CHAPTER 121

Pharmacists and Disease State Management

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Disease state management (DSM) is a systematic population-based approach to medical care that is being used with increased frequency in a variety of health care systems in an effort to standardize and improve provider adherence to treatment guidelines. The goal of DSM is to improve treatment outcomes while controlling health care costs. The historical patient care model in medicine has been an individualized physician-patient approach that can result in fragmented and suboptimal care. Although individual clinicians incorporate information gained from their training, personal experience, and the medical literature into their daily patient care activities, this does not always translate into optimal care. As an example, in a multicenter survey from five regions of the United States, only 18% of adult patients with coronary artery disease (CAD) receiving cholesterol-lowering medication for at least 3 months achieved their National Cholesterol Education Program (NCEP)[1] low-density lipoprotein (LDL) cholesterol target of $\leq$ 100 mg/dL.[2] This suboptimal treatment does result in higher vascular events, death, and health care costs.[3] Patients with hypertension face a similar problem. Based on the Third National Health and Nutrition Examination Survey (NHANES III), only 34% of all patients with hypertension were at or below a systolic blood pressure of 140 mmHg.[4]

DSM has been defined by Zitter as "a comprehensive integrated approach to care and reimbursement based fundamentally on the natural course of a disease with treatment designed to address the illness with maximum effectiveness and efficiency."[5] Therefore, in this management system, each patient may be proactively triaged at different stages in his/her disease process using a defined care plan established from evidence-based protocols or guidelines, rather than a series of fragmented encounters with various parts of the health care system. This integrated approach is developed with a quantifiable economic structure and a defined quality improvement process.

The Disease Management Association of America (DMAA) is a nonprofit membership organization founded in 1999 to represent the disease management community. The DMAA has defined those components needed for a full-service disease management program as shown in Table 121-1.[6] Programs consisting of fewer components are considered disease management support services.

As part of a prescription drug management program, DSM can be used as one of the methods to control medication utilization and pharmacy expenditures. Other methods include utilization management (eg, quantity limitations, prior authorizations), formulary management (open or closed), delivery systems, (eg, retail, mail order), and benefit design and consumer cost sharing (eg, copayments, coinsurance). This chapter will focus on DSM and steps involved in developing an effective program.

HISTORICAL BACKGROUND

Until the 1970s, the primary mode of health care reimbursement was through fee-for-service. In this model, health care costs skyrocketed, physicians relied largely on accumulated individual practice experience for disease treatment, and patient care interventions, rational or not, were reimbursed. New technologies added to the cost of health care, and in a fee-for-service environment their values were rarely assessed. Managed care was 'born' as the diagnosis-related groups (DRG) system was instituted in the early 1980s by the federal government as a means to reign in health care costs, with beneficial results observed by the early 1990s (Fig. 121-1).[7] Private payers, while watching their bottom line, also demanded that costs be curtailed. Neither the public nor private sectors, however, were willing to forego quality. Therefore, managed care is ever evolving to adapt to the seemingly diametric opposition of cost and quality. DSM is both an example of and a microcosm for this evolution. Managed care first targeted hospital and physician costs, as these were and are the most costly components of health care. After hospital and physician cost containment, managed care organizations (MCOs) addressed prescription drug costs (ie, the third most costly budget item) and by the mid-1980s most large MCOs had prescription drug management programs, either internally developed or contracted, with cost containment as their primary focus.[8] The skyrocketing cost of pharmaceuticals continues to be a driving force behind cost containment measures employed by MCOs.

Although quality and cost containment have always been mutual goals of managed care, skyrocketing costs, coupled with a 'silo' approach to hospital, physician, and pharmaceutical cost containment had a neutral—and sometimes negative effect on quality care delivery. Consumers of health care began to perceive a sacrifice in the quality of care to maintain the bottom line. The health care industry responded with the development of DSM programs that would, if effective, integrate health care services across the patient care continuum, positively influence quality care, and maximize efficiencies that would lead to cost containment. Initially, DSM programs were offered as outsourced products developed by stand-alone vendors or, more often, by pharmaceutical manufacturers. Justly or unjustly, however, the DSM programs developed by pharmaceuticals manufacturers were hurt by the perception that they were offered as a means through which pharmaceutical manufacturers could market their drugs and gain an increase in market shares. Many of these programs have since been abandoned, merged with other programs, or sold outright. Increasingly, DSM programs are developed and or operated through health care systems that work to identify proven processes and apply these to the care of patients enrolled in their system.

Table 121-1. Disease Management Association of America (DMAA) Definition of What Components Need to be Included for Full Service Disease Management Programs

COMPONENTS OF A DISEASE MANAGEMENT PROGRAM
• Population Identification processes
• Evidence-based practice guidelines
• Collaborative practice models to include physician and support-service providers
• Patient self-management education (may include primary prevention, behavior modification programs, and compliance/surveillance)
• Process and outcomes measurement, evaluation, and management
• Routine reporting/feedback loop (may include communication with patient, physician, health plan and ancillary providers, and practice profiling)

Full Service Disease Management Programs must include all six components. Programs consisting of fewer components are **Disease Management Support Services.**

Pharmacy benefit management (PBM), itself an industry with the main function of effectively managing the drug benefit program of MCOs through unit cost containment and utilization management, may also offer DSM as a means of increasing the quality and value of their services. PBM companies maintain a complete database of medications dispensed for enrolled patients. This information is very useful to anyone attempting to maximize drug efficacy and minimize cost. As an example, adherence to a medication regimen can be inferred through a patient's refill history, which is maintained in the PBM database; for another, a member-patient's medication list used to treat a particular disease state is available through this same mechanism.

Finally, another way in which DSM is evolving is through consolidation of programs and services. Although DSM programs focused on one disease has demonstrated cost and quality improvements, further efficiencies can be obtained if patient care is less piecemeal. It is believed that this "patient-centered" approach may allow synergistic benefits if the co-morbidities being treated are related.[9]

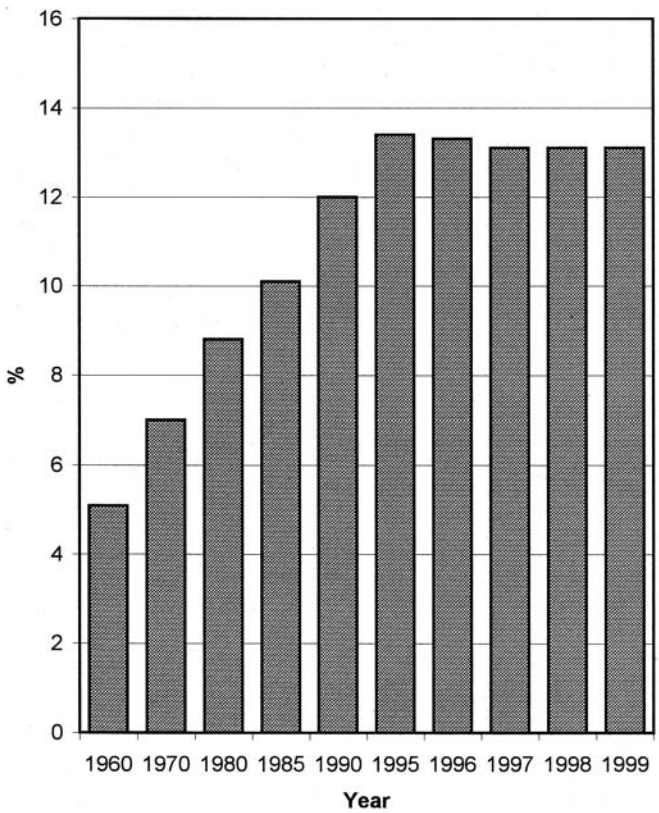

Figure 121-1. Total Health Expenditures as a Percentage of Gross Domestic Product, 1960–1999

Table 121-2. Appropriate Medical Conditions or Characteristics to be Targeted for a Disease State Management Program

CHARACTERISTICS
• Well-defined disease course
• High cost
• Chronic diseases or conditions
• High frequency
• Available outcomes benchmarks
• Measurable outcomes
• Treatment methods variable
• High incidence of non-adherence
• Preventable therapeutic misadventure is common or catastrophic
• Rare occurrence

DSM QUALIFIERS

Certain diseases or treatments lend themselves to DSM (Table 121-2). They include those in which the disease course is well-defined, and/or propel health care costs. Chronicity, prevalence, those with available benchmarks or definable, measurable outcomes, variability in treatment methodology, expensive therapies, and high incidence of nonadherence or preventable therapeutic misadventure are common characteristics. "Rare" diseases may qualify, because DSM programs can take advantage of economies of scale if cases from a broad geographic area are managed from a central location. Table 121-3 is an adaptation of the list of most costly medical conditions treated in the United States in 1997 to show DSM-appropriate conditions. Table 121-4 lists diseases or conditions successfully managed through a DSM program.[10] Many require drug therapy, providing the opportunity for pharmacists to play a key role in DSM.

PHARMACISTS AND DISEASE STATE MANAGEMENT

It is fairly well documented that pharmacotherapy-related outcomes can be improved by implementation of protocol-driven disease specific management programs by pharmacists collaborating with other health care providers. Noteworthy examples include an increased percentage of patients achieving NCEP LDL cholesterol targets following lipid-optimization,[11] a reduction in the length of hospitalization in patients taking warfarin guided by a pharmacist,[12] and a reduction in all-cause mortality in patients with heart failure receiving medication evalua-

Table 121-3. Selected Medical Conditions Among the Most Costly in 1997–Focus on Chronic Conditions Appropriate for Disease Management[7]

CONDITION	RANKING ($ MILLIONS)	TOTAL EXPENDITURE (THOUSANDS)	NO. OF PEOPLE AFFECTED
Heart disease	1	57,506	17,019
Mental disorder	4	29,731	20,152
Pulmonary disease	5	28,974	41,475
Diabetes	6	19,660	9,938
Hypertension	7	18,241	27,430
Cerebrovascular	8	16,333	2,252

Adapted from Cohen JW, Krauss NA. *Health Affairs* 2003; 22:129.

Table 121-4. Published Reports of Pharmacist Involved in Disease State Management (DSM) Programs

DISEASE STATES	FINDINGS	REFERENCE
Asthma	Significant reduction in ER visits and hospital admissions	Wantanabe et al.
Anticoagulation	Significant reduction in length of hospitalization	Dager et al.
	Significant reduction in total hospital costs	Mamdani et al.
Heart Failure	Significantly lower all-cause mortality	Gattis et al.
	Significant decrease in hospital readmissions	Riegel et al.
ICU Patients	Increase in cost savings related to pharmaceuticals	Baldinger et al.
	Significant reduction in preventable ADEs	Leape et al.
H. pylori	Cost-avoidance of $95 per patient	Segarra-Newnham et al.
Hyperlipidemia	Significant increase in patients meeting LDL-c goals	Ito et al.
Diabetes Mellitus	Reduction in mean HbA_{1c} by 0.7% vs 0.1% in controls	Grace et al.
	Decrease in total health care costs	Gerber et al.
Hypertension	Significant improvement in BP, QOL, and patient satisfaction	Carter et al.
General DSM	Decrease total monthly medical costs	Munroe et al.

H = *Helicobacter*; ICU = intensive care unit; ER = emergency room; ADEs = adverse drug effects; LDL-c = Low density lipoprotein cholesterol; QOL = quality of life; BP = blood pressure.

tion by pharmacy.[13] These examples employ outcome-related pharmacist cognitive services that were made possible from the fairly recent evolution of the profession over the past 35 years or so.

In 1976, the American Pharmaceutical Association (APhA, recently renamed the American Pharmacists Association) established the Board of Pharmaceutical Specialties given the charge of developing and administering board certification examinations to pharmacists with specialized training or experience. To be visionary for the future needs such as these, schools and colleges of pharmacy voted in 1992 to adopt the six-year Doctor of Pharmacy degree as the only professional degree in pharmacy.

Around the same time, the profession of pharmacy was moving toward the pharmaceutical care model of patient-centered, outcome-oriented practice (as first outlined by Hepler and Strand) and away from product-oriented procurement as its primary focus.[14] This patient-centered practice resulted from advances in information technology, the increased role of pharmacy technicians, and the evolution of pharmacy automation. These changes place pharmacists in a unique position to broaden their scope of practice and increase services where appropriate as collaborative care providers aimed at maximizing health-related outcome and minimizing drug-related misadventures—all the while assuring cost-effective use of pharmaceuticals. Health care administrators, physicians, ancillary care providers, and the public are increasingly recognizing the unique training and knowledge that pharmacists have in support of these activities.

Requirements for pharmacists who are involved in DSM vary from state to state and among health care organizations. Typically, pharmacists who are involved in DSM have advanced skill development either through a residency or fellowship program or have acquired skills from years of experience. Other methods of development are available through various certification programs that will provide some of the foundations needed to participate effectively in DSM. The National Institute for Standards in Pharmacist Credentialing (NISPC) offer programs in Certified Disease Management (CDM) for anticoagulation, asthma, diabetes, and dyslipidemia. The NISPC is a credentialing organization composed of the APhA, the National Association of Boards of Pharmacy (NABP), the National Association of Chain Drug Stores (NACDS), and the National Community Pharmacists Association (NCPA). Each set of DSM standards is created by a panel of experts composed of practitioners, academicians, PBM managers, and board of pharmacy members. The development of additional DSM standards will be based upon the needs and recommendations of practitioners, schools of pharmacy, payers, and the general health care community. The goals of the CDM credential program are to assist in validating the pharmacists specialized knowledge and skills. Credentialing earns pharmacists national recognition in specific disease states, increases revenue potential, and acknowledges their achievement and commitment to the profession and patient care. Further information is available at www.nispcnet.org.[15]

A Pharmacist's Role

Three strategies have been described[16] that, if followed, should help pharmacists develop practices that embody pharmaceutical care and DSM. First, careful planning of provided services should be carried out with buy-in from third party payers, physicians, and plan members. Second, close communication with the primary care physician regarding each patient's care should be maintained. And last, clear documentation of processes and outcomes should be maintained and measured against a reasonable benchmark.

The activities performed by pharmacists in managed care are not unique to this methodology and are discussed in more detail elsewhere in this book; however, it is interesting to note the ways in which these activities may benefit a DSM program. Pharmacists may provide primary care to patients in DSM programs through providing vaccinations, glucose and cholesterol screening and blood pressure monitoring in either the ambulatory care setting or in community pharmacy. In this role, pharmacists apply "pharmaceutical care" principles to manage patients with chronic medical problems, either making recommendations to a primary care or specialty physician, or prescribing under protocol. State law authorizes the latter, and rules may vary between states. In California, upon a physician's patient-specific authorization, pharmacists are authorized to initiate or adjust a drug regimen, order or perform routine drug therapy-related patient assessments such as vital signs, order drug therapy-related laboratory tests, and administer drugs and biologicals by injection, including immunizations.[17] In certain circumstances, pharmacists may be required to achieve advanced certification to perform these functions. For example, performing a fingerstick to assess blood sugar or cholesterol is beyond the scope of practice of pharmacists without first being certified to do so.

Pharmacists receive extensive training in pharmacology, pharmacokinetics, pharmacodynamics, and pharmacotherapeutics that makes them uniquely qualified to evaluate drug literature. Drug information activities performed by managed care pharmacists are used to support drug utilization review or medication use evaluation, as well as formulary management. All are important components for devising cost containment and utilization management strategies. These activities are also used to support an evidenced-based approach to DSM for developing population-based treatment plans and protocols. Further,

physician and allied health professional education by pharmacists is conducted to provide a balanced assessment of supporting literature and facilitate acceptance of the treatment plans.

The public also values educational functions the pharmacists provide. Patient counseling to educate patients on the proper use of medications as well as their risks and benefits, is a necessary function both ancillary to, and within a DSM program to maximize pharmacotherapeutic regimens. Pharmacists' patient counseling activities have been demonstrated to improve adherence to the therapeutic regimen, increase therapeutic efficacy and outcomes attainment, and potentially harmful medication errors.[15]

Pharmacists may serve as case managers in a DSM program. This is particularly advantageous when the drug therapy regimen used to treat the disease is susceptible to drug-drug, drug-food, or drug-disease complications. DSM programs incorporating pharmacists as case managers have been successfully deployed to care for patients with among others, diabetes mellitus, depression, smoking cessation, cardiovascular risk reduction, anticoagulation, and hypertension.

Careers in pharmacoeconomics and outcomes research are being pursued by pharmacists in academic and industrial settings. These activities are undertaken to determine the value of medications for the treatment and prevention of disease, and the research may involve either a drug-specific focus or population-based health care delivery. Most pharmacy schools provide a solid background in science, therapeutics, and economics required to produce pharmacist graduates equipped with the skills necessary to make a valuable contribution in this developing field. Postgraduate training (eg, graduate study, fellowships) enhances these skills and prepares pharmacists for independent research.

COMPONENTS OF A SUCCESSFUL DISEASE MANAGEMENT PROGRAM

DSM programs tailor population-based outcomes to individualized patient care. The challenge for successful management of patients using the DSM format is to demonstrate that the benefits derived from this form of patient care (in the form of cost and quality improvements) outweigh the resources used. There are certain characteristics that successful DSM programs share. A reliable and extensive medical informatics infrastructure allows for easy access to patients and their medical records. This includes telecommunications, computer networking, and data storage. Case managers working within a DSM program may monitor patients' progress using telephone surveillance and/or web-based telephone data collection devices. Integrated data collection and storage across the continuum of care, though not required, best serves the practitioners of DSM for patient follow-up and for reporting cost and quality outcomes. Complete data that is accurate and timely is essential to the success of a DSM program. Data collected should be analyzed and compared to benchmarked data points when available [as, for example, from the National Committee for Quality Assurance's (NCQA) Health Plan Employer Data and Information Set HEDIS)] to demonstrate quality outcomes. Medical claims, clinical and humanistic (satisfaction) data are all useful data points to benchmark.

As mentioned previously, one of the basic principles of DSM is identifying and offering a patient the best care for their disease. Successful DSM programs base goals on evidence-based outcomes. They incorporate treatment guidelines (eg, national guidelines if available or those developed by the health system after critical assessment of the literature) to reduce the amount of variability in practice that can lead to cost and quality inefficiencies. Development of treatment guidelines should be a cooperative consensus of all disciplines involved, as well as expert opinion and evidence from the scientific literature (eg, using published evidence grading).

Care in a DSM program should be physician-directed, yet take advantage of the expertise of a multi-disciplinary ancillary health care team (mid-level providers and pharmacists) to improve care and cost efficiency. Proper use of ancillary care for patient monitoring and management not requiring diagnostic skills of a physician can improve quality, reduce care costs, and have a positive effect on physicians workload, making room for patient visits requiring diagnosis-related activities.

Acceptance of the program by the primary care physician and/or health plan is of paramount importance to the success of a DSM program. Authorization from one or both entities is required for patients to have access to the DSM program. A key to acceptance may include shared risk, which also includes shared cost savings. Changing prescribing patterns and adherence to treatment guidelines might be enhanced by reasonable financial incentive. In addition, the practitioners affected by DSM programs need to be included early in development of the program to gain their support.

DSM programs should be financially viable. As such, demonstratable outcomes are only part of the story. They must be couched within a reimbursement system that acknowledges benefit of integrated care delivery. For example, payers should recognize that the costs for pharmaceuticals (eg, beta-blockers, angiotensin converting enzyme inhibitors) may increase in a DSM program targeting congestive heart failure, but that other, offsetting costs (eg, hospitalizations, surgical procedures, lost productive time, patient discomfort) should be reduced. In contrast, a DSM program that increases total health care costs with improvement in outcomes may be at odds with the goal of the heath care system.

Patient and physician education helps ensure that a DSM program is successful. Patients are empowered through learning about their disease. Signs of proper therapeutic management as well as therapeutic misadventure enable the patient to stay out of trouble, if they are taught how to identify these. Likewise, physicians are more apt to incorporate proven therapeutic modalities into patient care if they are informed of evidenced-based best practices as eluded to earlier.

Finally, continuous quality improvement (CQI) processes should be incorporated into the practice model to monitor and enhance care practices. Compliance with guidelines and assessment outcomes (humanistic, clinical, and economic) should be evaluated periodically and new evidenced-based information needs to be incorporated into the treatment guidelines as well.

DEVELOPMENT OF A DISEASE STATE MANAGEMENT PROTOCOL

The Protocol

One of the first tasks for the pharmacist planning to provide DSM is a detailed and specific protocol. Generally, this would be specific to a particular disease condition or area. The protocol should spell out in detail the responsibility of the pharmacist and specific endpoints for drug therapy.

The pharmacist wishing to develop such a protocol need not start from "ground zero." Numerous examples of DSM services and protocols have been published or are readily available from national organizations (see examples Table 121-2).[11–13, 18–27] In addition, extensive reviews on establishing and evaluating clinical pharmacy services providing DSM have recently been published.[28–31]

The protocol should clearly define pharmacist responsibility, including prescriptive privileges, authority to order and monitor selected laboratory indices, and consultation privileges. In addition, patient follow-up intervals and outcomes expected of pharmaceutical care should be included. Quality improvement measures may also be included as part of the protocol and are highly recommended as discussed above.

Documentation of the DSM activities is also a key element. Without proper documentation, the pharmacist will be unable to manage accurately and safely the patient's disease condition. In addition, without adequate documentation, the pharmacist will be unable to obtain compensation for services as well as determine the economics of the program. Finally, programs with poor or absent documentation of patient care activities may run afoul of various regulatory bodies such as the Centers for Medicare and Medicaid Services (CMS; formerly the Healthcare Financing Administration, or HCFA), the Department of Health and Human Services (DHHS) and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). Documentation of the complexity of the interventions (eg, such as amount of time spent with a patient, extent of an examination, the medical decision making involved) should be included.

Most of all, objectives within DSM protocols should be realistic. Unrealistic objectives that have a low likelihood of being attained will serve to frustrate the pharmacist and disappoint the patient. Of equal importance, failure to meet one's objectives while increasing the utilization of resources will be a conflict for one's health care system.

As mentioned in the previous section, when developing DSM protocols and determining objectives for such services, pharmacists should consult clinical practice guidelines established by government agencies, professional organizations, or international bodies. Historically, such guidelines are evidence-based and compose a consensus of experts in a disease area or diagnosis group. A comprehensive database of evidence-based clinical practice guidelines and related documents is available online through the National Guideline Clearinghouse at: www.guidelines.gov supported by the Agency for Healthcare Research and Quality (formerly Agency for Health Care Policy and Research, AHCPR).

The protocol should make some effort to define the organizational structure of the DSM program or clinic. The schedule of the clinic (days meeting, hours of clinic), how patients are checked in/out and screened, and the time periods allotted for appointments should be included. Consideration must be given for the amount of time necessary to consult new patients versus returning patients. Policies for patients who do not keep appointments, rescheduling patients, and how many times a patient can be rescheduled prior to being dropped from the service need to be established.

The ultimate goal is a DSM protocol that is dynamic and designed to minimize difficulty for the pharmacist and other practitioners. Efforts should be made, most commonly on a yearly basis, to review the protocol, update those areas based on management guidelines, and to reassess overall structure, function, and objectives.

Collaborative Agreement with Health Providers

Pharmacists who desire to establish DSM programs must be willing to invest time and energy to establish strong professional working relationships with other providers (eg, physicians, nurses, nurse practitioners, physician assistants) and staff members. Several keys to building working relationships is being responsive, doing more than what is expected of the pharmacist, and being willing to spend time with patients. Most often, examples of pharmacists providing DSM involve the pharmacist having identified a physician "champion" or advocate for their activity. Often this individual is a general practitioner in primary practice or a specialist in a particular disease area (eg, cardiologist, endocrinologist). In addition, support from physicians higher up the administrative hierarchy (Chief of Staff, Associate Chief of Ambulatory Care) can be invaluable in allowing the pharmacist to establish and manage disease-specific clinic activities and/or clinics.

Collaborative practice agreements with a provider should be established as part of the DSM protocol. When establishing collaborative practice agreements, pharmacists and physicians must evaluate their needs to determine the types of services the pharmacist will provide. The majority of states have passed legislation that allow pharmacists to practice collaborative drug therapy management with physicians. However, even without legislation, most medicine and pharmacy practice acts are broadly worded to allow collaborative practice arrangements (including drug therapy management) to exist between pharmacists and physicians. Some states may require pharmacists credentialing (as discussed above) in DSM to practice under a collaborative agreement with a physician. The pharmacist will need to evaluate his/her own individual state requirements.

Promoting/Influencing Stakeholders

Once the DSM protocol has been developed, the pharmacist must consider promoting their services and influencing stakeholders (eg, patients, physicians, and the MCO). This will require in some cases tremendous educational efforts. As mentioned in the previous section, a physician "champion" will be essential in most cases to develop a favorable partnership with the stakeholders. The pharmacist must be prepared and flexible enough to meet the concerns of all stakeholders. The collection of member and provider satisfaction data will help to ensure the longevity of the program.

Requisite Equipment and Set-Up

The minimum equipment and space required to practice DSM is a private area to interview and examine the patient. An examination room in a clinic or physicians office will usually be available for this purpose. In the case of a clinic that is telephone surveillance-based, a private desk area that includes a telephone and personal computer is necessary. If not already available in the examination area, a small desk, several chairs, and electrical power access will be required. This additional space would be required for equipment, such as computers, and to allow for processing of paperwork. In addition, a combination television/VCR is a very helpful option in case instructional videos need to be viewed by the patient. The ideal situation would be a separate interview/counseling room that would also double as the pharmacist's office.

Documentation and Forms

As previously emphasized, documentation is a key element of DSM. Before initiating the service, forms that document accurately and adequately all activities of the pharmacist should be available. There is little reason, in this era, to utilize paper forms for processing this information. Every effort should be made to computerize all documentation and interventions of the pharmacist. Many institutions and physician clinics are progressing rapidly to a paperless "electronic" medical record, and the pharmacist should embrace this in his/her DSM practice. The Veterans Affairs Medical Centers, for example, have been utilizing electronic medical notes and medical record for several years. There are numerous examples of commercial systems available for documentation and maintaining a medical record. The pharmacist is encouraged to research these and consider their use. If paper documentation is utilized in patient care, the pharmacist should make sure to develop forms which adequately document the complexity of the interventions (eg, amount of time spent with a patient, extent of an examination, the medical decision making involved) to allow good patient management and appropriate billing to occur.

Billing and Reimbursement

Billing and reimbursement issues have been the pharmacist's curse when attempting to make DSM pay for itself. Pharmacists are restricted in their ability to bill for services and there are discrepancies in compensation for their services.[32] The pharmacist is at a disadvantage in that the Social Security Act does not recognize the pharmacist as a provider of health care management services. Efforts are underway to change this. However, legislation will be required at a federal level, and this will likely take years to accomplish. At the current time, there are essentially three mechanisms to obtain reimbursement through the federal government and that is through the CMS that oversees Medicare and Medicaid financing. These include "incident to" billing, under an outpatient technical component using ambulatory patient classification (APC) codes, or for outpatient diabetes self-management training as part of a multidisciplinary team.

In institutions and physicians offices, the pharmacist can use the physician provider number ("incident to" billing) to seek payment for professional services. In most cases the pharmacist would bill under CPT code 99211 (this reflects a 5 to 15 minute consultation). However, this reimbursement rate is low and likely inadequate to support a pharmacists position in most cases. Also there are specific requirements (eg, the encounter must occur in a physicians office or clinic, physician must be present) that must be met to allow the pharmacists to use this type of billing. This may vary from state to state and by regional Medicare payers.

Billing at a higher CPT code for services such as 99212–99215 is controversial and may be determined by regional payers. For example, pharmacists in some states providing pharmacy DSM services are billing at the higher CPT codes and getting reimbursement from payers (eg, Medicare).

Medicare initiated a prospective payment system for reimbursement of outpatient visits in July 2000. The outpatient reimbursement is procedure-based (versus inpatient which is diagnosis-related reimbursement). Medicare-approved providers continue to bill professional services, but the outpatient technical component (ie, facility fee) is replaced by the new reimbursement system. This new system sets consistent reimbursement rates for outpatient services and charts nonprofessional procedures performed to known patient-care level APC codes known. As pharmacists cannot bill as a provider, their services become part of the overall facility reimbursement. The pharmacist's time to provide care increases the technical level allowing reimbursement which is often several times higher than the lowest "incident to" physician fee.

Finally, in January 2001 CMS (then HCFA) finalized rules on Medicare coverage of outpatient diabetes self-management training that allows payment of the pharmacist for diabetes training as part of a multidisciplinary team.

Unfortunately, payment for professional services for community pharmacists is more challenging and serves as a disincentive for the pharmacist to engage in DSM activities. Some possibilities are summarized below. Pharmacists approved by CMS as immunization providers may bill for immunizations. The first step in billing for services is to obtain a Medicare provider number to allow for billing. This can be accomplished by securing the necessary forms or submitting electronically at www.cms.hhs.gov. At the current time, the pharmacist is limited to billing insurance and third party carriers for in-person management only. No reimbursement is allowed for any form of telephone management. For in-person DSM, the pharmacist will be able to bill for laboratory services and for the non-MD health care provider visit. For example, if billing for anticoagulation management services, the pharmacist can bill a fee for obtaining the blood sample using a CPT code. For venipuncture-only the Medicare CPT code is G0001 and for venipuncture or finger stick it is 36415. The prothrombin time/International Normalized Ratio can be billed using CPT code 85610QW.

Other options are to charge a professional fee. Some pharmacists, particularly in community pharmacy, have found some success directly billing the patient a professional fee. Generally, attempts at billing private insurance carriers have been disappointing with many declining to reimburse the pharmacist based on lack of provider status at the federal level.

Potential Barriers

Potential barriers to DSM practices have been alluded to or discussed in some detail in previous sections of this chapter. The main barriers are acceptance by other providers of the services of the pharmacist and the reimbursement issues covered above. Each discipline that participates in the DSM program will have different interests, goals, and views. It is not paramount that there is total agreement on every issue. However, trust is one of the most important elements that needs to be established and confirmed.

Acceptance of other providers must be earned by investing the time and energy to create strong professional relationships with other providers and staff members. The pharmacist must be friendly, do beyond that what is expected, and be agreeable to spend time with patients.

As for reimbursement, success is a moving target, however documentation is a key element along with billing appropriately and adhering to legal requirements.

BUSINESS PLANS

It is common for pharmacists in managed care and at private health care facilities to create a business plan. Business plans are often very detailed and is beyond the scope of this chapter. The business plan may contain some background and description of the service, market analysis and strategy, operational structure and process, financial projections, milestones, schedule, action plan, risks, opportunities, conclusions, and any supportive documents. The business plan should be written in a manner to deemphasize or shift away from a "drug silo" cost assessment to an emphasis of the total direct health care costs. Some DSM programs may increase drug utilization, but lower total health care costs by reducing hospitalizations and emergency room visits.

QUALITY ASSURANCE

Evaluation of Outcomes

Evaluation of health outcomes is the ultimate measure of success of DSM. Measures of health outcomes should be an essential part of the management protocol. Usually, the initial step is a baseline evaluation of current indicators of performance for disease control and outcome. Measured outcomes of the DSM program may include well-known indicators of disease control such as glycosylated hemoglobin, blood pressure, or lipid concentrations, as well as secondary complications, hospitalizations, QOL, patient and physician satisfaction, mortality, or health care costs. As mentioned previously, these outcomes should be benchmarked to measures such as those from NCQA HEDIS or JCAHO.

In addition, measuring process-oriented outcomes, such as percentage of patients treated to established guidelines which are a component of the DSM protocol may be another useful measure of service quality. After implementation of the program, outcomes assessment leads to continuous modification of the program from feedback and constantly updated practice standards.

Ironically, one of the dichotomies of pharmacist's activities in DSM is that increasing the overall quality of care may require the need for increased prescription costs (ie, through maximization of existing prescriptions and new prescription orders)

to improve overall patient health and outcomes. Fortunately, studies have shown that pharmacists are able to ensure overall appropriate use of medications resulting in improved disease control, reduced health care use, and overall decreased health care costs.[11,8–21,25]

More difficult measures of quality of care associated with DSM include reduction of disease events and affects on survival (reduced mortality). Because long-term outcomes require longer-term data collection and a concurrent control group (using historical controls have their own inherent problems), which are not always practical, intermediate outcomes (ie, LDL cholesterol) may be more practical.

Final measures of quality of DSM services are humanistic (patient-specific) outcome measures such as patient satisfaction, quality of life (QOL) measures, and functional status. Recent study findings[33,34] have suggested more data or more specific questionnaires are required to document possible benefit of pharmacy care on humanistic outcomes. Patient satisfaction may assess numerous aspects of a DSM services including satisfaction with clinic process and waiting times, pharmaceutical care, disease control and endpoint attainment, and provider communication.

SUMMARY

Many diseases go untreated or are not managed optimally in the United States and other countries. DSM programs can be used as an effective strategy for enhancing patient outcomes and reducing management cost of diseases by ensuring consistent care using evidence-based treatment algorithms or protocols. In addition, education of patients and physicians is one key element in the success of a DSM program. The type and depth of training pharmacists receive during their formal pharmacy education and postgraduate training programs as well as enhanced recognition through board certification has opened up opportunities for collaborative care and other cognitive services within DSM programs. DSM programs are becoming more popular with health care systems and MCO and exemplify the unique expertise of the pharmacist toward making them effective. Thus the opportunity for pharmacists to enhance their role in disease-oriented approaches is here.

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CHAPTER 122

Development of a Pharmacy Care Plan and Patient Problem Solving

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INTRODUCTION

The practice of pharmacy has undergone several evolutionary leaps in the last four decades. Emphasis on the creation, preparation and dispensing of pharmaceuticals has given way to pharmacotherapeutic decision making and measurable patient outcomes, with increasing focus on patient safety. As this emphasis has shifted, academic pharmacy has adopted new paradigms and approaches in its preparation of future practitioners. Examples include introductory clinical pharmacy experiences, problem-based learning, and service learning opportunities. Students must understand their current and future roles in the ever-changing health care system, Further, students' didactic experience should include elements that develop and nurture their knowledge, skills, attitudes, and values. One central concept that often forms the framework for this approach to learning is that of pharmaceutical care.

Pharmaceutical care is a straightforward concept. It involves the pharmacist working in concert with his/her patients and other healthcare providers to identify, monitor, and achieve desirable health-related outcomes through the appropriate use of medications. While many consider the first reference to modern-day pharmaceutical care to be in 1989,[1] the theoretical construct was described several years before.[2] This expanded approach to care has been the subject of much discussion ever since, as well as recognized and supported in recent years by other healthcare providers.[3] And, while this advance appears to be logical and sensible, pharmaceutical care remains very difficult to define. At times, pharmaceutical care is perceived to include only a specific set of practitioners or practice settings. Further, in spite of a variety of excellent models for the provision of this care (ie, inpatient and outpatient), the delivery of pharmaceutical care is far from uniform within the profession.

In spite of our advancing knowledge and technology, drug-related problems and adverse drug events are a major source of morbidity and mortality in the United States. In a recent study, 4.4 adverse drug events were found to have occurred per 100 patient days in an inpatient setting, with 58% deemed to be preventable.[4] These results appear to be consistent with other studies.[5,6] Further, medication-related errors have been identified as a significant cause of emergency room visits and subsequent hospitalizations.[7–10] Thus, new approaches to the safe and effective use of medicinal products should be considered. One way this may be accomplished is through the enhanced utilization of the pharmacist in the drug delivery and utilization process.

Comparison to Clinical Pharmacy

Recently, the American College of Clinical Pharmacy (ACCP) has proposed the definition of clinical pharmacy to be "A health science discipline that embodies the application and development, by pharmacists, of scientific principles of pharmacology, toxicology, therapeutics, clinical pharmacokinetics, pharmacoeconomics, pharmacogenomics, and other life sciences for the care of patients."[11] The origin of the phrase appears to be related closely to the development of cognitive services in the inpatient setting[12] as well as concentrating on patients and their needs. As these services are intended to optimize the care provided to patients by pharmacists, there appears to be a significant amount of overlap with the provision of pharmaceutical care. In fact, all providers of pharmaceutical care may be considered to be practicing as clinical pharmacists. However, the explicit definition of pharmaceutical care requires the provider to assume a shared responsibility for therapeutic outcomes, as well as the communication of their efforts with other healthcare professionals. This requires an expanded view of pharmaceutical care as a strategy rather than a discipline. Further, while clinical pharmacy is, by definition, provided by pharmacists, it has been proposed that pharmaceutical care may be provided by a variety of healthcare professionals.[1]

This chapter is intended to contribute toward the pharmacy student and the practitioner's ability to provide pharmaceutical care. The care provided must be based upon a logical, effective, and patient-specific pharmaceutical care plan. This chapter is written to demonstrate what constitutes a pharmaceutical care plan and how it is created by the pharmacist.

Who Provides It?

Pharmaceutical care is an equally appropriate practice model for independent community practice, chain community practice, institutional practice, among other settings. While the specific services provided may differ among these practice environments, the underpinning philosophy of pharmaceutical care remains the same: achieving definitive outcomes for patients. Some examples of the various care settings include: outpatient clinics, emergency patient care centers, and specific inpatient units such as medical/surgical intensive care, infectious disease, transplant, pediatrics, trauma, internal medicine, and cardiac, among others. Indeed, several of these are featured in other chapters of *Remington*.

A central feature of pharmaceutical care is to identify, prevent and resolve drug-related problems (DRPs). Pharmaceutical care and pharmacist-managed drug-related problems may differ among practice settings and from patient to patient. Examples of pharmaceutical care services offered include: generic and therapeutic interchange, pharmacokinetic and therapeutic consultation, patient interviewing, patient counseling, team rounding, drug information, laboratory monitoring, and monitoring drugs with either high costs, narrow therapeutic windows, or potential adverse effects, to list just a few.

ROLE OF A PHARMACIST

The profession and roles of pharmacists are continuously evolving. There is a consensus among all major pharmacy organizations that pharmaceutical care is a viable and justifiable option and goal for the profession of pharmacy. Pharmaceutical care is defined by Hepler and Strand[1] as the responsible provision for providing drug therapy for the purposes of achieving definite outcomes. Pharmaceutical care focuses on activities that lead to positive patient outcomes, and accepting end results of medication therapy remains important in providing such services. According to Penna and colleagues,[13] to practice pharmaceutical care, a pharmacist must be a scientific problem solver, a good communicator, educator and learner. Primary activities involved in pharmaceutical care include: obtaining a medication history, identifying real and potential drug-related problems, developing a pharmacy care plan to include implementing and monitoring parameters to resolve and prevent drug-related problems, and evaluating the plan to determine if clinical outcomes have been achieved through documentation, patient consultation follow-up to determine if the desired clinical outcomes have been achieved. All this is achievable through competent skills and knowledge gained to provide reliable cognitive services. Cognitive services or value-added services (eg, patient drug or disease counseling) allow pharmacists to attain positive outcomes.[14]

Cognitive services are closely linked with the concepts of clinical pharmacy and pharmaceutical care. Key components of both include application of one's judgment, knowledge, and ability to solve DRPs. To practice effectively, pharmaceutical care focus must be placed on patient satisfaction. It is important to conduct a one-on-one patient session to review past disease and medical histories, current drug, herbal, dietary supplement, and non-drug therapies; related signs and symptoms; and desired outcomes. Collection of this information allows the pharmacist to identify patient drug-related problems and develop a pharmacy care plan to help resolve these problems.[15,16] Table 122-1 demonstrates the proposed nine steps to Pharmaceutical Care for Pharmacists.

In carrying out daily responsibilities, identifying DRPs or developing a pharmacy care plan, pharmacists must also address societal needs. Societal needs may be identified by providing value-added services for patients and performing these activities with ethical and professional prerogatives in mind. On a daily basis, pharmacists may be confronted with professional dilemmas that are legally, ethically and/or morally challenging (eg, patient confidentiality issues, pro-life issues). One must learn to balance these challenges while maintaining a level of personal comfort to practice successfully and deliver optimal care on behalf of the patient.[17]

Table 122-1. Nine Steps to Pharmaceutical Care

1. Develop a covenantal relationship between the pharmacist and the patient
2. Collect relevant drug, disease, and patient information
3. Interpret this information to identify all the patient's drug-related problems
4. Prioritize the patient's drug-related problems
5. Identify those drug-related problems for which the pharmacist will assume responsibility
6. Identify patient-specific outcomes for each drug-related problem for which the pharmacist has assumed responsibility.
7. Develop a therapeutic plan to attain the desired patient-specific outcomes for each drug-related problem
8. Develop a monitoring plan to assess whether predetermined outcomes have been attained
9. Implement and follow the pharmacy care plan, which consists of desired outcomes, therapeutic plan, and monitoring plan.

Adapted from Winslade NE, Bajcar JM, Bombassao A: Pharmacist's Management of Drug-related Problems: A Tool for Teaching and Providing Pharmaceutical Care. Pharmacotherapy 1997; 17(4):805; with permission.

STUDENT RESPONSIBILITIES

Education

According to the AACP Commission, the goal of pharmaceutical education is to "inculcate students with values necessary to serve society as caring, ethical, learning professional and enlightened citizens."[17] This is accomplished by providing a curriculum which enables students to learn, develop skills, and nurture values necessary to meet the needs of patients and society. Pharmacy education lays the foundation for students to acquire the knowledge and abilities required to be successful pharmacists in the future. Students are responsible for becoming active participants in this process, incorporating knowledge and developing skills in their career while embracing life-long learning.[17]

IMPORTANCE OF SKILLS

Skills necessary for the delivery of pharmaceutical care include patient care skills, clinical skills, application of drug knowledge and drug information skills, and professional skills (eg, interpersonal skills, service orientation). Collecting, collating, and organizing patient information from medical charts and computer databases is necessary. Equally important is the personal time a pharmacist invests in obtaining the information directly from the patient. The concept of patient-centered practice or patient care skills becomes evident when the pharmacist attempts to build a relationship of trust with the patient. This interaction will help identify and determine patients' preferences for their health-care outcomes. Patient encounters for students are planned to occur during internship and/or the experiential component (eg, fourth professional year clerkship rotations) of their curriculum. Routinely, students on rotation provide clinical pharmacy services under the direct supervision of a clinical pharmacy preceptor. The goal of the preceptor is to bridge classroom learning to real-life clinical experiences, enhance students' drug knowledge, and help develop the students' professional judgment and values. Clinical skills (eg, being capable to interpret blood levels and lab data, assess the patient's needs, apply therapeutic data to drug-related problems) are key factors for an optimal drug regimen. Furthermore, drug knowledge and information skills, as well as the ability to rationalize therapeutic decisions are equally important in achieving optimal patient care. Finally, professional skills remain essential for a successful, future practicing pharmacist. Professional responsibilities, whether learned through school during courses or heightened during clerkship rotations, distinguishes all health care professionals.[17] Examples of professional responsibilities for pharmacists may include holding high professional aspirations for the practice of pharmacy, a commitment to serve the community and humanity, serving as mentors for future pharmacists, and maintaining personal standards of integrity, competency, reasoning, and life-long learning.

For one to be proficient with skills gained or acquired, one must demonstrate competency or mastery of the skills learned. In pharmacy school, competency may be ascertained through successful outcomes on examinations, quizzes, and simulated patient exercises, among others. To test student competency and skill sets in a clinical setting, the use of algorithms and flow charts may be used on clerkship rotations. Flow charts (Fig. 122-1) encourage a uniform approach to problem solving and assist students in identifying DRPs, learning to ask appropriate questions, and becoming capable of formulating recommendations for monitoring and follow-up planning.[18]

Experiential practice and the work environment also help students gain experience toward identifying and resolving DRPs, not all of which will be clear-cut textbook scenarios. Awareness of such ambiguities exists throughout pharmacy practice and in other healthcare arenas. Professional prerogatives, ethical dilemmas, and the balance of both may be quite challenging. The American Pharmacists Association (APhA)

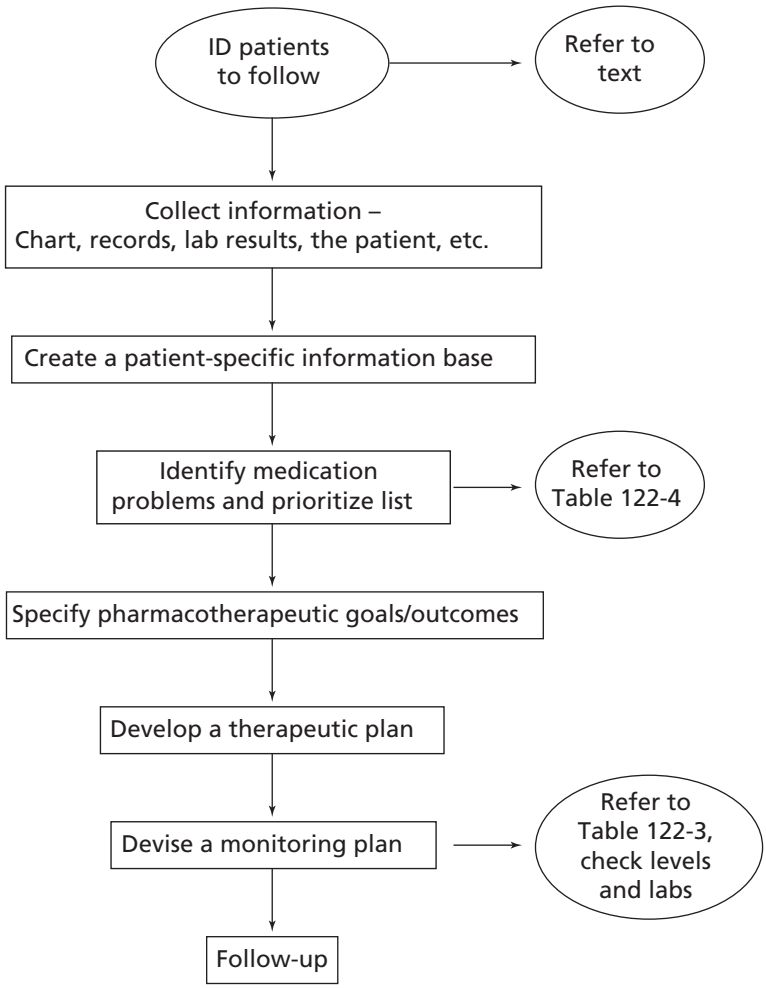

Figure 122-1. Example of a Flow Chart

Code of Ethics, states "a pharmacist should hold the health and safety of patients to be of first consideration and should render to each patient the full measure of professional ability as an essential health practitioner."[17] In some instances, a pharmacist's moral and ethical beliefs may conflict with his/her professional duty. For this reason, as a future pharmacist, it is important to be comfortable making decisions in the face of these uncertainties.[19]

Identifying Patients to Follow

To develop a pharmacy care plan and problem solve, the student will need to identify patients with DRPs to follow. Numerous studies have indicated that elderly patients (eg, older than 65 years of age) are at an increased risk for DRPs because, typically, they have multiple medical problems, have multiple drug therapies, and the physiological effects of aging on the disposition of drugs warrants close monitoring. Greater than three concomitant diseases, five or more medication regimens, twelve or more doses of drugs a day, and frequent medication regimen changes in the past year can lead to nonadherence and demand further investigation. Students may also learn by monitoring patients with compromised renal or hepatic function, those that demonstrate abnormal clinical laboratory values, and those who present with potential drug-drug interactions or duplicate therapies. Sometimes regulatory or reimbursement issues dictate or necessitate tracking the care of certain patients (eg, high cost drugs and therapies). By this selective process, one can effectively concentrate his/her activity on those patients who have the greatest potential for benefit from clinical services.[20]

DEVELOPING A PHARMACY CARE PLAN

Pharmacy care plan notes help to formalize and document a specific course of treatment for the patient. For example, when a patient is admitted to the hospital, the physician formulates a medical care plan for that patient. In parallel, the clinical pharmacist develops a pharmacy care plan for the patient. It is important that the plan be evaluated and revised according to the changing needs of the patient on a continuing daily basis.[21] Strand and colleagues developed a framework for the provision of a pharmaceutical care plan in their practice site, termed the pharmacist's workup of drug therapy (PWDT). Care plans will vary somewhat depending upon specific pharmacy settings. The PWDT allows the pharmacist to gather data, prevent or identify and resolve DRPs, and monitor the selected therapy (see Fig. 122-2A,B).[22]

The first step in formulating a care plan is to build a caring relationship with the patient, collect and organize information relevant to the patient, and create a patient-specific database. This relationship should be predicated on an honest and open

Example A: Documentation Form Used by PharmD Students for Interventions

COMMUNITY PHARMACY CLINICAL CONSULTATION

Patient's initials _____ Approximate age _____

Physician's initials _____ Date _____

Illness/conditions from profile or history (check):

____ Arthritis ____ Hyperlipidemia ____ Diabetes

____ Hypertension ____ Angina ____ Pregnancy

____ Asthma/COPD ____ CHF Other _____

Current Rx/OT medicatons and dose (from patient and profile):

_____ _____

_____ _____

Medications with which patient has had past problems (allergies, reactions):

_____

Drug-related problem(s): _____

_____

Subjective: _____

_____

Objective: _____

_____

Assessment: _____

_____

Plan: _____

_____

Follow-up with physician and/or patient: _____

_____

Consultation peformed at:

_____ _____

PharmD Student Pharmacist

Adapted from Anderson RJ, et al. Documentation of pharmaceutical care activities in community pharmacies by doctor of pharmacy students. *Journal of Pharmacy Practice* 1995;8:83–88.

Example B: Patient initials **Allergies/Reactions:**
Student name: **Write up date:** *Deepika Vadher, PharmD, BCPS*

CC:

HPI:

PMH:

Family Hx:

Social Hx:

Home medications/ OTCs/ Herbals: (List drug, dose, frequency and indication)

Emergency Room
Admit vitals: T BP HR RR
Ht: Wt: IBW: CrCl (est):

Admit Labs: Other labs:

Treatment in ER:

Studies/Labs Pending:

Consults:

ROS: Findings
GEN:
HEENT:
NECK:
CV:
PULM:
ABD:
GI:
GU:
EXT:
NEURO:

Differential Diagnosis:

Prioritized Problem List:

Hospital Course (Day ___)

- *Include problem, all supporting data/labs, pharmaceutical care plan, vitals, recent labs, recommendations, medications added or deleted, monitoring plans for efficacy and toxicities, consults, pending labs and discharge plans, etc*

Problems:	**Progress, supporting studies, labs, treatment regimens** (started, continued, discontinued, etc.)**and plans**	**Monitoring/ pending labs**	**Your Interventions**

Discharge Plans (Focus on new medications started, old medications deleted, disease state education, etc.)

Mercy Fitzgerald General Medicine Form – D. Vadher (rev.9/04)

Figure 122-2. *Continued.*

exchange of information to aid in solving patient problems and making recommendations to the attending physician or interventions on behalf of the patient. Both parties (pharmacist and patient) must mutually respect the pharmacist-patient relationship to address and provide optimal care. To provide such service, the pharmacist must communicate with the patient to ascertain his/her needs, wants, desires and goals, and evaluate if his/her wishes will be met with the prescribed or recommended treatment regimens.[23] Addressing patient-specific problems requires asking appropriate questions to help gain insight about the patient's understanding of his/her disease states, drugs and his/her attitude toward drugs, drug therapy, and drug usage patterns. Asking appropriate open-ended questions to gain comprehensive information is useful to help create a patient-specific database. Also, interviewing the patient helps build a rapport with the patient. However, before interviewing the patient, the pharmacist should review the patient's chart, medical card-ex, or prescription databases to determine the diagnosis, past medical history, medication history, and any other pertinent data (eg, recent labs, family and social history).[21] In an institutional setting, the pharmacist may examine the medical record and collaborate with the medical staff and patient to collect needed information. In a community setting, data collection may be limited to observations, conducting an interview with the patient, and in some circumstances, communicating with the physician or healthcare professional.

The next step in the development of a pharmacy care plan includes identifying DRPs and their subsequent prioritization. Collecting and processing relevant data should result in a list of patient-specific DRPs. This is accomplished by listing the patient's potential and actual medication-related problems and then ranking them by severity. The classic priority of problems, from most to least severe, first includes acute and then chronic problems. Finally, historical problems and other health-related risk factors are listed from most to least immediate. The medication history interview provides information regarding patient medication prior to admission and often will identify drug problems that will necessitate a change in drug therapy. Throughout this process, modifications must be made daily to address patient-specific problems.[23]

After collecting the information, the pharmacist should address the patient's needs, identify any potential problems and establish desired therapeutic goals and outcomes. The pharmacist's main responsibility is to maximize positive outcomes of drug therapy and minimize drug misadventures. Patient therapy should result in the achievement of definite outcomes that improve the patient's quality of life. Definite and desired outcomes that improve a patient's quality of life are (1) cure of a disease; (2) elimination, amelioration, or reduction of the patient's symptoms; (3) arresting or slowing the disease process; (4) preventing further disease or symptoms; and (5) returning the patient's physiological status to a normal healthy state. Pharmaceutical care is patient-oriented, and it involves developing, implementing, and monitoring a therapeutic plan that is designed to achieve these outcomes.[21,24]

The next step in the development of a pharmacy care plan involves therapeutic planning to achieve patient-specific outcomes or endpoints. The pharmacist's recommendation should incorporate therapeutic efficacy, safety, comfort and convenience, adherence, and cost considerations to the regimen. The best pharmacotherapy regimen for the patient should involve patient-specific, individualized drug dosing, frequency of drug administration, and duration of treatment. Most therapeutic problems will demonstrate more than one empirically acceptable solution. Thus, alternatives should always be considered and included in the plan. Viable alternatives require comparative analysis and critical review of the medical literature to reveal which agent(s) is(are) best suited for the patient based on clinical efficacy, safety, patient satisfaction, and cost.

The processes of problem-solving and the development of a care plan are incomplete until monitoring produces data that serves to empirically support the recommended solutions. One must assess specific, desired endpoints to document the attainment of outcomes and resolution/prevention of DRPs through a monitoring plan. The next step focuses on the monitoring parameters of serum drug levels or surrogate markers for the drug. Monitoring for efficacy and toxicity reflects the active involvement by the pharmacist. Monitoring for efficacy assesses whether a given drug regimen is working to achieve the therapeutic goals previously identified, and monitoring for toxicity determines if the patient is experiencing any unwanted adverse effects from the regimen (see Table 122-2 for a listing of representative drugs to monitor with therapeutic levels for each).[25]

The final step in the development of a pharmacy care plan involves following up on one's recommendations and re-evaluating the patient's problem list. It is imperative to continue to monitor the patient after discharge or counseling session as this act provides continuity of patient care. Times, dates, and mechanisms of follow up (ie, consultation in person or via a telephone call) should be documented in the care plan note. This allows the pharmacist-patient relationship to flourish and continue building toward a trusting, meaningful relationship.[14]

Table 122-2. Example of Drugs with Narrow Therapeutic Indices Requiring Pharmacist Monitoring [14]

EXAMPLES OF DRUGS WITH NARROW THERAPEUTIC INDICES	RECOMMENDED THERAPEUTIC SERUM LEVELS
Warfarin	INR 2-3 or 2.5-3.5 (dependent on indication)
Heparin	aPTT = 1.5-2.5 × the normal (ie, baseline 30 s → 45-75 s)
Aminoglycoside	Gent/tobra: <2-5-6 (8-10) Amikacin: {9-}15-24
Vancomycin	5-10 (trough)–20-50 (peak)
Digoxin	0.8-2 OR 1.5-2.5 (arrhythmia) mcg/ml
Theophylline	10–20 mcg/ml
Phenytoin	10–20 mcg/ml
Others:	
Valproic Acid	50–100 mcg/ml
Procainamide	3–10 mcg/ml

PREVENTION

A central feature of pharmaceutical care is to identify, resolve and prevent DRPs. Throughout the process of problem solving and identifying DRPs, importance should also be placed on the prevention of future, potential problems. Preventing future DRPs involves identifying: drug allergies, inappropriate dosages, drugs with narrow therapeutic indices that require frequent monitoring, exacerbation of disease due to suboptimal doses, patient nonadherence, herbal/dietary supplement product use, suspected drug abuse, and potential for drug-drug interactions. The presence of these DRPs leads to less-than-optimal therapeutic patient outcomes and could result in future hospitalizations. The cost to society of drug-induced hospitalization can be immense in morbidity, mortality, and treatment, and therefore, is a topic of great importance to clinicians, health care administrators, and society in general.

Drug-related hospital admissions may be precipitated by a host of factors including adverse drug reactions, drug-drug interactions, drug misuse, inadequate or improper therapy, and nonadherence leading to disease exacerbation or complications. To date, numerous studies have found an increased rate of hospital admission rates secondary to medication noncompliance and/or adverse drug reactions. The actual number of DRPs necessitating hospital admission may be higher than reported because of lack of documentation, further underestimating the problem.[24] Table 122-3 demonstrates examples of Pharmacy Care Plan notes.[26]

Table 122-3. Example of a Documentation Form for Drug Related Problems Used by PharmD Students on Rotation with Deepika Vadher Pharmacy Care Plan/Clerkship Rotation Worksheet

Patient initials _____ Student Name: _____ Date Written:_____

DRUG-RELATED PROBLEM	OUTCOMES	ASSESSMENT	THERAPEUTIC PLAN	THERAPEUTIC PLAN END POINTS	MONITORING PLAN	PLAN END POINT MET?
List problem and all supporting data (labs, review of symptoms, vitals, etc.)	Address the following: • Clinical or outcome • Pharmacotherapeutic	List and assess all drug and non-drug treatment related to problem.	Which drug or non-drug treatment should be instituted or changes made to existing drug therapy? (drug, dose, frequency, route, etc.)	List parameters for each outcome: (Goal BP, SCr, etc.)	For each desirable endpoint—what should be monitored and frequency of monitoring	Any interventions?
1)						
2)						
3)						
4)						

PROBLEM SOLVING

Initially, collecting and interpreting relevant patient information, identifying patient health-care needs, and formulating a DRP list may be challenging for the pharmacy student. These steps require that the student learn to recognize, obtain, and process relevant drug, disease, and patient information in a problem solving format. Problem solving involves identifying drug-related problems, suggesting interventions, and documenting patient outcomes. Each patient is unique, and how one approaches each particular problem is specific for that individual patient. Problem solving is a learned and developed skill which frequently requires fine tuning over time. As the saying goes, "the road to success is always under construction" and with due time one will sense a level of comfort in approaching and solving problems.[27]

Identifying Drug-Related Problems

As discussed earlier, the primary focus of pharmaceutical care is placed on the patient. Properly-educated, skilled and developed pharmacists have familiarity and knowledge of prescription medications, over-the-counter medications, and herbal/dietary supplements. This knowledge base serves as a very thorough and reliable method of obtaining the patient's mediation history. Once one has identified which patients to monitor, the next step involves identifying medication-related problems for the specific patient. After obtaining a thorough patient history, review the current medication regimen for allergies; drug-drug and drug-food interactions; nonprescription and herbal/dietary supplement medication use; adverse reactions; therapeutic duplication; and appropriate drug selection, dose, duration, and dose frequency to aid in processing a medication-related problem list.

The type of pharmaceutical problem identified in the community pharmacy setting may differ from that reported in the hospital practice environment. Therefore, it is important to be cognizant about one's practice site setting before identifying and focusing on related problems. In a study evaluating drug-related problems in the hospital and community settings, it was found that underdosing comprised 31.5% of student interventions in hospital settings versus 3% in the community setting. The incidence of potential drug interactions and adverse drug reactions was found to be four-fold greater in the community setting when compared to the hospital setting.[28] Table 122-4 demonstrates a listing of drug-related problems.[22,29]

Making Recommendations

Assessing the DRP list and making therapeutic recommendations or interventions requires clinical knowledge and a strong pharmaceutical foundation. Staying abreast of clinical knowledge and continually striving for improvement will aid in the transition from student learning to application of knowledge gained during clerkship rotations and the work environment. Access to information and becoming familiar and knowledgeable of where to obtain information may help address and resolve DRPs. Reliable and validated internet resources, drug information resources, the primary medical/science literature, and national guidelines may help guide the management of one's patient. In 1989, the federal government was charged with the development of guidelines (which were later endorsed by specialty groups and other organizations) to aid clinicians in the proper management and treatment of specific, clinical problems. Guidelines are educational tools that serve as a source of guidance to aid clinicians in their decision-making.

Table 122-4. Drug-Related Problems Encountered by Pharmacist Monitoring[16]

- Untreated condition
- Improper drug selection
- Underdose
- Failure of patient to receive drug
- Overdose
- Adverse drug reaction
- Drug-drug interaction
- Drug-food interaction
- Drug without indication
- Nonadherence
- Duplicate therapy
- Allergies
- Requiring renal or hepatic adjustments
- Miscellaneous-
- Poly-pharmacy

Another approach to aid in clinical decision making is to use the results of patient care research or literature, or, in other words, practice evidence-based medicine. Evidence-based medicine includes decision making regarding pharmacotherapy that has been found to be beneficial for the group of patients being studied. Making recommendations in conjunction with guidelines and practicing evidence-based medicine helps provide optimal patient care.

Documenting Recommendations

After identifying the DRPs and making clear, concise recommendations, the next step is to document the intervention. As a profession, pharmacists must share responsibility for patient outcomes and record their recommendations, defend/support their reasons, and demonstrate expected outcomes. Medical and nursing documentation is widely accepted. Routinely, physicians and nurses document clinical patient care activities. To justify continued clinical services in the past, pharmacists have documented administrative projects and protocols. However, these have not been necessarily related to direct patient care. The trend towards pharmaceutical care focuses on patient care and documentation, which will help develop and improve services rendered by pharmacists. Such services should include written or verbal documentation of recommendations.[29] Either form of documentation is appropriate, however, it is important to be clear and succinct. During one's initial experience with documentation, the student's preceptor will have to proofread and approve all documentation of recommendations prior to its transmission to allied healthcare practitioners. As students become more comfortable and proficient with documenting actions and plans, they may be able to act more independently—depending on the preceptor and practice setting.

SOAP NOTES

The suggested format for organizing patient notes in medical charts is to use the SOAP note. Written SOAP notes include **S**ubjective and **O**bjective data, **A**ssessment of the problems, and appropriate **P**lans. A strong database that includes information about the patient, the disease, and any drugs is necessary for effective clinical decision making and documentation.

Subjective data is elicited by interviewing the patient. General subjective patient data includes, among others, the patient's chief complaint, history of present illness, previous medical problems, current medications, allergies, social (eg, smoking, alcohol, illicit drug use) and family history, and history of adherence to medications. Objective data includes all pertinent patient vital signs, physical examination notes, and pharmacological review of systems and clinical laboratory values. The assessment portion includes primary and secondary diagnoses, which encompasses a comprehensive and relevant explanation of the DRPs, therapeutic alternatives, and the rationale for the recommended therapeutic plan. Finally, the plan should contain a description of the desired clinical and pharmacotherapeutic outcomes. The plan is developed based on the subjective and objective information and the final assessment of each problem. The therapeutic plan should include a detailed monitoring plan for each DRP and future patient education initiatives. Written recommendations are then incorporated into the patient's chart, which is a legal document.[27, 29]

Verbal documentation may entail direct communication with the healthcare provider about one's concerns and recommendations for a patient. Problems involving drug therapy should be discussed in a clear and concise manner with the proper healthcare team member. At times, the physician may be too distracted focusing on acute patient issues and may not have an opportunity to read a written recommendation, but may be available for verbal consultation. Verbal communication followed by chart documentation of the care plan helps to emphasize your concerns for the patient's wellbeing. Whether a recommendation is written or verbal, the pharmacist is an integral part of a healthcare team, whose focus is achieving positive optimal patient outcomes. Numerous studies indicate that physicians accept 80% to 90% of pharmacist-generated recommendations. This strongly supports the pharmacist's role in a patient care team.[30]

IMPORTANCE OF DOCUMENTATION

"If it is not documented, it has not been done." For the profession of pharmacy to evolve toward cognitive services and away from distributive functions, and to secure reimbursement for all new services, pharmacists must document value-added pharmacy services. Reimbursement from the provision of pharmaceutical care that is beyond customary dispensing and counseling should be an incentive for all practicing pharmacists. In the future, a successful pharmacist will be recognized by their impact on cost savings and the number of pharmaceutical interventions, rather than the number of prescriptions filled per day.[28]

IMPORTANCE OF PHARMACEUTICAL CARE

Throughout this chapter, much emphasis has been placed on the importance of pharmaceutical care. However, as with any change to a profession and how it is practiced, one encounters many barriers for implementation. Such barriers include: inadequate education and less-than-optimal skill development of pharmacists, pharmacist reluctance "to become involved and patient oriented," unnecessary and overly restrictive legal requirements, limited access to and communication of patient-specific information among practitioners, lack of time to implement new practice designs, limited market-driven demand, current lack of compensation for professional services, facility design and space utilization, and restriction issues. Legal and risk management issues with documentation may deter future pharmacists from providing and charting pharmaceutical care. However, with appropriate education and practical experience, these barriers will be overcome and pharmacists will learn to become comfortable with documentation and accept responsibility for patient care outcomes. Success requires dedication, personal effort, motivation, and energy to provide competent pharmaceutical care.

PATIENT EDUCATION

To provide adequate patient education, it is important that the patient knows the drug name, indication, dosage or strength, and frequency of his/her medication(s). Focus may be placed on patients with a history of nonadherence, new prescriptions, new diagnosis, chronic diseases, potential drug-drug interactions, or multiple daily medications. In some hospitals, the nursing staff is mainly responsible for medication counseling. However, pharmacists are better qualified to offer such services. Some hospitals have pharmacists conducting discharge counseling. Restructuring pharmacist responsibilities to provide pharmaceutical care will make the opportunity to provide discharge counseling for the profession attainable in healthcare settings. Through discharge counseling, the pharmacist, along with allied healthcare team members, may help the patient make the difficult transition from the controlled hospital environment to his/her home. Most states mandate outpatient counseling and this is a wonderful encouragement, inducement, and opportunity for the pharmacy student to develop this skill during the experiential component of the curriculum.

PATIENT ADHERENCE

Adherence to one's medication regimen is essential to optimize therapeutic outcomes and achieve maximum benefit to the patient. The pivotal role of the pharmacist toward optimizing

adherence encompasses many actions: assessing adherence problems, identifying predisposing factors contributing to nonadherence, providing comprehensive counseling, and recommending specific adherence strategies targeted to individual patient needs. Nonadherence can be a result of many factors including, but not limited to, medication regimen complexity (eg, how a dosage is administered, timing, form of medication), other existing conditions or diseases, and personal values and healthcare beliefs. Pharmacists remain uniquely positioned to assess and treat adherence-related problems that may adversely affect patients' health outcomes.

Adherence Assessment

Patients may be selective in the information they wish to receive. Nonadherence is a multivariant, complex problem, which may be influenced by patient's health beliefs, the extent to which they feel in control of their own health, their cultural norms, and strategies they have developed to cope with their illnesses. There are two methods to assess adherence: direct and indirect methods. The direct method employs blood-level monitoring and urine assay for the measurement of the drug and/or its metabolites/markers. Indirect methods of assessing adherence utilize, among others, patient interviews, tablet/capsule counts, refill records, and drug reminder sheets or tables, list a few.[31]

SUMMARY AND CONCLUSION

Pharmaceutical care may be provided by a wide range of practitioners and all pharmacists involved in the provision of patient care. Many of the principles of pharmaceutical care are also embraced in the practice of clinical pharmacy, making the two difficult to distinguish. Both approaches require the use of knowledge and skills gained in formal academic training and with experience, as well as a determined approach to life-long learning. Essential skills include oral/written communication and problem solving, and should be an integral part of the student's professional, on-campus education, and reinforced in the Advanced Practice Experience portion of the curriculum.

Often the end product of this care is the creation of a pharmaceutical care plan. Examples include a pharmacist's workup of drug therapy (PWDT) or SOAP note, and should include a prioritized list of issues, monitoring parameters, and specific outcomes to be achieved. This plan is built on trust and understanding between patient and provider, and focuses on mutually developed goals. The documentation of all provided services is critical, and serves to demonstrate the professional responsibility pharmacists assume in the provision of pharmaceutical care. This also serves to justify the need for, and reimbursement of, cognitive services.

As the role of a pharmacist continues to evolve, so too will the reality of pharmaceutical care. To date, the consuming public largely considers pharmacists to be knowledgeable and trusted, and often turns to them for advice and information. However, there are still many more of the public who are unaware of the skills of the pharmacist beyond those of dispensing. As pharmacist cognitive services are developed, implemented, and expanded to impact more of the general public, it is possible that the monitoring of many chronic diseases will be accomplished in the community or ambulatory setting. The continued, active participation in the identification, resolution, and prevention of drug-related problems will continue to impact patients positively and serve to define further the role of the pharmacist in the healthcare system.

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CHAPTER 123

Ambulatory Patient Care

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Various designations are used to categorize patients: institutionalized, noninstitutionalized, inpatient, outpatient, bedridden, and ambulatory. Strictly speaking, ambulatory patients are those who are able to walk (ie, those who are not bedridden). Therefore, ambulatory patients may be inpatients of an institution, such as a hospital or extended-care facility, if they are not confined to bed. However, the term ambulatory patient has become more restrictive in its modern usage simply to mean a noninstitutionalized patient.

Ambulatory patients referred to here are noninstitutionalized patients who have the responsibility for obtaining their medication, storing it, and taking it. They may or may not be outpatients, depending upon where they receive their treatment. They may even be in a wheelchair and, strictly speaking, not ambulatory, but if they are not institutionalized they will have the same basic responsibility for their medication as *walking patients*.

Whether patients consult a physician who may prescribe medication or whether they decide to treat themselves, the community pharmacist more than likely will come into contact with them. It is important, therefore, for the pharmacist to have an understanding of these patients so that as a pharmacist and member of the health-care team, the best possible health care for ambulatory patients may be provided through proper use of knowledge and judgment.

MEDICATION-RELATED NEEDS OF AMBULATORY PATIENTS

It is known that the ambulatory patient does not adhere always to the directions for taking medicine. There are a number of reasons for this, and the reader is advised to consult Chapter 115 for a thorough and enlightening discussion of patient compliance. Through the decade of the 1970s, numerous studies demonstrated that patients widely misuse medications, with frequency ranges between 20% and 82%.[1] This wide variation reflects study differences, medication class differences, and investigator interpretation of patient misuse of medication.

In one of the earliest studies, Latiolais and Berry[2] compiled a number of ways in which patients may misuse medications. Many of these same problems exist today and are

1. Overdosage
   a. Taking more than the prescribed dose at any one administration
   b. Taking more than the prescribed number of doses in any one day
   c. Taking a dose, prescribed as needed, at a time other than when needed
   d. Taking the same medication from two or more different bottles simultaneously
2. Underdosage
   a. Taking less than the prescribed dose at any one administration
   b. Omitting one or more doses
   c. Discontinuing the drug before the prescribed duration of time
   d. Omitting the dose of a medication, prescribed as needed, when it is needed
3. Taking a dose at a different time if a time has been specified in the directions
4. Taking a dose in a form other than that specified in the directions
5. Using the wrong route of administration
6. Taking medication that has been discontinued
7. Taking outdated medications
8. Taking someone else's medications
9. Taking two or more medications that are contraindicated therapeutically
10. Failing to get the prescription filled
11. Failing to understand how to use the administration unit properly (eg, inhaler)
12. Failing to understand how to use or administer the dosage form properly

Using the above criteria, the authors found that 42.8% of the patients sampled were misusing their medications and that 4.4% misused their medicine in such a manner as to pose a serious threat to their health. The types of misuse committed most frequently were overdosage and omission of doses. Overdosage represented 41.3% of the total misused prescriptions. Omitting one or more doses occurred in 23.6% of the misused prescriptions. Another result of this study showed that of the prescriptions being misused, patients actually were aware they were misusing about one-half of them.

This apparently deliberate misuse perhaps is more understandable when viewed with respect to the single most often mentioned reason, occurring fully one-third of the time, that the patient did not understand the instructions. The second most frequent reason given by the patients for not following directions was that they thought they needed another dose. Another frequent reason was that the patient thought he or she was cured and stopped taking the drug before the prescribed time.

In 1992, a study by Clepper estimated that one-half of the 1.8 billion prescriptions dispensed on an annual basis are taken incorrectly.[1] It also estimated that 90% of all outpatients make mistakes taking their medications. Further, these mistakes account for 10% of all hospital admissions in the general population and 25% of all hospital admissions in the elderly. As a result, health-care costs increase and work productivity decreases. However, the most alarming finding of this study was that patient noncompliance may be linked to more than 125,000 deaths annually.

Two of the most recent studies have provided estimates of the actual cost of medication misuse in the US. One study estimated these costs to be approximately $100 billion, with more than one-half due to loss of productivity and nearly one-third

due to hospital and nursing home admissions.[3] The other study estimated that medication morbidity and mortality costs the US economy about $76.6 billion annually.[4] This figure does not include costs associated with lost productivity.

It is inconceivable that patients knowingly would misuse medication in a way that would be injurious to their health. Similarly, with the high cost of health care, it is astounding that patients would not maximize the health care they do receive to gain maximum benefit from their expenditures.

As mentioned previously, a common reason for the misuse of medicine may be a lack of patient knowledge and understanding of the medication and how it is integrated into the treatment of a particular disease state. As an example, the scientific literature documents that patients with diabetes mellitus administer their insulin in an unacceptable manner, do not follow their diets, exhibit poor foot care, and do not test their urine and/or blood correctly.[5] Although bad habits and/or a lack of responsibility on the part of patients may account for some of these behaviors, lack of patient understanding of the importance of each treatment component for the prevention of disease complications is also a factor in many instances.

Other patient misconceptions also contribute to medication misuse. For example, *If one tablet is good, two will be even better,* is a common patient belief that is fraught with danger. Patients also frequently discontinue medicines inappropriately for a variety of reasons. In this context, a recent study identified the most common reasons for patients not having prescriptions refilled.[6] These reasons, in decreasing order of importance were that the

1. Medication was not working.
2. Medication was causing side effects.
3. Condition improved.
4. Patient received negative information about the medication.
5. Cost of the medication was too high.
6. Patient was confused about how to take the medication.

The noted philosopher and educator in medicine, Sir William Osler, in 1891, captured the essence of man and medicine when he stated that, "the desire to take medicines is perhaps the greatest feature that distinguishes man from animals." Unfortunately, his statement did not capture the mode in which man takes medicine, as demonstrated by the findings of the investigations described previously. These results clearly demonstrate the need for skilled professionals to assist patients to gain optimal benefit from their drug therapy. As medication experts who are often the most accessible health-care providers, community pharmacists are uniquely positioned and professionally obligated to fulfill this need for ambulatory patients.

THE PHARMACIST'S RESPONSIBILITY

In years past, the responsibility of the pharmacist was to dispense prescriptions accurately, provide medication counseling, and answer questions of concern to the patient. Recently, however, the profession of pharmacy has adopted pharmaceutical care as its mission and thereby extended the responsibility of the pharmacist.[7] Pharmaceutical care focuses pharmacists' attitudes, behavior, commitment, concern, ethics, functions, knowledge, responsibilities, and skills on the provision of drug therapy to individual patients. The goal is to achieve optimal outcomes that improve the patient's quality of life. These outcomes may include

1. Cure of the disease
2. Elimination or reduction of symptoms
3. Arresting or slowing the disease process
4. Prevention of disease
5. Diagnosis of disease
6. Desired alterations in the physiological processes

Pharmacist providers of pharmaceutical care assume responsibility to identify, prevent, and resolve medication- related problems on behalf of their patients. These problems have been defined broadly as undesirable events that are of psychological, physiological, social, or economic origin and may be the function of a patient:

1. Needing pharmacotherapy but not receiving it
2. Taking or receiving the wrong medication
3. Taking or receiving too little of the correct medication
4. Taking or receiving too much of the correct medication
5. Experiencing an adverse reaction to a medication
6. Experiencing a drug-drug or drug-food interaction
7. Not taking or receiving a medication that has been prescribed or
8. Taking or receiving a drug for which there is no valid indication.[8]

In this context, pharmacists collaborate with patients, patient caregivers, physicians, nurses, and other health-care providers to initiate, monitor, modify, and discontinue pharmacotherapy to avoid or resolve these medication-related problems. To that end, pharmacist providers of pharmaceutical care engage in a series of sequential steps to ensure that individual patients receive cost-effective pharmacotherapy that results in optimal therapeutic outcomes. These steps include having the pharmacist

a. Establish a committed relationship with individual patients
b. Collect, synthesize and interpret relevant patient information
c. Define and prioritize the potential and actual medication-related problems of the patient
d. Establish a desired pharmacotherapeutic outcome for each medication-related problem
e. Determine feasible pharmacotherapeutic alternatives to achieve each desired outcome
f. Select the best pharmacotherapeutic solution based upon individual patient circumstances
g. Design a monitoring plan to determine if the desired pharmacotherapeutic outcome has been achieved and
h. Implement the individualized pharmacotherapeutic and monitoring plans and evaluate and document the results of pharmacotherapeutic and monitoring plans.[8]

An advantage of pharmaceutical care over previous definitions of pharmacy practice is its applicability to all practice settings and to prescription *and* nonprescription therapies (see Chapter 114). Further, research demonstrates that pharmaceutical care services provided by pharmacists add value to the care of both institutionalized and ambulatory patients. This added value includes improvements in patient outcomes, enhanced patient compliance, and reduced health-care costs associated with medication misadventuring/misuse.[9]

In spite of these findings, realization of pharmaceutical care roles has been slow, particularly in ambulatory practice settings. To encourage further evolution of pharmaceutical care in ambulatory settings, the US Department of Health and Human Services' (DHHS's) Office of the Inspector General in 1990 summarized the current status of clinical services available in community settings, described barriers that limit the availability of these services, provided recommendations to reduce these barriers, and strongly recommended the establishment of strategies to deliver pharmaceutical care comprehensively in the ambulatory setting.[10]

Subsequently, the Omnibus Budget Reconciliation Act of 1990 (OBRA 90) was enacted and required each state Medicaid Agency to institute a Drug Use Review (DUR) program for covered outpatient drugs by no later than January 1, 1993. This act also required pharmacists to provide prospective utilization (ie, patient profile) review and counseling for Medicaid patients. It is hoped that societal and professional pressure will be such to ensure that all patients and not just Medicaid patients will receive these services. In fact, a number of states have legislated that these services will be provided to all patients.[11]

These legislative developments indicate a need for pharmaceutical care services in ambulatory practice settings. It is the intent of this chapter to operationalize further the concept of pharmaceutical care in this context so that community pharmacists may continue to evolve toward the realization of pharmaceutical care roles in their practices.

Establishment of a Committed Relationship with Individual Patients

The first step in the provision of pharmaceutical care is the establishment of a committed relationship with the patient. To that end, pharmacists must seek and be granted authority by their patients to intervene on their behalf. Pharmacists also may need to secure permission from other health-care providers and patient caregivers (eg, in cases in which the patient is a child or unable to visit the pharmacy in person) to provide pharmaceutical-care services. The key to doing so in all instances is effective communication.

Building a committed relationship cannot occur at a distance. The pharmacist must interact directly with the patient to earn his or her trust and to obtain permission to take responsibility for the outcomes of drug therapy. Thus, pharmacists in an ambulatory setting must take the initiative to introduce themselves and their services at the time the patient first presents a prescription.

Ideally, the pharmacist should invite the new patient into a private or semiprivate area of the pharmacy to explain the proposed relationship, it's benefits, and his or her commitment to the patient's well-being. Realistically, it may be impossible for the pharmacist to interview the patient at the time the prescription is originally dispensed, because of time constraints imposed by other professional responsibilities. In this case, the pharmacist should arrange to meet with the patient at another, mutually convenient time.

Committed relationships are rarely the result of a single interaction. In addition, by its very nature, pharmaceutical care is an iterative and ongoing process, as long as the patient has unresolved medication-related problems. Therefore, once a rapport has been established, the pharmacist must interact regularly with the patient to strengthen the relationship and to collect additional data necessary to ensure that the patient's pharmaceutical-care needs continue to be met.

COLLECTION, SYNTHESIS, AND INTERPRETATION OF RELEVANT PATIENT INFORMATION

As mentioned previously, the pharmacist's primary responsibility in the delivery of pharmaceutical care is to identify, prevent, and resolve medication problems. A key factor in the fulfillment of this obligation is the availability of essential patient data. These data have been categorized in various ways by different authors. The specific framework used to categorize patient data is less important than the consistent use of a single method to do so. This ensures that all potentially useful information is considered for each patient.

For the purposes of the present discussion, patient information is organized into three categories. Specific data items are grouped within each category as illustrated in Table 123-1. To make appropriate decisions about patient therapy, pharmacists must understand the utility of different types of information in the decision-making process. Further, they must realize that different decisions require different types of patient information. Thus, an appropriate and comprehensive database for a specific patient may or may not include all of the information included in Table 123-1.

In the context of ambulatory patients, useful demographic information includes the patient's name, age, gender, and race. Age, gender, and race are often important factors in the selection of medications and dose determinations. For example, medication doses are often lower in elderly patients because of diminished renal or hepatic function. Gender is important in the case of a female of childbearing age if medications that are being considered for treatment are potentially harmful to unborn children. Finally, race is an important factor in the treatment of hypertension in African-American patients because a number of antihypertensive medications are ineffective in this population.

Core medical information includes past medical problems and all current acute and chronic diseases, including assessments of their severity, prognoses, and associated patient complaints. In some instances, it also may be appropriate to collect information about a patient's physical impairments or disabilities. For example, a patient with limited manual dexterity secondary to an arthritic condition may have difficulty using a medication administration device such as a metered-dose inhaler.

It also may be appropriate in some cases for the pharmacist to collect additional medical information for a specific patient. For example, information relative to a patient's immune status would be important when the selected drug therapy can cause further immunosuppression. Similarly, home blood-glucose and blood-pressure measurements would be useful to assess the effectiveness of therapy for patients who suffer from diabetes mellitus and hypertension, respectively.

Essential therapeutic information includes the names of all prescription and nonprescription drugs used by the patient and their frequency of use and therapeutic indications. Drug allergies, previous adverse drug reactions, and intolerances also should be noted for each patient. In addition, because of the rising popularity of alternative therapies, pharmacists should inquire about the use of home remedies, vitamin/mineral sup-

Table 123-1. Patient Information for the Provision of Pharmaceutical Care

LIFESTYLE	DEMOGRAPHIC/MEDICAL	THERAPEUTIC
Ethnic background	Age	Past therapies[b]
Sexual history	Gender	Prescription drugs
Living arrangement	Race	Nonprescription drugs
Social support	Health status[a]	Alternative therapies
Health beliefs	Impairments/disabilities	Present therapies[b]
Expectations of care	Past medical problems	Prescription drugs
Financial/insurance status	Current medical problems	Nonprescription drugs
Daily activities	Severity	Alternative therapies
Tobacco, alcohol, caffeine use	Prognoses	Allergies
Dietary/exercise practices	Chief complaints	Adverse drug reactions
Perceptions of current diseases	Physical assessment data	Physicians
Perceptions of current therapy	Laboratory data	Other care providers
Compliance with current therapy		
Concerns about current therapy		

[a] Includes cardiac, hepatic, immune, nutritional, and renal status.
[b] Includes therapeutic regimens.

plements, herbal preparations, and other nontraditional therapeutic modalities (eg, acupuncture, aroma therapy).

Perhaps the most often overlooked category of information includes details related to the patient's life-style. Information in this category can be crucial under a variety of circumstances. Patient health beliefs and perceptions of illness and prescribed therapy are known to influence patient compliance strongly.[12] As a result, pharmacists should attempt to collect information about these perceptions and beliefs in all patient care situations.

In some situations, additional life-style information becomes important. As an example, the abuse of alcohol by a female patient who needs treatment for trichomoniasis would be important because the drug of choice for this disease (ie, metronidazole) causes a disulfiram-like reaction when alcohol is consumed. The sexual history of the patient in this situation also would be pertinent because treatment of male partners is necessary to prevent recurrence of the disease in the female. Because each patient presents with a unique set of circumstances, pharmacists must use professional judgment to determine which types of lifestyle information are essential for optimal patient care.

The pharmacist also must determine an appropriate source of each type of information. Common sources include the patient, the patient's caregiver or family, the pharmacy patient profile, medical records, laboratories, physicians, nurses, and other health-care providers. Appropriate sources vary from situation to situation. In each case, the pharmacist must consider a source's ability to provide accurate, reliable information and the ease with which the source may be accessed.[13]

As an example, consider the case of a retired, 67-year-old man who has suffered from diabetes mellitus for 30 years. When the patient and his wife visited the pharmacy for the first time to pick up prescriptions for insulin and syringes and to purchase test strips for his blood-glucose meter, the pharmacist on duty asked the patient to complete a new patient information form. Upon inspection of the completed form, the pharmacist concluded that blood-glucose measurements also would be important to obtain in this case to determine how well the patient's blood sugar is currently controlled. Alternative information sources in this instance would include the patient, the patient's wife, the patient's medical record, and the patient's blood-glucose meter, assuming it has dedicated memory to store test results, and the patient tests his blood regularly using correct technique.

The pharmacist may be able to obtain blood-glucose and glycosylated hemoglobin results for the patient by calling the patient's physician and asking for this information from the patient's medical record. However, these results may not be up-to-date unless the patient had recently visited the physician. Further, locating the physician for a consult may be difficult. The pharmacist could ask the patient directly or he could ask the patient's wife. In these instances, however, it is unlikely that either individual could remember more than one or two measurements. Moreover, the reliability of the reported results could be influenced by the memory or veracity of the person who reports them. Thus, the pharmacist in this instance concluded that if available, the most reliable and accessible source of blood-glucose measurements would be those stored in the memory of the patient's home blood-glucose meter.

In many instances, the most appropriate information sources are the patient or other individuals involved in the patient's care (eg, physicians). Thus, pharmacists must develop exemplary communication skills and prepare for interactions with these individuals in advance to obtain accurate and complete information in an efficient manner. Specifically, the pharmacist must be a skilled listener, speaker, and observer who formulates questions in advance to elicit the desired information about the patient.

Because pharmacists in ambulatory practice settings rarely have access to patient medical records, it is often necessary to conduct an interview with the patient to obtain critical background information. To save time, some pharmacists ask patients to complete an intake questionnaire prior to being interviewed. This instrument asks the patient for basic background health and demographic information that is elaborated further as appropriate during the interview process.

A successful interview begins with an organized approach that is driven by the nature and amount of information that is needed from the patient. For example, the approach taken during an initial patient visit to the pharmacy would be much different from subsequent visits when baseline information is typically updated.

Ideally, patient interviews should be conducted face-to-face in a quiet, relatively private area of the pharmacy. In addition, patients feel more comfortable when the pharmacist is seated at the same level near them, rather than behind a desk or high prescription counter. The pharmacist should begin the interview by greeting the patient, introducing himself or herself, and briefly explaining the purpose of the interview and the expected amount of time required for its completion.

Following this introduction the pharmacist should proceed with the interview, using an appropriate mix of question types to obtain the desired information. Generally, open-ended questions followed by appropriate probes are effective in this regard. Pharmacists also should attend to information communicated nonverbally by themselves and by the patients. In this context, note taking should occur only after the patient is finished speaking. This is because breaking eye contact while the patient is talking may be interpreted by the patient as disinterest on the part of the pharmacist and may limit patient responses. Further, pharmacists may miss important nonverbal cues if they are looking at their notes while a patient is speaking.

Pharmacists also must be aware of, and sensitive to, the influence of age, gender, and cultural, educational, family, and socioeconomic variables on patient responses during the interview. For example, a patient who is illiterate would be unable to complete a written patient information form. Rather the instrument would need to be administered verbally to the patient. As a further example, studies have demonstrated that patients in lower socioeconomic classes tend to seek medical attention and report bothersome symptoms less frequently than wealthier patients.[14] In this context, pharmacists may need to use more probing questions to obtain information from patients of lower socioeconomic status.

Occasionally, the most appropriate source of patient information is the patient's physician. Although the interaction between the pharmacist and physician is not considered to be an interview, many of the interview techniques outlined previously can facilitate the collection of patient information. Specifically, similar to the patient interview, the pharmacist should have a clear idea of the desired information and a logically sequenced set of questions to obtain this data prior to contacting the physician. In addition, pharmacists should begin the conversation by greeting the physician; introducing themselves and briefly explaining the nature of the desired information before asking specific questions is also appropriate.

Regardless of the source or type, patient information must be recorded in an organized and systematic manner. Recording systems vary widely. However, the system that is used should ensure that patient information is readily retrievable, provide for efficient evaluation of medication-related problems, and permit recording of pharmacist evaluations, recommendations, and patient-monitoring information.

Most community pharmacies employ computer-based medication profiles to record and maintain patient information. While the specific format of these records varies from program to program, an example of a typical patient medication profile is illustrated in Figure 123-1. These records typically include basic patient demographic and medical information and a list of all prescriptions filled at a particular pharmacy. However, because they typically do not provide for documentation of other therapies, monitoring information, and pharmacist recommendations, their utility for the provision of comprehensive pharmaceutical care is limited.

PATIENT'S NAME: Stacy Smith

ADDRESS: 313 Hummingbird Lane

PHONE NO.: 694-8374

DATE OF BIRTH: 3/17/69

KNOWN DISEASES	ALLERGIES/ SENSITIVITIES	ADDITIONAL INFORMATION
Asthma Sinusitis	Aspirin	multiple vitamin daily

Date	Rx#	Medication	Strength	Quantity	Dosage Regimen	R.Ph. Init.	Physician	Refills
9/21/97	12543	Ventolin	90mcg/act.	17g	ii puffs q6h prn	AR	Jones	6
9/21/97	20199	Serevent	25mcg/act.	13g	ii puffs bid	TS	Jones	1
10/19/97	20199	Serevent	25mcg/act.	13g	ii puffs bid	RS	Jones	0
10/19/97	12543	Ventolin	90mcg/act.	17g	i-ii q4h prn	RS	Jones	5
10/19/97	34578	Azmacort	60mg/act.	20g	ii puffs tid	AR	Jones	1
10/30/97	12543	Ventolin	90mcg/act.	17g	ii puffs q6h prn	AR	Jones	4
11/11/97	12543	Ventolin	90mcg/act.	17g	ii puffs q6h prn	AR	Jones	3
11/20/97	12543	Ventolin	90mcg/act.	17g	ii puffs q6h prn	AR	Jones	2

Figure 123-1. A typical patient profile.

A more useful alternative to the traditional patient profile is illustrated in Figure 123-2*A* and *B* and was developed for use in an ambulatory wellness clinic by the author. This pharmacist's patient data record provides fields to record all of the data contained on a patient profile. In addition, this record includes fields for the documentation of the patient's past medical and social histories and space for the pharmacist to record additional, patient-specific data, including monitoring information, interventions made on behalf of the patient, and the associated outcomes.

A variety of manual and computer-based tools are commercially available to overcome the limitations of patient medication profiles. For example, Problem-Oriented Medical Record (ie, POMR) cards were recently marketed by Global Publishing Network, Inc, as a manual system for monitoring and documenting patient care. An example is included as Figure 123-3. These cards include sections for patient background characteristics, medical history, medication profile, lab data, medication-related problems, progress notes, and pharmacist's recommendations. Although marketed primarily as a tool for institutional pharmacists, POMR cards also may be a cost-effective alternative for community practitioners.

Comprehensive, computer-based pharmaceutical-care systems also have become available recently from a number of vendors. CarePoint has developed a Windows-based system (ie, Guardian™) that enables pharmacists to collect detailed patient medical and medication histories and to document individual patient needs, interventions, outcomes, and impressions, using the SOAP format, eg, *S*ubjective patient data, *O*bjective patient data, data *A*ssessment and therapeutic *P*lan. The software also includes features to facilitate patient counseling, outcome monitoring, and third-party billing for pharmacists' cognitive services. A representative screen from the software is included as Figure 123-4.

HealthCare Computer Corporation's AlphaPC is a similar system that also has the capability to interface with a large number of other computer-based resources. For example, the system supports a variety of intake questionnaires, enabling pharmacists to choose the format that best suits their patients' needs. In addition, the system creates a series of patient education materials and pharmacist directions for their use when the patient suffers from a common, chronic condition (eg, asthma, diabetes). Finally, the system also can be connected to medical devices to record blood pressure, peak flow, and blood-glucose and blood-cholesterol measurements.

The recent development of innovative systems to collect, maintain, and analyze patient information clearly illustrates the profession's movement toward the realization of new, patient-centered practice roles. Further, as technology evolves, sophisticated tools to support additional pharmacist functions during the provision of pharmaceutical care likely will become available.

Definition and Prioritization of the Patient's Potential and Actual Medication-Related Problems

Evident in the previous section are the benefits of systematic collection and organization of patient databases (ie, efficient recording, retrieval, and evaluation of information). Similarly, the definition and prioritization of patients' medication-related problems requires a systematic approach to prevent problems from being overlooked. A variety of approaches have been developed and are described in the following paragraphs. More important than the specific approach chosen by the pharmacist, however, is the consistent application of a single approach to the evaluation of patient information. This also helps to avoid omissions in the patient's medication-related problem list and in the subsequent formulation of therapeutic goals.

Demographic Information	
Name: Tina Smith	Primary Care Physician: Bert Walker
Address: 2090 Mosside Drive	Occupation: Retail Sales Associate
Telephone #: 693-3148	Height: 5'8"; Weight 156lbs (actual 10/97)
Date of Birth: 8/11/65	Rx Insurance: $200.00 deductible then 80% covered

Date	Rx #	Medication	Regimen	R.Ph.	Physician	Refills
5/23	974	Hismanal 10mg #30	i po daily during allergy season	RW	Walker	2
4/10	328	Sporanox 100mg #30	ii daily	HS	Pitman	0
3/25	110	Imitrex 25mg #20	i po at onset of HA then i in 2 hours if needed	GR	Walker	0
3/10	328	Sporanox 100mg #30	ii daily	HS	Pitman	1
2/10	328	Sporanox 100mg #30	ii daily	HS	Pitman	2
12/2	110	Imitrex 25mg #20	i po at onset of HA then i in 2 hours if needed	GR	Walker	1

Acute/Chronic Medical Problems

migraines, hayfever, onychomycosis

Allergies/Intolerances (Reaction)

penicillin (rash)

Past Medical History

GERD 1995
shingles 1991

Social History

married 1990
divorced 1995

Lab/Monitoring Data

migraine diary suggests chocolate is a trigger

Pharmacist Notes/Interventions

5/23 - The patient brought in a new prescription for Hismanal which can interact with Sporanox to produce cardiac arrhythmias....questioned patient if she still is using the Sporanox....she said she sucessfully completed her treatment earlier this month. The diary is unremarkable for additional migraine triggers.

R.W.

3/10 - The patient brought in the migraine trigger diary that she has been keeping since 12/3. It appears that chocolate may be a migraine trigger. Evaluate diary again at the time of next visit.

B.T.

12/2 - The patient was given a migraine trigger diary and instructed on how to use it. She was also encouraged to bring it with her at the time of each visit to the pharmacy.

B.T.

Figure 123-2. *A,* A pharmacist's patient data record.

Demographic Information	
Name: Barry Sommers	Primary Care Physician: Steven Marshall
Address: 1341 Sinclair Drive	Occupation: Retired Prison Guard
Telephone #: 593-3078	Height: 6'1"; Weight 230lbs
Date of Birth: 7/21/35	Rx Insurance: $8.00 copay

Date	Rx #	Medication	Regimen	R.Ph.	Physician	Refills
7/15	890	HCTZ 25mg #30	i daily	MH	Spandel	2
7/15	110	Glipizide 10mg #30	i po qd	MH	Spandel	5
6/24	890	HCTZ 25mg	i daily	RT	Spandel	3
6/4	110	Glipizide 10mg #30	i po qd	JL	Spandel	6
6/4	328	Sular 20mg #60	ii daily	JL	Spandel	6
5/10	328	Sular 20mg #60	ii daily	MH	Spandel	7
5/10	110	Glipizide 10mg #30	i po qd	MH	Spandel	7

Acute/Chronic Medical Problems

NIDDM, hypertension, CHF (new 6/24)

Allergies/Intolerances (Reaction)

none

Past Medical History

left knee replaced 1998
right knee replaced 1995

Social History

married 1958, lives with wife, smokes 1 ppd x 40yrs

Lab/Monitoring Data

BP 135/85, Blood Glucose 180mg/dL on 7/15
BP 127/80, Blood Glucose 111mg/dL on 6/4

Pharmacist Notes/Interventions

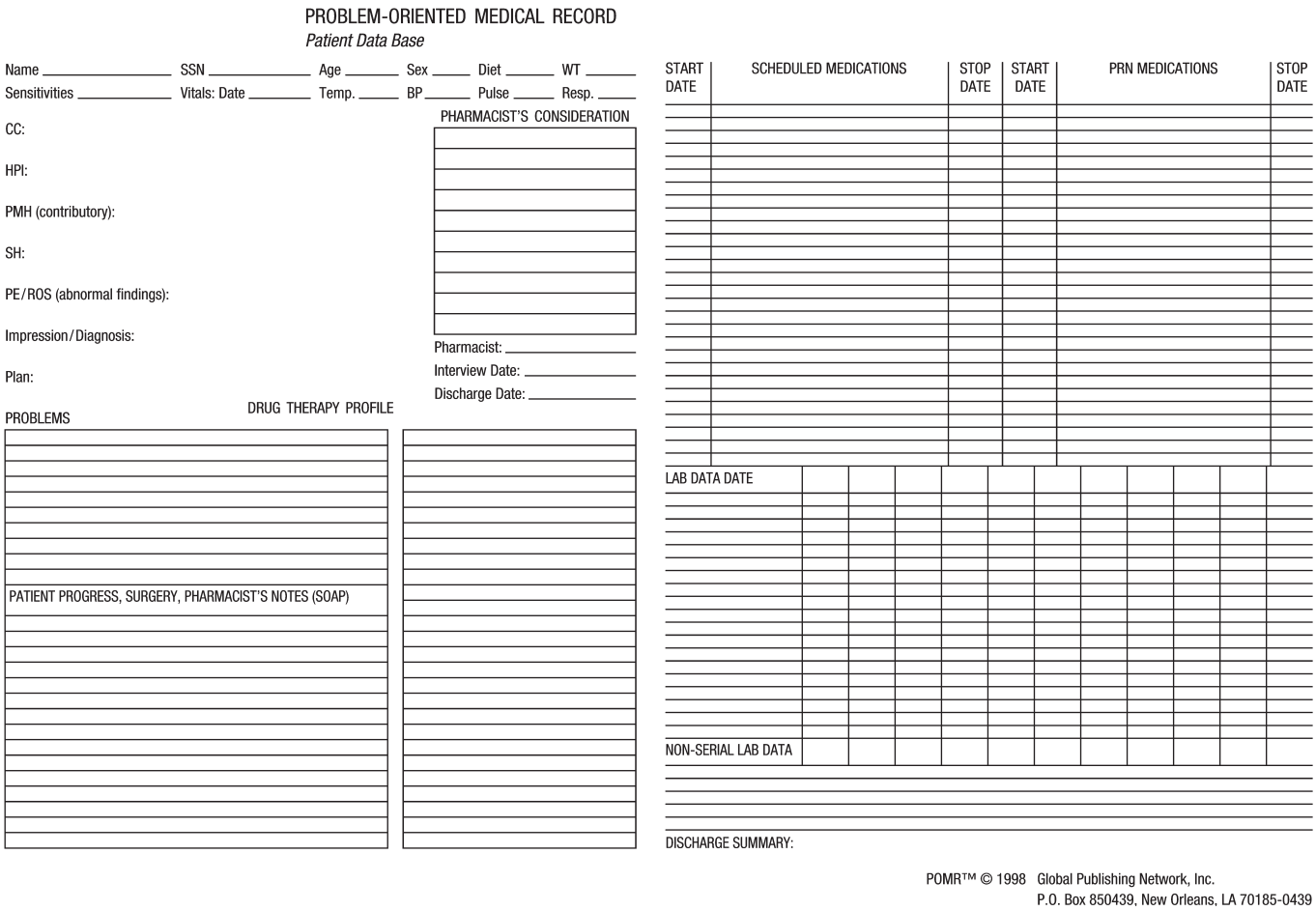
7/15 - The patient returned to the pharmacy today for refills and brought his meter and log book. The test performed here was unusually high for him. The logbook revealed a trend toward higher readings over the last 10 days. The meter appears to be operating appropriately. I will investigate further and follow-up with the patient/physician as needed. *M.S.*

6/4 - The patient brought in his meter today and performed a test while I observed - fasting measurement was 111mg/dL. Patient reported that readings have generally been in the 100-135mg/dL range since last visit but forgot to bring his log. His technique is fine.

J.L

5/10 - The patient purchased and was trained to use an Accu-Check Easy blood glucose meter and agreed to bring the meter with him on refill visits so pharmacist can reassess technique/obtain a measurement for the patient record. *M.S.*

Figure 123-2. *(Continued) B,* A pharmacist's patient data record.


PROBLEM-ORIENTED MEDICAL RECORD
Patient Data Base

Name _____ SSN _____ Age _____ Sex _____ Diet _____ WT _____
Sensitivities _____ Vitals: Date _____ Temp. _____ BP _____ Pulse _____ Resp. _____

CC:

HPI:

PMH (contributory):

SH:

PE/ROS (abnormal findings):

Impression/Diagnosis:

Plan:

PHARMACIST'S CONSIDERATION

Pharmacist: _____
Interview Date: _____
Discharge Date: _____

DRUG THERAPY PROFILE

PROBLEMS

PATIENT PROGRESS, SURGERY, PHARMACIST'S NOTES (SOAP)

START DATE | SCHEDULED MEDICATIONS | STOP DATE | START DATE | PRN MEDICATIONS | STOP DATE

LAB DATA DATE

NON-SERIAL LAB DATA

DISCHARGE SUMMARY:

Figure 123-3. The Problem-Oriented Medical Record (POMR).

One of the earliest approaches for the identification of medication problems is the 10-step method adapted from the work of Srnka and Self.[15] Using this method, pharmacists examine individual patient databases for actual and potential problems in the following 10 categories.

History of adverse effects
Potentially unwarranted/unintended changes in therapeutic regimen
Potential quantitative misuse (noncompliance, misuse, overuse)
Duplication of medications
Additive effects from similar medication use
Inappropriate dosage, route of administration, dosing schedule, or dosage form
Potential current adverse effects
Drug-drug interactions
Drug-disease interactions
Irrational therapeutic regimen

For example, the patient whose profile is illustrated in Figure 123-1 began receiving refills of her Ventolin more frequently than usual, beginning in October. In addition, she stopped having her other two asthma medications (ie, Serevent and Azmacort) refilled at the same time. Both of these potential problems would fall into the category of quantitative misuse. It would be important for the pharmacist to ask the patient tactfully about the reasons for these changes. Increased use of Ventolin may indicate that her condition is worsening. Further, the patient may be receiving sample units of Serevent and Azmacort from her physician or may be using another pharmacy to have prescriptions for these medications filled. Both scenarios could account for the apparent underuse of Serevent and Azmacort. In any case, the potential problem would be recorded by the pharmacist for further investigation.

The authors of the 10-step method suggest that pharmacists have a pocket card with the 10 categories available to aid the review of the patient profile each time they dispense a prescription. This pocket card provides them with a framework in which to review the profile and, with time, ultimately is committed to memory.

Strand et al advocate use of the eight medication-related problem categories outlined previously in the definition of pharmaceutical care.[8] These authors also stress the importance of clear and explicit problem statements. This is because problems stated in specific terms provide more guidance for the selection of an optimal problem solution. In this context, the authors recommend statements that describe each of two problem components:

1. The illness, symptoms, or risk factors
2. The actual or potential relationships to drug therapy.

To clarify the rationale behind this recommendation, consider the pharmacist's patient data record for Tina Smith, which is illustrated in Figure 123-2*A*. On 5/23 the pharmacist on duty noted a problem with the patient's new prescription. If this problem was defined simply as a drug interaction, the pharmacist would not know whether the solution is to

1. Discontinue a drug and recommend a new one
2. Increase the dose
3. Decrease the dose
4. Add a new drug
5. Discontinue all therapy
6. Implement some other appropriate action (eg, stagger medication doses)

In contrast, if the problem is stated as significant risk of serious cardiac arrhythmia due to an interaction between two med-

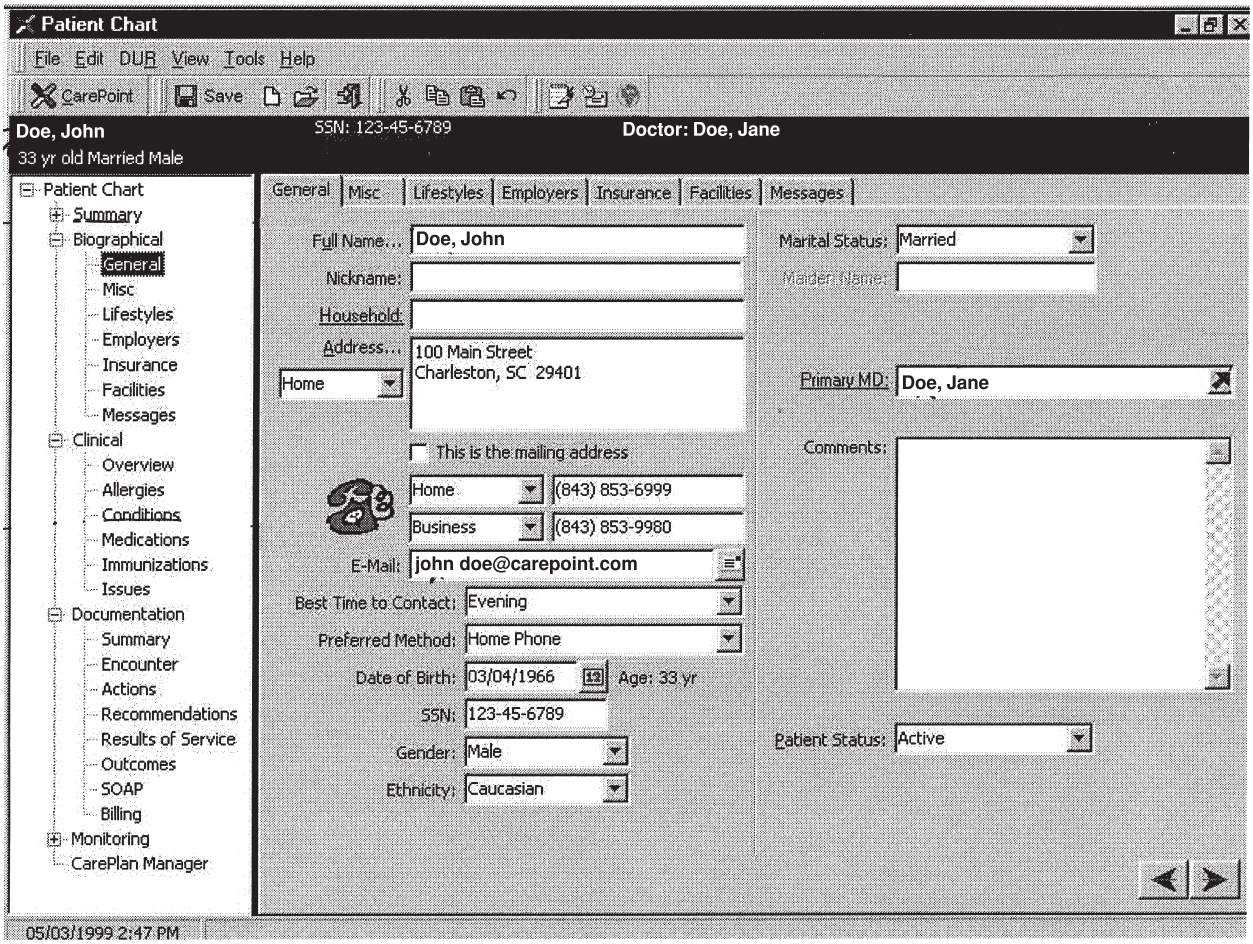


Figure 123-4. A Guardian patient chart.

ically necessary therapies (ie, Sporanox and Hismanal), the solution is much clearer. That is, under no circumstances should the two medications be used together by the patient. If the patient was still taking Sporanox, either the Hismanal or the Sporanox therapy must be discontinued and an alternative medication recommended as a replacement.

One of the most comprehensive systems for the assessment of medication problems was developed by Shimp and Mason as part of the American Society of Health System Pharmacists' Clinical Skills Program.[16] The system consists of two instruments. The Drug Therapy Assessment Worksheet (DTAW) prompts the pharmacist with a series of *guiding* questions to determine if problems exist in any of the following 11 drug-therapy problem categories:

Correlation between drug therapy and medical problems
Appropriate drug selection
Drug regimen
Therapeutic duplication
Drug allergy or intolerance
Adverse drug events
Interactions: drug-drug, drug-disease, drug-nutrient, and drug-laboratory test
Social or recreational drug use
Failure to receive therapy
Financial impact
Patient knowledge of drug therapy

Problems identified during completion of the DTAW then are transferred to a Drug Therapy Problem List (DTPL). This instrument consists of three columns that provide space for pharmacists to record the

1. Date on which the problem was identified
2. Drug-therapy problem
3. Actions or interventions employed to solve the problem

To illustrate how a pharmacist might use this system, consider the pharmacist's patient data record for Mr Sommers, illustrated in Figure 123-2*B*. For the drug-therapy category interactions: drug-drug, drug-disease, drug-nutrient, and drug–laboratory test, the DTAW prompts the pharmacist to answer the following questions.

a. Are there any drug-drug interactions?
b. Are they clinically significant?
c. Are any medications contraindicated (relatively or absolutely) given patient characteristics and current/past disease states?
d. Are there drug-nutrient interactions?
e. Are they clinically significant?
f. Are there drug-laboratory interactions?
g. Are they clinically significant?

The pharmacist who assesses the profile in Figure 123-2*B* using the DTAW would notice that the patient began receiving hydrochlorthiazide (HCTZ) following the diagnosis of congestive heart failure (CHF). Although HCTZ is commonly used to treat CHF, it is not usually a drug-of-choice in patients with concomitant diabetes mellitus because it can increase blood-glucose levels. In fact, inspection of the patient's blood-glucose

measurements in the Lab/Monitoring section of his record suggests that this drug-disease interaction may be occurring. Thus, the pharmacist would indicate on the DTAW that a problem exists and record his rationale for this belief in the column reserved for comments and notes. A specific statement of the problem would then be transferred to the DTPL. In this context, the pharmacist may formulate the problem as a clinically significant glucose intolerance possibly due to an interaction between the patient's therapy for CHF and hypertension (ie, HCTZ) and his preexisting diabetes mellitus.

After identifying all actual or potential medication-related problems in the patient database, the pharmacist must determine which problems to address first. For this purpose, the pharmacist must consider the probability that a particular problem will occur and the seriousness of the consequences if it does ensue. Problems that have the highest likelihood of causing the patient significant harm (eg, a patient with a history of anaphylaxis secondary to penicillin who has been prescibed amoxicillin) are generally ranked highest. The prioritized list of problem statements would then be used by the pharmacist to develop a specific goal for resolving each problem and subsequently to design pharmacotherapeutic regimens to achieve each goal.

Establishment of a Desired Pharmacotherapeutic Outcome for Each Medication-Related Problem

Pharmacotherapeutic outcomes are predefined medication-related goals for the resolution of problems identified in the previous step of the pharmaceutical-care process. Similar to problem statements, these outcomes should be clearly articulated to help the pharmacist identify feasible problem solutions and to evaluate results of the alternative that is ultimately chosen. Typically, these statements are simply the mirror image of the problem and fall into one of the three following categories:[8]

The patient is receiving appropriate pharmacotherapy for each definitively diagnosed disease.
The patient is receiving the appropriate dose of each medication at appropriate time intervals.
The patient is free from adverse drug reactions, side effects, and drug interactions.

In this context, a pharmacist would initially conclude from Tina Smith's pharmacist patient data record in Figure 123-2*A* (ie, prior to determining that the patient no longer takes Sporanox) that one of the patient's potential problems was a significant risk of serious cardiac arrhythmia due to an interaction between two medically necessary therapies (ie, Sporanox and Hismanal). Thus, the corresponding goal would be to provide the necessary pharmacotherapy for hay fever symptoms and onychomycosis without the risk of a serious drug interaction. Similarly, a pharmacist would determine from Mr Sommers' patient record in Figure 123-2*B* that the patient was experiencing clinically significant glucose intolerance due to an interaction between his therapy for CHF and hypertension (ie, HCTZ) and his preexisting diabetes mellitus. The corresponding goal in this instance would be to provide the necessary pharmacotherapy for CHF and hypertension without impairing glucose tolerance.

Once the pharmacist has articulated the desired pharmacotherapeutic outcome for each medication-related problem, he or she must define appropriate indicators for each goal. Indicators are measurable variables that can be used to monitor the effectiveness of the pharmacotherapeutic solutions to medication-related problems. To be optimally useful in this regard, indicators must be designed to include:

1. A patient factor
2. A progress factor
3. A time factor[8]

Patient factors are variables that can be measured to determine the impact of therapy and include reports of symptoms, laboratory values, and the results of quality-of-life assessments. Progress factors explicitly describe the degree of improvement in patient variables that can reasonably be expected to result from the pharmacotherapy. Finally, time factors characterize the time frame in which the pharmacotherapy should have achieved the desired degree of improvement.

For the patient illustrated in Figure 123-2*A*, an appropriate patient factor would be the severity of the patient's hay fever symptoms as measured by the patient on a scale of 1 to 5, with 1 signifying no relief and 5 representing complete relief of each symptom. An appropriate progress factor might be a value greater than 3 for each symptom, because complete relief of allergy symptoms secondary to antihistamine therapy occurs infrequently. An appropriate time factor for this level of relief would be 4 to 8 weeks. This is based on the time to reach steady state, which is indicated in the product's package insert.[17]

For the patient in Figure 123-2*B,* who has CHF, hypertension, and diabetes mellitus, an appropriate patient factor would be blood-glucose levels. The associated progress factor would be a return to normal fasting levels, ie $<$140 mg/dL. Finally, a reasonable time period for return to normal fasting blood-glucose levels would be approximately 2 days following discontinuation of therapy with HCTZ. This was determined by multiplying the average elimination half-life for HCTZ (ie, 10 hr) by five; ie, an estimate of the number of half-lives required for a drug to be eliminated from the body.[18]

Determination of Feasible Pharmacotherapeutic Alternatives to Achieve Each Desired Outcome

Following articulation of a goal for each medication-related problem, the pharmacist must generate a list of all feasible problem solutions. The reason for this brainstorming step is to ensure that all possible solutions have been considered before any one is chosen. It is also a useful backup tool when the first alternative selected is ineffective for a particular patient.

Generally, pharmacotherapeutic goals may be achieved by correction of a system problem, adjustment of current pharmacotherapy, or development of an entirely new pharmacotherapeutic plan. Thus, the pharmacist should begin the development of a list of feasible solutions by considering alternative solutions within each of these categories.

An example of a system problem would be a patient who has difficulty having prescriptions refilled regularly because of lack of transportation to and from the pharmacy. In this case, the pharmacist would work with the patient and other individuals (eg, caregivers, transportation services) to ensure that the patient receives medication refills in a timely fashion. An example of a minor therapeutic adjustment could be the downward adjustment of the theophylline dose for a patient who suffers from chronic bronchitis and is prescribed another medication known to impede theophylline metabolism, eg, an oral contraceptive. Finally, an example of a situation in which a new therapeutic plan would be appropriate involves a patient who has been prescribed erythromycin for a minor infection and who has previously suffered from intolerable nausea and vomiting when this medication was prescribed.

To facilitate the subsequent determination of an optimal solution in the next step, the pharmacist should take care to list alternatives in a consistent format. Strand et al recommend listing alternatives according to distinguishing characteristics.[8] This makes the advantages and disadvantages of each alternative more visible and therefore easy to compare with one another. In the context system problem described previously, a list could be developed to distinguish alternative

Table 123-2. Therapeutic Alternatives for the Treatment of CHF and Hypertension in a Diabetic Patient

CATEGORY	GLUCOSE	INSULIN SENSITIVITY	LD CHOLESTEROL	HDL CHOLESTEROL	TRIGLYCERIDES
ACE inhibitors	↓[a]	↑	(↓)	↔	↔
α-Blockers	↔	↑	(↓)	(↑)	↔
β-Blockers	↑	↓	↔	↓	↑
Calcium channel blockers	↔	(↑)	(↓)	↔	↔
Direct vasodilators	?	↔	↔	↔	↔
Thiazide diuretics	↑	↓	↑	(↓)	(↑)

[a] ↑, increase; ↓, decrease; (↑), possible increase; (↓), possible decrease; ↔, no effect; ?, unknown.

sources of patient assistance. For alternatives in the therapeutic adjustment example, the list might be created to distinguish alternative theophylline products according to available product strengths or dosage forms to accomplish the adjustment. In the final example, in which a new therapeutic plan was indicated, alternative medications could be listed according to available dosage forms, mechanisms of action, clinical efficacy, incidence of adverse reactions (eg, nausea and vomiting), or even cost.

To illustrate the generation of a comprehensive list of feasible alternatives for a specific example, consider the Mr Sommers' pharmacist's patient data record in Figure 123-2*B*. Using the recommendations of Strand et al and appropriate references,[19] the pharmacist could begin by listing alternatives to HCTZ for the treatment of hypertension and CHF according to mechanism of action, as illustrated in the first column of Table 123-2. Next, the pharmacist could further distinguish these six categories by listing the general effect each has on blood glucose and insulin sensitivity, as shown in the second and third columns of Table 123-2. Finally, because patients who suffer from diabetes mellitus are at increased risk for the development of atherosclerotic heart and brain disease, the pharmacist could determine and list the effects of each category on serum lipids.

In many instances it is also appropriate to list the approximate cost of individual medications in each category. However, in this instance, the patient has prescription coverage with a small copay. Thus, this information is not as useful as it might be in the case of an uninsured or underinsured patient.

Selection of the Best Pharmacotherapeutic Solution Based upon Individual Patient Circumstances

During this step, the pharmacist must determine which therapeutic alternative is best for the patient. In this context the pharmacist's recommendation for the solution of each medication-related problem should include the chosen medication, dosage form, dose frequency and duration, and any special instructions (eg, uncommon administration procedures) for the patient. At this point it is especially important to involve the patient in the selection of appropriate therapy. This helps to ensure that the patient is able and willing to comply with all associated therapeutic and monitoring instructions.

In the case of Mr Sommers, the pharmacist concluded from his research that an ACE inhibitor would be most appropriate. Upon questioning by the pharmacist, Mr Sommers expressed his desire to continue to be able to take all of his medications once daily in the morning. Upon further investigation, however, the pharmacist learned that it would be more appropriate to initiate therapy with a shorter-acting ACE inhibitor such as captopril, initally with 6.25 mg 3 times a day. Once the effective dose of captopril is achieved, the patient can then be switched to a once-daily ACE inhibitor such as lisinopril.[20] After the pharmacist explained this, the patient agreed that he would be able to manage multiple daily doses of captopril if they were only necessary for a short period of time.

Design of a Monitoring Plan to Determine If the Desired Pharmacotherapeutic Outcome Has Been Achieved

Prior to implementing any therapeutic recommendation, the pharmacist must develop a plan to monitor the patient's progress toward each goal established in a previous step. This plan should include appropriate pharmacotherapeutic monitoring parameters, realistic endpoints for each parameter, and the frequency with which each parameter will be assessed. The number and nature of each plan component depends on the

1. Properties of the recommended medications
2. Patient's background characteristics
3. Availability of practical, cost-effective monitoring methods.

Pharmacotherapeutic monitoring parameters are either quantitative or qualitative assessments of patient progress toward specific therapeutic goals. Quantitative assessments are objective measures of a particular variable and include blood pressure, pulse, temperature, serum drug levels, and blood-glucose determinations. Qualitative assessments are subjective determinations of change in a particular variable. Examples include patient self-reported changes in symptoms such as nausea, pain, and sedation.

It is important to note that some pharmacotherapeutic goals may necessitate the identification of multiple monitoring parameters while others will require only one. For example, a number of parameters could be used to monitor the resolution of a bacterial infection of the upper respiratory tract. These might include temperature, sputum color, cough, and/or white blood cell counts, depending on the patient's situation. In contrast, achievement of serum theophylline levels in the therapeutic range could only be determined by performing serum theophylline assays.

It is also important to mention that pharmacists must take care to ensure that the desired endpoint specified for each pharmacotherapeutic goal is realistic and achievable, based upon individual patient characteristics. For example, a score of 0 on a pain scale (ie, indicating no pain) may be achievable for a patient who has just undergone a tooth extraction, but would likely be unreasonable for a patient suffering from metastatic bone cancer. Similarly, an appropriate endpoint for chemotherapy in a patient in the earliest stage of breast cancer may be remission of the disease. However, a more appropriate endpoint for a similar patient in the terminal stage of the disease would be to reduce pain scale scores through the use of analgesics.

When choosing appropriate monitoring parameters for a given patient, the pharmacist must take into account the therapeutic efficacy of the selected medication and the potential for the medication to cause new problems (ie, side effects and adverse reactions). In the context of the pharmacist's recommendation of captopril to treat Mr Sommers' CHF and hypertension, blood pressure would be an example of a quantitative measure of therapeutic efficacy, and the severity of dyspnea on exertion would be a qualitative measure. Desired endpoints might be blood pressure measurements in the normal range for Mr Sommers' age and, at the very least, no change in the level of dyspnea on exertion.

Monitoring parameters to identify new problems as a result of captopril therapy might include the development of a maculopapular rash on the trunk or extremities (the most common side effect of captopril), alteration of taste perception, and the onset of a dry, hacking cough in the absence of other respiratory pathology. Realistic endpoints might be that symptoms, if they occur at all, do not interfere with Mr Sommers' daily activities. Monitoring data for all of the aforementioned parameters could be collected by the pharmacist each time Mr Sommers returns to the pharmacy for prescription refills.

Patient-specific characteristics also should be taken into consideration by the pharmacist when selecting appropriate monitoring parameters. Of particular importance are patient characteristics that may influence the pharmacokinetic disposition of the recommended medication. For example, captopril has been associated with the development of proteinuria and decreased renal function in some patients. Twenty percent of patients treated with captopril develop stable elevations in BUN and serum creatinine levels that may reach as high as 20% over baseline measurements. Others experience a more accelerated deterioration in renal function that necessitates discontinuation of captopril. However, most of these patients had evidence of preexisting renal disease.[21]

Although Mr Sommers does not apparently suffer from renal dysfunction at the present time, he is at risk for its development secondary to his diabetes mellitus. In addition, he suffers from CHF. Thus, the pharmacist in this situation also may recommend monitoring Mr Sommers' BUN and serum creatinine levels in addition to the parameters described previously. The pharmacist may recommend baseline measurement of BUN and serum creatinine and regular measurments (eg, every 3 months) for the first year of therapy.

Implementation of Individualized Pharmacotherapeutic and Monitoring Plans

The next step in the pharmaceutical-care process is to implement the pharmacotherapeutic and monitoring plans developed by the pharmacist. This involves securing physician approval for any changes in the originally prescribed therapy, counseling the patient about the proper use of the recommended therapy, and collecting monitoring data to evaluate the efficacy of the pharmacotherapeutic plan.

In some instances, it is necessary for pharmacists to secure authorization from a physician to initiate or modify a patient's pharmacotherapy. In the case of Mr Sommers, the pharmacist would need to contact Dr Spandel to seek approval to discontinue HCTZ and initiate therapy with captopril. The pharmacist in this case also would recommend monitoring Mr Sommers' BUN and serum creatinine and would request regular access to these laboratory results. In any situation in which the physician must be contacted, pharmacists can maximize the likelihood that their requests will be approved by following a few simple guidelines.

First, and most important, the pharmacist must prepare thoroughly prior to consulting with the physician. All necessary references must be checked, and relevant information, including citations, should be recorded in advance for rapid retrieval as needed during the consultation. Upon contacting the physician, the pharmacist should present a detailed but concise description of the problem. This should be followed by a specific solution for the problem, the pharmacist's rationale for the recommended solution, and supporting references. At the conclusion of the consultation, all information, including the outcome of the consult, should be documented in the patient's record.

The next implementation step is to educate the patient relative to the proper use of the chosen therapy. Effective counseling helps to ensure that patients adhere to prescribed therapies and enables pharmacists to identify and resolve medication-related problems as expediently as possible.[22–26]

OBRA 90 establishes minimum requirements for counseling individuals receiving benefits, consistent with applicable state laws and the pharmacist's professional judgment. At a minimum, the pharmacist should ensure that the patient knows

The name and description of the medication.
The dosage form, dosage, route of administration, and duration of drug therapy
Special directions and precautions for preparation, administration, and use by the patient
Common severe side or adverse effects or interactions and therapeutic contraindications that may be encountered—including their avoidance—and the action required if they occur
Techniques for self-monitoring drug therapy
Proper medication storage
Prescription refill information
Action to be taken in the event of a missed dose

In this context, the pharmacist who counsels Mr Sommers about his captopril therapy should tell the patient the following:

The name of the medication is captopril.
The strength of each tablet is 12.5 mg.
The doctor wants you to take one-half tablet by mouth 3 times a day.
This medication is being used to treat high blood pressure and congestive heart failure. It should be continued until the doctor decides otherwise.
The tablets should be broken or cut in half at the score mark in the center of each tablet. This medicine works best when it is taken on an empty stomach 1 hr before a meal. Ideally, this medication should be taken at the same time each day.
If you miss a dose, take it as soon as you remember unless it is close to the time of your next dose. In this instance, simply skip that dose and resume therapy with the next scheduled tablet.
Do not double doses.
This medication may cause dizziness or lightheadedness, especially after the first dose. Make sure you know how you will react to the medication before driving or operating dangerous machinery.
Minor side effects include coughing, changes in taste perception, and mild diarrhea and stomach upset.
Contact your physician if any of these symptoms become severe enough to interfere with daily activities.
Call your physician immediately if you experience fever, swelling of the face or extremities, trouble breathing, irregular heartbeat, nervousness, or tingling/heaviness in your legs.
Keep regularly scheduled appointments for laboratory tests and physician appointments. Consider use of a home blood-pressure-monitoring device for blood-pressure monitoring between physician visits.
Store this medication in a cool, dry place that is out of the reach of children.
Your doctor probably will adjust your dose before you run out of this medication; therefore, there are no refills on your current prescription.[27]

When taken at face value, the minimum counseling requirements set forth by OBRA 90 may be misleading because they may be interpreted as a one-time, one-way communication of information from the pharmacist to the patient. Indeed, while this type of interaction may fulfill the legal requirements of OBRA 90, it will not always, if ever, be sufficient to provide the level of professional service intended in the definition of pharmaceutical care.[28]

In fact, if the intent of pharmaceutical care is to optimize therapeutic outcomes, a one-way communication of drug information to the patient at the time of purchase rarely makes sense. This is apparent when one considers the frame of mind of patients at the time they pick up a prescription. In the worst case, the patient is feeling sick and is concentrating on little more than returning home to rest and recuperate. In less extreme circumstances, patients may be annoyed after having to take time off from work to perhaps spend hours in a physician's office followed by another period of waiting in the pharmacy. As a result, they are probably not overly enthusiastic about learning all there is to know about the prescribed medication in a few minutes of verbal counseling from the pharmacist.

In this context, some may argue that printed information to be read at a more convenient time would suffice as ade-

quate counseling for the patient. In fact, this approach has been used by some pharmacists as a means of dealing with the relative lack of time for verbal counseling at the time of dispensing. In addition, in an effort to increase the availability of prescription drug information to the public, the FDA proposed a rule commonly known as MedGuide in 1995. This rule set forth goals for the distribution of printed prescription drug information to consumers and would have required pharmaceutical manufacturers to include drug information for products that posed a serious health risk.

Although Congress passed legislation in 1996 that put the MedGuide proposal on hold, health professionals are being asked to voluntarily provide prescription drug information in the form of leaflets written in simple language. Consistent with DHHS's goal under its Healthy People 2000 program, this information must reach 75% of patients by the year 2000 and 95% of patients by 2006.[29] However, pharmacists should be cautioned not to rely entirely on printed drug information to educate their patients.

When used alone, written information may actually be less effective than a one-time, one-way communication of information from the pharmacist.[12] This is because there is no way to ensure that the patient will actually read the information prior to initiating the prescribed therapy. Further, there is no guarantee that the patient will contact the pharmacist with any questions that may arise after reading it. Even worse, the patient may be illiterate and unable to read the information at all. This is a real concern in the US, where over 20% of adults read at or below the fifth-grade level.[30]

A more effective approach to patient counseling would include two-way communication between the pharmacist and patient and would be augmented by printed information as needed, depending upon the specific situation. In addition, the approach must make efficient use of the pharmacist's and the patient's valuable time. Pharmacists employed by the Indian Health Service (IHS) have used one such approach for many years.

While traditional approaches to patient counseling focus on providing information, the goal of the IHS method is to verify that patients have acquired requisite drug information, using an interactive approach. For counseling on new prescriptions, the pharmacist asks the patient to answer the following questions.

What did the doctor tell you the medication is for?
How did the doctor tell you to take the medication?
What did the doctor tell you to expect?

Answers to these questions are then used by the pharmacist to determine the patient's specific information needs. The approach saves time, because the pharmacist must only supply the information that the patient does not already have. In fact, IHS studies have found the time required to counsel a patient about a new prescription takes a little under 2 minutes using this approach.[31]

To promote patient adherence and to monitor patient progress toward medication-related goals, IHS pharmacists use a second technique for refill prescriptions that takes only about 30 seconds. Using this approach, the pharmacist removes the cap from the prescription, shows the medication to the patient and asks, "What do you use this medication for? How do you take it? What kinds of problems are you having? Is there anything else I can do for you today?" Both techniques encourage pharmacist-patient interaction. Again, the pharmacist's questions are used to verify patient understanding and fill in any information gaps.[31]

Follow-up Evaluation and Documentation of the Results of Pharmacotherapeutic and Monitoring Plans

At predetermined intervals, the pharmacist must review collected monitoring data to determine if satisfactory progress is being made toward the desired medication-related goals. At the same time, the pharmacist must ascertain if any new problems have developed since the last review. If the desired outcomes have not been met or if new problems have occurred, the pharmacist, physician, and patient may need to make changes in the original pharmacotherapeutic and monitoring plans.

Changes are made following reconsideration of relevant information from earlier steps in the pharmaceutical-care process or from the collection of new information as needed. Suppose, for example, that Mr Sommers returned to the pharmacy 1 week after initiation of captopril and complained of intolerable coughing. In this case, the pharmacist would review the alternative therapies originally considered and select another medication to treat Mr Sommers without causing a cough. If the pharmacist, physician, or patient was not satisfied with any of the alternatives considered previously, the pharmacist would consult the literature to identify a more suitable therapy.

In any event, the final step in the pharmaceutical-care process requires that the pharmacist document all interventions and outcomes in the patient's record. This information then becomes baseline information upon which subsequent adjustments and/or new therapeutic decisions are made. This information also may be required if the pharmacist attempts to obtain reimbursement for pharmaceutical-care services from a third party.

BARRIERS TO PHARMACEUTICAL CARE

Although the profession of pharmacy has embraced pharmaceutical care as its new mission, the implementation of pharmaceutical care, particularly in ambulatory practice settings, has been slow. A variety of factors have impeded pharmacists' ability to implement pharmaceutical care and can be grouped into four general categories.

Individual pharmacist characteristics
Practice-setting constraints
Intraprofessional barriers
System impediments

An awareness of the potential barriers to pharmaceutical care and a working understanding of alternatives for surmounting these constraints may assist pharmacists during the transition to pharmaceutical-care practice.

Individual Pharmacist Characteristics

Individual pharmacist attitudes and background knowledge and/or skill deficiencies may hamper the implementation of pharmaceutical care in any practice setting. For example, some pharmacists have grown quite comfortable with traditional practice functions and may be fearful about changing to assume new, unfamiliar roles. In addition, they may be concerned that expanding professional practice roles will place them in conflict with patients who do not feel the need for pharmaceutical care and/or with other health-care professionals who believe they are more qualified to provide these services. Finally, some pharmacists might lack confidence in their educational preparation to provide an advanced level of care to their patients.

Indeed, the provision of pharmaceutical care will require many pharmacists to update their professional knowledge and skill base. First and foremost, pharmacists must develop a thorough understanding of what it means to provide pharmaceutical care. Many pharmacists mistakenly believe that they always have provided the level of professional service embodied in the definition of the concept. In reality, however, many fail to realize that pharmaceutical care is more than occasional interventions on behalf of the patient. Thus, pharmacists must take it upon themselves to develop an accurate understanding of the pharmaceutical-care process. Only then, will they be able to shift the focus of their practices from dispensing medications to the provision of patient-oriented, professional services.[32]

Pharmacists who commit to managing the pharmacotherapy of their patients must be familiar with current advances in the treatment of common diseases and with literature resources/databases that are available to assist them to make sound therapeutic decisions. Thus, some pharmacists may find it necessary to update their knowledge of therapeutics and drug information resources/capabilities.

Similarly, the provision of pharmaceutical care requires that pharmacists develop strong, effective problem-solving skills.[33] Most pharmacists have already developed basic problem-solving abilities. However, they may not have regularly applied these skills to the resolution of their patients' medication-related problems. As a result, some pharmacists may benefit from additional instruction on clinical problem solving.

Finally, oral and written communication skills are central to the provision of pharmaceutical care.[33] Among other things, strong communication skills are crucial for eliciting important information from patients, documenting pharmacists' therapeutic decisions, and counseling patients about the proper use of medications. Strong communication skills are also essential to convey information about patients' pharmacotherapy to physicians and other health-care providers. Because the levels of communication proficiency and frequency entailed for the provision of pharmaceutical care are generally higher than the requirements for traditional roles, some pharmacists may benefit from additional instruction prior to fully implementing pharmaceutical-care services.

One strategy for coping with the aforementioned barriers is for pharmacists to transition gradually to the provision of patient-oriented professional services. Adapting to change and the development of advanced practice abilities must develop over time. Thus, pharmacists should initially focus on the provision of limited pharmaceutical-care services to a specific group of patients. The group should be chosen to reflect an area of disease/therapeutics (eg, asthma care, diabetes care) in which pharmacists feel comfortable with their current level of expertise. Then, as pharmacists gain confidence and develop additional expertise, they can extend pharmaceutical-care services to additional patients.

An especially useful resource for pharmacists who want to develop new skills for the provision of pharmaceutical care is *The Pharmacists' Learning Assistance Network (PLAN)*. The *PLAN* is a continuing pharmaceutical education information service that is provided to pharmacists through the American Council on Pharmaceutical Education (ACPE). It was developed to enable pharmacists to pursue a curricular approach to professional development through organization and planning of their continuing pharmaceutical education needs. A computerized compilation of all continuing pharmaceutical education programs offered by ACPE-approved providers serves as the database for the service. The *PLAN* service may be contacted by telephone between 9:00 a.m. and 4:00 p.m. (Central Time) Monday through Friday by dialing (800) 533-3606. During this time professional staff members are available to discuss pharmacists' personal educational needs and available continuing education programs that may be useful to meet those needs.[34]

Practice-Setting Constraints

Resource constraints and other factors associated with a particular practice setting also are mentioned frequently as barriers to the provision of pharmaceutical care. For example, pharmacists often complain that they do not have time to provide pharmaceutical care in addition to their normal responsibilities.[32] When taken at face value, the assessment of these pharmacists relative to time available to provide pharmaceutical care is accurate. Upon closer scrutiny, however, other variables may be contributing to the perceived lack of time.

It is possible that pharmacists who perceive a lack of time for pharmaceutical-care services have not delegated enough nontechnical pharmacy functions to available support personnel or may not have taken full advantage of available technology (eg, fax machines, documentation software, automated dispensing equipment) in the dispensing process. In this context, pharmacists should scrutinize the tasks routinely performed to determine if any functions can be accomplished more efficiently through the use of technology or support personnel. Tasks that are reassigned to support personnel should then be added to the appropriate job descriptions. Training also must be instituted to enable support personnel to perform these new responsibilities. In this way, although time will be required to complete the aforementioned measures, pharmacists may be able to free additional time to provide patient care services in the long run.

Similarly, pharmacists should examine the workflow pattern in the pharmacy to make sure that departmental personnel can complete their assigned duties as efficiently as possible. Each dispensing station should provide easy access to prescription containers, labels, prescription files, patient records, telephones, and fast-moving prescription products. Space for direct, confidential pharmacist-patient interaction also should be located as close to the dispensing area as possible. These measures also may help to free pharmacist time for the provision of pharmaceutical care.[35]

A lack of financial resources also is mentioned often as a barrier to the provision of pharmaceutical care.[32] Purchasing additional equipment, hiring and training additional personnel, and redesigning the pharmacy can be quite expensive. A further complication exists when the management of the pharmacy organization is not committed to the provision of pharmaceutical care. In that situation, support for even minor modifications of the practice environment may be completely absent.

A gradual transition to the provision of pharmaceutical care also may be an effective means for pharmacists to contend with barriers in the practice setting. Most pharmacists should be able to offer pharmaceutical care to a limited number of patients without incurring large expenses. Then, as the number of patients receiving care is expanded, pharmacists can gradually modify the environment to be more conducive to patient-oriented services. The documented impact of these early efforts to provide pharmaceutical care also may be useful to persuade pharmacy management to provide resources for the transition.

Intraprofessional Barriers

Professional organizations, regulatory bodies, and schools/colleges of pharmacy also may be perceived as barriers to the implementation of pharmaceutical care insofar as their efforts fail to support practitioners adequately in their transition efforts. For example, until very recently professional pharmacy organizations have become increasingly fragmented into groups with widely different interests and competing agendas.[36] The resultant lack of consensus has weakened the profession politically. This is important because many debates relative to the profession are settled in the political arena (eg, OBRA 90). Thus, pharmacists from all practice settings and the organizations that represent them must work cooperatively to develop a common agenda for the implementation of pharmaceutical care if this new mission is ever to be fully realized by the profession.

As the practice of pharmacy transitions to pharmaceutical care, legislation governing the practice of the profession also must evolve to permit pharmacist provision of expanded patient care services. Outdated board of pharmacy regulations such as limitations on the nontechnical functions that can be performed by technicians or the restrictions on modes of prescription transmission can actually impede pharmacists in their efforts to implement pharmaceutical care. To prevent such obstacles, state boards and associations must work cooperatively with local colleges/schools of pharmacy and practitioners to identify and correct problematic rules and regulations.[32]

Schools/colleges of pharmacy must assume a variety of roles to support the transition to pharmaceutical care. They must

continually evaluate and modify their professional curricula to ensure that pharmacy graduates are prepared to assume contemporary patient care roles.[9,33] Similarly, they must assess the continuing education needs of their alumni and provide instructional opportunities for practicing pharmacists to develop further the professional knowledge and skills required to render pharmaceutical care.[9,33] Educational programs also should be developed to prepare practitioners to precept pharmacy students during the experiential component of professional curricula. Finally, colleges/schools of pharmacy must conduct research to demonstrate the value of pharmaceutical care to society.[32]

System Impediments

Several characteristics of the health-care system in the US also impede the provision of pharmaceutical care. Among these are the general lack of pharmacist reimbursement for pharmaceutical-care services, a lack of patient demand, and a lack of acceptance of pharmaceutical-care roles by other health professionals.

At present, pharmacists are not often reimbursed for pharmaceutical-care services. Rather, they receive remuneration for the drug products dispensed. However, as outlined previously, the body of evidence supports the feeling that pharmaceutical-care services add value to patient care by enhancing patient compliance, improving patient outcomes, and reducing health-care costs.

Consumers are beginning to recognize the value of pharmaceutical-care services. In addition, there is evidence to support the notion that patients are willing to pay for consultation if they know it is available, is of potential benefit, and what it costs. For example, one enterprising pharmacist in Indiana successfully offers families who purchase prescriptions at his pharmacy professional consultation services for a flat annual fee. The cost of the prescription then is based upon the cost to the pharmacy plus a handling charge. This pharmacist also, with some success, has billed insurance companies for pharmaceutical-care services that were provided to his patients.[37]

Third-party purchasers of health care also are beginning to recognize the value of pharmaceutical care and to compensate pharmacists who provide these services. As an example, a recent amendment to the Mississippi Medicaid plan permits reimbursement for disease-state management services provided by appropriately credentialed or certified pharmacists. Eligible pharmacists receive $20.00 for each 15- to 30-min patient consultation for the management of diabetes mellitus, asthma, hyperlipidemia, or coagulation disorders in that state.[38,39]

Although compensation for pharmaceutical-care services is still the exception rather than the rule, pharmacists should consistently bill patients and third-party payers for these services. Some pharmacists may be reluctant to ask patients for direct payment for pharmaceutical care. However, if they do not, patients will not demand coverage for these services from third-party payers for health care. In this context, third-party coverage of pharmaceutical coverage will not change.

Pharmacy organizations also must work with third-party payers to develop standardized pharmacy service terminology and universal systems for billing and claims transmission (see Chapter 93). This is because standardized third-party compensation policies are necessary for widespread pharmacist reimbursement for pharmaceutical-care services.[32,37]

Initially, patient demand for pharmaceutical-care services may be low. Patients may resist the adoption of pharmaceutical care for a variety of reasons. Some may be reluctant to spend additional time consulting with a pharmacist. Others may be concerned about cost. Some patients may feel that the pharmacist is trying to take over a portion of the physician's role and want to avoid angering their own doctor. Regardless of the specific explanation given by a patient for refusing pharmacist services, the underlying issue is that patients generally are unaccustomed to this level of service and do not fully understand the concept of pharmaceutical care.[32]

In this context, pharmacists should take the time to explain their services thoroughly to each patient. They should emphasize that pharmaceutical care complements rather than duplicates services provided by other health professionals. In addition, pharmacists should describe how patients benefit from pharmaceutical-care services. Pharmacists also may generate demand for pharmaceutical care through effective marketing of their services to their communities and through participation in national public relations and educational campaigns such as the annual *National Pharmacy Week* sponsored every fall by the APhA.

Finally, it is likely that some health-care professionals will resist pharmacists' assumption of patient care roles. For example, nurses and physicians may view pharmacist management of pharmacotherapy as an encroachment on their professional territory. Pharmacists should not be intimidated and/or discouraged by this lack of acceptance. Rather, they should forge relationships with health professionals one at a time, beginning with those individuals who are open to collaboration. Realistically, not all health professionals will completely accept pharmacists' expanded role. However, over time and with perseverance, most pharmacists will be able to establish themselves as integral members of the health-care team.

A Systematic Approach For Overcoming Barriers To Pharmaceutical Care

In a recent book, Hagel and Rovers et al advocate the use of a strategic planning process to assist pharmacists in the transition from a product-oriented business to a patient-centered practice. The authors assert that the primary reason that many pharmacists are still struggling to implement patient-centered care is because the system they work in is not conducive to the changes they desire to bring about. Thus, the authors' approach targets the practice rather than individual pharmacists and assists service implementers to answer the following fundamental planning questions.

- Where am I now?
- Where do I want to be?
- How do I get there?
- How will I know when I have arrived?

To that end, the book includes detailed chapters to assist implementers with everything from patient care planning to adjusting infrastructure, staff development and outcome evaluation.[40]

HEALTH EDUCATION

A primary concern of the pharmacist should be the welfare of humanity and the relief of human suffering. In fact, one oath contains the passage, "I will use my knowledge and skills to the best of my ability in serving the public and other health professionals." Today, there is little doubt that the continuing *buzzword* in contemporary pharmacy practice is *information*—specifically, consumer health information.

By virtue of the pharmacists' accessibility and familiarity with the community, it is obvious that they can exercise a dynamic impact, which can be translated into not only the triage function but also the dissemination of effective and useful health education. One study revealed that over 90% of those interviewed visited a pharmacy at least once a month, and 60%, at least once a week. The hours a pharmacy is open per week greatly exceed those of all other health facilities with the possible exception of the hospital emergency room. Although many consumers continue to view the pharmacist as *an invisible man behind a secret counter who delegates responsibility to technicians and clerks to deal directly with the public,* this attitude is being changed positively to reflect the pharmacist as a source of health information along with the physician. A vast majority of the public does not hesitate to ask the pharmacist about a

health matter and usually he or she is the first person, other than family or friends, who is consulted.

Frequently, the pharmacist is confronted with a variety of inquiries:

- A telephone call from a frantic mother whose child has just swallowed a number of chewable vitamin-iron tablets and wants to know what to do.
- A nervous teenage girl who wants to know how to use a home pregnancy kit.
- A habitual smoker who is interested in the success rate of the nicotine transdermal patches.
- An expectant mother who is afraid for her baby because she may have been exposed to a neighborhood child with German measles.

The situations are endless but typify the need for the pharmacist to be approachable and willing to help.

To answer these people or synthesize a plan of action, pharmacists must maintain professional competence and keep abreast of developments of drugs and disease states. At the same time they should serve as expeditors to solve patient problems. The familiarity of the pharmacist with the community lends itself to proper referral of patients to other health-care professionals, including providing addresses and telephone numbers. Indeed, the pharmacist is in a position to assess physicians on the basis of personal experience, the types of prescriptions they write or telephone, patient comments about the care they receive, and inquiries about physician follow-up. Beyond health-care assistance, the pharmacist also should be able to recommend nonmedical facilities that provide effective care (eg, a shoe store that exercises judgment and care in fitting jogging shoes). Further, pharmacists should know that pharmaceutical companies do offer physicians free drugs for needy patients. While individual manufacturer requirements for assistance may differ, the following are some common requirements:

- Eligible patients cannot be covered by Medicaid or a private insurance plan that has prescription-drug coverage.
- Physicians must initiate the request on behalf of the patient and, in some instances, provide a statement of the patient's financial hardship.
- No more than a 3-months' supply is available at one time, although requests may be renewed.

Pharmacists can advise interested patients to seek an alphabetical listing of drugs covered by specific pharmaceutical companies, including information on assistance for acquired immunodeficiency syndrome (AIDS) drugs, by contacting The Senate Special Committee on Aging, Dirksen Senate Office Building, Room G-31, Washington, DC 20510 (1-202-224-5364). Similarly, physicians can be advised to contact the Pharmaceutical Manufacturers' Association, 1100 15th St, NW, Washington, DC 20005 for a directory of manufacturers' assistance programs.

In 1993 there were 100 regional poison control centers in the US (of which 38 were certified through the American Association of Poison Control Centers), and every pharmacy should have the telephone numbers and addresses of those in the local area for quick patient referral. Although unintentional poisonings and deaths have dropped dramatically since child-resistant packaging was introduced, tragedies continue to occur among young children. The pharmacist must be able to deal effectively with these emergencies, exercise judgment, and be decisive with such inquiries.

Another alarming problem that has surfaced within recent years is child and spousal abuse. This is of concern to all communities, and pharmacists, by their involvement, can serve in several ways to help alleviate the problem. For example, be aware of the warning signs of abuse and neglect from the perspective of the child (eg, seems unduly afraid of parents, shows evidence of repeated skin or other injuries, shows signs of poor overall care) and the parent (eg, makes no attempt to explain the child's most obvious injuries or offers absurd, contradictory explanations; shows a lack of control or fear of losing control). Given the warning signs of child abuse and neglect, the pharmacist can coax information from the parent gently when either taking the initiative to do so or provided the opportunity. A simple conversation may be sufficient encouragement for an abusive parent to admit the need for assistance and guidance. At this point the pharmacist must have the name of an individual at the community abuse center with whom the parent can talk both before and during a crisis. Given uncooperative parents the pharmacist must exercise professional judgment and report the matter to local authorities. The pharmacist, like all citizens, is immune from civil and/or criminal liability when reporting any knowledge or suspicion of child abuse.

By participation with local authorities and professionals in information forums conducted by social workers, the pharmacist can provide information to the abusive parent on how drugs, including alcohol, can affect one's behavior, change one's mood, effect depression with long-term use, and induce psychotic reactions. When this information is blended with the physician-nurse discussion of physical injury incurred from abuse and with teacher awareness of reporting suspicions, it adds immeasurably to the dimension of such a symposium.

The pharmacist also should recognize the need for health education on a broader scale. Many of the health problems encountered by communities can be prevented or alleviated with proper education. But it must be the pharmacist who is willing to share the wealth of knowledge and information he or she has accrued. All persons are not knowledgeable about the extent of pharmacists' education and thus automatically do not think of them as a source of information. Thus, pharmacists must provide the impetus to focus attention toward the capability they have relative to health education. There are several ways they can achieve this.

One method is to make the pharmacy the health center of the community. The willingness to participate in *Poison Prevention Week* or *National Diabetes Month* focuses consumer education toward the pharmacy. Coupled with this is the distribution of pamphlets of public interest on health information for the community. A display of free health literature in the pharmacy demonstrates a commitment to effective health care. There are myriads of pamphlets available on a variety of topics (eg, *Diabetes, Dry Skin and You,* or *The Professional Treatment of Constipation*) from pharmaceutical manufacturers that can be used effectively to promote health care. This encourages inquiries from consumers and, if displayed neatly in the prescription waiting area of the pharmacy, may afford the opportunity to the patient to read health-related information while waiting for a prescription. The pharmacist should make an effort to question pharmaceutical manufacturers' representatives about the availability of such pamphlets for the community. Many times pamphlets are available, but unless requested, they remain confined to the box in which they are contained.

In the event there is an outbreak of a communicable disease (eg, pediculosis capitis at a local elementary school), the pharmacist should obtain and disseminate useful patient-related information. If this type of information is provided directly to the patient/caregiver at the time of medication puzrchase or in conjunction with the local school nurse, needless parental worry and confusion is avoided.

The AIDS crisis continues and ranks as the most significant global health concern of the 1990s. The impact of AIDS on society and on the health-care system is significant, and it is incumbent upon pharmacists to become knowledgeable about this disease process and to identify their role in efforts to stop its spread. Pharmacists can play two major roles in the community human immunodeficiency virus (HIV) disease effort:

1. They can actively participate in the provision of care, treatment, and information to people afflicted with HIV/AIDS.
2. By virtue of their accessibility, they are in an excellent position to provide HIV prevention information to consumers and the general public.

The provision of care for HIV and AIDS patients is similar to the treatment of other patients. However, the treatment of these patients is more complex, the disease can be debilitating, and the

emotional impact upon the patient, family, and health-care providers can be substantial. Aside from normal distributive functions, it is important that the pharmacist provide patient counseling and educational services (eg, treatment options, side effects, transmission information, risk reduction guidelines for sexual activity), emphasize patient compliance (including keeping scheduled medical appointments), provide emotional support, and provide referrals to appropriate resources (eg, financial, housing, health-care providers, or therapists).

The AIDS patient provides a unique opportunity for pharmacists, and they should interact with these patients in a way that encourages communication and confidence. It is very important that the patient feel *safe* with the pharmacist. Patients must feel that they are not being judged or scorned because of their disease or sexual orientation. Confidentiality is important to the AIDS patient; protecting it is a particularly important role for the pharmacist. Many patients have legitimate concerns that they may lose their jobs and/or be alienated from family and friends if their HIV status becomes known.

Pharmacists should be prepared to listen to a patient's desire to participate in nontraditional therapies. They should be open to discussing with patients the pros and cons of traditional and nontraditional options. It is estimated that health fraud in the US approaches $40 billion on an annual basis. Health fraud knows no bounds and frequently targets certain groups of people, including those with serious illnesses. Products and therapies of quackery waste people's limited financial resources, may offer ineffective or harmful therapy, predispose a patient to harmful adverse effects, and even persuade a patient to forgo traditional therapy that might be more beneficial. To help patients identify credible clinical trials, pharmacists can encourage them to call the AIDS Clinical Trials Information Service hotline (1-800-874-2572).

A key attribute to being a professional is being accessible to those one serves. In this context, the role of the pharmacist is illustrated aptly in the area of family planning. By sharing knowledge and information about oral contraceptive therapy, nonprescription modes of contraception control, prevention of venereal disease, and pregnancy testing and by assisting couples dealing with fertility impairment, the pharmacist demonstrates accessibility and increases the awareness of the public that the pharmacy is the place where knowledge and informed advice are available.

Pharmacy school curricula recognize the need for effective oral communication both on an individual patient basis and to larger numbers of assembled people (eg, civic and church groups, clubs) by implementing effective course work in the undergraduate curriculum. However, if the pharmacist does not accept the challenge and communicate information, then other, less-qualified persons may be asked by the consuming public to fill this informational void. Sometimes pharmacists are fearful of presenting talks or having discussions with interested groups because of a lack of self-confidence. At the same time they may feel that they do not have the capability to discuss a topic because of a lack of information.

Recognizing these shortcomings in its past graduates, schools/colleges now have electronic literature-searching programs in their libraries to educate and heighten students' awareness of literature resources. Schools/colleges are committing toward outcome-based curricula that are anchored toward the development of student oral communication skills, decision-making skills, and problem-solving abilities, among others. It is hoped that this will encourage greater involvement of the pharmacist in community discussion on health issues. However, one must still deal with the current situation, and pharmacists in practice should look to their local public libraries for information support or consider contacting either their alma mater or state/local pharmaceutical associations for meaningful information.

It is essential that pharmacists contribute to public informational forums and make the community aware of public-health problems. Information and guidance should not be confined solely to drugs and their use, but also should include health-related issues (eg, sexually transmitted diseases, hazards of smokeless tobacco). A true concern must center around the casual attitude of the public toward drugs, a concept that unfortunately is reinforced through commercial advertising and communication media.

Whenever possible, pharmacists must help restore consumer confidence when it has been put in a position of doubt. The classic examples occurred in 1982 and in 1986 with Tylenol-tampering incidents and in 1991 with a Sudafed-tampering incident. Several persons were killed because of the deliberate introduction of cyanide into capsules on the shelf. Pharmacists responded by displaying posters and informational bulletins that instructed consumers to complete the following:

- Read the label. The labels on OTC medicines with tamper-evident packages tell what seals and other features a person should look for.
- Inspect the outer packaging. Check for loose, torn, sliced, or missing wrappings as well as discolored products and unusual odors.
- Inspect the medication once it is opened. Look at it again before taking it. If it looks suspicious, be suspicious.
- Never take medications in the dark.
- The label should be read and medication inspected at every dose.

Unfortunately, there are innovative and creative individuals in the community who may create new problems. Thus, the pharmacist must maintain constant surveillance and be willing to allay fears.

In response to the initial event, the federal government passed amendments to its laws (18 USC 65) to provide for tamper-evident and tamper-resistant packaging of OTC products. This amendment (PL 989-127, Oct 1983) calls for several measures. While the act is complicated, it leaves the impression that there is not a thing that can be done to a commercial package that is not prohibited, and that is as it should be. The pharmacist must be careful not to destroy the tamper-evident or tamper-resistant component of the packaging inadvertently. To do so may bring the pharmacist under the Act as a violator. Products that have been opened by consumers (often for the purpose of noting how big the tablets are, or for comparing the product with one that is already being used by that individual) are rendered unsalable, and they must be removed promptly from the shelf and returned to the supplier.

Most OTC products are covered by the Act. Specifically excluded are insulin, dermatologicals, dentifrices, and lozenges. While nothing prevents manufacturers from placing those products into tamper-resistant or tamper-evident packaging, it is not required at this time.

Pharmacists always should remain above reproach in the eye of the public. They should avoid even the appearance of professional impropriety and thereby not create questions of ethics within the mind of the patient. The most important means pharmacists have in educating society on health matters is the personal contact they have with the public. Whenever possible, they should volunteer health information and encourage people to exercise proper judgment to maintain good health. Some have been very creative and have developed and written patient-oriented newsletters on timely subjects that reinforce the attitude that the pharmacist is both a drug information specialist and health-care educator and provider. Others have achieved this same end by writing health information columns for local newspapers or participating in local media programs to provide health-care information. Professional organizations (eg, NCPA) have been helpful, too, through the provision of print-based health information (eg, Pharm/alert) that the pharmacist can use and disseminate for public education.

Finally, by showing a professional interest in, and attitude toward, the clientele that frequents the pharmacy, the pharmacist makes people feel they are important and that they have someone upon whom they can depend for help. A notable example of this is in ostomy care. There are over 1.1 million ostomates in the US, with new ones increasing by

about 90,000 each year. In the end, though, it is the pharmacist who really benefits by the intangible return of fulfillment and enrichment from using skills and information learned through formal and continuing education and practical experience.

CONCLUSION

Pharmacy is evolving from a product-oriented to a patient-oriented profession. This role modification is extremely healthy for the patient, the pharmacist, and other members of the health-care team. However, the evolution will present pharmacists with a number of new challenges. Now, more than in the past, pharmacists must make the acquisition of contemporary practice knowledge and skills a high priority, to render the level of service embodied in the concept of pharmaceutical care. Pharmacy educators organizations and regulatory bodies must all work together to support pharmacists as they assume expanded health-care roles. Pharmacy and the health-care industry must work to ensure that the pharmacist is compensated justly for all services. But before this can happen it will be necessary for pharmacy to demonstrate *value-added* to the cost of the prescription. Marketing of the purpose of pharmacy in the health-care morass and of the services provided by the pharmacist is needed to generate an appropriate perceived value among purchasers and users of health-care services. Pharmacists should view themselves as dispensers of therapy and drug-effect interpretations as well as of drugs themselves. Service components of pharmacy should be identified clearly to third-party payers and be visible to consumers, so that they know what is available at what cost and how it may be accessed. In the future, pharmacy services must be evaluated on patient outcome (ie, pharmaceutical care) rather than the number of prescriptions dispensed, and pharmacy must evolve toward interpretation and patient consultation, related to the use of medication technologies.

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CHAPTER 124

Self-Care

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PHARMACISTS AND SELF-CARE WITH NONPRESCRIPTION PRODUCTS—Pharmacists are in a unique position because of their education, training, and ready accessibility to the public when it comes to self-medication by the public with nonprescription (over-the-counter or OTC) drugs. Experts estimate that the number of nonprescription products is in excess of 100,000, but the accuracy of this estimate is unknown. In the United States, nonprescription product sales exceeded $14 billion in 2001.[1]

Like other businesses, pharmacies are in a fight for survival. Recent years have seen closings of many small independent stores. Third-party plans have reduced prescription profits so dramatically that some retailers have turned to high volume strategies in an attempt to survive. One unfortunate result of high volume is decreased patient interaction time. Pharmacists are forced to spend long hours behind the prescription counter with no scheduled lunch hour and little patient contact. Even though counseling is required, it is often cursory and hurried. Management demands more work with less help, because hiring additional pharmacists and pharmacy technicians further reduces shrinking profits. This dismal picture is more prevalent in high volume chain stores.

Fortunately, some pharmacies realize that pushing for high volume is self-defeating in the long run, because it appeals to the patient who wants cheap products at the expense of quality. Some of these more enlightened locations have realized that another route key to survival is to cultivate a specialty or "niche."

There are several viable and profitable specialties, such as compounding. Unfortunately, articles in pharmacy journals and textbooks (eg, *Handbook of Nonprescription Drugs*) often advise embracing ethically and scientifically indefensible areas such as herbal supplements and homeopathic products. This is especially regrettable when the pharmacist has a wide range of nonprescription products that are ethical, safe, and effective.

Marketing one's practice location as a center for self-care through intense counseling on nonprescription products and devices is a logical and profitable specialty. Self-care is especially appealing because of several factors:

- Minor medical conditions can be advised competently by the pharmacist who has expertise and education in these areas.
- Most pharmacists have had a nonprescription products/self-care course as part of the professional pharmacy curriculum.
- The typical pharmacy already stocks a wide range of nonprescription products and devices, so that there is no need to purchase a special group of products.
- The nonprescription market contains many ingredients lacking proof of efficacy and/or safety. Pharmacist counseling helps patients choose products whose safety and efficacy is demonstrated.
- Effective counseling in the nonprescription area allows the pharmacist to extend the concept of pharmaceutical care.
- Although nonprescription products are available in non-pharmacy outlets, the patient will not be able to obtain legitimate self-care advice at these locations.
- Many pharmacies locate nonprescription products away from the immediate location of the pharmacy. The pharmacist cannot advise patients who need help with these items, which seriously compromises their ability to offer self-care counseling. Those who choose to place nonprescription products in close proximity to the pharmacy enhance their credibility as experts in self-care.
- In other stores, nonprescription products are positioned close to the pharmacy, but shelving is parallel to the pharmacy, rather than perpendicular, which also makes it impossible to see patients who need help. Choosing a store layout that allows the pharmacist to visualize the patients in the self-care aisles allows the pharmacist to render assistance when necessary.

The pharmacist who wishes to develop this niche should obtain current information on the various self-treatable conditions, as well as all of the nonprescription ingredients and the many precautions associated with their use.

THE MOVEMENT TOWARD SELF-CARE—During the 1960s, this country experienced a growing distrust of established entities, such as the government, organized religion, and legitimate medicine. One of the consequences was a compelling consumer desire to rebel against the traditional provider/patient relationship, in which the consumer meekly and unquestioningly followed the directions of the provider. Patients began to demand a greater personal involvement and responsibility for health-care maintenance and treatment, a trend that continues today.[2] Direct-to-consumer advertising of prescription products enhanced this by indirectly communicating to consumers an innovative medical paradigm in which patients should demand a particular prescription product from the physician based on the advertisements they had seen. Consumers also feel competent to guide their own medical therapy based on past personal experience or anecdotal information from friends and relatives in regard to a particular prescription or nonprescription product. This is partly due to the common myth that any nonprescription product or device advertised in the media is safe and effective for self-use without any medical supervision. Further, some patients feel that the nonprescription product label contains all information of importance and deny the possibility that a pharmacist consultation can add any value to the purchase. Partially as a result of these various market forces and misconceptions, nonprescription products cause many episodes of morbidity and mortality that might have been prevented with judicious pharmacist counseling.[3] It is an uncomfortable truth that the patient who enters a pharmacy with a preconceived self-care opinion about a particular product or course of action is often manifestly and profoundly incorrect, and it is in the highest tradition of pharmaceutical care that the concerned pharmacist correct the patient's mis-

conception and guide them to a more appropriate self-care decision.

THE PRESCRIPTION TO NONPRESCRIPTION (RX-TO-OTC) SWITCH—A second factor that greatly increases the validity of pharmacist counseling in self-care is the dynamic and constant switch of prescription products to nonprescription status.[4] During the past several decades, powerful new therapies have become available for self-care in widely divergent arenas. They include loperamide for diarrhea, ibuprofen/naproxen/ketoprofen for pain, hydrocortisone for dermatoses, minoxidil for androgenetic alopecia, nicotine patches and gum for smoking cessation, ophthalmic antihistamines for allergic conjunctivitis, histamine-2-blockers and omeprazole for gastroesophageal reflux, and pyrantel pamoate for pinworm. Unfortunately, due to widespread opposition, there is no "third class" into which switched medications move prior to their unsupervised release to the American public. This leads to the uncomfortable realization that a particular medication awaiting a switch is only available under a physician's prescription, requiring pharmacist counseling and refill authorization until midnight the day before the switch occurs. At 12:01 am on the day of the switch, the ingredient is suddenly deemed safe enough to be sold to any consumer in any location at any time, with no professional monitoring or advice being necessary. It can be purchased in any gas station, beauty shop, airport lobby, or hotel vending machine. Since there is no requirement for professional counseling prior to purchase of nonprescription products, the manufacturer assumes the full burden of communicating all of the risks and other information that was formerly provided by the pharmacist. Thus, the manufacturer of nonprescription products has a higher duty to directly warn the patient of risks associated with their use than the does manufacturer of prescription products. Pharmacists must embrace these products, stressing the value to the consumer of purchasing them in a pharmacy in order to obtain the counseling that enhances appropriate use.

CAN PATIENTS READ NONPRESCRIPTION PRODUCT LABELS?—Another major rationale for pharmacist involvement in self-care is the issue of patients and their ability to read and/or comprehend nonprescription product labels. The FDA mandated a new label that is intended to more clearly communicate issues in use of products to patients. However, the pharmacist can still add value to the purchase of nonprescription products by acting as a "learned intermediary." In this role, the pharmacist can point out specific contraindications to use of certain products, answering questions about dosing, adverse effects, and appropriate use.

There are still some patients who will be unable to properly read and/or interpret the label. Some suffer impaired vision (eg, glaucoma damage, detached retina, macular degeneration) that does not allow them to read the small print. Others suffer from tremor or other conditions that make it difficult to hold the container still for reading prior to purchase. Others cannot understand the terminology used on labels, perhaps because English is not their primary language. Still other patients have limited reading comprehension or may be completely illiterate. In all of these cases, pharmacist counseling can be of immense value.

HOW PATIENTS CHOOSE NONPRESCRIPTION PRODUCTS AND DEVICES—Persons do not always seek the advice of a physician with every illness. Symptoms of the ailment may be deemed minor enough to treat with a nonprescription product. The decision of the patient concerning which product to purchase often is based on prior experience with the product; advice received from a neighbor or relatives; and commercial advertisements by manufacturers. However, the pharmacist is the only expert in self-care with nonprescription products and devices. Pharmacists can develop an enduring self-care specialty by making defensible patient triage decisions that are based on scientific principles. Through this practice, it is often necessary to guide incorrect patient purchase decisions into a more suitable and appropriate path.

THE ROLE OF THE PHARMACIST

THE PAST ROLE—During the 1800s and early 1900s, it was common for the patient to seek the advice of a pharmacist for minor ailments and first aid. The involvement of the pharmacist in self-care changed dramatically in 1921 with the adoption of the American Pharmaceutical Association Code of Ethics, which deemed it unethical for a pharmacist to prescribe medications. This was interpreted to mean that pharmacists recommending a nonprescription medication would be committing a violation of ethics because they would be *counter-prescribing* (prescribing over the counter). During the later 1920s and 1930s, the pharmacist gradually withdrew from self-care. As a result, the pharmacist consulted about nonprescription drugs and/or treatments often refused to provide any information, forcing the patient to self-diagnose and self-treat. This attitude continued into the early 1970s, when pharmacists were taught not to tell patients the intended use or potential adverse effects of their prescription medications. Prescriptions were not labeled routinely with the contents so that the patient would be forced to ask the physician for additional information.

During this time, many pharmacists also felt uncomfortable counseling patients about minor ailments. Patients were often referred to the physician for all problems. Few colleges of pharmacy included any coursework involving nonprescription products. Pharmacists were not required to communicate to patients with any degree of skill, and could actually pass an entire work day without being asked to move to the front of the pharmacy to talk to the patient. The profession attracted a certain number of communication-apprehensive individuals, and the pharmacy curricula of the day did not include any training in communication. Thus, their communication skills were rudimentary and untested.

PHARMACY CHANGES IN THE 1970s—During the mid-1970s pharmacy was rejuvenated with the promotion and gradual introduction of clinical and *patient-oriented* concepts into the practice of pharmacy. Advising the patient on health matters not only became fashionable but was recognized as a responsibility of the pharmacist, ethically and legally. The pharmacist was encouraged to question the patient who had decided to self-medicate and triage the patient (ie, recommend a nonprescription medication or recommend that the patient seek medical attention). By 1969 the membership of the APhA voted to adopt a new Code of Ethics that held the health and welfare of the patient to be of first consideration for the pharmacist.

This brief historical perspective explains why the older, more mature pharmacist in practice today may feel somewhat uncomfortable in providing advice to persons who decide to treat themselves and why pharmacists may simply decline to offer this professional service. A number of pharmacists may have to be educated, or re-educated, on how to counsel the patient who elects to pursue self-care. Continuing-education providers should strive to educate pharmacists who did not have the benefit of a formal course in nonprescription drug therapy through intensive lectures replete with case studies and treatment algorithms.

THE PHARMACIST'S POTENTIAL ROLE TODAY—The move to self-care, the ongoing switch of potent medications to nonprescription status, and the inability to read and understand nonprescription labels effectively, all point to the potential importance of the pharmacist as a nonprescription product information source. It is clear that the pharmacist is in an ideal position to help consumers with their self-care needs, but the pharmacist *must* take a proactive role. Consumer trends indicate that the pharmacist slowly is gaining recognition as a legitimate source of information about nonprescription drugs/products. Consumers seek pharmacists who provide service, and media advertisements tout the pharmacist as a source to consult.[5] The factors (in descending order of importance) germane to the patient/consumer selection

of a pharmacist were:

1. Actively discussing instructions for the use of the pharmaceutical product, including effectiveness, anticipated side effects, and duration of treatment.
2. Being available for consultation.
3. Providing willingness to offer advice on general health problems.
4. Being friendly and approachable.

THE NONPRESCRIPTION PRODUCT LABEL—The FDA supports the concept of self-medication but, unfortunately, has not embraced the concept of the pharmacist as the first professional that the patient should consult before using the product. As pharmacists struggled to be included on the label of nonprescription products, they faced opposition from the nonprescription industry (who wished their marketing messages to reach the public undiluted by any "learned intermediary") and physicians (who balked at pharmacists being given co-equal status on the labels). Only in addressing drug interactions is the pharmacist's advice specifically mentioned on nonprescription product labels.

RESPONSIBILITIES OF THE PHARMACIST IN SELF-CARE

Self-care counseling is a primary-care activity that carries with it a great amount of professional responsibility. Communicating information about OTC products requires the same basic skills used for prescription medications and does not mandate additional specialized education/training or vast financial expenditures to be well done.

Many commercial enterprises use the old business maxim, "The customer is always right." However, in pharmacy, the customer is often not right in the potential choice of a self-care product or device. They may be mistaken in the need for a product, the choice of a product, and often the need to consult a physician or other primary care practitioner. It is the pharmacist's responsibility to correct the patient's misconceptions tactfully as a component of pharmaceutical care. To provide proper advice, the pharmacist must gather relevant information needed to decide whether the patient should not select a specific product, should choose a nonprescription product or device, or should be referred to the physician. This process is referred to as *pharmacist triage*.

THE TRIAGE FUNCTION OF THE PHARMACIST

Patients who wish to treat themselves may not seek the services of a pharmacist. Nonprescription products and devices are freely available in food stores, variety stores, vending machines in hotel lobbies, airports, and gasoline stations. The drawback to these purchases is that these venues lack a pharmacist to provide medically sound recommendations to the patient. Thus, the consumer then may choose a product or advice on the basis of recommendations from friends or family, the attractiveness of the packaging, or perhaps the memory of an entertaining media advertisement. While the vast majority of advertisements sponsored by nonprescription drug and device manufacturers are factual and accurate, patients are bombarded with hundreds of ads from less reputable manufacturers urging consumers to purchase products or devices that lack proof of safety and/or efficacy. Thus, without a pharmacist, patient safety may be seriously compromised. The presence of an educated/trained pharmacist is the value-added benefit of purchasing nonprescription drug products and devices at a pharmacy. Of course, this argument assumes that the pharmacist has embraced the concept of triage, moving from a protected area behind the prescription counter to engage patients actively. The pharmacist who talks to patients about nonprescription medications receives many questions daily.[6] The simplest of these questions is "Where can I find (name of product)?" However, the prudent pharmacist must learn to get *behind* this type of question, asking what type of problem has prompted this particular visit to the pharmacy. Failure to discover the nature of the medical condition can lead the patient to inappropriate use of a product. However, the pharmacist must understand that some patients are hesitant to provide any details and must be prepared for a cool rebuff from some patients. Other patients refuse to consider any advice from the pharmacist. This may be due to the greater relative influence of their friends, the advertising, or their own perception of the quality of the pharmacist interaction. However, the pharmacist should still make an attempt to educate the patient regarding a safer course of action.

In certain circumstances, the patient may ask about a specific medical condition where more complicated questions will be asked and triage decisions become critical. Patients can be placed into one of the following three categories.

No Need for a Product—The patient may have no perceptible need for a nonprescription product or device (eg, the healthy patient who has become convinced that unproven dietary supplements such as gingko and noni juice are necessary for everyday use). At times, another intervention will fit the concept of pharmaceutical care more closely than selling a product (eg, educating a patient about sleep-hygiene methods to treat insomnia rather than purchasing a nonprescription sleep-aid).

A Minor Medical Condition That Will Benefit From a Nonprescription Product or Device—There are numerous medical conditions that may be improved with self-care products and devices (eg, the common cold or athletes' foot).

A Medical Condition That Places the Patient Beyond the Realm of Self-Care—When the medical condition cannot be classified as minor or is clearly beyond the capacity of nonprescription products or devices, the patient must be referred for care from another practitioner (eg, MD, DO, podiatrist, optometrist, or dentist) who is able to properly diagnose and treat the condition through ordering lab tests and diagnostic examinations, and providing prescription medications when necessary. In the most severe cases, the patient should be instructed to go to the nearest emergency room and given directions if they are unfamiliar with its location.

Thus, many times in the average work day, the pharmacist who is willing to assist patients in self-care must implement pharmaceutical care through recognizing medical conditions, deciding whether they are self-treatable, knowing which products are appropriate for those conditions, and being able to persuade the patients which courses of action are most suitable. To carry out these sophisticated decisions, the pharmacist must possess a vast body of knowledge. The information needed to properly triage a patient can be divided into two categories: those related to the product and those related to the patient.

PRODUCT-RELATED DECISION FACTORS

The foremost factors to consider in nonprescription products and devices are safety and efficacy, both of which must be present. Safety without proven efficacy is a waste of money. Conversely, efficacy without proven safety presents an unacceptable risk to the patient.

Prior to the 1970s, objective data regarding safety and efficacy of nonprescription products and devices were difficult to find in professional medical literature. In the early 1970s, the U.S. Congress remedied that unfortunate situation by mandating a sweeping review of all nonprescription drug products and devices. This review dramatically improved the information available, but the downside has been the slow pace at which the review has been conducted. It is still proceeding one-quarter of a century later. Nevertheless, the Nonprescription Drug Review process of the FDA has been highly beneficial to pharmacists. It has provided a knowledge base that facilitates sound decisions regarding comparative product effectiveness and safety. The review process has generated substantial scientific research, producing impressive amounts of new information on

nonprescription medications. At the same time it has placed a burden upon the pharmacist to keep current about new information in this important subject area. A real handicap for the diligent pharmacist is obtaining factual, current information. Current pharmacy literature often provides synopses of the latest FDA rulings.

The major strength of the FDA review of nonprescription drug products and devices has been its objectivity. Full approval for any ingredient requires overwhelming evidence of safety and efficacy. Proof of efficacy must be demonstrated in placebo-controlled, double-blind studies with sample sizes sufficient to ensure statistical significance when the correct statistical tests are used. FDA personnel carefully examine each study submitted to uncover such shortcomings as bias in patient recruitment, poor questionnaire construction, insufficient blinding, and use of parametric statistics on nominal or ordinal data. The study must have been replicated in a nonrelated research center. Thus, strict adherence to the scientific method ensures that medications are proved efficacious. Proof of safety is determined through a comprehensive literature search to uncover studies that list adverse reactions and through examinations of all other extant literature on the specific ingredient. While no medication is free of adverse reactions, the risk must be small in relation to the proven benefit the consumer can expect from the product when used as directed.

If a nonprescription medication is proven safe and efficacious, it is given a designation known as Category I. These ingredients can be recommended by the pharmacist with confidence as long as all label warnings and dosing directions are carefully read and adhered to, and as long as all patient-related decision factors are taken into consideration.

Ingredients that lack proof of safety and/or efficacy are referred to as Category III ingredients. The pharmacist should take great caution in recommending these ingredients. If their efficacy remains unproven, any possible risks to which the patient would be exposed are unacceptable. If, on the other hand, their safety is unproved, any possible benefit is not worth the risk to patient safety.

Category II ingredients were determined to be unsafe and/or to lack efficacy. The FDA is usually able to force their removal eventually, but an article in the lay press exposed situations in which pharmacies continued to sell these banned products freely.[7] Selling products containing these ingredients exposes patients to chemicals already proven to be unsafe, or ineffective, or both, an indefensible business decision.

There are several reasons why pharmacists might recommend products that lack proof of safety and/or efficacy. For instance, companies have sponsored promotions in which an unidentified *mystery shopper* enters pharmacies and asks for help with a certain medical condition. These shoppers are actually acting for a certain company, and the pharmacist who recommends that company's product may win a cash prize, a free trip, or a new vehicle. Advertising campaigns encourage the pharmacist to suggest that company's product to all who ask, just in case the person might be the mystery shopper. Thus, the pharmacist might suggest a specific product out of selfish self-interest. Pharmacists are also approached by *rack jobbers,* who often ask to place a rack of merchandise in the pharmacy on consignment. The pharmacist does not purchase the items on the rack and has no cash outlay. When products sell, the pharmacist receives a set fee. The rack jobbers promise to restock the rack as needed. These products should be inspected carefully to ensure that their ingredients are actually safe and effective. This seductive approach may have been used by the manufacturers of Cal-Ban 3000, a diet aid that was marketed nationally. The ingredient in Cal-Ban 3000 had not been approved by the FDA.[8] Its labeling was confusing in listing its ingredient as *Cyamopsis tetragonolobus,* which was the scientific name of guar gum, a complex sugar that swells when wetted. The FDA was advised by health professionals of adverse reactions and discovered that ten hospitalizations from intestinal or esophageal obstruction had occurred. One death occurred from a blood clot that reached the lungs following surgical removal of a guar gum throat obstruction. The FDA forced the company to recall the product, levying a heavy fine. Had pharmacists been more wary about selling a product of unknown efficacy/safety, perhaps the medical problems could have been prevented. Some pharmacists sell unproven products out of a desire to please the customer. It is uncomfortable to have a confrontation with a patient who is convinced that an unproven product is the best choice for them. For example, a patient may be convinced that ginseng has helped him feel younger or that ginkgo has helped improve his memory. After many months of use, patients may become extremely upset with the pharmacist who then counsels them to discontinue these unproved products and seek legitimate medical care if their symptoms return.

Pharmacists also fear that they will lose business if they refuse to sell unproven products. They may not want to be viewed as an impediment to the patient. They also realize that patients may listen to the pharmacist, then purchase the products they wanted in the first place at a store down the street. Of course, pandering to the patient's every whim is ultimately self-defeating. The pharmacist must instead strive to build a reputation for professional integrity by refusing to sell questionable products and by offering logical reasons for such refusals. Such a refusal is in the highest traditions of pharmaceutical care and professional ethics.

Pharmacists may sell unproven products out of a belief that the product may actually work, even though data are lacking, or from the mistaken belief that "It can't hurt, can it?" These pharmacists will evidently continue to sell unproven products until they cause overt patient harm or until there is overwhelming evidence of a lack of efficacy. Unfortunately, congressional legislation has burdened the overworked FDA so that unscrupulous companies can continue to market their unproven products for a long period without making the barest pretense of carrying out legitimate scientific studies. The patient often has no idea that the products lack proof of safety and/or efficacy despite the fact that they are sold freely on the shelf of the pharmacy.

An example of the extreme care pharmacists should take in recommending nonprescription products is provided by phenylpropanolamine (PPA). PPA was first developed to maintain blood pressure, but was included in nonprescription products meant for oral nasal decongestion and weight control by the 1970s. PPA was first reviewed in 1976 by the FDA review panel for oral nasal decongestants, which recommended Category I status.[9] However, in 1985 the FDA published its tentative final monograph on OTC nasal decongestants.[10] In this publication, the agency placed PPA in regulatory limbo, declining to assign it any status because of concerns over blood pressure elevation. Out of concern for the safety of consumers, a prudent manufacturer should have withdrawn products containing PPA at that point or reformulated to a safer alternative (eg, pseudoephedrine), since the FDA was not convinced the ingredient was safe, but they continued to market PPA; they could have warned of the risk of PPA-associated hypertension and stroke, but did not do so. In 1990, Congress held hearings on PPA, causing the FDA to reopen the administrative record on PPA in 1991.[11] During the 1990s, debate raged over the safety of PPA, but patients continued to use PPA and pharmacists continued to recommend it. Many billions of doses were sold. Finally, a report (the Yale Hemorrhagic Stroke Project) demonstrated to the satisfaction of the Nonprescription Drugs Advisory Committee of the FDA that PPA caused hemorrhagic strokes in users, and the FDA in 2000 asked the pharmaceutical industry to discontinue marketing it.[12,13] Industry should have placed a voluntary warning about stroke on the label to fully warn consumers of its occurrence; in failing to do so they never clearly explained the potential risk of stroke to patients on the product labels to allow them to weigh the benefits of use against the risk of stroke be-

fore use (most packages had no mention of stroke on the label at all). Further, once the FDA requested a voluntary cessation on manufacturing of PPA-containing products, industry never issued an immediate active recall of all PPA-containing products (sold and unsold) with a widely publicized public health alert targeted to all potential consumers warning of the risk of hemorrhagic stroke. As a result, many millions of doses remained in medicine cabinets. Also, products containing PPA were found in secondary markets (eg, flea markets, deep discounters) several years later, often having passed their expiration dates. The FDA estimated PPA might have caused as many as 500 strokes yearly, so manufacturer refusal to withdraw products containing it in 1985 might have caused as many as 7500 stokes from 1985 to 2000.[14,15] According to a 2001 report from FDA personnel, the actual number of strokes yearly could have been far higher due to underreporting.[16] If pharmacists had recommended against the product starting in 1985 and refused to stock it, many of these strokes would have been prevented. The pharmacist must take a strong stand for patient advocacy in situations such as this where ingredients lack evidence of proven safety and/or efficacy and manufacturers refuse to withdraw the products or add voluntary warnings to fully apprise patients of the potential risks to the products they sell.

PATIENT-RELATED DECISION FACTORS

The pharmacist who sells only safe and effective ingredients may feel there is no need to counsel patients seeking self-care. This is a mistaken assumption, as the safe and effective ingredients have many restrictions on their use that must be observed to ensure that patient health is not compromised.

AGE OF THE PATIENT—The FDA and its panels have established the minimum ages above which nonprescription ingredients may be administered safely. Certain guidelines are still preliminary, but major changes in the lower age cutoffs are unlikely.

As a general rule, nonprescription products are not to be recommended to patients below the age of two years. (Teething products are an exception, being approved down to four months of age; there is also a pediatric ibuprofen product approved down to the age of six months.) Some products are not safe for dosing under the age of 6, 12, or 16, or 18 years (Table 124-1). These age cutoffs are not arbitrary. With each age cutoff, there is overwhelming evidence that providing the ingredient to those younger than indicated on the label without the supervision of a prescribing professional can be extremely dangerous. For instance, pharmacists are routinely asked about dosing of antihistamine-containing cold and allergy products for patients as young as one month of age. However, administration of antihistamines to those below the age of six years can result in paradoxical excitation (with the exception of loratadine). Similarly, use of antidiarrheals in those under the age of three years can result in life-threatening fluid and electrolyte abnormalities. Despite these warnings, various companies have distributed pediatric dosing charts that purport to provide safe doses for acetaminophen, loperamide, pseudoephedrine, and antihistamines down to ages as young as newborns.

DURATION/SEVERITY OF THE CONDITION—The range of conditions for which patients seek self-care is nothing short of amazing. The author has been asked to recommend nonprescription products for heavy-metal toxicity from inhalation of fumes from welding nickel pipe, brown recluse spider bites, nail and scalp fungi, loose teeth, boils, and eyeballs bruised so completely that the whites were totally blackened. Fortunately, these incidents are the exception, and most minor medical conditions for which self-care is sought will resolve regardless of whether a nonprescription product is used or not.

The pharmacist must remember that even a seemingly minor condition or symptom may reflect an underlying cause that is beyond self-treatment. For instance, while simple headache is usually benign, a headache that lasts for a certain period may indicate serious underlying pathology (eg, bacterial meningitis). Additionally, constipation of sufficient duration may indicate fecal impaction and/or megacolon/megarectum. For these reasons, many nonprescription products and devices carry a labeled safe maximal time cutoff for unsupervised use in self-care (Table 124-2). For instance, nonprescription diarrhea products carry the warning "Do not use for more than 2 days unless directed by a physician." The FDA seldom clarifies the exact meaning. For instance, how should the pharmacist handle the patient who already has had diarrhea for 3 days when seeking self-care products? Should the pharmacist advise an additional 2 days of therapy prior to seeking medical care? How about the patient who has a chronic diarrhea for 2 months? Obviously, both patients are in greater need of rehydration and electrolyte replacement than the patient with only a single diarrheal episode and both should be referred for physician care.

When examining the FDA-labeled maximal durations for self-use, the pharmacist should err on the side of patient safety. First, it is vital to ask "How long have you had this condition?"

Table 124-1. Selected Nonprescription Products and the Ages Below That These Should NOT be Recommended for Self-Care (According to FDA-Approved Labeling)[3]

AGE	PRODUCT(S)
None	Diaper rash products, topical protectant products
4 months	Gingival analgesic products for teething
6 months	Ibuprofen drops, sunscreen products
2 years	Glycerin suppositories, hydrocortisone, antacid products, dimenhydrinate (motion sickness), fluoride toothpastes, pyrantel pamoate, oral nasal decongestant products, sore throat products, antitussive products (except codeine), expectorant products, acetaminophen, children's loratadine syrup
3 years	Antidiarrheal products (except for loperamide)
5 years	Oral sodium phosphate/biphosphate products
6 years	Loperamide, anticavity rinse products, cyclizine (for motion sickness), psyllium (for constipation), methylcellulose, bisacodyl, antihistamine products (except loratadine, meclizine, and dimenhydrinate), cromolyn sodium nasal, codeine, ophthalmic vasoconstrictor/antihistamine combination products
12 years	Hypersensitive tooth products, meclizine, H2-blockers, hemorrhoid products, naproxen, caffeine, insomnia products, cerumen impaction products, skin hyperpigmentation products, topical terbinafine and butenafine, ketoconazole shampoo, vaginal antifungal products, ibuprofen 200 mg tablets
16 years	Ketoprofen
18 years	Minoxidil, nicotine cessation therapies

Table 124-2. Selected Medical Conditions and the Duration of Time Beyond Which the Patient Should be Referred for Professional Care (eg, Physician, Dentist, Podiatrist) (According to FDA-Approved Labeling)[3]

DURATION	MEDICAL CONDITION
2 days	Diarrhea, migraine
3 days	Fever, dry eye, red eye
4 days	Excessive earwax
7 days	Oral mucosal injury, canker sores, constipation, hemorrhoids, muscular injury, burns, vaginal irritation
10 days	Pain in an adult
14 days	Stomach upset, insomnia

or "When did the symptoms begin?" A judicious judgment allows appropriate triage decisions to be made. Diarrhea products only allow two days of self-care, so a strict interpretation of this timeline is preferable because of the potentially serious nature of diarrhea. In other words, the patient who has already had diarrhea for two days or more is beyond the realm of safe self-care and should be referred immediately to a physician (an emergency room visit may be required if a primary care physician is unavailable). Intraoral topical analgesics (eg, benzocaine) are only to be used for one week to ensure that the patient seeks professional care for a more serious cause of oral sores, such as an oral tumor. Again, a strict interpretation is needed, and the patient with an oral lesion of one week or more in duration should be referred immediately for an oral evaluation without being sold a product. On the other hand, corn and callus products caution against use for more than 14 days. Obviously, typical patients have had the corn or callus for many months to years and may be allowed to use the product for 2 weeks from the point they begin self-care.

CONTRAINDICATIONS—Just as is the case with prescription products, certain nonprescription products are unsafe for unsupervised self-use when the patient also has other medical conditions (Table 124-3). For instance, antihistamines are contraindicated in the patient with glaucoma, because they can cause a rise in intraocular pressure in a patient with narrow (acute or angle-closure) glaucoma, causing irreversible visual loss. Laxatives are contraindicated with rectal bleeding, since this is a cardinal sign of colorectal carcinoma. Oral nasal decongestants are contraindicated in the patient with hypertension. The typical patient seldom reads these warnings, and those that do may not understand them. The pharmacist can perform a particular service in explaining the warnings and offering alternative FDA-approved products that would be safer, when they exist. If there is no ingredient that is safe and effective, patients should be urged to seek the advice of the physician or other prescriber monitoring their condition.

CURRENT USE OF MEDICATIONS, FOODS, AND DRUGS—Some nonprescription ingredients have FDA-labeled precautions regarding drug interactions or warnings against concomitant ingestion with other medications, foods, or drugs of abuse (eg, alcohol, nicotine) (Table 124-4). The pharmacist might inspect a patient's profile or ask about routine medications to discover whether or not these precautions pertain to a specific patient. For instance, nonprescription cimetidine carries a label warning against concomitant use with theophylline, warfarin, and phenytoin. For patients taking these medications, the pharmacist could point out the other three alternative H_2 blockers, which do not carry this warning. Another example is nonprescription salicylates, which carry a warning against concomitant use of anticoagulants, as well as medications for gout, arthritis, and diabetes. At times, the pharmacist may choose to provide drug interaction warnings that exceed those the manufacturer includes. For instance, the risks of phenylpropanolamine-associated hypertension and hemorrhagic stroke were heightened if the patient also ingested caffeine; the manufacturers should have warned patients of this simple additive effect but failed to do so. Only those patients purchasing their products in a pharmacy might have been warned of this interaction.

Table 124-3. Selected Nonprescription Products and Medical Conditions That Contraindicate Their Use (According to FDA-Approved Labeling)[3]

NONPRESCRIPTION	PATIENT CONDITION(S) OR SYMPTOM(S) THAT CONTRAINDICATE PRODUCT/CLASS SELF-CARE WITH THE SPECIFIC PRODUCT/CLASS
Teething Products	Fever, nasal congestion
H2-Blocker Products	Persistent abdominal pain
Aspirin	Flu, chickenpox, in children and teenagers
Antihistamine Products (except Loratadine)	Emphysema, chronic bronchitis, glaucoma, difficulty in urination due to an enlarged prostate
Loratadine	Liver or kidney problems
Loperamide	Fever over 101°F, blood or mucus in the stool, liver disease
Pyrantel Pamoate	Pregnancy, liver disease
Hemorrhoid Products	Bleeding from the rectum
Nasal Decongestant Products	Heart disease, high blood pressure, thyroid disease, diabetes mellitus, difficulty in urination due to an enlarged prostate
Sore Throat Products	Fever, headache, rash, swelling, nausea and/or vomiting
Cerumen Impaction Products	Ear drainage or discharge, ear pain or irritation, rash in the ear dizziness; perforation of the eardrum, recent ear surgery

Table 124-4. Selected Nonprescription Products and Medications/Foods/Drugs With Which They Are Contraindicated or With Which Concurrent Use Should be Avoided (According to FDA-Approved Labeling)[3]

NONPRESCRIPTION	MEDICATIONS/FOODS/DRUGS WITH WHICH THEY ARE CONTRAINDICATED
Cimetidine	Theophylline, warfarin, phenytoin
Cyclizine, Meclizine	Alcohol, sedatives, tranquilizers
Mineral Oil	Meals, stool softeners
Oral Bisacodyl	Antacid or milk (within 1 hour)
Bismuth Subsalicylate	Medications for anticoagulation, diabetes, gout or arthritis
Diphenhydramine	Any other product containing diphenhydramine
Oral Nasal Decongestant Products, Dextromethorphan	Monoamine oxidase inhibitors (current use or within two weeks of stopping the MAOI)
Internal Analgesic Products	Three or more alcoholic beverages a day
Nicotine Cessation Products	Any other form of nicotine

DEMOGRAPHIC VARIABLES—Occasionally, a patient's demographic variables (other than age) may contraindicate a certain nonprescription product. For instance, nonprescription diuretics (eg, pamabrom, ammonium chloride) carry FDA approval only for menstrual-related water retention.[3] They are never to be recommended for any other cause of fluid retention (eg, possible congestive heart failure or renal dysfunction). Thus, gender disqualifies any male from the safe purchase and use of nonprescription diuretics. As another example, nonprescription hypopigmenting products containing hydroquinone are used legitimately for lightening skin that has darkened in response to sun exposure (eg, solar lentigines or sun-induced freckles), usage of oral contraceptives or estrogens, or during pregnancy. African-Americans and Hispanic Americans have used these products incorrectly in misguided attempts to lighten overall skin color. This may result in exogenous ochronosis, a paradoxical darkening of the skin. Thus, the pharmacist should counsel these patients against use of skin-hypopigmenting agents for overall skin lightening. Miscellaneous demographic patient factors should also be elicited, such as allergies to the specific ingredients present in the medication, and whether the patient is pregnant or breast-feeding.

PAST MEDICATION USE—As the pharmacist questions the patient, it is also important to ask about the products or devices already used to alleviate the condition. This also provides a clue regarding the duration of the condition. Instances of the improper use of unproven products (eg, homeopathic) or of application of home remedies can be uncovered and discouraged. The pharmacist also can discourage the use of unapproved and unsafe products such as those sold in health-food stores. Assuming the patient still has a few days of self-care remaining, the pharmacist can then recommend an appropriate product.

EXACT NATURE OF THE CONDITION—It is vital for the pharmacist to elicit a detailed history of the condition, even if the patient has formulated a self-diagnosis. This ability requires a thorough understanding of the minor medical conditions that are self-treatable and also of the various *red flags* that indicate a serious condition that requires referral to another health care professional. The pharmacist is hampered in discovering the exact nature of the condition for several reasons:

- The pharmacist typically has not undergone formal training in physical assessment, so that judgments must be rendered without a full spectrum of medical information being available. At times the disorder can be confirmed visually (eg, warts or athlete's foot), but in other situations (eg, vaginal candidiasis or hemorrhoids), the pharmacist depends wholly on the verbal information imparted by lay persons who may be fundamentally mistaken regarding certain aspects of their condition (eg, its appearance).
- The legality of pharmacist assessment is questionable, and the boundaries are vague and ill-defined. While the pharmacist can easily recognize poison ivy dermatitis, should the pharmacist examine throats to differentiate viral from bacterial pharyngitis? While the pharmacist can easily check a patient's head for head lice, should the pharmacist also check pubic areas for pubic lice? It has been suggested that retail pharmacists should conduct ear inspections for perforated eardrum, peer into the nostrils to recognize sinus congestion, and look into the fundus of the eye to recognize arteriovenous nicking.[17] But where does this stop? Would a pharmacist be justified in peering down the esophagus to recognize gastroesophageal reflux–induced esophagitis or conducting a digital rectal exam to differentiate hemorrhoidal bleeding from colorectal carcinoma? On what basis can the individual pharmacist decide what distinguishes acceptable assessment from the unacceptable? One must examine state pharmacy practice acts to remove these decisions from their seemingly arbitrary designations. The pharmacist is cautioned to ensure that the pharmacy practice act for that state allows pharmacist assessment prior to beginning to assess patients. In Oklahoma, a pharmacist's license was suspended because he did not "refrain from attempts at diagnosis and treatment that infringe upon the legally constituted rights and obligations of practitioners of the healing arts."[18,19] Resistance from the local medical society should be anticipated. Finally, the pharmacist should check malpractice insurance to ensure that these nontraditional but emerging pharmacist roles are covered in the case of legal complications.
- The typical pharmacy lacks otoscopes and equipment for appropriate assessments. Also, while many pharmacies have added areas for OBRA-mandated patient counseling, few pharmacies have examining rooms with a door for patient privacy. Male pharmacists may not fully understand the legal necessity of having a female employee present when examining a female patient.

The difficulties involved in pharmacists' assessment demonstrate that the pharmacist should not hesitate to triage the patient to a medical practitioner if there is any doubt about the condition being appropriate for self-care or if the validity of the patient's self-diagnosis is questionable.

There are many conditions that require referral, including nail and scalp fungi, boils or any other bacterial skin infection, sinus infection, ear pain, dental pain, swimmer's ear, eye infections, thumbsucking, nailbiting, nocturnal leg cramps, urinary tract pain/infection, and vomiting caused by anything other than motion sickness.

PAST EXPERIENCE WITH THE CONDITION—The pharmacist should discover whether the patient has experienced the condition previously. If so, was a physician or other legitimate practitioner consulted, and was a diagnosis made? For instance, consider the patient who enters the pharmacy with conjunctival redness and tearing. If the patient has been diagnosed with perennial allergic rhinitis, these symptoms constitute part of the syndrome and nonprescription products are appropriate. On the other hand, if the patient has not been diagnosed with allergic rhinitis, viral conjunctivitis is possible, necessitating referral.

As another example, corneal edema causes the patient to experience halos around lights and blurred vision. If previously diagnosed by a physician as due to some benign cause (eg, prolonged wearing of contact lenses), it is easily self-treatable with nonprescription 2–5% sodium chloride products. However, if the patient has not sought medical advice, the condition may be due to glaucoma, which requires immediate referral.

The female with a vaginal fungal infection is yet another example. If she has never had a physician-diagnosed vaginal fungal infection, she must obtain a physician diagnosis prior to using a nonprescription product. However, once she has received such a diagnosis, she can self-differentiate fungal vaginitis from other causes (eg, trichomonal) and can begin self-treatment. Thus the pharmacist must discover whether she is competent to self-treat, with judicious questioning prior to the sale of vaginal antifungals.

THE REASON FOR A SPECIFIC MEDICATION REQUEST—When patients have a product in mind, the pharmacist should discover why that specific medication is requested. Was the decision due to a previous successful experience with that product? Did they observe or read an advertisement? Did they hear a testimonial from a relative or friend?

The patient's motivation to purchase a specific product can have a profound impact on the pharmacist's actions, because previous use with positive results is one of the most potent arguments. Unless the product is not safe and effective, it is in the patient's best interest to switch to an alternate product, because of loss of confidence in a potential cure (eg, switching from a systemic analgesic to a topical analgesic for sore throat). On the other hand, if the motivation is simply an advertisement or advice from a well-meaning friend or relative, the pharmacist may be better able to offer an alternative product that may be a better choice.

COUNSELING TIPS

In the perfect pharmacist-patient self-care situation, the pharmacist always approaches the patient with a friendly "May I help you find something?" This lets the patient know that the pharmacist is available to provide the needed advice, facilitating communications. However, in busy retail establishments, pharmacists often cannot cruise the nonprescription aisles to converse with patients at their leisure. More often, it is the patient who seeks assistance and initiates the dialog when considering purchase of an OTC remedy. In these cases, pharmacists may give the unfortunate impression that they have been interrupted while carrying out a more important duty.

The patient may initiate the self-care conversation with several general types of questions that call for different types of pharmacist aid. For example:

What do you have for diarrhea? (provide relief for a patient's symptom)
What is the best antacid? (choose a specific product from a category of nonprescription products and/or devices)
Do you carry Lotrimin AF Cream? (locate a product for the patient)

As the pharmacist assesses the question and brings the various product- and patient-related decision-making factors to that specific situation, several important tips can be used.

EXERCISE ACTIVE LISTENING—The patient should be allowed to state the problem completely, and the pharmacist should provide the undivided attention that is necessary to minimize misperception and misunderstanding. The pharmacist should mentally summarize what the patient has said and provide positive feedback that conveys an understanding of the problem, with empathy and concern. Using the patient's own words or paraphrasing them demonstrates a full understanding of his problem(s). Rewording and paraphrasing also force the pharmacist to focus on the situation and understand its various aspects. This process also facilitates and enhances personal relations between the pharmacist and patient by exhibiting the concern expected of a caring professional.

QUESTION THE PATIENT THOROUGHLY—Quite often, the patient provides incomplete or contradictory information, much of which is necessarily subjective. To make the appropriate triage decision, the pharmacist must thoroughly

cover the patient-related decision-making factors listed previously (eg, age, duration of the condition, or exact nature of the condition). Other helpful information includes:

Does the condition come and go at certain times during the day?
How severe is the problem? If it is recurrent, is it worsening?
Do you have any other symptoms?
Have you noticed a specific trigger that worsens your symptoms or causes them to recur?

Questioning should be direct and to the point. With experience, the pharmacist should be able to gather needed information in a period of minutes. If the situation is more complex and time-consuming, the pharmacist can ask patients to return at a mutually agreeable time, contact them by telephone, or refer them directly to a physician.

INTERPRET VERBAL AND NONVERBAL COMMUNICATION—Every question asked of the patient should be phrased carefully to facilitate interpretation. The patient should be able to understand that the questions asked come from a genuine interest and desire to help. The pharmacist may ask two types of questions:

1. Open-ended questions, which draw forth information regarding the medical problem. For instance, " Can you tell me about your symptoms?" This question type provides flexibility for patient response and encourages more than a simple yes-or-no answer.
2. A direct question, which is useful when the information is a specific inquiry, eg, "How long have you noticed the burning sensation in your stomach?"

Nonverbal communication skills also serve a vital role in this situation. Body posture, facial expression, and distance maintained by the patient all provide perception of the patient as a whole. At the same time it is important to be aware of the patient's nonverbal behavior. Physical barriers to communication should be eliminated whenever possible. The pharmacist should make every effort not to talk down to the patient, neither verbally (ie, use the vernacular) nor physically (ie, the pharmacist and patient should be at the same eye level). These exchanges should be as private and uninterrupted as possible. Many pharmacies lack a private consultation area, but privacy can be achieved readily without expense by simply forming a triangle using the patient, the pharmacist, and the wall shelf or gondola as partitions. This automatically signals others that the consultation is private and should not be interrupted.

Whenever possible, the pharmacist should assess the patient physically, through observation or inspection. For example, the skin is assessed easily by inspection and palpation. However, the lung requires percussion and auscultation, not a realistic practice for the practicing retail pharmacist. The clear majority of pharmacists obtain physical data (eg, number of comedones per side of the face) exclusively through the use of observation. Further, there are clues to the overall state of health of the patient, and these provide insight into the seriousness of the problem. Facial expressions mirror pain and discomfort, pallor and lethargy may indicate an infectious process, and persistent coughing may be a sign of some systemic illness.

SPEAK TO A RESPONSIBLE CAREGIVER—When counseling the patient, the pharmacist may hear phrases such as:

"I can't do that without talking to my parents."
"My husband won't let me go to the doctor; we don't have insurance."
"I'm not sure what it looks like; it's for my grandmother."

In these situations, it may be prudent to call the individual from whom more information is necessary or who needs to be convinced of the serious nature of the problem.

GAINING THE PATIENT'S COOPERATION

After the pharmacist has questioned the patient thoroughly and considered various courses of action, the time comes when a recommendation must be made. The triage decision and its ramifications fall into several categories.

THE PHARMACIST CHOOSES NOT TO RECOMMEND ANY PRODUCT OR DEVICE—Many patients are simply worried that a product might be necessary. The pharmacist may inform them of the fact that their condition is likely to recede without any intervention and that no product will relieve their symptoms. An example would be to discourage smoking cessation to help coughing symptoms rather than purchasing a cough product. Some patients will be dissatisfied with this type of advice and remain convinced that a product will help them. They may simply purchase the product in another establishment in an effort to ignore the helpful advice of the pharmacist.

RECOMMENDING A SPECIFIC NONPRESCRIPTION PRODUCT OR DEVICE—When the pharmacist recommends a specific nonprescription product or device, most patients take the advice and purchase that product. However, a small group of patients insist on their first product choice, even though it clearly may be inappropriate. The pharmacist may urge them to reconsider, with the precaution that it is not the best product. When pharmacists recommend a drug treatment for a condition amenable to self-therapy, they should tell the patient of the condition itself, the monitoring guideposts to remember, and the duration of time before the patient should notice the benefit of treatment.

With acne vulgaris, for example, the objectives of topical treatment are to control an existing condition, impede acne in the developmental stages, and relieve the discomfort (ie, physical or psychological). The patient should be advised that continual, daily application of the medication to the entire face will gradually reduce the number of lesions, but that 2 to 3 weeks may elapse before any noticeable improvement. Indices that demonstrate acne may be worsening and require medical attention should be incorporated into the discussion. Adverse effects and potential toxicities should be noted. Using benzoyl peroxide as an example, the acne patient should understand that some skin redness and irritation may develop.

RECOMMENDING REFERRAL—This is one of the most difficult groups for which to provide advice. They enter the pharmacy asking for relief from what they perceive as a *minor* complaint, but are confronted with unwelcome advice to consult another health care professional. The pharmacist may even insist that they make an immediate visit to an emergency room. These medical alternatives involve an expenditure of money and time. All of the persuasive powers of the pharmacist must be brought to bear in this situation. Phrases such as the following may be used:

"If he were my child, I would take him to the emergency room immediately."
"The consequences of this could be as severe as loss of sight."
"I have heard of this type of problem resulting in a ruptured appendix if it is not diagnosed by a physician."

The goal of these and similar phrases is to impress upon the patient the potential gravity of the problem.

Patient harm may ensue when a pharmacist recommends a product until a patient can be checked by another health care professional. Some patients simply will not follow through and make the appointment, particularly if the product seems to work initially for his/her condition. An example is the patient who requests a nonprescription analgesic for tooth pain, promising to "visit the dentist tomorrow."

FOLLOW-UP—Whenever possible, the pharmacist should follow up with the patient, consistent with the concept of pharmaceutical care. To facilitate follow-up, pharmacists might note the patient's name and telephone number, after requesting permission to make a follow-up call. Patients might also be asked to share the results of the suggested triage decision back to the pharmacist. If the patient does not respond to the treatment plan, additional information and data assessment (eg, did the patient follow instructions correctly, taking the correct dose for the recommended duration?) may help determine a new course of action. Frequently, this reevaluation culminates with the referral of the patient to the physician for further treatment. If at

all possible the pharmacist should share information attained from the initial and the follow-up evaluation with the physician.

PRECAUTIONS

The pharmacist providing advice in self-care must take great caution in recommending products that lack proof of safety and/or efficacy. Examples include the numerous herbs and "dietary supplements," ear candles, athletic aids, obesity treatments, and other quack products and devices.

Another example of products that should not be recommended is homeopathic products. Homeopathy is an outdated branch of medicine that was developed in the early 1800s.[20] Among its theories are:

A. One treats a condition by administration of a product that causes the same symptoms. Thus, cockroach extract is used for asthma, candidal suppositories for vaginal *Candida,* caffeine for insomnia, ipecac for vomiting, and bronchial cancer extract for bronchial cancer.
B. If one drop of active ingredient is diluted with 99 drops of water and the flask is struck against a firm surface repeatedly in a process known as *succussion,* the water molecules will allegedly use the medication as a template and align themselves so that the diluted medication supposedly becomes stronger.
C. Each 1/10 dilution is known as 1X. Supposedly, the more diluted the medication is, the stronger it becomes, according to homeopathic practitioners. Some homeopathic remedies are as "strong" as 60X, by which time Avogadro's number has been surpassed, and there is no active ingredient in the final preparation.

All of these homeopathic theories directly contradict basic principles of pharmacology and the dose-response curve.[21] Further, there is no conclusive evidence that they work when subjected to the exhaustive and rigorous scrutiny required in double-blinded, placebo-controlled trials with sample sizes sufficient to ensure statistical and clinical significance.

Through a loophole intentionally placed in the 1938 federal law, homeopathic products are not required to prove efficacy as legitimate medication must. This double-standard should cause the pharmacist to pause when considering sales of these products. Several lawsuits against chain stores that sell these products have been settled out of court.

SUMMARY

Self-care is one of the most daunting challenges retail pharmacists face. This is partly because patients can purchase nonprescription products and devices for self-care in virtually any location. The problem is worsened because the patient is bombarded by advertisements from nonprescription product/device, herbal, and homeopathic manufacturers that promote one product to the exclusion of all others. When patients choose to purchase these items in a pharmacy, the pharmacist is challenged to discover product-related and patient-related factors that facilitate appropriate triage. In doing so, the pharmacist must use the highest principles of pharmaceutical care, employing a balanced and rational approach that rests on the precepts of legitimate scientific evidence rather than the seductive lure of expensive advertisements.

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CHAPTER 125

Diagnostic Self-Care

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Since the introduction of the first home pregnancy test in 1977, diagnostic aids and devices have expanded self-care into an information-based and profitable market. In one year, patients spend approximately $650 million on home tests and monitors.[1] In addition to nonprescription products, the pharmacist must also have a working knowledge of diagnostic aids and devices currently available to consumers. The market for these products has an average growth rate of 17% attributable to the relatively low cost, reliability, and user-friendliness of the exams.

Diagnostic devices have revolutionized the self-care industry. Consumers benefit from their easy accessibility. These devices include blood pressure monitors, home blood glucose monitors, HIV exams, cholesterol exams, and home tests for colorectal cancer. They help monitor chronic diseases, diminish doctor visits and associated costs, decrease hospitalizations, and allow consumers to become an active part of their own health care. With the trend toward pharmaceutical care and preventive medicine, the pharmacist can perform a vital public health role by counseling the consumer on newer diagnostic devices, thereby contributing to a reduction in deaths from colon cancer, helping patients monitor blood glucose, and aiding in the detection of drug abuse, among others.

Even though they have become more user-friendly, patients may still encounter problems with even the simplest devices. Consequently, pharmacists are often summoned to educate patients on proper use, and the validity and application of the results. It is essential that pharmacists ask questions about the disease or exam and make any appropriate recommendations based upon the available information. The pharmacist should remind the patient that any information attained as a result of counseling shall remain strictly confidential. The pharmacist should also mention that these test kits/devices must be used in collaboration with health-care professionals who can interpret and discuss the test results and their implications.

Diagnostic aids and tests are complex to use; patient understanding is maximized when a pharmacist is involved in the purchase and use of these products. If these products are purchased in a non-pharmacy outlet, the consumer does not have the opportunity to ask questions or receive reliable recommendations from an educated professional, thereby increasing the chances for product misuse.[1] Pharmacist counseling has direct benefits to the patient. The pharmacist is a highly educated drug-information specialist in over-the-counter (OTC) products. This, in conjunction with practical experience, makes the pharmacist the only health professional who understands the limitations of self-treatment with OTC products and who is also uniquely positioned to encourage the patient to seek the professional advice of a physician when necessary.

OBJECTIVES

Recently, the pharmacy profession enhanced the emphasis of pharmaceutical care, which encompasses proper self-care, preventive medicine, and follow-ups. Because of the increasing utilization of diagnostic test kits, it becomes necessary to discuss the issues surrounding these devices. The objectives of this chapter shall be to promote reader awareness of the following: the function of diagnostic test kits; pharmacist and consumer responsibility as it relates to counseling and utilization, respectively; the professional responsibility of pharmacists to contribute not only to consumer comprehension, but to other patient issues; the Food and Drug Administration's (FDA) concerns about these devices and any related recommendations; the scope of the marketplace for these items; and the various categories of in-home test kits and pertinent information regarding these devices. Pharmacists can enhance consumer understanding of the devices by gaining a thorough understanding of their use and counseling patients at every opportunity. The pharmacist has the ability to answer any consumer-related questions and recommend solutions to any problems, which will increase the effectiveness of the test kits and the impact of pharmaceutical care in the eye of the consumer.

FUNCTION

The function of testing devices is to provide accurate and reliable information to the patient in a short period of time. The exam must be easy to read and use, thus allowing the patient to make an informed decision based on exam results. The device should also carry label instructions that are understandable to a variety of patients regardless of their level of education or literacy. Instructions should be provided in a step-by-step approach, which may encourage confidence in self-administration and interpretation. The device should also instruct the patient on the next appropriate step to take after obtaining exam results. For example, if a blood glucose meter determined a blood glucose level that required the expertise of a clinician, this must be clearly explained to the patient. In some instances, a phone number may be included for professional consultation about any consumer-related questions or misconceptions. Manufacturer support may ensure that the device is utilized properly and that results are not tainted by misuse.

THE PHARMACIST

Clinicians must take the lead role in protecting patients, their peers, and themselves from the unfortunate consequences of

medication errors and device mishandling. Errors occur for a variety of reasons in every aspect of the health profession, including inaccurate communication between the clinician, the patient, or deficits in the knowledge and performance of the health care professional. Hence, the pharmacist's role in aiding with selection of the appropriate device, counseling about proper use, and interpretation of results is indispensable. The pharmacist is constantly accessible to the public, providing the opportunity to make a profound impact in the effectiveness of this growing market. It is the responsibility of the pharmacist to be familiar with these devices and to examine constantly any new literature related to the disease state or apparatus so that appropriate advice may be provided to the consumer. For example, product manufacturers should be periodically contacted to inquire about any recent developments and offer demonstrations to the pharmacy staff to guarantee proper training and application. Although most devices will include information booklets from the manufacturer, the pharmacist should take an active role in explaining the information to the patient. Proactively approaching the consumer may save money by detecting potential problems early, thus decreasing the likelihood of the patient purchasing a second exam because of mishandling. This "show and tell" theory will promote effectiveness and help perfect the patient's use of the product.

THE CONSUMER'S RESPONSIBILITY

Studies demonstrate that self-care is compromised by therapeutic failure of medication regimens, testing devices, and compliance tactics.[2] Strategies involving careful labeling, simplification of regimens, device instructions, and enhanced patient-pharmacist interaction may remedy this problem. Therefore, the consumer also has a shared responsibility in the correct use of these devices. First of all, any pertinent information related to the patient's physical examination or the disease state itself should be conveyed to the pharmacist. The pharmacist should be made aware of any allergies or potential adverse reactions. If the consumer has difficulty in reading materials or does not understand the instructions, that information should be relayed to the pharmacist, affording the opportunity for personal assistance. The consumer should ensure that all questions are documented, which will consequently promote constructive use of time and permit the pharmacist to respond to all concerns appropriately. It is important for the consumer to be patient and understanding because the pharmacist might be busy upon his/her arrival, necessitating a wait before counseling may occur. Towards the end of the consultation, the consumer should repeat the directions to the pharmacist to ensure understanding, and demonstrate proper use of the product.

PROFESSIONAL OPPORTUNITY

Martin and Pigarelli suggest that some diagnostic devices may produce 99% accuracy when administered properly.[3] This presents the pharmacist with an opportunity to make a difference in enhancing the device productivity. Pharmacists fit into a model in which the cost and benefits of medication and device usage are carefully managed to increase the quality of care. The precision of these devices will rely on the communication between the health care professional and the consumer. Unfortunately, the major productivity gap lies in the adherence of the patient to counseling and device instructions. Greater patient interaction with pharmacists has been recognized as a key component in solutions to medication errors and device misuse. A second study estimated that nearly 25% of hospital and long-term care admissions were attributable to non-adherence of advice or directions.[4] Therefore, reinforcement of instructions by the pharmacist during the interaction may be crucial for patient compliance with directions or counseling (eg, package insert or counseling), and may have a profound impact on the potential effectiveness of the device.

The pharmacist should seize the opportunity to converse with the patient about other ailments unrelated to the diagnostic exam. In some cases, patients may be reluctant to speak to a doctor or pharmacist in regards to clinically insignificant medical disorders. This unwillingness usually leads to self-diagnosis and treatment. Ferris et al conducted a study involving 95 women who were purchasing over-the-counter products used to self-treat vulvovaginal candidiasis.[5] The time period was September 1997 through December 1999, and the patients were required to answer an in-depth survey and complete a clinical examination. Laboratory tests were performed. Only 32% of patients made the correct self-diagnosis and an additional 19% had mixed vaginosis involving candidiasis and bacteria. One patient actually required hospitalization for her condition. Misdiagnosis in most cases, leads to inappropriate treatment. In turn, misdiagnosis and treatment has the potential to increase the severity of the patient's condition due to the delay in treatment with suitable medication. Although self-treatment may prove to be a less expensive option for the patient, it may also be detrimental to the patient's health. By asking open-ended questions, the pharmacist may be able to discover problems and aid the patient in selecting a suitable option for treatment or refer the patient to a physician.

FDA REGULATORY CENTERS

In 1982, an agreement prepared by the FDA detailed the working relationships between the organizations previously identified as the Bureau of Medical Devices (BMD), the Bureau of Radiologic Health (BRH), and the Bureau of Biologics (BOB). The purpose of this agreement was to identify the responsibilities of each entity for medical device activities.[6] Since then, there have been several major organizational modifications within the FDA. In 1982, BMD and BRH were joined to form the Center for Devices and Radiologic Health (CDRH). Also in 1982, BOB and the Bureau of Drugs were merged to form the Center for Drugs and Biologics (CDB), with biological products regulated by the Office of Biologics Research and Review (OBRR). However, in 1987, the CDB was divided into two major centers, with biological products regulated by the Center for Biologics Evaluation and Research (CBER).

Because both centers were responsible for similar regulations regarding diagnostic devices, the Intercenter Agreement between the CDRH and CBER was developed and became effective October 31, 1991. CDRH was designated as the lead Center in the FDA for regulating medical devices to ensure their safety and effectiveness. CDRH will use the device authorities of the federal Food, Drug and Cosmetic Act (FDC Act) as well as other authorities delegated to it for the devices regulated in that Center. For example, home diagnostic exams that do not require blood banking are controlled by the CDRH (eg, blood glucose monitors, pregnancy tests, or infertility exams).

The CBER was delegated the lead center for regulating certain medical devices utilized in or indicated for the collection, processing, or administration of biological products that utilize blood banking or blood extraction as a primary means of sample collection. This Center also uses the FDC Act and the Public Health Service Act (PHSA), as well as any other authorities delegated to it. *In vitro* tests, which are required for blood donor screenings and related to blood banking practices, (such as donor re-entry) are licensed under the PHSA. The CBER is also responsible for regulating all *in vitro* tests (including diagnostic tests which are not performed in association with blood bank practices, and any other medical devices intended for use with human immunodeficiency virus, type 1 (HIV-1) and type 2 (HIV-2), and any other retroviruses). Examples of *in vitro* reagents may include Hepatitis B Surface antigen, Hepatitis C Viral Encoded antigen, HIV-1, HIV-2, and Human T-Lymphotropic virus. These devices may include but are not limited to the following: collection devices, specimen containers, hospital or home test kits, and support kits intended for the inacti-

vation of these viruses. For a product that is a combination of a device and a biological product, the determination of the regulating Center is made based upon the primary mode of action.

FDA CONCERNS

Self-testing diagnostic and monitoring devices are often seen as a less expensive and more convenient alternative compared to a trip to the doctor's office. These devices are sold in increasingly high numbers. Self-monitoring for conditions such as diabetes mellitus and hypertension are made easier using these devices. However, this technology is not without its limits and could result in life-threatening problems for those who rely solely on the test without the expertise of a health-care provider.

Home test kits are inexpensive compared to a co-payment to the doctor and a great deal less time-consuming. An advantage is that they provide quick results. Women often use home pregnancy test kits for these reasons, as well as for the convenience of testing at home. Some women prefer a definite diagnosis prior to visiting their physician and home pregnancy tests may aid in confirmation. Early verification may enable clinicians to counsel women about their options and discourage any harmful behaviors such as smoking or alcohol consumption.

Because these exams offer early confirmation of problems, disease, or pregnancy, they have become increasingly popular among consumers. One sign of their popularity is the fact that many pharmacists are moving the home diagnostic exams from behind the counter onto freestanding displays. The Internet also makes these devices more accessible by offering direct home delivery.

Steve Gutman, MD, director of the FDA's clinical laboratory devices division, stated that consumers need to be wary about buying and using the kits on their own. "People need to carefully read the test-kit labeling and instructions, where important information and warnings about the product are listed," he says. Labeling demonstrates how the test works and steps to take in case of product failure. Home diagnostic exams are meant to be adjunctive to physician visits, not a replacement for them. "Although the menu of home testing products has expanded," Gutman says, "the advice is still the same."[7]

Although home test kits provide convenience, confidentiality, and cost-savings, physicians seem concerned about the availability of medical tests that may encourage self-diagnosis because of the possibility of result misinterpretation. For example, Sandy Stewart, PhD, a research engineer in the FDA's CDRH says that blood pressure monitors should be employed to track blood pressure readings between physician visits. "Users should never change their medications or spontaneously stop use based upon home blood pressure readings." If there are significant variations in the readings, the user should contact their physician immediately. "The blood pressure reading taken at the doctor's office must be the final word."[7]

The benefit of having a clinician involved is that the results may be evaluated within the context of the whole health picture and the decision for treatment options will not rely on one test result. Furthermore, receiving news of pregnancy, illness, or infection over the phone, or from the color of a test strip, may be overwhelming. "The first 72 hours following a positive HIV diagnosis is when people are most likely to hurt themselves," says Edward Geraty, a licensed clinical social worker with Behavioral Science Associates in Baltimore. It is imperative to have face-to-face contact when delivering a HIV diagnosis. "Without it," he says, "there is a psychological component of the person's illness that is completely negated from the process."

Accuracy is a critical consideration when it comes to home testing. False-positive results indicate that a condition is present when, in fact, it is not. Likewise, false-negative results may give the consumer a sense of security and lengthen the time until a patient obtains a valid diagnosis and treatment, if needed.

The Federal Trade Commission has the distinct responsibility of enforcing consumer protection laws. Recently, they have evaluated the results of several unapproved HIV home exams advertised and sold on the Internet for self-diagnosis. In each incident, the kits displayed a negative result when a known positive sample was applied. Similarly, the FDA recently examined a number of unapproved home HIV tests sold on the Internet that were confiscated during a criminal investigation.[8] None of the HIV tests produced accurate results. The FDA concluded that the outcome could have serious consequences for a user resulting in mental and emotional stress, lack of access to proper medical treatment, and possible transmission of disease to unaffected individuals. The CBER continues to investigate people and firms involved in the illegal sale of unapproved HIV home test kits in the United States.

FDA RECOMMENDATIONS

Follow Directions

In most cases, home diagnostic exams involve relatively simple procedures with straightforward instructions. The FDA requires that all test kits be simple enough for the average consumer to utilize the exam at home without direct supervision. For example, some pregnancy exams only require a stream of urine to produce colored indicator lines, whereas glucose monitors usually require placing a small blood sample onto a reagent strip. The consumer should carefully follow the directions as recommended by the manufacturer. If any questions exist, a health care professional should be contacted for clarification. Modification of directions or test kit samples is not recommended.

Storage

Home test kits should not be stored in places where they might be exposed to extreme temperatures. This may result in deterioration of the product over time. By storing the kits properly as recommended by the manufacturer, the consumer will lessen the probability of false results.

Expiration Date

Patients should check the expiration date before purchasing a diagnostic exam. Expired test kits may produce inaccurate results.

Nonadherence to Directions

Failure to follow directions with home test kits can compromise the integrity of the results. Non-compliance with device instructions, improper storage, shipment, or collection of specimens may diminish effectiveness. Inaccurate readings may be produced if urine samples are not collected at the appropriate time of day or if foods ingested mimic metabolites being measured. Extracted samples (eg, blood or urine) not applied within the recommended manufacturer time frame or exposed to severe temperature changes could generate false positive or false negative results.

FDA-Approved Devices

FDA-approved tests have undergone extensive analysis and review by the manufacturer of the product. For an in-home exam, the manufacturer must demonstrate to the FDA that the result of the test will benefit consumers and the kit is simple enough for consumers to decide whether the test is appropriate for their condition.[8] On the other hand, unapproved devices lack the

guarantee of accuracy or sensitivity and they have no documented history of dependability. Proper training to interpret results is not provided with the kits and they do not have a validated record of precision. Because of the aforementioned problems, the FDA has determined that unapproved tests may be inconsistent and inaccurate.

Internet Purchasing

The consequences of consumer health fraud range from significant financial loss to consumer avoidance of legitimate treatment.[7] The FDA wants consumers to be aware of a number of unapproved test kits available on the Internet, in magazines, or newspapers, for home use. Internet sites advertise test kits that falsely claim everything from FDA approval to detecting illness within 15 minutes or less. Consumers who purchase via the Internet may receive contaminated or counterfeit products, an improper test kit, or no product at all. The FDA confidently endorses home test kits available in reputable pharmacies or drugstores. Many of these products have undergone extensive review and testing by the CDRH or CBER divisions. Consumers may browse the FDA's web site at www.fda.gov/oc/buyonline/ for tips and warnings concerning Internet purchasing. Furthermore, www.fda.gov/cdrh/ode/otclist.html is an FDA site that contains a regularly updated list of approved home diagnostic exams sold over-the-counter.

GROWING MARKET

The marketplace for *in-vitro* diagnostic (IVD) products is among the most complex of all medical device sectors, involving public and private payers, prescribers and laboratory specialists, and an increasing variety of clinical and home use settings.[9] Making headway in this market requires manufacturers to undertake an intense period of research to understand their target market.

Currently in the realm of OTC diagnostic devices, the most active segments of the industry in terms of sales are clinical laboratory instruments and the emerging point-of-care (POC) testing systems (Table 125-1).[10] POC systems include automated testing devices, bedside diagnostic testing devices, and in-home diagnostic exams. The major clinical diagnostic laboratory instrument sectors include clinical chemistry, immunoassay, hematology, blood banking, urinalysis, microbiology, and emerging DNA and molecular testing. The average annual growth (AAGR) for the POC is expected to be 8.1% through 2007, while the laboratory instrument segment will grow at an estimated 6.4%.

Table 125-1. Point-of-Care System Sales

	2000		2005	
TESTING SEGMENT	SALES US ($ MIL)	MARKET SHARE	SALES US ($ MIL)	MARKET SHARE
Glucose	625	26	800	22
Pregnancy	500	20	700	19
Infectious disease	335	14	425	12
Critical care	275	11	375	10
Cholesterol	250	10	400	11
Coagulation	150	6	275	7
Cardiac markers	50	2	100	3
Drugs of abuse	50	2	55	1
Bilirubin	30	1	50	1
Other[a]	15	1	20	1
Total ($)	2280		3200	

[a]Other = fecal occult blood, *C. difficile*, prostate-specific antigen (PSA).
Adapted from Recognition and Initial Assessment of Alzheimer's disease and related dementia's. Clinical Practice Guideline 19. Rockville, MD: Department of Human Services, Public Health Service, Agency for Healthcare Policy and Research, 1996. AHCPR publication 97-0702.

United States

The United States is the largest IVD market in the world, with market shares and revenue totaling 9.7 billion dollars in 2000. In addition to being the largest market, the US is the largest IVD manufacturer, accounting for nearly 85% of all IVD products worldwide. Although the market share is enormous, there are two factors that may hamper continued economic growth. Consumer pressure to reduce prices has squeezed profits in the past. Undoubtedly, this trend will continue in the future. Another factor is the constantly challenging reimbursement issues for these devices. The US government is pursuing the establishment of reimbursement for various routine or esoteric exams.[11] Even with the projected 39% decline in market share in the US, IVD's largest companies are still expected to maintain healthy growth from international sales.

Point-of-Care Systems

Over the past couple of years, the market for POC diagnostics has experienced double-digit growth.[10] Researchers agree that future growth in this field will continue to be strong; however, not everyone agrees that double-digit growth can be sustained because of the Clinical Laboratory Improvement Amendment (CLIA). Approximately 95% of in-home diagnostic kits were CLIA-waived by the FDA. Some individuals believe that the market setting for POC diagnostics is severely constrained by the demand of physicians to designate that some new diagnostic exams be delegated as CLIA-waived, even if the device has not been designated for in-home use or to revisit to the requirements for CLIA-waiving.

In 1988, the CLIA law specified that laboratory requirements be based on the complexity of the test performed and established provisions for categorizing a test as waived.[12] On February 28, 1992, regulations were published to implement CLIA. In the regulations, waived tests were defined as simple laboratory examinations and procedures that were cleared by the FDA for home use. It had been determined that these test kits employ methodologies so simple and accurate so as to render the likelihood of erroneous results negligible and these exams would pose no reasonable harm to the patient if the test was performed incorrectly. Examples of CLIA-waived exams include but are not limited to: glucose monitors, ovulation tests, urine pregnancy exams, and urine ketone exams. Because more of these test kits are being marketed for in-home use, experts believe that the global IVD market will change and more dollars will be spent on these items.

ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is a progressive debilitating disease that has a devastating effect on the lives of affected individuals and their families. Approximately 4 million Americans over the age of 65 suffer from AD.[13] AD can be divided into four stages of dementia, known as the forgetful stage, confused stage, demented stage, and end-stage dementia. The classic triad of clinical changes includes memory impairment, visuospatial defects and language changes. These may occur in the absence of confusion (unlike delirium), mental retardation, or other neurological disorders. They cause a considerable decline in the patient's ability to function.

Patients with AD have an inability to perform basic activities of daily living. Early forgetfulness and problems performing basic tasks (eg, balancing check book, making complex decisions) occur, while social functioning often remains intact. The ability to accomplish familiar tasks (eg, driving, using a telephone) is usually preserved in AD. However, patients with AD have been noted to lose olfactory function (anosmia). Their sense of smell becomes distorted and familiar fragrances, in a variety of cases, cannot be distinguished. Eventually, they develop behavioral changes, such as wandering, getting lost, and

repeating the same questions. Visuospatial disturbances may manifest as a propensity to get lost and copy instructions.[14] In latter stages, patients may be unable to recall familiar objects or newly learned information. As the disease advances, they may develop irritability, psychosis, or disorientation and eventually, patients become completely dependent.

Diagnosis

Early diagnosis is the key to initiation of effective treatment options. Interviewing the patient and conducting a comprehensive clinical assessment usually reveals the most important diagnostic information. The clinician must extensively interview the patient to distinguish AD from other forms of dementia using the Diagnostic and Statistical Manual on Mental Disorders (DSM-4).

Screening

In an effort to provide an earlier diagnosis for AD patients, the development of a screening technique was devised. Knowing that anosmia and AD are linked, researchers began to conduct clinical studies on their relationship. In 1994, Soloman concluded that 90% of patients with AD showed varying degrees of anosmia.[15] In another experiment, the smell sensitivity of 80 normal elderly patients was compared with 80 AD elderly patients and the AD patients were found to have significantly poorer sense of smell. It was reported that 74% of the AD elderly claimed to have normal sensitivity after smelling the sample, yet, to recognize an aroma, they required a sample with an average concentration of *nine* times more than that needed by a normal elderly patient. It is noteworthy that the AD victims were not aware of the onset of anosmia, and, therefore, did not recognize their loss of olfactory sensitivity.

Home Diagnostic Exam

Subsequent to the development of the Pocket Smell Test (PST) and the Pennsylvania Smell Identification Test (PSIT), FMG Innovatives developed the Early Alert Alzheimer's Home Screening Test. This is the first home exam, based on the research involving the PSIT and PST, offered to patients as a noninvasive, self-administered test to screen for possible anosmia secondary to dementia. In 2003, the exam costs approximately $19.00 and affords patients the opportunity for early diagnosis.

Procedure

1. Open the screening booklet to the first page which is entitled ODOR #1.
2. Using the pencil provided, scratch the odor strip several times in a zigzag fashion to release the odor.
3. Place the odor strip directly under both nostrils and sniff.
4. Look for choices provided above odor strip. If patient is unsure or no smell is present, the closest answer choice should be selected.
5. Turn to the second page entitled ODOR #2. Repeat steps 2–4.
6. Continue this process until all 12 strips have been sniffed and an answer has been circled for each odor.

Scoring

After selecting the number of incorrect answers and placing them in the "TOTAL NUMBER INCORRECT" box, the patient or caregiver can read the results. Afterwards, if 4 or more incorrect answers exist, the patient should contact a physician. If there are less than 4 incorrect answers and symptoms of AD are present, a physician should still be contacted. This exam is intended as a screening tool and further testing is recommended.

Storage

1. Store test kit in a dry place below 86° Fahrenheit or 30° Celsius.
2. Do not scratch the odor strips until ready to use.
3. Do not allow odor strips to come into contact with any liquids.
4. Discard after use. Do not reuse.

HEPATITIS C

Over the last decade, Hepatitis C Virus (HCV) has emerged from obscurity as a disease (originally known as non-A, non-B Hepatitis) familiar only to a few experts, to one recognized as a major public health problem in the US and worldwide.[16] Responsible for a number of hepatic manifestations, HCV emerged in 1989 and was isolated through modern techniques of molecular cloning. The virus belongs to the flavivirus family and contains a single-stranded RNA genome approximately 10,000 nucleotides in length. Unfortunately, in approximately 80% of patients, infection with the virus is asymptomatic, and a physician may not discover abnormal liver function enzyme values upon examination of a blood specimen. Therefore, screening high-risk individuals is imperative in controlling the spread of this disease.

During the latter half of the last decade, the Centers for Disease Control (CDC) recommended that certain individuals be screened for HCV infection based upon their risk for infection (Table 125-2).[17] Those who inject legal or illicit drugs, patients on long-term hemodialysis, and individuals who received blood or blood components should all be tested routinely for HCV infection. Health care workers and infants born to seropositive mothers should also be tested. Infants born to seropositive mothers should not be tested until they have reached 12 months of age.[16] Immediate testing is not recommended because the infant will passively acquire antibodies to the virus and test positive even if he or she is not infected.

One of the largest obstacles in screening and diagnosing is the need to ask sensitive questions. In most cases, patients are not likely to come forward to be screened, but it is vital to reduce the cost associated with attempting to diagnose every high-risk patient. One strategy is to ask these questions in a standardized exam, which may remove the patient's anxiety associated with answering these questions. There are a variety of diagnostic tests used for screening patients at a physician's office (Table 125-3).

Table 125-2. Persons Recommended for Routine HCV Testing

1. Persons with specific medical conditions, such as:
   - Those who received clotting factors concentrated before 1987
   - Those who were treated with long-term dialysis
   - Those with persistently high ALT levels
2. Persons who have injected illegal drugs, including those who only experimented once or a few times
3. Prior recipients of transfusions or organ transplants, including those:
   - Who were informed that they received blood from a donor who later tested positive
   - Who received blood transfusions or components before 1992
   - Who received an organ transplant before 1992
4. Healthcare, emergency medical, and public safety workers
5. Infants over 12 months of age born to a seropositive mother

Adapted from Honeywell M, Hollis A, Thornton A, et al. *US Pharmacist* 2002; 27(5):HS81.

Table 125-3. Diagnostic Tests for Hepatitis C

1. Anti-HCV
   - Best screening test for patients with abnormal ALT/and or identified risk factors for HCV infection
2. Recombinant immunoblot assay (RIBA)
   - Supplemental assay employed for low-risk populations with a seropositive anti-HCV
3. Qualitative PCR
   - Detects HCV
   - Results expressed as present or absent
4. Quantitative PCR
   - Detects HCV
   - Sensitivity 100 to 1,000 copies/ml

Adapted from Honeywell M, Hollis A, Thornton A, et al. *US Pharmacist* 2002; 27(5):HS81.

In-Office Exams

The anti-HCV exam is usually suggested as the initial exam for screening patients with abnormal liver enzymes (eg, ALT) or other HCV risk factors. This assay is inexpensive and reliable. Its sensitivity is >90%, but its specificity varies according to the population tested.[16] For example, if a patient from a high-risk group is tested, the predictive percentage is approximately 93%, but in a low-risk population it may be as low as 50%. Therefore, a second test may be required to support the diagnosis. The recombinant immunoblot assay (RIBA) may be applied in this instance. This test utilizes sections of the HCV genome embedded in a nitrocellulose strip. A positive reaction is recorded when black bands appear after the strip has been placed in the patient's serum. If two or more bands appear, the result is considered to be positive; two bands or less is considered to be indeterminate. In immunosuppressed patients or patients undergoing chemotherapy, an antibody presence may be absent. If the patient is strongly suspected to have HCV, the polymerase chain reaction (PCR) may be useful. One other virologic assay, the branched chain DNA (bDNA), is sometimes ordered to help quantify the number of HCV-RNA copies per milliliter of blood.

Home Diagnostic Exams

The Home Access Hepatitis C Test was developed as an in-home exam created by Home Access Health Company. It is used to screen whole blood for Hepatitis C. This exam has been proven clinically safe and effective and was approved by the FDA in 1999. Comparative studies demonstrate that this exam is 99% accurate when measured against in-office exams in seropositive individuals.

Prior to testing, the patient should call a toll free number to activate a 14-digit test code and to obtain anonymous counseling from professional clinicians to ensure understanding of instructions or to answer any questions. Using the lancet included in the test pack, the patient should deposit a sample of blood onto the test card. The sample test card is then sealed and mailed in a self-addressed postage-prepaid mailer. Four to 10 business days should be allotted to process the results. The access number should be called and using the 14-digit PIN, the patient is given the test results and, if necessary, offered professional counseling regarding the results.

The exam is offered in most pharmacies across the continental US, and in 2003, costs approximately $56 per test. The American Liver Foundation (ALF) has recognized Home Access as an important advancement in the fight against liver disorders. Individuals who may be exposed to HCV are encouraged by the ALF to obtain counseling, testing, and if appropriate, medical treatment.

INFERTILITY

Infertility affects more than 2 million couples in the US and may be attributed equally to both males and females. Many couples have problems conceiving due to a male's low sperm count, decreased sperm quality, or other medical conditions.[18] Unfortunately, there is no identifiable cause for this dilemma in approximately one-fifth of cases. Until recently, the OTC approach to infertility focused on the female chemistry. Lake Consumer Products created a new benchmark by developing FertilMARQ (BabyStart), a home infertility test kit specifically designed for males. Given FDA approval in 2001, it is sold in retail pharmacies for approximately $40.

Procedure

Each test kit contains materials for two separate exams. Prior to testing, consumers must purchase a spermicide-free condom. Once the semen sample is collected using the condom, the contents are emptied into the coated cup included in the kit. This cup contains a material which accelerates the process of converting the sperm from a viscous formulation into a liquid. After 15 minutes, the male places a drop of the liquefied semen into a well on the plastic test cassette, which resembles a home pregnancy test strip, adds two drops of the blue solution and then two drops of the clear solution and waits. If, after 5 minutes, the sample in the test well changes color to a darker blue than the reference blue shown on the test cassette, the result is positive. A positive result means that the sample contains greater than 20 million sperm per milliliter of ejaculate which the World Health Organization (WHO) has determined is required for fertility.[48] A blue lighter than the reference blue is a negative result indicating that the sperm count is below the mark.

The test usually requires about 30 minutes to complete. The patient should repeat the test within 7 days, but not within 3 days after ejaculation.[19] If the test is negative, the patient should be referred to a physician or fertility specialist to determine if other unknown factors are influencing the decline in sperm count. As a part of the FDA approval process, these examinations were offered to consumers and matched professional in-office exams 87% of the time.

Concerns

FertilMARQ does not inform consumers of any factors that may contribute to infertility such as alterations in urine pH levels, white blood cell count, speed, and mobility of sperm movement towards the egg. Nor does it provide any information about the sperms morphology (size and shape). Robert Stillman, a reproductive endocrinologist, states that the latter reason may be crucial in evaluating a male's capacity to conceive. Some physicians believe that FertilMARQ may be considered as a diagnostic tool by consumers and results may be used in lieu of consulting with a physician, thereby, circumventing the ability of a physician to find the actual cause of infertility.

This test should not be used as a diagnostic tool but as an initial screen in similar fashion to doctors who routinely administer in-office pregnancy exams to substantiate at-home testing. It is anticipated that women will be major supporters of the product. Many may purchase this product on behalf of their male counterparts to aid in determining the cause of a couple's inability to conceive.

ASTHMA

Asthma is the most common chronic illness in children, with a prevalence of 5.8% in the US. Hospitalization rates and morbidity continue to increase despite scientific advances that have

improved our understanding of the pathophysiology of asthma, and the availability of new interventions. A recommended intervention to improve patient outcomes is the routine use of a peak flow meter (PFM). This device measures expiration from the lung and allows patients and caregivers to make informed therapeutic decisions. Although PFMs are not used in the initial diagnosis of asthma, these are commonly used at home to determine disease severity, thereby allowing the patient to decide whether treatment or hospitalization is required.

Introduced in the 1960s, PFM's have received increased attention in the recent past. In 1997, the National Asthma Education Program's Expert Panel recommended home monitoring of forced expiratory flow rate or Peak Flow Rate (PFR) for children with moderate to severe asthma to support clinicians in managing asthma more effectively.[20] The panel recommended PFM monitoring for the following: to detect asymptomatic deterioration in lung function, to monitor response to therapy, and to inform clinicians of needed changes in treatment, including emergency situations.

Peak Flow Rate

A normal PFR is based on the individual's age, height, sex, and race. A standardized "normal" may be obtained from a chart comparing the patient with a population without breathing problems. Interpretation of PFR is simplified for the patient by labeling three zones in the same manner akin to the colors of a traffic light. Be aware that the following zones are intended as a general guideline and a physician may alter these zones based upon the patient's specific condition.[21]

Green Zone. To be categorized in the green zone, the PFR should be between 80% and 100% of the baseline readings. In most cases, a measurement in this zone means that the patient's asthma is under reasonable control.

Yellow Zone. The yellow zone requires that the PFR be between 50% and 80% of the patient's baseline measurements. This may be indicative of airway narrowing and may require extra treatment. A therapeutic plan should be constructed, with the advice of a physician, allocating options for this zone. For example, if PFR is noted to be in the yellow zone, a physician may recommend that the patient inhale extra puffs of their prescribed Albuterol inhaler to help open the airways leading to the lungs.

Red Zone. Less than 50% of the baseline PFR signals a medical alert and immediate action should be taken. In some instances, a physician may decide that the red zone should be 80% or less of the baseline. In either case, severe airway narrowing may be occurring, and the patient should be instructed to take rescue medications immediately and possibly seek emergency care from a hospital emergency room. If the physician has developed a therapeutic emergency plan for the red zone, those instructions should be followed.

Peak Flow Meter Use

1. Before each use, make certain the sliding marker or arrow on the PFM is at the bottom of the numbered scale (zero or the lowest number on the scale).
2. Stand up straight. Any gum or food should be removed from the mouth. Take a deep breath (as deep as possible). The mouthpiece should be placed in the mouth, and the lips should be closed tightly around the mouthpiece. In one breath, the patient should blow out as hard and as quickly as possible.
3. The force of the air will cause the marker to move upward along a numbered scale. The number should be noted in a diary.
4. Repeat the entire routine three times. If the device has been used appropriately, the outcomes from all three trials should be similar.
5. The highest of three ratings should be recorded. The patient should not calculate an average of the ratings.
6. The PFR should be measured at the same time each day, and the clinician should help decide what time is appropriate (eg, between 7:00 and 9:00 AM and between 6:00 and 8:00 PM). Some individuals may need to measure PFR before and after the administration of medication. This may be an appropriate recommendation if daily testing times are inconsistent.
7. The patient should maintain a chart of PFR readings, and these should be discussed with clinicians during consultation.

Management Plan

It is important for the patient to measure the PFR consistently and to develop a therapeutic plan based on the readings. This may help to decrease the morbidity and mortality associated with asthma and also diminishes the number of hospitalizations and emergency care visits.

COLON CANCER

In 1998, an estimated 135,000 individuals were newly diagnosed with colon cancer, and of those people, 55,000 died from related complications. Colorectal cancer is the third most commonly diagnosed cancer and the second most deadly cancer in the US. The average American lifetime risk of developing colorectal cancer has been estimated to be about 5%.[22] Therefore, early detection has become vitally important and has been shown to reduce the mortality associated with this condition. The 5-year survival rate for patients with localized disease who are diagnosed early is estimated at 91%. This decreases to 60% in patients with regional spread and to 6% with distant metastases. These facts have encouraged pharmaceutical companies to develop self-care exams to facilitate earlier detection and treatment. Suggestions for colon cancer screening as recommended by the American Gastroenterological Association are found in Table 125-4.

Office Screening Techniques

Screening is most often applied to determine which individuals are more at risk for the development of colon cancer. Screening tools include the digital rectal examination (DRE), fecal occult blood test (FOBT), flexible sigmoidoscopy, colonoscopy, and double contrast barium exam (DCBE). The latter two generally have been recommended for individuals with a higher risk of colon cancer who have had abnormalities detected by other screening techniques.

The in-office examinations that test the stool for blood are Hemoccult, Hemoccult II, and Sensa. These tests consist of guaiac-impregnated cards that give a result regarding the

Table 125-4. Recommendations for Colorectal Cancer Screening

A. Screening is recommended if the following warning signs are noticed:
   1. Bleeding from the rectum
   2. Blood in the stool or in the toilet after a bowel movement
   3. A change in the shape and/or color of the stool
   4. Continuous cramping in the lower stomach
   5. A feeling of discomfort or an urge to have a bowel movement when there is no need to have one

B. Screening at an earlier age should occur in the following conditions:
   1. Past history of colorectal cancer or large polyps
   2. A close relative (eg, parent, sister, child) has been diagnosed
   3. A history of ulcerative colitis or Crohn's disease
   4. A hereditary colon cancer syndrome

C. Screening programs (with a digital rectal exam at each screening) recommended beginning at age 50:
   1. Fecal occult blood testing every year
   2. Flexible sigmoidoscopy every 5 years
   3. Double-contrast barium enema every 5–10 years
   4. Colonoscopy every 10 years

Data from Mandel J, Bond J, Church T, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. *N Engl J Med* 1993; 328:1365.

presence or absence of blood when treated with a developer solution. In the US, the majority of FOBTs are performed using these methods. Because cancerous and precancerous polyps bleed intermittently, these tests need to be repeated so that multiple samples may be analyzed minimizing the possibility of missing blood in the specimen.

Home Diagnostic Exams

ColoCare

In 1980, Helena Laboratories developed the first OTC diagnostic exam used to detect colon cancer. Although it was widely marketed as a home diagnostic test, it is also available for in-office use. Originally marketed as ColoScreen Self Test (CST) in 1980, ColoCare is used to determine the presence of fecal occult blood in a stool sample without removing the specimen from the toilet. Eliminating the necessity of handling a stool specimen allays most of the patient's apprehension about self-administration. This leads to an increase in patient acceptance, earlier diagnosis, and greater success in treatment of this pathological condition.

ColoCare, a third generation test, incorporates tetramethylbenzidine and cumene hydroperoxide as reagents. These have been proven to be comparable to guaiac methodology with an increased sensitivity for hemoglobin. Varying levels of water in the toilet bowl do not affect this test. In addition, diarrhea does not affect the effectiveness of the exam because it has not been shown to interfere with surface hemoglobin.

This diagnostic test has been designed to serve as a preliminary screen. Therefore, results obtained from this exam should not be considered as conclusive evidence of the presence or absence of gastrointestinal abnormalities. It is not intended to replace a physician's examination or consultation in regard to this condition.

PRE-TEST DIRECTIONS—Remove all toilet cleaners, disinfectants, or deodorizers from the toilet bowl. Flush toilet bowl twice before the bowel movement to remove any chemicals. If a noticeable color remains, flush once again. For two days before and throughout the testing period, the patient should be instructed to eat a normal, well-balanced diet that may consist of cooked chicken, tuna, or fish (not rare or raw). No red meat is allowed. The following medications should be avoided: aspirin, corticosteroids, reserpine, indomethacin, and other gastrointestinal irritants as these may cause gastrointestinal bleeding in the tract. Eating red meats or taking one of the aforementioned medications may stimulate a change in color on the test pad. Ascorbic acid (in excess of 250mg/day) and laxatives (containing mineral oil) may prevent a color change in the test when blood is present, thereby producing a false negative outcome.[23]

PROCEDURE—Before beginning this exam, patients should have a bowel movement.

1. Open foil pouch by tearing along the dotted line.
2. Remove one ColoCare pad from the pouch. Hold the pad along the outer edges. Carefully fold the open end of the pouch and tape closed to protect the remaining pads from exposure to moisture.
3. Hold the ColoCare pad with the printed side up. Carefully release the pad, allowing it to float on the water in the center of the bowl.
4. Observe the ColoCare pad for 30 seconds and note any blue or green appearance on the pad.
5. The two smaller squares on the bottom of the ColoCare pad are control areas and help the patient determine if the ColoCare pad is working properly. In 30 seconds, the small box on the left should turn bluish/green in color to demonstrate what the test result should look like if it is positive. The control box on the right should not change color demonstrating what a negative test result will be. If these boxes do not work as described, the test pad needs to be discarded and the procedure should be repeated after the next bowel movement.
6. The test results are determined by examining the pad for the presence of a blue and/or green color in the ColoCare test area (large square at the top of the pad). If color develops in this square, it may not be the same shade or intensity as the smaller square.
7. ANY BLUE OR GREEN DISCOLORATION IN THE LARGE SQUARE DENOTES THE POSSIBLE PRESENCE OF BLOOD, AND THE PATIENT SHOULD BE INSTRUCTED TO CONTACT A PHYSICIAN AS SOON AS POSSIBLE.
8. Using the first diagram on the reply card provided, the patient should be instructed to place an "X" in all areas (large and small) that changed color. The pad should be flushed along with the stool specimen and the examination should be repeated for the next two bowel movements.

ColoScreen/ColoScreen ES

Some individuals may still prefer the guaiac slide test as opposed to the ColoCare methodology. Therefore, Helena Laboratories also developed ColoScreen and ColoScreen ES to qualitatively detect fecal occult blood from a collected stool sample. Originally marketed in 1980, ColoScreen™ is a traditional guaiac test used to aid in the detection of a number of gastrointestinal disorders. It is composed of guaiac-impregnated paper enclosed in a cardboard frame, which permits sample application to one side, and development and interpretation on the other side. This process involves placing two fecal specimens, collected from each of three successive evacuations, onto the guaiac paper. This test is based on the oxidation of phenolic compounds, found in the guaiac, to quinines resulting in the production of a blue color. When a fecal specimen containing occult blood is applied to the test, hemoglobin will react with the guaiac. A psuedoperoxidase reaction will occur upon the addition of the developer solution, with a blue discoloration generated in direct proportion to the concentration of hemoglobin.

ColoScreen ES is an improvement over the original ColoScreen examination. It offers increased sensitivity and has been formulated to overcome the instability of guaiac solution and the hypersensitivity of benzidine and ortho-tolidine.

CHOLESTEROL

Cardiovascular disease is one of the leading causes of death in the US. In addition to hypertension, smoking, and diabetes mellitus, elevated serum cholesterol is considered an independent risk factor for the development of coronary heart disease (CHD) and cerebral vascular disease. Therapeutic life-style changes, early diagnosis, and improved management of dyslipidemia have the potential to reduce the impact cholesterol plays in the development of sequelae of cardiovascular disease. The Adult Treatment Panel III (ATP III) Guidelines[24] are found in Table 125-5.

When recommending patients for cholesterol screening, risk assessment becomes an important consideration. The major risk factors for CHD are age (>45 years for men and >55 years for women), smoking, hypertension, and a family history of premature heart disease. Recently, diabetes has been eliminated as a risk factor because it is now considered to be in the highest risk category for coronary events and has since been classified as a CHD risk equivalent. Other key changes in the new guidelines are located in Table 125-6[24]. Therefore, the pharmacist must continually be involved in monitoring for changes in patient medications, disease states, and dosages, which will allow patients at risk for CHD to be recognized and counseled regarding cholesterol screening and increase their familiarity with the devices used.

Home Diagnostic Exams

The BioScanner 2000 is the first home diagnostic exam that has the ability to perform multiple functions.[25] Currently, the

Table 125-5. Adult Treatment Panel III (ATP III) Guidelines for Life-Style Changes

1. Daily saturated fat intake below 7 percent of total calories and dietary cholesterol less than 200mg. The average American receives approximately 12 percent of total calories from saturated fat and has an average dietary cholesterol of 220–260mg in women and 360mg in men.
2. No more than 35 percent of daily calories from total fat, provided most are acquired from unsaturated fat, which does not raise cholesterol levels.
3. An increase intake of soluble fiber (grains, beans, peas, fruits, and vegetables) and plants stanols and sterols (found in certain margarines and salad dressings) that may lower low-density lipoprotein (LDL) levels.
4. Weight control and regular physical activity, which improves heart disease factors (eg, LDL).
5. All adults 20 years and older should test their cholesterol at least every 5 years, more often for individuals who are at a high risk for heart disease.

Adapted from Summary of the second report of the National Cholesterol Education (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 2001; http://www.nhlbi.nih.gov/guidelines/cholesterol/atp_iii.html. Accessed March 3, 2003.

BioScanner can screen for glucose, total cholesterol, HDL cholesterol, and ketones. Additional tests are being developed for this device including: triglycerides, LDL cholesterol, hemoglobinA_{1C}, hemoglobin, creatinine, and microalbumin. In 2003, the device retails for $172 and contains testing items as well as color-coded Memo chips, which contain the settings for each test. Memo chips are provided with each new pack of test strips and are responsible for the following:

a. Setting the device for the specific test to be performed (eg, glucose, ketones, and total cholesterol)
b. Identifying the lot number and expiration date of the strips
c. Setting the calibration curve for the specific lot
d. Locking out all expired test strips
e. Establishing the accuracy range of the instrument

Table 125-6. Key Changes in NCEP Guidelines

Treat cholesterol more aggressively for those with diabetes.

Make a lipoprotein profile the first test for high cholesterol.
- Previous NCEP guidelines only recommended a screening test for total cholesterol and HDL or triglycerides. The newly suggested screenings will measure LDL, total cholesterol, HDL, and triglycerides.

Develop a new level at which low HDL becomes a major risk factor for disease.
- The new guidelines establish 40mg/dl as the benchmark for signaling possible heart disease, which was increased from 35 mg/dl. An HDL 60mg/dl or higher shall be considered cardioprotective against heart disease.

Identify a "metabolic syndrome" or risk factors for heart disease.
- Factors such as too much abdominal fat, elevated blood pressure, elevated triglycerides, and low HDL often occur simultaneously and dramatically increase the risk for coronary events.

Initiate more aggressive treatment for elevated triglycerides.
- Recent studies identified that triglycerides are linked to heart disease. The new guidelines recommend treating borderline-high levels (eg, life-style modifications, physical activity, and medications).

Advise against the use of hormone replacement therapy (HRT) as alternative to cholesterol-lowering medications.
- HRT reduces the risk for major coronary events or deaths among post-menopausal women with heart disease. Cholesterol-lowering agents have been found to reduce coronary events in women with or without heart disease.

The cholesterol screening is fast, convenient, and requires no fasting. A sample of blood is placed on the test strip and results are available in one minute. BioScanner 2000 allows the storage of 250 glucose readings and 30 readings of any of the other exams. The device has a 2-minute automatic shut-off feature and is upgradeable for future exams.

Cardiocheck, also developed by Polymer Technology Systems, is another hand-held device that performs multiple functions. The health indicators available are total and HDL cholesterol, triglycerides, glucose, and ketones. The device costs $199 in 2003 and is also fully upgradeable. Cardiocheck is an updated version of the Bioscanner 2000 and is smaller, lighter, and consolidates lab testing affording multiple tests to be performed from a single needle stick.

Cholestrak, developed by Accutech, tests for cholesterol only. Results are available in approximately 15 minutes, and the exam costs approximately $20.00. It contains two foil-wrapped cholesterol tests, two lancets, and two result charts. The exam requires a finger prick with blood collection within 5 minutes of the finger prick. Results may be read within approximately 12–15 minutes.

Cholestrak Procedure

1. Thoroughly wash hands with soap and water.
2. Sit down and relax for 5 minutes (rub hands to warm them).
3. Prick the tip of middle or ring finger and withdraw a sample of blood.
4. Enough blood must be added to the well to cover the black "fill" circle within 5 minutes of pricking the finger.
5. Once the black fill circle is filled, wait for approximately 2–3 minutes.
6. Pull plastic tab on the right side of the testing device until the entire row is visualized.
7. The "OK" indicator will turn purple in 5 minutes, and the "END" indicator will turn green in approximately 10–12 minutes.
8. Using the Cholesterol Result Chart, match the number of the column labeled "test device reading" with the number to its right under the column labeled "Cholesterol mg/dl."
9. This is the measured cholesterol level. If the number is not on the card, call the CholesTrak Help Line.

Both Cardiocheck and Cholestrak must be sent to a laboratory to receive results. Although BioSafe developed Total Cholesterol and Cholesterol Panel, both measure total cholesterol. Cholesterol Panel Cholestrak also provides triglyceride, HDL and LDL cholesterol measurements. Results will be mailed to the patient within 1–2 weeks.

PREGNANCY TESTS

In the US, women are having more children than at any time in almost 30 years. In 1996, there were 6 million-plus pregnancies resulting in 3.9 million births.[26] It is believed that approximately one-third of all women, who believe they are pregnant, use a home pregnancy detection kit prior to seeking professional advice.

The FDA cleared the first home pregnancy detection kit in 1977. By July 1994, consumers spent $191 million on home pregnancy tests. Today, pregnancy detection tests are available for laboratory and in-home use.

Current pregnancy detection tests use monoclonal antibodies to detect human chorionic gonadotropin (hCG). The monoclonal antibodies are either antibodies or immunoglobulins that are capable of binding certain target chemicals, so that an extremely low amount of the target chemical can be detected. The "glycoprotein," hCG, can be detected once the fertilized ovum is implanted in the uterine wall.[27]

A sensitive blood or urine test may detect hCG as early as 8–9 days after ovulation. The plasma concentration of hCG doubles at least every 2 days, peaks between 60 and 70 days of

pregnancy, and then declines. Urine hCG levels in pregnant women can reach 25 mIU/ml 7–10 days after conception and reach peak levels of up to 200,000 mIU/ml by the end of the first trimester.[28] Although concentrations of hCG vary in women, more sensitive tests measure lower levels of hCG.

Home Diagnostic Exams

Pregnancy tests use similar technology to detect hCG concentration in urine. Pregnancy tests, which are performed using a urine sample, often require the use of an absorbent wick stick. The stick may either be placed into the woman's urine stream for 2–10 seconds or placed into a collected cup of urine.

PROCEDURE FOR USING TEST STRIPS

1. Remove device from the package.
2. Immediately place a test strip into a collected sample of urine with the arrow end pointing towards the urine. Do not immerse past the MAX (Marker Line).
3. Remove the strip after 3 seconds and lay the strip flat on a clean, dry, non-absorbent surface.
4. Positive results may be observed in as little as 40 seconds.
5. In most cases, negative results are best confirmed after 5 minutes (the manufacturer's recommended reaction time).

PROCEDURE FOR USING A MIDSTREAM TEST

1. Remove device from the package.
2. Remove cap from device.
3. The consumer should turn the test stick so that the handle is facing her and the absorbent tip is located on the bottom. The consumer should not touch the reaction tip.
4. During a midstream of urine, hold the test stick for an average of 6 seconds so that a sufficient amount of urine contacts the absorbent tip.
5. Seal the absorbent window with the cap.
6. Lay the test flat while it is developing and read the result in 3 minutes.
7. In 2–5 minutes, a rose-colored control band will appear in the window to indicate the test is complete.
8. View the indicator window for the result.

The product produces a reading in approximately 2–5 minutes. Results are obtained by viewing the presence or absence of a line due to a second set of reactions, which produces a color change. Most products use a *Control* window or a *Not Pregnant* indicator to demonstrate a positive or negative test outcome.

Timing

Many home pregnancy detection tests market the use of their products as early as the first day of a missed period. Variability in the timing of ovulation among women exists, and it is important to note implantation does not always occur before the expected onset of next menses. According to Wilcox et al, pregnancy is not detectable before the blastocyst implants. This study used an extremely sensitive assay for hCG and concluded 10% of clinical pregnancies were undetectable on the first day of missed menses.[27] Most home pregnancy detection tests should be used any time of day as soon as a missed menses occurs and any day thereafter.

False Negatives

Home pregnancy tests average 97% accuracy.[29] Studies show a 25% rate of false negatives and a significant (though smaller) number of false positives. Women using these products should be aware of possible causes of false-positive or false-negative results and consider the possibility of poor technique, performing the test too close to conception, use of an outdated test, contaminated specimens, and concomitant drug therapy.

Availability

Home pregnancy detection tests are widely available in retail stores and via various online shopping venues. In 2003, the exams cost under $20.00. Prices vary depending on the product selected, the quantity of test products, and sensitivity specifications.

Storage

Home pregnancy detection tests should be stored at room temperature 15–30°C (59–86°F).

OVULATION PREDICTION TESTS

Ovulation prediction home test kits use monoclonal antibody technology to detect luteinizing hormone (LH). LH is a glycoprotein hormone that stimulates the final ripening of an ovarian follicle, its secretion of progesterone, its rupture to release the egg, and the conversion of the ruptured follicle into the corpus luteum.[30] Produced by the pituitary gland, LH is normally present in human urine. LH levels increase significantly prior to a women's most fertile day of the month.

Ovulation prediction test kits are intended to detect the LH surge, which usually occurs during the middle of a woman's menstrual cycle, approximately 1–1 1/2 days prior to ovulation. Ovulation typically occurs 10–12 hours after the peak of a LH surge.[31] The length of a LH surge varies among women.

Many studies have concluded that an egg can only be fertilized 6–24 hours after ovulation. Therefore, advanced detection of ovulation is very important to women seeking pregnancy. Proper timing is a key to ensuring sperm reaches a viable ovum.

Ovulation prediction tests may also measure estrone-3-glucuronide (E3G). Estrone is a metabolite of 17β-estradiol, commonly found in urine, ovaries, and placenta; it has less biological activity than the parent hormone.[30] Ovulation home detection kits are available in the following options: dipstick/test strip, midstream urine kit, and several saliva-based testing devices. Most kits contain materials to conduct several separate tests (as many as 9).

Midstream and Test Strip Ovulation Tests

Midstream and test strip ovulation detection kits are qualitative tests. They simply predict whether LH or E3G levels are elevated and do not confirm the ability of women to become pregnant. Midstream ovulation tests are calibrated to an analytical sensitivity of 25 mIU/ml and test strips are calibrated to 20 mIU/ml.[31]

All instructions should be read fully prior to starting each test. Instructions for ovulation prediction test strips vary slightly among available kits. Most package inserts warn against early morning urine testing and suggest the sample be obtained between 11:00 AM and 3:00 PM and 5:00 PM and 10:00 PM. Some suggest testing twice a day. Testing should begin before ovulation is predicted (day 12–14 in the average cycle). Various charts are included in the package insert to help determine the most favorable testing time frame based upon the patient's menstrual cycle. Tests should be carried out at the same time each day. Liquid intake should be reduced for 2 hours prior to testing to prevent urine dilution.

PROCEDURE USING AN OVULATION TEST STRIP

1. Remove product from packaging.
2. Collect urine in the included plastic cup.
3. Immerse test strip into urine with arrow pointing towards the urine.
4. Do not immerse past MAX (maximum) line.
5. Remove test strip after 5 seconds (no longer than 7 seconds).

6. Place on clean, dry, flat non-absorbent surface.
7. Wait for colored bands to appear. Positive results may be observed in as short as 40 seconds. Negative results may be confirmed after the full reaction time (5 minutes) has passed.
8. After interpretation, discard test strip

Some test strips have a control band, which is located in the upper section of the result window. In a positive result, the test band may be equal to or darker than the control band, and ovulation is predicted to occur in the next 24–48 hours. In a negative result, the test band may present lighter in color intensity than the control band. When testing, during the first few days the tests may be negative, and then a weak positive will result, followed by a strong positive.

Test devices are individually foil sealed to ensure test integrity and shelf half-life. The shelf life is approximately 1 year. Kits should not be used beyond expiration date. Foil packets should be opened immediately prior to the test.

Test Limitations

There are various limitations to using test strips for ovulation prediction. The test strips are for *in-vitro* diagnostic use only and are not reusable. Test results are truly valid only if instructions are followed precisely. Prescription medications such as menotropins may affect results. The onset of menopause and certain medical conditions can result in false-positive results due to elevated levels of LH.

Ovulation Microscope

An ovulation microscope observes visual changes evident in a woman's saliva. Prior to ovulation, a fern-like pattern is produced by the saliva due to an increase in the level of salt and estrogen. Most saliva-based ovulation predictors offer 40X to 60X magnification.[32] Studies imply that a higher the magnification may produce greater accuracy in predicting peak fertility.

Test Limitations

There are various limitations to using the microscope for ovulation prediction. Not all women produce a fern-like pattern in their saliva, and the pattern may not be easily visible to all women. Women, who produce the fern-like pattern during some days of their fertile period, generally do not fern all fertile days. Disruptions in the pattern may occur due to smoking, eating, drinking, toothbrushing, inappropriately placing saliva on slide, and conditions in the location where testing is performed.[33]

Ovulation prediction microscopes are convenient, discreet, compact, and easy-to-use. In 2003, the average cost for a microscopic ovulation detection device was approximately $28.00.

Storage

Ovulation tests are very sensitive to extreme temperatures. Most package inserts indicate the product should be stored at temperatures between 59° and 86° F. Users should be cautious when ordering these products via mail order. Many companies do not permit refunds and exchanges on products damaged due to improper temperature regulation. Any remaining tests in the kit are usable through the manufacturer's expiration date.

URINARY TRACT EXAMS

On an annual basis, in 2000, urinary tract infections (UTI) were reported to affect 11% of women.[34] In 1997, urinary tract infections resulted in 8.3 million doctor visits.[35] These statistics are astounding, but understandable considering the number of patients who request a recommendation for a product to assist in the treatment of a UTI. Symptoms associated with UTI include pain on urination, urinary burning, urgency, or frequency.

Home Diagnostic Exams

The first urinary tract infection (UTI) detection product was marketed in 1997. The purpose of this test was to permit patients to detect a UTI or monitor the effectiveness of drug therapy after UTI diagnosis. Home UTI exams are qualitative tests. UTI detection home exams may detect either for the presence of nitrite (formed from bacteria), the enzyme catalase, or leukocyte esterase (formed from white blood cells) in the urine.[36] Nitrates taken in through dietary intake are normally excreted through the urine as nitrites. In patients with a Gram-negative UTI, the bacteria convert nitrate to nitrite. Positive results are identified as a dipstick color change or by the presence of foam in a sample test tube (Table 125-7).

Procedure for UTI Home Screening Test Kit

Prior to opening the test kit, patients should carefully read the directions and verify the product is not out of date. The testing environment is very important, and humid conditions should be avoided.

1. A test strip should be removed from the package quickly and the container top immediately replaced and closed tightly. The test strip should appear white, if not white it should be discarded.
2. Dip the test area of the strip into a freshly collected urine sample.
3. Tap the test strip against the edge of the cup to remove excess urine.
4. Wait 1 minute and then compare the test strip to the color strip located on the exterior of the vial of test strips.
5. A pink color indicates a positive result. Color changes that occur after 2 minutes should be ignored.

Concerns

Patients using home UTI diagnostic tests should be aware of the situations that can cause false-positive and false-negative test results. False positives may occur if patients have recently consumed phenazopyridine, rifampin, and other medications that discolor the urine and would interfere with test interpretation. If the patient ingests a medication that alkalinizes the urine, false-negative results are possible. Possible agents include ascorbic acid, fruit juices, and antibiotics. False negatives may also occur in patients who consume small amounts of nitrates (eg, vegetarians) and when urine has not had an adequate bladder retention time to form nitrites. There are a number of disease states that may increase the risk of UTI. These disease states include diabetes, neurological deficits, urinary calculi or obstruction, and a history of prior urinary tract infections.[37]

Table 125-7. Selected Home Diagnostic Urinary Tract Infection Exams

EXAM	REACTION TIME	POSITIVE RESULT INDICATOR
AZO	2 minutes	Dipstick color change
First Response Uriscreen	2 minutes	Foam present in sample tube
HealthCheck Uri-Test Urinary Tract Infection Screening Test	1 minute	Dipstick color change
UTI Home Screening Test Kit	<1 minutes	Dipstick color change (pink color)

Adapted from Boh LE. *Pharmacy Practice Manual: A Guide to the Clinical Experience*, 2nd ed. Baltimore: Lippincott, Williams & Wilkins, 2001.

HIV TESTS

Early detection of Human Immunodeficiency Virus (HIV) type-1 is important to reduce the spread of Acquired Immunodeficiency Syndrome (AIDS). Yet, a great deal of controversy exists on the appropriateness of home test kits for HIV detection. As a result, several detection kits have been introduced and withdrawn from the market in the US. Currently, Home Access HIV-1 Test System and Home Access HIV-1 Express Test System are the two tests available to patients today (Table 125-8). Test systems require patients to mail samples to the company for result processing.

The Home Access kits screen the blood specimen sample using an enzyme-linked immunoassay (ELISA) to test for antibodies to HIV-1. If a positive result is detected, an immunofluorescence assay (IFA) is used to confirm the result. Reliable results are only obtained if the patient follows the instructions carefully. Prior to performing the test, patients should locate the blood specimen collection card and remove the top page. The top page contains the confidential 11-digit Home Access Code Number. Users should read the informed consent section of the booklet and call the toll-free number included in the kit to register the confidential 11-digit number. This call indicates that the patient agrees to the informed-consent section of the booklet.

Procedure to Use the Home Access HIV-1 Detection Kit

1. Thoroughly wash hands with soap and water then dry hands completely.
2. Place the specimen collection kit on a clean, dry surface.
3. Unfold the blood specimen collection card to expose printed circle where blood should be placed.
4. Select a puncture site (preferred sites are middle and ring finger tips).
5. Patients should avoid the little finger and callused areas to ensure an adequate amount of blood may be collected.
6. Clean puncture site with alcohol pad and dry with gauze pad, which are included in the kit.
7. Hang hand by side of one's body for 30 seconds and shake it back and forth vigorously several times to stimulate blood flow to the fingers.
8. Place hand on table or countertop with palm up to avoid flinching or pulling away.
9. Hold lancet, included in kit, between first and second fingers of the other hand.
10. Press tip of lancet against target finger, use steady pressure to indent skin in selected location.
11. Use thumb to depress lancet trigger, using steady pressure.
12. Apply pressure to finger near puncture site. Allow large drops of blood to collect at site. Use thumb and first finger of other hand to increase blood flow.
13. Touch a large drop of blood to circle of blood specimen collection card. Additional drops may be placed around edges of primary drop to fill the circle completely.
14. Examine the back of card to ensure blood has completely soaked through. If it has not, place more blood on the front of the card. To acquire more blood, use the second lancet in the kit to create another puncture site.
15. Place adhesive bandage provided in kit over the puncture site. Place used lancet(s) in the lancet disposal container included in the kit.
16. Write the Home Access Code Number on the blood specimen collection card.
17. Allow 30 minutes for blood to dry. Place blood specimen collection card inside the specimen return pouch included in the kit.
18. Tightly seal the specimen return pouch and place it in a cardboard U.S. Mail envelope included in the kit (Home Access); or seal it in cardboard envelope and place it in a FedEx Overnight envelope (Home Access Express).
19. Call for results after seven business days (Home Access) or three business days (Home Access Express).

Table 125-8. Available Home HIV-1 Detection Kits

KIT	NO. OF TESTS PER KIT	TIME PERIOD TO RESULT AVAILABILITY	APPROXIMATE COST
Home Access HIV-1 Test System	1	One week	$40
Home Access HIV-1 Express Test System	1	Three days (excluding Sunday or Holidays)	$50

Data from Pray WS, Popovich NG. In Gennaro AR, ed. *Remington: The Science and Practice of Pharmacy,* 20th ed. Baltimore: Lippincott Williams & Wilkins, 2000:1738–1745; and Home Access [package insert], 1996.

Concerns

As health care providers, pharmacists should be aware of the following precautions associated with HIV-1 home test kit use:

- False positives and false negatives are associated with the use of the kit.
- Patients taking anticoagulants and/or hemophiliacs should not use the kit.
- Blood samples not received within 10 days may not be tested due to perishability.
- The product is approved by FDA for individuals 18 years of age and older; studies do not support the use of the products in patients under 18 years of age.
- Only the individual being tested should use the lancets provided in the test kit. Lancets should not be reused nor given to another person using a testing kit. Used lancets should be disposed of properly in the container provided with the kit.

Home HIV-1 detection kits provide patients with an opportunity to test in the privacy of their own homes. Patients may use "Silent Purchase Slips," small slips of paper often located near the products to eliminate the embarrassment associated with purchasing a Home Access HIV-1 Test System. Testing is anonymous and confidential. Results may only be obtained by using a test kit code number. Test results, counseling, and referrals are available 24 hours a day. Patients who obtain positive results should schedule an appointment with a physician to confirm test results and seek medical attention.

DRUG ABUSE

The abuse of illicit drugs, a widespread problem in the US, is perhaps the most commonly missed diagnosis in adolescents. In 2001, 22.4% of high school seniors reported use of marijuana and 2.1% reported cocaine use. In 2000, 7% of youth ages 12–17 also reported use of marijuana.[38]

There are several nonprescription home test kits available to detect the usage of illicit substances, including hair and urine sample kits. Table 125-9 lists selected nonprescription drug abuse detection kits. Home drug abuse detection kits are qualitative tests that indicate the presence or absence of certain detectable agents.

Hair Sampling

Currently, urine sampling is the gold standard for drug testing; however, hair analysis is gaining popularity as an alternative to urine sampling due to the ability of hair to trap within its substances that were in the blood at the time the hair was formed in its follicle.[39] The chemical residues in hair cannot be removed by washing, bleaching, or carrying out any other hair-care routine. Because hair grows 0.5 inch per month, a 1.5-inch sample detects use of drugs within the last 90 days. This

Table 125-9. Available Drug Abuse Detection Kits

DETECTION KITS	METHOD	DRUGS DETECTED	HOME/MAIL OPTION	TIME TO RESULT AVAILABILITY	DRUG DETECTION WINDOW	APPROX COST ($)
PDT-90 Personal Drug Testing Service	Hair	Amphetamines, barbiturates, benzodiazepines, cocaine, marijuana, methamphetamine, opiates, PCP	Mail	3–7 days	7–90 days	55.00
Rapid Drug Screen	Urine	Amphetamines, barbiturates, benzodiazepines, cocaine, marijuana, methamphetamine, methadone, opiates, PCP	Home	3 min	4 hours to 3 days	14.75
Parent's Alert	Urine	Amphetamines, cocaine/crack, barbiturates, benzodiazepines, marijuana, ecstasy, LSD, opiates/heroin, additives/diluents	Home	3–5 days		44.95

Data from Boh LE. *Pharmacy Practice Manual: A Guide to the Clinical Experience*, 2nd ed. Baltimore: Lippincott, Williams & Wilkins, 2001; Pray WS, Popovich NG. In Gennaro AR, ed. *Remington: The Science and Practice of Pharmacy,* 20th ed. Baltimore: Lippincott Williams & Wilkins, 2000:1738–1745; and PDT-90 Personal Drug Testing Service [package insert], 1997.

surveillance window yields valuable information regarding the long-term use of illicit substances.[40] Marketed in 1997, PDT-90 Personal Drug Testing Service was the first illicit drug detection product using hair analysis technology. This kit was developed for concerned parents interested in testing their children for illegal drug use.

Testing

Prior to sample collection, test kit directions should be read carefully. Obtaining a sample requires consent, both from an adult or the parental or legal guardian. Adult samples also require consent. The manufacturer does not recommend obtaining a sample without the consent of the individual. A hair sample should be collected from the crown of the head and mailed to the manufacturer of the product. Braided hair should be undone prior to collection. Toll-free telephone numbers are provided with kits to answer questions about sample collection, processing, or result notification.

Procedure for PDT-90 Personal Drug Testing Service

1. Remove all components from package.
2. Locate hair sample collection package, remove sample acquisition card, strip of foil, and integrity seal.
3. Remove strip of foil from sample collection package. Fold foil lengthwise to create a trough.
4. Using a sharp pair of scissors to take the sample, locate a small lock of hair that is 1/2 inch wide and one strand deep when held flat across the finger.
5. Cut the hair close to the scalp.
6. Place hair sample into foil trough, with the cut ends extending 1/4 inch beyond a slanted end of the foil. If the hair is short or curly, the hair should be wrapped before cutting it.
7. Press sides of foil together to trap hair sample inside. Remaining hair may be wrapped around foil.
8. Place the sample in the sample acquisition card. Remove the PDT-90 code card, containing a toll-free number and a confidential code number.
9. Place the integrity seal on the sample acquisition card, date it, and initial the card in the space provided.
10. Mail the sample acquisition card in the enclosed, first-class, postage-paid, return envelope.
11. Call the toll-free number after 5 business days to obtain the test result.

After 5 business days, the consumer calls a toll free number. During the telephone call, the consumer provides the code number that was located in the package. The company will then indicate which drugs, if any, were found in the hair sample.

Concerns

Drug testing should not be performed with hair samples obtained from a hairbrush to avoid sample contamination or the use of old dead hair samples.

Urine Sampling

Urine tests only detect usage within the last 2–3 days for most illicit drugs and do not provide an index of the degree of drug abuse over time.[39] Urine collection is objectionable due to its offensive nature and the ability for urine to be altered or substituted by devious subjects. Further, a urine test may not be feasible in patients unable to empty the bladder because of stress.[41]

Various agents may cause false-positive results including amphetamines, diphenoxylate, ephedrine, pseudoephedrine, methadone, chlorpromazine, dextromethorphan, promethazine, PCP, procainamide, doxylamine, thioridazine, and narcotics. False-negative results may occur due to ingestion of diuretics, excessive fluid intake, and urine contaminates such as bleach, lemon juice, salt, soap, or vinegar.[42]

DIABETES SELF-MONITORING TESTS

Diabetes is an extremely expensive disease for patients, their insurers, governments, and employers. Its direct and in-direct costs (eg, equipment, supplies, utilization of health facilities, and lost time from work) exceed $120 billion per year.[43] Home monitoring of blood glucose is critical to ensure proper management and treatment in insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM). Adequate treatment requires a continuous balance of insulin, oral medications, exercise, and diet. Successful modification of treatment requires patients to know and understand their blood glucose levels. Until the late 1970s, patients used urine glucose strips or glucose tablets to monitor the control of diabetes. Currently, self-monitoring blood glucose products (SMBGP) (Table 125-10) have replaced these items.

Blood Glucose Home Testing Devices

Technological advances in diabetes-testing have resulted in improved patient self-monitoring with the use of SMBGP. When performed correctly, self-monitoring is quick and accurate. Glucose testing requires a fingerstick using a lancet device to obtain a blood sample.

Table 125-10. Selected Home Blood Glucose Diagnostic Monitors

MONITOR	TIME TO RESULT (SECONDS)	NO. OF READINGS IN MEMORY	COMMENTS
Easy to use/Basic Monitors			
ExacTech RSG	30	~50	No calibration necessary
Glucometer Elite Basic	30	20	No buttons; no cleaning required
One Touch Basic	45	–	Large display; last result retrievable manually; possible to download previous 75 results; multilingual options
One Touch Fast Take	15	150	Large display; no cleaning required; possible to download previous results
Sophisticated Monitors			
Accu-Chek Advantage	40	100	No cleaning required; possible to download previous results; "Voicemate" option available
Glucometer Elite XL	30	120	Large display; possible to download previous results; multilingual options
Precision QID	20	10/~125	Large display; strips available for either whole blood or plasma; no cleaning required; Patient able to retrieve 10 readings; possible to download previous 125 results
One Touch Ultra	5	150	Large display; Product permits patient to obtain blood sample from the arm also
More Sophisticated Monitors			
Accu-Chek Complete	40	1000	No cleaning required; possible to download previous results; possible to display graphics and additional reports on meter screen
Glucometer DEX	30	100	Uses pre-filled cartridges with built-in strips; possible to download previous results
One Touch Profile	45	250	Permits user to record activities including meals, insulin dosing/timing; possible to download previous results; multilingual options

Data from Boh LE. *Pharmacy Practice Manual: A Guide to the Clinical Experience*, 2nd ed. Baltimore: Lippincott, Williams & Wilkins, 2001; Pray WS, Popovich NG. In Gennaro AR, ed. *Remington: The Science and Practice of Pharmacy,* 20th ed. Baltimore: Lippincott Williams & Wilkins, 2000:1738–1745; and PDT-90 Personal Drug Testing Service [package insert], 1997.

The process required to perform a blood glucose test using a SMBGP has been modified over time. Now, most SMBGPs are patient friendly, very easy to use, include large display screens, and provide multilingual options. Additional features may include audio readout, digital readout, memory, and printout capabilities.

Procedure for Applying Blood to Onetouch Ultra Test Strip

Prior to testing, the patient should read the directions carefully and code the meter to ensure the code number on the test strip bottle corresponds to the code number on the meter display. Control tests should be performed prior to using a new SMBGP and periodically thereafter as suggested in the product brochure. Patients using a SMBGP may obtain blood samples using one of several lancet devices (eg, Auto Lancet, Glucolet, Penlet, Penlet II, Softclix, and Soft Touch). Once the skin has been "pricked" with the lancet device, the following is a typical routine:

1. When the company symbol appears, touch and hold a drop of blood to the TOP EDGE of the test strip, where it meets the narrow channel.
2. The volume of the blood sample should correspond to the manufacturer's recommendation.
3. Hold the blood drop to the TOP EDGE until the confirmation window is completely filled. Then the meter will begin to count down.
4. Check the confirmation window.
5. If confirmation window does not fill completely before the meter begins to count down, do not add blood to test strip. Discard test strip and restart.
6. Read the results. Once the meter counts down from 5 to 1, the test result will display with date and time.
7. Used test strips, lancets, alcohol pads, and other supplies should be discarded properly.

Concerns

There are a number of concerns to keep in mind prior to suggesting an SMBG to a patient. Reliable results are best obtained by following the instructions carefully. Although patients may be required to draw blood samples as frequently as 5 times or more a day, the quality of information obtained out weighs this disadvantage. Patients should be advised to purchase and use the company recommended test strips for the equivalent meter. Patients should also be encouraged to wash and dry their hands thoroughly before and after testing.

Patients are often required to perform routine maintenance functions to ensure efficiency with their monitors. The routine functions may include: coding the meter, performing control tests, changing batteries, setting time and date, changing lancets, matching code numbers, and cleaning the meter. To aid with these tasks, patients should be referred to meter instructions and company toll free telephone numbers.

It is recommended that patients using SMBGP receive diabetes education prior to home testing and altering medication doses based on results. Typically, diabetes patients test 3–4 times a day.[44] In 2003, blood glucose test strips retail for approximately $60–$70 per box of 100.

Patients should be cautious of false-positive results due to anemia and false-negative results due to polycythemia.[45] Meters vary in blood drop sample size requirements. Glucose detection range varies among meters; the range is from 10 to 600 mg/dL. SMBGPs differ in price, and various insurance plans may not cover the cost of the meter and supplies. SMBGPs should be stored at room temperature.

Urine Glucose Tests

Urine glucose tests are noninvasive and provide a more economical option to patients unable to afford standard SMBGPs. Urine glucose strips use copper reduction or glucose oxidase for urine glucose detection. Urine glucose tests are problematic to use. They do not detect hypoglycemia, medication interferences, color vision abnormalities, and are unable to provide accurate specific values for results. For example, they only detect glucose in urine after the glucose threshold is exceeded in the kidneys. Further, they do not demonstrate what the current glucose level is but where it might have been several hours previously. Thus, diabetes patients should be discouraged from using urine glucose test strips as a primary marker. In 2003, prices varied from $7 to $10 per box of 50 strips.

Procedure for Using Urine Glucose Test Strips

1. Collect a fresh urine specimen in a clean, dry container.
2. Open diagnostic test bottle and remove one test strip. Hold the plastic end of test strip without touching the test area of the strip. Immediately replace cap on bottle.
3. Dip test area of strip into urine and remove it immediately (drawing edge of strip against the rim of the urine container to remove excess urine) or pass the test end of the strip through a stream of urine.
4. Begin timing.
5. Compare the glucose test area to the glucose color chart exactly 30 seconds after wetting.
6. Ignore any color changes that occur after 30 seconds.

Concerns

Urine glucose tests are affected by fluid intake. False-positive results may occur due to concomitant administration of ascorbic acid, cephalosporins, chloral hydrate, isoniazid, levodopa, methyldopa, high dose penicillins, probenecid, and salicylates. False negatives may occur due to ascorbic acid, aspirin, iron, levodopa, and methyldopa. Clinistix must be discarded 4 months after the bottle is first opened, and Diastix discarded after 6 months of opening. So, if patients use these, they should mark clearly on the label the date they open the product.

Urine Ketone Tests

Urine ketone testing is helpful when diabetes patients are ill or when blood glucose values exceed 250 mg/dL.[46] The presence of ketones (eg, acetone, acetoacetic acid, beta-hydroxybutyric acid) in the urine indicates that the body has attempted to break down stored body fat to use as a fuel source.[47] Diabetes patients are often advised to test periodically for ketones in the urine to assess the need for insulin dose adjustment.

Over the past decade, there has been an increased demand by patients on high protein diets for urine ketone test strips. Table 125-11 provides examples of urine ketone tests. Proper selection of urine ketone tests is based upon patients' needs. Urine ketone tests strips range between $7 and $32 per 50 test strips, in 2003.

Table 125-11. Selected Urine Ketone Detection Products

PRODUCT	DETECTABLE SUBSTANCES	COMMENTS
Ketostix	Ketones	Readily available in most retail settings
Keto-Diastix	Glucose, ketones	Readily available in most retail settings
Multistix	Bilirubin, glucose, ketones, occult blood, pH, protein, urobilinogen	Usually require retail setting to special order

Data from Boh LE. *Pharmacy Practice Manual: A Guide to the Clinical Experience*, 2nd ed. Baltimore: Lippincott, Williams & Wilkins, 2001; and Pray WS, Popovich NG. In Gennaro AR, ed. *Remington: The Science and Practice of Pharmacy,* 20th ed. Baltimore: Lippincott Williams & Wilkins, 2000:1738–1745.

Home HbA_{1C} Tests

Measurement of glycosylated hemoglobin (HbA_{1C}) that has been altered by exposure to excess glucose allows physicians to obtain an estimate of patients' glucose control over the preceding 2–3 months.[48] HbA_{1C} correlates with the likelihood of microvascular complications. Normal individuals should have a value of 4–6%; the goal for diabetics is less than 7%.[49]

Prior to purchasing a home HbA_{1C} detection test, patients should ascertain their laboratory HbA_{1C} value for comparison. Hemoglobin A_{1c} test kits include the Accu-Chek Hemoglobin A_{1c} Test Kit and the Biosafe™ Hemoglobin A_{1c} Test Kit.[50] In 2003, the testing kits ranged between $35 and $40.

FUTURE INNOVATIONS IN DIAGNOSTIC PRODUCTS

Increased patient desire to be proactive through self-monitoring and self-management has sparked a consistent demand for new, advanced, and easy-to-use home diagnostic testing devices. Currently, there are many home diagnostic test kits in development. Kits originally created for commercial laboratories are now more patient-friendly and manufactured for home use.

Alzheimer's Disease

At the 8th Annual International Conference on Alzheimer's Disease and Related Disorders, world-renowned clinicians gathered to discuss the recent developments in the area of dementia. There were a variety of topics discussed. Dr. Relkin provided information regarding the advancements and future trends in the area of diagnosis. The topics presented were as follows: cerebrospinal fluid (CSF) markers, biological markers, imaging and the possibility of visualizing neurofibrillary tangles and plaques in living patients.

Studies have demonstrated that certain CSF markers are altered in AD, and their measurement may sometimes assist in diagnosis. Using proteomic techniques (eg, 2-dimensional gel electrophoresis coupled with mass spectroscopy), researchers have been able to identify sets of proteins in CSF associated with AD.Brain imaging has also been employed frequently for diagnostic purposes. Magnetic resonance imaging (MRI) and computed tomography (CT) have been used in addition to single photon emission studies such as the positron emission test (PET) and magnetic resonance spectroscopy (MRS). It is believed that serial imaging studies spaced 1–2 years apart may prove useful in the diagnosis of AD because of average brain shrinkage of 2.5% per year compared with 0.4% visualized in normal patients. Because there are so many new approaches to the diagnosis of AD, the next few years may show a considerable shift in the way clinicians diagnose AD.

Hepatitis C

Currently, the majority of research conducted on antibody-detecting assays is focused on HIV screening and diagnosis. In addition to the blood specimen examinations, there is a test that uses oral fluid collected from between the cheek and the gum of the mouth to screen for HIV infection. This exam has been extensively tested and reviewed, and there has been some inquiry

about applying this technology to HCV exams. Unfortunately, this is not available for the detection of HCV, but it may be in the future.

Infertility

Current routine male semen analyses (eg, estimation of sperm concentration, motility, morphology) have limitations as fertility indicators. These analyses lack the potential to ascertain the functional capacity of spermatozoa, and they cannot predict the possible occurrence of *in-vivo* and *in-vitro* conception. In the last few years, efforts have been directed toward the development of the hypoosmotic swelling (HOS) and the acrosome reaction (AR) exam to assess the sperms functional capacity. Recently, progesterone receptor (PR) expression has also been discovered as a viable indicator of sperm function.

Asthma

Recently, investigators have studied the feasibility of using exhaled nitrous oxide to evaluate inflammation in mild to moderate asthma. Elevated nitrous oxide levels have been found in asthmatics because of their direct correlation to eosinophilic airway inflammation in both children and adults. Researchers suggested the possibility of applying this test as a marker for lung injury. Moreover, nitrous oxide has been successfully used as a marker for asthmatic response to treatment and is currently being investigated further for the possibility of other applications.

Recently, The FDA approved NIOX, a product developed by Aerocrine in Sweden, to be used in a physician's office to monitor asthma by recording changes in the levels of nitrous oxide obtained from a patient's breath. To use the device, a patient breathes into a mouthpiece that is connected by a tube to a special computer system that can give the physician an instant reading to facilitate making life-style recommendations or changing treatment parameters. Manufacturer-sponsored research demonstrated that most patients had a 30–70% decrease in nitrous oxide levels after 2 weeks of treatment with inhaled steroids. NIOX may prove to be of great benefit in adjusting treatment options in non- or mildly responsive asthmatics.

Colorectal Cancer

Early detection is the key to defeating colorectal cancer. If identified early, the 5-year survival rates improve 88%. For this reason, researchers are constantly developing new methods of detection. There are several new examinations being employed to screen patients for colorectal cancer and possibly afford patients effective treatment options early. The new examinations include: virtual colonoscopy, immunochemical fecal occult blood testing, and capsule video endoscopy.

Drug Abuse

Future home drug abuse detection kits are likely to be more consumer-friendly. There are consumer demands for more reliable saliva detection kits and home drug abuse detection kits that use blood samples. Forensic scientists are currently using a product, not for sale to consumers, which requires saliva samples to detect drug abuse. Company representatives indicated that they were performing clinical studies with the intent to seek FDA approval for sale of this product to consumers.

Diabetes

There are several companies experimenting with technologies to measure blood glucose levels with either minimal or no disruption to the skin. The following are diagnostic devices pending approval by the FDA: a device capable of using a low-level electrical current with a laser to produce virtually painless micropores through which glucose is extracted painlessly into a transdermal patch; a system that withdraws and tests interstitial fluid (ISF) on a disposable transdermal patch; an infrared glucose meter; a continuous glucose monitoring system using subcutaneous glucose sensors; a device using a transdermal patch and probe to measure ISF glucose; and a battery operated, hand-held meter that draws ISF from the body. These promising technologies offer the hope that improved monitoring devices could be developed to continuously provide blood glucose readings and even sound alarms warning of impending hypoglycemic reactions.

Additional Devices

Currently, additional diagnostic devices are in development for the following diseases: allergic disorders, cancer, glaucoma, infectious diseases, kidney disease, liver disease, and diabetes. Analyzers for home therapeutic drug monitoring by patients are also in development. Hand-held monitors, with changeable encoded computer chips, able to test blood chemistries including international normalized ratio (INR), lipids, glucose, HbA_{1c}, fructosamine, ketones, liver enzymes, and proteins, are all in the foreseeable future.

PHARMACISTS' RESPONSIBILITIES FOR DIAGNOSTIC SELF CARE

As the most accessible health care practitioner, the pharmacist plays a key role in recommending the most appropriate diagnostic device given the patient's circumstance. The development and FDA approval of new diagnostic devices requires pharmacists to remain abreast and understand the function and capabilities of these products.

A pharmacist must be patient and make certain the consumer understands how to use these products and know what to do when the test result is obtained. The patient-pharmacist relationship is important and a key element in ensuring the patient trusts that an appropriate recommendation will be provided and all information discussed shall remain confidential (Please refer to HIPAA regulations discussed in the *Laws Governing Pharmacy*, Chapter 111).

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CHAPTER 126

Preventive Care

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There is an old saying, "an ounce of prevention is worth a pound of cure." This has never been more true than in health care. Routine follow-up with primary care physicians and other health care professionals can aid in the early detection of many medical conditions (eg, cancer, diabetes, hypertension) and can encourage healthy habits that prevent the development of other conditions (eg, lung cancer, obesity). This chapter seeks to point out areas of preventive care that are wide-reaching to the general population and are areas that pharmacists of all practices should be aware of when interacting with patients.

To begin with, it is appropriate to provide some definitions of prevention. Primary prevention refers to preventing a disease from occurring (eg, childhood vaccinations). Secondary prevention refers to trying to reduce morbidity in presymptomatic subjects with established disease by its early detection and treatment (eg, screening of asymptomatic women and early treatment of detected cervical cancer). Tertiary prevention is implemented on patients with a view of cure, palliation, rehabilitation, or prevention of recurrence or complications (eg, treatment of symptomatic cancer). There are numerous interpretations among individual practitioners about these three definitions, and their use is not recommended by all. Instead, it has been suggested clinical interventions be defined by their objective, target population, and type ("reduction of mortality by increased use of statins in patients with a history of myocardial infarction") instead of by level of prevention ("tertiary prevention of myocardial infarction").

Health promotion and disease prevention were not always priorities of health care. It was not until 1979 that the *Healthy People: The Surgeon General's Report on Health Promotion and Disease Prevention and Promoting Health / Preventing Disease: Objectives for the Nation* were published. In 1990, Healthy People 2000 recommendations were released, and in 2000, Healthy People 2010 objectives were released.[1] There are 28 focus areas of Healthy People 2010 (Table 126-1). The intent is to increase the quality and years of healthy life and to eliminate disparities among the overall health of various communities, ethnic groups, and classes. Ten leading health indicators were identified in Healthy People 2010 to address major public health concerns. These are the most important preventable threats to health and are the focus of national goals to minimize these threats. These indicators involve the following: physical activity, overweight and obesity, tobacco use, substance abuse, responsible sexual behavior, mental health, injury and violence, environmental quality, immunization, and access to care.

Providing cost-effective health care throughout the country is a huge challenge and is being undertaken by the US Preventive Service Task Force (USPSTF). This task force is an independent panel of experts in primary care and prevention that systematically reviews the evidence of effectiveness of, and develops recommendations for, clinical preventive services. The first task force started working in 1984 to 1989 to develop recommendations for primary care clinicians on the content of periodic health examinations. It published the *Guide to Clinical Preventive Services* based off of this work. In 1990, the second USPSTF updated these recommendations for preventive services and released the second edition of the guidelines in 1996. These recommendations were incorporated into Healthy People 2010. The Agency for Healthcare Research and Quality (AHRQ) convened the third task force (USPSTF III) in 1998. It continued its work that will create the *Guidelines to Clinical Preventive Services, 3rd edition*. New recommendations can be found on the web site www.ahcpr.gov/clinic/uspstfix.htm as these become available. These recommendations are modified by individual health plans for their use, endorsed by the American Association of Health Plans, incorporated into HEDIS (Health Plan Employer Data and Information Set) and may result in changes in laws regarding health coverage. Part of the challenge of the USPSTF is to make recommendations for care based on cost-effectiveness. Accordingly, they have developed ratings for their recommendations, based on the levels of evidence, which are listed in Table 126-2.

SCREENING FOR DISEASE PREVENTION—Disease screening is effective when the screening test can detect a disease or its precursor before it becomes symptomatic and when early treatment can improve the patient's outcome. Effective screening tests should be highly sensitive (ie, correctly identifying a high proportion of persons with the disease) and highly specific (ie, correctly identifying a high proportion of persons without the disease). Effective screening tests should not cause harm from the test itself. These should also be of an acceptable cost burden to society so as to be utilized by the patients that need it.

DISEASE PREVENTION INTERVENTIONS—The first method of prevention for a particular disease is to eliminate the risk factors that a patient possesses. When one considers risk factors to disease, these are often broken down into modifiable and nonmodifiable risk factors. Modifiable risk factors are actions that the individual can make to change his/her own behaviors, such as smoking cessation, weight loss, and dietary changes. Nonmodifiable risk factors often include the presence of genetic risk factors, concomitant disease states, and abnormal lab values, and cannot typically be changed by the actions of the patient. A key element to preventive care is to make patients aware of the risk factors that exist for various diseases and to minimize the presence of these risk factors.

CHEMOPREVENTION—Chemoprophylaxis is the use of natural or synthetic compounds to block, reverse, or prevent the development of a disease or undesirable outcome. Increasing evidence in the literature supports the role of chemoprevention to prevent the development of various diseases, such as the use of tamoxifen to prevent breast cancer development, as

Table 126-1. Healthy People 2010 Focus Areas

Access to quality health services
Arthritis, osteoporosis, and chronic back conditions
Cancer
Chronic kidney disease
Diabetes
Disability and secondary conditions
Educational and community-based programs
Environmental health
Family planning
Food safety
Health communication
Heart disease and stroke
Human immunodeficiency virus infection
Immunization and infectious diseases
Injury and violence prevention
Maternal, infant, and child health
Medical product safety
Mental health and mental disorders
Nutrition and obesity
Occupational safety and health
Oral health
Physical activity and fitness
Public health infrastructure
Respiratory diseases
Sexually transmitted diseases
Substance abuse
Tobacco use
Vision and hearing

From the Healthy People 2010 web site www.healthypeople.gov, accessed July 24, 2003.

will be discussed later. For patients that are at high risk for the development of a disease, because of underlying risk factors, consideration of drug therapy to help prevent the development of a disease may be necessary. Typically, clinicians think of antibiotics and antivirals because of their evidence against several infective illnesses (eg, isoniazid for tuberculosis, amoxicillin for dental prophylaxis against subacute bacterial endocarditis, and antiviral agents after needlestick injuries to prevent HIV transmission). The topics in this chapter will go beyond discussion of anti-infectives and will present agents with evidence to prevent noninfectious diseases.

CLINICAL GUIDELINES—Many organizations provide guidelines for screening of various diseases, actions to prevent disease, and effective chemoprevention methods. These recommendations can be found at the National Guideline Clearinghouse web site at www.guidelines.gov/index.asp, which is sponsored by the US Agency for Healthcare Research and Quality in partnership with the American Medical Association and the American Association of Health Plans. Interested readers can also search the internet home pages of major national organizations, such as the Centers for Disease Control and Prevention, American Diabetes Association, American Heart Association, and the American Cancer Society, or perform Medline searches for the individual recommendations. Readers are encouraged to search these guidelines routinely, because they are updated on a regular basis, as new research and evidence becomes available.

The focus of this chapter is on methods of disease prevention, including screening recommendations, identification and modification of known risk factors, chemoprotective measures, as well as interventions to help reduce the morbidity and mortality of the disease. The intent is not to provide a substitute for current therapeutic texts, but to supplement these resources by focusing on the preventive care aspects. Readers are referred to appropriate chapters within this text that will discuss in more detail the areas of smoking cessation and substance abuse, as well as the role of complementary and alternative medicine in disease treatment and prevention.

OPTIMAL WEIGHT

BODY WEIGHT—Body weight is a routine measurement at a physician's office. However, body weight by itself does not adequately reflect an individual's health risk from obesity. From "ideal" or "desirable" body weight based on a person's height, a percentage of excess body weight can be calculated. Overweight is defined as 10–20% above desirable body weight, while obesity is defined as greater than 20% above desirable weight. Body mass index (BMI) is accepted as a better estimate of body fatness and health risk than body weight. BMI is the ratio of weight (kg) divided by height (meters) squared: BMI = kg/m^2. BMI can also be determined readily from tables. These tables do not accurately assess all populations, since they were mainly based on white, middle-class Americans who buy life insurance. Obesity is a complex, multifactorial chronic disease. It involves interactions between genetics, metabolism, appetite regulation, food availability, behavior, physical activity, and cultural factors. The National Institutes of Health released guidelines on the evaluation and treatment of obesity in 1998. Their definitions for obesity and overweight are provided in Table 126-3.

Less than half of the US adult population maintains a healthy weight (BMI $\geq$19 but $\leq$25). Obesity has increased in every segment of the population, regardless of age, gender, income, ethnicity, or socioeconomic group. Being overweight or obese is a proven risk factor for diabetes, heart disease, stroke, hypertension, osteoarthritis, and some forms of cancer. Analy-

Table 126-2. USPSTF Recommendation Definitions

A	Strongly recommends that clinicians [the service] routinely provide to eligible patients. (The USPSTF found good that the service improves important evidence health outcomes and concludes that benefits substantially outweigh harms.)
B	Recommends that clinicians routinely provide [the service] to eligible patients. (The USPSTF found at least fair evidence that the service improves health outcomes and concludes that benefits outweigh harms.)
C	No recommendation for or against routine provision of [the service]. (The USPSTF found at least fair evidence that the service can improve health outcomes but concludes that the balance of benefits and harms it too close to justify a general recommendation.)
D	Recommends against routinely providing [the service] to asymptomatic patients.(The USPSTF found at least fair evidence that the service is ineffective or thatharms outweigh benefits.)
I	Evidence is insufficient to recommend for or against routinely providing [the service]. (Evidence that the service is effective is lacking, of poor quality,or conflicting and the balance of benefits and harms cannot be determined.)

The U.S. Preventive Services Task Force (USPSTF) grades the **quality of the overall evidence** for a service on a 3-point scale (good, fair, or poor).

Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of evidence on health outcomes.
Poor	Evidence is insufficient to assess the effects on health outcomes because of limited number of power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

From www.ahcpr.gov/clinic/uspstfix.htm.

Table 126-3. Classification of Overweight and Obesity by BMI, Waist Circumference, and Associated Disease Risks

			DISEASE RISK[a] RELATIVE TO NORMAL WEIGHT AND WAIST CIRCUMFERENCE	
	BMI	OBESITY CLASS	MEN <40 INCHES WOMEN < 35 INCHES	>40 INCHES >35 INCHES
Underweight	<18.5		—	—
Normal[b]	18.5–24.9		—	—
Overweight	25.0–29.9		Increased	High
Obesity	30.0–34.9	I	High	Very High
	35.0–39.9	II	Very High	Very High
Extreme Obesity	>40	III	Extremely High	Extremely High

[a] Disease risk of type 2 diabetes, hypertension, and cardiovascular disease.
[b] Increased waist circumference can also be a marker for increased risk even in persons of normal weight.
From the National Heart, Lung, and Blood Institute, Obesity Guidelines, National Institutes of Health, 1998.

sis of data from NHANES III reveals that individuals with a body mass index ≥27 kg/m^2 have a greater than 70% chance of experiencing an obesity-related co-morbidity.[2] It has been estimated that 80–90% of people with type-2 diabetes are obese.[3] Increasing obesity in children has been linked to rising rates of childhood diabetes. More than one-third of all cases of hypertension in the US are related to obesity.[4]

OBESITY TREATMENT—Successful obesity treatment plans incorporate diet, exercise, behavior modification (with or without drug treatment), and/or surgical intervention. Prior to recommending any treatment, the clinician must evaluate the patient for the presence of secondary causes of obesity, such as thyroid dysfunction. If secondary causes are suspected, then a more complete diagnostic workup and appropriate therapy is important. The clinician should then evaluate the patient for the presence and severity of other obesity-related diseases, evaluating appropriate lab tests as indicated. Based on the outcome of this medical evaluation, the patient should be counseled on the risks and benefits of available treatment options. If obesity is present without other comorbid conditions, then the goal would be absolute weight loss. In the presence of comorbid conditions, relatively small reductions in total body weight can have significant effects on comorbidity. Weight loss of 5–10% of initial body weight has been shown in multiple studies to improve glucose intolerance and type-2 diabetes in obese individuals.[5–7] Weight loss has been shown to lower blood pressure, independent of sodium restriction in obese patients with hypertension.[8,9] The combination of diet and exercise-induced weight loss has shown favorable effects on lowering total cholesterol and increasing HDL cholesterol, and may eliminate the need for drug treatment.[10–12]

The average daily caloric intake for American men is 2800 kcal/day and 1800 kcal/day for women. Energy requirements are influenced by factors such as resting metabolic rate and activity level. The resting metabolic rate is higher at heavier weights, so larger people lose weight faster initially. As weight is lost, however, the resting metabolic rate decreases and intake must decline accordingly for weight loss to continue.

LONG-TERM BEHAVIORAL MODIFICATION—Long-term behavior modification is essential for successful weight loss. It may mean substituting undesirable habits with desirable ones (not using food as a reward, for example). To achieve weight loss, energy consumption must be less than energy expenditure. Because one pound of body fat contains about 3500 kcal, it is necessary to reduce the daily caloric intake by 500 kcal/day to achieve a weight loss of about 1 pound per week, or 1000 kcal/day to lose 2 pounds per week, both of which are considered reasonable goals. General recommendations for a balanced, low-calorie diet include limiting fat intake to 20–30% of total calories, and eating a minimum of five servings of fruits and vegetables daily. Choosing foods low in saturated fat and added sugars and high in nutritional value is important. Pharmacists should encourage patients to regularly eat an assortment of foods such as whole grains, low- or no-fat dairy products, and lean meat, fish, poultry, or beans. Appropriate portion-sizes for food is another behavior that needs to be retaught, as the "super-sizing" of American food portions is becoming more and more apparent.

For patients that have a BMI greater than 35 kg/m^2 and who are being followed by health care providers with specialized training, very-low calorie diets (VLCDs) may be useful. These VLCDs provide less than 800 kcal/day and produce a weight loss of 3.5–4 pounds per week. Surgical options such as gastric bypass or vertically banded laparoscopy are considered for patients with a BMI >40 kg/m^2. These procedures can cause weight loss of 1/3 of body weight, but are not without complications (eg, malabsorption, nausea/vomiting, gallstone formation). The long-term effects of these procedures on weight and overall health are still unknown.

There are three main mechanisms by which drugs can promote weight loss: (1) reduction of food intake, (2) blocking absorption of nutrients, and (3) increasing energy expenditure. Feeding behavior is influenced by the neurotransmitters serotonin, norepinephrine, and dopamine. These neurotransmitters inhibit feeding by suppressing appetite or producing feelings of satiety or fullness. Drugs such as amphetamines have been used for treatment of obesity since the 1930s, but because of their addictive component, became restricted as controlled substances in the 1970s. In the 1990s, the combination of fenfluramine and phentermine received much attention for its success in sustaining weight loss. Problems with cardiac valvular insufficiency and valvular structural abnormalities as a result of this combination, however, caused the FDA to withdraw fenfluramine, and a similar compound, dexfenfluramine, from the US market. Currently, there are two medications in the US approved for weight loss: sibutramine and orlistat. Sibutramine works by decreasing appetite and increasing metabolism through combined effects on serotonin and norepinephrine reuptake inhibition. Orlistat, on the other hand, works by selectively inhibiting gastrointestinal lipases, therefore, lowering dietary fat absorption. Several herbal products, such as chromium picolinate and ma huang, are also frequently used by patients for weight loss. However, evidence supporting these agents as safe and effective is sorely lacking.

EXERCISE—Increasing one's metabolism is a key component to weight loss. Unfortunately, in the US, citizens are increasingly becoming a nation of "couch potatoes." The increasing ease of food gathering and transportation has meant that there is a diminished opportunity to perform physical activity during our basic day-to-day living. In 1997, only 15% of adults performed the recommended amount of physical activity, and 40% of adults engaged in no leisure-time physical activity. One of the leading indicators of Healthy People 2010 is directed toward physical activity, and there are two objectives set forward.[1] The first objective is to increase the proportion of adolescents who engage in vigorous physical activity (defined as activity that promotes cardiovascular fitness on 3 or more days per week for 20 minutes or more per session) from the current 65% to 85%. The second is to increase the proportion of adults who engage in moderate physical activity (defined as activity for 30 minutes or more per day) from 15% to 30%.

Recommendations to increase physical activity in the community were released from the Task Force on Community Preventive Services in 2002.[13] Among the interventions that were strongly recommended based on the level of evidence were informational approaches such as community-wide campaigns that promote physical activity; behavioral and social approaches such as school-based physical education classes, social support interventions in community settings, and individually adapted health behavior change programs; and environmental and policy approaches such as creation of access to places to perform physical activity along with informational outreach activities.

CANCER

The most common causes of cancer and cancer death are shown in Figure 126-1. While it is beyond the scope of this chapter to discuss risk factors and preventive measures for all forms of cancer, the major ones, including colorectal, breast, skin, cervical, and prostate will be discussed.

Colorectal Cancer

INCIDENCE—For both men and women, colorectal cancer is the third leading cause of cancer-related deaths in the US.

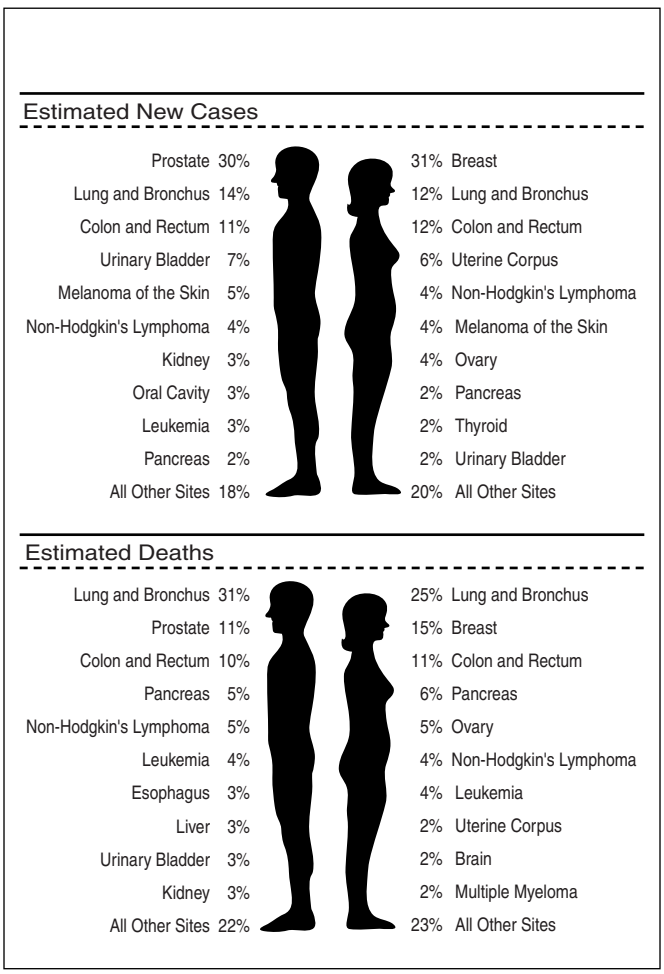

Figure 126-1. Ten leading cancer sites for the estimated new cancer cases and deaths by gender, US, 2002. (Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. Percentages may not total 100% due to rounding.) (From Jemal A, Thomas A, Murray T, et al. Cancer statistics, 2002. *CA Cancer J Clin* 2002; 52:23. © 2002 Lippincott Williams & Wilkins.)

Table 126-4. American Cancer Society Dietary Recommendations

Have most of your foods come from plant sources
Eat 5 or more servings of fruits and vegetables daily
Eat other foods from plant sources, such as breads, cereals, grain products, rice, pasta, or beans several times each day
Limit intake of high fat foods, especially from animal sources
Choose foods low in fat
Limit consumption of meats, especially high-fat meats
Be physically active: achieve and maintain a healthy weight
Be at least moderately active for 30 minutes or more most days of the week
Stay within your healthy weight range
Limit consumption of alcoholic beverages, if you drink at all

Adapted from http://www.cancer.org/docroot/PED/content/PED_3_2X_Diet_and_Activity_Factors_That_Affect_Risks.asp, accessed July 25, 2003.

The American Cancer Society estimates that 105,500 colon and 42,000 rectal cancers will be diagnosed in 2003, with about 57,100 deaths expected. Ninety-three percent of all colorectal cancers occur in patients older than 50 years of age. The median age at diagnosis is 72 years, and individual risk increases with increasing age. The American Cancer Society reports that the 1- and 5-year survival rates for patients with colon or rectal cancer are 83% and 62%, respectively. Even more importantly, when colorectal cancers are found early, in a localized state, the 5-year survival rate increases to 90%. However, only 37% of these cancers are detected at an early stage. Patients with colorectal cancer in the early stages may be asymptomatic or may have symptoms of rectal bleeding, persistent changes in bowel habits, with increased frequency or loose stools. Abdominal discomfort, pain, distention, constipation, and weight loss are all warning signs that deserve medical attention.

RISK FACTORS—Multiple risk factors are associated with the development of this malignancy, including genetic susceptibility, environmental, and life-style. It has been suggested that diets high in fiber are protective against the development of colorectal cancer. There has been conflicting data in support and against this recommendation. In addition, there is the suggestion, supported by numerous epidemiologic studies, that dietary fat increases one's risk of colorectal cancer. Most of the sources of fat in these studies were animal. But, it is unknown whether the source of fat is important, as is the question of saturated *versus* unsaturated fat. It is unclear whether the risk is associated with the fat source or the cooking or processing methods.[14] While current evidence indicates that animal meat and saturated fat intake appear to be associated with an increased risk of colorectal cancer, the magnitude of risk has not been determined. Dietary recommendations from the American Cancer Society are listed in Table 126-4.

Physical inactivity and elevated BMI are each independently associated with an increased risk of colon cancer.[15,16] Individuals with a total higher level of activity throughout life have the lowest risk. The risk of colon cancer may be increased as much as twofold in men who are in the highest quintile of body size. While the evidence is less consistent for women, the Iowa Women's Health Study showed that cancer risk for colorectal and breast cancer was 60% higher in women who were in the highest quartile of BMI compared to the cancer risk of women in the lowest quartile.[17] Potential mechanisms to this relationship include the observation that physical activity stimulates bowel peristalsis, resulting in decreased bowel transit time, and the possibility that exercise can alter levels of blood glucose, insulin, and other hormones, which may reduce tumor cell growth. Heavy alcohol consumption increases risk of rectal and colon cancer by as much as two to three times, although some studies have found no significant increase in risk.[14,16] The evidence is strongest for men, and no single source of alcohol is associated with a greater risk.

A prospective cohort of over 1 million Americans showed that long-term cigarette smoking is associated with an adjusted colorectal cancer mortality ratio of 1.32 (95% CI, 1.16–1.49) for men and 1.41 (95% CI, 1.26–1.58) for women smokers, compared to men and women who had never smoked.[18] Increased risk was evident after >20 years of smoking for men and women combined as compared with patients who never smoked. Risk among current and former smokers increased with duration of smoking and average number of cigarettes smoked per day; risk in former smokers decreased significantly with years since quitting. These authors suggested that as much as 12% of colorectal deaths were attributable to smoking.

SCREENING FOR COLORECTAL CANCER—Despite clear evidence to the benefit of screening for colorectal cancer, The Centers for Disease Control and Prevention estimated that in 1999 only 20.6% of US men and women over 50 had a fecal occult blood test in the year prior to the survey, and only 33.6% had a sigmoidoscopy or colonoscopy within the past 5 years.[19]

The US Multisociety Task Force on Colorectal Cancer released updated guidelines in 2003.[20] This panel recommends offering screening for colorectal cancer in average-risk men and women at age 50 (Fig 126-2). The strongest evidence-based recommendations include offering annual fecal occult blood testing (FOBT) or flexible sigmoidoscopy every 5 years. Each of these screening tests has been associated with reductions in mortality. FOBT uses a guaiac-based test of two samples from each of three consecutive stools. Patients with a positive specimen should be followed up with colonoscopy. Flexible sigmoidoscopy reduced mortality by two-thirds for lesions within reach of the sigmoidoscope. This panel found theoretical evidence supporting the combination of annual FOBT and flexible sigmoidoscopy every 5 years. No direct evidence of efficacy, but strong rationale, supports the recommendation of double-contrast barium enema every 5 to 10 years, or colonoscopy every 10 years. Both double-contrast barium enema and sigmoidoscopy are found to be less sensitive for detecting cancers than a colonoscopy and therefore are recommended at more frequent intervals. Colonoscopy is the most sensitive and specific of all of the available screening tests, but offers the disadvantage of greater cost, risk, and inconvenience to the patient. In 2001, Medicare rules allowed for a colonoscopy screening every 10 years to beneficiaries. While newer methods for screening for colorectal cancer are being developed, such as virtual colonoscopy and DNA analysis of stool samples, there is insufficient evidence to support these methods for screening tools.

Other recommendations have been made by the USPSTF, which in 2002 recommended screening all adults aged 50 and older. The panel found that benefits from screening substantially outweigh harms, but that the quality of evidence, magnitude of benefit, and potential harms vary with each method. Furthermore, it found that screening tests are cost-effective ($50,000 per year of life saved).[21] The American College of Gastroenterology recommends colonoscopy screening every 10 years as the preferred screening strategy, with an alternative being the flexible sigmoidoscopy every 5 years plus annual FOBT.[22] In contrast, the American Cancer Society recommends annual FOBT, flexible sigmoidoscopy every 5 years, annual FOBT plus flexible sigmoidoscopy every 5 years, double-contrast barium enema every 5 years, or colonoscopy every 10 years.[23] The American Cancer Society does not recommend digital rectal examination as a stand-alone screening test for colorectal cancer.

Pharmacists often have the opportunity to discuss colorectal screening when counseling patients on the use of polyethylene glycol purge products, such as Colyte and Nulytely. Careful attention should be paid to the timing of these products so that procedures can take place as scheduled. Pharmacists should be aware that there are differences in the guidelines with regards to method and frequency of colorectal cancer screening, but the

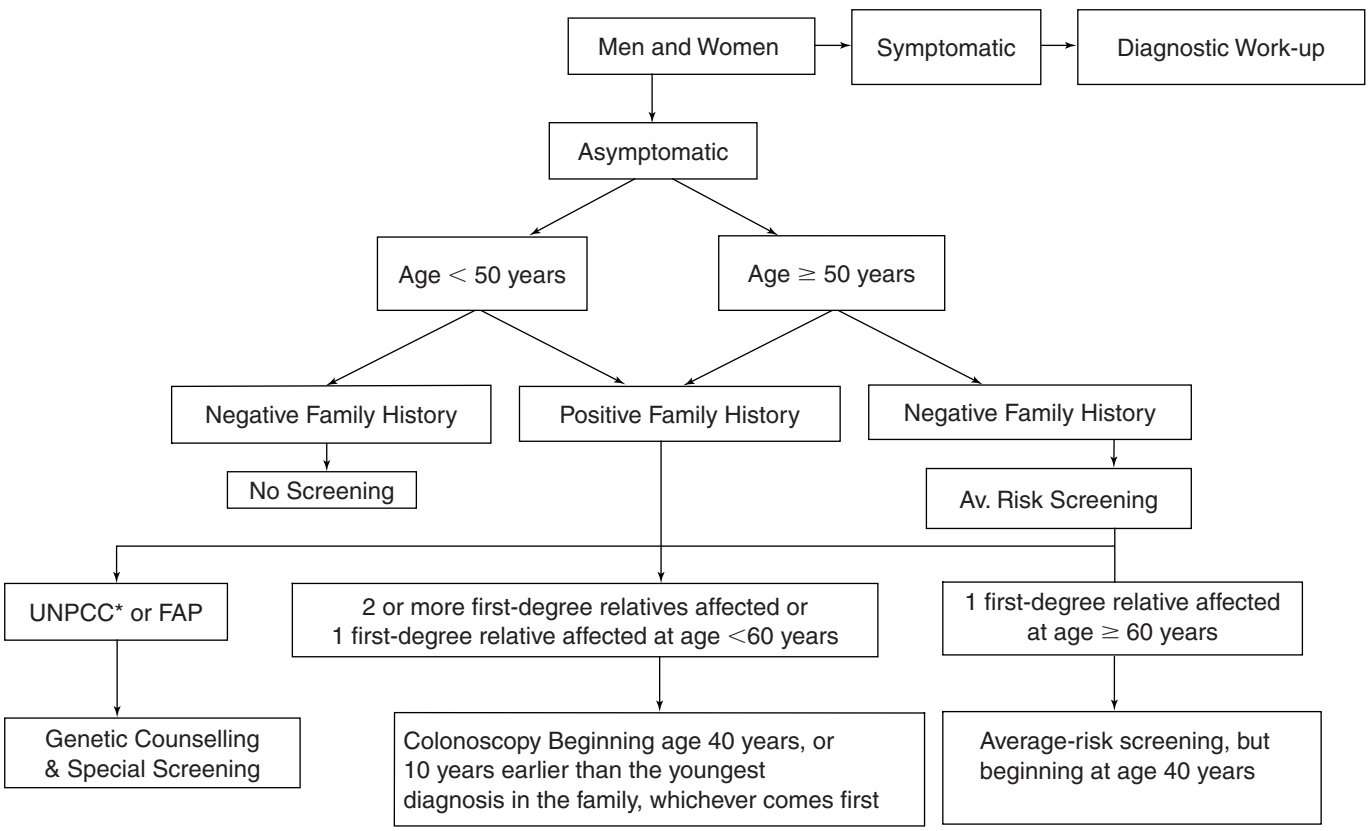

Figure 126-2. Algorithm for colorectal cancer screening. +, Either colorectal cancer or adenomatous polyp; *, HNPCC = hereditary nonpolyposis colorectal cancer and FAP = familial adenomatous polyposis. (Reprinted from Winawer S. Colorectal cancer screening and surveillance. *Gastroenterology* 2003; 124:544, with permission from the American Gastroenterological Association.)

accepted starting range for screening all adult patients at average risk is 50 years. Mass media campaigns have increased the awareness of the need for colon cancer screening, and counseling by pharmacists is a good way to help reinforce these recommendations. Additionally, pharmacists should be aware of patients displaying any of the colorectal cancer warning signs (eg, bleeding, changes in bowel habits, weight loss, abdominal pain) so that they can be referred to appropriate medical care and diagnostic work-up.

CHEMOPREVENTION OF COLORECTAL CANCER—

Aspirin—Regular use of non-steroidal anti-inflammatory drugs and aspirin use (at least two doses per week) is associated with a reduced risk of the development of colorectal cancer. In the Nurse's Health Study, colorectal cancer development was decreased in women who took aspirin regularly for 10 consecutive years, with the highest reduction occurring with an intake of four to six tablets per week.[24] A population-based study of non-aspirin NSAID users who had taken NSAIDs for at least 48 months in the previous 5 years revealed a relative risk of colorectal cancer of 0.49 (95% CI, 0.24–1.00) for users as compared to nonusers.[25] However, the Physician's Health Study, the first randomized trial of aspirin *versus* placebo, reported no decrease in colorectal cancer risk (RR = 1.03; 95% CI, 0.83–1.28) with aspirin 325 mg every other day for 12 years.[26] The potential mechanisms by which these agents exert their protective effects appear to be linked to their inhibition of cyclooxygenase-2 (COX-2) and free radical formation.

The question of whether aspirin should be recommended for patients with a prior history of colorectal cancer was recently addressed in two major trials. The first trial randomized 635 patients to 325-mg enteric-coated aspirin or placebo daily for a median duration of 31 months.[27] One or more adenomas were found in 17% of the aspirin patients and 27% of the placebo patients ($p = 0.004$). The mean ($\pm$ SD) number of adenomas was lower in the aspirin group than the placebo group (0.3 ± 0.87 vs. 0.49 ± 0.99, $p = 0.003$). The adjusted relative risk of any recurrent adenoma in the aspirin group, compared to placebo was 0.64 (95% CI, 0.46–0.91). Time to the detection of a first adenoma was longer in the aspirin group than in the placebo group (hazard ratio for the detection of a new polyp 0.64; 95% CI, 0.43–0.94; $p = 0.022$). The authors concluded that aspirin use is associated with a significant reduction in the incidence of colorectal adenomas in patients with previous colorectal cancer.

The second trial randomized 1121 patients with a recent history of adenomas to receive placebo, 81 mg aspirin, or 325 mg aspirin daily.[28] Follow-up colonoscopy was performed 3 years after the qualifying endoscopy. The incidence of one or more adenomas was 47% in the placebo group, 38% in the 81 mg aspirin group, and 45% in the 325 mg aspirin group (global $p = 0.04$). Unadjusted relative risks of any adenoma compared to placebo were 0.81 for the 81 mg aspirin group (95% CI, 0.69–0.96) and 0.96 in the 325 mg aspirin group (95% CI, 0.81–1.13). Advanced neoplasms were found in 12.9% of placebo patients, 7.7% in the 81 mg aspirin group, and 10.7% in the 325 mg aspirin group. For advanced neoplasms, the relative risks were 0.59 (95% CI, 0.38–0.92) for the 81 mg group, and 0.83 (95% CI, 0.55–1.23) in the 325 mg aspirin group. The authors concluded that low-dose aspirin has a moderate chemoprotective effect on adenomas in the large bowel.

These trials suggest that aspirin reduces the risk of recurrent adenomas in patients with a history of colorectal cancer or adenomas. At this time, cost-effectiveness analyses do not support the use of aspirin for primary chemoprevention in lieu of the current screening recommendations. The question of whether aspirin should be recommended for secondary chemoprevention in patients with a history of colorectal neoplasm needs to consider the protective and harmful effects of aspirin with long-term use.

Folic Acid Supplementation—Several cohort trials have suggested that increased consumption of folic acid in the diet, in the form of supplements and eating high folic acid containing food, reduces one's risk of colorectal cancer. A large, prospective cohort of over 88,000 nurses in The Nurses Health Study, showed that taking a multivitamin with greater than 400 mcg folic acid reduced the risk of colorectal cancer (RR = 0.25, 95% CI, 0.13–0.51) after 15 years of use.[29] It has been suggested that the long time needed to see benefit may be due to an early effect of folic acid on colon carcinogenesis.[30] In 2003, the USPSTF stated that the evidence was insufficient to recommend for or against the use of vitamins A, C, or E, multivitamins with folic acid, or antioxidant combinations for the prevention of cancer or cardiovascular disease (Grade I recommendation).[31]

Calcium Supplementation—Calcium may prevent the development of colon cancer by binding to bile acids and fatty acids in the bowel lumen or by directly inhibiting the development of epithelial cells.[30] The exact benefit of calcium in the prevention of colon cancer has been questionable. One recent randomized trial in 930 patients with a history of colorectal adenomas demonstrated a significant reduction in the formation of new adenomas in patients receiving calcium supplements (3 gm calcium carbonate) compared to placebo (RR = 0.75 (95% CI, 0.60–0.96; $p = 0.02$).[32] Pooled results from the Nurses Health Study and the Health Professionals Follow-up Study, totaling 87,998 women and 47,344 men showed an inverse association between higher calcium intake of >1250 mg/day *versus* ≤500 mg/day and distal colon cancer (pooled RR = 0.65, 95% CI, 0.43–0.98), but incidence of proximal cancer was not significant.[33] There appeared to be minimal benefit in additional calcium carbonate intake beyond 700 mg/day, suggesting a possible threshold effect.

Although there is evidence supporting the use of hormone replacement therapy for the prevention of colorectal cancer, its use for this indication is no longer recommended (see HRT discussion later in this chapter). Results of a large American Cancer Society cohort do not support a substantial effect of vitamins C or E supplement use on overall colorectal cancer mortality.[34] Pharmacists should be aware of measures that patients can take to help prevent the development of colorectal cancer (eg, increasing physical activity, maintaining proper body weight, limiting fat intake, smoking cessation, minimizing alcohol intake, and using aspirin or an NSAID regularly). Further research is being conducted in this area to determine what other modifiable risk factors exist.

Breast Cancer

INCIDENCE—Breast cancer is the most common site of cancer and is second only to lung cancer as the leading cause of cancer death in American women. It is estimated that more than 192,000 new cases of breast cancer will be diagnosed and that more than 40,000 women will die of breast cancer each year. The incidence of breast cancer has been increasing over the last 4 decades. There are three main reasons for the increase in this incidence: an increase in the development of the disease itself due to changes in body hormones, body habitus, and dietary factors; increases in the detection because of mammography and regular clinical breast examinations; and because women are living longer and the mortality from other causes is decreasing.

While most people think of breast cancer as purely a disease of women, more than 1500 cases of male breast cancer were projected to be diagnosed in the United States in 2001. The incidence of breast cancer increases with increasing age. One in eight women will develop breast cancer during their lifetime. The cumulative probability of developing breast cancer increases with increasing age, but more than half of the risk occurs after age 60 years.[35]

RISK FACTORS—Risk factors for the development of breast cancer can be broken down into three categories: hormonal, genetic, and environmental. Hormonal factors such as early menarche, which is defined as menstruation beginning before age 12, has been shown to increase the cumulative lifetime risk of breast cancer development compared to menarche at age 16 or later.[36] Conversely, early menopause has been shown to result in a reduction in risk. Both nulliparity and having a first child later in life (after age 30 years) have been reported to increase the lifetime risk of developing breast cancer twofold. Conflicting data exists about the influence of oral contraceptive pills (OCPs) on the development of breast cancer. There are clear benefits to the use of OCPs, including a reduction in ovarian cancer risk by 40% and reduction in endometrial cancer risk by 60%.[37] Due to recent evidence from the Women's Health Initative, use of hormone replacement therapy is not recommended for patients to prevent the occurrence of breast cancer. Further discussion on HRT occurs later in this chapter.

GENETIC FACTORS—A past medical history of breast cancer is associated with a relative risk of 5.0 for the development of a contralateral breast cancer. A previous history of cancer of the uterus or ovary has also been associated with an increased risk. Family history of breast cancer has a strong association with a woman's own risk for developing the disease. The following statements about the estimates of the risks asso-

ciated with family history include the following[38]:

1. Any first-degree relative with breast cancer increases a woman's risk of breast cancer 1.5–3-fold, depending on age;
2. Higher relative risk is associated with breast cancer with onset younger than age 45 years in one or more first-degree relatives;
3. Having multiple affected first-degree relatives has been inconsistently shown to elevate risks;
4. A second-degree affected relative increases a woman's risk of developing breast cancer by 50% (relative risk = 1.5); and
5. Affected family members on the maternal side and the paternal side contribute similarly to the risk.

Two breast cancer genes, BRCA1 and BRCA2, have been mapped to chromosome 17 and 13, respectively. Women with a strong family history of breast or ovarian cancer, or both, who are carriers of the BRCA1 have an estimated lifetime risk of 85% for breast cancer and 60% for ovarian cancer. Carriers of the BRCA2 mutation have similar risks for breast cancer, but much lower risks for ovarian cancer.[39] Current estimates of the risk of breast cancer in a woman who carries a BRCA1 or BRCA2 mutation and has a family history of multiple cases of breast or ovarian cancer, or both, range from 76% to 87%.[40–43] Estimates of the risk of ovarian cancer in a woman with such a history range from 32% to 84% for carriers of BRCA1 mutations, but are much lower for carriers of BRCA2 mutations.[41–43] These results were derived from studies of high-risk families and may not apply to all carriers of BRCA1 or BRCA2 mutations. There are no clear recommendations for prophylactic treatment for carriers of these mutations. Bilateral prophylactic mastectomy is one alternative, but this has failed to prevent cancer occurrence in some patients. Close follow-up (ie, mammography every 6 months) for carriers of the BRCA mutation is recommended by some.

ENVIRONMENTAL FACTORS—Case control and prospective studies in the US have generally failed to show an association between dietary fat and breast cancer risk. The relationship between vitamin A and breast cancer risk is unclear. In contrast, most studies suggest some benefit from β-carotene, vitamin C, and/or dietary fiber.[44] Other factors with conflicting evidence of their effects on breast cancer include obesity, alcohol intake, and radiation exposure.

PREVENTION AND EARLY DETECTION—Efforts at breast cancer prevention revolve around risk factor modification and identification. However, genetic risk factors including family history and previous history of other malignancies cannot be ignored. Isolation and screening for breast cancer genes in high-risk patients help identify candidates for prophylactic bilateral mastectomy. Chemoprevention includes interventions directed at inhibiting neoplastic development through pharmacologic measures. Retinoids and tamoxifen are two drugs being studied for their use in breast cancer chemoprevention.

MAMMOGRAPHY—Controversy exists in screening recommendations for annual mammography. It is generally accepted that annual mammograms should be performed in women ≥50 years of age, and reduction of mortality is associated with regular use of screening mammography. The controversy exists for women younger than 50 years of age. The American Cancer Society currently recommends a baseline mammogram for women between 35 and 40 years of age, and annual screening in women 40 years of age and older, while the NCI and USPSTF do not recommend routine screening in the 40–49 years age group, holding off on recommending annual mammography until age 50, due to finding no benefit to screening in the 40–49 year age group.[45–49] A summary of the differences in recommendations for the prevention of breast cancer can be found in Table 126-5. The results of the Canadian National Breast Screening Study-1, comparing (1) breast cancer mortality in 40–49-year-old women who received either screening annual mammography, breast physical examination, and instruction on breast self-examination on 4 or 5 occasions to (2) community care after a single breast physical examination and instruction on breast self-examination failed to show a reduction in breast cancer mortality in the annual mammography screening group (group 1) after 11 to 16 years of follow-up.[50]

BREAST SELF-EXAMINATIONS—Currently the American Cancer Society recommends that all women over the age of 20 years perform monthly breast self-examinations (BSEs). There is evidence to support this recommendation due to patients' ability to help diagnose the disease at an earlier stage and demonstrate a higher 5-year survival when compared to women who did not perform them.[51] However, reports from the published randomized clinical trial sponsored by the NCI in over 250,000 women in Shanghai, China, found that women who received intensive instruction in BSE did not reduce mortality from breast cancer and that programs to encourage BSE in the absence of mammography would be unlikely to reduce mortality from breast cancer. The BSE group was more likely to be diagnosed with benign breast lesions.[52] Although these results fail to show the benefit of BSE on mortality, it is still accepted as an effective screening tool for the discovery of breast cancers and is still generally recommended by most clinicians. Clinical breast examinations can occur during the course of a routine visit, but should occur no less often than every 2 years, beginning at age 35.

CHEMOPREVENTION—The Breast Cancer Prevention Trial P-1, part of the National Surgical Adjuvant Breast and Bowel Project (NSABP), was the main reason for the approval of tamoxifen for breast cancer risk reduction in high-risk women, defined as age >35 years with a 5-year predicted breast cancer risk of 1.67% as calculated by the Gail Model.[53,54] This trial showed that tamoxifen decreased the incidence of invasive and noninvasive breast cancer by about half when compared to placebo in high-risk patients treated for 5 years, and the authors felt that despite side effects, its use is appropriate in women at increased risk of the disease.[55] Previous trials for this indication had been less successful.[56,57] Initial results from the International Breast Cancer Intervention Study IBIS-1 have been released. These investigators compared tamoxifen 20 mg/day vs. placebo for 5 years in women at increased risk of breast cancer. They found a risk reduction of 32% for breast cancer, no increased risk for endometrial disease, and an increased risk of thromboembolic events in the tamoxifen group (OR 2.5, 95% CI, 1.5–4.4, p = 0.001). The authors concluded that overall risk *versus* benefit to prophylactic tamoxifen is still unclear, mortality from nonbreast cancer causes is not increased from tamoxifen, and that temporary cessation of tamoxifen should be considered after major surgery or periods of immobility, in addition to appropriate antithrombotic measures. Patients at high risk of thromboembolic disease should not use prophylactic tamox-

Table 126-5. Guidelines for Early Detection of Breast Cancer

	AMERICAN CANCER SOCIETY	USPSTF	NATIONAL CANCER INSTITUTE
Breast self examination	Monthly (20+)	NR	NR
Clinical breast examination	Every 3 years (20–40)	Annual 50–69 with mammography	Every 3 years (20–40) annual (40+)
Mammogram	Annual (40+)	1–2 years (50–69)	NR (40–49) Annual (50+)

NR = not recommended.

ifen.[58] Data from the on-going STAR (Study of Tamoxifen and Raloxifene) trial is not yet available, but seeks to determine the incidence of breast cancer in high-risk patients receiving raloxifene 60 mg/day or tamoxifen 20 mg/day for 5 years. Clinicians will need to wait for these results before recommending raloxifene for this indication.[59] Readers interested in further information about the topic of tamoxifen for the prevention of breast cancer are referred to the following review.[60] For women at low or average risk of breast cancer, the USPSTF found fair evidence that tamoxifen and raloxifene may prevent some breast cancers. The panel concluded, however, that the potential harms of chemoprevention may outweigh the potential benefits in women who are not at high risk of breast cancer (Grade D recommendation). Clinicians should discuss chemoprevention with women at high risk for breast cancer and at low risk for adverse effects of chemoprevention, and inform patients of the potential benefits and harms of chemoprevention (B recommendation). For women at high risk of breast cancer, the USPSTF found fair evidence that treatment with tamoxifen can significantly reduce the risk of invasive estrogen-receptor-positive breast cancer and that the likelihood of benefit increases as the risk of breast cancer increases. Less evidence supports the benefit of raloxifene. The USPSTF found good evidence that tamoxifen and raloxifene increase the risk of thromboembolic events (eg, stroke, pulmonary embolism, and deep venous thrombosis) and symptomatic side effects (eg, hot flashes) and that tamoxifen, but not raloxifene, increases the risk of endometrial cancer. Their conclusion was that the balance of risks and benefits may be favorable in high-risk women, but will need to also consider individual patient preferences.

Prostate Cancer

INCIDENCE—Prostate cancer is the most common cancer in American men and is the second-leading cause of cancer-related deaths. Accepted risk factors for prostate cancer include age greater than 50 years, race, and family history. African Americans have a 5-year survival approximately 15% less than whites, perhaps due to the combination of higher levels of testosterone compared to white males and increased androgen receptor activation. Low-fat diets and other dietary considerations such as β-carotene, lycopene, and vitamin E may be protective, although these are still unproven. Smoking has not been associated with an increased risk of prostate cancer, but smokers with prostate cancer have an increase in mortality. Alcohol consumption does not appear to be associated with the development of prostate cancer. Many patients with localized prostate cancer are asymptomatic, while those with more invasive disease develop symptoms of alterations in urinary frequency, hesitancy, and flow, and new-onset impotence. Metastases from prostate cancer develop in the bone and lymph tissue. Some nonspecific signs of more advanced disease include anemia and weight loss. The prostate specific antigen (PSA) test involves taking a simple blood sample and detecting the enzyme levels. While it is simple and readily available, it does generate false-positives and false-negatives and cannot be recommended alone as a screening tool. Normal ranges for PSA differ by age and race (white vs. African American), and range from 0 to 6.5 ng/ml by some, while the American Cancer Society states that levels above 4 ng/ml are abnormal. Elevated PSAs occur commonly in patients with benign prostatic hypertrophy and prostatitis, making it difficult to distinguish the condition based on values alone. Diagnosis of prostate cancer is confirmed by transperianal or transrectal prostate biopsy.

SCREENING FOR PROSTATE CANCER—As with many other screening recommendations, controversy exists with regard to who should be screened for prostate cancer because clear-cut evidence on reductions in mortality are not yet available. The American Cancer Society recommends digital rectal examination (DRE) and prostate specific antigen (PSA) be offered annually to men beginning at age 50 years with at least a 10-year life expectancy, and to younger men (45 years old) who are considered to be at high risk for prostate cancer development (eg, those with a strong family history, African Americans). If both tests are normal, no further diagnostic work-up is required. If either is abnormal, further work-up by transrectal ultrasound is indicated.[61] In contrast to this, the American College of Physicians recommends that instead of routinely screening all men, physicians should describe the potential benefits and harms of screening, diagnosis, and treatment, listen to the patient's concerns, and then decide on a course of therapy.[62]

The prognosis for prostate cancer depends on the extent of disease. A 5-year overall survival was estimated at 90% for whites and 75% for African Americans. Localized disease has survival rates as high as 100% in some studies, while more advanced disease has less favorable survival rates of around 30% for white males and slightly less for African American males. This is another example of a disease that is nearly always curable if detected early.

CHEMOPREVENTION—Evidence regarding chemoprevention against prostate cancer is currently limited. Selenium 200 mcg daily was associated with a significant (63%) reduction in the incidence of prostate cancer in 974 men with a history of either basal cell or squamous cell carcinoma. Thirteen prostate cancers occurred in the selenium-treated group and 35 cases in the placebo group. When results were restricted to patients with a PSA ≤4 ng/ml, a significant (74%) reduction was still found. There was no change in the incidence of the primary endpoint of basal and squamous cell carcinoma of the skin.[63] The benefit of finasteride in primary prevention of prostate cancer was shown in the Prostate Cancer Prevention Trial.[64] A total of 18,882 men ≥55 years of age with a normal digital rectal examination and a PSA ≤3ng/ml were randomized to treatment with finasteride 5 mg daily or placebo for 7 years. Prostate cancer was detected in 18.4% of men in the finasteride group, and in 24.4% in the placebo group, for a 24.8% reduction (95% CI, 18.6–30.6%, $p < 0.001$). Of concern, however, was the fact that high-grade cancers were more common in the finasteride group, compared to placebo (37% vs. 22.2%; $p < 0.001$). Additionally, sexual side effects were more common in finasteride-treated men, while urinary symptoms were more common in placebo-treated men. While finasteride may prevent or delay the appearance of prostate cancer, the risk of side effects and increased risk of high-grade prostate cancer leaves the question regarding its place in therapy for routine primary prevention unanswered.

Cervical Cancer

INCIDENCE—The American Cancer Society estimates that in 2003 there will be 12,200 new cases of cervical cancer diagnosed, with 4,100 women dying from the disease. Risk factors for cervical cancer include having multiple sexual partners, age at first intercourse, exposure to human papilloma virus, and smoking. Cervical cytology, by way of Papanicolaou (Pap) smear screening can detect both precancerous lesions and presymptomatic invasive squamous cell cancer of the uterine cervix, both of which may be treated effectively. In the US between 1973 and 1998, age-adjusted incidence of invasive cervical cancer fell from 14.2 to 7.5 per 100,000 women, and mortality from 5.2 to 2.5 per 100,000 women.[65]

SCREENING—Although the efficacy of Pap smear screening has been well documented, the optimal interval at which repeat screening should be performed is not clear. Until recently, standard medical practice recommended annual screening of women who are sexually active, or age 21, whichever comes first, which some organizations still recommend.[66] Suggestions to increase the interval from 1 to 2 or even 3 years have been adopted by others.[67] Some guidelines recommend two or three annual smears to initiate screening, and if those are negative,

intervals up to 3 years between smears may be appropriate.[68–70] The USPSTF recommends against routinely screening women over the age of 65 who are considered low risk as evidenced by previously negative Pap smears due to increased risks of potential harms and invasive testing compared to a low perceived benefit (Grade D recommendation), while the American Cancer Society recommends screening until age 70. Newer technologies, such as liquid-based cytology (eg, ThinPrep) and HPV DNA testing, may have improved sensitivity over conventional Pap smear screening, but are of a considerably higher cost and possibly lower specificity and there is insufficient evidence to support their use as the initial screening method (Grade I recommendation).

Skin Cancer

INCIDENCE—Non-melanoma skin cancer is the most common cancer in the United States, with an estimated annual incidence of more than 600,000 cases, and the majority of these cases occur as basal cell carcinoma. Squamous cell carcinomas represent 20% of non-melanoma skin cancers and are more significant because of their ability to metastasize. Non-melanoma skin cancers are very common, especially in the elderly. However, they cause limited morbidity and mortality. Melanoma is considered the deadliest of the skin cancers. The American Cancer Society estimates that in 2003 there will be 54,200 new cases of melanoma in this country, and about 7,600 people will die.[71]

Melanoma mortality ranks as the sixth leading cause of cancer deaths and is disproportionately higher in men and women over the age of 65 years. Roughly half of US deaths from melanoma occurred in men 50 years of age and older. While the incidence of melanoma is variable worldwide, it appears to be increasing universally. Once diagnosed, five-year survival rates are improving and are currently at 88%. The strongest predictor of prognosis is the thickness of the primary tumor. Melanomas less than 1 mm in depth have a small chance to metastasize.

RISK FACTORS—Patients with a strong genetic predisposition are at increased risk for the development of melanomas. Hereditary dysplastic nevus syndrome (HDNS) is characterized by a predisposition to develop dysplastic nevi and cutaneous melanoma. Heavy sun exposure increases one's chances of developing melanomas. It was previously thought that only exposure to UV-B rays increased one's risk of development, but now it is known that exposure to UV-A rays are also important. Melanoma incidence is related to the latitude and the intensity of the sun exposure. Patients at higher risk include those with fair hair color (red or blond) and light-colored eyes (blue, gray, or green), and who have a higher tendency to burn or hardly tan. Development of nonmelanoma skin cancers such as squamous cell and basal cell carcinomas is directly related to lifetime exposure to the sun. This association has not been found with melanomas, suggesting that the relationship to the development of melanoma is more complex than just related to total sun exposure. Patients with a history of severe sunburns appear to be at higher risk for development of melanoma than those with chronic sun exposure without sunburn. Intensive exposure to sunlight and subsequent sunburns is more hazardous during infancy and childhood than during adult life.

PRESENTATION—A normal mole is generally an evenly colored brown, tan, or black spot on the skin. It can be either flat or raised, and round or oval. Moles are generally less than 6 millimeters (1/4 inch) in diameter (about the width of a pencil eraser). A mole can be present at birth, or it can appear during childhood or young adulthood. Several moles can appear at the same time, especially on areas of the skin exposed to the sun. Once a mole has developed, it will usually stay the same size, shape, and color for many years. Moles may eventually fade away in older people. Most people have moles, and almost all moles are harmless. However, it is important to recognize changes in a mole that can suggest a melanoma may be developing.

The initial presentation of melanoma is often a lesion, which can be found anywhere on the body, but most commonly on the trunk of men and lower legs of women. Typically, melanomas are classified using the ABCD(E) system as follows: **A**symmetry; **B**order irregularity; **C**olor variability, **D**iameter greater than 6 mm, and **E**levation or enlargement. Once identified, suspicious lesions should be biopsied, and the diagnosis can be made.

SCREENING—There is some controversy as to the benefits of routine screening for melanoma. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely screening for skin cancer using a total body skin examination for the early detection of cutaneous melanoma, basal cell cancer, or squamous cell skin cancer. Evidence is lacking that skin examination by clinicians is effective in reducing mortality or morbidity from skin cancer (Grade I recommendation). The American Cancer Society recommends skin examination as part of a cancer-related checkup every 3 years for people aged 20–40, and on a yearly basis for anyone over 40.[71] The American College of Preventive Medicine (ACPM) recommends that periodic total cutaneous examinations be performed, targeting populations at high risk for malignant melanoma, including individuals with family or personal history of skin cancer, predisposing phenotypic characteristics, and increased occupational or recreational exposure to sunlight, or clinical evidence of precursor lesions (eg, dysplastic or congenital nevi), but does not recommend routine screening.[72] However, the NIH Consensus Panel recommends screening for melanoma as part of routine primary care, while the American College of Obstetricians and Gynecologists recommends yearly, or as appropriate skin examination of women aged 13 and older based on risk factors.[73] There is agreement among the organizations of the need to educate the public to change behaviors that may decrease the risk of skin cancer, including sun avoidance, sun protection, and skin self-examination.

PREVENTIVE MEASURES—Sunscreens fall into two categories—thick paste-like ointments that block all solar rays, and light-absorbing sunscreens rated by "sun protective factor" (SPF). The SPF is a ratio of the number of minutes for treated *versus* untreated skin to redden with exposure to UV-B. An SPF of at least 15 is recommended and protects against 93% of UV-B. There is no scale for UV-A, which causes photoaging, or UV-C, the most carcinogenic ray that is blocked in the atmosphere by ozone. Sunscreens should be applied to all areas of skin exposed to the sun, particularly when the sunlight is strong. Advise patients to always follow directions when applying sunscreen, using a one-ounce, or palmful of sunscreen, 30 minutes before going outside, and to reapply it every 2 hours. Many sunscreens wear off with sweating and swimming and must be reapplied for maximum effectiveness. Patients should be advised to use sunscreen even on hazy days or days with light or broken cloud cover because the UV light still comes through.

The American College of Preventive Medicine finds insufficient evidence to recommend for or against sunscreen use. Nonmelanoma skin cancers may be reduced with regular, daily sunscreen use. There is insufficient evidence that chemical sunscreens protect against malignant melanoma, and they may, in fact, increase risk, due to increased sun exposure.[74]

Pharmacists can have a role in skin cancer prevention by encouraging patients to avoid sun exposure during peak times of the day (10 AM to 4 PM), wearing protective clothing, and wearing sunscreen with an SPF of at least 15 when outside. Special attention should be paid to those at highest risk, including children. Use of tanning beds, which contain mainly UV-A rays, should be discouraged, and patients should be educated about the risks of using them, including photoaging, ocular damage, and skin cancer. Pharmacists should be aware that fair-skinned men and women over age 65, patients with atypical moles, and those with more than 50 moles constitute known groups at substantially increased risk for melanoma. Clinicians

should remain alert for suspicious skin lesions and help the patient seek appropriate medical care. A melanoma vaccine is currently in development.

DIABETES MELLITUS

INCIDENCE—Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia. It is associated with abnormalities in carbohydrate, fat, and protein metabolism, and long-term complications include microvascular complications such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications such as cardiovascular disease and stroke. Approximately 17 million people in the US, or 6.2% of the population, have diabetes. While an estimated 11.1 million have been diagnosed, unfortunately, 5.9 million people (or one-third) are unaware they have the disease.[75] Type-1 diabetes results from the body's failure to produce insulin, the hormone that "unlocks" the cells of the body, allowing glucose to enter and fuel them. It is estimated that 5–10% of Americans who are diagnosed with diabetes have Type-1 diabetes. Type-2 diabetes results from insulin resistance (a condition in which the body fails to properly use insulin), combined with relative insulin insufficiency. Approximately 90–95% (16 million) Americans have Type-2 diabetes. Gestational diabetes affects about 4% of all pregnant women, resulting in 135,000 cases in the United States each year.

DIABETES-RELATED COMPLICATIONS—Diabetes was the sixth leading cause of death listed on US death certificates in 1999, with heart disease as the leading cause of diabetes-related deaths. Adults with diabetes have heart disease death rates about 2 to 4 times higher than adults without diabetes. The risk for stroke is 2 to 4 times higher among people with diabetes. About 73% of adults with diabetes have blood pressure greater than or equal to 130/80 mmHg or use prescription medications for hypertension. Diabetes is the leading cause of new cases of blindness among adults 20–74 years old. Diabetes is the leading cause of treated end-stage renal disease, accounting for 43% of new cases. About 60–70% of people with diabetes have mild to severe forms of nervous system damage. More than 60% of non-traumatic lower-limb amputations in the United States occur among people with diabetes. Poorly controlled diabetes before conception and during the first trimester of pregnancy can cause major birth defects in 5–10% of pregnancies and spontaneous abortions in 15–20% of pregnancies. During the second and third trimesters, poorly controlled diabetes can result in excessively large babies, posing a risk to the mother and the child. People with diabetes are more susceptible to many other illnesses, and once they acquire these illnesses, often have a worse prognosis than people without diabetes. For example, they are more likely to die with pneumonia or influenza than people who do not have diabetes.

RISK FACTORS—Risk factors for Type-1 diabetes include autoimmune, genetic, and environmental factors. Risk factors for Type-2 diabetes are included in Table 126-6. Gestational diabetes occurs more frequently among African Americans, Hispanic/Latino Americans, and Native Americans. It is also more common among obese women and women with a family history of diabetes.

Table 126-6. Risk Factors for Type 2 Diabetes

Age ≥45 years
Overweight (BMI >25 kg/m^2)[a]
Family history of diabetes (parents or siblings with diabetes)
Physical inactivity
Race/ethnicity (African-Americans, Hispanic-Americans, Native Americans, Asian-Americans, and Pacific Islanders)
Previously identified IFG or IGT
History of GDM or delivery of a baby weighing >9 lbs
Hypertension (≥140/90 mmHg in adults)
HDL cholesterol ≤35 mg/dl and/or a triglyceride level ≥250 mg/dl
Polycystic ovary syndrome
History of vascular disease

[a] May not be correct for all ethnic groups.

Table 126-7. Categories of Glucose Tolerance

Fasting plasma glucose
Normal: <110 mg/dl
Impaired fasting glucose (IFG): ≥110 mg/dl and <126 mg/dl
Diabetes mellitus: ≥126 mg/dl
Two-hour postload plasma glucose (oral glucose tolerance test)
Normal: <140 mg/dl
Impaired glucose tolerance (IGT): ≥140 mg/dl and <200 mg/dl
Diabetes mellitus: ≥200 mg/dl

DIAGNOSIS—The fasting plasma glucose test is the preferred way to diagnose diabetes. Normal fasting plasma glucose levels are less than 110 milligrams per deciliter (mg/dl). Fasting plasma glucose levels of more than 126 mg/dl on two or more tests on different days indicate diabetes. Sometimes, random blood samples may be used to test for diabetes when symptoms are present. A random blood glucose level of 200 mg/dl or higher indicates diabetes, but it must be reconfirmed on another day with a fasting plasma glucose or an oral glucose test. The oral glucose tolerance test begins with a fasting plasma glucose. After this test, 75 grams of glucose is ingested in a sweet-tasting liquid (100 grams for pregnant women). Blood samples are taken up to four times to measure blood glucose response. In a person without diabetes, the glucose levels rise and then fall quickly. In someone with diabetes, glucose levels rise higher than normal and fail to come back down as quickly.

People with glucose levels between normal and diabetic have impaired glucose tolerance (IGT). People with IGT do not have diabetes. Each year, only 1–5% of people whose test results show IGT actually develop diabetes. Upon retesting, as many as half of the people with IGT have normal oral glucose tolerance test results. Weight loss and exercise may help people with IGT return their glucose levels to normal. See Table 126-7 for Categories of Glucose Tolerance. A woman has gestational diabetes when she has any two of the following: a fasting plasma glucose of more than 95 mg/dl, a 1-hour glucose level of 180 mg/dl or higher, a 2-hour glucose level of 155 mg/dl or higher, or a 3-hour glucose level of 140 mg/dl or higher.

Once the diagnosis of diabetes is made, a glycosylated hemoglobin test (HbA1C) is used to monitor blood glucose control. Hemoglobin is the protein in red blood cells that carries oxygen. Glycosylated hemoglobin forms when glucose in the blood attaches to the hemoglobin. Because blood cells stay in circulation for 2–3 months, the glycosylated hemoglobin level is a good measure of a person's average blood glucose level over the previous 2–3 months. Although a high glycosylated hemoglobin level almost always means IGT or diabetes, people with IGT or diabetes can have normal levels. So this test is not used to diagnose diabetes. The goal for HbA1C is <7%.

COMMUNITY-BASED PROGRAMS—Although there is ample scientific evidence showing that certain risk factors predispose individuals to development of diabetes, there is insufficient evidence to conclude that community screening is a cost-effective approach to reduce the morbidity and mortality associated with diabetes in presumably healthy individuals. While community screening programs may provide a means to enhance public awareness of the seriousness of diabetes and its complications, other less costly approaches may be more appropriate, particularly because the potential risks are poorly defined. Thus, based on the lack of scientific evidence, community screening for diabetes, even in high-risk populations, is not recommended. The ADA Evidence Grading System for Clinical Practice Recommendations is listed in Table 126-8. Using this grading scale, and that of the USPSTF, The Recommendations for Screening for Diabetes for the two organizations are summarized in Table 126-9.

Table 126-8. ADA Evidence Grading System for Clinical Practice Recommendations

DESCRIPTION
A Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:
Evidence from a well-conducted multicenter trial
Evidence from a meta-analysis that incorporated quality ratings in the analysis
Compelling nonexperimental evidence, ie, "all or none" rule developed by the Center for Evidence Based Medicine at Oxford*
Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:
Evidence from a well-conducted trial at one or more institutions
Evidence from a meta-analysis that incorporated quality ratings in the analysis
B Supportive evidence from well-conducted cohort studies, including:
Evidence from a well-conducted prospective cohort study or registry
Evidence from a well-conducted meta-analysis of cohort studies
Supportive evidence from a well-conducted case-control study
C Supportive evidence from poorly controlled or uncontrolled studies, including:
Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results
Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls)
Evidence from case series or case reports
Conflicting evidence with the weight of evidence supporting the recommendation
E Expert consensus or clinical experience

* Either all patients died before therapy and at least some survived with therapy or some patients died without therapy and none died with therapy. Example: use of insulin in the treatment of diabetic ketoacidosis.
From *Diabetes Care* 26:S1–S2, 2003. Reprinted with permission from the American Diabetes Association.

RECOMMENDATIONS FOR SCREENING OF COMPLICATIONS—Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg should have their blood pressures confirmed on a separate day. Orthostatic measurements of blood pressure should be performed to assess for the presence of autonomic neuropathy. Advise all patients not to smoke and include smoking cessation counseling and other forms of treatment as a routine component of diabetes care. In adult patients, test for lipid disorders at least annually and more often if needed to achieve goals. In adults with low-risk lipid values (LDL <100 mg/dl, HDL >60 mg/dl, triglycerides <150 mg/dl), repeat lipid assessments every 2 years. Perform an annual test for the presence of microalbuminuria in Type-1 diabetic patients with diabetes duration of ≥5 years and in all Type-2 diabetic patients, starting at diagnosis. Current recommendations for retinal screening include baseline screening in Type-1 diabetes when patients have had the disease for 5 years. Type-2 diabetics should have screening at the time of diagnosis. Subsequent examinations for Type-1 and Type-2 diabetic patients should be repeated annually by an ophthalmologist or optometrist who is knowledgeable and experienced in diagnosing the presence of diabetic retinopathy and is aware of its management. Examinations will be required more frequently if retinopathy is progressing. Annual foot examinations are recommended for all diabetics, and a visual inspection should be performed at each visit. Annual influenza vaccinations are recommended for all diabetics older than 6 months of age. They should also have one dose of pneumococcal vaccine, regardless of age. A one-time revaccination is recommended for individuals >64 years of age previously immunized when they were <65 years of age if the vaccine was administered >5 years ago. Other indications for repeat vaccination include nephritic syndrome, chronic renal disease, and other immunocompromised states, such as post-organ transplantation.

PREVENTION OF DIABETES—The hypothesis that Type-2 diabetes is preventable is supported by observational studies and two clinical trials on diet, exercise, or both in patients at high risk for the disease. In the Diabetes Prevention Program, a large prevention study of people at high-risk for Type-2 diabetes, 3,234 nondiabetic persons with elevated fasting and post-load plasma glucose were randomized to placebo, metformin 850 mg twice daily, or a life-style modification program with the goals of at least a 7-pound weight loss and at least 150 minutes of physical activity per week. The average follow-up period was 2.8 years. The incidence of diabetes was 11% for the placebo group, 7.8% for the metformin group, and 4.8% for the life-style group. The life-style intervention reduced the incidence by 58%, and metformin reduced the incidence by 31%, both of which were significant *versus* placebo. The life-style

Table 126-9. Recommendations for Screening for Diabetes

USPSTF:

The USPSTF concludes that the evidence is insufficient to recommend for or against routinely screening asymptomatic adults for Type 2 diabetes, impaired glucose tolerance, or impaired fasting glucose (Grade I).

The USPSTF recommends screening for Type 2 diabetes in adults with hypertension or hyperlipidemia (Grade B).

ADA:

Evaluation for type 2 diabetes should be performed within the health care setting. Patients, particularly those with a BMI ≥25 kg/m^2[a], should be screened at 3-year intervals beginning at age 45; testing should be considered at an earlier age or be carried out more frequently in those who are overweight if additional diabetes risk factors are present. (Grade E)

The FPG is the recommended screening test. The OGTT may be necessary for the diagnosis of diabetes when the FPG is normal. The FPG is preferred for screenings because it is faster and easier to perform, more convenient, acceptable to patients, and less expensive. (Grade C)

Diagnostic testing should be performed in any clinical situation in which such testing is warranted; health care providers should not consider whether a person meets screening criteria in such cases. (Grade E)

Screening outside of health care settings, or community screening, has not been shown to be beneficial and may result in some harm; this type of screening is not recommended. (Grade E)

[a] May not be correct for all ethnic groups.
Data from US Preventive Services Task Force. Screening. Diabetes Mellitus, Adult Type II and American Diabetes Association. Screening for Type 2 Diabetes. *Diabetes Care* 2003; 26:S21.

group was significantly more effective than metformin in decreasing the incidence of diabetes. Treatment with metformin was most effective among younger, heavier people (those 25–40 years of age who were 50–80 pounds overweight) and less effective among older people and people who were not as overweight.[76]

The STOP-NIDDM Trial was a multi-centered, randomized, placebo-controlled trial comparing acarbose 100 mg three times daily to placebo in 1,429 patients with impaired glucose intolerance, with the primary endpoint being the development of diabetes using a yearly oral glucose tolerance test. A total of 221 of the 682 (32%) acarbose patients developed diabetes, whereas 285 of the 686 (42%) placebo patients developed diabetes after a mean follow-up period of 3.3 years, demonstrating a 25% risk reduction ($p = 0.015$). Weight loss contributed to the decreased risk of diabetes, but acarbose reduced the risk of diabetes even after adjustment for change in weight ($p = 0.0063$). The effects were consistent across age, sex, and body-mass index.[77] A follow-up of this study showed that treatment with acarbose in patients with impaired glucose tolerance decreased the risk of cardiovascular disease by 49% and hypertension by 34%.[78] There are no known methods to prevent Type-1 diabetes, although several clinical trials are currently in progress.

PREVENTION OF LONG-TERM COMPLICATIONS—Research studies in the United States and abroad have found that improved glycemic control benefits people with either Type-1 or Type-2 diabetes. In general, for every 1% reduction in HbA1C, the risk of developing microvascular diabetic complications (ie, eye, kidney, nerve disease) is reduced by 40%. Blood pressure control can reduce cardiovascular disease (ie, heart disease, stroke) by approximately 33% to 50% and can reduce microvascular disease (ie, eye, kidney, nerve disease) by approximately 33%. In general, for every 10 mmHg reduction in systolic blood pressure, the risk for any complication related to diabetes is reduced by 12%. Improved control of cholesterol and lipids (eg, HDL, LDL, and triglycerides) can reduce cardiovascular complications by 20–50%. Detection and treatment of diabetic eye disease with laser therapy can reduce the development of severe vision loss by an estimated 50–60%. Comprehensive foot care programs can reduce amputation rates by 45–85%. Detection and treatment of early diabetic kidney disease can reduce the development of kidney failure by 30–70%.

TREATMENT OF DIABETES—To survive, people with Type-1 diabetes must have insulin delivered by a pump or injections. Many people with Type-2 diabetes can control their blood glucose by following a careful diet and exercise program, losing excess weight, and taking oral medication. Many people with diabetes also need to take medications to control their cholesterol and blood pressure. Among adults with diagnosed diabetes, about 11% inject insulin and take oral medications, 22% inject insulin only, 49% take oral medications only, and 17% do not use either insulin or oral medications. As stated previously, the recommended goal for glycemic control is a HbA1C less than 7%. Once glycemic control has been reached, testing of HbA1C should continue every 3–4 months for those on insulin, and every 6–12 months for those not prescribed insulin. One quality assurance mechanism monitored through HEDIS is the percentage of patients with diabetes in a health plan who have HbA1C measured within the past year.

Blood pressure control is essential for prevention of complications of diabetes. Current goals of blood pressure are $<130/80$ mmHg for patients with diabetes. ACE inhibitors are the drugs of choice for hypertensive patients with microalbuminuria, proteinuria, or heart failure. Diabetics who smoke should be asked about their tobacco use at each visit, and should be strongly advised to quit. Diabetics who have known CHD should have annual lipid screening done, with treatment based on lipid profile. Aspirin is recommended for secondary prevention of CHD in patients with diabetes.

SELF-MANAGEMENT OF DIABETES—Diabetics should be encouraged to perform self-monitoring of blood glucose. It is useful to have values from all times of day, both fastings and nonfastings. Pharmacists in all settings can be involved in patient education of how to use blood glucose meters with the overall goal of preventing diabetes related complications.

ROLE OF THE PHARMACIST—Pharmacists can play an integral role in teaching patients about diabetes and its related complications. Reinforcement of the importance of management should be performed at every available opportunity, by educating patients on medications, proper control of blood sugars, control of hypo- and hyperglycemic symptoms, sick care management, vaccinations, and monitoring for signs of diabetes-related complications. Many pharmacists have gone on to become certified diabetes educators, and have practice sites in community pharmacies and ambulatory care clinics.

Pharmacists in ambulatory care are becoming more involved in the management of diabetes. Further discussion of this topic can be found in Chapter 121.

CARDIOVASCULAR DISEASE

INCIDENCE—Results from the AHA Heart and Stroke Statistical Update 2002 showed that 61.8 million Americans (1 in 5) have cardiovascular disease. Of these, 12.6 million have coronary artery disease, or CAD (angina, acute myocardial infarction). Each year, 1.1 million Americans will have a myocardial infarction and 600,000 will have a stroke. Death from cardiovascular diseases remains the number one killer of adult males and females.[79]

There are two screening strategies to reduce morbidity and mortality from CAD. The first involves screening for modifiable cardiac risk factors, such as hypertension, elevated serum cholesterol, cigarette smoking, physical inactivity, and diet. The second strategy is early detection of asymptomatic CAD. The principal tests for detecting asymptomatic CAD include resting and exercise ECGs, which can provide evidence of previous silent myocardial infarctions and silent or inducible myocardial ischemia. Thallium-201 scintigraphy, exercise echocardiography, and ambulatory ECG (Holter monitoring) are less commonly used for screening purposes.

Hypertension

INCIDENCE—It is estimated that more than 50 million Americans have hypertension. The etiology is usually unknown (primary or essential hypertension) and is rarely identified from a specific cause (secondary hypertension). Genetic factors have a role in the development of essential hypertension. Some secondary causes of hypertension include renal dysfunction, adrenal tumor, Cushing's syndrome, hyperthyroidism, pregnancy, and drug-induced causes. Drugs commonly associated with increased blood pressure include adrenocorticosteroids, amphetamines, oral decongestants, cyclosporine, non-steroidal anti-inflammatory drugs, and oral contraceptives. Herbal therapies such as ma huang, ginger, and licorice are associated with increases in blood pressure. If a secondary cause is found, treatment should target the underlying condition and any offending drugs should be discontinued.

RECOMMENDATIONS—Hypertension is a major risk factor for coronary heart disease, stroke, retinopathies, and renal dysfunction. The goals of treatment of hypertension are to limit target organ damage, thereby reducing the morbidity and mortality associated with the disease. Despite increases in awareness and treatment of hypertension, National Health and Nutrition Examination Survey III (NHANES III) results showed that only 29% of patients were controlled to below 140/90 mmHg. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) was released in 2003.[80] These guidelines put a new emphasis on the importance of control of systolic blood pressure (BP) in persons older than 50 years,

which has been recognized as a more important risk factor than diastolic BP. New to these guidelines is the classification of prehypertension, where systolic blood pressure is 120–139 mmHg, or diastolic blood pressure is 80–89 mmHg. Patients falling in this classification should have health-promoting life-style modifications to prevent CVD (discussed below). Target blood pressure for patients who do not have diabetes is <140/90 mmHg and is more aggressive at <130/80 mmHg in diabetics and patients with chronic kidney disease. Chronic kidney disease is defined by (1) reduced excretory function, with an estimated glomerular filtration rate of less than 60 ml/min per 1.73 m^2 (corresponding to a creatinine of >1.5 mg/dl in men or >1.3 mg/dl in women), or (2) the presence of albuminuria (>300 mg/day or 200 mg albumin per gram of creatinine). The classifications of Blood Pressure for Adults Aged 18 Years and Older is listed in Table 126-10.

LIFE-STYLE MODIFICATIONS—Non-drug therapies have been shown to lower BP, enhance antihypertensive drug efficacy, and decrease cardiovascular risk. Recommendations for non-drug therapy include weight reduction, with a goal of maintaining normal body weight; adopting a DASH eating plan (Dietary Approaches to Stop Hypertension), which includes having a diet rich in fruits, vegetables, and low-fat dairy products, with reduced saturated and total fat content; dietary sodium restriction to less than 100 mEq/L (2.4 g sodium or 6 g sodium chloride); physical activity, engaging in regular aerobic physical activity such as brisk walking at least 30 minutes per day on most days of the week; and moderation of alcohol consumption, limiting consumption to no more than 2 drinks per day in most men and no more than 1 drink per day in women and lighter-weight persons. All patients with hypertension and those in the prehypertensive category should be advised to make life-style modifications in addition to any pharmacologic treatment that they receive. Continued reinforcement and encouragement of these changes at health encounters may help patient adherence with these changes.

DRUG THERAPY CONSIDERATIONS—Some effective drug therapies for hypertension include β-blockers, diuretics, and ACE inhibitors. JNC-7 recommends thiazide-type diuretics as initial therapy for most patients with uncomplicated hypertension, either alone or in combination. There are certain high-risk conditions that are compelling indications for the initial use of other antihypertensive drug classes (ie, ACEI, ARBs, β-blockers, CCB). Many patients will require 2 or more antihypertensives to achieve their goal BP. If the BP is more than 20/10 mmHg above goal BP, consideration should be given to initiating two-drug therapy, one of which should be a thiazide. Support for the initiation of diuretics as first-line therapy for hypertension is based on the results of The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), which showed that diuretics are as effective and safe as ACEI and calcium channel blockers.[81]

BLOOD PRESSURE MEASUREMENTS—Because hypertension is often termed a "silent killer," blood pressure measurements should be performed at each health care encounter. This includes visits to the doctor's office, but is increasingly becoming incorporated into regular pharmacy encounters as well, as pharmacists begin taking on an increasing role in disease state management. Further discussion of this topic can be found in the *Disease State Management* chapter of this text. Healthy People 2010 has a target to increase to 95% the percentage of Americans screened for hypertension within the past 2 years, and to increase to 50% the percentage of patients with controlled blood pressure, up from the 1990 rate of 27%.[1] Pharmacists in all settings should be aware of current recommendations for screening and management of hypertension so that they will be able to direct the care of patients appropriately. Additionally, pharmacists are involved in teaching patients how to check their blood pressures at home, as patients are taking on a larger role in their self-care.

Hyperlipidemia

RECOMMENDATIONS FOR TESTING AND MONITORING—Recommendations regarding the diagnosis and management of hyperlipidemia are provided by the National Cholesterol Education Program, which regularly updates these guidelines as new information becomes available. The current Adult Treatment Panel III recommendations state that all adults aged 20 years or older should obtain a fasting lipoprotein profile (total cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and triglycerides) once every 5 years.[82] If the testing opportunity is non-fasting, only the values for total cholesterol and HDL-C will be usable. In such a case, if total cholesterol is ≥200 mg/dl or high density lipoprotein is <40 mg/dl, a follow-up lipoprotein profile is needed for appropriate management based on LDL-C. The relationship between LDL-C levels and coronary heart disease risk is continuous over a broad range of LDL-C levels from

Table 126-10. Classification and Management of Blood Pressure for Adults Aged 18 Years or Older

				MANAGEMENT		
					INITIAL DRUG THERAPY	
BP CLASSIFICATION	SYSTOLIC BP, MMHG[A]		DIASTOLIC BP, MMHG[A]	LIFE-STYLE MODIFICATION	WITHOUT COMPELLING INDICATION	WITH COMPELLING INDICATION
Normal	<120	And	<80	Encourage		
Prehypertension	120–139	Or	80–89	Yes	No antihypertensive drug indicated	Drug(s) for the compelling indications[b]
Stage 1 Hypertension	140–159	Or	90–99	Yes	Thiazide-type diuretics for most; may consider ACEI, ARB, β-blocker, CCB, or combination	Drug(s) for the compeling indications Other antihypertensive drugs (diuretics, ACEI, ARB, β-blocker, CCB) as needed
Stage 2 Hypertension	≥160	Or	≥100	Yes	2-Drug combination for most (usually thiazide-type diuretic and ACEI or ARB or β-blocker or CCB)[c]	Drug(s) for the compelling indications Other antihypertensive drugs (diuretics, ACEI, ARB, β-blocker, CCB) as needed

[a] Treatment determined by highest BP category.
[b] Treat patients with chronic kidney disease or diabetes to BP goal of less than 130/80 mmHg.
[c] Initial combination therapy should be used cautiously in those at risk for orthostatic hypotension.
From Chobanian AV, Bakris GL, Black HR, et al. *JAMA* 2003; 289:2560.

Table 126-11. Adult Treatment Panel III Classification of Low-Density Lipoprotein (LDL-C), Total, and High Density Lipoprotein Cholesterol (HDL-C)

LDL-C (MG/DL)	
<100	Optimal
100–129	Near optimal/above optimal
130–159	Borderline high
160–189	High
≥190	Very High
TOTAL CHOLESTEROL (MG/DL)	
<200	Desirable
200–239	Borderline high
≥240	High
HDL-C (MG/DL)	
<40	Low
≥60	High

From NCEP III Guidelines, National Heart, Lung, and Blood Institute, National Institutes of Health.

low to high. Therefore, the Adult Treatment Panel III adopts the classification of LDL-C levels shown in Table 126-11; this also shows the classification of total and HDL-C levels.

The category of highest risk consists of coronary heart disease and coronary heart disease risk equivalents. The latter carry a risk for major coronary events equal to that of established coronary heart disease, ie, >20% per 10 years (more than 20 of 100 such individuals will develop coronary heart disease or have a recurrent coronary heart disease event within 10 years), based on large epidemiologic evidence from trials conducted in Framingham, Massachusetts. Coronary heart disease risk equivalents comprise: other clinical forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease), diabetes, and multiple risk factors that confer a 10-year risk for coronary heart disease >20%. Diabetes counts as a coronary heart disease risk equivalent because it confers a high risk of new coronary heart disease within 10 years, in part because of its frequent association with multiple risk factors. Furthermore, because persons with diabetes who experience an acute myocardial infarction (AMI) have an unusually high death rate either immediately or in the long term, a more intensive prevention strategy is warranted. Persons with coronary heart disease or coronary heart disease risk equivalents have the LDL-C goal (<100 mg/dl). The second category consists of persons with multiple (2+) risk factors in whom their 10-year risk score for coronary heart disease is ≤20%. Major Risk Factors that Modify LDL-C Goals are summarized in Table 126-12. Other lifehabit risk factors for hyperlipidemia not included here are obesity, physical inactivity, and atherogenic diet; emerging risk factors consist of lipoprotein (a), homocysteine, prothrombotic, and proinflammatory factors, impaired fasting glucose, and evidence of subclinical atherosclerotic disease. These risk factors may be incorporated into future guidelines as more evidence develops.

The third category consists of persons having 0 to 1 risk factor; with few exceptions, persons in this category have a 10-year risk <10%. Their LDL-C goal is <160 mg/dl. See Table 126-13 for a summary of LDL goals.

EFFECTIVE TREATMENT—Effective drug treatment for hyperlipidemia consists of bile acid sequestrants, niacin, statins, fibric acid derivatives, and cholesterol uptake inhibitors. The largest amount of evidence on the benefits of lipid-lowering therapy is found with the statins. Results from large-scale trials of statin therapy have shown them to be effective for reducing total mortality, coronary mortality, revascularization rates, and stroke in patients with cardiovascular disease. For patients without underlying cardiovascular disease, statins are effective for reducing the incidence of first major coronary events, AMI, unstable angina, and revascularization procedures. Despite adequate treatments available, results from NHANES III showed that only 28% of eligible patients were being treated with cholesterol-lowering therapy.[83] Recently, the results of the Heart Protection Study, a randomized trial of 20,536 adults with coronary disease, other occlusive arterial disease, or diabetes, to simvastatin 40 mg daily *versus* placebo, showed a significant reduction in all-cause mortality (12.9% vs. 14.7%; p = 0.0003).[84] Rates of AMI, stroke, and revascularization were all reduced by about one-third, when allowances were made for noncompliance. This is significant because it may demonstrate that statins produce a substantial reduction in major vascular events in patients without diagnosed coronary disease who have cerebrovascular disease, peripheral arterial disease, or diabetes, irrespective of the blood lipid concentrations when the treatment is initiated. These benefits were in addition to those of other treatments.

NON-DRUG TREATMENT—Therapeutic Life-Style Changes (TLC) are essential for reducing risk for CHD. Features recommended by the ATP III include reducing intake of saturated fat to <7% of total calories and reducing cholesterol to <200 mg/day; enhancing LDL lowering by addition of plant sterols/stanols (2 g/day) and soluble fiber (10–25 g/day); weight reduction; and increased physical activity. These life-style changes should be performed in addition to any pharmacologic treatment.

The National Committee for Quality Assurance (NCQA) has included cholesterol management after an acute event as one of its performance measures in the Health Plan Employer Data and Information Set (HEDIS). Managed care organizations will be scored on the percentage of their members screened for LDL-C and with LDL-C <130 mg/dl within 1 year after AMI, coronary artery bypass grafting (CABG), or percutaneous transluminal coronary angioplasty (PTCA).

Results from the Lipid Treatment Assessment Project (L-TAP) show that only 38% of patients are treated to their LDL-C target goals.[85] Reasons for this may include failure to initiate therapy, increase the dose, and monitor lipid levels; fear of combination of therapy; and non-adherence to drug therapy. Pharmacists in ambulatory clinics and community pharmacies have a role in helping to manage lipid-lowering therapy for their patients by providing interventions in treatment and monitoring and helping patients adhere to their medication regimens by educating them about their disease.

Aspirin and Anticoagulation

Decisions about aspirin therapy need to take into account the potential benefits compared to the risk for coronary heart disease, as well as the potential harms, such as gastrointestinal and intracranial bleeding. The optimum dose of aspirin for chemoprevention of heart disease is unknown. Primary and

Table 126-12. Major Risk Factors (Exclusive of LDL-C) that Modify LDL-C Goals[a]

Cigarette smoking
Hypertension (blood pressure >140/90 mmHg or on antihypertensive medication)
HDL-C <40 mg/dl[b]
Family history of premature CHD
CHD in male first-degree relative < 55 years
CHD in female first-degree relative <65 years
Age
Men ≥ 45 years
Women ≥ 55 years

[a] In Adult Treatment Panel III guidelines, diabetes is regarded as a coronary heart disease risk equivalent
[b] HDL-C ≥ 60 mg/dl counts as a "negative" risk factor; remove one risk factor from the total count
From ATP-III Guidelines, National Heart, Lung, and Blood Institute, National Institutes of Health.

Table 126-13. Risk Categories that Determine LDL-C Goals

RISK CATEGORY	LDL-C GOAL	LDL-C TO INITIATE TLC	LDL-C TO CONSIDER DRUG THERAPY
CHD or CHD risk equivalent 10-yr. risk >20%	<100 mg/dl	≥100 mg/dl	≥130 mg/dl 100–129 mg/dl: drug optional
2+ Risk Factors 10-yr. risk ≤20%	<130 mg/dl	≥130 mg/dl	10-yr. risk 10–20%: ≥130 mg/dl 10-yr. risk <10%: ≥160 mg/dl
0–1 Risk Factors	<160 mg/dl	≥160 mg/dl	≥190 mg/dl 160–189 mg/dl: drug optional

TLC = therapeutic life-style changes.
CHD = coronary heart disease.
From ATP-III Guidelines, National Heart, Lung, and Blood Institute, National Institutes of Health.

secondary prevention trials have demonstrated benefits with regimens ranging from 75 mg daily, 100 mg daily, to 325 mg every other day. Meta-analysis of 5 primary prevention trials showed that aspirin therapy reduced the risk for CHD by 28%. These trials also suggested that the rate of gastrointestinal bleeding is approximately 2–4 per 1,000 middle-aged individuals given aspirin for 5 years. Enteric-coated or buffered preparations do not clearly reduce the adverse gastrointestinal effects.

The USPSTF strongly recommends that clinicians discuss aspirin chemoprevention with adults who are at increased risk for coronary heart disease (Grade A recommendation). Men older than 40 years, postmenopausal women, and younger people with risk factors for coronary heart disease (hypertension, diabetes, or smoking) are at increased risk for heart disease and may wish to consider aspirin therapy. Currently, the American Diabetes Association recommends aspirin 75–325 mg daily in all adult patients with diabetes and macrovascular disease. The American College of Cardiology and the American Heart Association in 1997 recommended that daily aspirin therapy at 75–325 mg/day be considered for all patients at elevated risk of subsequent events due to a history of vascular disease. They stated that consideration should be given to a patient's particular cardiovascular risk profile, the demonstrated benefits of aspirin on reducing the risk of a first AMI, and aspirin side effects.[86] Aspirin is not generally recommended in patients less than 21 years of age due to the increased risk of Reye's syndrome.

ATRIAL FIBRILLATION AND STROKE—Atrial fibrillation (AF) is the most common sustained arrhythmia and is an important independent risk factor for stroke. It occurs in more than 2 million people in the United States. Prevalence increases after age 40 and rises rapidly after age 65. The median age of patients with AF is approximately 75 years. The rate of ischemic stroke in patients with AF and not treated with antithrombotic therapy averages about 5% per year. Management of AF is related to control of the arrhythmia itself, restoring and maintaining sinus rhythm, or ensuring that the ventricular rate is controlled, such as with the use of β-blockers, sotalol, or amiodarone, and prevention of thromboembolic complications. The risk for thromboembolism increases in patients with a prior stroke or TIA, history of hypertension, congestive heart failure, advanced age, diabetes mellitus, and coronary artery disease. Intensity of anticoagulation involves a balance between prevention of ischemic stroke and avoiding hemorrhagic complications. The American College of Chest Physicians recommendations for anticoagulation in patients with atrial fibrillation are found in Table 126-14. For patients that have suffered a recent stroke or TIA as a result of a cardioembolic event, oral anticoagulation (warfarin), with a target INR of 2.5 and range of 2–3 is recommended.[87] The Sixth ACCP Consensus Conference on Antithrombotic Therapy recommends that every patient who has experienced a noncardioembolic stroke or TIA and has no contraindications receive an antiplatelet agent regularly to reduce the risk of recurrent stroke or other vascular events. Aspirin, 50–325 mg daily, Aggrenox 200 mg twice daily, or clopidogrel 75 mg daily are all acceptable options for initial therapy. Aggrenox is more effective than aspirin alone and may be more effective than clopidogrel, with a similarly favorable serious adverse effect profile.

CHRONIC STABLE ANGINA—For patients that have already suffered an AMI, therapy should be routinely prescribed in patients without contraindications. These agents should also be considered first-line therapy for patients with angina.

The ACC/AHA 2002 guidelines for the management of patients with chronic stable angina recommendations for drug therapy to prevent MI and death in asymptomatic patients are presented in Table 126-15. Recently, an important trial, called Heart Outcomes Prevention Evaluation (HOPE), showed that use of the ACE inhibitor ramipril (10 mg/d) reduced the incidence of cardiovascular death, AMI, and stroke in patients who were at high risk for, or had, vascular disease in the absence of heart failure.[88] The primary outcome in HOPE was a composite of cardiovascular death, MI, and stroke. However, the results of HOPE were so definitive that each of the components of the primary outcome by itself also showed statistical significance. Furthermore, only a small part of the benefit could be attributed to a reduction in blood pressure (22–23 mmHg). These results led to the addition of ACEI to these newest recommendations.

UNSTABLE ANGINA—The American College of Cardiology and the American Heart Association recommend that patients with unstable angina and non-ST-segment elevation MI be placed on aspirin as soon as possible after presentation of symptoms, and continued indefinitely. Recent changes to the guidelines were made to include the addition of clopidogrel, and the combination continued up to 9 months.[87a]

VITAMINS FOR CHD PREVENTION—Homocysteine is a sulfur-containing amino acid generated during the metabolism of methionine from dietary protein. Vitamins B6, vitamin B12, and folic acid are important cofactors in this metabolic process, and deficiencies of these vitamins may cause

Table 126.14. Recommendations for Patients with Atrial Fibrillation Considered for Chronic Oral Anticoagulation Therapy

AGE	MAJOR RISK FACTORS[a]	RECOMMENDATIONS FOR LONG-TERM THERAPY
<65	No major risk factors	Aspirin
<65	Major risk factors	Warfarin[b]
65 to 75	No major risk factors	Aspirin or Warfarin[b]
65 to 75	Major risk factors	Warfarin[b]
>75	All patients	Warfarin[b]

[a] Previous TIA, stroke, or systemic embolism; poor left ventricular function (moderate to severe left ventricular dysfunction on echocardiography, or recent CHF); hypertension
[b] Goal INR = 2.5; range = 2.0 − 3.0.
Data from Albers GW, Dalen JE, Laupacis A, et al *Chest* 2001;119:1945S.

Table 126-15. Recommendations for Drug Therapy to Prevent MI and Death in Asymptomatic Patients

Class I
1. Aspirin in the absence of contraindication in patients with prior MI. *(Level of Evidence: A)*
2. Beta-blockers as initial therapy in the absence of contraindications in patients with prior MI. *(Level of Evidence: B)*
3. Lipid-lowering therapy in patients with documented CAD and LDL cholesterol greater than 130 mg/dL, with a target LDL of less than 100 mg/dL. *(Level of Evidence: A)*
4. ACE inhibitor in patients with CAD* who also have diabetes and/or left ventricular systolic dysfunction.*(Level of Evidence: A)*

Class IIa
1. Aspirin in the absence of contraindications in patients without prior MI. *(Level of Evidence: B)*
2. Beta-blockers as initial therapy in the absence of contraindications in patients without prior MI. *(Level of Evidence: C)*
3. Lipid-lowering therapy in patients with documented CAD and LDL cholesterol 100 to 129 mg/dL, with a target LDL of 100 mg/dL. *(Level of Evidence: C)*
4. ACE inhibitor in all patients with CAD[a] or other vascular disease. *(Level of Evidence: B)*

[a] Significant CAD by angiography or previous MI.

From Gibbons RJ, Abrams J, Chatterjee K, Daley J, Deedwania PC, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Chronic Stable Angina). *Circulation* 2003;107:(1):149–58 © 2003 Lippincott Williams & Wilkins.

an elevated homocysteine level. Accumulation of homocysteine levels has been associated with increased risk of heart disease, and the American Heart Association has recognized homocysteine as a potential risk factor for vascular disease. Several studies have demonstrated an inverse relationship between folic acid consumption and homocysteine levels. In the Nurses Health Study, women who were in the lowest quintile of folic acid and vitamin B6 consumption had nearly a 2-fold increased risk of coronary heart disease.[89] For those patients that do not obtain adequate reduction of homocysteine through dietary measures, supplementation of folic acid, alone or with pyridoxine and cyanocobalamin, is useful. The optimal dose of folic acid is uncertain, but appears to be around 1 mg/day, causing a maximum reduction in homocysteine levels of about 25%. Currently there are no randomized controlled trials that demonstrate a benefit to homocysteine reduction on mortality, although trials are ongoing. As mentioned previously, in 2003, the USPSTF stated that the evidence was insufficient to recommend for or against the use of vitamins A, C, or E, multivitamins with folic acid, or antioxidant combinations for the prevention of cancer or cardiovascular disease (Grade I recommendation).[31] In 1999, A Statement from the American Heart Association was made stating that routine screening for hyperhomocysteinemia cannot be recommended at the present time due to lack of definitive evidence for clinical benefit. They stated that the clinician may consider determining levels in patients who are at "high risk" for hyperhomocysteinemia, including those with a strong family history of premature atherosclerosis, advanced age men and postmenopausal women, hypothyroidism, impaired kidney function, lupus, and those taking certain medications, such as niacin, theophylline, and methotrexate. A reasonable therapeutic goal for homocysteine levels in patients at risk for cardiovascular disease is <10 μmol/L.

The Heart Protection Study, a randomized trial of 20,536 patients with coronary disease, other occlusive arterial disease, or diabetes, compared placebo, vitamin E 600 mg, vitamin C 250 mg, and B-carotene 20 mg over a 5-year period. No significant differences were found in any of the outcome categories, including all-cause mortality, deaths from vascular or nonvascular causes, nonfatal myocardial infarction, or coronary death, nonfatal or fatal stroke, or coronary or noncoronary revascularization.[84] Results from the Physician's Health Study, a prospective cohort of 83,639 male physicians in the United States with no history of CVD or cancer, failed to show an association of self-selected supplement use (vitamin E, vitamin C, and multivitamins) on total CVD or CHD mortality after a mean follow-up period of 5.5 years.[90] These results suggest that while vitamin supplementation for patients at risk of coronary artery disease does not appear harmful, their use should not take the place of the proven therapies of aspirin, β-blockers, lipid-lowering therapy, and ACEI. There is currently no basis for recommending that patients take vitamin C or E supplements or other antioxidants for the express purpose of preventing or treating CAD.

HORMONE REPLACEMENT THERAPY

In 1993, the Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial, which tested healthy postmenopausal women with no history of CHD with placebo, unopposed estrogen, or one of 3 combination estrogen/progestin combinations, had suggested that hormone replacement therapy may be beneficial for the prevention of coronary heart disease, due to benefits of increasing HDL-C, lowering LDL-C, and lowering fibrinogen levels.[91] Newer results from HERS suggested that patients with a history of CHD should not begin treatment with HRT for the prevention of AMI due to the increased incidence of CHD events during the first year of therapy, and a lack of overall benefit on the development of CHD and prevention of AMI.[92] In 2003, data was released from the Women's Health Initiative trial, comparing the safety and efficacy of estrogen plus progestin *versus* placebo for an average of 5.2 years in postmenopausal women without a history of CHD. Absolute excess risks per 10,000 person-years attributable to estrogen plus progestin were 7 more CHD events, 8 more strokes, 8 more PEs, and 8 more invasive breast cancers, while absolute risk reductions per 10,000 person-years were 6 fewer colorectal cancers and 5 fewer hip fractures. The absolute excess risk of events included in the global index was 19 per 10,000 person-years. Coronary heart disease mortality was not significantly increased. These results demonstrated that the risk-benefit profile of HRT is not a viable option for primary prevention of chronic diseases.[93] Also in 2002, the HERS II results (after an additional unblinded follow-up period of 2.7 years after the 4.1 year average duration of HERS) showed no significant decreases in rates of primary CHD events or secondary cardiovascular events among women treated with HRT compared with placebo.[94]

The results of the Women's Angiographic Vitamin and Estrogen (WAVE) trial found that postmenopausal women with heart disease who took hormone therapy either alone or in combination with high-dose antioxidant vitamins A and E did not have fewer heart attacks. Unlike the WHI study, WAVE participants did have prior evidence of heart disease, and although a much smaller study, adds to the evidence that HRT is not helpful in either preventing or treating heart disease.[95]

After evaluating evidence of both the benefits and harms of combined estrogen and progestin therapy, the U.S. Preventive Services Task concluded that HRT does not decrease and may increase the incidence of CHD. The effects of HRT on CHD mortality are less certain.[96] Further discussion of this topic will continue in the osteoporosis section.

OSTEOPOROSIS

DIAGNOSIS—Osteoporosis is a disease in which bones become fragile and more likely to break. In the absence of proper prevention or treatment, osteoporosis can progress painlessly until a bone breaks. Bone mineral density (BMD) reflects the balance between bone resorption and formation. Peak BMD is reached from age 20–35 for men and women. Osteoporosis occurs when resorption exceeds formation, with resultant bone loss. It is diagnosed based on T-scores, with the gold standard measurement being dual energy x-ray absorptimometry (DXA) of the hip and spine BMD. A T-score is the number of standard deviations away from the mean BMD for the young normal population. Patients with normal bone mass have T-scores greater than −1, osteopenia is a T-score of −1 to −2.5, and a T-score less than −2.5 is defined as osteoporosis by the World Health Organization. While skeletal x-rays demonstrate osteoporosis, they do not reliably do so until bone loss is greater than 20–30%. X-rays are of limited value in estimating bone mass.

SEQUELA—Annually, osteoporosis is responsible for 1.5 million fractures, typically in the hip, spine, and wrist. There are 10 million Americans (8 million women and 2 million men) with osteoporosis, and another 34 million Americans with low bone mass. Osteoporosis can be classified as postmenopausal (ie, due to estrogen deficiency), age-related, or secondary (ie, caused by certain medications such as steroids, or diseases such as malabsorption, cancer, or kidney or liver disease). Risk factors for osteoporotic fractures can be found in Table 126-16. Interested readers are referred to the National Osteoporosis Foundation website at www.nof.org.

Postmenopausal women who present with fractures should be evaluated by BMD testing to confirm the diagnosis and determine the disease severity. There is general consensus that measurement of BMD should be considered in patients receiving glucocorticoid therapy for 2 months or more and in patients with other conditions that place them at high risk for osteoporotic fractures. The USPSTF recommends that women age >65 years be screened routinely for osteoporosis and that patients with increased risk for osteoporotic fractures begin screening at age 60 (class B recommendation). No recommendation for or against routine screening is made for postmenopausal women younger than 60 or in women age 60–64 who are not at increased risk for osteoporotic fractures (class C recommendation).

Prevention of Osteoporosis

DIETARY APPROACHES—Adequate intake of calcium and vitamin D are important for the prevention of bone loss. It is recommended that adults age 19–50 years ingest 1000 mg of elemental calcium/day, while those older than 51 years should ingest 1,200 mg/day. Requirements of vitamin D increase as one gets older, going from 200 IU/day for those 19–50 years, to 400 IU/day for those 51–70 years, and 600 IU/day for those older than 71 years. Most Americans do not meet the requirements of calcium intake in their food, from sources such as milk, yogurt, cheese, ice cream, and fortified orange juice. Often these patients need to obtain calcium from one of the many available supplements. Between 5 and 15 minutes of casual daily exposure (without sunscreen) to sunlight is usually sufficient to produce one's vitamin D requirements. Patients who spend little time outdoors, or keep their bodies covered, with minimal sun exposure, need to find other sources. Dietary sources of vitamin D include fatty fish, dairy products, and liver. Milk is fortified with 400 IU/quart of vitamin D. Patients that have limited sun exposure and do not drink milk may need to use vitamin D supplements. Caffeine has been inconsistently associated with decreased bone mass. Teenage girls who drink a lot of carbonated beverages have an increased risk of fractures, in part due to decreased consumption of milk and therefore calcium, in favor of carbonated beverages.[97] Other possible dietary factors that influence risk for fractures include low vitamin K intake, low protein intake, and excessive vitamin A intake.

Table 126-16. Risk Factors for Osteoporotic Fracture

Personal history of fracture after age 50
History of fracture in a first-degree relative
Current cigarette smoking
Low body weight (less than 127 pounds)
Estrogen deficiency (early menopause <45 years) or bilateral oviarectomy; prolonged premenopausal amenorrhea (>1 year)
Caucasian or Asian race
Advanced age
Female sex
Low calcium and vitamin D intake (lifelong)
Alcoholism
Impaired eyesight despite adequate correction
Recurrent falls
Inactive life-style
Poor health/frailty
Medications: glucocorticoids, excessive thyroid replacement, long-term heparin, lithium, chemotherapy

The four items in **bold** are key factors in determining risk of hip fracture independent of BMD.

LIFE-STYLE MODIFICATIONS—Smoking increases one's risk of hip fracture and is associated with decreasing BMD. It is recommended to avoid tobacco use to help improve BMD. Alcohol use has been associated with a low BMD and an increased risk of fractures, but this has not been consistently demonstrated. Moderation of alcohol consumption is recommended despite this lack of evidence, especially when one considers the increased risk of falls associated with excessive alcohol intake. Physical activity for patients with osteoporosis should be encouraged. Regular exercise, especially resistance and high-impact activities, contributes to the development of high peak bone mass and may reduce the risk of falls in older individuals.

PHARMACOLOGIC INTERVENTIONS FOR PREVENTION AND TREATMENT—The National Osteoporosis Foundation suggests initiating therapy to reduce fracture risk in women with T-scores below −2 in the absence of risk factors and in women with T-scores below −1.5 if other risk factors are present. In patients over 70 with multiple risk factors, treatment may be warranted without BMD testing, due to the high risk of osteoporosis. The U.S. Food and Drug Administration has approved hormone replacement therapy, bisphosphonates, raloxifene, and calcitonin for osteoporosis prevention or treatment, or both. Bisphosphonates inhibit osteoclast-mediated bone resorption and have been shown to increase BMD at the spine and hip in a dose-dependent manner, as demonstrated from RCT. They consistently reduce the risk of vertebral fractures by 30–50%. Alendronate and risedronate reduce the risk of nonvertebral fractures in women with osteoporosis and adults with glucocorticoid-induced osteoporosis. Raloxifene, a selective estrogen-receptor modulator (SERM), has been shown to reduce the risk of vertebral fracture by 36% in large clinical trials. Salmon calcitonin has demonstrated increases in BMD at the lumbar spine, but exhibits less clear effects on the hip. RCT have demonstrated that estrogen therapy increases bone density and decreases bone resorption. The greatest benefit from HRT occurs during the first years following menopause. Unopposed estrogen should not be used in patients with an intact uterus due to the increased risk of endometrial cancer. Women with a history of unexplained vaginal bleeding, breast cancer, or thromboembolism should not take HRT. Results from the HERS II trial showed that treatment for 6.8 years with HRT in older women with coronary disease doubled the rate of venous thromboembolism and increased the risk of biliary tract surgery by 1.44 (95% CI, 1.10–1.90, p = 0.01).[98]

A meta-analysis of 22 trials of estrogen reported a 27% reduction in nonvertebral fractures (RR 0.73, 95% CI, 0.56–0.94).[99] The HERS trial found no reduction in hip, wrist,

vertebral, or total fractures with hormone therapy (relative hazard for total fractures 1.04; 95% CI, 0.87–1.25).[92] The WHI trial found significant reductions in total fracture risk (RH 0.76; 95% CI, 0.63–0.92) in healthy women taking combined estrogen and progestin. The USPSTF concluded that there was good evidence that HRT increases bone mineral density and fair to good evidence that it reduces fractures.

In response to the release of the HERS and WHI trials, the North American Menopause Society (NAMS) updated its recommendations regarding the use of HRT. It recommends that alternatives should be considered to HRT due to the associated risks, weighing the risks and benefits of each, despite the fact that HRT is approved for treatment of postmenopausal osteoporosis. Additionally, the NAMS feels that lower than standard doses of HRT and estrogen therapy should be considered, based on the Women's Health, Osteoporosis, Progestin, Estrogen (HOPE) Trial.[100] This trial showed equivalent menopausal symptom relief and preservation of bone density without an increase in endometrial hyperplasia with lower doses of HRT.[101] Some authors feel that women using postmenopausal HRT for reasons other than control of menopausal symptoms should be advised to stop.[102] Other authors feel that long-term HRT should be offered to women at high risk of osteoporosis or with established osteoporosis.[103] Clinicians should carefully consider each individual patient's risks and benefits before deciding on the use of HRT for osteoporosis, as the debate will likely continue for some time. Pharmacists can help patients in their decision-making process by keeping informed about new research that is conducted and recommendations that are released.

ALZHEIMER'S DISEASE

INCIDENCE—Alzheimer's disease (AD) is the most common form of dementia among older people. It involves the parts of the brain that control thought, memory, and language.

AD usually presents in patients over age 65, but can occur as early as age 40. AD affects 3% of individuals aged 65–74 years, doubling every 5 years beyond age 65. Women are affected twice as often as men. Genetic factors for early onset cases (40–64 years) include chromosomal changes, including 1, 14, and 21. Late-onset AD (≥65 years) is primarily influenced by the apolipoprotein E (apo E) genotype, with the Apo E4 allele serving as a risk factor for development of AD. Environmental risk factors for AD include alcohol abuse, stroke, repeated or severe head trauma, lower levels of education, and small head circumference.

CHEMOPREVENTION—In a study looking at dietary intake of antioxidants in 5,395 people, higher intakes of vitamins C and E, flavinoids (found in cranberries, green and black tea, and peas and beans), and β-carotene were associated with reduced risk for Alzheimer's disease among smokers. In nonsmokers, vitamins C and E showed a potential protective effect, with risks reduced by 34% and 43%, respectively, among those with greatest intake of the vitamins, compared with those consuming the lowest amounts.[104]

In a second study, only dietary vitamin E was linked to reduced risk of Alzheimer's disease in a study of vitamin C, vitamin E, and β-carotene. Among 815 community-dwelling residents who were 65 years or older, increased intake of vitamin E from foods only was associated with a 70% lower risk of the disease. The protective effect was found only among people with a certain genotype, those without the apolipoprotein E4 gene.[105] It had been suggested from prospective and case-control trials that women taking estrogen lowered their risk of developing AD by 50%. However, results from the Women's Health Initiative Memory Study (WHIMS) contradict this. It randomly assigned 4,894 postmenopausal women aged 65 years or older and free of probable dementia at baseline to estrogen plus progestin or placebo. After an average of 4 years of follow up, 61 women were diagnosed as having dementia, 40/2229 women in the hormone group and 21/2303 in the placebo group.[106] In a related study, also from WHIMS, global cognitive function did not improve when compared with placebo. Most women on the hormone treatment did not experience clinically relevant adverse effects on cognitive function; however, a small increased risk of clinically meaningful cognitive decline occurred in the hormone group.[107] One possible explanation of this increased risk may be due to an increase in vascular-related dementia. This adds further fuel to the increased risks of HRT and that they should not be used for preventive measures.

THYROID DISEASE

DIAGNOSIS—Thyrotoxicosis, or hyperthyroidism, occurs when tissues are exposed to increased levels of thyroxine (T4), triiodothyronine (T3), or both. It occurs more commonly in women, with an annual incidence of 3 per 1,000. Hypothyroidism occurs in 1–2% of women, and 0.2% of men, with the incidence increasing with increasing age. Primary hypothyroidism (due to thyroid gland dysfunction) is the most common, with typical causes being Hashimoto's disease, or iatrogenic (due to exposure to radiation or thyroid surgery). Secondary hypothyroidism occurs as a result of diseases of the pituitary or hypothalamus. Common symptoms in hypothyroidism include fatigue, weight gain, cold intolerance, bradycardia, constipation, depression, and skin and hair dryness. Hyperthyroidism, on the other hand, presents with symptoms nearly opposite, including weight loss, heat intolerance, tachycardias or palpitations, hyperdefecation, nervousness, and hyperhydrosis.

SCREENING—The preferred method of screening for thyroid dysfunction is the thyroid stimulating hormone (TSH) test. A free thyroxine test should be done when the TSH level is undetectable or is ≥10 mU/L. Patients who have an undetectable TSH level and an elevated free thyroxine level have overt hyperthyroidism. Patients who have a TSH level >10 mU/L and a low free thyroxine level have overt hypothyroidism. Patients exhibiting either of these conditions are likely to benefit from appropriate treatment. In the case of hypothyroidism, treatment typically includes long-term thyroid replacement therapy. For thyrotoxicosis, treatment consists of propylthiouracil or methimazole, iodine-containing compounds, radioactive iodine, and surgery. Subclinical hypothyroidism occurs when patients exhibit slightly elevated TSH, but normal T4 and T3, and may or may not have symptoms. Currently there is insufficient evidence to recommend for or against treatment of subclinical hypothyroidism.

The exact age to begin screening for thyroid disease is debatable. The American College of Physicians and the American Society of Internal Medicine recommend screening women older than 50 years of age for unsuspected but symptomatic thyroid disease. However, the American Thyroid Association recommends that adults begin screening at the age of 35 years, and repeat screening every 5 years thereafter. The most compelling evidence is in women, but may be justified in men in the context of the periodic health exam.[108–111]

DEPRESSION

INCIDENCE—Approximately 20% of the US population is affected by mental illness during a given year. Of all mental illnesses, depression is the most common disorder, affecting more than 19 million adults in the United States. Major depression is the leading cause of disability and is the cause of more than two-thirds of suicides each year. Depression is associated with other medical conditions, such as heart disease, cancer, and diabetes as well as anxiety and eating disorders. Depression also has been associated with alcohol and illicit drug abuse. An estimated 8 million persons aged 15–54 years had coexisting mental and substance abuse disorders in 2002. The total estimated direct and indirect cost of mental illness in the United States in 1996 was $150 billion.

FACTORS CAUSING DEPRESSION—Certain drug therapy is associated with depression, eg, antihypertensive medications, (including reserpine, methyldopa, clonidine, hydralazine, and propranolol), and hormone therapy (oral contraceptives or corticosteroids). It has been suggested that isotretinoin may cause depression, although the mechanism is unknown. If a medication is suspected of causing psychiatric symptoms, patients should discuss their symptoms with their health provider so that the medication can be discontinued and an alternative therapy selected, if appropriate. Or the patient can begin treatment with a pharmacologic agent for depression.

Adults and older adults have the highest rates of depression. Major depression affects approximately twice as many women as men. Women who are poor, on welfare, less educated, and unemployed are more likely to experience depression. In addition, depression rates are higher among older adults with coexisting medical conditions. For example, 12% of older persons hospitalized for problems such as hip fracture or heart disease are diagnosed with depression. Rates of depression for older persons in nursing homes range from 15% to 25%. Seasonal affective disorder occurs commonly during winter months in patients who have reduced exposure to sunlight, possibly due to a disturbance in the natural circadian rhythm, which is sometimes treated with bright-light therapy.

DIAGNOSIS—The diagnosis of depression is made by qualified health professionals using the criteria in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). Several screening tests are administered before a diagnosis is made, using various questionnaires such as the Beck Depression Inventory and the Zung Self-Rating Depression Scale (SDS). Questionnaires are also available for children.

TREATMENT—Depression is treatable. Available medications and psychological treatments, alone or in combination, can help 80% of those with depression. With adequate treatment, future episodes of depression can be prevented or reduced in severity. Treatment for depression can enable people to return to satisfactory, functioning lives. The Healthy People 2010 Leading Health Indicator is to increase the number of adults with recognized depression who receive treatment, from 23% in 1997, to 50% in 2010.[1] The USPSTF recommends screening adults for depression in clinical practices that have systems in place to assure accurate diagnosis, effective treatment, and followup (B recommendation). They found good evidence that screening improves the accurate identification of depressed patients in primary care settings and that treatment of depressed adults identified in primary care settings decreases clinical morbidity. However, the USPSTF concludes the evidence is insufficient to recommend for or against routine screening of children or adolescents for depression (I recommendation).[111a]

Pharmacists can be effective at identifying patients with risk factors for depression and observing patient behavior for signs of depression that may suggest the need for further evaluation and treatment. By identifying potential modifiable causes and encouraging patients to seek medical treatment, pharmacists can have an impact in reducing the morbidity and mortality of this disease.

RESPONSIBLE SEXUAL BEHAVIOR

Unintended pregnancies and sexually transmitted diseases (STDs), including infection with the human immunodeficiency virus that causes AIDS, can result from unprotected sexual behaviors. Abstinence is the only method of complete protection. If used correctly and consistently, condoms can help prevent both unintended pregnancy and STDs.

In 1999, 85% of adolescents abstained from sexual intercourse or used condoms if they were sexually active. In 1995, 23% of sexually active women reported that their partners used condoms. The Healthy People 2010 goal is to increase from 85% to 95% the number of adolescents in grades 9–12 who are not sexually active, or sexually active and use condoms, and to increase from 23% to 50% the number of sexually active unmarried women, age 18–44, who report condom use by their partners.[1]

Sexually transmitted diseases are common in the United States, with an estimated 15 million new cases of STDs reported each year. Almost 4 million of the new cases of STDs each year occur in adolescents. Women generally suffer more serious STD complications than men, including pelvic inflammatory disease, ectopic pregnancy, infertility, chronic pelvic pain, and cervical cancer from the human papilloma virus. African Americans and Hispanics have higher rates of STDs than whites. The total cost of the most common STDs and their complications is conservatively estimated at $17 billion annually in the US.

Human Immunodeficiency Virus (HIV)

INCIDENCE—Worldwide, 42 million people are estimated to be living with HIV/AIDS. Of these, 38.6 million are adults, 19.2 million are women, and 3.2 million are children under 15. Currently the Centers for Disease Control and Prevention (CDC) estimates that between 800,000 and 900,000 Americans are living with HIV. It is estimated that approximately 40,000 new HIV infections occur in the US each year. Also, the number of people living with AIDS is increasing, as effective new drug therapies are keeping HIV-infected persons healthy longer and dramatically reducing the death rate.

GUIDELINES FOR PREVENTION AND TREATMENT—The CDC regularly provides updates to their guidelines for the prevention and diagnosis of STDs, including HIV. These guidelines recommend testing for HIV in all patients who seek evaluation and treatment of STDs.[112] This should be performed in addition to counseling (both pretest and posttest counseling). HIV infection is diagnosed by tests for antibodies to HIV-1 and HIV-2. Antibody testing starts with a sensitive screening test such as enzyme-linked immunosorbent assay (ELISA). Reactive screening tests must be confirmed by a supplemental test, such as Western Blot, or by immunofluorescence assay. If confirmed by a supplemental test, a positive test indicates that a person is infected with HIV and is capable of transmitting the virus to others. HIV is detectable within 3 months after infection in at least 95% of patients. Although a negative antibody test result indicates that a patient is not infected, it cannot exclude the possibility of a recent infection. Patients with a new diagnosis should receive initial behavioral and psychosocial counseling on-site. Providers should be alert for medical or psychosocial conditions that might require immediate attention. Patients should be encouraged to notify their partners (including sex partners and needle sharing) and to refer them for counseling and testing.

Needlestick injuries are fairly common occurrences in the health care field. Guidelines are available from the US Public Health Service for the management of occupational exposure to HIV, HBV, and HCV and recommendations for postexposure prophylaxis. These guidelines are updated regularly, and include such topics as implementation of a bloodborne pathogen policy, treatment recommendations after needlestick injuries, monitoring for adverse effects, and laboratory testing to monitor for seroconversion.[113]

Health care providers should be knowledgeable about the symptoms and signs of acute retroviral syndrome, characterized by fever, malaise, lymphadenopathy, and skin rash, which occur within the first few weeks after HIV infection. This presentation occurs before the antibody test results become positive. Current guidelines suggest that patients with recently acquired HIV infection might benefit from antiretroviral drugs and may be candidates for clinical drug trials. Anyone with an acute HIV infection should be referred immediately to an appropriate HIV care provider. Once detection has been confirmed, this should prompt education efforts to reduce the

spread of HIV to others. This includes counseling patients on high-risk behaviors (eg, sharing of intravenous needles, unprotected sexual behavior).

Chlamydia Infection

INCIDENCE—*Chlamydia trachomatis* is the most common sexually transmitted bacterial pathogen in the US, with an estimated 3 million new infections occurring each year. Chlamydia infections are a major cause of urethritis, cervicitis, and pelvic inflammatory disease (PID) in women and are an important cause of infertility, chronic pelvic pain, and ectopic pregnancy, as well as adverse pregnancy outcomes. Chlamydial infections are associated with a 3–5-fold increased risk for acquiring HIV. Perinatal transmission to infants can cause neonatal conjunctivitis and pneumonia. In men, chlamydia infections cause urethritis, epididymitis, and chronic complications including prostatitis and possibly infertility. Most women and men are asymptomatic, and chlamydia is readily transmitted between sexual partners, allowing for important reservoirs for new infections.

RISK FACTORS—Women and adolescents through age 20 years are at highest risk for chlamydia infection, but most reported data indicate that infection is prevalent among women aged 20–25. Age is the most important risk factor. Other patient characteristics associated with a higher prevalence of infection include being unmarried, African-American race, having a prior history of sexually transmitted disease, having new or multiple sex partners, having had cervical ectopy, and using barrier contraceptives inconsistently. Individual risk depends on the number of risk markers and local prevalence of the disease.

DIAGNOSIS—Clinicians should be observant for signs that suggest chlamydial infection during pelvic examinations of asymptomatic women (eg, discharge, cervical erythema, cervical friability). Positive results are found by cultures of endocervical or urethral samples, or by nucleic acid amplification tests. In patients where chlamydia is detected, assessment for the presence of other sexually transmitted diseases should occur.

TREATMENT—Effective and low-cost treatment of chlamydia is available, including a 7-day course of doxycycline or a single dose of azithromycin, with alternatives including erythromycin, ofloxacin, or levofloxacin. To minimize further transmission of infection, patients treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen. To minimize the risk for reinfection, patients should also be instructed to abstain from sexual intercourse until all of their sex partners are treated.

SCREENING—Repeat infection confers an elevated risk of pelvic inflammatory disease (PID) and other complications when compared with initial infection. Therefore, recently infected women are a high priority for repeat testing for chlamydia. For these reasons, clinicians and health care agencies should consider advising all women with chlamydial infection to be rescreened 3–4 months after treatment. Partners of infected individuals should be tested and treated if infected, or treated presumptively. Clinicians should be sensitive to the potential impact of diagnosing a sexually transmitted disease on a couple.

Screening for chlamydia is a HEDIS measure. The indicator is the proportion of sexually active women between the ages of 15 and 25 who were screened for chlamydia infection at least annually. The USPSTF strongly recommends that routine screening for chlamydial infection occur in all sexually active women aged ≤25 years, and other asymptomatic women at increased risk for infection (A Recommendation). The USPSTF found good evidence that screening for high risk women decreases the incidence of PID. For asymptomatic low-risk women in the general population, the USPSTF makes no recommendation for or against screening routinely for chlamydial infection (C Recommendation), and concludes that the evidence is insufficient to recommend for or against routinely screening asymptomatic men for chlamydial infection (I Recommendation).[114]

Gonococcal Infections

INCIDENCE—In the United States, an estimated 600,000 new *Neisseria gonorrhoeae* infections occur each year. Most infections in men produce symptoms that cause them to seek treatment soon enough to prevent serious events, but this may not be soon enough to prevent spreading to others. Among women, many infections do not produce recognizable symptoms until complications (eg, PID) have occurred. Both symptomatic and asymptomatic cases of PID can result in tubal scarring that can lead to infertility or ectopic pregnancy. Because gonococcal infections among women often are asymptomatic, an important component of gonorrhea control in the US continues to be the screening of women at high risk for STDs. Recommended antibiotics for the treatment of gonococcal infections include single oral dose cefixime, ciprofloxacin, ofloxacin, or levofloxacin, or single dose intramuscular ceftriaxone.

DUAL THERAPY FOR GONOCOCCAL AND CHLAMYDIAL INFECTIONS—Patients infected with *N. gonorrhoeae* often are coinfected with *C. trachomatis*; leading to the recommendation that patients treated for gonococcal infection also be treated routinely with a regimen effective against uncomplicated genital chlamydia infection. Routine dual therapy without testing for chlamydia can be cost-effective for populations in which chlamydial infection accompanies 10–30% of gonococcal infections, because the cost of therapy for chlamydia (eg, $0.50–$1.50 for doxycycline) is less than the cost of testing. Some specialists believe that the routine use of dual therapy has resulted in substantial decreases in the prevalence of chlamydial infection.

PRENATAL CARE

STD SCREENING—Recommended screening tests for sexually transmitted diseases in all pregnant women include the following at the first prenatal visit: HIV, syphilis, and hepatitis B surface antigen. Screening for *Chlamydia trachomatis* is recommended in the first trimester and again in the third trimester in patients at increased risk for chlamydia, such as those with more than one sex partner. Screening for *Neisseria gonorrhoeae* and hepatitis C antibodies should be performed at the first prenatal visit in women at risk or those living in areas where the prevalence is high. Screening for bacterial vaginosis may be conducted at the first visit in asymptomatic patients at high risk for preterm labor, but routine testing in all patients is not currently supported.[115]

The USPSTF recommends that clinicians routinely screen all asymptomatic pregnant women aged 25 years and younger and others at increased risk for infection for chlamydial infection (B recommendation). The USPSTF makes no recommendation for or against routine screening of asymptomatic, low-risk pregnant women aged 26 years and older for chlamydial infection. (C recommendation).

FOLIC ACID DURING PREGNANCY—The American Academy of Pediatrics and the United States Public Health Service recommend that all women of childbearing age who are capable of becoming pregnant should consume 400 micrograms (0.4 milligrams) of folic acid daily to prevent neural tube defects. Because there is a high rate of unplanned pregnancies in the US, efforts at promoting food fortification to provide all women a daily intake of 400 mcg of folic acid is encouraged. In the absence of optimal fortification, women should consume 400 mcg of folic acid daily in addition to eating a healthy diet. Currently, the most convenient, inexpensive, and direct way to meet the recommended dosage is by taking a multivitamin containing 400

mcg of folic acid, but efforts to increase the availability of folic acid-only supplements should be encouraged for women who prefer not to take multivitamins. Because the risk for neural tube defects is not totally eliminated by folic acid use, routine prenatal screening for neural tube defects is still advisable.[116]

Women with a history of a previous pregnancy resulting in a fetus with a neural tube defect should be advised of the results of the British Medical Research Council (MRC) Vitamin Study.[117] This randomized trial compared one of four high-dose folic acid supplementation groups: 4 mg folic acid; multivitamin plus 4 mg folic acid; neither the multivitamin nor folic acid; or multivitamin without folic acid. Outcome information was available for 1,195 pregnancies. Folic acid supplementation was associated with a 71% reduction in the recurrence of neural tube defects. Multivitamins alone were not effective and did not contribute to additional benefit. During times in which a pregnancy is not planned, these high-risk women should consume 400 mcg of folic acid per day. However, they should be offered treatment with 4 mg of folic acid per day starting 1 month before the time they plan to become pregnant and throughout the first 3 months of pregnancy, unless contraindicated. Women should be advised not to attempt to achieve the 4 mg daily dosage of folic acid by taking multivitamins, which typically contain 400 mcg folic acid each, because of the possibility of ingesting harmful levels of other vitamins, such as vitamin A. It should be noted that 4 mg of folic acid did not prevent all neural tube defects in the Medical Research Council study. Therefore, high-risk patients should be cautioned that folic acid supplementation does not preclude the need for counseling or consideration of prenatal testing for neural tube defects.

No intervention or observational studies address prevention for other high-risk persons. Women with a close relative (eg, sibling, niece, or nephew) who had a neural tube defect (risk is approximately 0.3–1.0%), women with Type-1 diabetes mellitus (risk is approximately 1%), women with seizure disorders being treated with valproic acid or carbamazepine (risk is approximately 1%), and women or their partners who have a neural tube defect (risk may be 2–3%) and are planning a pregnancy should discuss with their physician the risk for an affected child and the advantages and disadvantages of increasing their daily periconceptional folic acid intake to 4 mg.

UNIVERSAL PRECAUTIONS

Universal precautions include the use of gloves, gowns, masks, and protective eyewear to prevent parenteral, mucous-membrane, and non-intact skin exposures to pathogens carried in the blood, such as HIV, hepatitis B, hepatitis C, and others. These pathogens may be carried in blood and body fluids such as semen, vaginal secretions, and cerebrospinal, pleural, synovial, peritoneal, pericardial, and amniotic fluids. When exposure to body fluids is expected, wearing proper protection is essential to infection control. Hand-washing is the single most important method to prevent transmission of infectious agents. Hands should be washed before and after each contact with patients, body fluids, and contaminated or soiled materials; between dirty and clean procedures on the same patient, after removing gloves; before and after performing invasive procedures; after using the rest room; and whenever hands are visibly soiled. The U.S. Occupational Safety and Health Administration (OSHA) and U.S. National Institute for Occupational Safety and Health (NIOSH) guidelines require use of special masks—National Institute for Occupational Safety and Health certified N-95 respirators—when caring for patients with contagious tuberculosis; use of these masks requires education to ensure proper fit.

HEPATITIS B—Immunization with hepatitis B vaccine is mandated by Occupational Safety and Health Administration for all persons whose job might involve exposure to blood or blood-containing body fluids. This consists of a series of three IM injections into the deltoid over a period of several months. Individual doses of the vaccine are dependent on the actual product used. If patients extend the interval beyond what is recommended, the series can simply be completed, with no need to start over. Response to the vaccine can be measured by anti-Hepatitis B levels (anti-HB) at 1–6 months after completion of the vaccine series. Vaccine nonresponders or inadequate responders may need subsequent booster vaccinations.

TUBERCULOSIS—In adults, screening for tuberculosis using the Mantoux skin test should be performed before health care employment to ensure active tuberculosis is detected early and treated. A test is considered positive in a healthy health care professional if an area of induration of at least 10 mm is detected. For persons with underlying conditions or known household exposure to tuberculosis, 5 mm of induration is considered positive. If the Mantoux test is positive, the employee is referred for evaluation and appropriate management. The frequency of repeat skin testing for purified protein derivative (PPD)-negative employees should be based on the risk of exposure to people with active tuberculosis. Risk factors will vary from employee to employee; yearly testing should be considered in practices where there has been a high rate of documented tuberculosis or skin test conversion among families and patients or among health care professionals. Consultation with local health departments is useful to determine the prevalence of tuberculosis in the local area.[118]

IMMUNIZATIONS

CHILDREN—Prior to the practice of routine immunizations, vaccine-preventable diseases were a major cause of morbidity and mortality in children. Recommendations for childhood vaccinations are approved by the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians.[119] Each year these guidelines are updated, and the recommendations from 2003 include vaccination against the following diseases: hepatitis B, diphtheria, tetanus, pertussis, Haemophilus influenzae Type b (Hib), polio, measles, mumps, rubella, varicella, and Streptococcus pneumoniae. For children in high-risk states and for certain high-risk groups, vaccination against hepatitis A is recommended. Annual vaccination against influenza is recommended for high-risk factors (eg, asthma, cardiac disease, sickle cell, HIV, diabetes) household members of persons in high-risk groups, anyone wishing to obtain immunity. The recommended vaccination schedule for adolescents and children can be found at www.cdc.gov.

The Healthy People 2010 Leading Health Indicator for vaccinations is to increase the proportion of young children who receive all vaccines that have been recommended for universal administration from 73% in 1998 to 80% by 2010: four or more doses of diphtheria/tetanus/acellular pertussis (DTaP) vaccine, three or more doses of polio vaccine, one or more dose of measles/mumps/rubella (MMR) vaccine, three or more doses of Hib vaccine, and three or more doses of hepatitis B (Hep B) vaccine.[1]

Barriers to childhood vaccinations include fear of adverse reactions, the unfounded fear that in fact vaccinations cause autism, concern over the long-term impact of the vaccine on the immune system, fear of multiple injections at one time, areas of poor access to vaccines, and lack of motivation by the parents. Strategies for high immunization levels include proper record keeping, recommendation to get the vaccine and reinforcement to return for follow up, reminder and recall messages to patients and providers, reduction of missed opportunities, and reduction in barriers to immunization within the practice.

ADOLESCENTS AND ADULTS—In 2002, the Advisory Committee on Immunization Practices approved for the first time a schedule for the routine vaccination of persons aged ≥19 years. It has been accepted by the American Academy of Family Physicians and the American College of Obstetrics and Gynecology, and will be updated annually.[120] This includes recommendations on tetanus, diphtheria, influenza, pneumococcus,

Table 126-17. Topics for Preventive Counseling in Adults and Adolescents

Tobacco use
Substance abuse, driving under impairment
Nutrition
Optimal body weight
Exercise
Injury prevention: seat belts, gun safety, household safety
Dental hygiene
Responsible sexual behavior
Stress management
Sleep hygiene

Hep B, Hep A, measles, mumps, rubella, varicella, and meningococcus. Included in these recommendations are recommendations for adults with certain medical conditions, such as pregnancy, diabetes, heart disease, renal failure, asplenia, and immunocompromised conditions such as HIV and malignancies. Both schedules can be found at www.cdc.gov.

Boosters against tetanus and diphtheria are recommended every 10 years by the CDC, while the American College of Physicians Task Force on Adult Immunizations supports giving a single Td booster at age 50 years for persons who have completed the full pediatric series.

Immunizations against influenza and pneumococcal disease can prevent serious illness and death. Pneumonia and influenza deaths together constitute the sixth leading cause of death in the United States. Influenza causes an average of 110,000 hospitalizations and 20,000 deaths annually; pneumococcal disease causes 10,000–14,000 deaths annually. For adults, the Leading Health Indicator is to increase the proportion of noninstitutionalized adults who are vaccinated annually against influenza (from 64% in 1998 to 90% by 2010) and ever vaccinated against pneumococcal disease (from 46% in 1998 to 90% by 2010). Coverage levels for immunizations in adults are not as high as those achieved in children, yet the health effects may be just as great. Low-income and minority children and adults are at greater risk for under-immunization. Barriers to adult immunization include not knowing immunizations are needed, misconceptions about vaccines, fear of injections, and lack of recommendations from healthcare providers.

TRAVEL IMMUNIZATIONS—With improvements in transportation, the ability to travel to far off lands is increasingly easy. With this comes the need for vaccination against infectious diseases found in these countries. Recommendations for travel vaccines are regularly updated by the CDC web site www.cdc.gov/travel. Pharmacists can assist patients planning to travel abroad to consult an international travel clinic weeks before their expected travel to identify the risks of the particular trip. Travel recommendations will be made based off of the length of the trip, previous travel to the area, the exact location of travel, the expected activities on the trip, the type of accommodations, the food supply that is available, and the health of the traveler. Additional information will be provided about food and water precautions to avoid diarrhea and insect-borne illnesses. Providing information such as boiling drinking water, avoiding uncooked foods or undercooked foods will help prevent the chances of diarrhea. Efforts to minimize getting bitten by mosquitoes, such as wearing light-colored clothing, minimizing perfume, avoiding outdoor activities at dusk or night time, and using insect repellants containing DEET, should be recommended. Vaccinations that may be recommended during international travel include malaria, typhoid fever, yellow fever, cholera, rabies, hepatitis A, hepatitis B, meningococcal, or Japanese encephalitis virus. Specific instructions for each vaccine with regard to timing and number of doses, and potential adverse effects should be reviewed with the patient.

OPPORTUNITIES FOR PHARMACISTS—Pharmacists in all settings are increasing their visibility as a provider of immunizations, as many states, ie, 30 in 2003, now allow pharmacists to administer vaccines within their practice. Training programs such as those offered by the American Pharmacists Association have aided pharmacists in vaccination administration techniques, and have provided them with information to help develop this area of practice in their setting. Further, schools/colleges of pharmacy are now including immunization training in the curricula. The addition of pharmacists as vaccine providers can help achieve overall immunization goals, which are to reduce the morbidity and mortality associated with vaccine-preventable illnesses, and to improve overall vaccination rates.

SUMMARY AND CONCLUSIONS

Preventive care is a challenge that should be undertaken by health care providers in all practice settings. A summary of recommended preventive counseling topics can be found in Table 126-17. Pharmacists should "seize the moment" to educate and counsel patients regarding these various topics when the opportunities arise. Throughout this chapter, disease screening guidelines have been discussed. A current summary of recommendations can be found in Table 126-18. Several medications have evidence to their usefulness for chemoprevention of various diseases. A list of such medications and the diseases

Table 126-18. Preventive Services Screening Recommendations

MEN AND WOMEN
Colorectal cancer
Average risk: Age 50 and older
Higher risk: Age 40 and older
Depression
Screen adults in practices equipped to diagnose, treat, and follow up
Diabetes
Routine community screening is not recommended
Hyperlipidemia
Fasting lipid profile, starting at age 20 years, every 5 years
Hypertension
Screening at each health encounter
Influenza vaccine
Annually, beginning age 65, earlier in higher risk patients
Pneumococcal vaccine
At least one beginning at age 65
Skin Cancer
Variable; routine screening not recommended by some, while others recommend
Tetanus Booster
Every 10 years
Thyroid screening
Age 35 and every 5 years
MEN
Prostate cancer
PSA and DRE: Average risk: men age 50 and older; age 45 and older for higher risk
WOMEN
Breast cancer
Annual mammography: Age 50 and older; some recommend beginning at age 35
Breast self-examination: monthly, beginning at age 20
Clinical breast examination: At least every 2 years
Cervical cancer
Annual Pap smears: Begin when sexually active or age 21 (whichever comes first)
Chlamydia
Annually in sexually active women age 25 and older and others at increased risk
Pregnant women age 25 and younger and others at increased risk
Osteoporosis
Average risk: Age 65
Higher risk: Age 60

Table 126-19. Drugs with Evidence to Prevent Disease Development

DISEASE PREVENTED	DRUG OR DRUG CLASS
Alzheimer's	Vitamin E
Breast Cancer	Tamoxifen and Raloxifene
CAD	Aspirin, Statins
Colorectal cancer	Aspirin, COX-II Inhibitors
Prostate cancer	Finasteride, Selenium
Diabetes	Metformin and Acarbose
DVT	Heparin, LMWHs, Warfarin
Nephropathy	ACEI and ARBs
Osteoporosis	Bisphosphonates, Statins
Hip fracture	Calcium/Vitamin D, Bisphosphonates
NSAID-induced ulcer	Misoprostil and PPIs
Stress ulcer	H2 blockers, Sucralfate
CVD	ACEI
Exercise-induced asthma	Salmeterol, Formoterol
Pregnancy	OCPs
Emergency contraception	Mifepristone, Levonorgestrel
Neural tube defects	Folic acid
Vaccine-preventable illnesses	Vaccinations
Tobacco-related illnesses	Smoking cessation aids
Vitamin deficiencies	Various vitamins
Various infections (SBE, HIV, TB)	Various antibiotics, antivirals

they help prevent can be found in Table 126-19. Opportunities for pharmacists to help bring about awareness of recommendations and risk factors for the development of disease, and educate patients as to the benefits of prevention, occur daily. It is important for the pharmacists on the "front line" to have a general understanding of current recommendations for screening and disease prevention so that they can provide appropriate counseling and care for their patients.

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CHAPTER 127

Hospital Pharmacy Practice

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The practice of hospital pharmacy has evolved in tandem with hospitals and the delivery of health care in the United States. A hospital is "an institution where the ill or injured may receive medical, surgical, or psychiatric treatment, nursing care, food and lodging, etc." as defined in Webster dictionary. While this definition continues to reflect accurately the purpose of today's hospitals, there has been an evolution in the scope of illness and injury care in hospitals, the services provided and the hospital organization itself. Major factors in this evolution have been the advances in medicine and technology and the changing medical needs and expectations of today's society.

The advancements in medicine and technology have allowed care that once required the intensive care of a hospital setting to be delivered in less intensive settings. As a result, we have witnessed the development of ambulatory surgery centers, skilled nursing facilities, home health services, outpatient treatment centers, and multiple chronic disease monitoring programs. Health care leaders continually search for the delivery model that meets the quality, safety, and access expectations of patients at an affordable cost. This quest led to a progression from individual stand-alone hospitals to health systems. These "health systems" include the acute care services that only hospitals are equipped to provide and a cadre of other services that may include primary care, specialty outpatient care, home care, nursing home facilities, hospice care, ambulatory surgery programs, and a network of physicians and other health care providers.

For this chapter, hospital pharmacy is defined as the practice of pharmacy in hospital settings and includes the organizationally related facilities or services. The pharmacy is defined as that department or division of the hospital wherein the procurement, storage, compounding, manufacturing, packaging, controlling, dispensing, and distribution of medications are performed by legally qualified, professionally competent pharmacists and their assistants. In addition to the traditional functions, the practice of pharmacy in a hospital also includes a broad responsibility for the safe and appropriate use of medications, which includes, among other things, the rational selection, dosing, and monitoring of the patients' overall medication-therapy. These professional responsibilities are fulfilled through collaboration with other health care professionals in the daily care of each patient. This collaboration often leads to the development of protocols, guidelines, formularies, policies, and safe medication practices in support of optimal medication use. The responsibilities of pharmacy services, role of hospital pharmacists, and the practice environment combine to make this a rewarding practice with unique characteristics.

UNIQUENESS OF HOSPITAL PHARMACY PRACTICE—A major factor making hospital pharmacy practice unique is the organizational structure of a hospital: a formalized pattern of authority, responsibility, and coordination that affects every department of the overall health care team. The administrator (highest hospital administrative position) implements the policies and philosophies of the governing board, delegates authority, and passes on responsibility to department leaders to carry out the patient care, teaching, research, and public-health objectives of the hospital. Department leaders, such as the director of pharmacy, are expected to coordinate their services and activities with other department leaders. The business and finance departments handle the financial affairs; the building services departments provide the essential maintenance and security functions; the human resources department implements personnel policies; the clinical laboratory department performs a multitude of patient laboratory tests and services; the nursing service provides continuous care; and dozens of other departments influence and affect the services of all hospital departments. Pharmacists work with various departments to assure the safe, efficient, and cost-appropriate distribution and use of medications, as well as practice as a team with physicians, nurses, and other health care professionals to care for patients of the hospital.

In addition to the internal forces operating within the hospital, the following is a listing of some external forces that affect the practice of pharmacy in the hospital setting:

- Accreditation agencies exert their influence on professional standards of practice as they affect patient care.
- Licensing agencies exert legal influences on hospital operations.
- The federal government imposes standards and regulations on hospitals, such as the *Conditions of Participation for Hospitals* under Medicare. Third-party payers exert their influence on the methods by which hospitals may bill and be reimbursed for services rendered to patients.
- The Office of Inspector General (OIG) establishes and enforces compliance standards for hospitals to detect and prevent fraud and abuse in the health care industry.
- Social agencies and governmental welfare agencies influence the services provided to medically indigent and totally indigent patients.
- The governing board and public opinion exert their influences over the policies, objectives, and philosophies of hospital operations and practices.

Because the hospital is an institution of and for the community, it is influenced heavily by the needs, expectations, and demands of the members of that community. These influences directly or indirectly impact the practice of pharmacy that must support the mission and goals of the hospital.

The hospital pharmacy has several basic general functions. These functions have been outlined in a document approved by the American Hospital Association (AHA), "Statement on Functions of a Hospital Department."[1] It reads as follows:

> A department carries out its functions according to the philosophy and objectives of the hospital. The governing board estab-

lishes the philosophy and objectives. Accordingly, the pharmacy director reports to the administrator of the hospital. Within the organizational pattern, the functions of the department are:

1. To provide and evaluate service in support of medical care pursuant to the objectives and policies of the hospital.
2. To implement for departmental services the philosophy, objectives, policies, and standards of the hospital.
3. To provide and implement a departmental plan of administrative authority that clearly delineates responsibilities and duties of each category of personnel.
4. To participate in the coordination of the functions of the department with the functions of all other departments and services of the hospital.
5. To estimate the requirements for the department and to recommend and implement policies and procedures to maintain an adequate and competent staff.
6. To provide the means and methods by which personnel can work with other groups in interpreting the objectives of the hospital and the department to the patient and community.
7. To develop and maintain an effective system of clinical and/or administrative records and reports.
8. To estimate needs for facilities, supplies, and equipment and to implement a system for evaluation, control, and maintenance.
9. To participate in and adhere to the financial plan of operation for the hospital.
10. To initiate, utilize, and/or participate in studies or research projects designed for the improvement of patient care and the improvement of other administrative and hospital services.
11. To provide and implement a program of continuing education for all personnel.
12. To participate in and/or facilitate all educational programs that include student experiences in the department.
13. To participate in and adhere to the safety program of the hospital.

It is within this framework that the hospital pharmacist practices. The responsibility is to develop a high quality comprehensive pharmaceutical service, properly coordinate and meet the needs of the numerous diagnostic and therapeutic departments, the nursing service, the medical staff, and the hospital as a whole in the interest of continually improving patient care.

Hospital pharmacy has significantly grown in recent years that it has developed a body of specialized knowledge through its documented literature. It has created a workforce of well-qualified hospital practitioners who have adopted a sound philosophy of professional service and high standards of practice. There is special education and training at the graduate level; and there is a vigorous professional society—The American Society of Health-System Pharmacists (ASHP). This professional organization strives to meet the needs of pharmacists practicing in hospitals and other organized health care settings. The ASHP is actively involved in the provision of continuing education programs, publications, and other services designed to help the institutional practitioner in providing a high level of professional service. The ASHP Best Practices Standards provide documents that offer a point of reference for use by pharmacists in developing and evaluating their programs and services.

Curricula for the professional degree program, Doctor of Pharmacy (PharmD), include an experiential component in hospital practice. Most of the colleges/schools offer an undergraduate course in hospital pharmacy, while a few offer a graduate educational program leading to a Master of Science degree in hospital pharmacy. Concurrently, some of these graduate programs may be coordinated so students can complete a hospital pharmacy residency with their graduate work. The first programs of this type were at the Philadelphia College of Pharmacy and Science (1947), the Jefferson Medical College Hospital (1947), the University of Maryland (1947), the Johns Hopkins Hospital (1947), and the University of Michigan (1948). These combined educational and training programs have contributed much to develop and nurture career-minded, well-trained hospital pharmacists. Graduates of these programs have taken leadership positions in hospitals throughout the country and have demonstrated their capabilities through the development of comprehensive pharmaceutical services of broad scope and high quality.

The increasing complexity of medication therapy continues to fuel the need for hospital pharmacists with the skills and expertise that meet the pharmaceutical service needs of hospitals. Hospital pharmacists long recognized the need for additional education and training and developed additional formal education such as residency programs to accomplish these ends.

THE HOSPITAL

Hospital pharmacists practice within the framework of the hospital's organizational structure. For them to function effectively, it is essential that they understand what a hospital is, how it is organized, what its functions are, and how the pharmacy service fits into the overall patient care program.

DEFINITION—As stated by the AHA, the primary function of the institution is to provide patient services, diagnostic and therapeutic, for particular or general medical conditions.[2] Traditionally, a hospital has been defined in terms of its *form,* which includes its physical makeup and the quantitative nature of its services. This definition is exemplified best by the *Registration of Hospitals Program* of the AHA. To be registered under this program, an institution must meet certain requirements that constitute the definition of a hospital. Thus, the program differentiates between a hospital and other institutions such as extended-care facilities, convalescent homes, and homes for the aged.

REQUIREMENTS FOR REGISTRATION BY AHA AS A HOSPITAL[2]

1. The institution shall maintain at least six inpatient beds, which shall be continuously available for the care of patients who are nonrelated and who stay on the average in excess of 24 hours per admission.
2. The institution shall be constructed, equipped, and maintained to ensure the health and safety of patients and to provide uncrowded, sanitary facilities for the treatment of patients.
3. There shall be an identifiable governing authority legally and morally responsible for the conduct of the hospital.
4. There shall be a CEO to whom the governing authority delegates the continuous responsibility for the operation of the hospital in accordance with established policy.
5. There shall be an organized medical staff of fully licensed physicians that may include other licensed individuals permitted by law and by the hospital to provide independent patient care services in the hospital. The medical staff shall be accountable to the governing authority for maintaining proper standards of medical care, and it shall be governed by bylaws adopted by said staff and approved by the governing authority.
6. Each patient shall be admitted on the authority of a member of the medical staff who has been granted the privilege to admit patients to inpatient services in accordance with state law and criteria for standards of medical care established by the individual medical staff. Each patient's general medical condition is the responsibility of a qualified physician member of the medical staff. When nonphysician members of the medical staff are granted privileges to admit patients, a qualified physician makes provision for prompt medical evaluation of these patients. Any graduate of a foreign medical school who is permitted to assume responsibilities for patient care shall possess a valid license to practice medicine, or shall be certified by the Educational Commission for Foreign Medical Graduates, or shall have qualified for and have successfully completed an academic year of supervised clinical training under the direction of a medical school approved by the Liaison Committee on GAT Medical Education.
7. Registered nurse supervision and other nursing services are continuous.

8. A current and complete medical record shall be maintained by the institution for each patient and shall be available for reference.
9. Pharmacy service shall be maintained in the institution and shall be supervised by a registered pharmacist.
10. The institution shall provide patients with food service that meets the nutritional and therapeutic requirements; special diets shall also be available.

Hospitals are registered with the AHA as one of four types: general, special, rehabilitation and chronic disease, and psychiatric.

General: The primary function of the institution is to provide patient services, diagnostic and therapeutic, for a variety of medical conditions.

Special: The primary function of the institution is to provide diagnostic and therapeutic services for patients who have specified medical conditions, both surgical and nonsurgical.

Rehabilitation and Chronic Disease: The primary function of the institution is to provide diagnostic and therapeutic services to handicapped or disabled individuals requiring restorative and adjustive services.

Psychiatric: The primary function of the institution is to provide diagnostic and therapeutic services for patients who have psychiatric-related illnesses.

The broad purpose or mission to which that health system aspires also defines hospitals. Hospitals often serve as the focal point for the coordination and delivery of patient care to its community. Thus today, a hospital may be viewed as an organized structure that assembles the health professions, the diagnostic and therapeutic facilities, equipment and supplies, and the physical facilities into a coordinated system for delivering healthcare to the public.

Services provided by hospitals include those for patients in the institution itself (hospitalized patients) and also for patients in ambulatory-care clinics, emergency rooms, and emergency care centers, those in physicians' offices at hospitals, those in extended-care facilities and nursing homes either affiliated with or owned by the hospital, at home, through home health care services, those at wellness centers and those at community or neighborhood health clinics. In most communities, hospitals serve as the focal point of emergency care and treatment in the event of natural disasters, catastrophic accidents, and terrorist attacks.

Certain other definitions are required for proper understanding of the differences between hospitals and patient care institutions other than hospitals. In its accreditation program, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) defines long-term care facilities and divides them into two categories: a Long-Term Health Care Facility and a Resident-Care Facility.[3] These facilities are defined as follows:

Long-Term Health Care Facility—A facility for inpatient care other than a hospital, with an organized medical staff, medical staff equivalent, or medical director, and with continuous nursing service under professional nurse direction. It is designed to provide, in addition to the medical care dictated by diagnoses, comprehensive preventive, rehabilitative, social, spiritual, and emotional inpatient care to individuals requiring long-term health care and to convalescent patients who have a variety of medical conditions with varying needs.

Resident Treatment Facility—A facility providing safe, hygienic living arrangements for residents. Regular and emergency health services are available when needed, and appropriate supportive services, including preventive, rehabilitative, social, spiritual, and emotional, are provided on a regular basis.

These two broad categories cover the various types of long-term care designated by governmental agencies for licensure, certification, and/or reimbursement purposes, including skilled nursing care and intermediate care. Patient care is also delivered in other settings such as

Clinic: A facility or area where ambulatory patients are seen by appointment, treated by a group of physicians practicing together, and where the patient is not confined, as in a hospital. The term *clinic* also is used to indicate the outpatient diagnostic facility operated by a hospital and also facilities operated by other agencies for the care of indigent and medically indigent patients. In the past, the term *clinic* usually has been reserved for facilities of a teaching nature where medical students and resident staff offered treatment to patients unable to afford private practitioners. While the concept of clinics caring for medically indigent patients continues today, networks of clinics are valuable components of today's health care delivery model in the United States.

A*mbulatory Surgery Center:* A facility where patients are admitted, surgical procedures are performed, and patients are discharged following assessment. Recovery from the procedure continues while the patient at home or in other settings.

DEVELOPMENT AND EXPANSION—Greek temples were forerunners of the modern hospital in the sense that they provided refuge and treatment for the sick and also provided for the teaching of young medical students. Temples as the Temple of Aesculapius (Greek god of Medicine) existed in 1134 BC, while the temple at Kos, Greece, was where Hippocrates (born about 460 BC) practiced. Hospitals had their origin in Indian and Egyptian culture during the 6th century BC. The evolution of the hospital is related to the sociological development of the individual's expansion of interest beyond himself and his family to the welfare of the community. Although early hospitals were instituted to remove certain people (eg, the insane, the incurable, the contagious) from society to protect it other hospitals were developed through religious and divine motives. The temples of the gods in early Greek and Roman civilization were used as hospitals where healing was associated with divine powers, while continued illness or death was associated with a lack of purity.

The first hospital on the American continent was built by the Spaniards (led by Cortez) in 1524—The Hospital of the Immaculate Conception in Mexico City. In 1663, the name was changed to The Hospital of Jesus of Nazareth. In the American colonies, a hospital was built in 1663 on Manhattan Island for sick soldiers. The first incorporated hospital in the United States was the Pennsylvania Hospital, established in 1751 through the efforts of Dr. Thomas Bond. It provided physicians in Philadelphia with a place to treat their private patients. Since 1873, the United States population has more than doubled, but the number of hospitals has increased from 149 to approximately 5,800.[4]

One of the major factors in the development and expansion of hospitals was the religious influence. Prior to the Christian era, hospitals were temples dedicated to the god of medicine in which the care of the sick was accompanied by magical, mystical, and religious ceremonies. The doctrines of Jesus Christ intensified the emotions and virtues of love, pity, and charity. These strong motivating forces toward one's fellow man gave impetus to the expansion of hospitals.

Another major factor in the development and expansion of hospitals was the military influence. Much of the stimulus toward medical and surgical progress over the centuries has come from the urgent need for care of the battlefield wounded. This was true during the Roman Empire; it was also true in the US before, during, and after the Civil War. The Civil War, however, focused attention on the inadequacy of hospital construction and also on the lack of nursing care. President Lincoln requested Catholic Sisters to care for wounded army personnel because hospital care was so poor. The Army's work set a pattern for improvement in patient care and combined the military and religious influences on hospital development.

Other factors that influenced the development and expansion of hospitals included:

- The Flexner report on medical education (1910), which caused revolutionary developments in medical education *per se* and in medical internship training, which helped the development of minimum standards for patient care in hospital surroundings.
- The activities of Florence Nightingale during and after the Crimean War, which served as the basis for revolutionizing the

quality of nursing care in hospitals and for the development of schools of nursing.
- The public interest in hospitals through greater dependence and improved confidence in hospital care.

With public dependence and confidence came public support, and this support provided the finances for further development, expansion, and improvement in hospital facilities. This public interest extended its influence into private hospitalization insurance and government participation in health care through Social Security and other health-related agencies. One of the most significant governmental programs that affected the development and expansion of hospital facilities in the United States was the adoption (in 1946) by the Congress of the Hospital Survey and Construction Act. Commonly known as the Hill-Burton program, this act provided federal funds for hospital construction on a matching basis with local communities. From 1946 to 1973, hundreds of new hospitals were built, while hundreds of other hospitals undertook major expansion programs of existing facilities through the availability of government finances through the Hill-Burton Act.

The Congress made funds available for construction and improvement of various health care facilities, including medical and nursing schools, outpatient and extended care facilities, and specialized diagnostic and therapeutic facilities in hospitals, and adopted a number of legislative amendments. In addition, the Social Security Amendments of 1965 (Medicare) had a long-range impact on the development and expansion of hospitals because funds are made available to pay for services of medically indigent patients.

In 1983, Congress enacted significant changes in the method by which hospitals are reimbursed for Medicare patients to hold down escalating hospital costs. A Prospective Payment System was developed to reimburse hospitals at a specific rate based upon the diagnosis of the patient, ie, the diagnosis-related group (DRG). This system of payment has influenced the mechanism by which private insurance companies reimburse the hospital for patient for care. This emphasis on cost containment has prompted a shift from care in hospital settings to care in less expensive ambulatory care settings for many medical services.

Beyond the three basic essentials of human existence (ie, food, clothing, shelter), the hospital has become a necessary instrument for providing a fourth basic element of survival—health. Health care in the United States has come to be defined as a right for all, rather than a luxury for a few. The hospital serves as a major instrument through which health professions are able to provide health care to the people of the community.

CLASSIFICATION—Hospitals may be classified in different ways, including

- type of service
- length of stay
- ownership
- bed capacity

Hospitals are classified by *type of service* such as general, special, rehabilitation and chronic disease, and psychiatric.

Hospitals are classified by *length of stay* as either short-term or long-term. A short-term hospital is one in which the average length of stay of the patient is less than 30 days. Patients with acute disease conditions and emergency needs are usually hospitalized for less than 30 days. General hospitals are short-term, because acutely ill patients usually recover in less than 30 days. Alternatively, a long-term hospital is one in which the average length of stay of the patient is 30 days or longer. Such patients have long-term illnesses, such as psychiatric conditions.

Hospitals are classified by *ownership* usually as governmental or nongovernmental. Hospitals falling into these categories of ownership are:

Governmental Hospitals

Federal
- Armed Forces,
- Veterans Administration
- US Public Health Service

State
- County
- City (municipal)
- City-County

Nongovernmental Hospitals

Nonprofit
- Church related or operated
- Other nonprofit

For profit
- Individual
- Partnership
- Corporation

Federal hospitals are owned and operated by various branches of the federal government. The United States Army, Air Force, and Navy hospitals are usually general medical and surgical hospitals, provided to care for military personnel, although there are specialized mental institutions within these groups. The Veterans Administration (VA) hospitals provide care for additional specialized groups of our population and operate general medical and surgical hospitals and also some mental hospitals.

State hospitals are owned by the state and controlled by a board of control or division of the state government or a similar organization responsible to state government. They are maintained by state appropriations and consist mainly of psychiatric hospitals. In some instances, state hospitals are general hospitals affiliated with a university involved in the training of physicians and other professional personnel, often referred to as teaching hospitals.

County hospitals are owned by the county and financed and controlled similarly to state hospitals, only on a county level. They are usually general hospitals caring for the indigent.

City hospitals are owned, financed, and controlled by the city government. They are usually general hospitals caring for the indigent.

In the nongovernmental hospital group, most institutions are general medical and surgical hospitals, varying only in their control and eligibility for receipt of state funds for charity or indigent patient care. The *proprietary* or *private hospital organized for profit* may be privately or publicly held. These hospitals often represent an investment interest of their owners, and profits are legally shared among the owners.

The *nonprofit,* nongovernmental hospitals are supported financially by fees from paying patients or by contributions from the several religious orders or churches. These hospitals are owned and controlled either by the religious order or diocese, as exemplified by the Catholic churches, by a separate governing board, as in churches of other denominations, or by a not-for-profit corporation in the community.

Community hospitals or private, nonprofit hospitals are owned and operated by members of the community, but with no relationship to the local government. Fees from patients from the community and surrounding area finance them. The cost of providing medical care for the indigent is a problem for the community hospital, and this cost is partially met through local, state, and federal assistance.

Hospitals generally are classified by *bed capacity* according to the following pattern:

Under 50 beds
50–99 beds
100–199 beds
200–299 beds
300–399 beds
400–499 beds
500 beds & over

Using these four general classifications, the approximately 5,800 hospitals in the United States are 85% nongovernmental, short-term, general or special hospitals. These 5,800 hospitals represent approximately 987,440 beds and admit about 35.6 million patients annually.[4]

FUNCTIONS—Traditionally, the hospital's basic purpose for existence has been the treatment and care of the sick and injured. In conjunction with this basic function, hospitals have been concerned with teaching, particularly of medical students, ever since the pre-Christian Era of Greek medicine. Research has been another function of the hospital. In modern times, a fourth function has been assumed by hospitals, namely, public health (ie, preventive medicine, wellness). Thus, the four fundamental functions of hospitals are patient care, education, research, and public health.

Patient Care—Patient care involves the diagnosis and treatment of illness or injury, preventive medicine, rehabilitation, convalescent care, and personalized services. The modern hospital is charged with maintaining and restoring health to the community that it serves through its patient care services. The other three functions are really the servants of patient care, because they contribute either directly or otherwise to the care of the sick and injured. Emergency care of the injured commands prime attention in any hospital—fully as important as the care of the inpatient. Outpatient care also has become an important part of the hospital's responsibility to the community.

Education—This is an important function of the modern hospital, whether it is or is not affiliated with a university. Education as a hospital function is of two major forms:

1. Education of the medical and allied health professions. This form includes physicians; nurses; medical social service workers; medical record librarians; dietitians; radiology and laboratory technicians; medical technologists; respiratory, physical, and occupational therapists; hospital administrators; pharmacists; and others. The hospital's educational program for these groups includes formal programs (such as medical, nursing, and pharmacy schools); in-service training programs for professional personnel, such as residencies; and on-the-job training programs for nonprofessional personnel. Such educational programs are essential; it is only in a hospital that such concentrated facilities are available to provide the necessary practical learning experience for dealing with saving human lives.
2. Education of the patient. This is an important hospital function, the scope of which is seldom realized by the public. It includes providing general education for children confined to long-term hospitalization; special education in the area of rehabilitation—mentally, socially, physically, and occupationally; and special education in health care, for example, teaching patients with diabetes or cardiac disorders to care for their ailment or teaching patients with colostomies to care for their personal needs.

Research—Hospitals conduct research as a vital function for two major purposes: the advancement of medical knowledge against disease and the improvement of hospital services. Both purposes are directed toward the basic aim of better health care for the patient. Examples of research activities in the hospital include devising new diagnostic procedures, conducting laboratory and clinical experiments, developing and perfecting new surgical procedures or techniques, and evaluating investigational medications. Other examples include research to improve administrative procedures for greater efficiency and lower cost to the patient; and designing, developing, and evaluating new equipment and facilities to improve patient care.

In the past, research in hospitals was performed primarily by medical staff. However, in recent years there has been a significant increase in research activities in the various hospital departments by other disciplines. Nursing, for example, is now engaged in significant research designed to improve patient care. Many medications are evaluated in hospitalized patients before they are marketed, and thus, the clinical evaluation of investigational medications presents many opportunities for the hospital pharmacist to participate in research. Pharmacists are involved in many other types of research, such as pharmacokinetic studies involving individualization of medication-dosing in patients, biopharmaceutical studies of medication products and radiopharmaceutical dosage formulations, and pharmacoeconomic studies, as well as administrative and professional studies on medication-distribution systems, the effectiveness of clinical roles of pharmacists, and medication utilization studies.

Public Health—The prime objective of this fourth and relatively new hospital function is to assist the community in reducing the incidence of illness and improving the general health of the population. Examples of public health activities are the close working relationships many hospitals have with public-health departments of communicable diseases; the participation in disease management or detection programs such as diabetes, hypertension, and cancer; the participation in mass public inoculation programs such as those against influenza and various childhood diseases; and the participation of hospital ambulatory care departments in teaching routine hygienic practices, wellness clinics, smoking cessation, and exercise and fitness programs, as well as ways in which patients should care for themselves when illness strikes. Hospital pharmacists have an opportunity to contribute to this function by providing health information brochures and services to outpatients and by instructing patients on the safe use of medications and poison prevention measures.

The terrorist attacks that took place in the United States on September 11, 2001, have redefined the hospital's relationship with public-health agencies. Historically, hospitals have taken part in responding to naturally occurring disasters or catastrophic accidents, such as tornadoes or train wrecks. Hospitals, in cooperation with local health authorities, had developed plans to handle a large number of casualties. However, communities now face a potential of orchestrated terrorism ranging from localized bombings to devastating scenarios such as the use of chemical or biological weapons or nuclear devices inflicting casualties on a massive scale. Hospitals in many communities are collaborating with local, state, and federal authorities to develop comprehensive emergency management plans that include response to large-scale chemical or bioterrorism attacks. The Department of Homeland Security and the Department of Health and Human Services work on a national level to respond to events such as public exposure to biological agents (eg, anthrax, botulism). Stockpiles of pharmaceuticals, including antibiotics and supportive care equipment such as ventilators and personal protective equipment, are warehoused and will be immediately delivered to an affected area. Locally, the disaster team must be prepared to respond to the immediate needs of the community until the supplies and therapeutic agents arrive and the contents are distributed. The pharmacy department should ensure needed supplies of pharmaceuticals are readily available. The pharmacist should work with their colleagues in other hospitals and drug wholesalers to establish a plan to treat their potential patients and the hospital's employees.

STANDARDS OF PRACTICE—In the United States, a level of protection for the public is provided through an accreditation process requiring that hospitals comply with certain standards of care. The accreditation program is conducted on a national basis, and its purpose is to determine the quality of care rendered to patients. This is achieved through the establishment of minimum standards of quality of patient care and the invitation to all hospitals to meet or surpass these standards by improving their services and facilities.

Accreditation of hospitals began in 1918 when The American College of Surgeons initiated its Hospital Standardization Programme. The purpose was to elevate the quality of surgical care provided in hospitals. The program involved setting up minimum standards of practice for the operating rooms, but it also identified the need for similar standards in all departments of the hospital. The first list of approved hospitals, published in 1919, contained 89 approved hospitals out of 692 surveyed. The American College of Surgeons standardization program was assumed by the Joint Commission on Accreditation of Hospitals (JCAH) in 1951.

The JCAH transitioned to a broader scope accreditation and in 1988 changed its name to the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). The JCAHO establishes standards and provides accreditation services for other components of health care delivery including, home care, ambulatory care, behavioral health care organizations, as well as hospitals.

The JCAHO is an independent, voluntary agency, and its actions are not subject to ratification by the organizations represented by its component members. One of its objectives is to make known to the public the names of those hospitals that have invited its scrutiny and have been accredited by it through meeting the minimum standards established for good patient care. The net effect of the program is to enable the public to discriminate between hospitals that are accredited and those that are not.

During the years the American College of Surgeons administered the accreditation program, the pharmacy was not included among the essential divisions of the hospital but, rather, was listed as a complementary division. The JCAH continued this classification for several years. However, in 1956, the pharmacy department was included among the essential services of the hospital, and thus, official recognition was given to the importance of the pharmacy. In 1965, the JCAH amended its standards for medical staff functions by requiring a Pharmacy and Therapeutics Committee. Previously, the JCAH had only considered this committee to be a desirable one rather than an essential committee on the medical staff. This action placed a greater emphasis on medication use standards, was instrumental in expanding the role of pharmacists in the medication use process and medication safety.

Another major impetus to the development of standards of practice in hospitals came about with the enactment of the So-

cial Security Amendments of 1965 (Medicare). This law set forth certain conditions that hospitals are required to meet for purposes of participating as providers of services to recipients of federally financed programs. These requirements are published as a manual entitled *Conditions of Participation—Hospitals* (available from the US Department of Health and Human Services, Social Security Administration, Washington, DC). Among the requirements for hospital participation is accreditation by an organization recognized by the Centers of Medicare and Medicaid Services including the JCAH and the American Osteopathic Association (AOA). This manual also includes the conditions of participation for the various departments of the hospital, including the pharmacy department. These conditions played a major role in challenging hospitals, particularly, small hospitals to consider appointing pharmacists to their staffs, providing comprehensive pharmacy services, and establishing pharmacy and therapeutics committees.

Standards of practice in hospitals are also influenced by other organizations. In 1999 and 2001, respectively, the Institute of Medicine, an advisory group to the National Academy of Sciences, issued reports titled "To Err is Human: Building a Safer Health System" and "Crossing the Quality Chasm: A New Health System for the 21st Century." These reports detailed the problem of medical errors in health systems and outlined improvement strategies. This resulted in a tidal wave of interest from the media, regulatory agencies, and the public in patient safety in hospitals. The outcome has been a renewed focus on patient safety in hospitals and organizations such as JCAHO as standards are continually revised.

ORGANIZATION AND ADMINISTRATION—The governing body has total accountability within the organization's structure in most hospitals. This board, commonly referred to as the board of trustees, board of directors, or board of regents, is accountable to provide direction for the organization and oversight of the operations. The board commonly hires a CEO to lead the organization and make recommendations to the board. This officer is commonly referred to as the CEO, President, or Superintendent. In the case of the federal hospitals, there is usually a federal structure through which local hospitals are organized and report. State, county, and city hospitals often have a governing board appointed by the designated political officer. In the nonprofit, nongovernmental hospital, there is usually a governing board, board of trustees, board of governors, or other titled group that assumes overall responsibility for the proper operation of the hospital so that adequate service can be rendered to the sick and injured at as low a cost as is compatible with efficiency.

The governing body has ultimate accountability for the operations, strategic direction, and appropriation of resources to fulfill the mission of the hospital. However, many duties to implement the policies and strategic plan of the Board are delegated to the responsibility of the CEO. These responsibilities include the selection of competent personnel including the medical staff, control of hospital funds, and supervision of the physical plant. By reason of certain court decisions, the responsibility for injury or other act by a member of the hospital staff on the hospital grounds reverts back to the governing board, although the individual hospital personnel is involved.

The governing board has its own internal organization, consisting of a president or chairman, vice-chairman, secretary, and treasurer. On many boards, the CEO of the hospital serves as the secretary. There are usually standing committees appointed, such as

- The executive committee
- The hospital committee dealing with personnel appointments, especially those of the medical staff, and with other activities of a departmental nature
- The finance committee, which is concerned with the hospital budget, room rates, and other financial matters
- A committee on public relations, which is concerned with educating the community on the value of the hospital and with maintaining a desirable relationship with the community

There may be other committees appointed as needs arise, such as an expansion and development committee when the hospital is concerned with the need for construction of additional hospital beds.

The CEO of the hospital must produce a two-way channel of communication between the board and the hospital staff and personnel. The CEO reports all essential facts concerning the operation of the hospital to the Board and receives from the Board all directives it issues.

For CEOs to carry out the overall responsibilities assigned by the governing board, they need assistance. Depending on the size of the hospital, there may be one or more administrators reporting to the CEO. The administrator responsible for that service also appoints a leader for each department. The department leaders have the responsibility of operating the departments effectively and properly, within the overall policies and philosophies established by the hospital's governing board.

Among the many departments that make up the modern hospital, there are some in which the services involve primarily the *professional care* of the patient, while the services of other departments involve mainly the *business management* of the hospital.

Some of the departments that deal with the professional care of the patient (diagnostic or therapeutic) include:

Ambulatory Care	Medical Records (HIMS)
Anesthesia	Medical Social Service
Blood Bank	Nuclear Medicine
Clinical Laboratories	Nursing Service
Dental Service	Occupational Therapy
Dietary and Nutrition Service	Pharmacy Service
Electrocardiograph Laboratory	Physical Medicine
Emergency Room	Radiology Therapy
Medical Library	Respiratory Therapy

Departments that deal with the business management or administrative side of the hospital include:

Accounting	Engineering & Maintenance
Admitting	Housekeeping
Biomedical Engineering	Information Systems
Business Office	Materials Management
Cafeteria	Patient and Employee Safety
Central Transportation	Patient Representatives
Credit & Collection	Personnel & Payroll
Public Relations	Risk Management
Marketing	Telecommunications
Care Improvement	Volunteer Service

THE MEDICAL STAFF—The medical staff of a hospital falls in a different category organizationally than the departments listed previously. In some cases, physicians are independent agents taking care of their patients, and they use the hospital, its departments, facilities, and services to care for these patients. The governing board of the hospital, and the community that it represents, exercises effective control over the medical staff. Although the governing board neither originates nor implements medical policy, it is responsible for the policy, and while the board members are not competent to pass judgment on the professional care of the patient, they are, as representatives of the ownership of the hospital, liable for dereliction of duties established by law. Thus, the board delegates a portion of its duties and responsibilities to its appointed medical staff to originate medical policy and carry out this policy in good faith. This requires that the medical staff be organized to govern itself and appraise its own work and yet be responsible to the governing board for the details of its work.

For a physician to be appointed to the medical staff of a hospital, an application for membership must be made. The credentials committee of the medical staff, which determines

whether the physician is competent to practice in the claimed specialty, considers this application and appropriate credentials. The credentials committee also evaluates the qualifications of the physician to perform certain specialized procedures (eg, cardiac transplant, laser surgery, radiation oncology therapy). The credentials committee, if favorably impressed, makes its recommendation to the medical staff for appointment. Assuming this is approved, the recommendation goes to the governing board for final approval, upon which the physician is designated a member of the medical staff of the hospital for a specified period of time, usually one year, subject to renewal.

The organized medical staff of a hospital has certain duties:

- Providing professional care to patients of the hospital
- Maintaining its own efficiency
- Self-governance
- Participating in the educational program of the hospital
- Auditing its own professional work
- Advising and assisting the administrator and the governing board regarding medical policies

There are two main types of hospital staffs: *open* and *closed*.

An *open staff* is one in which certain physicians other than those on the attending or active medical staff are allowed to use the facilities, providing they comply with all rules and regulations of the institution. These physicians are termed members of the *courtesy* medical staff; the hospital is termed an *open-staff* hospital.

A *closed staff* is one in which all professional services, private and charity, are provided and controlled by the attending or active medical staff. A hospital with this type of staff is termed a *closed-staff* hospital. The closed staff, although it has minor drawbacks, is the more desirable for the average hospital and especially for the teaching hospital because it allows careful selection of a group of specialists with excellent reputations.

The medical staff may consist of any of the following groups: an honorary staff, a consulting staff, an active staff, an associate staff, a courtesy staff, and a resident staff. The *honorary medical staff* is composed of physicians who have been active in the hospital but who are retired and those whom it is desired to honor because of outstanding contributions. The *consulting medical staff* consists of specialists who are recognized as such by right of passing specialty boards or belonging to the national organization of their specialty and who serve as consultants to other members of the medical staff when called upon. The *active* or *attending medical staff* is the group primarily concerned with regular patient care. It is the group most actively involved in the hospital. In internal staff government, the medical staff is the authoritative body. The *associate medical staff* is composed of junior or less-experienced members of the staff. Appointment to this group is the first step toward active or attending staff membership. The *courtesy medical staff* consists of those physicians who desire the privilege of attending private patients, but who do not desire active staff membership. The *resident medical staff* is composed of residents, who are full-time employees of the hospital. These persons provide specific services in the care of the patient, for which they receive education and experience.

FINANCING HOSPITAL CARE—The technological developments of our industrialized society and the rapid advances of the medical sciences increase the financial burdens of hospitals annually. Hospitals, in their efforts to provide the best care available, must keep up with these advances by obtaining the newest diagnostic and therapeutic equipment, facilities, and products. In addition, the increasing cost of labor is reflected in the increased cost of the personalized services available in the modern hospital.

For centuries hospitals have struggled with the problem of finances adequate to cover operating expenses and fund capital purchases to improve services and care continually. At one time hospitals were a place where people went to die; the public cared little about their financial struggles. But, as the hospital developed into a place where people went to get well, the public took a more positive interest in the financial problems. In other words, the public has come to recognize that hospitals must have adequate funding to continue to provide patient care and protect the public health.

Sources of Income—There are several main sources of income for hospitals: patients, government, third-party hospitalization insurance, voluntary contributions, endowment funds, and investments.

Because most hospitals in the United States are private (nongovernmental operated), the bulk of income to these institutions is from the patient, either directly or indirectly. Funds may come from the patient directly, or they may come through hospitalization insurance (usually referred to as third-party payments). Most of the population is covered by hospitalization insurance commonly purchased by employers.

Another third-party principle involves the workmen's compensation regulations in the various states. These vary among the states, but essentially each involves the employer taking out an accident insurance policy that will pay for emergency treatment or hospitalization of the employee in case of accident or injury on the job.

Medically indigent patients are those who do not have sufficient income or insurance to pay for their own personal health needs. Although some private organizations provide assistance to this group of patients, the bulk of the financial assistance comes from tax funds through local, state, and federal agencies. The list of public, tax-supported programs for health-care assistance is formidable and becomes complex in determining what department, division, or agency of the federal, state, county, or city government is involved. In addition, dependents of members of the Armed Forces, members of the Public Health Service and their families, and the veterans of foreign wars receive health care through public tax funds.

The Social Security Amendments of 1965 and 1972 extended the benefits for hospitalization, physician's services, and outpatient services from the original Social Security Law. A substantial portion of hospital costs is provided under federal auspices.

Other sources of income for hospitals are the voluntary contributions of individuals, corporations, foundations, and community fund-raising campaigns. Some of these are direct contributions to the hospitals; others are made available in the form of grants for research; still others are given for major expansion or remodeling programs. Private health-assistance agencies assist individuals who need help by subsidizing the cost of their hospitalization and other health-care needs.

Many hospitals are fortunate in receiving substantial sums of money for the purpose of setting up endowment trust funds and for use by the hospitals in other ways. In addition, some hospitals receive some income through investments, such as in portfolios.

HEALTH MAINTENANCE ORGANIZATIONS—A health maintenance organization (HMO) is a public or private organization that provides and/or manages comprehensive health services to individuals enrolled win the HMO of the health plan. The purpose of such organizations is to provide high quality comprehensive or total health care services, emergency care, inpatient hospital and physician care, ambulatory physician care, prescription services, and preventive medical services while managing the cost of care. This type of comprehensive care while balancing the cost of care often is referred to as managed care.

In 1973, Congress passed the *Health Maintenance Organization Act of 1973* (Public Law 93-222), which provided new authority to the Department of Health, Education and Welfare (now Health and Human Services) to develop new HMOs. According to the Act, an HMO is an organizational entity that includes four essential attributes:

1. An organized system for providing health care in a geographic area that accepts the responsibility to provide or otherwise assure the delivery of health care;
2. An agreed-upon set of basic and supplemental health maintenance and treatment services to;
3. A voluntarily enrolled group of persons; and
4. For which services the HMO is reimbursed through a predetermined, fixed, periodic prepayment made by or on behalf of each person or family unit enrolled in the HMO without regard to the amount of actual services provided.

Among many other things, this legislation authorizes an HMO to "maintain, review and evaluate a drug use profile of its members receiving prescription drugs, evaluate patterns of drug utilization to assure optimum drug therapy and provide for in-

struction of its members and health professionals in the use of prescription and nonprescription drugs." Thus, opportunities for the development of challenging new roles for pharmacy have developed within HMOs in the broad areas of rational medication therapy including diagnostic and curative, as well as preventive therapy. Many would agree that pharmacy practice within these organized health-care facilities is characteristic of institutional pharmacy practice.

INTEGRATED HEALTH SYSTEMS—Recently, there has been a marked change in hospitals and their diversity of services. Many hospitals have merged with other hospitals and other patient care services such as home health care, ambulatory care clinics, long-term care, and wellness facilities. These systems often are known as *health systems,* because the overall governance of the system is unified. Directors of hospital departments are often administratively responsible for pharmaceutical services in multiple hospitals, ambulatory care pharmacies, long-term care pharmacy services, and home health care pharmacy services. As these *hospitals* evolve into health systems, various supportive systems such as computer systems, medication distribution systems, and clinical pharmacy services are provided and managed by one pharmacy administrative group for all units in the health system.

THE HOSPITAL PHARMACY

The separation of pharmacy from medicine took place in charitable institutions operated under governmental or ecclesiastic authority. The fact that business interests played no part in the delivery of care to patients in these institutions led to an eventual division of labor to improve the quality of care. This division of labor in the physician-apothecary function led to the recognition of pharmacy as a discipline separate from medicine. Because the division occurred in hospitals, the hospital pharmacist was the first recognized practitioner of the profession of pharmacy.

The development of hospital pharmacy in different countries was vitally affected by educational standards and the caliber of its practitioners. Thus, hospital pharmacy as an important professional specialty virtually was neglected in America for almost 168 years, from the time that Jonathan Roberts became the first hospital pharmacist at the Pennsylvania Hospital (Philadelphia) in 1752 to approximately 1920.

NATIONAL PROFESSIONAL SOCIETY—Although the existence of the American hospital covers a span of more than 200 years, only during the past four decades or so has there been a rapid expansion of pharmacy services leading to the present vast and complex hospital pharmacy system. As the movement toward the organization, expansion, and growth of the hospital pharmacy system in the US began to take shape, there also developed a movement toward the organization of hospital pharmacists. As Niemeyer et al[5] point out, the critical years for hospital pharmacy were the two decades from 1920 to 1940. The awakening in the 1920s came about as a result of a growing realization by hospital pharmacists of the problems, potentialities, and importance of their specialty. The advances in the 1930s resulted from their determination for organization, recognition, and establishment of higher standards of practice.[6]

The activities of hospital pharmacists during this critical period resulted in the formation of the American Society of Hospital Pharmacists in 1942, later renamed the American Society of Health-System Pharmacists (ASHP) in 1995. The development of the Society within the sphere of American pharmacy has been due in large part to the adoption of a philosophy of service by hospital pharmacists that places the patient as the focal point for the existence of pharmacy practice, as indicated in the ASHP Vision Statement for Pharmacy Practice in Hospitals and Health Systems (2001).[7] The unity that binds hospital pharmacists through their national professional society stems from them being a goal-oriented group. The common bond among them is the development of higher standards of professional practice and service because *the patient needs them*. The membership, exceeding 30,000, represents a significant proportion of the pharmacists practicing in the institutional setting. Despite only being in existence since 1942, the ASHP has made significant contributions toward the improvement of hospital pharmacy through its leadership in the development of standards of practice, continuing education to maintain professional competency, various publications to support practice, standards for residency training, and residency accreditation services.

The Official Bulletin of the American Society of Hospital Pharmacists began in June 1943, which became the *American Journal of Hospital Pharmacy* in 1958. In addition, *Clinical Pharmacy* was published to provide in-depth articles dealing with clinical practice. In 1995, these two significant journals were combined to provide a journal on a semimonthly basis and were later merged into the *American Journal of Health-System Pharmacy*.

The *International Pharmaceutical Abstracts* (IPA) was introduced by the ASHP. This abstract service provides extensive coverage of the pharmaceutical literature and now is available for online computer searches.

AHFS Drug Information (American Hospital Formulary Service) is a comprehensive, unbiased source of current information on medications provided in print and electronic means. This is a comprehensive reference often used throughout the country and on an international basis. This reference supports pharmacists in their role as pharmaceutical consultants to the medical profession and other hospital staff.

The residency training programs in hospital pharmacy are accredited by the ASHP and serve as a basis for ensuring a high quality of training of future practitioners. In addition to a residency in pharmacy practice with emphasis on pharmaceutical care, specialized residencies in nuclear pharmacy, community pharmacy care, pediatric pharmacy, psychiatric pharmacy, geriatric pharmacy, drug information pharmacy practice, oncology pharmacy, primary care, internal medicine, clinical pharmacokinetics, critical care, nutrition support, pharmacotherapy practice, infective diseases practice, managed-care, home care, long-term care and management serve to provide a means to develop practitioners with specialized skills to meet future practice needs. Pharmacy technician training programs are also accredited by the ASHP, and these standards provide a basis for consistent technician training.

Other national organizations such as the American College of Clinical Pharmacists (ACCP), the American Association of Colleges of Pharmacy (AACP), and the American Pharmacists Association (APhA) have also supported the advancement of hospital pharmacy practice.

STANDARDS OF PRACTICE

The movement to develop standards of practice in the hospital was initiated by the American College of Surgeons during the early 1900s, when surgeons recognized the need to standardize and improve on surgical procedures, operating room techniques, and medical record keeping on surgical operations. The College found that to improve the overall care of surgical patients, standards needed to be developed in other departments of the hospital as well as in the operating room. As a result of their initiative, the first *Minimum Standard for Pharmacies in Hospitals* was presented to the 18th Hospital Standardization Conference of the American College of Surgeons in 1935. In 1942, when the ASHP was organized, a standing Committee on Minimum Standards was appointed for the purpose of maintaining and developing better minimum standards. The original standard of the American College of Surgeons was revised by the ASHP in 1950. This revised Standard was approved by

the American Pharmaceutical Association, American Hospital Association, and Catholic Hospital Association and received editorial endorsement by the AMA. The *Minimum Standard for Pharmacies in Hospital,* evolved into a yearly publication called the *Best Practices for Health-System Pharmacy*. This publication provides a helpful set of principles on which to develop good professional practices within the hospital. *Best Practices for Health-System Pharmacy* is published annually, and the documents are available on the ASHP web site.

The JCAHO and the AOA continually revise their standards regarding the use of medications to assist hospital administrators and pharmacists review their pharmacy services. These standards, while not totally inclusive of a broad scope and high quality pharmacy service, do challenge the hospitals to meet optimum achievable standards of practice in providing high quality, safe, and effective medication use and services.

Another standard of practice relating to institutional pharmacy is the federal requirement imposed under the Social Security Amendments of 1965 (Medicare) and subsequent amendments. In addition, most state health departments have guidelines on hospital pharmacy and medication use systems.

ORGANIZATION—Within the organizational structure of the hospital, the director of pharmacy reports to an administrator of the hospital on the proper operation and management of the pharmacy. The director of pharmacy formulates and implements departmental administrative and professional policies of the pharmacy, subject to the approval of the administrator. The professional and clinical policies relating to hospital-pharmacy practice, which have a direct relationship to the medical staff, are formulated and developed through the pharmacy and therapeutics committee and are subject to administrative approval (see *Pharmacy and Therapeutics Committee*).

The organizational structure of the hospital pharmacy may be as illustrated in Figure 127-1. However, the structure differs significantly depending on the mission and services of the hospital. This chart attempts to illustrate the coordination and integration of all the technical elements of practice that must be implemented effectively into a total pharmaceutical service. For example, there are technical and professional elements of a clinical pharmacy service. On the other hand, there are clinical components of professional, technical, and support services. Likewise, there are educational, technical, and clinical implications to the research and supportive components to a pharmacy service. Therefore, the organizational structure of a modern hospital pharmacy in terms of the overall elements comprising its services and medication use leadership should be considered rather than viewing it from a clinical *versus* an operational standpoint. This philosophical approach to the organizational

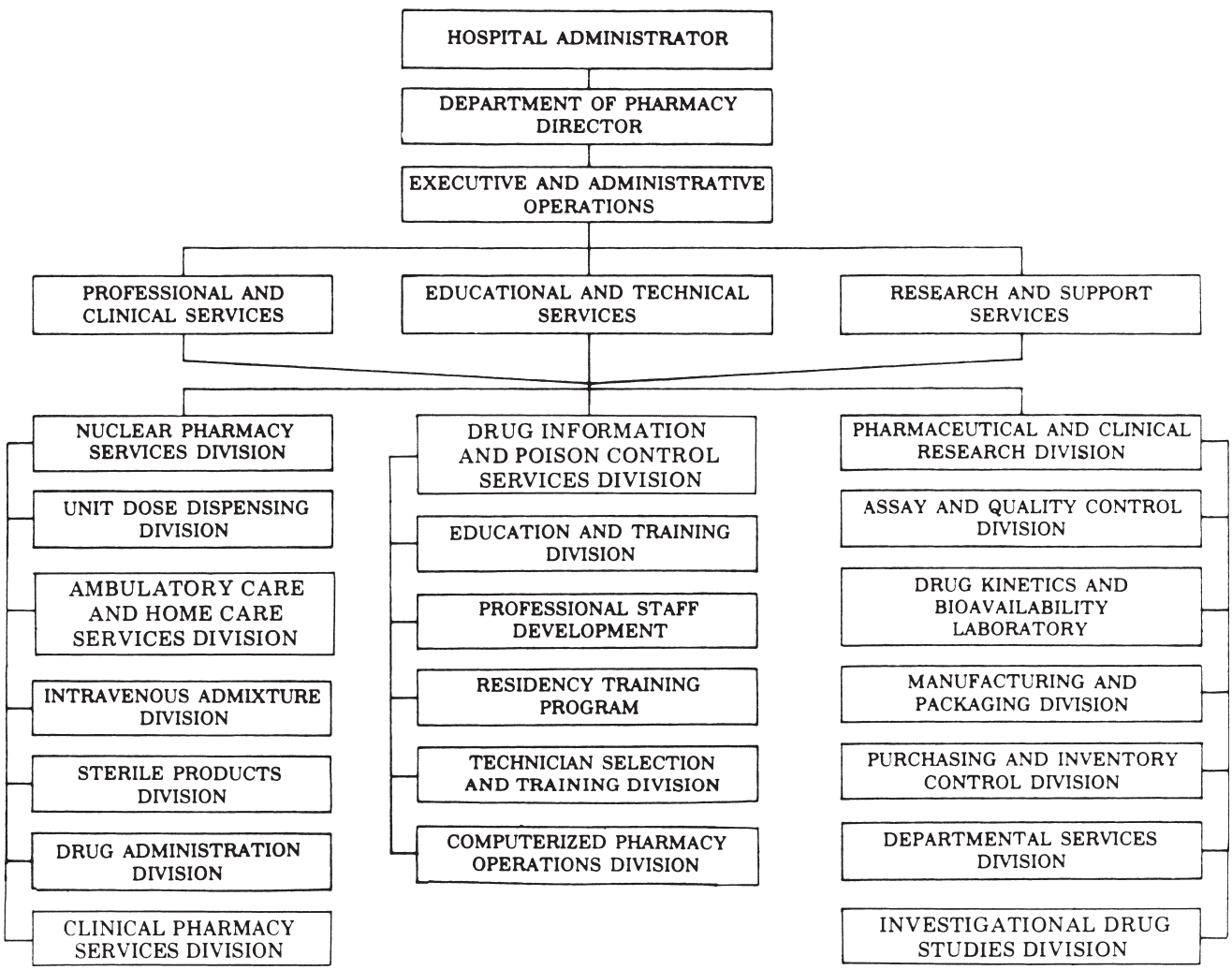

Figure 127-1. Typical organizational structure of a pharmacy department.

and operational aspects of hospital pharmacy is essential for effective use of all the pharmaceutical sciences that underlie the profession of pharmacy.

A close examination of this organizational chart shows the many ramifications of the practice of pharmacy in today's modern hospital. Hospital pharmacy staff primarily can be grouped into three categories: pharmacists, technicians, and clerical. The Pharmacist category includes those pharmacists who practice in medication distribution roles and those in clinical or direct patient care roles. Other pharmacists in the hospital include those who specialize in various areas of practice, such as leadership positions and pharmacy residents. The following is a comprehensive job description of the pharmacist's responsibilities in general hospital pharmacy activities and in clinical functions and responsibilities.

PHARMACIST RESPONSIBILITIES

I. General Responsibilities
  A. Policies and Procedures
    1. Ensures that policies and procedures are established and followed
    2. Ensures that all state and federal medication-related regulations and accreditation standards are followed
  B. Competence
    1. Maintains professional competence in areas of responsibility
  C. Training and Education
    1. Ensures that new personnel are trained properly
    2. Communicates with all pharmacy staff regarding new developments and assists in employee evaluations
    3. Provides medication information to pharmacy, medical, and other health-care personnel
    4. Provides patient education and counseling regarding medication therapy and medication-related disease prevention
    5. Assists in medication training of those staff who administer medications
    6. Provides education to pharmacy, nursing and medical students and residents
  D. Documentation
    1. Provides for proper record keeping and billing
      a. Patient medication records
      b. Extemporaneous compounding records
      c. Dispensing, automation and intravenous admixture records
      d. Investigational medication records
      e. Controlled substance records
      f. Reports (eg, monthly workload, financial, clinical programs)
      g. Prescription files
      h. Billing information
  E. Interdisciplinary
    1. Participates in multidisciplinary committees focused on:
      a. Development and maintenance of the medication formulary and medication-related policies
      b. Conducts medication use evaluations and development of medication usage guidelines and protocols
      c. Implements medication use and medication safety performance improvement projects
      d. Evaluates and approves investigational medication studies conducted in the hospital
      e. Other medication therapy-related issues
II. Dispensing responsibilities
  A. Dispensing area
    1. Checks for accuracy of computer entry and doses selected prepared by pharmacy technicians:
      a. Medication order
      b. Intravenous admixtures
      c. Unit dose
      d. Floor stock
    2. Provides for proper medication control:
      a. Ensures that medications are stored properly.
      b. Ensures that medications are dispensed properly (eg, investigational medications)
      c. Ensures adequate controlled substance procedures are in place
    3. Ensures that good techniques are used in compounding intravenous admixtures, chemotherapy, and extemporaneous preparations
    4. Coordinates the activities of the area with the available staff to make the best possible use of personnel and resources
    5. Keeps the dispensing area neat and orderly
    6. Coordinates the overall pharmaceutical needs of the patient-care areas with the dispensing area (eg, delivery schedules)
  B. Patient-care area
    1. Medication order review
      a. Reviews each medication and IV order for appropriate dosage, frequency, route, duration, monitoring parameters, and medication selection in combination with the patient's demographics, laboratory results, diagnosis, and other clinical parameters
      b. Reviews medication orders and the patient's current medication regimen to minimize adverse drug reactions, therapeutic duplication, drug interactions, and other contraindications
      c. Discusses medication order clarifications or recommendations with the prescriber and documents any changes
      d. Ensures that the medication orders are entered accurately into the appropriate pharmacy system
    2. Medication Administration
      a. Supervises medication administration and patient care area; Reviews each patient's medication administration form periodically to ensure that doses are being administered and charted correctly, that the transcription is accurate, and controlled substance documentation is complete
      b. Collaborates with nursing on missed doses, rescheduling the doses as necessary
      c. Ensures that proper medication administration techniques are used
      d. Acts as pharmacist liaison between the pharmacist and the patient care and medical staffs
      e. Communicates with nurses and physicians concerning medication administration problems
      f. Periodically, inspects the medication areas on the patient care areas to ensure that adequate levels of floor stock medications and supplies are maintained and ensures adequate medication security and controls
      g. Ensures that other supportive services performed by the department of pharmacy are carried out correctly
      h. Coordinates all pharmacy services on the patient care area
      i. Identifies medications brought into the hospital by patients
    3. Medication monitoring
      a. Obtains patient medication histories and communicates all pertinent information to the physician
      b. Assists in medication product and entity selection and in the selection of dosage regimens
      c. Monitors patients' total medication therapy for
        (1) Effectiveness/ineffectiveness
        (2) Side effects
        (3) Toxicities
        (4) Allergic reactions
        (5) Drug interactions
        (6) Appropriate therapeutic outcomes
      d. Orders or obtains clinical laboratory data and medication levels to monitor medication regimens for therapeutic efficacy, adverse effects and toxicity
      e. Identifies specific patient types, drug products, or therapeutic categories for targeted monitoring of patients and medication therapy
      f. Attends medical or health-care team rounds and performs consults for selected patient populations
      g. Counsels patients on
        (1) Medications to be self-administered in the hospital
        (2) Discharge medications
      h. Participates in cardiopulmonary emergencies by
        (1) Procuring and preparing needed medications.
        (2) Documenting all medications given
        (3) Performing cardiopulmonary resuscitation, if necessary

A growing number of hospital pharmacists specialize in specific patient populations (eg, geriatric, pediatric), patients with targeted therapeutic needs (eg, infectious disease, nutrition, pain management) or patients on a specific medical service (eg, oncology, cardiology). Pharmacists in hospitals are often given the authority by the hospital's Pharmacy and Therapeutics Committee and medical staff to write orders for alterations in medication therapy or associated laboratory orders according to established guidelines or protocols (eg, therapeutic substitutions, adjustment of selected medication doses or frequency based on patient conditions or laboratory values, ordering of laboratory tests to assist in monitoring medication therapy). In some hospitals, pharmacists and other allied health professionals must complete a hospital privileging process to provide selected patient services or perform medication prescribing. The privileging requirement occurs most frequently where there is a pharmacist-directed clinic in which the pharmacist provides direct patient care services in the ambulatory clinic areas (eg, pharmacist anticoagulation or hypertension clinic).

With continuing development of computer and pharmacy technology, automation and an automated medical record, the pharmacist's distributive and technical roles will be reduced continually, allowing more focus on patient care activities. The American Council on Pharmaceutical Education, the agency responsible for the accreditation of professional degree programs in pharmacy, has established the doctor of pharmacy (ie, PharmD) degree as the entry level degree for pharmacists. This degree program provides more clinical education and experiential preparation to fulfill these roles. Pharmacy residency programs provide additional training for pharmacists to practice in clinical roles or specialty areas of practice. For licensed pharmacists who wish to attain additional recognition for their knowledge in particular specialty areas, the Board of Pharmaceutical Specialties (BPS) has developed a certification process to recognize certain areas of specialty practice (eg, nuclear pharmacy, pharmacotherapy, nutritional support).

Pharmacy technicians provide the technical support for a hospital pharmacy. Technician roles are expanding to perform hospital pharmacy functions that do not require the skills and training of a pharmacist, allowing pharmacists to enhance their focus on assuring that the desired outcome of patients' medication regimen is achieved. Because individual state boards of pharmacy regulate and often specify the functions that technicians can perform under the supervision of a pharmacist, their roles vary among states. In addition, state boards may also specify the number of technicians relative to the number of pharmacists that can be utilized in the pharmacy.

The *White Paper on Pharmacy Technicians 2002: Needed changes can no longer wait*[8] discusses the functions, training, and regulation of technicians. Training of technicians is variable and certification is voluntary in most states. Less than half of technicians working in hospitals have received formal training, and the remainder have been trained primarily on the job. There are formal technician training programs nationwide, many of them at technical schools or community colleges, and there is a national accreditation service for pharmacy technician training programs. The Pharmacy Technician Certification Board (PTCB) started a voluntary national certification program for pharmacy technicians in 1995. In many states, technicians must be registered with the State Board of Pharmacy. Some states require certification for technicians, and many other hospitals are requiring technician certification as a condition for employment. With increased numbers of accredited training programs and expanding technician certification, technicians will be better prepared to move into roles of additional responsibility.

There follows a comprehensive job description of typical technician responsibilities.

TECHNICIAN RESPONSIBILITIES

I. General responsibilities
   a. Ensures that policies and procedures are followed
   b. Maintains competence in areas of responsibility
   c. Ensures new personnel are trained properly

II. Technical responsibilities
   a. Selects and prepares patient-specific unit dose and floor stock medications
   b. Utilizes aseptic technique to prepare and mix intravenous, parenteral nutrition and other admixtures
   c. Packages medications into unit dose and unit of use packaging
   d. Performs routine inspection of patient care and medication storage areas for medication control, security, and controlled substance accountability
   e. Orders, receives, and restocks medications and associated supplies into pharmacy and patient care inventory
   f. Collects patient demographic, laboratory, and other information to provide a complete medication profile and to provide data for pharmacist review
   g. Monitors the utilization of medications and IVs and reorders as necessary
   h. Returns outdated medications and tracks medication wastage
   i. Utilizes and manages computer software and medication related technology (eg, automated medication dispensing systems, parenteral nutrition admixture pumps, bar code technology)

III. Reporting and Documentation
   a. Documents medication preparation, packaging, and compounding
   b. Enters charges and credits to ensure billing accuracy
   c. Performs audits of medication processes and completes associated reports
   d. Completes controlled substance documentation

In smaller hospitals, sometimes staffed by only a single pharmacist, it is challenging for the pharmacists to maintain expertise in all areas of hospital pharmacy practice. In a large hospital, with a number of pharmacists who specialize in certain areas of practice, each may become expert in one or more disciplines. The staffing pattern in hospital pharmacy varies, with the scope and quality of pharmaceutical service being offered. Most hospitals with fewer than 50 beds employ at least one pharmacist and one technician. As the size of the hospital increases, so does the number of personnel in the pharmacy. For example, in a 300-bed progressive hospital, the pharmacy may be staffed with a director of pharmacy, an operations manager, a clinical specialist, from 10 to 20 staff pharmacists, 5 to 15 technicians, and a full-time department secretary. In the very large hospitals with several hundred beds, the staffing pattern in the hospital pharmacy may consist of a director of pharmacy, two or more associate or assistant directors, one or more managers, as many as 40 to 60 or more staff pharmacists (many of whom specialize in various clinical areas), 5 to 10 pharmacy residents, and about as many technical personnel as professional personnel. In addition, several clinical pharmacy faculty associated with a college of pharmacy also may be active within the department.

Pharmacy leadership provides management of pharmacy services and coordination of medication use throughout the hospital. This leadership role requires knowledge and the application of a variety of skills, including:

- Strategic planning
- Financial management
- Workload and productivity monitoring
- Budgeting and cost-containment
- Human resource management (eg, staffing, recruiting, performance evaluation, education, training)
- Quality assessment and performance improvement
- Policy, procedure, standard, and guideline development
- Customer satisfaction monitoring
- Medication safety monitoring and improvement
- Interdisciplinary and interprofessional partnership and collaboration

The director of pharmacy uses these skills and other management tools to ensure that all the services and functions are fulfilled adequately. Whereas, most hospital pharmacy managers have historically been pharmacists, non-pharmacist managers responsible for technicians, technology, and business managers are becoming more prevalent, especially in larger hospitals.

FACILITIES—There are great variations in the amount of floor space devoted to the pharmacy in hospitals of the same size and type. Such variations have a direct bearing on the scope of service that can be developed and conducted by the pharmacy. Helpful guides for planning hospital pharmacy facilities are available in the pharmacy literature.

In the small hospital with one pharmacist, only one room usually is required for the pharmacy (ie, a combination of dispensing, manufacturing, administrative, and all other features of a complete pharmaceutical service). When sterile products are to be prepared, there should be a separate room or area for such work. An area of this type is required for reconstituting lyophilized injections, ophthalmic preparations, packaging unit-dose injections into syringes, and preparing intravenous admixtures, all of which must remain sterile.

Hospitals of 200 beds and larger provide the opportunity for departmentalization of pharmacy activities. There should be a separate area for inpatient services and unit dose dispensing; outpatient service; an office for a manager; a compounding, repackaging, and labeling room; a storeroom; a sterile products and IV-admixture clean room; a room or area for a departmental computer; a separate area for drug information services; and space assigned on various patient care areas for unit dose medication storage, automated dispensing technology medication administration preparation, and clinical pharmacy services. As the hospital size advances to 500 to 1000 or more beds, the space requirements of pharmacy service will also increase.

MEDICATION SAFETY—Hospitals, independent of size and services offered, are highly complex organizations with multiple communication formats, interprofessional handoffs, and sophisticated yet complicated technology. Medication use within a hospital is subject to many opportunities for unintended results due to the combination of defects within this complex system and the reliance on human operators. The hospital pharmacist must assume a leadership role in developing a plan to eliminate or create awareness around system defects and to minimize the harm to the patient if an error occurs. Coordination with other hospital committees and departments such as the Pharmacy and Therapeutics Committee, Patient and/or Medication Safety Committees, Performance Improvement, and Risk Management departments is essential to preventing medication errors. The plan should incorporate key elements of:

1. Implementing best practices in medication use
2. Creating a medication use system that is fully understood by users and thus considered transparent
3. Maximizing safety with automation and technology
4. Conducting educational and training programs regarding medication safety
5. Reducing patient harm resulting from a medication accident

Establishing consensus around best practices in medication use at a hospital can be facilitated using a variety of resources such as ASHP's Best Practices in Hospital Pharmacy, and the Institute for Safe Medication Practices (ISMP) and National Patient Safety Foundation (NPSF) recommendations. Examples of actions to implement best practices include: eliminating the use of dangerous abbreviations, removing concentrated electrolytes from patient care areas, developing a mechanism to distinguish "look alike/sound alike" medications and creating a quality assurance program around high risk medications such as heparin or chemotherapy drugs.

Continually improving the safety of the hospital pharmacy systems requires that users have a complete understanding all system components and the system is considered "transparent." Transparency of the medication use system is important because it allows latent defects to become clear and easily understood by its human users. Transparency can be created proactively through the use of an open and blameless reporting system for errors. It can also be created by using a process known as a Failure Mode and Effects Analysis (FMEA). This tool is used to map out complex procedures carefully, breaking them down to each step, analyzing and prioritizing any identified risk or defect, and developing an action plan to address the defects. A simplified form of FMEA methodology can be used in evaluating new drugs for inclusion in the hospital's formulary. Automation and technology can be used to help eliminate or reduce medication errors by reducing reliance on human functions in the system. These technologies include bar code verification systems, robotics, smart IV pumps, clinical information support, and alerts and computerized physician order entry systems. The medication safety plan should incorporate a systematic program to evaluate new and existing technology, apply human factors design analysis or an FMEA, and create an implementation strategy that addresses the concerns of the end user prior to any installation so as to not inadvertently introduce risk into the system.

The plan should include the development of medication safety education programs for all relevant health care providers. Education should include recent developments in safety science as well as the lessons learned within the hospital's safety reporting system. Training programs should include orienting the new employee to identified areas of high risk within a given process, such as the compounding of medications for intravenous administration. Training should be conducted for any significant changes in processes or systems.

Finally, the hospital's medication safety plan should include a systematic and ongoing program to develop protocols to reduce variation and patient harm. These protocols may include communication and decision trees for patient transfers to the intensive care unit, the use of reversal agents, and the use of an extravasation kit.

The hospital's medication safety plan developed with pharmacy leadership and multidisciplinary professional participating can be an effective tool in reducing the likelihood of a medication error and improving the safety of patients.

PHARMACY AND THERAPEUTICS COMMITTEE—The American College of Surgeons recognized this need in 1935 when it adopted the first *Minimum Standard for Pharmacies in Hospitals*. The Pharmacy and Therapeutics (P&T) Committee also is recognized by the JCAHO as an essential committee of the hospital's medical staff. The P&T Committee is a committee of the medical staff and is chaired by a physician while the director of pharmacy commonly functions as secretary. Typically, it includes representation from medical staff specialties, pharmacy, nursing, administration, quality, laboratory, and other pertinent departments.

The ASHP has formulated and adopted a statement embodying the definition, purpose, organization, functions, and scope of a P&T Committee. This statement defines the primary purpose of the P&T Committee as policy development and education and is an effective guide to organizing such a committee.

Historically, some have thought that the sole purpose of a pharmacy and therapeutics committee was to develop a formulary and operate a formulary system. However, the function of this committee includes policy development and governance of the medication use process. Thus, the role is much broader than the formulary system. A hospital's medical staff could have an effective P&T Committee without having a formulary system. On the other hand, a hospital could not properly operate a formulary system without a P&T Committee unless the medical staff served as a *committee of the whole.*

During recent years, with the development of the clinical pharmacy movement, a number of clinical pharmacists on the staff of some departments have developed expertise in specific therapeutic specialty areas. Therefore, it was a logical development that a subcommittee structure could be developed under the pharmacy and therapeutics committee. For example, infectious disease physician specialists along with a clinical phar-

macist who specialized in anti-infective pharmacology and therapeutics could provide the appropriate expertise to the pharmacy and therapeutics committee in this area of medication therapy. The organizational chart in Figure 127-2 illustrates an effective approach for the medical and pharmacy staffs to develop and implement a rational medication therapy program, a subcommittee structure of specialists in defined areas of therapeutics.

Another significant activity of the P&T Committee is performing Drug Usage Reviews (also known as Drug Usage Evaluations (DUEs) or Medication Use Evaluations (MUEs) studies). The committee, with active involvement by the pharmacy, determines the medications or therapeutic indication to be studied, determines the appropriate medication usage criteria, collects data, evaluates actual usage data against approval criteria, and makes recommendations for improvement in the appropriate use of the medication therapy studied. In addition, the Committee is charged by JCAHO to monitor Adverse Drug Reactions (ADRs) and medication errors, as a part of the quality assurance standards of the medical staff. The P&T Committee is involved in hospital medication safety prevention and management efforts and oversees medication use policies and systems.

FORMULARY SYSTEM—The formulary system and formularies have existed in the US since the days of the American Revolution and in European hospitals for centuries prior to this. The need for hospital formularies continues to increase due to:

- The increasing number and complexity of medications available
- Increased utilization due to direct-to-consumer and physician marketing strategies of the pharmaceutical industry
- The obligation of health care providers to exercise good stewardship in the appropriate use of medications

This is substantiated by the fact that the federal government requires the establishment of Professional Review Organizations (PROs), whose purpose it is to monitor and control the quality of services rendered to patients. The federal Maximum Allowable Cost (MAC) programs also are emphasizing cost control for patients on federally funded programs.

The formulary system—because it has attempted to outline the scientific data on a medication, including its toxicities, untoward side effects, safety profile, and beneficial effects—has been a controversial method of appraising medication therapy. While the pharmaceutical industry promotes the virtues of a brand name medication, the formulary system evaluates the virtues and defects of that medication in comparison with other brands with similar therapeutic uses. This often leads to therapeutic guidelines promoting the use of medications in various clinical situations.

The increasing use of alternative and complementary therapies by patients is creating challenges as hospitals make decisions on whether to include these agents on formulary. Often, adequate scientific data is not available, the products are not standardized, and since the products are not required to meet FDA medication formulation standards, the hospital cannot be assured of their content.

The ASHP has created several documents that can help physicians, pharmacists, and administrators with development of a formulary and with operating a hospital formulary system. Hospital pharmacists have viewed the hospital formulary system as a means to manage the medication inventory and provide high quality, safe, effective medications that meet the need of the patients. Essentially, the formulary system provided a mechanism to avoid brand duplication and therapeutic duplication, as well as promoting rational medication therapy. The success of this system is due to *peer review* in a hospital, whereby physicians agree to practice by the policies and procedures established by the committee process.

Many useful reference sources are available to assist the P&T Committee to develop an effective, ongoing rational medication therapy program and formulary system in the hospital. The knowledgeable drug-information specialist and the clinical pharmacist can use these reference sources effectively to encourage the medical staff of the individual hospital to select those medications its members consider most effective therapeutically, together with the preparations in which they may be administered most effectively. In addition, these committees have focused increasingly upon the pharmacoeconomics of medication therapy, prompting them to be more selective or restrictive in the medications available for patient care. According to the 2001 ASHP National Survey of Pharmacy Practice in Hospital Settings, more than 90% of hospitals use clinical, therapeutic, cost, and pharmacoeconomic information in the formulary management process, while nearly two thirds consider quality-of-life issues. Nearly 70% use clinical practice guidelines in the formulary management process, and 78% have a medication use evaluation program designed to improve prescribing.[9] The safety profile of the medication (eg, sound-alike medication, administration error potential) should be included in the formulary analysis.

An active P&T Committee with a well-developed formulary system provides assurance that the medical staff, the pharmacy staff, and the administration of the hospital have taken the necessary steps to assure the patient of an effective, safe, and cost-appropriate medication therapy program.

PURCHASING—The principal function in purchasing is to establish standards and specifications for all medications, chemicals, diagnostic agents, intravenous solutions, and pharmaceutical equipment. The pharmacist is responsible for the

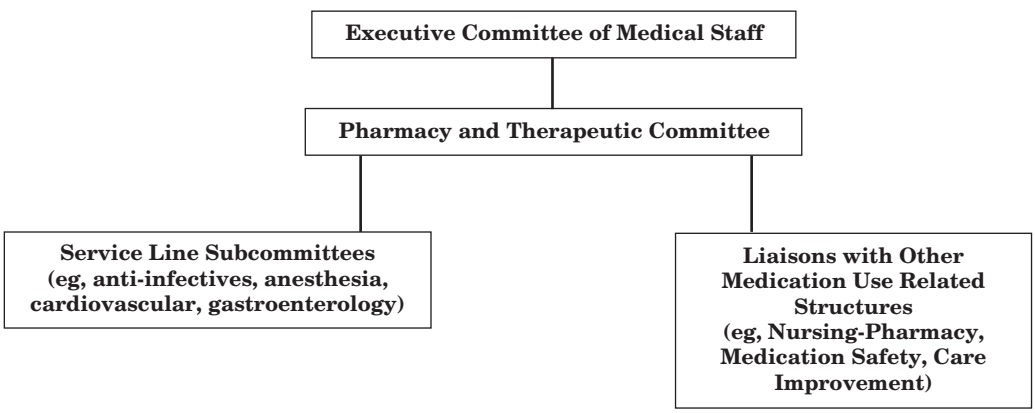

Figure 127-2. Organization of a Pharmacy and Therapeutics Committee.

quality of medications dispensed to patients. The P&T Committee serves as a potent force in helping the pharmacist establish adequate specifications for the purchase of quality pharmaceuticals.

Most hospitals have joined Group Purchasing Organizations (GPOs) or buying groups to pool their usage so that one uniform contract can be negotiated for all members of the group. Most hospital pharmacies now are obtaining all of their contract pharmaceuticals through one, single wholesaler, who provides the pharmaceuticals to the hospital for a small percentage fee. This system is known as the *prime-vendor* system and enables the hospital to order all pharmaceuticals from the prime vendor. Thus, multiple purchase orders are eliminated, and ordering is further facilitated through the use of a computer system. Most hospitals order electronically on a daily basis. This provides for a minimum inventory at the hospital and an optimum inventory rate of 10 to 20 times annually. In addition, the prime vendor can provide the hospital with coordinated purchase data and cost control reports. However, some pharmaceuticals must be obtained directly through the manufacturer.

Annual or semiannual inventories should be taken as a check on the theoretical inventory record maintained by either pharmacy or accounting. Various procedures are used to take a medication inventory. Many hospitals are using electronic data processing in inventory value determinations.

There has been an increasing frequency of drug product shortages in recent years, making it more difficult for pharmacies to maintain an adequate supply of select drug products. The Pharmacy Department and the P&T Committee have a role in determining and acquiring alternative pharmaceuticals to meet the needs of the hospital's patients and communicating this information to the medical and hospital staff.

MEDICATION-DISTRIBUTION SYSTEMS—The medication distribution system in hospitals is very complex and involves several health care professionals. The usual flow is physicians prescribe, pharmacists dispense, and nurses administer medications. However, to have this simple tripartite order executed, many steps must take place in between. The overall medication distribution and utilization process in the hospital involves an infinite number of procedures, personnel, departments, equipment, and storage. As an illustration, trace the path of a typical medication from procurement to administration to the patient.

Before a medication can be purchased, specifications must be prepared. This usually is performed through the medical staff and the pharmacist by means of a P&T Committee. Requisitions outlining the specifications for the medications selected are prepared and processed in the pharmacy. Medication shipments are accepted by the receiving department and distributed to the pharmacy, where they are checked and stored for future use. Inventory control procedures must be established. In the meantime, invoice for payment must be processed through the accounting department by a coordination of efforts among the pharmacy, purchasing, receiving, and accounts payable.

Physicians must prescribe medications before they can be administered. Upon receipt of the medication order (prescription), the pharmacist must review the order for appropriateness, given the patient's medication therapy regimen and clinical condition. Any recommendations due to patient condition, medication formulary status, or more appropriate therapy are communicated to the physician. In the pharmacy, the medications are transferred from the storage area to the dispensing area. There they may have to be prepackaged (for future use), compounded or manufactured, and have assay and control procedures performed. They must be packaged in correct quantities for use by the nurse to administer to the patient, labeled properly, checked for accuracy, and distributed to the patient care area. Here, the medications are stored again for continuous use by the patient, according to physicians' orders. The nurse obtains the necessary medication, prepares the medication for administration, brings it to the patient, ensures that the patient is the one who is to receive the medication, and records this information in the patient's record. Additionally, the nurse and pharmacist monitor the patient for therapeutic and adverse effects.

In the meantime, the pharmacy processes these medication orders for billing purposes and sends these charges electronically to the business office. There, they are posted to the patient's account. Then, through coordination between the pharmacy and the accounting department, data are accumulated and based on the cost of medications issued.

While the mechanics of this operation are taking place, other activities must be completed. Problems must be resolved in the procurement phase regarding medication shortages, overshipments, undershipments, or other shipping errors; errors in billing may have to be rectified. Outdated or deteriorated medications and/or drug product recalls may necessitate these having to be returned to the manufacturer. Recall procedures have to be established. Further information, such as dosage, toxicity, and side effects, may be required from the physician or nurse before the order or prescription can be filled.

The medication use cycle is complex and passes through many health care professionals to provide the appropriate medication to the patient. The average patient receives 20 doses of medication per day while in the hospital. At each step, there is an opportunity for a medication error that may or may not adversely affect the patient. Thus, the medication use system is subject to ongoing review by the P&T Committee and Safety Committee to optimize the safety of the system. Computers, automation, clinical pharmacist practitioners and bar-code technology can be incorporated into the medication system to optimize efficiency and safety.

Medication is administered to a hospital patient only upon the order of a physician (or designated allied health professional). Thus, a prescription order originates in the patient's medical record, where physicians write all the orders (prescriptions) for the patient. Because the patient's medical record remains at the patient care area, it is essential that some means be used to transmit the prescription order from the patient care area to the pharmacy. These orders are transmitted to the pharmacy usually in one of four ways:

- The medical record has a duplicate copy so that the pharmacy can obtain a carbon copy of the physician's original medication order.
- Patient care personnel transcribe the physician's order onto an inpatient prescription or requisition form; however, the transcription method is no longer recognized as acceptable practice.
- Physicians input the order into a computer terminal and the order is transmitted to the pharmacy.
- The physician writes the medication order on a separate blank, commonly for home use.

Most hospitals use procedures whereby the pharmacist obtains a direct copy of the physician's medication orders. The pharmacy department makes medications available at the patient care area for patient use usually in one of four ways:

1. A floor stock system
2. Individual labeled prescription for each patient
3. Patient-specific unit dose dispensing either filled in the central pharmacy or at the patient care area
4. Decentralized automation with a computerized link from the patient's profile to the automation to allow appropriate medication availability for the individual patient, or
5. A combination of the above.

Systems 1 and 2 are considered poor medication control methods in comparison with systems 3 or 4; however, until all hospitals adopt these unit-dose concepts, pharmacists often must operate with less desirable systems.

Medications dispensed under a *floor stock system* are of two classes: no charge and charge. No charge floor stock consists of a predetermined list of medications that are available on the patient care area of the hospital for use at no specific charge to the patient. Usually these items are inexpensive pharmaceuticals that have universal patient use (eg, alcohol, lotion, water for injection, normal saline injection). Usually, orders are re-

ceived from each patient care area. In other hospitals, the pharmacy assumes the responsibility for restocking and maintaining the no charge floor stock medications. Under such a system, the nurse is relieved of having to maintain an inventory control, fill out a daily requisition order, and return the medication items to the shelves. Adequate controls can be set up on the basis of usage in relation to number of patient days per given interval of time. Some hospitals have adopted electronic data-processing procedures or bar code technology to handle the totaling and cost extension of medications issued and the preparation of monthly medication usage reports for each patient care area.

Charge floor stock is medication that is available at each patient care area of the hospital and for which a charge is made to the patient. Certain medications are required to be used almost immediately after the physician prescribes them, and it is not practical to obtain them from pharmacy in each instance, yet the cost and the volume of usage necessitate a charge to the patient. Such medications are usually injections or other single dose forms. A common method of handling charge floor stock medications is to attach a small removable label, bar code label, or pre-stamped pharmacy requisition form bearing the name of the medication to the charge floor-stock medication. When nurses access the medication, they merely remove the label and affix it to the usual inpatient prescription or requisition slip. This is then used for billing purposes and to replace the medication on the patient care area. The floor-stock system is also used in small hospitals where pharmacists are not available to dispense individual doses for patients. Most hospitals are switching to point-of-care automated dispensing technology for storage, charging, and inventory control of floor stock medications, particularly controlled substances. This eliminates the need for most of the manual inventory control, automates charging, and enhances controlled substance medication security and documentation.

Individual prescription patient medications are compounded and dispensed similarly to other prescriptions, except that the name and location of the patient is included on the label. The individual prescription method of distribution is used predominately in small hospitals where a pharmacist is not on the premises all the time.

In hospital pharmacy practice, medications are kept secure in a patient care area. The nurse or an assistant is responsible for administering the appropriate medication to each patient in the patient care area. Thus, it is important to know what medication is being administered. It is the nurse's professional responsibility to observe the patient for untoward adverse reactions and report this to the patient's physician. Individual prescriptions are commonly multiple doses of medications to be administered during the patient's hospital stay. A typical inpatient prescription label would contain the following information:

Mr. John Jones	Digoxin 0.25 mg	Room 608E
Number		#10
Lot #	Exp Date	
Doctor's name	Date	

To expedite the dispensing of inpatient prescription medications, hospital pharmacists have adopted the practice of prepackaging frequently used medications in standard administration quantities. It is not unusual for most of the inpatient prescription medications under this system to be prepackaged. Prepackaging medications requires accurate procedures, controls, and records to trace the identity of the medication at all time. Thus, a prepackaging control record form is used for documentation of manufacturer's control numbers, expiration date, pharmacy control number that appears on each prepackaged container label, and the pharmacist responsible for checking the prepackaging operation. In the case of a medication recalled by a manufacturer, the pharmacist easily can trace prepackaged quantities of the medication in question.

Hospitals pharmacies distributing medications use *the individual inpatient prescription system and the floor stock medication system* often use a combination of the two. Medications that are free floor stock are charged against the patient care service; however, in the final analysis, the patient does pay for the medications, because the cost is included as a part of the patient care service portion of the daily room rate.

Because of the large number and variety of medications stored on patient care areas—including individual patient prescriptions, free and charge floor stock, narcotics and other controlled medications, investigational medications, and emergency medication tray—it is an important responsibility of the pharmacist to inspect these medications routinely. Proper storage conditions must be adhered to, dated medications must be checked, narcotic medications must be safeguarded, and discontinued medications must be removed from the patient care area. To ensure proper control of medications in the patient care area, the pharmacist or the designated support person prepares a report to the nursing and pharmacy managers. The condition of a patient care area medication station may warrant attention by personnel from both departments. In some hospitals, pharmacists are assigned to specific patient care areas to coordinate the medications and address the medication therapy problems at the patient care area level. These pharmacists function as part of the patient care team.[10] Some hospitals also have technicians assigned to specific patient care areas to assist in the technical medication coordination activities.

The safest most accepted method of dispensing medications to hospitalized patients is called *unit dose dispensing* and has become the standard of practice in most hospitals today. In this system, the pharmacist prepares each dose of medication ready for administration, rather than issuing containers of medications to patient care areas where the nurse must prepare the medication for administration. For example, tablets and capsules are labeled and dispensed as a single dose for each patient, liquids are measured, lyophilized injections diluted and measured accurately into sterile syringes, parenteral medication admixtures added to intravenous solutions prior to use, and oral powders and other unusual dosage forms measured and mixed appropriately. Most of these procedures involve pharmaceutical techniques that are the pharmacist's responsibility. Hospital pharmacists use various models for the safe and efficient distribution of medications in their hospitals. Such distribution models may involve a centralized pharmacy and/or decentralized pharmacies in the patient care areas, centralized automation and/or decentralized automated dispensing technology, and information scheduling and retrieval.

The unit dose dispensing concept has changed many of the traditional functions of the hospital pharmacist. For example, the traditional prepackaging system of multiple doses of medications has evolved to the use of tablet and capsule strip packaging, labeling machines, and liquid unit dose packaging equipment. This is necessary since all medications are not available from the industry in unit dose packages. The traditional individual inpatient prescription also is eliminated and thereby eliminates prescription labeling. Free and charge floor-stock medication activities essentially are eliminated. A 2002 ASHP national survey of hospital-based pharmaceutical services in indicated that 89% of all hospitals employed the unit-dose-dispensing system; 81% dispensed more than three quarters of oral doses as unit doses and 63% of injectable doses to non-critical care patients.[11] This medication distribution system has become the standard of practice.

Unit dose dispensing lends itself to automation and the interface of that automation with various information systems supporting the medication use process. In practice there is a centralized philosophy and a decentralized philosophy to the use of automation. The centralized approach includes robotic technology operating from a central area. Medications are retrieved and placed in patient specific containers for transport to the patient care area and administration as directed by in-

formation received through an interface with the pharmacy information system. The decentralized approach involves the use of automated dispensing technology placed in the patient care areas. This technology is interfaced with the pharmacy information system and provides the caregiver access to medications prescribed for their patients. Both central and decentral technologies are capable of interfaces with information systems used in other components of the medication use process such as administration, documentation, and billing. This eliminates the traditional nurses' medication Kardex® (profile), medication ticket, and manual record of medication administered system of patients' medication therapy profiles. Additionally the creation of a single information source to support the medication use process eliminates the potential for conflicting information and provides a common record for all caregivers.

The General Accounting Office (GAO) studied several distribution systems in its *Study of Health-Care Facilities Construction Costs* (December 1972) and reported that in addition to safer and better patient care through minimization of medication errors, the unit-dose system was to be recommended because of its favorable life cycle cost-to-benefit ratio. The JCAHO also recommends the unit-dose distribution system. The ASHP *Statement on the Pharmacist's Responsibility for Distribution and Control of Drug Products* (1996) and the ASHP *Technical Assistance Bulletin on Hospital Drug Distribution and Control* (1981) provide the best demonstrated practices in hospitals for the medication use process.

PATIENT SELF-ADMINISTRATION OF MEDICATIONS IN HOSPITALS—Pharmacists have generally considered a unit-dose dispensing system as a panacea for hospital medication problems. However, unit-dose dispensing systems primarily have been *pharmacy-centered* rather than *patient-centered.* Many hospitals have developed patient self-administration programs as an alternative medication administration method for selected patients.

The self-administration of medications by patients in the hospital offers many advantages. It allows patients to assume more responsibility for their direct care, to learn how to use medications properly, and to be able to anticipate potential side effects and other medication-related problems. It provides a salient opportunity for the pharmacist to help educate patients on the safe and proper use of medications, and, thereby, alleviates much dedicated time spent by nurses and physicians performing this essential function. The objective is that patients should become more knowledgeable about their medication, thus enhancing proper and safe use of medications during hospitalization and after their discharge.

Self-administration of medications by patients can be implemented effectively on numerous hospital services, such as obstetrics, surgery, medicine, physical medicine and rehabilitation, and even in psychiatry.[12,13] Generally, patients with stable medication regimens, receiving chronic medications and in good physical and mental health are appropriate candidates for self-administration. Again, a procedural manual should be prepared that outlines the methods used to implement a patient self-administration program as part of a unit-dose distribution system. A self-administration medication program provides patients possession of their medication and makes them responsible for its administration. The nurse and pharmacist then make rounds to ensure that patients are using their medication properly.

A nurse-administered medication program is the appropriate system for most hospitalized patients. This program is used for patients who are not capable of self-administering their medications or for those medications that patients cannot administer by themselves.

INVESTIGATIONAL MEDICATIONS—These medications are often studied in the hospital setting where patients are supported by various diagnostic and treatment resources. The hospital pharmacist is in a strategic position to participate in the evaluation of investigational medications.

There are, however, many problems associated with the use of investigational medications in the hospital, some of which are as follows:

- Legal liabilities for the hospital if there is improper handling of investigational medications in the overall care of the patient.
- Nurses, as agents of the hospital, usually are responsible for administering investigational medications to patients. In performing this act, it is essential that sufficient information on the proper dosage, route of administration, possible adverse/toxic reactions and side effects, precautions, and proper labeling is available to them.
- Investigational medications, as they are made available from the manufacturer to the principal investigator, are not labeled sufficiently in many instances to prevent the possibility of error in their administration to patients.
- Because investigational medications fall in the area of research, in contrast to accepted methods of treatment, there are legal implications revolving around the need for written, informed consent by patients.
- In the case of double-blind studies, it is essential that the person holding the code be readily available 24 hours a day, 7 days a week, in the event a patient's condition warrants "breaking the code."

The FDA has delineated the legal requirements for proper records on the use of investigational medications. In case of a recall due to severe toxicity resulting from an investigational medication, it is essential that records of its use on specific patients in a hospital be readily available. In cases in which the lot number of the medication is a significant factor, such records also should be available.

In cases in which investigational medications are used for outpatients, it is essential that such medications be labeled and packaged to conform to legal requirements, such as child-proof packaging requirements and controlled substances requirements. Information must readily be available to assist physicians in other hospitals who may be required to treat patients suffering from over dosage, toxic symptoms, or illnesses or condition unrelated to the investigational medications.

It is essential that the supply of an investigational medication be available 24 hours per day if nurses are to maintain uninterrupted dosage schedules in the best interest of the patient. The hospital pharmacist needs to maintain adequate dispensing records (Fig 127-3) for all investigational medications dispensed.

Thus, the problems associated with the proper handling of investigational medications provide ample justification to warrant the establishment of sound policies and procedures governing their use in the hospital. This is a responsibility of the medical staff. The P&T Committee or Investigational Review Board (IRB) in collaboration with the P&T Committee should have the responsibility to formulate policies and procedures relative to the handling of investigational medications. To assist the committees, the ASHP developed a guideline on Pharmaceutical Research in Organized Heath-Care Setting and on Clinical Drug Research (1998) embodying basic principles applicable to the safe handling of investigational medications in the hospital. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has developed a quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.[14] The hospital pharmacist, as a key member of the P&T Committee, makes a real contribution to better patient care and safety by participating in formulating policies and procedures for handling investigational medications in the hospital. Often, pharmacists serve on the Institutional Review Board of a hospital and are involved with the review of all investigational studies involving humans. The pharmacist can provide valuable insight on the design, economics and ethics involved in medication studies in human patients.

Clinically, many hospital pharmacists are involved with the care of patients receiving investigational medications such as

THE UNIVERSITY OF KANSAS MEDICAL CENTER
PHARMACY DEPARTMENT

INVESTIGATIONAL DRUG DISPENSING RECORD

Name and Synonyms _____

Strength and Dosage Form _____

Manufacturer _____

Principal Investigator _____

Date	Patient Name	Case Number	Physician	Rx # or Location	Lot Number	Amount Dispensed	Amount on Hand

Figure 127-3. Investigational Drug Dispensing Record.

patients on an oncology medical service. These pharmacists often participate in patient monitoring, medication preparation and administration of investigational medications. Patient consent and patient information are essential in such activities. Pharmacists often provide specific written medication information to patients so that they may have a better understanding of their medication regimen and the various side effects or problems to expect.

A single prescription for a single patient does not raise the question of investigational medication use. Preparing large quantities of medications that have not been approved for human use by the FDA can violate the federal law. To avoid legal violation, a sponsor of a medication investigation must file a *Notice of Claimed Investigational Exemption for a New Drug* (IND) with the FDA. A pharmaceutical manufacturer usually files such a form; however, others may serve as the sponsor, such as a physician, pharmacist, an institution, such as a hospital, or the hospital pharmacy department.

An abbreviated form of IND is acceptable to the FDA when a physician wants to study a medication that is not sponsored by a manufacturer. The physician may serve both as sponsor and investigator, or the hospital pharmacy may serve as sponsor and the physician as investigator. Some hospital pharmacy departments serve as sponsors on many abbreviated INDs for special medication dosage forms that are not available commercially. The required forms for the sponsor and investigator plus the new-medication regulations are available from the FDA.

INTRAVENOUS ADMIXTURES—Hospital pharmacists are well trained to organize, develop, and operate a centralized pharmacy intravenous admixture service.[15] These services have been found to:

- Save nursing time for other professional nursing roles
- Provide a system for screening physical-chemical incompatibilities and dispensing stable preparations
- Minimize pharmaceutical calculation errors
- Reduce the risk of medication error by providing additional checks.[16]
- Centralize responsibility for preparation of parenteral admixtures.
- Label admixtures with rate of infusion as prescribed by the physician and provides a standardized label format
- Provide an aseptic environment for the preparation of admixtures
- Conform to the standards recommended by the JCAHO
- Conform to the guidelines established by the National Coordinating Committee on Large-Volume Parenterals
- Provide a mechanism for appropriately creating patient charges
- Provide for the preparation of solutions that are not commercially available

The JCAHO wisely promulgated the concept that the pharmacist should be involved in the preparation of medications preparing intravenous admixtures. In its 2004 *Standards for Accreditation,*[17] frequently, the JCAHO refers to the subject of the safe and accurate handling of all medications, including intravenous admixtures. One especially relevant statement is:

> *When an on-site, licensed pharmacy is available, only the pharmacy compounds or admixes all sterile medications, intravenous admixtures, or other drugs except in emergencies or when not feasible (for example, the products stability is short).*

In rising to the challenge posed by the JCAHO, it is essential that the pharmacist be involved in preparing intravenous admixtures. The responsibility for preparing intravenous admixtures is actually the same as that assumed for the unit-dose distribution system. It is important that specific guidelines for an effective intravenous admixture program are formulated.

The ASHP has furnished a document entitled *Quality Assurance for Pharmacy-Prepared Sterile Products* (1996).[18] These guidelines promote greater attention to clean-room technology, personnel training, validation, and quality assurance procedures. Specific guidelines for compounding cytotoxic and hazardous medications are also provided by the ASHP in a technical assistance bulletin. The intravenous admixture service can serve as a base for other pharmacy services such as chemotherapy compounding, allergy extract preparation, and parenteral home care programs.

AMBULATORY CARE SERVICES—As ambulatory care activities continue to increase within the institutional setting, the hospital pharmacist becomes more and more involved in providing services to these patients. These patients are often seen in clinic settings, by home care services, by hospice services, infusion centers, etc. Pharmacists practicing in ambulatory care settings have expanded many of the service concepts initiated in the hospital and the community pharmacy settings. They include special patient information brochures, patient dosing calendars, special packaging, patient education for home care, review of prescribing practices and recommendations for improvement, development of therapeutic protocols, etc. In addition, pharmacists in some clinics have collaborative practice agreements with physicians that allow the pharmacist to monitor selected patients and prescribe or adjust specific medication therapy in accordance with the agreement or protocol (eg, anticoagulation, hypertension, asthma, diabetes). These collaborative practice agreements can be established in most states. However, as of this publication, pharmacists are not currently recognized by the Center for Medicare and Medicaid as a provider, and therefore cannot bill independently for these services. The ASHP has promulgated a guideline to assist pharmacists entitled *Minimum Standard for Pharmaceutical Services in Ambulatory Care* (1999). These activities will continue to increase as more emphasis is placed on ambulatory care as part of the total patient care program by hospitals and, ultimately, when pharmacists achieve provider recognition.

TECHNOLOGY AND AUTOMATION IN PHARMACEUTICAL CARE—Significant progress has been made through the use of computers and hardware technology such as automation devices, robots, and point of care automated dispensing technology.[19,20] This development has been in concert with the pharmacist's responsibility for medication distribution and control. Intravenous solution compounders provide

efficient methods of aseptically formulating various sterile solutions and additives into a final intravenous admixture product. Robotics connected to the pharmacy computer are able to package and select medications that are patient-specific for distribution by pharmacy. Other robots can select the appropriate medication, count a specified quantity, place the medications into a dispensing vial, and label the vial with patient-specific directions for ambulatory care pharmacy practice. Prescription dispensing machines can select the appropriate prescription medication vial, label the vial with the patient-specific information and instructions, and provide written patient teaching information upon receipt of electronic physician order. Decentralized point of care stations located on patient-care areas can provide the nurse access to medications for patient administration. These decentralized point-of-care systems are akin to bank automated teller machines (ATMs) in that they are controlled centrally and provide only restricted authorized access. They should be programmed only to allow access to medications for which that patient has an order on designated floor stock medications. As these new technology systems develop, the pharmacist must incorporate them safely into the hospital's medication distribution system to continue appropriate medication control throughout the hospital.

CLINICAL PHARMACY—The concept of *clinical* or *patient-oriented* pharmacy service has gained tremendous acceptance in hospital pharmacy. The hospital environment offers the hospital pharmacist a multitude of opportunities to develop meaningful clinical roles in the safe and rational use of medications in hospitalized, as well as ambulatory patients. This chapter does not include a detailed discussion of the hospital pharmacist's clinical roles and responsibilities because they are discussed elsewhere in this publication.

It is important to note that significant progress is being made in providing ongoing clinical pharmacy services in hospitals. Various service functions are described in the ASHP *Statement on the Role of the Pharmacist in Patient-Focused Care* (1995).

As increased emphasis is placed on cost containment in hospitals and improved medication-therapy utilization, the pharmacist has been valuable in monitoring patient medication utilization and promoting rational therapy. The pharmacist can best carry out the mandate of the P&T Committee relative to appropriate medication therapy. An evolution of clinical pharmacy practice is occurring in that pharmacists are embracing the concept of pharmaceutical care. In essence, the pharmacist is becoming a medication-therapy manager.

Pharmacists often document their clinical workload for various administrative purposes. This documentation often involves recording clinical interventions, financial impact of their interventions, and impact on patient care. Historically, pharmacists have used forms developed within hospital pharmacy departments, and, increasingly, are using computers or handheld personal digital assistants (PDAs) to document workload numbers.

Documentation of clinical services, pharmaceutical care, and associated patient outcomes is important to illustrate the role and contribution of the pharmacist. The patient-specific information and the pharmacists' assessment, plan, recommendations and monitoring should be recorded in the patient's medical record so the information can be shared with other caregivers.

FUTURE PRACTICE—In reviewing the activities of hospital pharmacy practice, one must conclude that no two hospital practices are alike. Hospital pharmacy practice has made significant strides over the past three decades in changing the practice of pharmacists to provide a more patient-oriented pharmacy service. Medication distribution systems have been improved (unit dose and intravenous admixture services), and patient oriented clinical services have been implemented in large and small hospitals alike. Computerization and automation have increased efficiency and provide improved patient and management databases. Practice in hospitals has adjusted to the changing environment of health care. The challenge for the institutional pharmacist and the profession as a whole is to provide pharmaceutical care to all patients by shifting emphasis (not responsibility) from medication distribution to patient care. What the future holds for hospital pharmacy practice in the year 2010 is only speculation. However, it is very likely that dispensing automation, technology, automated medical records and prescriber order entry will free pharmacy staff time spent on technical activities. Technician roles and responsibilities will expand in overseeing medication automation and technical dispensing functions. Pharmacist roles will continue to focus on managing and optimizing medication therapy for inpatients and ambulatory patients, developing medication guidelines and protocols, and optimizing safe medication systems and services. With the significant progress in the last few years, one can be assured that the role of the hospital pharmacist on the health care team will be significant and will be directed at meeting the medication therapy needs of the patient. Thus, the hospital environment provides a rewarding career for the pharmacist.

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CHAPTER 128

Emergency Medicine Pharmacy Practice

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OVERVIEW OF EMERGENCY MEDICINE AND EMERGENCY MEDICINE PHARMACY PRACTICE

Emergency medicine (EM) is an extremely exciting and rewarding area of pharmacy practice. The emergency department's (ED) unpredictability, potential chaotic activity, and patient complexity epitomize the specialty of EM.[1] Clinicians who work in the ED must be able to multi-task and identify the urgency of a task. Clinical services including nursing, pharmacy, social work, radiology, respiratory therapy, and home-care play a critical, central role in the optimal management of a patient presenting to the ED.

The ED serves as one of the first point of care destinations for any patient. A unique quality of EM is that no patient in extremis may be denied or refused care.[2] In this day of budget constraint and diminishing resources, the ED has become the safety net of last resort in a society with millions of underserved, uninsured patients.[1] There are various types of EDs ranging from relatively low-acuity to large trauma centers. Despite the differences in design, the one commonality is the wide spectrum of diseases that are encountered in the ED.

Pharmacists have played a key role in the ED since the 1970s.[3] Initial services focused on inventory control and cost-containment issues and the development of 24-hour pharmacy satellites to ensure accurate inventory of all medications and appropriate intravenous admixture preparation.[4] Clinical pharmacy services have evolved to include identification of drug-related problems, adverse drug reaction surveillance, pharmacokinetic and toxicology consultation, on-call pharmacy services, and provision of cardiopulmonary resuscitation.[3–8] However, a recent survey demonstrated an overall lack of pharmacy services in the ED. The authors surveyed hospital pharmacy departments with pharmacy practice residencies. They documented that only 3.4% of hospitals (n = 4/119)) reported having an ED satellite pharmacy. Further, only 13 (10.9%) of the remaining hospitals surveyed had a clinical pharmacist whose primary responsibility was to provide services to the ED.[4] These results illustrate that the majority of teaching hospitals in the US do not have pharmacy services in the ED. However, 30% (31/119) of the survey respondents stated that they planned to look for funding for ED pharmacy services in the future. This illustrates the potential growth and demand for pharmacists and pharmacy services in the ED.

DRUG-RELATED ISSUES IN THE EMERGENCY DEPARTMENT

Many ED visits and subsequent hospital admissions are in some part, if not entirely, related to a drug-related problem. Drug-related problems can be classified into eight categories: untreated indication, improper drug selection, subtherapeutic dosage, failure to receive drugs (includes patient noncompliance/nonadherence), overdosage, adverse drug reaction, drug interaction, and drugs used without an indication.[9] Although most drug-related problems can be resolved without a major impact on patient health, many are associated with significant morbidity and mortality.[10,11] A probability model estimated that morbidity and mortality associated with drug-related problems account for $76.6 billion in hospital costs, 17 million EM visits, and 8.7 million hospital admissions annually in the US.[12]

Several published reports have documented the problem of drug-related hospital admissions due to adverse drug reactions.[10,11,13] Hospital admissions secondary to all categories of drug-related problems as described above are likely much higher than those solely described for adverse effects.[9] A systematic search of reports published in the English language suggests drug-related problems account for as many as 28% of ED visits, of which as many as 24% result in hospital admissions. Approximately 70% of the drug-related visits to the ED were deemed preventable.[14] A clinical pharmacist in the ED may aid in identifying and resolving drug-related issues with subsequent reductions in recidivism, morbidity, mortality, and economic burden placed on the US health-care system.

SCOPE OF DISEASE

Some of the more common disease states presenting to a general adult ED include: acute stroke, sepsis, status epilepticus, acute respiratory exacerbations (eg, asthma, chronic obstructive pulmonary disease [COPD]), acute coronary syndromes (ie, both ST and non-ST-elevation myocardial infarction), congestive heart failure, cardiac arrhythmias, hypertensive urgencies/emergencies, thromboembolic disease (ie, deep vein and pulmonary thrombosis), acute peptic ulcer disease, acute pancreatitis, diabetic ketoacidosis, and various pain management issues. Depending on the location of the hospital (eg, proximity to an expressway, lower socioeconomic neighborhood), an ED pharmacist may also encounter patients presenting with trauma, various infectious diseases (eg, meningitis, malaria, tuberculosis, pneumonia, endocarditis, urosepsis, skin and soft-tissue infections) and drug overdoses.

PATIENT SELECTION

The ED clinician faces the challenge of addressing pharmacotherapeutic issues of diverse critically ill and non-critically ill as well as ambulatory patients simultaneously. One mechanism to help identify patients who would most benefit from a pharmacotherapeutic consultation is based on the general prin-

ciple of triaging. In simplest terms, triage can be defined as the sorting or prioritizing of items (eg, patients, tasks).[15] Generally, patients with conditions requiring immediate stabilization involving drug therapy (eg, status epilepticus, diabetic ketoacidosis, acute coronary syndromes, cardiac arrhythmias, drug-overdose) should be assessed by the pharmacist first. Other situations, such as therapeutic drug monitoring, various infectious diseases, and patients on medications with a narrow therapeutic index, may be seen after the urgent patients are seen, with admitted or stable patients seen thereafter. Further triaging by the pharmacist may be quite different from that of a nurse or a physician. Another excellent triage mechanism is a direct referral by a fellow clinician (eg, physician, nurse, social work) for a pharmacotherapeutic consultation. In addition, the type of hospital and the individual priority programs identified at that particular institution might help guide the pharmacist in developing a triage system. Furthermore, a pharmacy clinician's skill set and training (eg, focus on trauma or critically ill patients, ambulatory care patients) may also influence the priority given to development of specific pharmacist-based programs in the ED (eg, toxicology consultation, pharmacist-driven medication refill program, asthma management).

EVALUATION OF THE ED PATIENT

Usually, time is a limiting factor in the ED. Thus, it is important to stress that the pharmacist's assessment or evaluation of the patient may occur concurrently with other clinicians. In general, when patients present to the ED, they have very limited formal medical information with them (ie, medical chart, consultation notes, laboratory data). However, if the patient is able to communicate effectively, his/her history is of great importance in patient assessment. Diagnosis of various conditions has been estimated to be based 76% on history, 12% on physical exam, with 12% attributed to ancillary studies (eg, laboratory, radiographic studies).[1] The initial patient examination should focus on the urgent, pharmacy-relevant concerns of the patient. Other medical problems not related to the patient's chief complaint should be addressed by a primary care provider, outside the scope of the ED visit.

Before the patient interview, the clinician should become familiar with the ambulance report, the triage nurse assessment, and the physician's evaluation to date and an old patient chart, if it is available. It is essential for the pharmacist to determine if the patient's chief complaint or reason for ED presentation may be related to particular medications/drug(s), and then develop a pharmaceutical care plan for management in the ED, and for continuation upon admission or discharge.

To this end, it is essential to perform a complete medication history focusing on prescription, over-the-counter medications, herbal and alternative therapies. The medication history should be performed in consultation with the patient or family members as many patients may take their medications differently than that indicated on the prescription vial. Another excellent resource is the patient's usual community pharmacy. For patients who tend to return to the same hospital, the ED pharmacy clinician should refer to medications prescribed/dispensed during previous visits to the ED or other clinics. Inpatient pharmacists on various clinical services may be able to provide a pharmacy-related history (eg, medication history, medication adherence, allergy status, medication-related issues, past medical history). By contacting the in-patient pharmacy clinician, the ED clinician can convey the patient's current medication-related concerns to the pharmacist that will be taking care of the patient if he/she is admitted.

In general, the medication assessment in conjunction with a head to toe evaluation of the patient will help ensure all the drug-related issues are identified/discovered. However, in the event the patient/family may be unable/unavailable to provide any medical or medication history, the physical examination and history from the scene (ie, obtained from the paramedics) takes on even greater importance. In cases where no information is available, the pharmacy clinician, in similar fashion to the ED physician, must use 'detective' skills in combination with his/her knowledge of disease, pharmacology and toxicology to identify potential drug-related problems. In many cases, decisions regarding the ED management will need to be made without the benefit of an extensive work-up.

CONTINUITY OF CARE (SEAMLESS CARE) CONCEPT

Seamless care may be defined as the continuity of patient care between an institution and the community setting, with the goal of optimizing the patient's potential for wellness with as little disruption as possible to the patient's therapy.[16,17] Seamless care involves the transfer of relevant information between caregivers, with the overall intent to improve patient care and health outcomes.[18] Continuity of patient care can occur in a number of different ways (eg, ED to inpatient floor, ED to community partners, ED to patient). It is also important to remember that seamless care is a dynamic process, whereby information may also be transferred back to the ED to optimize patient care in the ED or during hospitalization.[17]

Seamless Care in the Hospital

Communication among health care providers within the hospital environment is a key component in striving to optimize patient care. The prompt initiation and continuation of optimal pharmacotherapy in the ED improves the likelihood of a faster resolution of disease and decrease the hospital length of stay.[19] It is routine for physicians and nurses to 'give report' from the point of origin of the patient (ie, ED) to the floor where the patient is to be admitted (ie, intensive care unit (ICU), in-patient, another institution to where the patient is transferred). A similar interaction should occur between the ED and in-patient pharmacists. Such communication should include details of the patient's presentation, ED course and treatment as well as the intended pharmacotherapeutic plan. The ED pharmacist may start a formal patient profile that is then transferred with the patient once he/she is admitted. This may occur electronically in a fully computerized medication administration record. This process reduces the likelihood of unnecessary medication changes upon admission and improves the continuity of care. In fact, increased communication among health professionals throughout the continuum of in-patient care has been shown to reduce the likelihood of errors.[20]

Seamless Care in the Community

Just as communication between the ED and other health care providers may improve care in the in-patient setting, the same can be accomplished in the outpatient setting upon ED discharge. Discharge from a hospital can be a very confusing and stressful experience for a patient, as he/she attempts to understand and recall elaborate medication changes and other directions despite feeling unwell.

Medication management is an especially important post-discharge issue. Many medications may have been added, deleted, or modified in some manner. This is confusing for the patient and for the health care providers in the community (ie, family physician, community pharmacist).[21] Furthermore, continuity of care (including monitoring of therapies started in the hospital) is more likely to occur if the community providers have a clear understanding of the reason for changes made in the patient's drug therapy.[22] For example, a pharmacy discharge letter is sent routinely to family physicians and community pharmacists for patients discharged from the geriatric unit at the Royal Victoria Hospital in Quebec, Canada. Specific in-

formation communicated in the discharge letter includes: medications upon admission, medications upon discharge, diagnosis (hospital admission), various laboratory values, reasons for treatment modification, and any required follow-up. Physicians, pharmacists, and nurses deemed the letter as being helpful in facilitating the transmission of pertinent information regarding the patient's drug regimen to the community health care providers.[22]

Telephone calls made to patients directly after an ED visit have been shown to increase patient satisfaction, increase patient adherence to follow-up appointments, and improved patient compliance to discharge instructions.[23–26] Dudas et al. demonstrated that follow-up telephone calls after discharge made specifically by pharmacists were associated with increased patient satisfaction, resolution of medication-related problems, and fewer return visits to the ED.[27] The authors also observed a trend toward fewer hospital readmissions within 30 days of discharge for patients receiving a telephone call. Approximately 15% of patients reported new symptoms or concerns during the follow-up telephone call, while 19% were unable to obtain all of their medications prescribed upon discharge. Therefore, the pharmacist who made the follow-up call may have been able to intervene and, subsequently, helped in preventing return ED visits.

PREVENTION OF HOSPITAL RE-ADMISSION

Effective means of sharing the pharmaceutical care plan with either in-patient clinicians or community health care providers is essential in helping to prevent re-admission or future ED visits.[14,17,18,22–27] Leaving a detailed note in the patient's medical record is an excellent means of sharing the care plan with multiple disciplines. For patients who are being discharged directly from the ED, a letter or note written in collaboration with the ED physician is also a great mechanism to provide useful information to the family physician and/or community pharmacist. Finally, the practitioner must remember to communicate the care plan to the patient. This care plan should include patient education and counseling regarding drug therapy and importance of compliance. Once patients understand why their medications are altered (and even understand why they take various medications), it is likely they will be adherent to the prescribed regimen. Ultimately, it is the patient who is responsible for the direction of their health care; hence, it is important to involve him/her in the decision-making process whenever possible.

PHARMACY SERVICES IN THE EMERGENCY DEPARTMENT

Scope and Standards of Practice

There are currently no standards of practice for ED pharmacy services. Pharmacists in the ED setting perform a broad range of distributive, clinical, teaching, and research activities. Some of these activities in teaching hospitals have recently been described by Thomasset et al. and are summarized in Table 128-1.[4] The nature and extent of pharmacy services and pharmacist activities vary from institution to institution.

Distributive Services

Traditionally, drug distribution services in the ED have involved ward stock supply of medications. Provision of unit dose packaging with a 24-hour supply of medication has been limited in the ED setting because a decision regarding patient disposition is usually made quickly. This has also meant that, traditionally, there has been inadequate accountability of medication use in the ED setting. In recent years, ED overcrowding has become a greater issue due to downsizing of hospital beds and a shortage of ICU beds (ie, due to nursing shortages). As a result, patients admitted to the hospital do tend to stay in the ED for prolonged periods of time waiting for a bed.[28–30] According to the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) standards, a patient's medication profile should be reviewed once they are in the hospital for 24 hours.[31] This necessitates a pharmacist's review of medications in the ED, and also raises the issue of provision and accountability of medication use in this setting.

With the advent of technology, many institutions have elected to place automated drug dispensing machines (eg, Pyxis machines) in the ED setting as is common in the ICU or operating room (OR) settings. These are operational either 24 hours a day or only at night, when pharmacy services from either a central location or another satellite pharmacy are not available. These systems provide accountability for drug use and may be related to the individual obtaining the medication as well as the individual patient for whom the drug is intended. They may also facilitate evaluation of drug inventory levels as well as drug utilization reviews. However, pilfering and inappropriate drug selections are not prevented, nor is a patient's medication order reviewed prior to dispensing with this method.

An ED pharmacy satellite staffed with pharmacists and pharmacy technicians is likely the most optimal method of providing fast, accurate, and accountable drug distribution to ED patients. Pharmacy satellites in the ED have been described in the literature since 1985.[32] They have been shown to be cost-effective compared with traditional ward stock systems.[33] Having the pharmacy prepare IV admixtures in the ED pharmacy satellite removes this responsibility from the nurses whose time and effort should be directed to nursing patient care activities. Like the ICU and OR, the ED is a 24-hour operation and pharmacy services should be provided on a 24-hour, 7 days a week basis.[32] As such, most medications, particularly parenteral medications, are needed immediately for patient care and should be available within minutes in the ED setting. Pharmacists have the responsibility of ensuring appropriate stock of all medications used in the ED and, in particular, should be able to quickly provide adequate supplies of commonly used parenteral therapies and uncommonly used antidotes (for toxicological exposure and in instances of exposures

TABLE 128-1. Clinical Pharmacy Services Provided to Emergency

SERVICE	NO. (%) HOSPITALS
Medication-error or adverse-drug-reaction reporting	71 (59.7)
Order clarification	64 (53.8)
Drug or toxicology information	60 (50.4)
Formulary adjustment	51 (42.9)
Cardiopulmonary resuscitation participation	42 (35.3)
Allergy screening	42 (35.3)
ED inservice meetings	44 (37.0)
Drug interaction screening	39 (32.8)
Antimicrobial dosing	36 (30.3)
Drug-use review	36 (30.3)
Renal dosing	33 (27.7)
Drug therapy recommendation	33 (27.7)
Pharmacokinetic dosing	29 (24.4)
Patient education and counseling	24 (20.2)
Research activities	23 (19.3)
Assessment of patient contraindications to therapy	22 (18.5)
Serving as preceptor for students and residents	22 (18.5)
Medication history review	11 (9.2)
Other	13 (10.9)

Originally published in Thomasset KB, Faris R. *Am J Health-Sys Pharm* 2003;60:1561.

to weapons of mass destruction), as well as other commonly used medications used in the ED.[34,35]

Clinical Services

Although there are published guidelines for the scope of practice for pharmacotherapy specialists,[36] clinical pharmacists in primary care,[37] and those practicing in the critical care setting,[38] there are no published guidelines regarding the optimal scope of pharmacy practice or pharmacy-related activities in the ED.[4] The applicability of the aforementioned guidelines to the ED setting may be limited for several reasons. First, the medication needs of patients in the ED may differ from those in the inpatient and primary care settings. Secondly, rapid patient turnover prevents pharmacists from providing standard clinical services and reduces their ability to perform activities that are routine in other settings.[4] Given these caveats, the American College of Clinical Pharmacy (ACCP) practice guidelines for pharmacotherapy specialists may nevertheless be applicable to EM pharmacy clinicians.[36] There are three areas of practice the Guidelines outlined: patient care, education, and research.

Direct Patient Care

The ACCP Guidelines outline the pharmacy clinician's patient care responsibilities in terms of designing, implementing, monitoring, evaluating, and modifying pharmacotherapy to ensure effective, safe, and economical care.[36] In the ED setting, this might involve obtaining a complete medication history including documenting non-prescription, vitamin, herbal, and alternative/complementary therapy use. The clinician should obtain a complete medication history making use of all available and appropriate resources including the patient, medical record, the hospital or community pharmacy, family members, family physician, or provincial/state prescription computer medication records (eg, PharmaNet system in Canada). Various physical assessment skills, interpretation of laboratory studies and diagnostic investigations are necessary to facilitate the implementation of the patient's pharmaceutical care plan. Patient education or counseling is another area of focus for the ED clinician. The pharmacist is a ready source of drug information for the other clinicians in the ED and should be able to retrieve information readily. All of these efforts may decrease the number or frequency of return visits to the ED.

Documentation of patient-specific issues or pharmacotherapeutic care plans in the medical record is also essential for medical-legal reasons and to help facilitate seamless care. Examples of ED pharmacist-driven activities include an ED-based medication refill clinic, toxicology consultation, participation in an acute stroke team, participation in the CPR team, outpatient deep vein thrombosis clinic, outpatient treatment protocol for skin and soft skin tissue infections, facilitation of procedural sedation, and acute pain management, as well as many others.

CHALLENGES TO PATIENT CARE

A variety of barriers may exist to the provision of patient care by the pharmacy clinician in the ED. Communication issues such as language barriers may initially present as a challenge to patient care depending on the ethnic diversity in the surrounding community. Although most hospitals provide interpretative services, these may not be available in a timely manner. In addition, patients who are unable to provide pertinent information, such as those who present with decreased level of consciousness may also pose a problem. These barriers are not unique to the pharmacist, and affect all ED clinicians, and thus, are usually surmountable. Using the patient's family or friends is an excellent resource for obtaining a history or facilitating an assessment. Patients may also come in with prescription vials with their community pharmacy's name or phone number. The patient's community pharmacist is another resource as he/she can help inform the ED pharmacist of any on-going issues (eg, compliance). Accessing old medical charts (eg, paper charts or electronically through a computer system) may also prove to be a timely resource.

There may also be barriers to carrying out clinical pharmacy activities effectively. ED physicians and nurses may not be aware of the specialized knowledge base, training level and skills of an ED pharmacist. As with any new pharmacy service, the pharmacist may need to educate the other health care workers to overcome any resistance he/she may encounter. Full integration of the pharmacy clinician in the ED requires not only competence, skill, and confidence, but also administrative support from the ED and the pharmacy department or academic unit(s) involved. The pharmacist must also spend a considerable amount of time learning about the unique medications that are used in the ED and the unique 'culture' in the ED setting to be effective.

CRITICAL PATHWAYS

Critical pathways are comprehensive patient care plans incorporating all aspects of patient care relating to disease management based on standards of care, current literature, and benchmarking.[39] Critical pathways are also referred to as CarePath, CareMap, clinical pathway, clinical path of care, case management plan, multidisciplinary action plan, collaborative care tract, and Plan of Care in the literature.[40] Critical pathways describe the care of the patient in full including pharmacotherapy, non-pharmacological strategies, interventions, activities, and outcomes (ie, from diagnosis to post-discharge care).[39] Critical pathways standardize patient care and have been shown to reduce the length of hospital stay for coronary artery bypass patients[41,42] and community-acquired pneumonia.[19] They also improve quality of care for patients with acute stroke[43] and acute coronary syndromes.[44] Some of the general goals of the pathway are to aid in the continuity of care, to decrease fragmentation of services, to guide the patient and family through expected treatment and progress, to optimize cost-effectiveness of health care delivery, and to increase satisfaction of patients, families, staff, physicians, and third-party payers.[45]

The ED pharmacist should be involved in the development and implementation of pathways where drug therapy is extensive, expensive, or high risk (eg, ST-elevation myocardial infarction).[39] The pathway serves as an excellent tool not only for improving patient care but also for conducting pharmacy-driven research (eg, drug utilization reviews, pharmacoeconomic, outcomes research), which subsequently aids in establishing and justifying the pharmacy clinician's presence in the ED, and thus improving patient care.

EMERGENCY PREPAREDNESS

The ED pharmacist and pharmacy satellite have a unique responsibility to assist in the planning for, and to participate actively in, the coordinated response in the advent of an unintentional (eg, natural) or intentional (eg, bioterrorism) disaster. Because ED personnel are linked intricately with local and regional emergency medical services and local and regional disaster planning networks, the pharmacist in the ED has many key roles.

The American Society of Health-System Pharmacists (ASHP) Position Statement on this issue describes how a health-system pharmacist may help in this kind of event.[46] Briefly, the ED pharmacist should be involved in institutional and local disaster planning committees to assist in the selec-

tion of pharmaceuticals and related supplies for local and regional emergency inventories. The expertise of the pharmacist allows the planning committees to help develop and disseminate guidelines for the diagnosis and treatment of victims of terrorism attacks. For each biological agent, information should be readily available regarding symptom onset, treatment, post-exposure prophylaxis, patient isolation precautions, and the availability of antidotes at local hospitals. The pharmacist may help develop a procedure for obtaining and preparing antidotes that might not be available or stocked in sufficient quantities because national antidote stockpiles do not arrive quickly and are not designed to supplant local or regional resources.[47,48] The job of a pharmacist during a bioterrorism strike is to make and disseminate antidotes and information rapidly; provide dosage and vaccination schedules for both treatment and prophylaxis, and counsel patients.[34,49–51] During such an event pharmacists will need to find methods to meet the tremendous demand for various medications and to advise prescribers about treatment options. They will receive many telephone calls simultaneously asking for supplies and treatment alternatives.[52] To test the deployment of emergency preparedness plans, the ED pharmacist and pharmacy satellite should participate in organized, institutional disaster drills.

EDUCATION

The pharmacotherapy specialist is responsible for the education of other health care professionals and students, patients, and the public regarding rational use of medications in the ED.[36] The pharmacist is the expert in the field of pharmacotherapy. It is the pharmacy clinician's responsibility to keep current with cutting edge literature, including interpretation and its application to EM. Furthermore, it is also important to educate the rest of the pharmacy department staff regarding new practices in the field of EM to help keep them up-to-date. Most clinical pharmacy specialists will also have an affiliation or a cross-appointment with the faculty/college of pharmacy and/or the school of medicine, with ensuing formal teaching responsibilities. These formal teaching obligations may include coordination of a course or acting as a preceptor to pharmacy or medical students, residents and fellows.

Methods of Education

There are many different teaching opportunities in the ED. The choice of teaching method will depend on the audience and learning objectives. Pharmacist-directed educational activities may include regularly scheduled in-services, journal clubs, or pharmacology rounds. Pharmacists may also choose to participate in ED morbidity and mortality, toxicology, and follow-up rounds. The teaching session may be optimized when done in collaboration with other health care members (eg, nurse educator, physician).

In-services may be provided in traditional classroom style or in electronic format such as through e-mail distribution or web-based continuing education. E-mail is an excellent means of dissemination of information to an audience that is difficult to gather at a common meeting time (eg, due to shift work in the ED). Electronic in-services should be short, concise, and relevant. Avorn and Soumerai conducted a randomized controlled trial of "academic detailing," which involves non-biased information sent to a group of physicians combined with personal educational visits by clinical pharmacists.[53] The authors found academic detailing reduced the prescribing of target medications in addition to financial savings compared to the control group who only received written information. Furthermore, the effect persisted for at least nine months after the start of the intervention, with no significant increase in the use of expensive substitute medication. In a similar study conducted at an academic medical center, Solomon et al. found a reduction in the number of days of inappropriate levofloxacin and ceftazadime antibiotic administration from 8.8 to 5.5 days ($p < 0.05$).[54] The principles of academic detailing are easily applicable to the ED setting.

The pharmacy clinician is the ideal person to initiate and/or facilitate an ED journal club. The pharmacist has an excellent background in medical literature evaluation skills and, consequently, can teach others. The objective of a journal club is to impart basic literature evaluation skills and new clinically relevant knowledge to participants. The selected articles should be pertinent to the ED clinician. A fruitful benefit of a departmental journal club is to utilize evidence-based medicine to impact the choice of new therapies or optimize the use of existing drugs.

Morbidity and mortality rounds are an excellent teaching opportunity and an opportunity to showcase the pharmacy clinician's expertise. The pharmacist brings a unique perspective to patient care, which may enable him/her to identify and resolve drug-related issues that may not be obvious to the other health care team members.

The importance of patient education by pharmacists cannot be overstated. By educating patients in a variety of settings, pharmacists have been shown to improve patient compliance with pharmacotherapy and non-pharmacotherapeutic lifestyle changes in diseases such as asthma, diabetes, hypercholestoremia, heart failure as well as others. All of these diseases are associated with a high rate of recidivism and frequent ED visits. Patient education in the ED may decrease return ED visits and improve outcomes. This may be a very cost-effective investment to be undertaken by EDs and Departments of Pharmacy in the era of ED overcrowding.

Research and Publications

The third guideline the ACCP set forth for pharmacotherapy specialists is in the area of research.[36] The clinician is encouraged to participate in the generation of new knowledge, which pertains to pharmacotherapy affecting ED patients. The research may either be directed by the pharmacist or involve the pharmacist as a co-investigator. There are multiple examples of publications in the pharmacy and EM literature that documents pharmacists' involvement and leadership in conducting research in the ED setting.[52–55] As an example, Rudis et al. recently published several articles dealing with the optimal method of phenytoin loading in the EM.[55] Another example of pharmacist directed research affecting patient care was completed by Spina and Dillon focusing on the effect of dosing probenecid in combination with cefazolin in the ED.[56] Active pharmacist participation in research-related activities (eg, patient identification and recruitment, generation of research ideas and planned analysis for drug studies) in the ED is also very important.[57,58] Moreover, it is important to publish and present research, case reports, or topic summaries in journals and conferences that are read and attended by other clinicians who work in EM in an attempt to increase their exposure and experience with emergency room pharmacotherapy specialists.[55,57,59–63] The ED pharmacist may also be involved with providing input for clinical trials involving drug therapy in the ED, particularly as it relates to study design, data collection, and selection of appropriate outcome measures.

Preparation and Training

The practice of EM can be quite demanding and challenging, and, thus, requires a unique individual. Qualities of successful pharmacy clinicians in the ED include professional competence and confidence, 'tough skin,' compassion, and motivation. The individual should also possess excellent communication and presentation skills. The pharmacist must first have appropriate training regarding the clinical use of drugs ('at the bedside') in the ED. Electrocardiogram interpretation

skills and advanced cardiac life support (ACLS) training as a provider and instructor is also an asset for clinicians working in the ED.

In Canada, in addition to completing an undergraduate baccalaureate degree in pharmacy, a post-baccalaureate professional degree (doctor of pharmacy) is strongly recommended. Further, prior to entering the doctor of pharmacy program in Canada, a hospital pharmacy residency program also aids in the preparation of the clinician. In the US, upon earning the entry-level doctor of pharmacy degree, the clinician may consider a one year's general residency and then complete a specialty residency program in his/her second year. For example, a one-year specialty residency program focusing in the area of EM, critical care, and toxicology is offered by Detroit Medical Center/Detroit Receiving Hospital, and accredited by the ASHP. There are other residency and fellowship programs that focus in critical care and toxicology, and place greater or lesser emphasis on EM. A list of specialty residencies that provide EM training can be found at www.accp.com.

The pharmacy student who wishes to explore a career as a pharmacist in the ED should choose experiential rotations that will allow for direct patient care in the acute care setting, such as in the ED, the ICU and in clinical toxicology. Coursework in acute care as well as courses in physical assessment will provide the student with much needed background for rotations in the ED and ICU. During their experiential training, students should develop clinical thinking and deductive reasoning skills in preparation for a clinical 'hands on' career in EM. The student should also seek out opportunities to shadow an ED clinician (ED physician, nurse, or pharmacist) or volunteer in an ED setting.

The EM pharmacist may also wish to seek certification (note Chapter 120) with the Board of Pharmaceutical Specialties in the area of pharmacotherapy (BCPS). Board certification implies that an individual possesses a high level of expertise in the area of pharmacotherapy. The American Board of Applied Toxicology (ABAT) was established to recognize exceptional knowledge, experience, and competence in the area of toxicology, which is of definite value for the EM clinician in dealing with toxicological exposures.

STRESS IN THE ED

One of the issues that any new health care provider in the ED will confront sooner or later–and may not be able to prepare for ahead of time–is the stress that is inherent is working in an ED. From one perspective, this 'stress' may be the price health care providers 'pay' for the privilege and gratification that comes from saving lives. All EM clinicians will face events which prove at one time or another to be stressful and/or traumatic.[64–67] Stress in the ED may result from a particularly severe patient presentation such as a death of a child, a case of domestic violence, or a mass casualty motor vehicle accident. Stress can also result from a chaotic or heavy workload, disruptive patients or inappropriate responses from health care providers. Several studies have found a neuroendocrine response (ie, cortisol secretion) to stressful situations and self-perceived work stress in the ED among physicians and nurses.[66,68]

Reaction to these stressful situations may vary from humor to frustration, anger, depression or dissociation. The response to stressors in the ED depends on the individual, their level of experience, training and exposure and the surrounding environment.[64–67,69,70] It is vital for all health professionals to be aware of stressors in the ED and to find positive and constructive outlets for feelings of frustration, stress or anxiety. Humor is often used in the ED setting to diffuse such events, to relieve tension, and to cope with often unspeakable trauma.[70] However, there must also be opportunities to either informally or formally discuss these events with other ED clinicians or psycho-behavioral professionals.[69,71–73] All of these resources may be helpful to promote a long career for health care providers in EM.

EVALUATION OF EM PHARMACY PRACTICE

The quality of patient care and pharmacy services provided to ED patients should be evaluated on a regular basis to ensure an optimal level of service is provided. According to the ACCP, there are different aspects of care that need to be evaluated including the process of delivering care and assessing health outcomes.[37] The rationale for establishing an acceptable or ideal process of delivering patient care is that the care should lead to better patient outcomes and quality of care. Furthermore, the information generated in the evaluation process will also likely serve as a source for potential publication or conference presentation.

LOGISTICS—HOW TO GET STARTED

Given that EM pharmacy practice may be intriguing and one may wish to become an EM practitioner, how does one proceed to secure such a position? The first step is to decide on the level of services and practice environment one wishes to work in. Is it at a trauma center or a teaching hospital, etc.? Then, one would have to gather information documenting the need for a pharmacist in the department. It is important to get the support of the pharmacy personnel, and also from clinicians in the ED and hospital administrators.

Writing a proposal is a crucial step, which should involve ideas of potential services or projects that will be implemented including time frame for completion and methods of assessment. Hospital administrators are usually interested in efforts that would optimize patient care and at the same time provide cost savings. Once the hospital or university is interested in having a pharmacy clinician in the ED, the question of funding will need to be addressed. Funding for most hospitals may be the limiting or complicating factor. However, proposing that the department of pharmacy and EM share the financial burden may be a reasonable option for both parties. Other potential sources of funding include grant money from various organizations. The proposal should include an adequate time frame for implementation and assessment of projects and establishing patient care. A 2-year "pilot" study is a reasonable time frame for implementation and evaluation of services.

Also, it is advantageous to review the medical and pharmaceutical literature to identify other practitioners who have been successful in developing and creating an EM service. Networking at conferences with these individuals is also an invaluable means to learn from others and gain their advice/guidance.

FUTURE

The demand and need for ED pharmacists is likely to grow in the near and distant future. The increasing focus on patient safety and optimization of pharmacotherapy; the recognition of the pharmacist as a key member of the healthcare team in the in-patient and outpatient settings; and the continual need to improve the cost-effectiveness of drug therapies in the acute care setting all will increase the demand for the services of an ED pharmacist to provide clinical, distributive, teaching and research services in the ED setting.

CONCLUSION

The ED is an exciting and ideal place for a pharmacist to practice pharmaceutical care, to conduct or participate in research, to educate allied health clinicians and students, and to be of service to patients. The ED is a nontraditional practice site and is emerging as a growing specialty area as the expertise of the pharmacist in this arena is becoming recognized. Further research is needed to determine the extent of existing pharmacy services and pharmacist activities in the ED so that outcomes of pharmacist interventions and activities may be quantified.

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CHAPTER 129

Long-Term Care

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Long-term care has changed dramatically over the last 200 years. In the late 1700s, people who lived to old age were either taken care of by their children or were wealthy enough to afford in-home caretakers. Old-age homes and retirement communities began to appear in the 1800s. Pension and welfare systems were developed. In the 1930s, the Great Depression necessitated the Social Security Act of 1935 to create a national welfare system. For-profit homes were built in which state and Federal governments shared the cost of caring for the aged. Health care licensing systems were created by Hill-Burton in the 1940s. The 1950s and 1960s saw the government become the primary payor for nursing home care and costs began to escalate. Medicare and Medicaid were created in 1965 to provide government health insurance. Medicare and Medicaid payments to nursing facilities exploded, causing Medicare to restrict nursing home coverage. Decreased payments to nursing homes caused a diminished number of staff to care for a growing number of residents and the quality of nursing home care became a concern.[1] The Omnibus Budget Reconciliation Act of 1987 (OBRA 87) was enacted in part to address these quality-of-care concerns. OBRA 87 required that all nursing facilities certified by Medicare retain the services of a consultant pharmacist to ensure that all medication regimens provided to residents were periodically reviewed. The term *consultant pharmacist* generally refers to a pharmacist who practices in a long-term care setting to provide drug regimen review (DRR), medication storage and administration oversight, and staff and resident education.

Pharmacist involvement in long-term care activities grew as a result of these regulations, which include oversight of provision of medications to nursing facilities and consultant pharmacist duties. Pharmacists practicing in the field of geriatrics must not only be cognizant of these guidelines, but must also be able to manage patients with multiple disease states taking multiple medications. Nursing home care has been much improved with the enactment of OBRA '87 and its revision in 1999. While these regulations provide guidelines to medication management of the elderly, pharmacists must also be aware of the quality of life of the patient when recommending drug therapy interventions, including the complexity of the medication regimen, compliance issues, and side effect profiles of therapy.

POPULATION AND NURSING HOME CHARACTERISTICS

In 1950 there were approximately 12 million Americans aged 65 and older. That number is expected to approach 70 million by the year 2030.[2] Because of this, the need to address the issues of long-term care becomes paramount. The impact of the growing elderly population has far-reaching effects on government and private finances, number and quality of nursing facility beds, and availability of home health care services. Health care systems will be providing care to a larger number of sicker patients, as the group of elderly over the age of 85 has increased >274% in the last 34 years. By the year 2050, nearly half of Americans will live to their 85th birthday and will comprise approximately 5% of the total US population.[3]

The male-female ratio continues to decline with age. In 1999, there were 100 women over the age of 85 compared to 49 men. Approximately 35% of women aged 65 to 74 were widowed, compared to 77% of women >85 years old. Older women had a higher poverty rate than older men—for those 65 to 74, 10.7% and 7.0%; 75 and over, 15.1% and 7.5%, respectively.[4] From 1994 to 1996, people aged 65 or older visited their physicians 11.4 times per year and accounted for more than 12 million patient discharges from non-Federal hospital stays. Patients >85 years old were twice as likely to be hospitalized than those aged 65 to 74.[2]

More than 1.5 million Americans resided in nursing homes in 1997. Approximately half of these residents were over the age of 85 and 75% of them were women.[2] In 1999, the number of nursing home residents had risen to 16.4 million in 18,000 nursing homes. Assistance with activities of daily living (ADLs) is the most common reason for admission to a nursing facility. These ADLs include bathing, dressing, toileting, and eating (Table 129-1). Often, residents are unable to follow a medication regimen, whether due to the complexity of the regimen itself or problems with remembering to take medications.

Nursing home care costs currently exceed $40,000 per resident per year. Medicare and Medicaid paid $51 million for nursing home care for residents >65 years old in 1995. This was greater than 70% of the total long-term care expenditures for Medicare/Medicaid in that year. Private long-term care insurance accounted for less than 1% of payments for nursing home care.[5] In 1998, total long-term care spending totaled >$117 billion, with Medicare paying 39%, Medicaid 17.8%, private insurance 7.4%, and 29.5% out-of-pocket payments. Most residents of nursing facilities receive Medicare, Medicaid, Veterans' Administration benefits, and/or use private insurance. Nearly 67% of nursing home residents received Medicaid in 1998.[6] A total of 33 million Americans received Medicare benefits in 1996.[2] Long-term care expenditures for older Americans with disabilities, including those receiving nursing home or community-based care, reached $123 billion in 2000, with more than 65% paid by the government.[7] The projected total long-term care costs (both institutional and community care) by all payors in 2020 is approximately $207 billion and in 2040 rises to $346 billion.[8]

Table 129-1. Characteristics of Nursing Homes

Total Number of Nursing Facilities		18000
Average Number of Beds/Facility		105
Average Occupancy Rate		87%
Private Pay/Day	Skilled Nursing	$146
	Intermediate Care	$114
	Residential	$101
Per Diem	Medicare	$213
	Medicaid	$105
Percentage of Residents with Assistance With ADLs	Bathing	94%
	Dressing	87%
	Toileting	56%
	Eating	47%

Data from National Center for Health Statistics. The National Nursing Home Survey: 1999 Summary Page. Available at: http://www.cdc.gov/nchs/products/pubs/pubd/series/sr13/160-151/sr_152.htm. Accessed March 5, 2003.

Definitions of Long-term Care Facilities

Table 129-2 provides current definitions of long-term care facilities used by the Centers for Medicare and Medicaid (CMS). "Skilled nursing facility" defines a facility that meets specific regulatory certification requirements set out by CMS to provide inpatient nursing care that does not meet the level of care required in a hospital setting. Previous terms for these facilities included *extended care facility, nursing facility, intermediate care facility,* and *skilled nursing home*. The certification requirements for CMS no longer differentiate between "skilled" and "intermediate" care. Intermediate care facilities/mental retardation exist to provide care for developmentally disabled individuals requiring care not meeting the level of skilled nursing or hospitalization.

GOVERNMENT AND PRIVATE PROGRAMS IMPACTING LONG-TERM CARE

There are many government and private certification programs that affect nursing facilities. Table 129-3 provides a selected list of these. Certification by government programs is required in all nursing facilities that care for residents receiving Medicare, Medicaid, and Veterans' Administration benefits. Payment for care-related services is based on the facility's ability to maintain a level of care set out by these government bodies. Accreditation by the Joint Commission on Accreditation of Healthcare Facilities (JCAHO) is voluntary. All of the above-mentioned agencies provide standards and regulations that facilities must comply with to maintain certification.

Legislation has also had a significant impact on long-term care, both in terms of financing health care for elders and improving quality of care in nursing facilities. The Social Security Act of 1935, the Omnibus Budget Reconciliation Act of 1987 (revised 1999), the Omnibus Budget Reconciliation Act of 1990, the Health Insurance Portability and Accountability Act of 1996, and the Balanced Budget Act of 1997 are a few. Currently, there is considerable controversy over the proposed addition of a prescription drug benefit for Medicare beneficiaries.

Table 129-3. Selected Programs and Regulations Governing Long-Term Care

Centers for Medicare & Medicaid Services (CMS) (formerly HCFA, Health Care Financing Administration)
Health Insurance Portability and Accountability Act of 1996 (HIPAA)
Omnibus Budget Reconciliation Act of 1987, updated 1999 (OBRA 87)
Omnibus Budget Reconciliation Act of 1990 (OBRA 90)
Social Security Act of 1935 (SSA 1935)
The Joint Commission on Accreditation of Healthcare Facilities (JCAHO)
Veterans Health Administration (VHA)

The Social Security Act of 1935

The 1934 Committee on Economic Security met with the intention to produce a complete system of social insurance, to include workers' compensation, health insurance, disability insurance, old-age benefits, and survivors' benefits. Unfortunately, many of the health benefits proposed were not included in the January 1935 report to Congress, and it would take nearly three decades until all of the committee's visions were realized.[9] The United States Congress did enact the Social Security Act of 1935 (SSA), which created the Old-Age and Survivors Insurance (OASI) program. This provided retirement benefits to workers age 65 and older. The program became effective in 1937 and is financed by payroll tax paid by employees and employers. The Disability Insurance program was added to the SSA in 1956. In 2001, 39 million beneficiaries received benefit payments from the OASI, with total benefit payments of $372.3 billion. The number of OASI beneficiaries is projected to reach 72 million in 2030. In 2001, the estimated average monthly social security benefit payment was $874.[10] Revenues for Social Security are currently 14% less than expenditures and it is projected that Social Security will be depleted by 2030. At that time, revenues will only pay 70–75% benefits to beneficiaries.[11]

Medicare and Medicaid

The history of Medicare dates back to the enactment of Title 18 of the Social Security Act, "Health Insurance for the Aged" in 1965 (Table 129-4). This created Medicare Part A (Hospital Insurance) and Part B (Supplemental Medical Insurance). Benefits are payable to people >65 years old, Social Security

Table 129-2. Definitions of Long-Term Care Facilities

Skilled Nursing Facility (SNF)	(1) A facility (which meets specific regulatory certification requirements) which primarily provides inpatient skilled nursing care and related services to patients who require medical, nursing, or rehabilitative services but does not provide the level of care or treatment available in a hospital. (2) A nursing facility with the staff and equipment to give skilled nursing care and/or skilled rehabilitative services and other health-related services.
Intermediate Care Facility/Mental Retardation (ICF/MR)	A facility which primarily provides health-related care and services above the level of custodial care to mentally retarded individuals, but does not provide the level of care available in a hospital or skilled nursing facility.
Extended Care Services	An alternate name for "skilled nursing facility services"

Data from Centers for Medicare & Medicaid Services. The Glossary page. Available at: http://cms.hhs.gov/glossary. Accessed March 5, 2003.

Table 129-4. The History of Medicare

DATE	EVENT
1965	Title 18—"Health Insurance for the Aged" of the Social Security Act created Medicare. Part A—Hospital Insurance (HI) Part B—Supplemental Medical Insurance (SMI)
1972	Medicare expanded to include disabled persons who qualify for benefits under Disability Insurance program and certain individuals with end-stage renal disease.
1986	State and local government employees hired after March 31, 1986 and not covered under Social Security required to be covered by Medicare.
1997	The Balanced Budget Act of 1997 expanded delivery of health care under Medicare with the Medicare (+) Choice Program. (Medicare (+) Choice Program allows more types of health insurance plans, including managed care, to serve Medicare beneficiaries.)
1997	The Balanced Budget Act of 1997: home health services not associated with a hospital or skilled nursing facility stay for individuals enrolled in both HI and SMI were transferred from the HI program (Part A) to the SMI program (Part B) effective January 1998.
2000	Congress enacted the Benefits Improvement and Protection Act (BIPA) to increase payments to health insurance plans in an effort to stop plans from withdrawing from the Medicare (+) Choice Program.

Data from Facts From EBRI. August 2002 EBRI Fact Sheet. The Basics of Medicare Page. Available at: http://www.ebri.org/facts/0802fact.htm. Accessed March 5, 2003.

beneficiaries under age 65 with disabilities, and individuals needing renal dialysis or transplantation.[12] All Medicare providers are subject to Federal health care quality standards to qualify for payment. Because Medicare does not cover all needed services, the Balanced Budget Act of 1997 was enacted to expand delivery of health care under the Medicare (+) Choice program. Under this program, more types of health insurance plans, both private insurance and managed care, may provide services to Medicare beneficiaries. These private health insurance programs are referred to as "Medigap." The Centers for Medicare and Medicaid (CMS), formerly the Health Care Financing Administration (HCFA), is responsible for overseeing the administration of Medicare and Medicaid. Title 19 of the Social Security Act, "Grants to States for Medical Assistance Programs," was also enacted in 1965, creating Medicaid. Medicaid is a state program that provides medical services to individuals receiving state public assistance and augments hospital and nursing facility services that are mandated under Medicaid. The discretion for payment for services lies with the individual states.[12] States must cover certain persons who are poor, aged, blind, or disabled.[13] Currently, Medicare does not provide outpatient prescription drug benefits, while Medicaid will provide such benefits based on individual state drug programs and formularies.

Veterans' Health Administration

The Department of Veterans' Affairs provides many health care benefits to veterans of the United States Armed Services. These benefits vary based on many factors, including wartime service, service-connection of illness or injury, and whether or not the health care service was provided by a Veterans' Administration (VA) facility or provider.[14] A veteran who is a resident of a nursing home or is permanently housebound may be eligible for a benefit entitled "Aid and Attendance," which includes prescription medication. Veterans' Administration hospitals and services are available in every state. Veterans' Service Officers, who can be found in most areas, aid in the provision of multiple services to veterans. The Veterans' Millennium Health Care Act was signed into law on November 30, 1999 and will provide increased access to long-term care, both in institutions and community-based care.[15]

The Omnibus Budget Reconciliation Act of 1987

The Omnibus Budget Reconciliation Act of 1987 or The Federal Nursing Home Reform Act was enacted in 1987 and took effect in 1990. This landmark legislation was brought about due to serious concerns about the quality of care in the nation's nursing facilities. Long-term care facilities utilizing Medicare and Medicaid funding must provide services that help each resident attain and maintain the highest practicable physical, mental, and psychosocial well-being.[16] Provisions are made in the OBRA 87' guidelines for quality of life, activities of daily living, resident assessment (MDS–Minimum Data Set), rights to remain in the nursing home, and freedom from unnecessary physical and chemical restraints. The impact of these regulations on pharmacy practice has been enormous. Requirements for dispensing pharmacy services, drug regimen review, and unnecessary psychoactive drugs have changed the practice of consultant pharmacy. These regulations were revised in 1999 to include selected Beer's criteria of inappropriate drugs in the elderly (Table 129-5). Prior to the revision, the unnecessary drug regulations primarily covered antipsychotics, anxiolytics, and sedative/hypnotics. The addition of the Beer's criteria to the regulations added other medications that may have detrimental side effects in the elderly or have little evidence of efficacy. Quality indicators have been developed based, in part, on OBRA 87. These include monitors of prevalence of depressive symptoms, use of psychoactive medications, and use of nine or more medications per resident.

The Omnibus Budget Reconciliation Act of 1990

The Omnibus Budget Reconciliation Act of 1990 requires that each state establish a system of drug use review (DUR) which would ensure that drugs used for Medicaid patients are appropriate, medically necessary, and not likely to result in adverse effects.[17] The prospective DUR process requires pharmacists to screen prescriptions for potential problems, offer to counsel patients about medications, maintain patient profiles, and document certain actions. One impact of OBRA 90 on long-term care is for nursing facilities with independent residential living areas. Residents in independent living facilities are generally required to take their own medications without significant intervention by the nursing staff. Pharmacies providing medications to these residents should have a mechanism in place to counsel these residents about their medications and provide documentation of this counseling.

The Health Insurance Portability and Accountability Act of 1996

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) is a broad set of rules and procedures for protecting the privacy of patient health information. The finalized rules were released on August 9, 2002 and providers of health care must comply by April 14, 2003. Pharmacists and pharmacies, as providers, must take reasonable steps to limit the use or disclosure of private health information to the minimum necessary to accomplish the intended purpose of the use or disclosure. This does not apply to treatment activities, therefore, contacting a prescriber to verify the contents of a prescription is allowed without consent from the patient.[18] Nursing facilities must educate staff about HIPAA and the confidentiality of patient information. It is not acceptable to discuss patient information in an open nurses' station, hallway, cafeteria, or any

Table 129-5. Beers' Criteria

GENERIC	BRAND	HIGH SEVERITY?
Propoxyphene and combination products	Darvon Darvocet N-100	No
Indomethacin	Indocin	No
Phenylbutazone	Butazoladin	No
*Pentazocine	Talwin	Yes
Trimethobenzamide	Tigan	No
Methocarbamol	Robaxin	No
Carisoprodol	Soma	No
Oxybutynin	Ditropan	No
Chlorzoxazone	Paraflex	No
Metaxalone	Skelaxin	No
Cyclobenzaprine	Flexeril	No
*Flurazepam	Dalmane	Yes
*Amitriptyline	Elavil	Yes
*Doxepin	Sinequan	Yes
*Meprobamate	Equanil, Miltown	Yes (If recently started)
*Chlordiazepoxide	Librium	Yes
*Diazepam	Valium	Yes
*Disopyramide	Norpace	Yes
*Digoxin	Lanoxin	Yes (If recently started)
Dipyridamole	Persantine	No
*Methyldopa	Aldomet	Yes (If recently started)
Reserpine	Serpasil	No
*Chlorpropamide	Diabinese	Yes
*Dicyclomine	Bentyl	Yes
*Hyoscyamine	Levsin, Levsinex	Yes
*Propantheline	Pro-Banthine	Yes
*Belladonna alkaloids	Donnatal	Yes
*Clindinium/ chlordiazepoxide	Librax	Yes
Antihistamines	Several	No
Diphenhydramine	Benadryl	No
Ergot mesyloids	Hydergine	No
Iron supplements >325mg/day	Several	No
*Barbiturates	Several	Yes (If recently started)
*Meperidine	Demerol	Yes
*Ticlopidine	Ticlid	Yes

* Denotes inclusion in Tag#329, OBRA 1987 Guidance to Surveyors—Revised 1999
Data from Beers MH. *Arch Intern Med* 1997; 157:1531.

other public place. The HIPAA regulations provide for assessment of monetary sanctions for each HIPAA violation. The National Association of Chain Drug Stores (NACDS) and the American Pharmaceutical Association (APhA) have HIPAA implementation guidelines available.

The Joint Commission on Accreditation of Healthcare Facilities

The Joint Commission on Accreditation of Healthcare Facilities (JCAHO) has been providing accreditation to long-term care facilities for several years. JCAHO accreditation is not required for facility reimbursement for services by Medicare or Medicaid, but is encouraged by some private insurance plans. The goal of the Joint Commission is to improve the quality of health care. Sentinel events, which can include adverse drug reactions, must be reported to JCAHO by accredited facilities. Medication use standards are found primarily in the standards concerning care and treatment of residents (TX) in the JCAHO Standards for Long-Term Care.

Proposed Prescription Drug Benefit for Medicare Beneficiaries

Prescription drugs accounted for 1% of the total national health expenditure of $2.7 billion in 1960. That figure rose to 9.9% of $140.6 billion in 2001.[19] Medicare beneficiaries account for 15% of the US population, but incur 40% of out-of-pocket spending on prescription drugs. Nearly 75% of Medicare beneficiaries have prescription coverage from private health plans or retirement plans, but employment-based health plans are scaling back benefits for prescription drugs and increasing copayments. Medicare beneficiaries spent $87 billion on prescription drugs in 2002. The Congressional Budget Office estimates spending per Medicare beneficiary on outpatient prescription drugs to be $2439 in 2003 and $5816 in 2012. Individuals with Medicare benefits but no drug coverage had an average of 25 prescriptions filled in 1999. Those with drug coverage filled an average of 32 prescriptions. Medicare beneficiaries with Medicaid coverage received an average of 39 prescriptions. The need for a Medicare prescription drug benefit is enormous, but controversy exists as to how it should be provided. Of the proposals that have been issued, most include a deductible to be met before benefits commence. Others suggest a $1000 cap on prescription drug payments after the deductible is reached; and others a $4000 to $6000 stop loss after which Medicare would resume payments for prescription drugs. Questions of eligibility and percentage of individual state responsibilities have yet to be answered. The estimated cost of the benefit is between $200 billion and $500 billion per year between the years of 2005 and 2012.[20] One option that has been discussed is the use of a discount drug card. Many pharmacy organizations, including APhA (American Pharmacists Association), NACDS (National Association of Chain Drug Stores), and NCPA (National Community Pharmacists Association) have criticized this discount card as outside of the legislative authority of the Federal Government.[21] The concern of these organizations rests in the provision of appropriate pharmaceutical care as opposed to simply discounting prescription drugs without utilization review. A further concern for pharmacists is a reimbursement system that discounts beyond average wholesale price and without a reasonable dispensing fee. While the current controversy focuses on the community and outpatient pharmacy practice arena, many Medicare beneficiaries reside in long-term care facilities. While provision will likely be made to include these individuals in any prescription drug benefit, such provision will be complex due to the frequent duality of coverage by Medicaid and Medicare.

PHARMACY PRACTICE IN LONG-TERM CARE

Policies and Procedures

Policies and procedures for organizational aspects, medication orders, ordering and receiving medications from the pharmacy, medication storage in the nursing facility, disposal of medications, medication administration, and medication monitoring are required in long-term care facilities. Sample policy and procedure topics are provided in Table 129-6. The policy and procedure manual establishes guidelines and processes that define how pharmacy services are delivered to the facility. This manual should clearly define the scope of services of the pharmacy and responsibilities of both the nursing facility and the pharmacy. A multidisciplinary approach should be used in writing a policy and procedure manual to ensure that all disciplines involved in pharmacy services agree with and are able to easily use the manual. Most long-term care pharmacies provide services to several facilities and have a basic manual format that can be individualized to the needs of each facility. The requirements of federal and state laws governing pharmacy services in long-term care must be included in the

Table 129-6. Suggested Policy and Procedure Topics

Disposal of Medications and Medication-Related Supplies
Controlled Medications Disposal
Discharge Medications
Medication DestructionI
Returning Medications to Pharmacy
Syringe and Needle Disposal

Medication Administration
Controlled Medications
Enteral Tube Medications
Equipment and Supplies
General Guidelines
Infusion Therapy Products
Injectable Medications
Irrigation Solutions
Medication Administration By Route
Preparation of Emergency Medications
Reconstitution of Injectable Medications
Self-Administration of Medications

Medication Monitoring
Consultant Pharmacist Quarterly Report
Documentation and Communication of Consultant Pharmacist Recommendations
Drug Regimen Review
Medication Administration Monitoring - Med Pass Survey
Psychoactive Drug Monitoring
Quality Improvement
Standing Monitoring Orders for Routine Medication Monitoring

Medication Orders
Prescriber Medication Orders
Standing Orders
Stop Orders

Medication Storage
Bedside Medication Storage
Controlled Medication Storage
Infusion Therapy Product Storage
Medication Storage

Miscellaneous
Adverse Drug Reactions
Drug Product Problem Reporting
Drug Product Recalls
Investigational Medications
Medications Dispensed by Physicians
Medications Errors
Pass Medications
Syringe and Needle Inventory

Ordering and Receiving Medications from Pharmacy
Drug Information
Emergency Pharmacy Service and Kits
Floor Stock Medications
Infusion Therapy Product Labeling
Medication Labeling
Medication Packaging
Medications Brought in by Resident or Family
Ordering and Receiving Medications (Noncontract)
Ordering and Receiving Medications (Provider Pharmacy)
Pharmacy Hours and Delivery Schedule

Organizational
Noncontract Phamarcy
Provider Pharmacy
Consultant Pharmacist Provider Requirements
Infusion Therapy Produces Provider Requirements
Pharmaceutical Services Committee
Pharmacist/Provider Collaborative Practice Agreement

Data from D'Achille KM. Model Policy and Procedures for Pharmaceutical Care in the Long-Term Care Setting. ASCP, 1999.

manual. Table 129-7 provides a listing of relevant federal regulations and where each regulation may be found in the Centers for Medicare and Medicaid *Guidance to Surveyors*. Because of the changing environment of long-term care, the policy and procedure manual ideally should be reviewed and updated annually. The American Society of Consultant Pharmacists provides a reference entitled *Model Policy and Procedures for Pharmaceutical Care in the Long-Term Care Setting* that encompasses all topics required in nursing facilities.[22]

Drug Regimen Review

Drug regimen review (DRR) encompasses nearly all clinical activities of the consultant pharmacist. Each drug regimen must be reviewed at least monthly by the pharmacist when servicing a nursing facility. Reviews may be done quarterly in residential facilities and intermediate care facilities for the mentally retarded (ICFs/MR). Any irregularities found during the review must be reported to the attending physician and director of

Table 129-7. Relevant Regulations and Standards

REGULATION/STANDARDS	CMS REGULATION(S)	TAG #S	MDS SECTION	JCAHO STANDARD(S)
Pharmacy Provider	483.60(a)	F426		CC.3.1
	483.75(h)(1), (2)	F500		
Consultant Pharmacist	483.60(b)(1)–(3)	F427		TX.1
	483.20(b)(2)	F272	O	PE.2
Drug Regimen Review	483.60(c)(1), (2)	F428–30		PE.2
				TX.4
	483.25(l)(1)(i)–(vi)	F329	B-P	TX.4.1
Infusion Therapy Products				TX.2.4.2
Noncontract Pharmacy	483.60(a)	F426		CC.3.1
	483.75(h)(1), (2)	F500		
Medication Preparation and Documentation	483.60(a)	F426		CC.3.1
	483.25(m)(1), (2)	F332–3		TX.3
				TX.4.1
Parenteral Meds Preparation	483.25(k)(2)	F328	L4, P1, G, K, P	TX.2.4.2
Controlled Medications	483.60(b)(2)–(3)	F427		TX.2.10
Enteral Meds Preparation	483.25(k)(2)	F328	L4, P1, G, K, P	TX.2.4.2
Self-Adminsitration of Medications	483.10(n)	F176		TX.3.1
Freedom from Chemical Restraints	483.13(a)	F222	A, C, E, G, J, K, M	
Freedom from Unnecessary drugs	483.25(l)(1)(i)–(v)	F329		TX.4
Freedom from Antipsychotic drugs	483.25(l)(2)(i)	F330	B-P	
Gradual dosage Reduction of Antipsychotic drugs	483.25(1)(2)(ii)	F331		

CMS = Centers for Medicare & Medicaid Services; MDS = Minimum Data Set; JCAHO = The Joint Commission on Accreditation of Healthcare Facilities.

nursing of the facility. After the attending physician receives the consult written by the pharmacist, he/she must provide documentation of agreement or disagreement with the recommendations. The director of nursing can be provided a summary report of recommendations for review and follow up to ensure that all consults have received a response in a timely manner. Neither the director of nursing nor the physician is required to agree with the report or provide a rationale for acceptance or rejection of the recommendation.

Among the indicators that will be assessed by state and federal surveyors monitoring facilities for compliance with federal regulations is DRR. The number of DRRs performed per month will be compared to the average monthly facility census. If the number of reviews falls significantly short of patient census over several months, the facility may be found in noncompliance with regulations. The pharmacist should perform drug regimen reviews in the facility. Data sources necessary to perform appropriate drug regimen review may be found only in the resident chart and medication administration record.

The average number of prescriptions per resident in 1974 was 6.1. In general, this includes both routine and PRN (as needed) medications. The adequacy of DRR could be questioned if a significant number of residents take an average number of medications above this number. Current practice guidelines for many disease states common in the elderly call for use of multiple medications, which may cause an increase in the average number of medications per resident. Documentation by medicine, pharmacy, and nursing concerning reasons for use and efficacy are important in justifying continued use of medications. Adequacy of drug regimen review may also be questioned if the consultant pharmacist performs an excessive number of reviews on the same day. A total of 100 reviews performed on one day should be considered the maximum recommended in order to perform acceptable drug regimen review. The pharmacist performing reviews should determine the significance of any irregularity found. If an irregularity is found to be significant, the physician and/or nursing should be notified immediately and documentation should be provided of that communication to nursing and the attending physician. A signed and dated statement by the pharmacist may be provided for a nonsignificant irregularity to be responded to at a later time. The pharmacist is only responsible for documenting the irregularity and making a recommendation for resolution. It is then the responsibility of the facility to ensure communication to the attending physician. Irregularities that require nursing intervention should be reported to the director of nursing for resolution.

Examples of irregularities can include the following:

1. Multiple orders for the same drug by the same route
2. Drugs administered without regard to stop order policies
3. As needed (PRN) drug orders administered routinely for more than 30 days
4. Residents receiving three or more laxatives concurrently
5. Use of antipsychotics or antidepressants for less than 3 days
6. Concurrent use of two or more hypnotic drugs
7. Concurrent use of two or more antipsychotic drugs
8. Use of thyroid drugs without routine assessment of thyroid function (usually annual)
9. Use of a drug affecting blood pressure without a weekly recorded blood pressure
10. Use of anticoagulant therapy without assessment of clotting function at least monthly
11. Use of insulin or oral hypoglycemics without routine monitoring of blood sugar
12. Use of iron therapy without a red blood cell assessment
13. Use of urinary anti-infectives for chronic urinary tract infections if a urinalysis has not been performed at least once in the first 30 days of therapy
14. Use of three or more analgesics at the same time
15. Use of diuretics without determination of serum potassium within 30 days of initiation of therapy
16. Use of anticholinergic drug therapy with antipsychotic drugs without documented extrapyramidal side effects
17. Orders for drugs for which there is a known drug allergy
18. Inappropriate crushing of solid dosage forms that could result in resident discomfort or disruption of dosage form

The pharmacist should ensure that all medication orders have a corresponding diagnosis documented in the patient record. As needed (PRN) medication orders should include a reason for use in the order. The appropriate medication order includes the drug, dose, route of administration, frequency, and reason for use. Confusion in administration and documentation could result if a range of doses and frequency are given, for example 1 or 2 tablets every 4 to 6 hours. If an as needed (PRN) medication has not been given for greater than 30 to 60 days, a recommendation should be written for discontinuation of the medication. Routine laboratory monitoring should be ordered for appropriate medications. The pharmacist should ensure that the laboratory monitoring is ordered and that results are available in the patient record on a timely basis. Often, lab monitoring is ordered less frequently than would be found in an acute-care setting, for example, a potassium level may be appropriately obtained quarterly in the long-term care setting, but would be drawn much more frequently in a hospital. Significant drug-drug and drug-disease interactions should be identified. A consultant pharmacist should review a drug regimen for the above irregularities monthly, but may also choose to target a specific drug, disease, or laboratory value monthly. This may reduce the sometimes overwhelming nature of drug regimen review and provide focused data for drug use evaluation. The American Society of Consultant Pharmacists provides a reference entitled *Drug Regimen Review: A Process Guide for Pharmacists* that offers information regarding guidelines for appropriate drug regimen review.[23]

Unnecessary Drug Regulations, OBRA 87, Revised 1999

The Omnibus Budget Reconciliation Act of 1987 was enacted to improve the quality of care in the nation's nursing facilities. One of the most important issues addressed was that of unnecessary drugs, those medications that may be used as chemical restraints for difficult behavior problems. The concern was that many of these drugs were used to control residents for the convenience of staff. There is evidence that a substantial decrease in the use of antipsychotic drugs in nursing home residents resulted from the enactment of OBRA 87. According to one longitudinal study, there was a 26.7% reduction in antipsychotic drug use during a 30-month period from April 1, 1989 to September 30, 1991.[24]

The unnecessary drug regulations from OBRA 87 are presented in Table 129-8. These regulations require that each resident's drug regimen be free from unnecessary drugs. An unnecessary drug can include any medication that has an excessive dose, is duplicate therapy, or is used for an excessive duration. Monitoring of medication use is required, as is an adequate reason for use. Initially the unnecessary drug regulations focused on the use of antipsychotic medications. The regulation requires that facilities should not initiate antipsychotic drug therapy for any resident who is not already taking an antipsychotic when admitted to the facility unless the drug is being used for a specific documented condition with gradual dose reductions performed to ensure necessity of therapy. Environmental, medical, and behavioral interventions must be performed and documented as further justification of need for antipsychotic drug therapy. These interventions may include reducing nursing unit lighting at night, appropriate temperature regulation in resident rooms, assessment of pain, monitoring for fecal impaction and urinary tract infection, medication side effects, and behavioral care plans.

OBRA 87 also defined appropriate diagnoses for the use of antipsychotic medications in nursing facilities. Most of these diagnoses require symptoms of psychosis, whether schizophrenia, delusional disorder, psychotic mood disorders, or atypical

Table129-8. Unnecessary Drug Regulations OBRA 1987, Revised 1999

(1) Each Resident's drug regimen must be free from unnecessary drugs. An unnecessary drug is any drug when used:
- (Tag F329) (i) in excessive dose (including duplicate therapy); or
- (ii) for excessive duration; or
- (iii) without adequate monitoring; or
- (iv) without adequate indications for its use; or
- (v) in the presence of adverse consequences which indicate the dose should be reduced or discontinued; or
- (vi) any combinations of the reasons above.

(2) Antipsychotic drugs—Based on a comprehensive assessment of a resident, the facility must assure that:
- (Tag F330) (i) Residents who have not used antipsychotic drugs are not given these drugs unless antipsychotic drug therapy is necessary to treat a specific condition as diagnosed and documented in the clinical records; and
- (Tag F331) (ii) Residents who use antipsychotic drugs receive gradual dose reductions, and behavioral interventions, unless clinically contraindicated, in an effort to discontinue these drugs.

Data from Omnibus Budget Reconciliation Act OBRA 1987 (revised 1999) PL 100-203 Nursing home Reform Act; Guidance to Surveyors—Long Term Care Facilities; pp 114–128.

psychosis (Table 129-9). Residents with organic mental syndromes, including Alzheimer's dementia and vascular dementia, must have associated psychotic or agitated behaviors in order to justify the use of an antipsychotic. The guidelines also suggest that antipsychotics should not be used if specific behaviors are the only indication for use (see Table 129-9). Examples of such specific behaviors include wandering, indifference to surroundings, uncooperativeness, impaired memory, or agitated behaviors that do not present a danger to the resident or others. Residents receiving antipsychotics must be monitored for both efficacy of the medication and potential side effects. Efficacy monitoring would include observing for episodes of specific psychoses or agitated behaviors for which the medication is being used. Movement side effects (motor restlessness, tremors, involuntary movements of tongue or mouth, gait instability), anticholinergic side effects (constipation, dry mouth, urinary retention, blurred vision), and hypotension should be monitored. While there are no specific requirements for frequency of monitoring provided in the OBRA 87 regulations, episodes of behaviors and side effects are generally documented on every shift in most nursing facilities. Routine assessment of involuntary movements is also suggested. The AIMS (Abnormal Involuntary Movement Scale) and the DISCUS (Dyskinesia Identification System–Condensed Use Scale) are most often used for this purpose. Both scales require the resident to perform specific movements of the face, neck, and limbs to assess for possible long-term side effects of antipsychotic medication use. As these side effects are associated with longer-term use of therapy, the performance of these scales is suggested prior to initiation of antipsychotic use and every 3 to 6 months thereafter.

All psychoactive medications require monitoring of side effects and efficacy. This includes not only antipsychotics, but also anti-anxiety medications and sedative/hypnotics. Antidepressant medications are not included in the unnecessary drug regulations because of evidence that depression is underrecognized in the elderly population and any regulation of use of antidepressants may lead to reduced diagnosis and treatment. Many nursing facilities use one form to monitor all psychoactive medications and reduce required paperwork. Often, the provider pharmacy will furnish these forms preprinted with the resident and medication information. Med Pass, Incorporated (PO Box 750218, Dayton, Ohio, 45475-0218, 800-438-8361, sales@med-pass.com) has developed forms to aid in the monitoring of psychoactive medication use in the nursing facility. The American Society of Consultant Pharmacists also has a forms book available that contains examples of usable forms for this purpose.

Dosage reduction requirements of OBRA 87 also include all psychoactive medications (Table 129-10). Attempts at medication reduction should be performed at least twice in 1 year for short-acting benzodiazepines and antipsychotics and three times in 1 year for sedative/hypnotic medications before the further reduction or discontinuation of the drug can be deemed "clinically contraindicated." There are no specific requirements for the percent of reduction undertaken, but a 10% to 25% reduction at any one time can be suggested. This percent reduction will allow for evaluation of symptom emergence without causing a medication withdrawal reaction. Residents taking long-acting benzodiazepines for diagnoses other than a

Table 129-9. Appropriate Diagnosis for the Use of Antipsychotic Drugs

Acute psychotic episode	**Antipsychotics should not be used if one or more of the following is/are the only indication:
Atypical psychosis	Agitated behaviors which do not represent danger to the resident or others
Brief reactive psychosis	Anxiety
Delusional disorder	Depression
Huntington's disease	Fidgeting
Organic Mental Syndromes (now called delirium, dementia, and amnestic and other cognitive disorders by DSM-IV) with associated psychotic and/or agitated behaviors	Impaired memory
	Indifference to surroundings
	Insomnia
Psychotic mood disorders (including mania and depression with psychotic features)	Nervousness
	Poor self care
Schizoaffective disorder	Restlessness
Schizophrenia	Uncooperativeness
Schizophreniform disorder	Unsociability
Tourette's disorder	Wandering

Data from Omnibus Budget Reconciliation Act OBRA 1987 (revised 1999) PL 100-203 Nursing Home Reform Act; Guidance to Surveyors—Long Term Care Facilities; pp 125–126.

Table 129-10. Unnecessary Drug Regulation-Required Dose Reduction (OBRA 87)

Long-Acting Benzodiazepine Drugs	Daily use <4 continuous months unless an attempt at a gradual dose reduction is unsuccessful (long-acting benzodiazepine use is appropriate only if short-acting benzodiazepine use has failed).
Short-Acting Benzodiazepine Drugs	A gradual dose reduction should be attempted at least twice in one year before one can conclude that a gradual dose reduction is clinically contraindicated.
Sedative/Hypnotic Drugs	A gradual dose reduction should be attempted at least three times within six months before one can conclude that a gradual dose reduction is clinically contraindicated.
Antipsychotic Drugs	A gradual dose reduction should be attempted twice in one year before one can conclude that gradual dose reduction is clinically contraindicated.

Data from Omnibus Budget Reconciliation Act OBRA 1987 (revised 1999) PL 100-203 Nursing Home Reform Act; Guidance to Surveyors—Long Term Care Facilities; pp 114–128.

neuromuscular disorder must also undergo a dosage reduction. Long-acting benzodiazepines should only be used when there is documented treatment failure with the use of a short-acting benzodiazepine. It is not sufficient for the physician to simply write an order "clinically contraindicated." There must be justification based on a clinical reason for use, psychiatric consultation, improvement in resident condition, and interdisciplinary monitoring. The exception to the requirement for "gradual dose reduction" is for those residents who have been diagnosed with a psychotic condition (schizophrenia, delusional disorder) taking an antipsychotic medication. However, it is still recommended that these residents undergo dose reduction as appropriate to their medical condition, as continued use of the drug may not be needed.

Recommended daily doses of psychoactive medications can also be found in the OBRA regulations (Table 129-11). At or below these doses, geriatric patients will be less likely to suffer significant side effects. Use of doses above the recommendations will require explanation by the nursing facility, beyond the monitoring and dose reductions previously mentioned. Many nursing facilities provide this further documentation through the use of mental health consultation and multidisciplinary committees that monitor medication use and behavioral symptoms. Some of the medications listed in Table 129-11 were not available when the original regulations were written in 1987, but were added in 1999. Future revisions of the OBRA regulations will likely continue to provide updates to the recommended daily doses.

The 1999 revision of the OBRA 87 guidelines included use of medications other than psychoactive drugs that may be inappropriate in the elderly. This list of drugs and diagnoses/drug combinations was partially adapted from a paper entitled *Explicit Criteria for Determining Inappropriate Medication Use by the Elderly* by Mark H. Beers.[25] The list of inappropriate drugs found in the OBRA regulations are summarized in Table 129-5, along with the risk of severity of adverse events associated with use of each drug. The guidelines direct surveyors to assess resident use of these medications and ensure appropriate documentation of need for use. This documentation should provide adequate reason for use, justification for use of the drug over other options, and monitoring of drug efficacy and side effects. Inclusion in the list was determined based on efficacy, risk of side effects, and adverse effects on concomitant medical conditions.[25] For example, propoxyphene should be avoided in the elderly because it offers few advantages over acetaminophen in pain control and has significant neurologic and cardiotoxic side effects. Drugs with high anticholinergic side effects, such as amitriptyline, diphenhydramine, and dicyclomine, may cause constipation and urinary retention. Sedative/hypnotic medications should be avoided in residents with severe chronic obstructive pulmonary disease and sleep apnea. The reader is referred to the 1997 Beers article for further information regarding specific reasons for medication inappropriateness.

Table 129-11. Recommended Daily Doses of Psychoactive Drugs (OBRA87)

LONG-ACTING BENZODIAZEPINES		
GENERIC	BRAND	DAILY ORAL DOSE
Flurazepam	Dalmane	15 mg
Chlordiazepoxide	Librium	20 mg
Clorazepate	Tranxene	15 mg
Diazepam	Valium	5 mg
Clonazepam	Klonopin	1.5 mg
Quazepam	Doral	7.5 mg
Halazepam	Paxipam	40 mg
SHORT-ACTING BENZODIAZEPINES		
GENERIC	BRAND	DAILY ORAL DOSE
Lorazepam	Ativan	2 mg
Oxazepam	Serax	30 mg
Alprazolam	Xanax	0.75 mg
Estazolam	ProSom	0.5 mg
OTHER ANXIOLYTIC AND SEDATIVE DRUGS		
GENERIC	BRAND	DAILY ORAL DOSE
Diphenhydramine	Benadryl	50 mg
Hydroxyzine	Atarax, Vistaril	50 mg
Chloral Hydrate	Many Brands	750 mg
Temazepam	Restoril	7.5 mg
Triazolam	Halcion	0.125 mg
Zolpidem	Ambien	5 mg
ANTIPSYCHOTIC DRUGS		
GENERIC	BRAND	DAILY ORAL DOSE
Chlorpromazine	Thorazine	75 mg
Promazine	Sparine	150 mg
Triflupromazine	Vesprin	20 mg
Thioridazine	Mellaril	75 mg
Mesoridazine	Serentil	25 mg
Acetophenazine	Tindal	20 mg
Perphenazine	Trilafon	8 mg
Fluphenazine	Prolixin, Permitil	4 mg
Trifluoperazine	Stelazine	8 mg
Chlorprothixene	Taractan	75 mg
Thiothixene	Navane	7 mg
Haloperidol	Haldol	4 mg
Molindone	Moban	10 mg
Loxapine	Loxitane	10 mg
Clozapine	Clozaril	50 mg
Prochlorperazine	Compazine	10 mg
Risperidone	Risperdal	2 mg
Olanzapine	Zyprexa	10 mg
Quetiapine	Seroquel	200 mg

Daily oral doses represent those doses above which higher doses would need to be explained by the nursing facility.
Data from Omnibus Budget Reconciliation Act OBRA 1987 (revised 1999) PL 100-203 Nursing Home Reform Act; Guidance to Surveyors—Long Term Care Facilities; pp 117–121.

Medication Errors and Adverse Drug Reactions

Tags F332 and F333 of the OBRA guidelines define accepted rates of medication errors in a nursing facility and require that residents are free from significant medication errors (Table 129-12). The facility must monitor for medication errors and ensure an error rate of less than 5%. A medication error is defined as the administration of a drug that is not in accordance with: (1) the physician's order, (2) manufacturer's specifications, or (3) accepted professional standard. A significant medication error is one that causes the resident discomfort or jeopardizes his/her health or safety. Examples include: warfarin administered to a resident without a valid order; omission of a dose of an antibiotic; digoxin 0.25mg given when ordered dose is 0.125mg. The facility must have a policy and procedure in place for staff reporting of medication errors and the error rate should be reported to the Quality Assurance committee in the facility. It is suggested that the nursing facility monitor the occurrence of significant adverse drug reactions (ADR). An ADR is an unintended, undesirable, and unexpected effect of a prescribed medication or a medication error that results in: discontinuation of the drug or modification of the dose; initial or prolonged hospitalization; disability; treatment with further prescription medication; cognitive deterioration or impairment; or death. The JCAHO standards for long-term care TX.4.14 through TX.4.14.2 provide guidelines for the reporting and treatment of adverse drug reactions. 42 CFR 483.25(l) and 42 CFR 483.60(c)(2) of the CMS surveyor guidelines refer to adverse drug reactions. Surveyors for CMS will refer to the revised 1999 OBRA guidelines on unnecessary drugs when assessing for potential adverse drug reactions. If an ADR has occurred, the surveyors will review the resident chart for documentation of facility acknowledgment of

Table 129-12. Medication Error Regulation (OBRA87, Revised 1999)

The facility must ensure that:
(Tag F332) It is free of medication error rates of five percent or greater.
(Tag F333) Residents are free from any significant medication errors.

Medication Error: The observed preparation or administration of drugs or biologicals which is not in accordance with:
1. Physician's order
2. Manufacturer's specifications (not recommendations) regarding the preparation and administration of the drug or biological
3. Accepted professional standards and principles which apply to professionals providing services.

Medication Error Rate:
Medication Error Rate =
(Number of Errors Observed/Opportunities for Errors) × 100
A medication error rate of 5% or greater includes both significant and nonsignificant medication errors. It indicates that the facility may have systemic problems with its drug distribution system.

Significant and Nonsignificant Medication Errors:
Significant Medication Error—An error which causes the resident discomfort or jeopardizes his or her health or safety
*Determining Significance—The relative significance of medication errors is a matter of professional judgment.
1. Resident Condition
2. Drug Category
3. Frequency of Error

*Examples of significant and nonsignificant medication error may be found in OBRA 87 (revised 1999); Guidance to Surveyors—Long Term Care Facilities, Tag Number F333, pp 120–135.7.
Data from Omnibus Budget Reconciliation Act OBRA 1987 (revised 1999) PL 100-203 Nursing Home Reform Act; Guidance to Surveyors—Long Term Care Facilities; pp 129–131.

the adverse drug reaction and any treatment in response to the ADR. The MedWatch program of the Food and Drug Administration serves as a mechanism for reporting adverse drug reactions. If any of the above consequences result from an adverse drug reaction, a MedWatch report should be submitted. MedWatch forms may be downloaded at http://www.fda.gov/medwatch/ for use in submission. The FDA has recently added online submission of ADRs on this website.

Medication Pass Observation

Consultant pharmacists should monitor and make recommendations concerning medication administration passes on at least a quarterly basis. CMS surveyors observe medication administration as a part of the survey process for certification of the facility for Medicare/Medicaid. The objective of the med pass survey is to observe preparation and administration of medications in order to assess compliance with 42 CFR 483.25(m) (medication errors). The pharmacist should observe a minimum of 20 to 25 opportunities for error (both doses administered and doses ordered but not administered). The med passer should compare the medication label with the medication administration sheet to ensure that the drug, dose, and time are appropriate. The resident should be identified by the med passer to avoid administration to the wrong resident. In general, the med passer should adhere to the "5 rights"—right resident, right drug, right dose, right time, right route. Adequate hydration must be provided to the resident when administering medication. If medications are to be crushed for administration, ensure that the dosage form is suitable for crushing (ie, not sustained release or enteric coated). Medication carts should be locked when not in direct view of the medication passer to make certain that unauthorized individuals do not have access.

The acceptable medication error rate is less than 5% without any significant medication errors. A summary of this observation should be provided to the director of nursing and the Quality Assurance committee. As previously mentioned, The American Society of Consultant Pharmacists and Med Pass, Inc. can provide examples of medication pass observation worksheets and checklists.

The Minimum Data Set (MDS)

42 CFR 483.20 of The Omnibus Budget Reconciliation Act of 1987 requires that the facility conduct initial and periodic comprehensive assessment of each resident's functional capacity. This includes demographic information, community lifestyle and daily routine, cognitive patterns, communication, vision, mood and behavior patterns, psychosocial well-being, physical functioning, continence, disease diagnosis and health conditions, dental and nutritional status, skin conditions, activity pursuits, medications, special treatments and procedures, discharge potential, documentation of summary information obtained through resident assessment protocols (RAPs) and documentation of staff participating in the assessment. This assessment must be completed within 14 days of resident admission, quarterly, annually, and whenever there is a significant change in condition. The facility must use its state-approved resident assessment instrument. The facility must maintain 15 months of assessment data in the resident's clinical record that is readily available to all professional staff. The Resident Assessment Protocols (RAPs) are identified through responses to the individual sections of the MDS (triggers). These triggers identify residents who either have or are at risk for developing specific problems that require further evaluation. The RAPs provide the framework for individual resident care plans. Section O of the MDS involves medication use. Section O1 lists the number of medications the resident is taking (7-day look back), Section O2 is for new medications (90-day look back), Section O3 is injections (7-day look back), and Section O4 records the number of days that the resident received an antipsychotic, anxiolytic, antidepressant, hypnotic, or diuretic (7-day look back). Each medication should be coded based on the drug's pharmacological classification, not how it is being used. Doses are coded based on the number of days received, not the number of doses received. A PRN (as needed) medication is coded based on number of days given. Section U of the MDS is a list of medications that the resident has received in the last 7 days. This list includes the name of the medication and the dose ordered, the route of administration, the frequency of use, the amount administered (number of tablets/capsules), number of times a PRN medication was given, and the National Drug Code. The nursing facility likely will have a nurse serving as an "MDS Coordinator" to ensure that assessments are done on a timely basis. In general, the consultant pharmacist will not be asked by the facility to document on the MDS, but the pharmacist should be aware of the contents of the individual resident MDS for pertinent care issues and spot-check Section O for completion during drug regimen review. Updated information regarding the MDS can be found at http://cms.hhs.gov/medicaid/mds20.

Quality Indicators

The 1999 revision of the OBRA 87 regulations incorporated the use of quality indicators based on the MDS (Table 129-13). Five of the 24 indicators are derived from Section O. These are: (1) prevalence of symptoms of depression without antidepressant therapy; (2) prevalence of residents who take nine or more medications; (3) prevalence of antipsychotic use in the absence of psychotic or related conditions (high and low risk); (4) prevalence of antianxiety/hypnotic use; (5) prevalence of hypnotic use more than two times in last week. Consultant pharmacists need to be aware of these quality indicators and

Table 129-13. Quality Indicators Based on the Minimum Data Set (MDS)

ACCIDENTS	1. Incidence of new fractures
	2. Prevalence of falls
BEHAVIOR/ EMOTIONAL PATTERNS	3. Prevalence of behavioral symptoms affecting others (high risk and low risk)
	4. Prevalence of symptoms of depression
	5. Prevalence of symptoms of depression without antidepressant therapy
CLINICAL MANAGEMENT	6. Use of 9 or more different medications
COGNITIVE PATTERNS	7. Incidence of cognitive impairment
ELIMINATION/ INCONTINENCE	8. Prevalence of bladder or bowel incontinence (high risk and low risk)
	9. Prevalence of occasional or frequent bladder or bowel incontinence without a toileting plan
	10. Prevalence of indwelling catheter
	11. Prevalence of fecal impaction
INFECTION CONTROL	12. Prevalence of urinary tract infections
NUTRITION/ EATING	13. Prevalence of weight loss
	14. Prevalence of tube feeding
	15. Prevalence of dehydration
PHYSICAL FUNCTIONING	16. Prevalence of bedfast residents
	17. Incidence of decline in late loss ADLs (activities of daily living)
	18. Incidence of decline in ROM (range of motion)
PSYCHOTROPIC DRUG USE	19. Prevalence of antipsychotic use in the absence of psychotic or related conditions (high risk and low risk)
	20. Prevalence of antianxiety/hypnotic use
	21. Prevalence of hypnotic use more than two time in last week
QUALITY OF LIFE	22. Prevalence of daily physical restraints
	23. Prevalence of little or no activity
SKIN CARE	24. Prevalence of stage 1-4 pressure ulcers

Data from Center for Health Systems Research and Analysis. Quality indicators page.
Available at: http://www.chsra.wisc.edu/CHSRA/Quality_Indicators/ toc.htm. Accessed March 6, 2003.

the facility performance on them. Quality indicators should be incorporated into the consultant pharmacist reports to the facility, along with an explanation of any deviation from the norm. If the facility has a high rate of residents taking more than nine medications or a high rate of use of antipsychotic medications in the absence of psychotic conditions, the facility will have to justify this to CMS surveyors. Consultant pharmacist drug regimen review recommendations and drug use evaluation may aid in providing justification. Prevalence of falls should be of interest to the consultant pharmacist when determining appropriateness of sedating drug therapy. Bowel and bladder incontinence and fecal impaction patterns may direct the consultant pharmacist to evaluate the facility's use of laxative medications. Prevalence of residents receiving tube feedings should prompt the consultant pharmacist to evaluate the drug regimen of those residents to ensure that all medications are suitable for tube administration and do not interact with tube feedings.

Interdisciplinary Health Care Teams

Interdisciplinary teams are defined as health care teams that have members from different disciplines; those members have interdependent, collaborative roles and meet to plan treatment and evaluate patient response.[26] Many disciplines can be involved in interdisciplinary care teams in long-term care (Table 129-14). While the MDS requires most of these disciplines to provide documentation on the resident assessment, care team meetings can aid the facility in integrating care such that the entire group is responsible for resident function and outcome. The interdisciplinary model works well in long-term care because the resident is being treated for chronic conditions, for which each discipline can contribute to a treatment plan with creative interventions that allow for the best possible functioning of the resident. Care plan meetings generally involve nursing, dietary, recreation, and social services. Pharmacy, respiratory therapy, physical therapy, and occupational therapy are consulted as needed based on the discussion in the care plan meeting. Ideally, these meetings would include the pharmacist, but most consultant pharmacists are responsible for many facilities and only spend a few days per month in each facility. One area in which a pharmacist may become more involved is behavioral care and treatment. There is a trend in nursing facilities toward developing a functional behavioral care committee that meets on a monthly or quarterly basis. This committee discusses residents with problem behaviors that are disruptive or dangerous to self and/or others. Disciplines represented include nursing, social services, recreation, psychology or psychiatry, medicine, and pharmacy. Because use of medications is often a large part of the discussion, having the pharmacist available to provide input regarding choice of drug therapy (or lack of effective drug therapy for the particular behavior), dosing, drug interactions and side effects, and regulatory requirements can optimize the resident outcome. Interdisciplinary care teams help to promote a level of respect for individual disciplines and the need for all in the care of residents in long-term care.

ETHICAL AND QUALITY OF LIFE CONSIDERATIONS

An individual's entitlement to the concern, respect, and protection of the community does not diminish with age.[27] This is considered to be the first principle of gerontology and is the principle which, if subscribed to by geriatric practitioners, can ease some of the ethical dilemmas that frequently arise. In this age of increasing technology, increasing cost of health care, and reduced number of individuals with comprehensive health care coverage, issues in the care of elderly patients are debated. Questions have been raised about the benefit of expenditures made in the last year of a patient's life by those who argue that medical resources should be rationed and given to those who can receive the most benefit in terms of longevity. The American Geriatric Society's policy on the allocation of health care resources points out that before any debate on rationing of medical resources can take place, practitioners should first focus efforts on unnecessary spending and waste in all areas of health care and not target a specific population, such as the elderly.[28] The general perception of nursing homes is that these facilities exist to provide comfort and care to geriatric patients in the end of life without going to extraordinary measures to prolong life. In reality, nursing homes are the end-of-life residences of many elderly individuals, and these facilities are expected to adhere to strict regulations regarding the rights of residents to health care.

CFR 42 483.10 of the Omnibus Budget Reconciliation Act encompasses resident rights. This regulation states that the resident has a right to a dignified existence, self-determination, and communication with and access to persons and services in-

Table 129-14. Multidisciplinary Approach to Resident Care

Pharmacy	Respiratory Therapy	Nursing
Medicine	Occupational Therapy	Dietary
Recreation	Social Services	Physical Therapy

side and outside the facility. Exercising these rights means that residents have autonomy and choice, to the maximum extent possible, about how they wish to live their everyday lives and receive care, subject to the facility's rules, as long as those rules do not violate a regulatory requirement.[29] Autonomy and self-determination in health care requires that health care practitioners have a respect for the individual and his/her right to decide what, if any, medical treatment is acceptable and appropriate. Practitioners can aid the person in this decision by providing clear and complete information about the benefits and risks of a particular treatment. While often difficult to ethically accept, those providing care to elderly nursing facility residents will encounter residents who refuse treatment. Documentation should be provided in the medical record concerning the counseling the resident received and a form of resident documentation of resident refusal. A resident should never be coerced into a treatment or made to feel that reprisals will result from refusal. While the responsibility for the outcome of the refusal of treatment lies with the resident, health care practitioners must continue to offer and provide optimal care regardless of the outcome. When a resident refuses treatment, the competency of the resident to make medical decisions can be called into question. Competency of an individual is a legal determination of ability to make decisions in one's best interest. Care must be taken by the health care team to recognize that the elderly are especially vulnerable to a transient lack of competency that has many causes, including medication side effects, delirium secondary to infection, and depression. Before pursuing a ruling on an individual's competency, the facility should ensure that all medical and psychiatric reasons for lack of decision-making abilities are ruled out. Often, a resident will be admitted to a facility with a durable power of attorney (POA) or health care representative/power of attorney (HCR/POA) already appointed. It is important to differentiate between these two terms. The durable POA is a surrogate appointed by the individual to handle his/her property and financial affairs. The HCR/POA is a person appointed by the individual to act in the individual's best interest in matters of health care should the individual be unable to do so. Either of these may be revoked by the individual as long as the person is deemed competent. If a resident does not have a HCR/POA and is deemed not to be competent to make medical decisions, the legal system will appoint a guardian for the resident. Guardianship proceedings often result from an urgent need for a responsible individual to make decisions.

The Federal Patient Self-Determination Act of 1990 was enacted in December 1991 in an attempt to offer patients the opportunity to make their wishes known prior to the need for a HCR/POA or guardian in the form of an advance directive. This Act requires all health facilities to maintain policies and procedures regarding written advance directives. Facilities must document whether or not a patient has an advance directive, but does not require that the facility prepare the document.[30] Advance directives essentially document the individual's wishes for health care should that individual become incapacitated. A patient may make statements about wishes for life-sustaining treatments, including cardiopulmonary resuscitation (CPR), mechanical ventilation, artificial hydration and nutrition, intravenous antibiotics, transportation to the hospital from the nursing facility for treatment of acute illness, and dialysis. These advance directives should be placed in a prominent place in the resident chart, along with the "code status" of the resident. The "code status" refers to the resident's wishes for CPR. Documentation must be made by the physician regarding "DNR" (do not resuscitate) or "full code" (CPR). The physician must talk to the resident or his/her agent prior to this documentation. The *living will* is another term used for advance directives.

The concept of *quality of life* is central to understanding decisions regarding what may or may not be in a resident's best interest. Quality of life is a nebulous term that is variably defined based on the circumstance. Quality of life is generally referred to as multidimensional, incorporating an individual's physical health and functioning, psychological health and functioning, social and role functioning, and perceptions of general well-being. Prolongation of life by life-sustaining measures does not ensure that the individual will continue to maintain a quality of life that is acceptable to him or her. Persons admitted to long-term care facilities are often facing considerable losses in terms of independence and previous lifestyle. They commonly have significant chronic medical conditions and receive multiple medications that may reduce their perceptions of a meaningful life. A resident may express to staff that he/she is not worth the time spent taking care of him/her and believe that no medical treatment can change the inevitable outcome of their demise. In these situations, the medical issues challenging a resident have little to do with the resident's well-being. The facility staff should make every effort to get to know a resident's likes and dislikes and activities enjoyed prior to admission. Residents often have roommates not of their choosing, are told when to eat and take medications, bathe based on a staff schedule, tolerate many individuals in a limited space, and cope with the fact that they live in an institution. It becomes more understandable that residents who are able to make their own medical decisions may choose not to pursue aggressive treatment when these factors are recognized. The practice of geriatrics, whether medicine, pharmacy, nursing, social services, or recreation, should always involve a cognizant effort on the part of the practitioner to recognize issues of quality of life.

GERIATRIC PHARMACOLOGY

There are many age-related changes in the pharmacokinetics of drugs that effect the geriatric patient's ability to appropriately process and eliminate medications. Table 129-15 provides a summary of these changes.

Absorption

Changes occurring in the gastrointestinal tract due to age can be expected to affect the absorption of drugs administered orally. The increased gastric pH that occurs secondary to gastric atrophy may alter drug ionization and solubility and decreased blood flow to the GI tract may decrease the rate and extent of drug absorption. Gastric atrophy also contributes to a decreased surface area for absorption. Decreases are seen in gastric emptying rate and intestinal motility. While most drugs are absorbed via passive transport, a few require active transport, which is reduced in the elderly, leading to a decreased bioavailability of the drug. Of more significance may be the decreased first-pass effect and hepatic extraction that is a function of aging, which may cause enhanced bioavailability of drugs that have a high first-pass effect. Absorption of drugs through the skin is poorly understood in geriatric patients. Evidence exists that while older patients may eventually attain serum levels transdermally similar to those of younger adults, the time to reach these levels may be longer.[31]

Distribution

The distribution of drugs in the body depends on factors such as blood flow, plasma protein stores, body fat, and total body water. Decreased cardiac output and tissue perfusion can lead to decreased renal and hepatic blood flow. A reduction in total body water causes a decrease in the volume of distribution of water-soluble drugs promoting increased plasma concentrations of these drugs. The elderly are more likely to have greater body fat and less lean body mass, which will increase the volume of distribution and terminal half-life of fat-soluble medications. The loading doses of some drugs may be affected by the altered volume of distribution caused by aging. For example, the loading dose of digoxin should be reduced in patients with

Table 129-15. Age-Related Pharmacokinetic Changes

PARAMETER	PHYSIOLOGIC CHANGES
Absorption	↓ active transport = ↓ bioavailability
	↓ first-pass effect = ↑ bioavailability
	↑ gastric pH
	↓ absorptive surface
	↓ splanchnic blood flow
	↓ gastrointestinal motility
	↓ gastric emptying rate
Distribution	↓ volume of distribution = ↑ plasma concentrations of water-soluble drugs
	↑ volume of distribution = ↑ t1/2 of fat-soluble drugs
	↑/↓ free fraction of highly plasma protein bound drugs
	↓ cardiac output
	↓ total body water
	↓ lean body mass
	↓ serum albumin
	↑α_1-acid glycoprotein
	↑ body fat
	↓ tissue perfusion
Metabolism	↓ clearance = ↑ t1/2 for oxidatively metabolized drugs
	↓ clearance = ↑ t1/2 of drugs with high hepatic extration ratio
	↓ hepatic mass
	↓ hepatic blood flow
	↓ enzyme activity
Excretion	↓ clearance = ↑ t1/2 of renally eliminated drugs
	↓ renal blood flow
	↓ glomular filtration rate
	↓ tubular secretion
	↓ renal mass

renal dysfunction due to a reduction in volume of distribution and increased serum drug levels. Substantial changes may occur in serum albumin and α_1-acid glycoprotein. Nutritional deficiencies that include a lack of protein intake may cause a reduction in serum albumin. This can lead to a higher free fraction of drugs that are highly bound to albumin, such as phenytoin. When a routine serum level of phenytoin is drawn, a serum albumin should also be obtained to correct the phenytoin level for the reduced albumin. Other acidic drugs, such as naproxen and warfarin, may be affected by the serum albumin level. α_1-acid glycoprotein is increased in the plasma secondary to inflammation or cancer and can lead to enhanced levels of β-blockers, quinidine, and tricyclic antidepressants, causing a reduced free fraction of drug and reduced drug effects.[32]

Metabolism

The liver is responsible for the majority of drug metabolism, including Phase I (oxidative) and Phase II (conjugative) metabolism. It has been suggested that age-related declines in Phase I metabolism are likely due to age-related reduction in liver volume, rather than decreased enzymatic activity. Drugs that are metabolized by Phase I, including diazepam and theophylline, can be expected to have reduced clearance and increased half-life. Medications such as lorazepam and oxazepam, which undergo glucuronidation, are unaffected by age.[31] For this reason, use of short-acting benzodiazepines such as lorazepam and oxazepam are recommended over use of the longer-acting diazepam. Because of reduced blood flow to the liver, drugs that have a high hepatic extration ratio will have an increased plasma half-live and reduced clearance. While aging can cause a reduced enzymatic activity in the liver, elderly individuals who smoke may have liver induction of the P450 CYP1A2 enzyme. Drugs metabolized by CYP1A2 can be expected to have reduced plasma levels due to increased metabolism. Some examples include amitriptyline, mirtazapine, clozapine, olanzapine, haloperidol, ondansetron, propranolol, theophylline, verapamil, and warfarin.

Elimination

Most drugs are primarily excreted renally. Aging is associated with reduction in renal mass. Glomerular filtration rate, tubular secretion, and renal blood flow are also reduced. The assumption is that most elderly individuals have declining renal function, but as many as one-third may have no renal impairment evident as measured by creatinine clearance. Although the estimation of the creatinine clearance is a useful tool in assessing renal function, it should only be used as a guide, as elderly patients often have a reduction in muscle mass, which is the primary source of serum creatinine. The most often used equation for estimating creatinine is the Cockcroft/Gualt equation:[33]

$$\text{CrCl (males)} = \frac{(140 - \text{age in years}) \times (\text{total body weight in kg})}{72 \times \text{SCr in mg/dl}}$$

For females, the result must be multiplied by 0.85.

ACE inhibitors, aminoglycosides, digoxin, furosemide, lithium, metformin, and vancomycin are examples of drugs whose elimination is impaired by age-related reductions in renal function. Digoxin and lithium have narrow therapeutic indices that require close monitoring of both drug serum levels and renal function in order to avoid significant side effects.

Altered Pharmacodynamics

Evidence exists that the elderly have an enhanced response to drug therapy. Many possible reasons for this have been suggested, including changes in number of receptors, changes in receptor affinity, postreceptor alterations, and age-related impairment of homeostatic mechanisms.[31] Elderly patients may have a greater response to opiates and benzodiazepines, causing an increase in analgesia and central nervous system side effects. They may be less responsive to β-blockers, either due to a reduction in the number of β receptors or alterations in receptor affinity for the drug. The anticoagulant effects of warfarin are enhanced in older individuals, leading to a greater risk of bleeding and a need for reduced and carefully monitored dosing. The elderly may have an increased sensitivity to drugs that affect dopamine. This includes metoclopramide, levodopa, dopamine agonists, and antipsychotics with significant dopamine-antagonist properties.[32]

DISEASE CONSIDERATIONS

In order to perform clinically guided drug regimen review, the pharmacist must have an understanding of common disease states that are likely to be present in the elderly population. Table 129-16 provides an overview of disease states by organ system. While it is beyond the scope of this chapter to provide in-depth discussion of each disease state, a brief overview of the disease and points relevant to the consultant pharmacist will be presented. Tables 129-17 and 129-18 provide useful websites for clinical guidelines for many disease states and information regarding the needs of geriatric patients. Table 129-19 lists selected geriatric care references that may aid the clinician in the treatment of the elderly.

Cardiovascular

Age-related changes in the cardiovascular system and reduced physical activity affect cardiovascular function in the elderly. A decrease in arterial elasticity contributes to an increase in afterload which causes an elevation in blood pressure. Left

Table 129-16. Common Geriatric Disease States

Blood Disorders
Anemia of Chronic Disease
Iron Deficiency Anemia
Thrombocytopenia
Vitamin B12 Deficiency

Bone/Rheumatologic
Bone Fractures
Osteoarthritis
Osteoporosis
Paget's Disease
Rheumatoid Arthritis

Cardiovascular
Atherosclerosis
Cardiac Arrhythmias
Coronary Artery Disease
Heart Failure
Hyperlipidemia
Hypertension
Thromboembolism
Valvular Heart Disease

Dermatological
Herpes Zoster
Psoriasis
Rosacea

Endocrine
Diabetes Mellitus
Hyperthyroidism
Hypothyroidism

Gastroenterologic
Cholecystitis
Constipation
Diverticulitis
Dysphagia
Esophageal Dysmotility
Gallstones
Helicobacter pylori Gastritis
Hiatal Hernia
Peptic Ulcer Disease
Reflux Esophagitis

Neurologic
Alzheimer's Dementia
Essential Tremor
Parkinson's Disease
Peripheral Neuropathies
Stroke
Vascular Dementia

Ocular
Cataracts
Glaucoma

Psychiatric
Alcohol Abuse
Anxiety
Depression
Insomnia
Late Life Psychosis

Respiratory
Asthma
Chronic Obstructive Pulmonary Disease
Lung Cancer

Urinary Tract
Bacteriuria
Benign Prostatic Hyperplasia
Diabetic Nephropathy
Renal Failure
Urinary Incontinence

Table 129-18. Useful Web Sites

TITLE	WEB SITE
American Association of Retired Persons	www.aarp.com
American Pharmaceutical Association	www.aphanet.org
American Society of Consultant Pharmacists	www.ascp.com
American Society of Health System Pharmacists	www.ashp.com
Centers for Medicare & Medicaid	http://cms.hhs.gov
Cytochrome P450 Drug Interactions	http://medicine.iupui.edu/flockhart
ElderWeb	www.elderweb.com
Herbal Therapy	www.uiowa.edu/~idis/herballinks
Medscape	www.medscape.com
MedWatch	www.fda.gov/medwatch
National Institute on Aging	www.nia.hih.gov
Quality Indicators	www.chsra.wisc.edu
Veterans' Adminsitration	www.va.gov

ventricular diastolic filling is reduced and contraction and relaxation of the ventricle is prolonged, leading to heart failure.[34] Progressive heart failure becomes a vicious cycle of sympathetic response to decreased cardiac output causing tachycardia and left ventricular hypertrophy that further damages the heart muscle. Coronary artery disease, valvular heart disease, arrhythmias, and hyperlipidemia are common in the elderly.

Current guidelines for many of the cardiovascular diseases now include the use of several medications at one time to effectively treat these conditions. According to the ACC/AHA Practice Guidelines, patients with heart failure should receive a diuretic and an ACE inhibitor as maintenance therapy. Those who can tolerate a β-blocker should receive a low dose of metoprolol or carvedilol to reduce the increased heart rate that is a response to reduced cardiac output. Evidence suggests that spironolactone, as an aldosterone antagonist, may reduce the deleterious effects of aldosterone on the heart. Digoxin should be considered when there is a need for symptomatic control of heart failure and should be used along with an ACE inhibitor, diuretic, and beta-blocker.[35]

Atrial fibrillation (AF) is the most common cardiac arrhythmia seen in geriatric patients.

AF is often associated with structural heart disease and heart failure. It is a supraventricular tachycardia that occurs in isolation or in association with other arrhythmias. Patients with AF may have drug therapy for heart rate control, which allows the arrhythmia to continue, or for rhythm control. Restoration and maintenance of sinus rhythm will help to alleviate symptoms, prevent thromboembolism and reduce the risk of stroke. Drugs used to control heart rate are considered safer than those with an antiarrhythmic effect. Antiarrhythmics, such as amiodarine, propafenone, quinidine, digoxin, and sotalol may be used in an effort to convert AF to sinus rhythm. Digoxin, non-dihydropyridine calcium antagonists, and beta-blockers may be used for rate control in AF.[36] Anticoagulation with warfarin is recommended for all patients with atrial fibrillation to reduce the risk of thromboembolism and stroke. If a patient cannot tolerate warfarin, aspirin may be used, but is not as effective.

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Express, full report due Fall 2003) suggests that normal blood pressure is <120/80 mmHg. *Prehypertensive* is a new term used in the JNC VII and is defined at a blood pressure of 120–139/80–89 mmHg. Hypertension is divided into two stages. Stage 1 hypertension is a blood pressure of 140–159/90–99 mmHg, stage 2 hypertension is a blood pressure of >160/100 mmHg.[37] Initial drug choices for hypertension should include di-

Table 129-17. Selected Clinical Guidelines Web Sites

TITLE	WEBSITE
Agency for Healthcare Research and Quality (AHRQ)	www.ahrq.gov/clinic/cpgonline.htm
American College of Cardiology	http://www.acc.org/clinical/statements.htm
American Medical Directors' Association (AMDA)	www.amda.com
CDC Prevention Guidelines	http://aepo-xdv-www.epo.cdc.gov/wonder/PrevGuid/prevguid.shtml
eGuidelines	http://www.eguidelines.co.uk
Healthlinks: Evidence-Based Practice and Guidelines	http://healthlinks.washington.edu/clinical/gidelines.html
National Guideline Clearinghouse (NGC)	http://www.guideline.gov.index.asp
National Heart, Lung, and Blood Institute	http://www.nhlbi.nih.gov/guidelines
National Library of Medicine	http://text.nlm.nih.gov
Primary Care Clinical Practice Guidelines	http://medicine.ucsf.edu/resources/guidelines
SUMSearch	http://SUMSearch.uthscsa.edu
Turning Research into Practice (TRIP)	www.tripdatabase.com

Table 129-19. Selected Geriatric Care References

Carstensen LL, et al. *The Practical Handbook of Clinical Gerontology*. Thousand Oaks, CA: Sage Publications, 1996.
Clark TR. *Nursing Home Survey Procedures and Interpretive Guidelines*. American Society of Consultant Pharmacists.
Dipiro JT, et al. *Pharmacotherapy: A Pathophysiologic Approach*, 5th edition. New York: McGraw-Hill, 2002.
Hazzard, WR, et al. *Principles of Geriatric Medicine and Gerontology*, 5th edition. New York: McGraw-Hill, 2003.
Kane RL, et al. *Essentials of Clinical Geriatrics*, 4th edition. New York: McGraw-Hill, 1999.
Koda-Kimble MA, et al. *Applied Therapeutics: The Clinical Use of Drugs*, 7th edition. Philadelphia: Lippincott Williams and Wilkins, 2001.
Semla TP, et al. *Geriatric Dosage Handbook*, 8th edition. American Pharmaceutical Association, 2003.
Tallis, RC, Fillit HM. *Brocklehurst's Textbook of Geriatric Medicine and Gerontology*, 6th edition. London: Churchill Livingstone and Elsevier Science Limited, 2003.

uretics and beta-blockers. These drug classes have been shown to reduce the morbidity and mortality associated with hypertension. ACE inhibitors may be a drug of first choice in patients with diabetes or heart failure, as these drugs may also have a renal protective effect. Patients having had a recent myocardial infarction should receive a beta-blocker to reduce the risk of subsequent MI. Diuretics and long-acting dihydropyridine calcium channel blockers are preferred for older persons with isolated systolic hypertension.[37] The JNC VII also suggests that most persons with significant hypertension will require two or more antihypertensives to control their condition.

The NCEP Guidelines for the treatment of hyperlipidemia suggest that drug therapy be initiated when the low-density lipoprotein cholesterol is >130 mg/dL. Drug therapy can include the *statins* (HMG-CoA reductase inhibitors), niacin, and bile acid sequestrants. If the patient is exhibiting hypertriglyceridemia, a *fibrate* such as gemfibrozil or fenofibrate may be used, but caution should be taken if gemfibrozil is to be used in combination with a statin as the risk for myalgias and rhabdomyolysis is increased.[38] Current evidence suggests that geriatric patients of any age may benefit from the use of a statin to reduce the risk of a cardiac event. Ezetimibe is a new medication for the treatment of hypercholesterolemia that is used in combination with dietary therapy or statins which inhibits the absorption of cholesterol in the small intestine.

Respiratory

Many residents of nursing facilities suffer from chronic obstructive pulmonary disease (COPD), often from smoking tobacco. The quality of life of patients with COPD changes dramatically based on their perceived ability to "catch their breath." Residents who use oxygen are often preoccupied with the oxygen availability in their tanks, the time of the next nebulizer treatment, and anxiety concerning the inability to breathe. Beta-agonists, such as albuterol, remain the mainstay of the treatment of COPD. Albuterol is a short-acting beta-agonist with an onset of action that can rapidly improve respiratory function. Side effects may include an increase in heart rate and anxiety, and reductions in serum potassium. Albuterol is often combined with ipratropium, an anticholinergic, which competitively inhibits cholinergic receptors producing bronchodilation. Long-acting beta-agonists, such as salmeterol, may be used; the patient should be aware that salmeterol should not be used as a "rescue" medication. Corticosteroids are often used in patients with COPD, either for acute exacerbations or long-term therapy when the individual progresses to more significant disease. Inhaled corticosteroids, including fluticasone and beclomethasone, are generally initiated after use of albuterol/ipratropium is not sufficient to control symptoms. Patients should be told to rinse the mouth after use of the inhaler to avoid drug-induced oral fungal infections. The anti-inflammatory efficacy of oral corticosteroids in COPD is not without a price. Diabetes mellitus, osteoporosis, psychological disturbance, and hypokalemia can result from the long-term use of corticosteroids.[39] Some studies have shown that patients receiving oral prednisone at a dose of >5mg/day for several months have a significant risk of osteporosis. Anxiety concerning shortness of breath is a significant problem for patients with COPD. Treatment of this anxiety can often improve the quality of life of the patient. Benzodiazepines, such as lorazepam, can be effective, but the lowest dose possible should be given to prevent respiratory depression.

Neurologic

Common neurologic disorders include Parkinson's disease, Alzheimer's disease, vascular dementia, stroke, and peripheral neuropathies. Stroke often occurs as a result of cardiovascular disease and hypertension. This event can be life-changing for the patient and can result in permanent disability or admission to an institution. Many stroke patients develop hemiparesis, or paralysis on one side of the body. Physical and occupational therapy can be instrumental in aiding these patients in a return to an acceptable quality of life. Antiplatelet therapy is often initiated after a stroke to prevent a recurrence, with aspirin being the most commonly used agent. Warfarin may be used as an alternative. Peripheral neuropathies often occur as a result of poorly controlled diabetes. Drug therapy can help to reduce the pain associated with the neuropathies, but often is only partially effective. Amitriptyline is a very effective medication for peripheral neuropathy, but its use is limited by anticholinergic side effects. Gabapentin has recently been approved for use in post-herpetic neuralgia and is used off-label for neuropathies.

Parkinson's disease results from a markedly decreased number of nigrostriatal dopamine neurons and from nigrostriatal dopamine loss. While primarily a disease of motor function, some patients can develop neuropsychological abnormalities and dementia later in the course of the disease. Anticholinergics, levodopa, and dopamine agonists are the mainstay of therapy for Parkinson's disease. Controversy exists over the optimal time to initiate levodopa due to concerns that dopamine, as a free radical, may cause more damage to the nigrostriatum. Strategic dosing of levodopa is important to minimize "wearing off" and "on-off" problems associated with levodopa therapy. Levodopa-carbidopa is available in regular and sustained release dosage forms to deal with these issues. COMT (catecholamine-O-methyltransferase) inhibitors may increase the amount of levodopa that crosses the blood-brain barrier by interfering with the metabolism of levodopa in the periphery. Tolcapone, the first COMT inhibitor released on the market, is associated with possible hepatotoxicity and guidelines exist for monitoring of liver function. Use of entacapone has largely replaced tolcapone due to a reduced risk of liver abnormalitites with entacapone. Parkinson's patients receiving drugs that boost dopamine in the brain are at risk for symptoms of psychosis, including hallucinations and delusions. Because use of dopaminergic agents is the most effective way to treat the movement problems associated with Parkinson's disease, many patients are resistant to discontinuing or reducing the dose of these drugs. Atypical antipsychotic agents such as quetiapine, risperidone, olanzapine, and clozapine may be used in low doses to minimize psychotic symptoms while not interfering with the need for elevated dopamine in the nigrostriatum.

Dementia is a common condition in nursing home residents. Alzheimer's dementia, Lewy body dementia, and vascular dementia are a few forms. Unfortunately, at this time, definitive diagnosis of Alzheimer's can only be accomplished at autopsy. It is a diagnosis of exclusion. When the individual with dementia is admitted to a nursing facility, he or she has generally declined enough in the course of the disease that control of behavioral symptoms and wandering are the greatest concerns. The acetylcholinesterase inhibitors (tacrine, donepezil, galantamine, and rivastigamine) are available as treatment for mild to moderate Alzheimer's dementia, but the goal of therapy with these agents should be to slow progression of the disease, not to improve cognition. Behavioral treatments for agitation in dementia include short-acting benzodiazepines, trazodone, and anticonvulsants, such as valproic acid and gabapentin. Antipsychotics may be used if documentation can be provided of psychotic symptoms.

Ocular

Visual disturbances secondary to hypertension and diabetes mellitus are common in the elderly population. Unfortunately, little treatment is available for these problems once they have arisen. Use of large-print books and books-on-tape can aid a visually impaired resident who enjoys reading. The resident room should be arranged simply so that the individual has a reduced risk of tripping or falling on furniture and other room items. Glaucoma is an ocular disorder that is characterized by changes in the optic nerve. Elevated intraocular pressure may be involved in the pathogenesis of glaucoma, but is no longer considered to be diagnostic for glaucoma.[40] The beta-blockers (timolol, bisoprolol) are considered to be first-line therapy for glaucoma. Other therapies include topical carbonic anhydrase inhibitors, prostaglandin analogues, and brimonidine. Pilocarpine, epinephrine, and apraclonidine are now considered second line agents in the treatment of glaucoma. The consultant pharmacist should ensure that these medications are appropriately administered such that optimal benefit is obtained, meaning that if a resident is receiving several different drops, the drops should be administered with enough time in between to allow for absorption in the eye.

Psychiatric

Recent evidence suggests that major depression is under-recognized in the elderly population, with the prevalence approaching 20% in females aged 65 to 80.[41] As has been previously mentioned, elderly individuals admitted to nursing facilities suffer life-changing losses in independence and self-esteem. As such, the symptoms of depression can manifest themselves in several ways in geriatric patients, including dementia, isolation, agitated behavior, weight loss, and psychosis. Antidepressants with high anticholinergic side effects should be avoided in the elderly patient. Sertraline, fluoxetine, citalopram, escitalopram, venlafaxine, and bupropion can be considered to be among the antidepressants of first choice for geriatric patients. Anxiety and insomnia often accompany the myriad of chronic diseases that may be present in the older patient. Treating the signs and symptoms of the chronic disease can in many cases alleviate this anxiety and insomnia, but if this is not effective, benzodiazepines, buspirone, and zolpidem can be helpful. If a patient has a diagnosis of sleep apnea, use of a sedative/hypnotic medication should be avoided, as well as the use of a benzodiazepine in a patient with a history of substance abuse.

Bone/Rheumatologic

Osteoporosis and related bone fractures occur frequently in the elderly. Most older persons will have some degree of bone loss related to lack of calcium intake and physical exercise. While osteoporosis has been associated in the female patient with the loss of estrogen after menopause, male patients who have an inadequate diet or take chronic oral corticosteroids may also be at risk. Current recommendations for adequate calcium intake are 1200 mg of calcium and 400–600 IU vitamin D per day. Single doses of calcium should not exceed 600 mg due to lack of absorption of calcium at higher doses. Calcium tablets should be taken with a meal to improve absorption and reduce the likelihood of gastrointestinal upset. Bisphosphonates, risedronate, and alendronate are adsorbed to bone and become a permanent part of the bone structure, preventing bone resorption. These drugs are indicated for the prevention and treatment of osteoporosis. Due to a risk of esophageal ulceration associated with these agents, the patient should take this medication on an empty stomach and remain in an upright position for 30 minutes after ingestion. Calcitonin is also available in injectable and intranasal form for the treatment of osteoporosis. The occurrence of a hip fracture in an elderly patient can cause significant morbidity and mortality. The consultant pharmacist should be aware of medications contained in a resident's drug regimen that could contribute to the risk of falls and act to minimize their use as much as possible.

Gastrointestinal

Swallowing difficulties can present a significant problem to the geriatric patient. A patient with dysphagia, often the result of a stroke, loses the ability to swallow due to lack of muscle control in the esophagus. Choking and aspiration pneumonia are common consequences of dysphagia, and residents with this problem will often require a mechanical soft or pureed diet and thickened liquids. Benzodiazepine anxiolytic medications can be associated with dysphagia secondary to muscle relaxant effects and should be considered when a resident develops dysphagia without signs or symptoms of stroke. This effect is not related to newly initiated drug therapy and may occur at any time during therapy. Patients with significant gastrointestinal complaints should be evaluated for *Helicobacter pylori* infection, a common cause of gastritis in the elderly. Testing for *H pylori* is relatively simple, and it is easily treated. The course of therapy often involves some combination of a macrolide antibiotic, amoxicillin, H2 antagonist or proton pump inhibitor, and/or bismuth subsalicylate in high doses for a 2-week course of therapy. Gastroesophageal reflux disease can be caused by lower esophageal sphincter relaxation associated with aging, exacerbated in those who smoke tobacco. Proton pump inhibitors and H2 antagonists are effective in treating this condition. NSAID-induced gastric ulcers can be a significant source of morbidity and mortality for the geriatric patient. Some evidence exists that COX 2 inhibitors (celecoxib, rofecoxib, valdecoxib) may exhibit a reduced risk of GI bleeding over traditional NSAIDs (nonsteroidal anti-inflammatory drugs). This may be due to a possible reduced deleterious effect of COX 2 inhibitors on the gastroprotective mucosal layer of the stomach as compared to NSAIDs. Constipation remains the most frequent gastrointestinal complaint in elderly individuals. Physiologically, these patients have a prolonged gastric emptying time and decreased gastric motility. Frequently, drug regimens containing multiple medications further effect gastric emptying and motility. Opiate analgesics, anticholinergics, antihistamines, tricyclic antidepressants, calcium channel blockers, NSAIDs, and iron and calcium supplements may all cause constipation. The surveyor guidelines of the OBRA 87 regulations require that documentation of necessary drug therapy be provided for use of three or more laxatives for a resident. Counseling of the resident and education of the facility staff may be necessary regarding appropriate expectations for bowel function and the use of laxatives.

Urinary Tract

Creatinine clearance decreases at the rate of approximately 0.75 ml/min/1.73 m^2 per year beginning in the fourth decade of life.[42] As has been previously mentioned, evaluation of renal function in the elderly using creatinine clearance can be problematic, as this equation is a function of serum creatinine, which is reduced in the elderly secondary to reduced muscle mass. A calculation of creatinine clearance should be made whenever possible for effective drug regimen review to assess the appropriateness of not only drug therapy, but also of dosing. Diabetic nephropathy is characterized by proteinuria of >300 mg/24 hr, an increase in blood pressure, and reduced glomular filtration rate. Microalbuminuria (proteinuria) is also an independent risk factor for myocardial infarction and stroke. ACE inhibitors and angiotensin receptor blockers have been shown to be beneficial in slowing the progression of renal disease in patients and should be considered in patients with progressive diabetic nephropathy.[43]

Benign prostatic hyperplasia is common is elderly males and causes significant distress related to urinary continence. The increased size of the prostate impedes urinary outflow due to a blockage of the bladder neck. Excessive α-adrenergic tone of the prostate may lead to contraction of the prostate gland around the urethra. α-blocking drugs such as terazosin and doxazosin are often used in the treatment of BPH. Finasteride, which blocks 5α-reductase and decreases serum dihydrotestoterone levels, is also effective. The patient taking these medications should be aware that clinical onset of drug action may take several weeks to months.

Endocrine

Much controversy currently exists regarding when to initiate treatment for hypothyroidism. Primary hypothyroidism is defined as an elevated TSH (thyroid stimulating hormone), and a low free T_4 level. Patients with a TSH between 6 and 10 μU per mL may be defined as having subclinical hypothyroidism and may be treated on the basis of documented signs and symptoms of hypothyroidism. These patients have a higher risk of developing overt hypothyroidism than those with a documented normal TSH. Levothyroxine is used as exogenous replacement therapy in patients with hypothyroidism. The TSH level may be used to monitor efficacy of levothyroxine replacement therapy, with the free T_4 obtained as necessary to substantiate TSH findings. When levothyroxine is initiated or the dose changed, a 6- to 8-week period should elapse before obtaining another TSH level. The dose initiation or change may not be reflected in the TSH level before this time.

Diabetes mellitus is a significant health problem in elderly patients. Dietary habits, obesity, and cigarette smoking can all contribute to an individual's risk of developing diabetes. It is especially troublesome in the long-term care environment to impress upon residents the need to comply with the recommended diet and exercise programs. Because quality of life is very important in the care of the elderly in the long-term care facility, often all that can be done is counseling and frequent fingerstick blood glucose measurements. The facility is responsible for providing an appropriate diet through the dietary department, but can often do little about food items brought into the facility by family members and friends. Continued monitoring and documentation of counseling is essential in ensuring that the facility is doing all that it can to provide optimal care to the resident.

Sulfonylureas, insulin, metformin, α-glucosidase inhibitors, and thiazolidinediones are all used in many different combinations in the treatment of diabetes in the older individual. Care must be taken in the use and monitoring of metformin due the risk of lactic acidosis in patients with low oxygen states, including heart failure, renal impairment, and respiratory dysfunction. The dose of metformin must be held prior to and after an intravenous dye procedure, as this procedure may lead to diminished renal function. There is some evidence the thiazolidinediones may be associated with changes in cardiovascular function, and this needs to be further studied before any definitive recommendation concerning their use may be made.

The appropriate use of hormone replacement therapy (HRT) in postmenopausal women is currently the cause of much debate. The results of the Women's Health Initiative study of the benefits and risks of combined estrogen and progestin therapy in women with an intact uterus were published in 2002. This arm of the study was stopped early because the risk of cardiovascular events, including coronary heart disease, stroke, and thromboembolic disease, and invasive breast cancer was greater than the beneficial effects of the therapy.[46] Data from the Women's Health Initiative study was further evaluated for the incidence of dementia and mild cognitive impairment in postmenopausal women (The Women's Health Initiative Memory Study). Women aged 65 years and older were more likely to develop dementia of any type if they had taken HRT. HRT did not prevent the development of mild cognitive impairment.[47] The Cache County Study examined the relationship between use of HRT and the risk of Alzheimer's disease in a group of elderly women with an average age of 73 years. The conclusion of this study was that prior use of HRT was associated with a decreased risk of Alzheimer's disease, but only if the use exceeded 10 years duration.[48] The American Heart Association has published recommendations for the use of HRT in the prevention of cardiovascular disease (CVD). These guidelines state that HRT should not be used for secondary prevention of CVD, and the decision to stop therapy in women who have been receiving long-term HRT should be based on noncoronary benefits of continued use and the patient preference.[49] Many clinical trials have shown a benefit of HRT in the reduction of bone fractures and colon cancer. The risks and benefits of the use of hormone replacement therapy must be weighed carefully for each individual patient.

Anemias

Iron deficiency anemia and anemia of chronic disease are often confused, and the laboratory evaluation of both may overlap. The consultant pharmacist should request several laboratory values in order to make this distinction: serum iron level, TIBC (total iron binding capacity), % saturation, ferritin. In both conditions, the serum iron level and percent saturation will be low. The difference lies in the values for TIBC and ferritin. In iron deficiency anemia, the TIBC will be elevated and the ferritin value low. In anemia of chronic disease, the TIBC will be low and the ferritin elevated. Most elderly patients with anemia suffer from anemia of chronic disease, for which iron therapy has no effect. Iron therapy serves to increase the ferritin level, ferritin being the stored form of iron. Adding additional iron to an already elevated ferritin level will not effectively treat the anemia. Iron supplementation can cause significant gastrointestinal distress and constipation. If supplementation is needed, the maximum recommended dose in the elderly is 325 mg/day.[44]

Pain Management

The appropriate management of pain is one of the biggest challenges facing practitioners in long-term care. The assumption by many elderly patients and practitioners is that pain is an inevitable consequence of aging and, as such, should simply be tolerated. Often, residents in long-term care facilities will not complain of pain and must be questioned by staff in order to adequately assess pain. Many hospitals and nursing facilities have begun to add pain assessment to monitoring of vital signs. Several pain scales are available that simplify the assessment process by allowing the resident to identify a face on a scale or give a number from 1 to 10 to

quantify and qualify pain. Pain assessments should be performed on all nursing facility residents to provide a baseline by which to evaluate further complaints of pain.

The American Geriatrics Society has developed clinical practice guidelines for the management of chronic pain in older persons.[45] NSAIDs, acetaminophen, and opioid analgesics form the backbone of effective pain management. Risks and benefits of NSAID use in a particular elderly patient must be evaluated prior to initiation of drug therapy. Gastrointestinal bleeding is a problematic side effect of these drugs and use of H2-receptor antagonists and proton pump inhibitors is only partially effective in offsetting this effect. COX-2 inhibitors may provide the benefit of anti-inflammatory pain relief with a reduced risk of GI bleeding. Opioid analgesics are likely underused in the geriatric population because of fears of drug-dependency and addiction. This should not be a consideration in relieving pain in the end of life or in significant pain situations. Constipation, impaired consciousness, and hypoxia may result from the use of opioid analgesics and should be closely monitored. Codeine is metabolized by the P450 CYP2D6 isoenzyme system in the liver to an active form. Patients who also take P450 2D6 inhibitors (paroxetine, fluoxetine, cimetidine, quinidine) should receive another opioid analgesic, as the efficacy of codeine will be limited in these patients. Propoxyphene use should be avoided in geriatric patients, as the active metabolite, norpropoxyphene, is both cardio- and neurotoxic. There is also evidence that propoxyphene is no more effective than acetaminophen in pain relief. Acetaminophen can be found in many opioid combination products, and this should be accounted for in any further dosing of acetaminophen to ensure that the maximum daily intake of acetaminophen does not exceed 4 grams. Tramadol is an opiate analgesic that has a secondary mechanism of action thought to involve monoamines, including norepinephrine and serotonin. The dose of tramadol should not exceed 400 mg/day to avoid the risk of drug-induced seizures.

Adjuvant medications used in pain management include anticonvulsants (carbamazepine) and tricyclic antidepressants. Caution should be exercised in the use of tricyclic antidepressants in the elderly due to anticholinergic side effects that may produce confusion, constipation, and urinary retention. Recently, gabapentin has been approved for use in postherpetic neuralgia and is often used off-label for neuropathic pain. Gabapentin may also have an anxiolytic effect that may be beneficial for patients suffering from acute and chronic pain. Other anxiolytics, such as lorazepam and buspirone, may be considered for use in the management of pain.

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CHAPTER 130

Aseptic Processing for Home Infusion Pharmaceuticals

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The provision of home care has existed since the turn of the last century, when societal concerns regarding immigration, industrialization, and infectious diseases spawned the need for visiting nurses. Early homecare services primarily consisted of midwife and nursing assistance for births, and the care of influenza and tuberculosis patients. This early form of home care paved the way for the development of alternate site healthcare. In the past, the term *home care* generally referred to community-based nursing services provided to patients in their homes. Today, the term has been expanded to include home/alternate site healthcare and encompasses: long-term care, and skilled nursing facilities, assisted living and subacute facilities, home care, diagnostic centers, outpatient clinics, ambulatory surgery, rehabilitation facilities, and emergency service markets.[1] The types of alternate site or home-care services are outlined in Table 130-1.

Since 1993, home health care has become the fastest growing segment of health care. In 1999, the US Supreme Court rendered a decision in *Olmstead v. L.C.*, affirming the Americans with Disabilities Act of 1990, which "increased pressure on federal and state programs to deliver advanced health care services to patients at home."[2]

Home infusion is an important component of the alternate site, home health care industry. Home infusion therapy provides therapies to a patient in either the home or alternate site care setting, and emerged as a result of significant changes that occurred in the delivery of health care in the United States. Home infusion therapy involves the prolonged and usually repeated injection of pharmaceutical products (eg, medications, nutrients, or other solutions) most often delivered intravenously, subcutaneously, intramuscularly, enterally, or epidurally. Commonly prescribed home infusion therapies include: antibiotics, chemotherapy, TPN, pain management, immune globulins, corticosteroids, inotropics, hydration, tocolytics, human growth hormone, blood clotting factors, colony-stimulating factors, steroids, other miscellaneous intravenous drugs as well as enteral nutrition.[1] According to the ASHP Guidelines Minimum Standard for Home Care Pharmacies,[3] a home care pharmacy is one that provides primarily, if not exclusively, home infusion products.

Infusion therapy always originates with a prescription from a physician who is overseeing the care of the patient and is designed to achieve physician-defined therapeutic endpoints. A home infusion provider must be a licensed pharmacy. Currently, there are approximately 4,000 pharmacies nationwide providing infusion therapy services. These pharmacies include: local, regional, and national organizations and can be independently owned or hospital-affiliated.[4] Home nursing services are often provided in conjunction with infusion therapy to ensure proper patient or caregiver training and education and to monitor the clinical care of the patient in the home; alternatively, home nursing services can also be provided by a qualified home health agency.

A more recent practice setting offshoot of home infusion pharmacy is the "specialty pharmacy." The most commonly accepted definition of specialty pharmacies are those that serve patients who have rare or chronic diseases with high-cost injectable, infusion, or biotech drugs.[5] Specialty pharmacy patients are generally harder to serve in that oftentimes specialty pharmacy products are often in short supply relative to mass-marketed pharmaceuticals and have more difficult delivery mechanisms (injectables). Oftentimes, the cost of the patient's specialty medication can exceed $10,000 per year. Examples of diseases managed by specialty pharmacies include: hemophilia, and related bleeding disorders, hepatitis, immune disorders, growth hormone deficiencies, multiple schlerosis, rheumatoid arthritis, and RSV.

Home infusion pharmacy services differ dramatically from most retail pharmacy operations. While retail pharmacies primarily dispense oral medications, infusion pharmacies must have the equipment necessary to safely prepare and store sterile parenteral products. This includes: laminar flow hoods to reduce the risk of microbial contamination, modified storage areas for certain drugs, and additional compounding equipment and supplies for mixing drugs.

The dramatic increase in the alternate site healthcare market has largely occurred due the nationwide effort to control health-care costs. During the 1980s, the US healthcare system underwent dramatic changes. In particular, with the introduction of the diagnosis-related groups (DRGs) as a cost-control measure, home care offered a cost-effective alternative following the post-acute hospital stage.[1] Driven by heightened emphasis on cost-effectiveness and cost-containment, technological advances have developed that enabled the safe and effective administration of IV therapies in the home.

Sterile Products in the Home

Because hospital stays have been dramatically reduced, injectable pharmaceuticals are increasingly administered to patients in the home (for both acute and chronic conditions), often by laypersons. The conditions of administration for parenteral products used in the home have introduced numerous concerns for pharmacists to be able to give reasonable assurance to patients that the products received and administered are safe and effective. Home infusion therapy has raised many issues requiring pharmacist's attention including: the use of many sterile products before quality control testing can be complete, potential exposure of the products to temperatures outside the desired storage range during shipping and/or delivery, and, in the home, administration by persons lacking professional

Table 130-1. Types of Alternate Site or Home-Care Services[1]

Pharmaceutical	Includes high-tech infusion therapies, potential and oral medications, inhalation therapies, and clinical monitoring
Skilled Nursing Services	
Semi-skilled Nursing Services	
Custodial Care	
Home Respiratory Therapy / Durable Medical Equipment	
Hospice Care	

skills, administration through devices that may not be adequately protected against contamination, and the lack of definitive evidence of stability for the 30- to 60-day shelf life often required.[6]

Given the realities of the conditions listed above, pharmacists must ensure that their aseptic technique for preparing and dispensing sterile products for home use is beyond reproach. Additionally, pharmacists must do all they can to influence the home-care environment so that the quality of their products will be maintained until the administration of the products to the patient is complete. It is the intent of this chapter to highlight those issues that are essential to ensuring proper aseptic technique is used for the preparation of safe and effective sterile home-care pharmaceuticals.

Aseptic technology is the application of a scientific understanding of the characteristics of viable microorganisms, applied in such a manner that the microorganisms are eliminated, with a high probability of success, from all of the process steps involved in compounding sterile pharmaceutical dosage forms. Regardless of where aseptic processing (compounding) is practiced on products prepared in an institutional setting, a home infusion pharmacy, or a pharmaceutical manufacturing facility, the principles are the same; only the practices differ. Practices will differ because of the nature of the product being produced, the size of the batch, the length of its projected shelf life, and the extent of the regulatory requirements involved. This chapter focuses on the distinctive practices of aseptic compounding applicable to sterile products used in the home. This practice is referred to as "home infusion pharmacy." Compounding is the preparation, mixing, assembling, packaging, and labeling of a drug or device as the result of a practitioner, patient, pharmacist (or Triad) relationship in the course of professional practice.[7]

The dispensing activities of home infusion pharmacies are licensed and regulated by their respective state boards of pharmacy, but there are no specific federal regulations governing these pharmacies, as is the case with the pharmaceutical industry.

Legal and Regulatory Oversight

Each home infusion pharmacy is governed by the State Board of Pharmacy laws for that particular state. While many states have adopted regulations that govern sterile products compounding, many have not. Currently, there is no principle authority on pharmacy compounding in the US. There are, however, health care accrediting organizations such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the Accreditation Commission for Health Care, Inc. (ACHC), yet, neither organization addresses the specific needs of the home infusion or specialty pharmacy. Typically, these accreditations have become a vital prerequisite for doing business. Many third-party payers require home infusion organizations to be JCAHO or ACHC accredited for reimbursement to be rendered.[1]

Patient morbidity and mortality have resulted from incorrectly prepared or contaminated pharmacy-prepared sterile products. Patients receive sterile compounded products that have been stored for extended periods of time before use; and this allows for the growth of a pathological bioload of microorganisms.[8]

The FDA recently published a study that lends credence to its concerns regarding the under-regulated practice of pharmacy compounding. Regulators sampled 29 drugs from 12 pharmacies and found that more than one-third (10 of 29) failed either a drug assay or pyrogen test; nine out of ten drugs were subpotent, and one in ten was pyrogenic.[9] Tragic results of pharmacy compounding have reached the mass media in such outlets as the Associated Press and National Public Radio (NPR). A California-based compounding pharmacy extemporaneously prepared betamethasone in response to a national shortage. The drug was contaminated with *serratia* bacteria, and 38 people received spinal injections of contaminated betamethasone. Dozens of people were hospitalized and treated with antibiotics.[9] Mishaps such as this make a strong case for tighter control of compounded pharmaceuticals.

Other professional organizations have published guidelines on compounding and dispensing sterile products. The United States Pharmacopeia (USP) and the National Formulary and supplements all have legal implications for pharmacists.[11] The National Association of Boards of Pharmacy (NABP) has published less detailed model regulations for use by state boards of pharmacy[12] and the American Society of Parenteral and Enteral Nutrition (ASPEN) has published a special report on safe practices for parenteral nutrition products.[13]

In recent years, two other organizations have developed standards and technical assistance bulletins on the preparation of sterile products. The American Society of Health-Systems Pharmacists (ASHP) has published the *Technical Assistance Bulletin on Quality Assurance for Pharmacy-Prepared Sterile Products*[8] (ASHP-TAB), and the United States Pharmacopeia (USP) general chapter <1206>, *Sterile Drug Products for Home Use*[11], also provides guidance on compounding sterile pharmaceuticals.

The industrial perspective for the preparation of sterile injectable (parenteral) products is presented in Chapter 41 and is referenced when overlapping material is encountered. The reader is encouraged to read the entire chapter to glean applicable aseptic processing principles and practices. Expanded, highly relevant information also can be found in the chapter by Levchuk[14] and the book by Buchanan, McKinnon, Scheckelhoff, and Schneider.[15]

DISTINCTIVES OF ASEPTIC PROCESSING FOR HOME-CARE PHARMACEUTICALS (HCPS)

A reasonable distinction can be drawn between HCPs with a low risk of becoming contaminated under controlled aseptic processing conditions and those with a relatively high risk of such contamination occurring. The USP chapter defines these risks into two levels, low-risk and high-risk.[11] Detailed descriptions of these levels are given in the USP, and the reader should refer to the USP chapter for those details. Similarly, the ASHP has also classified risk levels, using three categories, the descriptions differing from those of the USP in relatively minor ways.[8]

The ASHP and USP guidelines contain valuable information for pharmacists involved in the preparation of sterile products for administration in either the hospital or home setting. However, each guideline contains unique information that is not contained in the other. All pharmacists who compound sterile products are encouraged to read both sets of guidelines and to determine the appropriate risk level of the sterile products that they prepare. As always, professional judgment should be exercised when applying these guidelines to specific pharmacy practice settings to ensure the highest level of product quality. A

comparison of the ASHP and USP classifications and a discussion of the quality requirements for the preparation of pharmacy-prepared sterile products can be found in the articles by Avis[16] and Lima.[17]

Low-risk processing of HCPs normally consists of starting with sterile, commercially available pharmaceuticals, including large-volume injectables (LVIs), such as amino acids, high concentrated dextrose solutions, and sterile water for injection, small-volume injectables (SVIs), and sterile powders, packaged in sealed primary containers. Aseptic compounding of these products then occurs by combining, diluting, subdividing, or otherwise manipulating the products in a noncomplex manner to produce other products to meet the prescribed needs of one or at most, a small group of patients. The devices used to accomplish the manipulations are also sterile, clean, packaged, and disposable. These devices enable the manipulative transfers of liquids with limited exposure to the environment–a closed system. The primary requirement of this type of aseptic compounding is to maintain the sterility and freedom from contamination and the overall quality required of the HCPs when dispensed.

The risk of contamination increases if the HCPs are compounded using components that are not sterile, if the compounding is performed using open tanks or complex or multiple procedures, if an environmental exposure over a relatively long period of processing time is needed, or when a relatively long shelf life is anticipated. Such conditions meet the classification of *high risk*. The pharmacist should be trained to be able to differentiate the risk levels required for the preparation of a given HCP and designate the procedures to be used during for compounding.

Because most HCPs used in the home are not prepared from raw materials but from pharmaceutically manufactured products, and compounding manipulations generally consist of accurately measured liquid transfers, quality control testing requirements are fairly limited. However, the pharmacist is ultimately responsible for the final quality of all of the products dispensed, and confirmatory tests should be performed when appropriate. In such cases, adjustments must be made for sampling, for example, by preparing duplicate products so that one can be tested or by a planned program of sampling (for example, one out of a set of ten similar or identical product units will be tested).

Other distinctive characteristics of HCPs include: a relatively short shelf life of 30 to 60 days, rapid distribution by commercial transportation systems, and storage and administration to the patient by caregivers in the home. As stated previously, these dispensing activities fall under the oversight of the respective state boards of pharmacy and not of the Food and Drug Administration (FDA).

COMPOUNDING FACILITIES

Compounding facilities should be designed to provide adequate space for the work load anticipated and for the appropriate future expansion in work load. All too frequently, expansion space is not initially provided for in the compounding pharmacy and, as the service demands and compounding volume increases, the ability to maintain environmental and process control becomes compromised due to overcrowding.

The pharmacy compounding area must be designed to prevent the contamination of the HCPs during aseptic compounding. Therefore, the work area must be cleanable and sanitizable, with a minimum amount of particle shedding and crevices or other sites where dirt and microorganisms can accumulate. This means the compounding room must have structural surfaces of ceiling, walls, and floors, and work surfaces and storage surfaces that are smooth and resistant to cleaning and sanitizing. Stainless-steel work surfaces and epoxy-coated structural surfaces (or the like) are preferred because they generally meet the required surface characteristics. Equipment and instruments must also meet these general requirements, as much as possible. Equipment with noncleanable, particle-shedding motors, gears, and other such structures should be contained, preferably in stainless-steel enclosures.

The arrangement of the compounding area should be planned for convenient work flow, with minimal crossover and controlled progression through barrier structures, doors, or pass-throughs from uncontrolled rooms (such as storerooms) to increasingly cleaner-controlled environments. The preceding environment serves as a buffer area to reduce the ingress of contaminants into the next area of a higher level of cleanliness.

The most critical work area, the area where the HCPs are compounded, is the Class 100 area (contains no more than 100 particles of 0.5 μm and larger per cubic foot) where the aseptic compounding manipulations will be performed. Compounding activity typically occurs on a laminar airflow workbench (LAFW), with an air stream cleaned by passage through a high-efficiency particulate air (HEPA) filter. The laminar flow air stream efficiently and continuously sweeps the work area with clean air at a velocity of 90 fpm ± 20%. For more details concerning air cleanliness classes, clean air operations, and laminar airflow, the reader is referred to Chapter 41.

An example of a medium-sized compounding pharmacy facility floor plan, taken from the USP,[11] is shown as Figure 130-1. Using this example, the compounding procedures followed for controlling the ingress of contamination may be illustrated as follows. The compounding supplies are brought from the storage room to the demarcation line on stainless steel or plastic carts. The supplies are then carefully removed from the primary packaging and are transferred to a cleaned and sanitized cleanroom cart. The cart is cleaned with filtered isopropyl alcohol (IPA). The supply items are then brought into the buffer room, with the cart wheels sanitized at the entryway.

Clean, sanitized supplies may be stored temporarily in the buffer room but, preferably, the needs for each compounding shift should be used directly from the cart. The supply cart(s) is positioned conveniently for use by the operator(s) (compounders) at the LAFW. At the end of each shift, or more

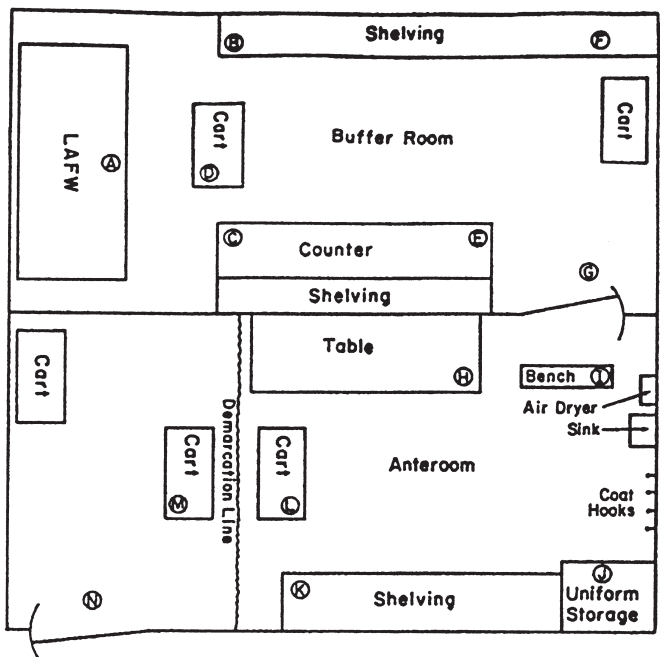

Figure 130-1. Example floor plan. Encircled letters are suggested environmental sampling sites. (From the USP 26-NF21. All rights reserved, © 2003. United States Pharmacopeia.)

frequently if needed, the operator should clean and sanitize the inside of the LAFW, other work surfaces, reorganize the work areas, and then remove the supply cart(s) from the buffer room, with any unused supplies. Assigned compounding personnel should remove trash and clean and sanitize the floors during the off-shift, following an established standard operating procedure (SOP).

The above example is given for illustrative purposes only. Compounding pharmacies and their operation will vary in accordance with the needs, design of facilities, and workload of the given home infusion pharmacy. Many hospitals and home infusion pharmacies have begun to use isolators for preparing HCPs. Isolators have been introduced to the US, but have been used for over two decades in England, Canada, and other European countries.[18,19] By design, the unit isolates the Class 100 critical area from its surrounding controlled area with sides of stainless steel, windows or of transparent plastic. By design, barrier isolators are more efficient than laminar flow hoods for aseptic compounding. When compared to a cleanroom, isolators are more economical to install and operate, require less space, are less costly to maintain, and ensure a clean environment in less time than what is typically required for cleanroom maintenance.[1]

The isolator's critical area is sterilized (not just sanitized) before use. Access for compounding personnel, also isolated from the critical area, is provided through glove ports or halfsuits sealed in the walls. Sterile or externally sanitized supplies are introduced into the critical area through *pass-through* entry ports, the weakest link in the process if sanitization rather than sterilization is used. Reports indicate that contamination rates for HCPs compounded in isolators can be markedly reduced.

Environmental Control

Microorganisms and dust particles are ubiquitous to any workplace, even a traditional cleanroom. When microorganisms are suspended in air, they are most likely to gain entrance into an open container of drug product or onto any other exposed surface. Therefore, the objective of environmental control in a cleanroom is to minimize the presence of all contaminants insofar as possible, particularly those that are airborne. With aseptic compounding, it is particularly important to control microorganisms in the environment where products intended to be sterile are processed, because there is no final sterilization step at the end of the compounding process. Therefore, microorganisms must be prevented from reaching any critical site. As defined by the USP, a critical site is any opening providing a direct pathway between a sterile product and the environment or any surface coming in direct contact with the product and the environment.[11]

To prevent microorganisms from reaching a critical site, the critical environment should be sterile or as close to sterile as possible. Normally, the equipment of choice is a certified Class 100 LAFW. When effectively cleansed, sanitized, and operated, a Class 100 environment is attainable. Either a vertical or horizontal LAFW can be used for most HCP compounding unless the products are toxic or carcinogenic in nature. Then, only a vertical LAFW biocontainment cabinet should be used. The immediate compounding work surface should be nonpermeable and resistant to liquid cleaning and disinfecting agents. It should be made of polished stainless steel with coved seamless joints. In addition to frequent cleaning, a validated disinfectant should be used on all compounding and adjacent surfaces at least as frequently as at the end of each shift.[11] A valuable source of additional information about the use of disinfectants is a Parenteral Drug Association (PDA) Task Force report.[20] It should be noted that disinfectants can only be expected to supplement effective cleaning. They will not overcome inadequate cleaning and sanitizing and are not to be relied upon as sterilizing agents. Further, because of the risk of microbial resistance, it is good policy to rotate disinfectants at least every 6 months.

Although a certified Class 100 LAFW is effective in maintaining an aseptic environment, the laminar air flow is relatively gentle, and its overall efficiency is affected by its surroundings. Consequently, the LAFW should be surrounded with a buffer zone only slightly less environmentally controlled, as illustrated in Figure 130-1. All critical aseptic compounding should be performed within the Class 100 environment and operators should be well trained in aseptic compounding techniques. The buffer room should be a Class 10,000 cleanroom or better and should be used for the final decontamination of external surfaces of supplies before introducing them into the LAFW as well as for short-term storage of clean supplies to be used in the LAFW. The number of persons in the buffer room should always be limited to those properly authorized and trained in aseptic compounding procedures and limited to the number of individuals necessary to perform the required tasks.

The anteroom shown in Figure 130-1 is intended to be used for decontaminating supplies, equipment, and personnel prior to entrance into the buffer room. It is used to interrupt the potential flow of contaminants and microorganisms from the storage room into the buffer room, a very critical step in controlling potential contamination of HCPs. For example, in the anteroom, supplies would be removed from their shipping cartons, cleaned, and sanitized externally before placing them onto clean and sanitized carts for entry into the buffer room. The supply items would then be cleaned and sanitized externally again before placing them into the LAFW. Further, descriptive details of these control steps can be found in the USP.[11]

Environmental Monitoring

Monitoring the environmental cleanliness and microbial bioburden of the cleanroom provides the home infusion pharmacy with data that indicates how effectively compounding staff follow procedures for cleaning and maintaining the compounding environment.

An assessment of the level of control achieved and maintained in a clean room environment may be performed by measuring total particle counts (both viable and nonviable particles) in air samples of at least 10 ft^3, usually done by the use electronic samplers. The results are available instantly. Viable particle counts of the cleanroom are performed with one or more of methods, such as: settling plates, surface or contact plates, slit-to-agar samplers, or centrifugal samplers. However, the results are not available until after incubation, usually 48 hours. The incubation time is necessary to allow the microorganisms to multiply (grow) so that colonies become visible. The presence of microorganisms in the cleanroom are visually detected by the presence of a colony count which is expressed in 'colony-forming units' (cfus). The cfu serves as macro evidence that microbial bioburden exists in the cleanroom. However, it is not known whether or not each colony arose from a single or multiple microorganisms. A sufficiently large sample must be taken in order to detect microorganisms at least some of the time. This fact must be considered particularly in Class 100 compounding environments where the number of microorganisms is expected to be very low. In such situations, it may be necessary to sample a volume of 30 ft^3 or more. Additional details on environmental monitoring can be found in Chapter 41.

ENVIRONMENTAL MONITORING PROGRAM—An environmental monitoring program should be established for the compounding pharmacy to assist in the detection of out-of-control microbial limits. The environmental monitoring program also assesses if the appropriate level of cleanliness has been achieved and maintained in the cleanrooms. Using two or three of the sampling methods listed above, one selects the sites, frequency, and length of time (for volume monitoring) required to give adequate information concerning the level of microbial control being maintained. This is best determined by performing sampling at many sites daily for a minimum of two weeks, preferably confirmed by repeating the sampling six

Table 130-2. A Sample Dynamic Environmental Microbial-Monitoring Program

SITE	BASELINE cfu	LOW-RISK ACTION LEVEL	HIGH-RISK ACTION LEVEL
Settling Plates[a]			
A	0, 1	3	2
D	2, 3	6	4
E	4, 5	10	6
J	5	10	7
L	8	15	10
Contact Plates			
D	2, 3	6	4
E	4, 6	10	7
J	6	12	8
L	8	15	10
STA or Impaction Sampler[b]			
A	0, 1	3	2
E	5	10	7
H	8	15	10

[a] Based on 3-hr exposure, except 1 hr for "A." See Fig. 119.1 for site locations.
[b] Based on 10-ft^3 samples.
Data from the USP23-AF18.

months later. As a minimum, at least the index finger of each operator should be rolled onto a contact plate. From the averaged data obtained, a selected, reduced number of sites should be chosen that, when monitored routinely, would best indicate whether or not appropriate environmental control is being maintained. Test sites should include both sites within the Class 100 environment as well as sites that could be expected to show the first sign of unacceptable increases in microbial levels if control is being lost.

A sample environmental sampling program based on the floor plan of Figure 130-1 is described in the USP,[11] and an example of a collected data set is listed in Table 130-2.[10] The USP chapter[11] provides practical information for establishing an environmental monitoring program as well as how to determine acceptable and out-of-limit environmental conditions. The example data for action levels (the cfu count signaling possible loss of control and requiring action to correct) for both low-risk and high-risk products are given with appropriately lower action levels when high-risk products are being processed. This is an example program for guidance and results should be adjusted for each home infusion pharmacy based upon baseline monitoring and trends. A program providing fewer data points, and still probably acceptable if all controls were in place, would be to use only settling and contact plates for testing.

A meaningful environmental monitoring program provides critical information that is essential for assuring that the risk of contamination of HCPs is under control and minimized. Without environmental monitoring data, the acceptability of aseptically prepared products as sterile is very uncertain. Extensive details concerning the development of a monitoring program and the methods used for its monitoring will be found in PDA Technical Report No. 13.[21] Although geared towards the pharmaceutical industry, the basic principles and methods of an environmental monitoring program are given, and their application to a home infusion pharmacy can be readily extracted.

COMPOUNDING DEVICES

Home infusion pharmacies rely heavily upon automated compounding devices for the aseptic preparation of sterile products. These compounding devices typically fall into two categories: those used for the preparation of intravenous total parenteral nutrition (TPN) solutions (total nutrient admixtures (TNAs)) or large-volume hydration solutions and those used for SVIs, such as antibiotics and medications for pain management. The SVI devices are used to admix solutions into smaller drug-delivery systems, such as empty plastic bags, syringes, and other disposable elastomeric devices.

Home infusion pharmacy personnel must ensure that the equipment, apparatus, and devices used to compound sterile products are capable of consistently operating properly and within acceptable quantity tolerance limits as established by the device manufacturer. The pharmacy should have written policies and procedures for equipment calibration, annual maintenance, operational monitoring, and quality control procedures. Pharmacy personnel must document routine equipment maintenance and calibration checks and personnel should be qualified through both specific training and experience to use, in an expert manner, any of the equipment or devices required for preparing sterile products.

LARGE VOLUME INJECTABLE (LVI) COMPOUNDING DEVICES—LVI products can be compounded by using one or two basic methods: by gravity or by the use of an automated compounding device. Gravity compounding involves the manual aseptic transfer of sterile base solutions such as amino acids, dextrose, and lipid emulsion from one container to another using gravity-driven transfer. The remaining additives such as electrolytes, vitamins, and trace elements are also added manually with each additive transferred separately using a syringe. Gravity compounding involves low equipment costs, but has a high labor component. The risk of microbial contamination using the gravity method of compounding is higher due to the multiple manipulations made into the final container during the additive transfer process. Additionally, because each additive is added manually, the risk of touch contamination is greater.[22]

Most automated compounding devices used to prepare TPN and TNA liquids are electromechanical devices that measure opaque and transparent suspensions and solutions by gravimetric or volumetric methods. Some automated compounders can be used for the transfer of base solutions only, with the remaining additive components added manually versus other, more sophisticated automated compounders that can be used to compound the small volume additives and the base solutions.

Some automated compounding devices use calibrated gravimetric weighing to convert and monitor the actual volume dispensed. With volumetric compounders, base solutions are transferred from the source container to the final container using a rotary peristaltic pump. With each turn of the rotor, fluid is pulled from the source container and pushed into the final container. Often, these compounding devices are used as standalone instruments or they can be interfaced with a computer. TPN-compounding devices use a microprocessor system control, which provides the device with a measure of *self-test,* to ensure the integrity of the electrical control functions. The computer interfaced with these devices provides for the correct data transfer in an automated fashion consistent with standard pharmacy checking methods. The accuracy of the compounding unit is achieved through weighing the actual solution being delivered, converted by a specific gravity calculation to the required volume transferred. Thus, if any air is inadvertently transferred, it will not alter the accuracy of the compounded solution.[23]

Automated compounding devices have multiple channels for pumping the solutions of amino acids, dextrose, pooled electrolytes, and/or intravenous fat (lipid) emulsions into the final dispensing container or bag. TPN compounders do not normally use a sterilizing 0.22-micron filtration step as part of the admixture preparation process because of the resistance to flow induced by the filter and that because it is a closed system for dispensing sterile solutions. However, if an electrolyte pool is created for subsequent dispensing into individual TPN bags, the final solution should be filtered through a 0.22-μm filter prior to attaching the unit to the automated compounder. This step is included because the process is using an open system with a relatively long exposure of the solution to the environment. Further, this step eliminates any inadvertent microbiological and touch contamination introduced during the compounding process.

Table 130-3. Commonly Automated Pharmacy Compounding Devices Used to Prepare Home Infusion Products

AUTOMATED SYSTEM	MANUFACTURER	METHOD OF TRANSFER	NO. OF STATIONS	RANGE OF VOLUMES DELIVERED FROM EACH STATION	ADDITIONAL INFORMATION AVAILABLE FOR PN CALCULATIONS, QA CHECKS, & TRANSFER OF RX TO COMPOUNDER?
Nutrimix Macro	Abbott	Subtractive Gravimetric	4	10–4,000 mL	Yes
Nutrimix Micro	Abbott	Volumetric	10	—	Yes
Automix 3+3	Baxter	Additive Gravimetric	6	10–5,000 mL	Yes
Automix 3+3/AS	Baxter	Additive Gravimetric	6		
Micromix	Baxter	Additive Gravimetric	10	0.3–4,000 mL	Yes
Exacta-Mix	Baxa	Volumetric	6	1–9,990 mL	Yes
MicroMacro	Baxa	Volumetric	12	0.2–9.9 L	Yes
MicroMacro 23	Baxa	Volumetric	23		
HyperFormer	B. Braun	Volumetric	6	1–3,000 mL	No

Adapted from Chrai S, et al. *J Parenter Sci Technol* 1986; 10:104.

THE SOLUTION-COMPOUNDING PROCESS—Generally, in home infusion practice, pharmacy technicians perform the actual compounding of sterile products. The vast majority of states in the US allow technicians to compound sterile products under the direct supervision of a licensed pharmacist.

Prior to actually compounding an intravenous solution, the individual starting components should be selected by a technician and then checked by a pharmacist. This checking is performed to minimize any risk of selecting an incorrect product(s). These components are usually sterile, packaged, commercial IV products that have been subjected to quality control testing and release by the manufacturer. The external surfaces of the packages are then cleaned and sanitized, and the packages are brought into the cleanroom.

The operator should calibrate the automated compounder on a daily basis per the manufacturer's directions and recommendations. Usually, these calibration checks are documented in a QC log book and/or on a compounding (batch) record. The technician then connects the compounding device's transfer set to the device itself. Each different type of compounder has its own unique plastic solution-transfer set. Typically, these sets cannot be interchanged between the different compounding devices because the configurations are purposely different. The appropriate dispensing containers are then connected to the compounding device.

Next, the operator performing the compounding programs the device by entering the specific volumes of each of the different solutions, ie, amino acid, dextrose, electrolyte pool, and/or fat emulsion used into the device itself. The usual volume ranges for these liquids are from 10 to 5000 mL. The specific gravity of each of the respective solutions is then programmed into the compounding device's computer. Limits for specific gravities are usually 0.50 to 3.00 for each pump station, and specific solution specific gravities are provided by the pharmaceutical manufacturer.

Prior to actually starting the machine, operators should visually check the solution level in each of the stock solution containers to be sure there is an adequate supply and should ensure that the final product bag has been properly connected to the transfer set. Operators also should ensure that there are no kinks, clamped sites, or other obstructions in the tubing.

Immediately after the appropriate amounts of solutions have been transferred into the final dispensing container, the bag is removed from the compounder, air is expelled, and the bag is sealed. Bags are either crimped manually or with a device that uses radiofrequency waves to heat-seal the bags. The expected weight of the final TPN bag should have been calculated. The final compounded bags of product can then be weighed on a scale to provide a second gravimetric QC check for accuracy.

Some of the current compounding devices provide for as many as 23 different pump stations. Microcompounders allow for the accurate, aseptic dispensing of electrolytes for compounded TPN/TNA solutions with aliquot volumes as low as 0.2 mL.

Many nutritional compounding devices interface with software packages and simplify the formulation of TPN solutions, particularly by automating the complex calculations that help to minimize errors. Additionally, these instruments generate compounding records and prescription labels for the compounded product. Prescription labels can be generated in a variety of different formats, including providing a complete listing of all ingredients and quantities dispensed as well as a summary of clinical information, such as the total number of calories; amounts of proteins, carbohydrates, and fats; and solution osmolarity. Refer to Table 130-3 for a list of commonly used pharmacy compounding devices.

SMALL VOLUME INJECTABLE (SVI) COMPOUNDING DEVICES—In addition to nutritional compounding devices, home infusion pharmacies can also use compounders to prepare SVI solutions. These compounding devices are most frequently used for the pooling of electrolyte solutions and/or for reconstituting drugs over prolonged compounding operations. The solutions are dispensed into smaller drug-delivery systems such as plastic syringes, vials, disposable elastomeric pumps, cassettes, or empty bags.

Volume delivery for these types of compounding devices typically ranges from 0.01 to 9,999 mL.[24] Like the nutritional compounding devices, these compounders also employ brand-specific transfer sets. Prior to operation, the pump should be calibrated per the manufacturer's instructions. The operator then aseptically connects the transfer set to the compounding device's pump rotor. The transfer set is then primed and, using a universal spike adapter, is connected to a primary-source container. The operator then enters the desired pump volume(s) on a numeric keypad, and the solution is dispensed into the final container. Each unit is filled completely in one filling step, one unit at a time.

As the pump operates, it will deduct and record the delivered amount from the source-container volume. Once all the units have been filled, the transfer tubing is disconnected from the final unit, and any air remaining present is aspirated.

When filling specific drug-delivery systems, such as elastomeric devices, it is very important to adhere to the manufacturer's recommended speed setting. Because of the high pressures required to fill these devices accurately, transfer-set tubing wear can be quite high. Therefore, it is recommended that the transfer tubing set be examined after filling 50 units, for possible replacement.[24] Many of the SVI compounders have a memory recall function for storing dispensing information for subsequent compounding procedures.

Compounding Device Quality Control

As stated previously, TPN/TNA bags or small infusion drug delivery systems can be double-checked by weighing the final container or product to provide a second gravimetric check of the quantity of the final solution dispensed. Additionally, many compounding devices used in pharmacy practice come with

some type of computerized bar-code verification system. Such systems clearly identify the different solutions used in the compounding process and prevent the compounding device from operating if an error has been made.

The refractive index (RI) also can be used to determine the accuracy of some compounded nutrient solutions. The RI serves as a gross predictor of compounding accuracy, for example, for dextrose solutions or dextrose containing solutions. The RI is the ratio of the normal velocity of light in air to the velocity in the solution being tested. The use of RI as a quality control test is particularly useful for neonatal and pediatric TPN solutions, for which accuracy of compounding is particularly important. The RI is based upon specific constants for dextrose and amino acids and their relationship to that of the final compounded TPN.[25]

PERSONNEL

Personnel are generally recognized as the principle source of contamination in a cleanroom because of the inherent shedding of both viable and nonviable particles from their body surfaces and clothing. Uniforms are worn to help contain these particles, but the personal hygiene and characteristic physical activities of each operator plays a critical role in the shedding of particles into the compounding environment. Therefore, training personnel to understand their personal characteristics and how to control their emission of particles while performing good aseptic practices (GAPs) is very critical.

GOWNING—Assuming good personal hygiene, the shedding of particles will increase as the level of the operator's activity increases. Because home infusion pharmacists and technicians will normally be standing or sitting at an LAFW, their level of activity will be moderate. However, they will be reaching into the critical work area and air currents may bounce from the front of their uniforms back into the critical work site, and they will be exhaling toward the work area. Therefore, sterile gloves should be worn along with very clean, nonshedding gowns, face masks, and hair covers. Gowns should be long sleeved, snug-fitting at the wrist, closed front, and knee length. The frequent practice of wearing scrubs is questioned because of their normally high load of lint. Synthetic polymer gowns are preferred. Further, gowns should never be worn outside the buffer room; they should be captive to the cleanroom.

Sterile gloves should be worn, although these will quickly become contaminated from the surfaces of sanitized (not sterile) packages, LAFW surfaces, and other surfaces contacted. They should be resanitized frequently with sterile IPA. Face masks may be omitted if working at a VLAFW, and the transparent shield is always kept between the mouth and the critical work area. Shoe covers also should be worn to reduce tracking contamination onto the floor of the buffer room.

PRACTICING GOOD ASEPTIC TECHNIQUE—Pharmacists and technicians must be trained to understand their natural propensities for contaminating the environment and the impact their activities have on introducing that contamination into the HCP with which they are working. In general, the greatest concern is to prevent microbial contamination, but particulate matter and other physical and chemical contamination are also of concern. Therefore, operators must learn to practice good aseptic techniques (GAPs) automatically, to minimize the risk of contaminating the HCP that is being prepared. It is generally recognized that in the context of GAPs, the greatest risk of introducing contamination into a sterile product is through touch contamination by the operator. Therefore, special attention must be given to learning how to avoid this potential problem.

Space limitations do not permit detailed descriptions of practices that constitute GAPs, which are best learned by personal tutoring and practice. However, Avis has provided a list of key practices that should be followed,[16] and these are reproduced on Figure 130-2.

1. Practice good personal hygiene, be organized and level-headed.
2. Be healthy, without eczema or other skin rashes and free from allergies or other conditions causing sneezing and coughing.
3. Wash hands and arms thoroughly or disinfect with foamed alcohol.
4. Put on uniforms properly, avoiding contaminating the outside of the clean/sterile uniform components.
5. Replace a uniform or parts of a uniform that become contaminated while gowning or working.
6. Put on sterile latex gloves as the final gowning step.
7. Sanitize all internal surfaces of the LAFW (except the HEPA filter face) with an appropriate sanitizing agent, usually IPA.
8. Sanitize latex gloves (usually with IPA) as frequently as necessary while performing GAPs to maintain the aseptic condition of the outer surfaces.
9. Replace gloves with new sterile ones if they become punctured or torn.
10. Move with slow, smooth, gentle motions.
11. Do not talk unnecessarily.
12. Do not disrupt HEPA-filtered laminar air flow within the critical area.
13. Do not interpose arms or any other nonsterile object above a critical site in vertical laminar air flow (VLAF) or behind a critical site in horizontal laminar air flow (HLAF).
14. Do not spray or splash disinfectants where the liquid might enter a product container or reach other product contact sites.
15. Do not introduce any packages into the buffer room unless they have been adequately sanitized or sterilized externally.
16. Minimize in and out movement at the LAFW.
17. Arrange sterile supply items in the critical area so as not to interrupt the laminar air flow and to provide for efficient processing of the product(s).
18. Resanitize gloves with IPA after handling any package if the outside had uncertain sterility or surfaces such as switches of mixing pumps.
19. Cooperate with other operators and mutually assist in maintaining proper GAPs.
20. Pass through doorways, plastic curtains, or other passageways slowly and carefully to minimize the generation of wild, potentially contaminating air currents.
21. Do not leave open vials, tanks, or other critical sites exposed to the environment during breaks or other delays in operation.
22. Inspect all supply items before using and the finished product after preparation for evidence of defects.
23. Remove used supply items and clean/sanitize work area as needed.
24. Prepare and apply appropriate labels and complete documents away from the critical area or, preferably, pass product outside so that a second person can perform the paper work.
25. Remove used uniforms carefully to avoid distributing accumulated body contamination before exiting the gowning room.
26. Leave the HEPA filter blower operating all the time.

Figure 130-2. Key GAP practices. (From Avis KE. Assuring the quality of pharmacy-prepared sterile products. *Pharmaguide to Hospital Medicine* 1996: 9(2): 11–12. Copyright 1996, Lawrence DellaCorte Publications. All rights reserved.)

TRAINING

Because the potential for success in preparing a sterile HCP is so dependent upon the capability and reliability of the pharmacist or technician, the training and evaluation of such personnel must be given high priority. To be an effective practitioner of GAPs, the operator should understand the body of knowledge supporting such practices. Therefore, one of the objectives of aseptic compounding training is to transmit a basic level of knowledge (ie, the characteristics required of a sterile dosage form the reasons for the high standards of purity required for such products, quality control measures that apply, the facilities required and their operation, the environmental requirements for processing, the role of operators in performing GAPs. A brief summary of this body of knowledge is provided in this chapter, but other cited references should be consulted for more details.[7,11,15,16].

Methods

The most perfect body of knowledge retained only in the individual's mind will not result in reliable and proficient compounders. Compounding staff must be motivated to apply their knowledge of aseptic technique effectively. Therefore, didactic instruction must be coupled with experiential instruction, and both must be conveyed with enthusiasm and motivational examples.

ASEPTIC COMPOUNDING DIDACTIC INSTRUCTION—Intellectual knowledge can be acquired by formal lectures, through informal discussion methods, and or by one-on-one instruction. Each method has its own unique advantages and disadvantages. The formal lecture provides the most organized approach to transmitting the desired body of knowledge. All participants are ensured to have been exposed to the same information, but this does not guarantee that all individuals take in the same body of knowledge equally. Relatively large groups can be trained at one time and visual aids can be used effectively.

Informal discussion has the advantage of encouraging learning through active participation of the learner. However, it is more difficult to maintain organized control of the schedule of topics to be covered. The relevance to one's specific work needs usually can be implemented more effectively and the enhanced understanding of the student can be judged directly if the instruction is one-on-one. Because of the frequently small number of trainees, one-on-one aseptic technique training is commonplace. With such instruction, it is the responsibility of the instructor to give diligent attention to the risks of interruptions, inadequate preparation, and differences from instructor-to-instructor or from time-to-time in the quality of instructions given. When performed effectively, one-on-one instruction can be the most effective method for teaching sterile products compounding.

EXPERIENTIAL TRAINING—The ability to perform the GAPs required to prepare sterile HCPs safely, accurately, and elegantly is the objective of experiential training. Typically, this type of training should be given by an expert supervisor or designated trainer using mock sterile products (vials of sterile water vs. actual drug product) to establish the principles for the level of skill required of the learner. Subsequent practice to develop improved skills may be done under the tutelage of an experienced operator, with the supervisor continuing to provide oversight. Before being permitted to prepare actual sterile products for patient use, the trainee must be approved by the supervisor and successfully pass the compounding validation program. Retraining should be required whenever an operator fails compounding revalidation, when direct observation suggests the development of careless technique, or at least on an annual basis.

VALIDATION OF OPERATORS—Aseptic compounding validation may be defined as documented evidence that provides a high degree of assurance that a specific compounding process will consistently produce a product meeting its predetermined specifications and quality attributes.[7]

Before operators, pharmacists, or technicians may be permitted to prepare HCPs of any risk level for use by patients, they must demonstrate their basic knowledge and manipulative proficiency to prepare such products, that is, to be 'validated' to perform aseptic compounding. Greater expertise and proficiency is required for operators who will be responsible for the preparation of high-risk HCPs.

The following is an example of a compounding validation procedure that may be used for operators who have completed a basic training program and are certified by a supervisor as ready to be validated.

Sample Validation Program for Operators

The program consists of three portions, all three of which must be satisfactorily passed for the operator to be considered validated to compound HCPs. The program may be modified to meet the needs of a particular home infusion pharmacy, but the requirements should be at a level that will ensure proficiency of the operator. Revalidation should be required on an annual basis to ensure continued satisfactory performance.

TESTING FOR UNDERSTANDING—The pharmacist-in-charge or their designee shall administer a written or oral test consisting of at least 25 objective test items, most of which challenge the student's knowledge and understanding of aseptic technique. To successfully pass the test, a minimum of 23 items (92%) must be answered correctly.

OBSERVATION AND EVALUATION OF GAPS—Five different aseptic manipulations, representative of those that are routinely performed in the pharmacy, including at least one of the most complex methods, should be selected by the supervisor. The trainee is then required to perform these five procedures in accordance with the GAPs demonstrated in the training program, while being directly observed by the supervisor. Any observed deviations from GAPs shall be recorded. To pass this test no deviations from GAPs are permitted.

TRANSFER OF CULTURE MEDIUM—Using the most-complex type of HCP the trainee will be expected to prepare in actual practice, the trainee will prepare 20 of these simulated products in series, at one time, without the supervisor present. Sterile soybean casein digest (SCD) medium will be used in place of an actual drug product, otherwise the process will be simulated in all respects.

Post-compounding, the 20 *units* will be incubated at 30 to 35° C for up to 14 days and inspected for the development of any turbidity after 3 and 7 days. If any visible turbidity develops at any time during the incubation period in one or more of the containers, the test is terminated, and the trainee has failed the test. Turbidity indicates that at least one microorganism has gained entrance into the unit container and has grown, most likely due to a failure in GAP by the trainee.

If the trainee fails any portion of the example tests, retraining and retesting should be required. However, at the discretion of the supervisor, retraining and retesting may only be required for the failed portion(s) of the examination. Due to the tendency for even the best operators to gradually become less proficient over time, revalidation should be planned for all operators at least annually.

QUALITY-CONTROL REQUIREMENTS

The physical, chemical, and biological quality of an injectable product intended for administration to patients in the home must be of the highest quality attainable. This quality must be *built in* to the product in each step of the aseptic compounding process, that is, in the starting components, the design and operation of the compounding facilities, the control of the envi-

ronment, and the qualifications of operators all contribute to the final quality of the product, either in a positive or negative manner. Therefore, the control of quality is a continuous process throughout the compounding of the product. Testing of the finished product can only confirm the quality built into the product during its preparation.

The home infusion pharmacy must develop written procedures to ensure the quality of each finished product, also called standard operating procedures (SOPs) or policies and procedures (P&Ps). SOPs then become the protocols to be followed meticulously to replicate established, reliable compounding procedures. These also become the basis for training new pharmacists or technicians.

In the aseptic processing of products intended for use by home patients, the starting components are typically clean, sterile, and quality-controlled; that is, they have been released as having met the pharmaceutical manufacturer's quality standards. Therefore, the challenge for the pharmacist is to maintain the final product free from the ingress of contaminants, particularly microorganisms and other foreign particles, during the process steps.

PRODUCT SIMULATION TESTING—Many HCPs contain ingredients that are nutrients for microorganisms. Even though other components of the product may inhibit growth, the ingress of even one microorganism during the aseptic compounding process may permit multiplication to occur with the reproduction of many microorganisms occurring within the product within a few hours. To prevent the development of such intolerable conditions, the compounding process must be controlled. Once a process is properly controlled, it can be validated as capable of producing the prescribed quality product. To evaluate the level of microbiological control achieved, a balanced culture medium (eg, soybean casein digest medium) may be substituted for the product during a simulation of the process, called a *media fill*. After incubation of the simulated product prepared, if no growth is observed in the culture medium by the 14th day, it can be concluded that no contaminating microorganisms were introduced during the process. This is the most rigorous biological evaluation of the process currently available for quality control. It is the most important test to be performed relative to the processing of HCPs and is the basis for validation of the aseptic process and the compounder's aseptic technique. Simulation testing should represent the range of compounding procedures typically encountered in the pharmacy, from simple transfers to the procedure with the most challenging manipulative complexity (eg, *worst case*).

FINAL PRODUCT RELEASE TESTING

Without question, the most critical quality-control focus is on the control of the aseptic compounding process for preparation of sterile products. Nevertheless, select product release testing should be performed, although modified because of the nature of the products, the very small lot sizes (often a single unit for a single patient), and their relatively short shelf life. There are four key categories of final product release testing: visual inspection, compounding accuracy, sterility testing, and pyrogen testing.

PHYSICAL INSPECTION—The simplest but practical and essential evaluation is physical (visual) inspection. All HCPs should be physically examined, that is, by critically looking at the product with a pharmaceutical assessment. The pharmacist should know if the color, clarity, and other appearance characteristics are appropriate. If there is any visible alteration from the expected, the pharmacist should be alerted to the possibility of some type of degradation, and an investigation should be performed. Furthermore, the USP requires that all final containers be inspected individually for the presence of visible particulate matter. If any particles are observed against either a white or black background, the container should be discarded.

COMPOUNDING ACCURACY—Compounding accuracy in the preparation of HCPs is normally considered to be the responsibility of the pharmacist-in-charge, using accurate measuring and compounding devices and appropriate, careful techniques. Established SOPs should require the measurements by one technician or pharmacist to be checked by a second pharmacist. For example, if syringes are used to measure a prescribed volume of a component, the syringe plunger should be drawn back to the measurement site used so that its accuracy can be determined by the pharmacist checker. As discussed previously, with automated mixing pumps the volume setting can be checked before it is moved for the next delivery. Electrolyte pool solutions used in PN, calculations should also be double checked.

STERILITY TESTING—As stated above, the best assurance of sterility of an HCP is through the evidence of validated aseptic compounding procedures. Compounding records verifying the sterility of the initial components of the product and of the devices used for preparing the HCP, the control of the Class 100 workspace and its buffer areas, and the qualifications of the operators, provide the greatest assurance that the final HCP is sterile. Therefore, a sterility test is not typically performed on a single or small lot of HCPs. However, a sterility test performed on a sample representative of a group of products prepared under essentially identical conditions (eg, the preparations of a single technician during a single work shift) may be appropriate. Operators must consider that the USP sterility test is a destructive test; that is, the test unit(s) is consumed in performing the test and would not be available for subsequent patient administration. Additionally, the test has practical limitations in that it requires a minimum incubation period of 7 days, during which most HCPs would already have been administered to the patient before test results would be known. Conversely, sterility testing should be performed on any lots of products made from nonsterile starting ingredients or when batches of HCPs are produced in open tanks, that is, when the product is exposed for a substantial period of time to the environment, often in a Class 1,000 or less clean room. The test requirements would be based upon the specifications for small lots of products as described in the USP[26] and adjusted for the small lot sizes.

Of the two test methods described by the USP, the membrane filtration technique is preferred. This method has the advantages that:

1. It concentrates small numbers of microorganisms and gives greater probability of recovery.
2. Large volumes of product can be filtered and thus tested.
3. The product is filtered away from any viable microorganisms, and any inhibitory effects from the product are minimized.

This method also provides a higher probability of detecting any viable microorganisms that may be present. The testing methods are described in the USP.[26] Because sterility testing and other analytical laboratory tests will not be performed in the pharmacy but in another facility, the pharmacist-in-charge is responsible for ensuring that the contracted testing laboratory is capable of performing all tests properly.

PYROGEN TESTING—The presence of pyrogens (the products of metabolism of microorganisms) normally is of little concern. But testing would be required under circumstances similar to the requirements for sterility testing. Detectable levels of pyrogens would normally occur only in the presence of a relatively high number of microorganisms; usually something that is not likely with most HCPs. However, pyrogen testing is a sensitive test and of particular value when microorganisms had been present in equipment or other areas of the compounding process even though they are dead at the time of testing. The *Bacterial Endotoxins Test,* the test method normally used, is described in Section <85> of the USP.[27]

EXPIRATION DATING—Although the shelf life of HCPs is normally not required to be more than 30 to 60 days, this dating is long enough given the nature of HCPs and the uncertain

storage conditions that may occur during transportation and storage in the patient's home. Pharmacists must give careful consideration to the potential for sterile product degradation. A home infusion pharmacy usually does not have the capability of studying chemical drug degradation, nor is it possible, considering the many formulation variations that can occur with the prescribing privileges of physicians. Therefore, pharmacists are limited to the information that can be obtained from the drug's manufacturer, the pharmaceutical literature, and their professional judgment. Each of these sources, at best, can only provide the basis for a theoretical stability assessment. Only product-specific, experimentally determined stability data can provide a real determination of physical and chemical stability over time. The biological prediction of stability, that is, the likelihood of microorganisms growing in the product, can only be ensured by the level of reliability of the aseptic compounding methods used. Due to the nutrient nature of many HCPs and the inherent risk of even one microorganism gaining entrance into the product, the length of shelf life with uncertain conditions of storage should be conservatively limited.

For all HCPs, compounding documents should be available to provide a record of the product's complete processing history. These documents should refer to, and be founded upon, a complete set of SOPs that clearly describe the established procedures used to determine product stability and compounding methodology. The documented process history should be carefully reviewed for completeness, accuracy, and evidence of compliance with SOPs and other quality standards for the product before it is released for use in a patient.

LABELING

After a sterile product is prepared, it must be properly labeled to communicate the necessary information to ensure its appropriate use.[16] This is particularly true for product labels for sterile products used in the home environment, because of the following requirements:

- Labels must be understandable by a lay person, because the end user may be a patient, or family member.
- Labels should avoid medical abbreviations or potentially confusing terminology.
- Labels must give clear directions for administering the product via the prescribed method of administration. Instructions must be included for operating any infusion pump devices or other required administration techniques.
- Labels must be understandable by other health-care professionals, so that if the patient is treated at another site (eg, an emergency room) the correct administration of the drug can be continued.

Recognizing these requirements, the elements of a label for a home infusion pharmaceutical should include[15]:

- Prescription information-prescription number, date, and prescribing physician.
- Patient information—patient name and other identifying information, such as a patient number or address, if appropriate.
- Directions for use (eg, the time and frequency of administration, infusion rates, and pump settings) for the infusion device selected.
- Handling or storage requirements, including requirements for refrigeration and warming to room temperature before use, if applicable.
- Name and amount of drug present; if the admixture contains more than one dose, the label should indicate the amount of drug for one dose, the volume of the dose, and the total amount of drug and total volume present.
- Name and volume of the admixture solution.
- Expiration date under the recommended storage conditions; length of time product may be stored at room temperature, if appropriate.
- Initials of persons who prepared and checked the admixture.
- Auxiliary labels as appropriate.

Because home-care patients require significant detailed information about their products, many home infusion pharmacies choose to supplement the label with additional patient informational materials. If an auxiliary label does not provide enough space, supplemental instruction sheets may be provided. It is the dispensing pharmacist's responsibility to ensure that all of the information needed by the patient or caregiver is provided.

If caregivers in the home must add ingredients to the HCP that are not stable for prolonged periods (such as insulin or vitamins), the product label should clearly indicate the amount and volume of each ingredient to be added just prior to infusion. Highlighting this information with a bright color, use of a separate additive label, or other techniques may be used to ensure that these additives are not omitted.

PARENTERAL NUTRIENT ADMIXTURES—Labeling of parenteral nutrient (PN) admixtures requires special attention. Total parenteral nutrition formulations are complex admixtures containing amino acids, dextrose, and lipids, as well as water, electrolytes, vitamins, and trace elements. PN labels are used by clinicians as a source of prescription information when patients are seen in outpatient settings or admitted to other sites of care. For this reason, PN formula information must be expressed in a manner that is clearly understandable not only by caregivers in the home, but also throughout the health-care system.

Currently, methods of macronutrient labeling vary widely among different organizations and sites of care. One of the most common ways of expressing nutrient quantities is as the final concentration of each ingredient, such as dextrose 25%. Calculations are required to determine the total nutrients included per day or per container. Other organizations label their parenteral nutrition formulations by specifying the volumes and initial concentrations before admixture of each ingredient (eg, 500 mL of 50% dextrose). Still other pharmacy's may label their PN formulas with the absolute quantity of each ingredient per preset volume of PN (eg, dextrose 250 g per liter), or home infusion organizations can also label PN formulas in terms of total quantities of each ingredient per day, such as dextrose 340 g per day. Electrolyte additives may be expressed in millimoles or milliequivalents per liter or per total volume. Unfortunately, this lack of labeling standardization causes confusion and the potential for errors, especially when patients are transferred between health-care environments.

Errors in managing the preparation of PN solutions can result in serious harm or even death for the patient. In fact, the misinterpretation of prescription labels has led to several serious patient incidents.[28] In one case, hospital personnel misinterpreted the dextrose content on the label of a home PN formulation, resulting in a pediatric patient's death.[28] The prescription label read *300 mL of 50% dextrose*. The hospital pharmacy misinterpreted this as a final concentration of dextrose 50%. The patient died after receiving the incorrect formulation for two days.

Another incident involved the misinterpretation of a label resulting in an iron overload with resultant liver toxicity in a child receiving PN with iron dextran.[29] The home PN label read iron dextran 1 mL, the intention being to use a 1 mg/mL iron dextran dilution prepared by the pharmacy. However, the solution was prepared with the undiluted 50 mg/mL concentration and not a 1 mg/mL solution, resulting in a 50-fold error in the dose that was administered.

As a result of these tragic events, the American Society of Parenteral and Enteral Nutrition (ASPEN) established the National Advisory Group (NAG) on Standards and Practice Guidelines for PN.[30] The purpose of this group was to identify problematic areas in PN therapy and to make recommendations and develop guidelines that fostered safer practices. Specific problem areas noted in the NAG included: nutrient requirements, labeling, compounding formulas, stability issues, filtering, and quality assurance. PN labeling was one of the areas identified by the group as problematic.

The NAG recommended that the macronutrient content of PN admixtures be labeled in grams per total volume and that other additives be labeled in total quantities per total volume[30]

This labeling method supports the use of a once-per-day nutrient admixture system, which is a cost-efficient method of PN compounding.[31] Organizations accustomed to labeling in other formats, such as amounts per liter, sometimes supplement the label with a second column indicating the latter information.

Auxiliary labels may also be useful to list other information such as individual concentrations of electrolytes in milliequivalents or millimoles, total and nonprotein calories per day, and the percentage of total and nonprotein calories provided as carbohydrate and fat.[30]

STORAGE IN THE PHARMACY

Monitoring the storage conditions in the pharmacy is necessary to ensure that sterile products retain their respective quality attributes. Controlled-temperature storage areas such as refrigerators and freezers should be monitored at least once daily, with results documented on a temperature log. Suitable temperature-recording devices include calibrated continuous recording devices (preferred) to a National Bureau of Standards (NBS) calibrated thermometer. Continuous recording devices should be minimally checked daily to confirm that the device is working properly and has not malfunctioned. Pharmacy staff should take care to avoid causing significant temperature aberrations, such as from holding refrigerator doors open too long or overloading the refrigerator.[11]

PACKAGING AND SHIPPING

The pharmacist's responsibility for ensuring the quality of sterile products used at home does not end when the product is dispensed from the pharmacy. Care must be taken that the handling of such products outside the pharmacy and at the site of administration ensures that the product maintains its original quality attributes, particularly sterility and stability. This requirement should be balanced with the need to deliver sterile products in a timely manner and at a frequency that minimizes delivery costs but avoids product waste because of changes in orders or expired shelf life of products.[15]

Transportation of the product to the site of administration must take place via a delivery or shipping system. In this chapter, delivery refers to the personal delivery of the sterile product by an employee of the home infusion organization (eg, the home care nurse who will administer the product, a delivery employee) while shipping refers to the use of a common carrier, or courier, such as a commercial package-handling service, or the mail. Each of these delivery methods has its unique challenges.

Delivery usually is assumed to be faster and more reliable than shipping. This can lead to a cavalier attitude about the need for properly packaging sterile products during delivery, because it is assumed that the product will be delivered to the home (or other administration site) within a short time. Oftentimes, long delivery routes, employee breaks and meals, or adverse traffic conditions can delay product delivery and adversely expose products to extremely hot or cold temperatures in the delivery van or nurse's car. Additionally, the shifting of packages during transportation can potentially lead to damaged products and/or hazardous spills.

Similarly, shipping products via a common carrier can also subject the product to extremes in temperatures and rough handling. When commercial air and truck carriers are used, the home infusion pharmacy is responsible for taking actions to ensure the quality of their services. Before using a commercial carrier, the pharmacy should confirm the carrier's capabilities for maintaining required delivery schedules, transit times, safe handling, and temperature control. The pharmacy should develop an effective system for monitoring the carrier's shipping performance. Some carriers provide electronic or telephone confirmation of delivery times. If this is not available, a review of delivery receipts or telephone follow-up calls with the patient or caregiver can be used to monitor the delivery timeliness of the carrier. Other important indicators to monitor include the condition of the products upon receipt and personnel courteousness.

Careful product packaging is essential to protect the integrity of the sterile products during shipping and delivery. Packaging materials should be selected to maintain required product temperature, minimize breakage, and to avoid leaks. Required components of product packaging includes: insulation for temperature control, cushioning to avoid product shifting and breakage, and a sealed leak-proof container to minimize the risk of leakage if a liquid product is damaged in transit.

INSULATION—Refrigerated sterile products for home use should be packaged in an insulated container to maintain temperatures within the USP recommended storage temperatures of 2° to 8°C. For personal deliveries, a sturdy reusable cooler is a cost-effective insulated container. For shipping, insulated containers, consisting of a Styrofoam inner liner with a cardboard outer box, are commercially available. A low-cost alternative involves placing a smaller cardboard box inside a larger cardboard box and filling the space between the boxes with Styrofoam packing peanuts. In either case, ice bricks or kool-it blocks are used inside the package to maintain product temperature. Tape should be used to completely seal box edges; this will also facilitate maintaining product temperature.

Even sterile products that do not require refrigerated storage may be labeled for storage at controlled room temperature (<85°F). In one study, the USP found that more than 90% of approximately 200 packages shipped from its Rockville, Maryland headquarters were exposed to unacceptably high temperatures during shipment. Temperature indicators in two-thirds of the packages registered spikes between 86° and 104°F at some point in transit.[31] Although ice bricks are not required, use of an insulated container for shipping or delivery, especially in the warm summer months, can help to avoid excessive heat.

CUSHIONING—Packaging materials such as Styrofoam packing peanuts, bubble wrap, Styrofoam wrap, or shredded or crumpled newspapers are useful to prevent damage due to product shifting. For best damage control, the box containing the product should be completely filled with the selected packaging material. Any free air spaces within the box increases the risk of product shifting, and contributes to decreased temperature control.

Packaging materials can also be used to avoid excessively cold product temperatures during transit. Avoid subjecting HCPs to freezing and extremely cold temperatures. Some protein-containing drug products can be denatured by freezing. Using a cardboard barrier to separate the drug product from the ice bricks can be helpful.

CONTAINERS—Within the package, the sterile drug product itself should be packaged in a primary container, usually made of glass or plastic that is designed to protect and contain the product. The primary container should minimize the risk of leaking, unless it is broken or otherwise damaged. Sometimes an outer wrap, in the form of a zip-lock plastic bag, is used to contain the liquid drug product in the event that the primary container is damaged and leakage occurs. The outer wrap is also useful to separate the drug product from food items when stored in the patient's refrigerator.

Chemotherapeutic drugs or other hazardous materials should be double bagged. Should an unexpected spill occur, hazardous spill kits should be available to use in containing and cleaning up the spill thus minimizing the hazard. When shipping hazardous materials, check both OSHA and local department of transportation (DOT) requirements for specific guidelines.

PACKAGE VALIDATION—Home infusion pharmacists should validate the packaging materials that they use to ensure that such materials maintain product temperatures within the acceptable range during shipping. The placement and number of ice bricks, product size and placement, air space within the

package, insulation thickness, choice of packaging materials, expected ambient temperatures, and duration of shipping all influence the maintenance of the product's temperature.

Small, reusable computerized temperature probes are available for monitoring temperatures during normal shipping conditions. The temperature probe is placed as close as possible to the drug in the package to be evaluated. The product is then packaged and shipped or delivered via standard procedures. Upon receipt, the temperature probe should be returned to the pharmacy and the temperature data downloaded. The computerized probe records the temperatures experienced by the package during the entire delivery cycle. Ideally, the packaging system should maintain the product within the desired temperature range for the anticipated duration of shipment plus some additional margin of safety, in case the delivery is delayed.

Temperature indicators are also available. These indicators record a color change or other visual display of the maximum temperature experienced by the product during transit. Although these devices are not yet inexpensive enough for use with every shipment, they can be useful for initial validation and periodic retesting.

A less costly but less evaluative method of package evaluation involves post transit temperature checks. A thermometer is used to test the product temperature immediately upon product receipt, or the package is simply examined to assess whether the drug product is cold (but not frozen). Checking the temperature upon package receipt has limitations in that it gives an indication of the current temperature but does not reflect whether temperature fluctuations occurred during transit.

Designing a shipping package to meet both temperature and cost requirements will necessitate some experimental testing. Possible solutions for commonly encountered problems are listed in Table 130-4.

Evaluation and possibly redesigning the shipping package should be continued until a package is developed that adequately maintains the product within the desired temperature range for the anticipated duration of shipping. Once the package has been designed and the procedure for packing is complete and validated, the information should be put incorporated into a standard operating procedure (SOP) by home infusion pharmacy personnel. This SOP will ensure that packing techniques, configurations, and materials for groups of products with common storage characteristics will be standardized. Procedures also should be developed for products with unique storage conditions. Packaging should not vary from the established materials and procedure without retesting, as different packaging materials and configurations differ in their resistance to heat penetration or loss. Occasionally, shipments should be retested, especially whenever transit conditions vary, seasonal temperature changes occur, changes in transit times, or use of different packaging materials.

Table 130-4. Designing a Package for Shipping Refrigerated Sterile Products

POTENTIAL PROBLEMS	POSSIBLE SOLUTIONS
Temperature too cold (<2°)	• Fewer ice bricks • Cardboard barrier around product
Temperature too warm (>8°)	• Add more ice bricks • Use thicker insulation in box • Use more packaging materials to avoid air space in package
Temperature not maintained long enough for expected duration of shipment/ delivery	• Add more ice bricks • Try larger ice bricks • Use a cardboard barrier around product plus more or larger ice bricks

STORAGE IN THE HOME

Sterile products must be stored under controlled conditions until the product is administered. Each drug product should be labeled to indicate its storage requirements and expiration date, including, if appropriate, the time of day beyond which the product should not be used.

Refrigerated products usually are stored in the patient's own refrigerator. The patient/caregiver should be trained to check the refrigerator temperature on a daily basis to ensure proper storage is maintained. If the patient does not have a refrigerator, alternative arrangements must be made. At one time it was common practice for the home infusion organization to provide patients with a refrigerator. In today's cost-conscious health care environment, other options, such as using a neighbor's refrigerator or storing the product with a visiting home health nurse, may be considered.

Unless otherwise indicated, sterile admixtures for home use should be refrigerated until the time of use. Even under ideal conditions, there is always some risk that microorganisms may gain entry into the sterile product. Therefore, HCPs should be stored at refrigerated temperatures to inhibit microbial growth, even if stability issues do not require such storage. There are a few exceptions including:

- Sterile products intended for administration promptly after compounding may be retained at room temperature. It should be noted that delivery time should be included when determining whether the product will be administered promptly; if in doubt, the product should be refrigerated during delivery.
- Reservoirs of medications, such as narcotic analgesics, intended for infusion over more than one day via an ambulatory infusion pump, should either be started promptly after preparation or be refrigerated until the start of infusion. Administration should be completed within seven days.
- Sterile products, such as 5-fluorouracil that should not be refrigerated after preparation should be used within 28 hours of preparation.[11]

The cumulative storage conditions experienced by a sterile product must also be considered. For example, products are commonly removed from the refrigerator and allowed to equilibrate to room temperature, only to be replaced in the refrigerator for later use, if not used as planned. The originally assigned expiration date may be invalidated by these circumstances. In this situation, the pharmacist must consider the cumulative effects of room-temperature storage when determining whether or not the product is stable for use. This may be fairly straightforward for products that have a well-accepted duration of stability at room temperature. For example, 24-hour stability at room temperature is the accepted limit for parenteral nutrition solutions, and 7 days at room temperature is the norm for multi-day infusion reservoirs containing narcotic analgesics. For other sterile products, the manufacturer, their product literature or other reputable source should be consulted for limits on room-temperature stability.

Product labeling should be used to explain requirements for storage and expiration dating. A separate information sheet should include instructions for proper storage, interpretation of expiration dating, and how to observe signs of unsuitability for use. Home-care products should be stored out of the reach of children and pets.

Home assessments should be performed to confirm compliance with appropriate drug storage conditions, cleanliness, separation of drugs from food items, avoidance of improper use or reuse of drugs or supplies, and proper disposal of drug waste. Home inventory quantities should be monitored as an indicator of compliance. If improperly stored, expired, or damaged products are found, the patient should be asked for consent to return or dispose of these items.[11]

Patients receiving sterile products in the home should be instructed about appropriate methods of waste disposal. Needles or other sharp objects should be placed in a commercially available sharps-disposal container, or alternatively, can be stored

130-5. Training Content for Administration of HCPs

- Inspection of products upon receipt for damage and temperature maintenance.
- Product storage requirements.
- Visual inspection before administration for leaks, cracks, particulates, precipitation, discoloration, oiling out, or other evidence of loss of product integrity.
- Label check to confirm right product, drug, dose, and administration time.
- Proper handwashing technique.
- Procedures for aseptic preparation of the product in a clean preparation area.
- Handling and set-up of infusion apparatus and supplies.
- Catheter care and maintenance.
- Clinical monitoring of the patient and the therapy.
- Emergency actions for common complications such as infection, catheter breakage or displacement, tubing disconnection, catheter occlusion, equipment battery change, or equipment malfunction.
- Emergency contact numbers and procedures.
- Proper waste disposal.

Data from USP 26-NF21.

in an impervious and sealable container (eg, empty coffee can.) The sharps container should be kept out of the reach of children. A process should be established for routine waste removal from the home. Options for sharps removal include having home infusion pharmacy personnel pick up the waste container, mailing the sharps container in a sealed package to an EPA-approved incineration facility, or having the patient or caregiver bring the sharps container to a health-care facility for disposal.

Most drug products are not hazardous, and empty containers, tubing, and the like may be disposed of with other household trash; however, local disposal requirements may be prescribed by the landfill where the waste will be sent. Additionally, special consideration to waste disposal must be given if the patient has a communicable disease such as HIV or hepatitis. Waste from hazardous products administered in the home, such as chemotherapy, should be stored in a separate area of the home and should be retrieved by the home infusion organization for incineration.

ADMINISTRATION

The individual or caregiver responsible for administering sterile products in the home must be properly trained. Basic training topics are listed in Table 130-5.

Certain methods of drug administration are unique to home care. These include: ambulatory infusion pumps, implantable infusion devices, and disposable infusion devices. All of these devices expose the sterile drug products to elevated temperatures (eg, body temperature) during administration. Reference data should be consulted to confirm that product stability will be maintained during storage and administration at these elevated temperatures during the intended period of administration.[11]

The home infusion pharmacist is ultimately responsible for compounding sterile products of acceptable strength, quality, and purity with appropriate packaging and labeling in accordance with good pharmacy practices, state pharmacy regulations, official professional and compendial standards, and current scientific principles. Pharmacists practicing in the home infusion setting should continually expand their knowledge about aseptic compounding by participating in seminars, reviewing the professional literature, and consulting professional pharmacy trade organizations.

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CHAPTER 131

The Pharmacist's Role in Substance Use Disorders

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Substance abuse and drug addiction permeate our society today, irrespective of one's socioeconomic status. Alcohol dependence is estimated to affect more than 7% of the adult population in the United States[1] and is responsible for 130,000 deaths annually.[2] Tobacco use is responsible for more than 440,000 deaths each year in the United States, and greater than 150 billion dollars is spent annually in direct and indirect costs attributable to smoking.[3] Over 70% of current smokers would like to quit; however, less than 3% of all smokers are able to successfully stop smoking each year.[4,5] Total direct and indirect costs associated with illicit drug use exceed $97.7 billion.[6] Even with these staggering numbers, substance use disorders are frequently overlooked as health care issues that pharmacists can impact.

As health care professionals, pharmacists are well positioned to take a major role in the disease management of substance use disorders and other comorbid conditions.[7] Pharmacists have knowledge of the pharmacology, pharmacokinetics, mechanisms of action, drug interactions, and adverse events associated with prescription medications and abused substances.[8] Therefore, taking an active responsibility in assessing patients and assuring the appropriate use of treatments for substance use is another opportunity in the ever-increasing role of the pharmacist.

Substance Use Disorders

Substance use disorders are a broad spectrum of behaviors related to the inappropriate use of legal or illegal products. These disorders encompass drug addiction, alcoholism, nicotine addiction, and inhalant abuse, to name a few. Addiction is defined as a disease process characterized by the continued use of a specific psychoactive substance, or the continuation of a particular behavior despite physical, psychological, or social harm. Patients exhibit addictive behavior usually due to dependence upon the substance. Dependence is classified as either physical or psychological. Physical dependence, a physiological state of adaptation to a specific psychoactive substance, is characterized by the emergence of withdrawal effects during abstinence, which may be relieved in total or in part by re-administration of the substance. Psychological dependence is a subjective sense of need for a specific psychoactive substance, either for its positive effects or to avoid negative effects associated with its abstinence. Consumption of the abused substance continues due to fear of withdrawal symptoms. Tables 131-1, 131-2, and 131-3 list common withdrawal symptoms associated with tobacco, alcohol, and opioid cessation.[1] Tolerance is defined as repeated exposure to the same dose of a psychoactive drug resulting in a diminished effect, so that higher dosages than usual are required to achieve a similar response. Tolerance commonly occurs in alcohol, tobacco, and opioid abuse, causing the user to consume larger quantities of the substance to gain the same desired effect. Abstinence is defined as refraining from the use of the substance for a period of time, while a relapse is considered to occur when the individual resumes use of the substance after a period of abstinence. A lapse is considered to be a single episode of using the substance that does not lead to resuming continuous use of the substance.

Brief Interventions

Pharmacists are gaining increasing responsibility for direct patient care and are in an ideal position to provide brief interventions for substance use disorders. Usually, brief interventions are conducted in a primary care setting; however, these short dialogues with patients can take place in any setting where a pharmacist has an opportunity for one-on-one counseling with a patient (eg, retail, hospital, outpatient clinics). The purpose of a brief intervention is to reinforce behaviors toward abstinence in four or five successive patient interactions. Table 131-4 outlines a helpful strategy that can be used during brief counseling sessions known as the "5 A's." These consist of **A**sking, **A**dvising, **A**ssessing, **A**ssisting, and **A**rranging and can help the pharmacist focus each session and provide effective counseling within a short period of time.[9]

In general, such interventions begin with an assessment of the patient's substance use problem and a discussion of the potential health consequences with continued substance use. The pharmacist then offers advice on strategies to either cut down or abstain from use of the substance. Such strategies can include setting specific goals for reducing the number of alcoholic drinks consumed per day or cigarettes smoked per week and agreeing to written contracts that specify measures of progress toward changes in behavior.[10,11]

Recognizing the Addicted Patient

Identifying substance use in a patient should not be a challenge for the pharmacist. Asking a patient if he or she smokes, drinks alcohol, or uses other psychoactive substances should become as natural as asking a patient if he or she has any medication allergies. This information should be included in the demographic section of the patient's profile. Many patients will respect the confidentiality and privacy offered by their pharmacist; however, some patients may be dishonest in answering questions related to licit or illicit substance use, or they may become angry when questioned.

Table 131-1. Diagnostic Criteria for Nicotine Withdrawal

A. Daily use of nicotine for at least several weeks.
B. Abrupt cessation of nicotine use, or reduction in the amount of nicotine used, followed within 24 hours by four (or more) of the following signs:
   (1) dysphoric or depressed mood
   (2) insomnia
   (3) irritability, frustration, or anger
   (4) anxiety
   (5) difficulty concentrating
   (6) restlessness
   (7) decreased heart rate
   (8) increased appetite or weight gain.
C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

From The American Psychiatric Association. *Diagnostic and Statistical Manual for Mental Disorders,* 4th ed, text revision. Washington DC: American Psychiatric Association, 2000.

Knowing as much information as possible about substance use is critical when dispensing prescription medications. Table 131-5 describes the various drug interactions with cigarette smoking. For example, smoking induces the cytochrome P-450 system in the liver causing drugs such as caffeine, clozapine, olanzapine, tacrine, and theophylline to be metabolized more quickly. Higher doses of these medications are required in smokers and dosage adjustments are necessary in patients that quit smoking. Tobacco use may also cause a pharmacodynamic interaction with medications such as benzodiazepines and beta-blockers, altering their expected response. Smokers may have less sedation and drowsiness with benzodiazepines and a decreased antihypertensive effect with beta-blockers.[12] This information may help motivate patients to make a smoking cessation attempt or remain abstinent. Disease states and medications that should automatically trigger the pharmacist to ask about the patient's smoking status are listed in Table 131-6. Common indicators that should prompt questioning regarding smoking status include prescribed medications for chronic obstructive pulmonary disease, asthma, diabetes, hypertension, and cholesterol lowering medications. Common interactions also occur between alcohol and prescription medications. Interactions can be pharmacokinetic, as described above with cigarettes, or pharmacodynamic, often resulting in an additive effect with alcohol on the central nervous system. Pharmacokinetic interactions depend on the patient's level of drinking. With moderate alcohol consumption, competition occurs for the cytochrome P-450 metabolic pathway. Alcohol has a greater affinity for these enzymes, resulting in decreased metabolism of the medication and higher levels of it in the body. In chronic heavy drinkers, cytochrome P-450 activity is enhanced, resulting in potentially subtherapeutic levels of the medication.[13] Patients taking medications with sedative effects should be counseled on the additive sedation that can result when these products are taken in conjunction with alcohol.

Table 131-2. Diagnostic Criteria for Substance Abuse

A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
   (1) recurrent substance use resulting in failure to fulfill major role obligations at work, school, or home (eg, repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
   (2) recurrent substance use in situations in which it is physically hazardous (eg, driving an automobile or operating a machine when impaired by substance use)
   (3) recurrent substance-related legal problems (eg, arrests for substance-related disorderly conduct)
   (4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (eg, arguments with spouse about consequences of intoxication, physical fights).
B. The symptoms have never met the criteria for Substance Dependence for this class of substance.

From The American Psychiatric Association. *Diagnostic and Statistical Manual for Mental Disorders*, 4th ed, text revision. Washington DC: American Psychiatric Association, 2000.

Table 131-3. Diagnostic Criteria for Opiate Withdrawal

A. Either of the following:
   (1) cessation of (or reduction in) opioid use that has been heavy and prolonged (several weeks or longer)
   (2) administration of an opioid antagonist after a period of opioid use
B. Three (or more) of the following, developing within minutes to several days after criterion A:
   (1) dysphoric mood
   (2) nausea or vomiting
   (3) muscle aches
   (4) lacrimation or rhinorrhea
   (5) pupillary dilation, piloerection, or sweating
   (6) diarrhea
   (7) yawning
   (8) fever
   (9) insomnia.
C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

From The American Psychiatric Association. *Diagnostic and Statistical Manual for Mental Disorders,* 4th ed, text revision. Washington DC: American Psychiatric Association, 2000.

Willingness to Change: The Transtheoretical Model

One of the most helpful concepts to understand when assisting a patient with a substance use disorder is the Transtheoretical Model for Change.[14] This model illustrates the process one goes through with *any* type of behavior change, whether it is quitting smoking or drinking alcohol, losing weight, or starting a new exercise regimen. Once the patient's readiness to change is determined, appropriate counseling may be more readily of-

Table 131-4. The "5 A's" for Brief Intervention

Ask about substance use	Identify and document substance abuse at every visit.
Advise to quit	In a clear, strong, and personalized manner urge user to quit.
Assess willingness to make a quit attempt	Is the substance abuser willing to make a quit attempt at this time?
Assist in quit attempt	For the patient willing to make a quit attempt, use counseling and pharmacotherapy to help him or her quit.
Arrange follow-up	Schedule follow-up contact, preferably within the first week after the quit date.

From Fiore MC, Bailey WC, Cohen SJ, et al. *Treating Tobacco Use and Dependence: Clinical Practice Guideline.* Rockville, MD: U.S. Department of Health and Human Services. Public Health Service, June 2000.

Table 131-5. Drug Interactions with Cigarette Smoking

DRUG	MECHANISM	COUNSELING COMMENT
Acetaminophen	Induction of CYP1A2	Patients may require less acetaminophen for pain relief if they quit smoking.
Caffeine	Induction of CYP1A2	Patients attempting abstinence may want to decrease their caffeine intake. Slower metabolism of caffeine causes insomnia, also a withdrawal symptom of nicotine.
Clozapine	Induction of CYP1A2	May require a lower dose once they stop smoking.
Diazepam	Unknown	Sedation may improve with abstinence. Smokers require higher doses.
Insulin	Increased catecholamines and cortisol; decreased subcutaneous absorption	Patients may be able to lower their insulin dose once they stop smoking.
Propoxyphene	Unknown	Pain may be controlled with lower doses after quitting smoking.
Propranolol	Increased release of catecholamines	Drug efficacy, blood pressure, and chest pain may improve with abstinence.
Tacrine	Induction of CYP1A2	Patients may require a lower dose once they stop smoking.
Theophylline	Induction of CYP1A2	The dosage of theophylline may need to be empirically lowered by one-third to one-fourth of the total daily dose once the patients stop smoking.
Tricyclic antidepressants	Increased hepatic metabolism	Patients may require a lower dose once they stop smoking.
Warfarin	Increased hepatic metabolism	Patients may require a lower dose once they stop smoking.

fered.[15] Recommending that a patient change a specific behavior before the decision to change has been made may lead to defensive behavior from the patient and frustration for the pharmacist.

The goal of the Transtheoretical Model for Change is to offer advice and motivation to move the patient forward to the next stage until the behavior change is imminent. The model is designed to be cyclical, meaning a patient may lapse or relapse and need counseling to restart the process. The patient may proceed completely or partially through the model of change several times before the behavior change becomes permanent.

The first stage of change is *precontemplation*. At this stage, a patient has not really thought about making a behavior change. The patient may appear defensive when asked about his/her substance use and whether stopping this use is in sight. Although the patient may not want to change at this stage, it is still very important to ask the patient about his/her habits and to offer advice to quit smoking or stop other substance use. Pharmacists and other health care providers need not get frustrated and surrender to a patient's lack of motivation at this stage. Repetition by asking the patient about their habits at this stage and counseling on the benefits of abstinence should continue at every visit until the patient is motivated to change.

For example, explaining the health risks of continuing to smoke may be used as a tactic to motivate a patient to quit smoking; however, this can sometimes backfire. Providing the patient with positive reasons to quit, such as decreased shortness of breath, monetary savings, possibly less medication in some instances, and a cleaner living environment, is more motivational than applying scare tactics. Saying a few words to the patient or providing a pamphlet with the benefits of stopping smoking may be enough to make the patient think about stopping smoking and motivate him/her to move forward to the next stage of quitting. Table 131-7 outlines some of the health benefits of stopping smoking.

Contemplation is the next stage of behavioral change. At this point, a patient is thinking about making a change, but has not yet identified a date or plan to do so. This stage is like a teeter-totter; the patient can move on to prepare for this change or fall back to not even considering it. Patients who are considering stopping smoking may be at this stage for some time before preparing for an actual quit date. Patients who use alcohol may continue to drink excessively for a long period of time without any immediate detrimental effects. They may realize that there is a problem, but think they have control over the situation and try to stop on their own, often with failure. Unfortunately, in those addicted to drugs or alcohol, it may take severe impairment before they fully understand the need for change.

Pharmacists, physicians, nurses, and other health care providers can have a positive impact on patients in the contemplation state. A few vital counseling tips can help make the difference between a patient's decision to change or continue their substance use. The goal is to motivate the patient to prepare for the change sooner rather than later. Sharing information on the benefits of abstinence from abused substances such as alcohol and tobacco, while providing different

Table 131-6. Cues for Smoking Cessation Counseling

MEDICATION OR DISEASE STATE	COMMENT
Antibiotics for otitis media	Exposure to second-hand smoke increases the incidence of ear infections in children.
Bisphosphonates and Calcium supplements	Cigarette smoke lowers a woman's estrogen level, making her more susceptible to bone fractures.
Diabetes	Heart disease is the most common cause for death in patients with diabetes. Smoking increases the risk of heart disease and may also contribute to insulin resistance.
Hyperlipidemia	Smoking lowers high-density lipoprotein (HDL) cholesterol.
Hypertension	Blood pressure is elevated after smoking due to vasoconstriction.
Inhalers	Smoking is the major cause of COPD. Smoking may also trigger asthma symptoms.
Mouth rinse for gingivitis	Smoking increases the incidence of gingivitis and tooth loss.
Oral contraceptives	Use of oral contraceptives and smoking increases the risk for stroke, myocardial infarction, and blood clots in women older than 35.
Prenatal vitamins	Smoking during pregnancy may cause congenital malformations and low birth weight.
Proton pump inhibitor or H_2 blockers	Smoking delays the healing of ulcers and worsens gastroesophageal reflux (GERD).

Table 131-7. Time Course of Health Benefits from Smoking Cessation

20 Minutes:	Blood pressure drops to normal. Pulse rate drops to normal. Body temperature of hands and feet increases to normal.
8 Hours:	Carbon monoxide blood level drops to normal. Oxygen blood level increases to normal.
24 Hours:	Chance of heart attack decreases.
48 Hours:	Nerve endings start regrowing. Ability to smell and taste is enhanced.
2 Weeks to 3 Months:	Circulation improves. Walking becomes easier. Lung function increases up to 30%.
1–9 Months:	Coughing, sinus congestion, fatigue, and shortness of breath decrease. Cilia regrow in lungs, increasing ability to handle mucus, clean the lungs, and reduce infection. Body's overall energy increases.
1 Year:	Excess risk of coronary heart disease is half that of a smoker.
5 Years:	Lung cancer death rate for average smoker (one pack a day) decreases by almost half. Stroke risk is reduced to that of a nonsmoker 5 to 15 years after quitting. Risk of cancer of the mouth, throat, and esophagus is half that of a continuing smoker.
10 Years:	Lung cancer death rate is similar to that of a nonsmoker. Pre-cancerous cells are replaced. Risk of cancer of the mouth, throat, esophagus, bladder, kidney, and pancreas decreases.
15 Years:	Risk of coronary heart disease is that of a nonsmoker.

From Cancer Facts and Figures, 1996, American Cancer Society.

methods to stop current behavior may motivate a patient to prepare for change.

Preparation is a vital stage for most patients to be successful with behavior change. For smokers, this stage usually occurs very close to the selected quit date. A few days to a month are often enough time for the patient to develop and practice their quit plan. Patients may move quickly from *preparation* to *action*, even without a complete quit plan. A few may be successful for the short-term, but may then relapse once an unplanned barrier is encountered. Therefore, assisting a patient with arranging and practicing a quit plan prior to the quit date may improve the success of the quit attempt. Support from friends, family, and coworkers is very important during both the preparation and action stage to ensure success.

Action is the stage in which the patient has changed their unwanted behavior from between 1 day and 6 months. This stage is often misinterpreted as the "end" of the cycle, because the patient has reached the goal of changing their behavior. Actually, this period of time requires the most counseling and encouragement in order to maintain the change. Smokers during this stage may be using medication and behavior modification techniques to stay abstinent. Despite medication and behavioral assistance, patients may still experience withdrawal. Contacting the patient on their quit date and seeing the patient in person one to two weeks after the quit date may prevent relapse. Congratulating the patient on quitting and offering assistance with any possible barriers the patient has encountered may help with continued abstinence. Encouraging the patient to remember his/her reasons for stopping smoking and the benefits he/she has noticed since the quit date are also important.

The *maintenance stage* begins after the patient has changed their unwanted behavior for 6 months. The patient will still need support and encouragement to maintain their behavior change. Congratulating the patient on continued abstinence and discussing the benefits he/she has experienced are important. Previous smokers may still have cravings for many years after their quit date. A reminder of the risks of returning to the substance use, the benefits of stopping, and the difficulty of making the change deters many from returning to their addiction. To prevent relapse, identify specific triggers and prepare the patient for these encounters. Encouraging a drinker to stay away from bars or restaurants that serve alcohol and to avoid hanging out with people they know will lead them to drink again may help prevent relapse.

Relapse can occur at any time. In smokers, it most commonly occurs within the first year after stopping. During the course of smoking cessation, most smokers make several quit attempts before being successful. All patients, regardless of whether they use alcohol, tobacco, or other drugs, should be encouraged to resume their efforts and to avoid treating this as a failure. Learning from each attempt at change may prevent relapse from occurring on the next attempt.

TOBACCO DEPENDENCE

Smoking History

Prior to obtaining a smoking history, baseline medical information should be obtained including the past and current medical history, current medication use, and alcohol and drug use. Baseline smoking information to be collected from a patient includes the number of cigarettes smoked in packs per day (ppd) (20 cigarettes = 1 pack), number of years smoked, number of previous quit attempts and methods used, reasons the patient wants to quit smoking, smoking triggers, barriers to successful quitting, and the reasons for any past relapses.

Trigger Planning

There are many behavioral and pharmacological strategies for smoking cessation depending on the patient's stage of change. If a patient is ready to quit, effective smoking cessation strategies must incorporate the "habit" and "withdrawal" components of tobacco addiction. Treatment must address withdrawal symptoms and cravings that are often responsible for relapse within the first few weeks, as well as the behavioral factors that often cause relapse later in the quit process.

Developing a quit plan involves a number of steps. If the patient is ready to quit, an important first step is to select a quit date. The selected date should not be too far in the future, but should give the patient enough time to prepare for that date. Ideally, the quit date should be set within the upcoming 1–2 weeks; however, for some patients it may be later than this. This date should be marked on a calendar, and friends and family should be informed of this important date. Prior to the quit date, smoking-related paraphernalia (eg, cigarettes, lighters, matches) should be thrown away.

Patients should be encouraged to critically evaluate their smoking habits prior to their quit date and identify their personal smoking triggers. This involves quantifying the number of cigarettes smoked per day, especially if the patient is unsure of the exact number and when he or she smokes. One method is to keep a "tally sheet" or a record of when, where, and why each cigarette was smoked for several days. This may also be useful in identifying an individual's smoking triggers. Triggers can be certain times, events, or people that produce an urge to smoke. Common triggers include after meals; when socializing; when drinking coffee, soda, or alcohol; and stress at work or stress from major life events. Each patient should identify his or her own specific triggers and write them down. The next step is to brainstorm and come up with a list of activities or actions that can be performed to deal with specific triggers. The idea is to have very specific activities already selected that can be utilized during a craving to overcome the desire to smoke and

prevent a lapse or relapse. One counseling technique to assist with trigger planning is called the "4 D's." These include **D**elay, **D**o something else, **D**rink water, and **D**eep breathing. For example, those who like to smoke after meals may decide to brush their teeth or go for a walk instead. Those who like to smoke while driving can carry a water bottle, have a squeeze ball with them, or listen to relaxing music while in the car. Prior to quitting, patients who like to drink coffee in the morning can drink the coffee first and delay smoking their first cigarette by 30 minutes. Patients can also delay for 1–3 minutes when they are experiencing a craving. Each patient should identify several actions that will help manage his or her triggers and should actively engage in these activities during the quit process. It is also useful to review and examine past quit attempts and reasons for failure. Evaluating what was helpful and what factors caused the relapse can be important information to have for any subsequent quit attempts.

Individual Counseling

As a pharmacist, it is often difficult to determine exactly how to counsel a patient on stopping smoking. In the retail setting, the demands of dispensing prescriptions, answering telephones, and counseling patients on medications make it difficult to take time to discuss smoking cessation. In the hospital setting, this activity may not be viewed as a pharmacist's role at all; however, all health care professionals should take part in the effort to help patients stop smoking.

Every patient should be advised to quit smoking by every health care provider. A physician's advice alone improves abstinence rates compared to no intervention. Having a greater variety of health care providers involved in treatment for smoking cessation increases abstinence rates.[9] A 6-month study evaluating the efficacy of community pharmacists offering smoking cessation treatment found that brief counseling by a pharmacist along with nicotine replacement therapy is as effective as that same treatment offered by physicians and nurses. A combination of brief counseling by pharmacists, nicotine replacement therapy, and group counseling resulted in an abstinence rate at 6 months of 44%.[16]

Patients and health care providers have been led to believe that group sessions or self-help materials are the only effective means of helping a patient quit smoking. Actually, less than 10% of smokers will attend group sessions.[17] Therefore, if individual advice to quit is not offered, health care providers are missing 90% of smokers! The goal is to capture the individual's attention in the pharmacy, hospital, or clinic in order to motivate that patient to quit smoking.

Fear of defensive behavior from the patient, misunderstanding of the addiction by the pharmacist, and the pharmacist oftentimes never having smoked are perceived barriers to offering individual counseling. Pharmacists should not assume patients know and understand the health and life consequences of smoking. Providing the patient with individualized empathetic counseling may be motivating. Studies have shown that talking to the patient on an individual basis for just 3 minutes increases abstinence rates.[9] The "5 R's" provide a template for relaying an individualized approach to patients. These include **R**elevance, **R**isks, **R**ewards, **R**oadblocks, and **R**epetition and may motivate a patient to get ready to quit smoking. Table 131-8 lists the 5 R's. Also, with each encounter, the pharmacist gains new information and experience about medication efficacy, side effects, and trigger planning that can be applied to future patients.

Individual counseling offers the benefits of convenience, privacy, and individual attention. The time spent counseling is focused on the individual's specific needs. For example, if more time needs to be spent on behavioral modification, then this is possible. If the patient has special educational needs or requires close medication monitoring, then individual counseling is beneficial. Individual counseling has also been shown to achieve higher abstinence rates. As little as 10 minutes of counseling doubles the abstinence rate compared to no intervention at all.[9] Whether the patient returns for further instruction, uses self-help materials, or attends a group session, each patient should be asked and advised to quit smoking.

Group Counseling

Group sessions are able to offer group support, imitation, and competition. If the pharmacist has never smoked, sometimes it is difficult for the patient to believe that the pharmacist understands how difficult it is to quit smoking. This situation is avoided in a group setting as it allows patients to share experiences and questions with others in the group who are also going through the quitting process. The support from others makes quitting less lonely. Imitation of successful group members or competition within the group may also motivate patients to quit smoking.

Group sessions are difficult to conduct without some training or at least some planning. Establishing limitations and structure for the group alleviates unforeseen barriers to success. An enrollment process, including an application, can help create structure and identify a patient's willingness to participate. The application can also be used to collect a smoking history, determine if there are any learning or language barriers, and aid in coordinating dates and times for group sessions.

Including all patients that are at the same level of motivation is crucial. One or two participants who are not ready to quit

Table 131-8. The "5 R's" to Enhance Motivation to Quit Tobacco.

Relevance	Relate individualized factors (ie, current disease states, medications, family, cost) to how the patient will benefit from stopping smoking.
Risks	Patients may already know some risks to continuing to smoke. Examples: cancer, heart attack, and stroke. Also provide the patient with risks that relate personally to them. Examples: high blood pressure, increased shortness of breath, and bronchitis.
Rewards	Patients often enjoy smoking, so the rewards need to outweigh the benefits of continuing to smoke. Examples: saving money, improved smell and taste, healthier body, more time, freedom from the addiction, and improved self-esteem.
Roadblocks	Ask the patient what concerns or barriers they have to stopping and problem-solve with them ways to overcome these with this quit attempt. Examples: spouse smokes, weight concerns, fear of failure, stress, and other addictions.
Repetition	Do not give up on the patient! Continue to assist the patient until the patient quits smoking.

From Fiore MC, Bailey WC, Cohen SJ. Treating Tobacco Use and Dependence. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, June 2000.

smoking can shift the balance for other group members by offering excuses as to why now is not a good time to quit smoking. A simple question to ask on the application is "When do you see yourself stopping use of tobacco?" Include patients that answer similarly in the same group.

If the sessions will follow an agenda, a closed enrollment is beneficial. With a closed enrollment, all members of the group start and end at the same time. New members are not allowed into the group at different times needing to "catch up" to the others. This type of enrollment improves group cohesiveness and as each week passes, the group becomes more like a "family." This enrollment also ensures that the agenda for the meeting is met.

The group leader is as important as the participants. The group leader needs to facilitate the discussion for the meeting. Facilitating the meeting also means avoiding lecturing to the participants and ensuring that all participants have the opportunity to talk. This may mean going around the room asking for input or calling on participants. The facilitator should avoid allowing one person to dominate the group discussion.

Defining the optimal time frame and number of sessions for stopping smoking has been studied.[9] At least four group sessions significantly improves the quit rate. Meetings may be scheduled with half of the sessions preparing the participant to quit smoking and half occurring after the participant has stopped smoking to prevent relapse. Ideally, 31–90 minutes of counseling has been shown to increase abstinence rates. Sessions that are longer tend to lose the interest of the participant and do not improve the abstinence rate.[9]

Telephone Counseling

Telephone counseling has many benefits and is becoming more common as state-funded quit lines are being implemented across the country. Quit lines have been shown to double abstinence rates at one year in people who attempt to quit.[18] Quit lines offer the advantages of ease of use and availability, as many are staffed 24 hours per day, every day of the year. Pharmacists can save time and increase convenience for the patient with brief telephone contacts as a method of follow-up. This personalized, brief intervention can help maintain motivation to quit smoking and prevent relapse.

Cold Turkey/Tapering Method/Aversive Smoking

Cold turkey, aversive smoking, and tapering are alternative methods for smoking cessation that do not involve the use of medications during the quit process. The cold turkey method involves selecting a date and then quitting tobacco use on that date, while tapering or "cigarette fading" involves gradually cutting down on the number of cigarettes smoked per day or per week until cessation is reached. Cold turkey and tapering have not been shown to improve quit rates.[9] Smoking to the point of feeling ill is called aversive smoking. Rapid smoking and rapid puffing are aversive techniques that have been shown to double the quit rate compared to no intervention.[9] These techniques are not used frequently today due to the health risks associated with this type of smoking.

Medications for Smoking Cessation

Based on current guidelines, tobacco addiction is considered to be a chronic disease that often requires repeated interventions for success. Currently, first-line agents include bupropion SR (Zyban), nicotine gum, nicotine inhaler, nicotine nasal spray, and nicotine patches.[9] Nicotine lozenges have just been released and are not currently included in the guidelines; however, it is likely that they will also be considered as first-line agents. Every patient who is attempting to quit, except in special circumstances (ie, pregnancy, within 2 weeks post-myocardial infarction) should be offered at least one of these agents. When compared to placebo, each agent has been shown to approximately double the quit rate.[9] There are no guidelines to determine which of the first-line agents should be used in various situations; therefore, choice of first-line therapy is made based on a number of factors. These factors include the patient's smoking history and habits, past experience with any of the agents, coexisting medical conditions (ie, depression), contraindications to any of the agents, and patient and caregiver preference. Treatment can and should be individualized based on these factors. Prior to beginning a specific therapy, it is important for the patient to understand the proper use and dosing of that agent.

Combination therapy with two nicotine replacement products or with a nicotine replacement product and bupropion SR may improve the response rate in those trying to quit over that of single therapy.[19–22] Nicotine replacement therapy (NRT), if dosed according to the current guidelines, provides nicotine equivalent to smoking about 1 pack per day; therefore, in heavier smokers, withdrawal and cravings may still occur. One effective option is to use a nicotine replacement product on a scheduled basis and have available an additional agent that the patient can use when needed throughout the day. Effective combinations might include using a patch on a scheduled basis daily and adding an agent such as the nicotine gum, lozenge, or inhaler on an as needed basis. This provides additional nicotine replacement and may be especially useful for those patients who smoke greater than 1 ppd or who have failed monotherapy. Tables 131-9, 131-10, and 131-11 include dosing information on the first-line medications approved for smoking cessation.

Special Populations of Smokers

PSYCHIATRIC DISORDERS AND OTHER ADDICTIONS—Many psychiatric and substance abuse treatment programs have typically not addressed smoking as an addiction and, in the past, may have actually encouraged smoking. For example, until recently smoke-free AA meetings were not available and smoking at these meetings was commonplace. People with psychiatric disorders (ie, schizophrenia, depression, bipolar disorder, anxiety disorders) or other addictions (ie, alcohol, opiates) are estimated to be two to three times more likely to be tobacco dependent than the general population.[23] Biological, genetic, psychological, and social factors are all thought to play a role. In addition, patients may be managing medication side effects and disease symptoms by adjusting their smoking habits due to drug and disease state interactions.[24] Although few studies are available, the use of the first-line agents alone or in combination plus behavioral therapy may be effective in this subgroup of the population. In clinical practice, schizophrenic patients often have a difficult time quitting smoking and need a significant amount of follow-up and reinforcement. Patients with a history of depression who attempt to stop smoking risk a relapse of depression for the first 6 months after quitting.[25] For this reason, bupropion SR may be a good choice in these patients.

CARDIOVASCULAR DISEASE—Abstinence rates for cardiovascular patients at one year are greater than 50%, making this population one of the most motivated groups to quit smoking.[26] NRT and/or bupropion SR should be offered to these patients to ease withdrawal symptoms. Nicotine has sympathomimetic effects that increase blood pressure and heart rate and may cause coronary artery vasospasm. However, the amount of nicotine in NRT is much lower than the amount of nicotine in cigarettes. Studies have found that NRT does not cause myocardial infarction in the general population, nor does it exacerbate cardiovascular events in patients with pre-existing disease.[27, 28] Before using NRT, caution should be exercised in patients with a history of myocardial infarction, serious arrhythmias, or worsening angina within the past 2 weeks. A physician's monitoring and assessment of this type of patient is

Table 131-9. Nicotine Replacement Therapy: Transdermal Patches

	NICOTROL®	NICODERM CQ® GENERIC	PATIENT INSTRUCTIONS	POTENTIAL SIDE EFFECTS
Availability	5, 10, 15 mg OTC	7, 14, 21 mg OTC	Stop smoking. Peel the backing off the patch. Place the patch on a relatively hairless area between the neck and waist. Start wearing the patch the morning of the quit day and keep the patch on all day and night (remove 16 hour patch at bedtime and 24 hour patch at bedtime only with sleep disturbances). Change the patch daily, rotating it to a new site.	Local cutaneous reaction (erythema, pruritus, edema), headache, sleep disturbances (seen with 24 hour patch). Use cautiously in cardiovascular patients within 2 weeks post myocardial infarction, those with serious arrhythmias, and those with severe or worsening angina.
Patch Replacement Schedule	16 hours	16 or 24 hours		
Dosing Guidelines	15 mg × 6 weeks 10 mg × 2 weeks 5 mg × 2 weeks	>10 cigarettes/day: - 21 mg × 6 weeks - 14 mg × 2–4 weeks - 7 mg × 2–4 weeks <10 cigarettes/day, cardiovascular disease, or weigh <100 lbs. - 14 mg × 6 weeks - 7 mg × 2–4 weeks		

advised since these patients were excluded from most clinical trials. Bupropion SR has little effect on the cardiovascular system. Non-significant trends of increased blood pressure in patients treated with both bupropion SR and the nicotine replacement patch were seen in one study.[19]

PREGNANCY—Smoking during pregnancy has been shown to cause a number of adverse outcomes including spontaneous abortion, fetal growth retardation, preterm delivery, and sudden infant death syndrome.[29] Many women are motivated to quit smoking during pregnancy; however, there is little data available regarding the most efficacious method. Pregnant smokers should first be given extensive counseling on the benefits of stopping smoking and on behavioral techniques that may be beneficial. For heavier smokers unable to stop, NRT or bupropion SR may be an option.

SMOKELESS TOBACCO PRODUCTS/CIGARS—Advertisements promoting cigars and smokeless tobacco products, and possibly current restrictions on smoking in public places, have caused an increase in the use of these forms of tobacco. The use of cigars has increased 50% since 1993, primarily among males aged 18–24 years old. The rate of women smoking cigars has increased fivefold from 1990 to 1996.[30]

Cigar smoke is usually not purposefully inhaled, and the nicotine is absorbed through the buccal lining in the mouth. Cigars contain between 100 and 200 mg of nicotine, while most cigarettes contain about 8.4 mg of nicotine.[31] Only one-fourth of cigar smokers inhale; however, the lips, tongue, throat, and larynx of all cigar smokers are exposed to the carcinogens contained in cigars. The risk of lung cancer in cigar smokers who do not inhale is twice that of nonsmokers. The risk of oral, throat, and esophageal cancer is similar to that of cigarette smokers. Cigar smokers who inhale 5 cigars per day have about the same risk of lung cancer as a 1 pack per day cigarette smoker. Occasional cigar smokers are twice as likely as those who have never smoked cigars to start smoking cigarettes. Cigar smoking increases the risk of relapse in previous cigarette smokers.

Quitting cigar smoking decreases the risk of many cancers, chronic obstructive pulmonary disease, and coronary heart disease. Studies evaluating the effectiveness of pharmacotherapy to help regular cigar smokers are lacking.

Smokeless tobacco, also called spit tobacco, comes in two forms, snuff and chew tobacco. Snuff is available in sachets, moist, or dry. The user places a pinch or dip between the cheek and gum and the nicotine is absorbed through the buccal area. Dry snuff is the form more commonly available in Europe and is inhaled through the nose. Chew tobacco is available as loose leaf, plug, or twist form. The user of chew tobacco also places a "wad" in the cheek for buccal absorption.

Ninety-two percent of spit tobacco users are male. The use of these products tripled between 1972 and 1999.[32] Snuff or chew tobacco increases the risk of oral, pharynx, and esophageal cancer. Tobacco specific nitrosamines, formaldehyde, arsenic, polonium, and many other carcinogens are found in smokeless tobacco products. Increased blood pressure, cardiovascular disease, oral leukoplasia, and many dental complications are increased with smokeless tobacco use. Two to three times the amount of nicotine is absorbed in the buccal lining compared to cigarettes resulting in users of smokeless tobacco becoming highly addicted.

An oral examination with counseling, usually completed by a dentist, is an effective method to help smokeless tobacco users discontinue use.[33] Studies using nicotine replacement therapy and bupropion SR have conflicting results with long-term abstinence rates similar to placebo.[34–36] Smokeless tobacco users are likely to need aggressive therapy, possibly combination therapy and counseling with follow-up to maintain abstinence.

Monitoring

Blood pressure, pulse, weight, and carbon monoxide (CO) or a cotinine level should be assessed before medication is initiated and again after the quit date. CO is a poisonous gas that smokers inhale each time a cigarette is smoked. Carbon monoxide can be measured with the use of a small hand-held CO monitor which measures the amount of CO exhaled in parts per million (ppm). Some monitors can also convert the CO measurement to percentage of carboxyhemoglobin (% COHgb), which is the estimated amount of CO displacing oxygen on hemoglobin. Typically, cigarette smokers have CO levels between 15 and 40 ppm or between 3.0 and 7.0% COHgb. Cigar and pipe smokers may

Table 131-10. Nicotine Replacement Therapy

	GUM (NICORETTE)	ORAL INHALER (NICOTROL INHALER)	NASAL SPRAY (NICOTROL NS)	LOZENGE (COMMIT)
Availability	2 mg, 4 mg OTC Original, Orange, Mint	10 mg/cartridge Prescription only	10 mg/ml Prescription only	2mg, 4mg OTC
Dosing Schedule	2 mg: <25 cigarettes/day 4 mg: ≥ 25 cigarettes/day Begin with 1 piece every 1–2 hours for 6 weeks, then 1 piece every 2–4 hours for 3 weeks, then 1 piece every 4–8 hours for 3 weeks.	6–16 cartridges/day for the first 12 weeks Must use a minimum of 6 cartridges/day for the first 3–6 weeks (up to 12 weeks), then taper over 6–12 weeks.	1–2 sprays in each nostril/hour Gradually decrease rate over 6–8 weeks.	2mg: first cigarette >30 minutes after waking 4mg: first cigarette ≤30 minutes after waking Weeks 1 to 6: 1 lozenge every 1 to 2 hours (at least 9/day) Weeks 7 to 9: 1 lozenge every 2 to 4 hours Weeks 10 to 12: 1 lozenge every 4 to 8 hours
Dosing Guidelines	Stop smoking. Chew gum until a "tingling sensation" is felt. Place nicotine gum between cheek and gums ("Park") and leave gum there until tingling disappears. "Chew" and "park" gum for 1–2 hours, then use a new piece. Park in different areas.	Stop smoking. Individualize dosing to each patient. Short, shallow puffs minimize coughing and throat irritation. An open cartridge is good for one day. May take one week to adjust to side effects.	Stop smoking. Individualize dosing to each patient. Do not sniff, swallow, or inhale through the nose as the spray is administered.	Stop smoking. Suck on the lozenge until the taste becomes strong, then place the lozenge between the gum and cheek. Do not chew, bite, or swallow. When the taste fades, repeat the process until the lozenge is dissolved.
Duration of Therapy	12 weeks	18–24 weeks	12 weeks	12 weeks
Maximum Dose	2 mg: 30 pieces/day 4 mg: 20 pieces/day	16 cartridges/day	Do not exceed 10 sprays/hour or 80 sprays/day.	Do not exceed 20 lozenges/day.
Potential Side Effects	Jaw soreness, Hiccups, Nausea, Vomiting, Headache	Local irritation of throat and mouth, Coughing, Rhinitis	Hot/peppery sensation in nose and throat, Sneezing, Coughing, Watery eyes, Runny nose	Hiccups, Heartburn, Nausea
Comment	Avoid eating or drinking anything except water 15 minutes prior or after use of the gum to maximize absorption. If the gum is used properly, side effects will be minimized. The gum is difficult to use on a scheduled basis and patients may have withdrawal from lack of compliance. The original flavor tastes bad.	The inhaler mouthpiece looks like a plastic cigarette or cigarette filter. The cartridges contain nicotine that is absorbed in the buccal lining of the mouth when the patient puffs on the mouthpiece. Food and drink decrease the absorption of nicotine from the inhaler. Scheduled use is most efficacious.	The nasal spray has the fastest onset of action of the NRT products. Twenty percent of patients use the nasal spray at higher than recommended doses or for longer than recommended.	The lozenge has a mint flavor and is sugar-free. Scheduled use will enhance the efficacy of the lozenge.

have CO levels > 40 ppm, as these products emit high levels of CO. In clinical trials, a nonsmoker is often defined as having a CO < 10 ppm; however, in clinical practice, nonsmokers often achieve CO levels of 1 or 2 ppm. CO monitors with disposable mouthpieces are manufactured by *Bedfont* (Innovative Medical Marketing; T/A Bedfont Scientific, USA; 30 Jackson Road, Suite B-3; Medford, NJ 08055; 609-654-5561; Info@bedfontusa.com) and cost between $400 and $800. The CO monitor is a useful tool to provide the patient with immediate feedback regarding his or her smoking cessation efforts. However, if the patient is a light smoker, has severe restrictive or obstructive pulmonary disease, or has abstained from smoking for the past 8 hours, the reading may not be a true measurement of abstinence.

Cotinine is a metabolite of nicotine that can be measured in the blood, saliva, or urine. Cotinine can be detected in the serum for up to 7 days; however, if the patient is using nicotine replacement therapy, cotinine levels will remain elevated.[37] Cotinine measurements require laboratory analysis; therefore, they should be reserved for physician use in certain situations, especially prior to surgeries or procedures where the patient has committed to abstinence. Cotinine levels are often reported in research trials and are typically < 10 ng/mL for nonsmokers, but may be 300 ng/mL for a 1 ppd smoker.[38]

Relapse Prevention

Many potential barriers exist that may lead to relapse. Without a trigger plan, medication, and counseling, only 3–5% of patients who try to quit smoking are successful at 1 year.[39] For

Table 131-11. Bupropion SR (Zyban)

DOSAGE FORM	SUSTAINED-RELEASE TABLET DO NOT SPLIT OR CHEW TABLET.
Availability	150 mg Prescription only
Dosing Schedule	150 mg daily × 3 days; then 150 mg twice daily Space dosages 8 hours apart. Take last dose before 6 PM.
Dosing Guidelines	Initiate while patient is still smoking. Set quit date for 1–2 weeks after starting bupropion SR.
Duration of Therapy	7–12 weeks No clinical data to support use for more than 12 weeks.
Maximum Dose	300 mg daily
Potential Side Effects	Dry mouth (10%), Insomnia (30%), Dizziness (8%), Constipation (8%), Tremor (2%), Seizure (0.1%)*
Contraindications	History of seizures, bulimia, anorexia nervosa, or head trauma. Concomitant use of MAO inhibitors or Wellbutrin.

*Dose-dependent <= 300mg/day.

this reason, providing encouragement, motivation, congratulations, and assistance with barriers after the quit date and for at least 1 year is important. Asking the patient about previous quit attempts and causes for relapse may help in preparation for the current quit attempt. Common reasons for relapse include withdrawal symptoms, weight gain, and stress. Preparing the patient for these barriers before the quit date as part of the quit plan and then continuing the support after the quit date is important.

Withdrawal symptoms may be more intense or prolonged in some individuals. Using smoking cessation medications in combination or for longer periods of time may alleviate this cause of relapse. Educating the patient to be able to identify withdrawal symptoms (ie, cravings, irritability, trouble concentrating, insomnia) and to act quickly may help to prevent relapse. Before increasing or adding additional smoking cessation medications, an assessment should be made of whether current medications and trigger plans have been utilized appropriately.

Weight gain is a major barrier to stopping smoking, especially among women.[40] Smoking cessation usually results in less than a 10-pound weight gain over the first few months of abstinence for most patients. A small percentage of patients are at risk to gain more weight including those who smoke greater than 15 cigarettes per day, African Americans, and patients under the age of 55.[41] Women also tend to gain more weight than men. Reasons for the weight gain include decreased metabolism, improved taste and smell, and increased eating as a reward or to satisfy the hand-to-mouth habit.

It is important to be proactive with a patient that is concerned about weight gain or relapsed in the past due to weight gain. Patients need to be educated that it is likely that they will gain weight when they stop smoking, but this weight gain is a return to the weight they would have been had they never smoked. The health concern of gaining weight is negligible compared to continuing to smoke. A patient would have to gain 75 pounds before the risk of stopping smoking outweighs that of continuing to smoke.[42] Patients need to be counseled that stopping smoking is their primary concern. Starting a new exercise regimen or strict diet in addition may be too many habit and lifestyle changes at once and cause failure. However, clinical trials have shown that a diet and exercise program along with stopping smoking in patients concerned about weight gain may not be detrimental.[43,44]

Advise the patient to avoid substituting food for smoking cigarettes or rewarding the quit attempt with food. Counsel the patient to be smart about their food choices. Preparing healthy snacks such as carrot sticks, celery, broccoli spears, watermelon, and strawberries ahead of time helps the patient reach for these low-calorie snacks when cravings hit. Instead of eating, drinking a lot of water, keeping the hands busy, and staying active may alleviate unwanted pounds.

If weight gain is a concern that may prohibit the patient from stopping smoking, medications such as bupropion SR or nicotine gum should be considered. Studies using these medications have shown that patients maintain or lose weight while using the nicotine gum, bupropion SR, or the combination of bupropion SR and nicotine replacement therapy. However, this effect lasts only while the medications are being taken. After the medications are stopped, patients may then gain weight if they do not receive counseling on a healthy diet and exercise.

Moderate exercise may be beneficial to help with the decreased metabolic rate after stopping smoking and may also help relieve stress, which is often cited as a trigger. Preparing the stressed smoker with relaxation techniques and possible exercises can help avoid relapse during stressful situations. The pharmacist can suggest going for a walk during a lunch break or after meals, performing light weight lifting twice a week to relieve tension, practicing deep breathing to help in stressful situations, and listening to relaxing music. Guided imagery is another useful relaxation technique. This exercise involves taking a break at some point in the day and finding a quiet, relaxing place to sit. The patients then close their eyes and imagine themselves in a serene setting such as walking through a field of flowers or on the beach looking at a sunset. This exercise can be done alone, but also may be guided by another person. It takes some practice to become proficient, but it can be a very effective tool. To also help prevent relapse, the pharmacist should educate the patient that nicotine withdrawal can cause irritability and tension and should ensure that the patient has proper medication and support to help relieve these withdrawal symptoms.

Establishing Smoking Cessation Services

Smoking cessation services are usually very welcomed by patients and other health care providers. Receiving training to become a smoking cessation facilitator is beneficial in order to become skilled at helping smokers with behavioral modifications such as stress management and trigger planning. Training can also help with providing group education and marketing the service.

There are many resources including training programs, guidelines, web sites, and brochures available to initiate a smoking cessation service. The internet has a wealth of information for both the pharmacist and patient. Many patients enjoy the convenience of smoking cessation programs offered online. These programs should be supplemented with medication counseling and smoking cessation advice. Tables 131-12 and 131-13 provide details on available pharmacist and patient resources.

Marketing smoking cessation services is important. Marketing should include notifying local physician offices, dentists, and organizations such as the American Lung Association and American Cancer Society. Several days have been identified to help patients stop smoking including the "Great American Smoke-Out" and "World No Tobacco Day" that are ideal days to promote smoking cessation services and products. Posters for the "Great American Smoke-Out" and other special days are often provided by the sponsoring organizations free of charge. In outpatient settings, flyers detailing the smoking cessation program can be distributed with prescriptions. If the site of practice is hospital-based, consultations to provide smoking cessation counseling prior to discharge are very beneficial and are a highly needed service. Marketing this service to cardiovascular and pulmonary units would likely generate many consultations.

Table 131-12. Pharmacist's Resources for Establishing a Smoking Cessation Service

Treating Tobacco Use and Dependence. Clinical Practice Guideline.	www.surgeongeneral.gov	This thorough resource is a necessity for learning about effective behavioral and pharmacologic treatments.
Mayo Clinic	www.mayoclinic.org	Four-day nicotine dependence counselor training and program development seminar. CE for pharmacists is not offered.
American Lung Association	www2.lungusa.org/tobacco 1-800-LUNG-USA	Become a facilitator for the Freedom from Smoking program by calling a local ALA office. Sign on to the Freedom from Smoking online program and learn more about relaxation exercises and helpful suggestions to offer your patients. There is usually a fee to be trained as a facilitator and to purchase smoking cessation packets for the groups. After completing the training, a fee for providing Freedom from Smoking groups may be charged to participants.
Pamphlets and Brochures	American Cancer Society www.cancer.org 1-800-ACS-2345	Pamphlets and brochures are available on quitting smoking and smoking and pregnancy. Information about dip and a Spanish smoker's guide are available.
	Centers for Disease Control and Prevention www.cdc.gov/tobacco/	Pamphlets, fact sheets, advocacy groups, designated smoking cessation days, and statistics on smoking are available.

Offering educational books, brochures, or quit smoking paraphernalia (ie, water bottles, mints, car fresheners) and demonstrating smoking cessation medications (ie, nicotine inhaler) may make the program more attractive or marketable. Monitoring carbon monoxide, blood pressure, weight, and medication interactions may also add to the smoking cessation counseling.

Smoking cessation services are both rewarding and challenging. Waning commitment from patients highly addicted to nicotine, as well as lack of insurance coverage for medications, are barriers to this type of service. It is very rewarding helping a patient become smoke-free for good. Patients often do not realize how addicted to cigarettes they are until they quit. Reimbursement for smoking cessation is slowly gaining acceptance.

Table 131-13. Smoking Cessation Patient Resources

Special Days	New Year's Day	January 1st	Many smokers every year attempt to start the year without smoking.
	Tobacco Free Awareness Week	January 19th-25th	Encourages smokers who quit January 1st to continue to be successful. Also educates the public about the dangers of secondhand smoke and advocates smoke-free environments.
	Kick Butts Day	April 2nd	This day is for school children to stand up against tobacco.
	World No Tobacco Day	May 31st www.wntd.com	Global event to reduce tobacco dependence in individuals and to inform the public about the negative impact of tobacco use.
	Great American Smoke-Out	Third Thursday in November	Smokers are encouraged to throw away their cigarettes and not smoke for 24 hours.
Resources for Patients	Internet	www.Quitnet.com	This site offers an active chat room, expert counselors, quit plans, and information in Spanish.
		www.ffsonline.org American Lung Association	This site contains 7 modules including very nice worksheets on weight gain, relaxation exercises, and medications.
		www.smokeclinic.com	This site offers an individualized profile and 10 sessions to help a smoker quit for good. The smoke clinic contains a resource section for health care providers and the smoker. There is a $49.90 fee for using the program.
		www.smokefree.gov National Cancer Institute	Concise web site for steps to stopping smoking and instant messaging service where smokers can receive advice on stopping smoking.

Public Aid reimburses for all smoking cessation medications. Some insurers cover medications and group or individual meetings if the service is offered by an approved provider. This usually requires contacting the insurance company and submitting a description of the smoking cessation service to be provided. Requiring patients to pay for smoking cessation services enhances their commitment to quit smoking. However, many patients will provide the excuse that they cannot afford smoking cessation medications or services, yet they continue to pay $5 per pack of cigarettes.

Persistence with smoking cessation efforts from health care providers, with pharmacists being the most accessible, will lead to a more educated population willing to quit smoking.

ALCOHOL DEPENDENCE

Pharmacists in both retail and hospital settings face great challenges in dealing with patients who abuse alcohol. Since alcohol use is socially accepted throughout our society, patients tend to downplay warnings about the effects of alcohol consumption despite the potential adverse health consequences. Identifying patients who are dependent on alcohol is important because of the health effects and the potential for drug-alcohol interactions with over-the-counter (OTC) and prescription medications. Adverse consequences of drinking are not limited to alcoholics; even occasional drinkers can put themselves at risk if they consume alcohol in combination with other psychoactive or sedating agents. Disulfiram-like reactions can occur in select populations with even the slightest ingestion of alcohol. It is the role of the pharmacist to understand the mechanisms by which medications and alcohol interact and to provide appropriate interventions and counseling about risky drug-alcohol interactions when necessary.

The first step in dealing with the patient that consumes alcohol is to assess their drinking habits. Asking questions about alcohol use may elicit anger and suspicion in some patients, while others will be very honest and straightforward about their use. A pharmacist should be non-accusatory and assess each patient with caution and empathy. For example, questions about alcohol use posed to a lifelong non-drinker can be seen as rude and offensive. Alcoholics tend to underestimate how much they really drink. For example, a person who claims to consume six drinks a day may, in fact, consume as many as twelve drinks a day. Sometimes, a person with a heavy drinking problem will welcome questions related to their alcohol use. Embarrassed to seek assistance on their own, they may be looking for an avenue of help. As with any brief intervention, pharmacists should reinforce the importance of refraining from alcohol use during each encounter with the patient.

One quick method to assess alcohol abuse is the CAGE questionnaire. Physicians, nurses, or pharmacists can administer this brief intervention during any patient encounter. Table 131-14 lists the CAGE questions.[45] Item responses on the CAGE questionnaire are scored 0 or 1, with a higher score an indication of an alcohol problem. A total score of 2 or greater is considered clinically significant. The CAGE questions can be used in the clinical setting using informal phrasing. It has been demonstrated that they are most effective when used as part of a general health history and should not be preceded by questions about how much or how frequently the patient ingests alcohol.

Table 131-14. CAGE Questions

Cut down—Have you ever felt you should **c**ut down on your drinking?
Annoyed—Have people **a**nnoyed you by criticizing your drinking?
Guilty - Have you ever felt bad or **g**uilty about your drinking?
Eye opener—Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (**e**ye opener)?

From Ewing JA. *JAMA* 1984; 252:1905. Copyright © 1984, *American Medical Association*. All rights reserved.

Table 131-15. Definition of a Standard Drink

	VOLUME (OUNCES)	ALCOHOL CONTENT (%)
Beer	12	4.5
Wine	5	12.9
Spirits	1.5	41.1

What is a Drink?

Table 131-15 shows the accepted beverage size and alcohol content for beer, wine, and distilled spirits.[46] This quantification of a standard drink should only serve as a general guide. The amount of alcohol consumed is difficult to quantify due to lack of standard measurements for a drink. The size of a drink depends on the type of alcohol consumed and the means in which it is delivered. For beer, wine coolers, and similar bottled and canned beverages, the drink size is consistent due to packaging.[46] For wine and distilled spirits, the size of the drink is dependent upon the person pouring the beverage. A drink consumed in the home may differ in size to one served at a bar or restaurant.

The alcohol content also varies within beverage classes. The standard alcohol content for the majority of beers consumed in the United States is 4.5%. However, some states have laws mandating lower alcohol levels. Light beer may have as low as 3.0% alcohol, whereas the microbrewery and specialty beers have an alcohol content greater than 9.0%.[46] Similar variations in alcohol content occur in the wine and distilled spirits categories. Distilled spirits have the largest variation, ranging from 30% to 94% alcohol by volume.

Alcohol Metabolism

Alcohol is a very small molecule and can be found almost everywhere within bodily fluids once it is consumed. Alcohol easily dissolves into water and does not concentrate in any one area within the body. Alcohol does not dissolve into fat tissues. Since females generally have a greater ratio of fat to body water than males, blood alcohol concentrations (BACs) tend to be higher when women drink equal amounts of alcohol compared to men. Every state in the United States has set legal limits for safe BACs for the operation of a non-commercial motor vehicle. Currently, BACs range from 0.08% to 0.10%. Although these standards define the legal limits, impaired driving can occur at much lower levels.[47]

Alcohol and Medications

Adverse reactions from alcohol can occur whether or not a person is a heavy drinker. Many OTC cough, cold, and oral hygiene products contain alcohol. Although the amount of alcohol in these products is usually less than 10%, certain populations may be very sensitive to these levels. A genetic variation in alcohol metabolism occurs primarily in people of Asian descent, although it occurs rarely in Caucasians as well. Consumption of even small amounts of alcohol in this population causes an unpleasant flushing reaction that includes hot flashes, facial flushing, nausea, and vomiting. This reaction occurs due to an inability of this subpopulation to completely metabolize acetaldehyde, a byproduct of alcohol metabolism in the liver. Thus, pharmacists should have a heightened awareness of this reaction and counsel patients taking these OTC products.

Several medications can produce a "disulfiram-like" reaction. This reaction blocks the oxidative metabolism of acetaldehyde causing acetaldehyde accumulation. People who consume alcohol with these medications or disulfiram will experience nausea and flushing from the acetaldehyde accumulation.[10] When alcohol is consumed in combination with disulfiram, the reaction

may be so unpleasant that it prevents future episodes of alcohol ingestion in most patients. Thus, disulfiram is a medication used as aversive therapy in chronic drinkers**.** A list of common prescription medications that can precipitate this reaction are listed in Table 131-16. In patients with chronic medical conditions, this reaction can be serious, resulting in the dilation of blood vessels, a drop in blood pressure, and an increase in heart rate. A warning label should be placed on all prescriptions that have the potential to cause this "disulfiram-like" reaction.

Alcohol produces a sedative effect in the central nervous system (CNS). A misperception of many social drinkers is that alcohol can boost confidence and self-esteem. This brief feeling of confidence is a result of alcohol decreasing (depressing) inhibitions. As a person continues to ingest alcohol, they will experience impaired judgment, slowed reflexes, and fatigue. When alcohol is taken in combination with a sedating medication (prescription or OTC), the CNS depressive effect is synergistic, meaning that the combination of the two produces a greater amount of sedation than each one combined (ie, 1 + 1 = 3). Labels on OTC medications generally have warnings about drinking alcohol due to this increased risk of sedation. Pharmacists should counsel patients not to combine alcohol with prescription or OTC products, especially if they are driving or operating heavy machinery.

Alcoholism as a Disease

Table 131-2 lists the DSM-IV-TR criteria for alcohol dependence.[1] Signs of alcohol dependence manifest both physiologically and socially. A person abusing alcohol will often develop tolerance, requiring larger amounts of intake over a long period of time. Withdrawal often occurs following a period of abstinence and drinking tends to happen more often out of fear of withdrawal. The patient recognizes that he/she should cut down on drinking, but individual efforts to control drinking often fail. The alcohol user will experience ever-increasing periods of time spent on drinking activities, while other important activities will fall by the wayside. Alcoholism affects all parts of a person's life, both at home and at their place of employment. Continued use can result in the loss of loved ones and unemployment.

Alcohol and drug use should be recognized and treated as a medical disease. Medically, alcoholism is a chronic, relapsing disease with a biologic component, a genetic component, and a social component. Unfortunately, the stigma associated with substance abuse and the professionals who treat it serve as a barrier to providing patients much needed therapy. This stigma results in health care providers failing to properly recognize clinical clues or completely ignoring substance use altogether.[48]

Table 131-16. Medications That Cause Disulfiram-Like Reactions

TYPE OF MEDICATION	GENERIC NAME	BRAND NAME
Antibiotics	Cefoperazone	Cefobid
	Cefotetan	Cefotan
	Chloramphenicol	Various
	Griseofulvin	Fulvicin, Grifulvin, Grisactin
	Isoniazid	Nydrazid, Rifamate, Rifater
	Metronidazole	Flagyl
	Nitrofurantoin	Furadantin, Macrodantin
	Sulfamethoxazole	Bactrim, Septra
	Sulfisoxazole	Pediazole, Various
Cardiovascular Medications (Nitrates)	Isosorbide dinitrate	Dilatrate, Isordil, Sorbitrate
	Isosorbide mononitrate	Ismo, Imdur
	Nitroglycerin	Nitro-Bid, Nitrostat
Diabetes Medications (Sulfonylureas)	Chlorpropamide	Diabinese
	Glyburide	DiaBeta, Glynase, Micronase, Various
	Tolazamide	Tolinase, Various
	Tolbutamide	Orinase, Various

From Weathermon R, Crabb DW. *Alcohol Research & Health* 1999; 23:40.

Pharmacotherapy of Alcoholism

Currently, two FDA approved agents are available for the treatment of alcoholism: disulfiram and naltrexone. These agents are further categorized as aversive and anticraving medications.

AVERSIVE PHARMACOTHERAPY

Disulfiram (Antabuse) is the oldest pharmacologic agent used for the treatment of alcohol abuse. Used first in 1951, disulfiram is still dispensed as a deterrent against alcohol consumption. As discussed earlier, disulfiram blocks the oxidative metabolism of acetaldehyde, an intermediate by-product of alcohol, causing acetaldehyde accumulation. Thus, drinking alcohol within 12 hours of taking disulfiram produces a number of discomforting side effects. For example, within 5–15 minutes of consuming alcohol, disulfiram may cause facial flushing, followed by headache, tachycardia, hyperpnea (ie, deep, rapid breathing), and sweating. Severe nausea and vomiting can also occur and may lead to hypotension and dizziness. The intense reaction of alcohol and disulfiram is intended to serve as a deterrent to future consumption. Unfortunately, compliance with the medication limits the effectiveness and patients have learned to stop using disulfiram 1–2 days prior to a drinking episode. Experience demonstrates better abstinence rates when the patient is very motivated, or when spouses or treatment staff supervise disulfiram administration compared to when the patient self-administers the medication.

ANTICRAVING PHARMACOTHERAPY

NALTREXONE—Naltrexone is an opiate-receptor antagonist similar in structure to naloxone, which is used for opiate reversal. In contrast to disulfiram, concomitant use of naltrexone and alcohol does not cause detrimental side effects. In response to alcohol, endogenous opioids activate certain brain cells and induce some of the rewarding effects of alcohol. By blocking the actions of these endogenous opioids, naltrexone prevents alcohol from exerting these effects and may reduce the patient's desire to drink. However, naltrexone does not prevent the consumption of alcohol.[8] Initial studies of naltrexone demonstrated a reduction in the number of drinks, but it did not maintain a high level of abstinence. Newer clinical studies have not shown any benefit of naltrexone over placebo in delaying relapse to heavy drinking.[49]

ACAMPROSATE—Acamprosate has similar effects on alcohol craving as naltrexone, although it does not show any activity on opioid receptors.[50] Although the specific mechanism of action is unclear, acamprosate is thought to reduce cravings through binding to gaba-aminobutyric acid (GABA) receptors. Acamprosate also has serotonergic properties and activity as a noradrenergic antagonist.[51] In European trials, acamprosate demonstrated increased abstinence rates consistently when used as part of a multidisciplinary approach that included psychosocial or behavioral therapies. Subjects in one trial had a 43% abstinence rate after 48 weeks of acamprosate compared to a 21% abstinence rate in the control group.[52] The acamprosate treated subjects also stayed sober for a longer duration of time compared to the controls. In all trials, for those who did not quit drinking, acamprosate reduced the number of drinking days during the study period. Side effects for acamprosate were generally mild, with the most frequently reported side effect being

diarrhea. Acamprosate has not yet met efficacy criteria held by the FDA and is still undergoing clinical trials in efforts to gain approval in the United States.

Alcohol Counseling

More than one alcohol treatment method is often necessary to promote abstinence and prevent relapse. Patients with alcohol disorders have better outcomes when they also participate in an organized treatment program. Whether this treatment program is mandated or voluntary, the alcoholic has an opportunity to interact with peers and professionals who are skilled and trained to help them through the recovery process. For example, the combination of pharmacotherapy and group counseling or Alcoholics Anonymous (AA) has been found to be more successful than treating alcoholism with pharmacotherapy alone.[53] Pharmacists should be able to refer patients to appropriate alcohol treatment centers, counseling groups, or AA organizations within their community. Alcohol counseling and treatment can be conducted in an inpatient or outpatient setting depending on the severity of the disease. There is no 'quick-fix' for a person in recovery, and any person entering treatment should realize that battling the disease of alcoholism is usually a life-long process.

Alcoholics Anonymous

AA is one of the first successful peer-based support programs developed outside of a clinical setting. AA is defined as "A fellowship of men and women who share their experience, strength, and hope with each other that they may solve their common problem and help others recover from alcoholism." The only requirement for membership is a desire to stop drinking. Two former alcohol abusers founded the association in 1935 and developed the "twelve-step" model of recovery. Since then, the twelve steps of AA have been adopted and utilized by people with all types of addictions and behavior problems (eg, Narcotics Anonymous, Overeaters Anonymous, and Gamblers Anonymous). Support groups such as Al-anon and Alateen have been developed for the friends and families of those in recovery. AA is now worldwide, and persons in recovery can find a meeting in almost every community. Information about AA and methods to locate AA meetings can be found at www.alcoholics-anonymous.org. For more information about Al-Anon/Alateen, call 1-888-4-AL-ANON (weekdays, 8 am to 6 pm EST) or visit the website, www.al-anon.alateen.org.

OPIATE ADDICTION

Pharmacists may have greater difficulty in detecting and intervening with patients addicted to narcotics or other illicit street drugs. Signs and symptoms of opiate addiction are as variable as the number of prescription and street drugs that are abused. A person who is 'high' on a narcotic may exhibit erratic behavior, or they may appear completely normal while experiencing a level of euphoria. Street drugs are constantly changing, and clandestine chemists often invent new delivery methods to streamline the drug supply chain.

Like tobacco and alcohol use disorders, the Transtheoretical Model for Change can be applied to those persons who are attempting to recover from opioid and illicit substance use; however, these substances provide a greater reward in the CNS, and it can be much harder to discontinue use without other interventions. Opioid withdrawal is often prolonged and painful, often resulting in clinically significant distress or impairment in social, occupational, or other important areas of functioning (see Table 131-3). Due to new treatment methods and novel drug therapies, pharmacists have a greater role in the treatment of opiate addiction.

Pharmacologic Treatment

METHADONE—Methadone maintenance and treatment programs exist throughout the United States. Methadone substitution is the preferred method of opioid maintenance and withdrawal for heroin addiction because of its long half-life and less profound sedation. Pharmacists have traditionally been responsible for the mixing and dispensing of daily doses of this Schedule II drug. Methadone substitution is highly regulated and requires strict documentation of the quantities and doses dispensed. Administering the correct dose of methadone is critical. Methadone is given orally in the smallest amount (generally 30 mg/day) that will prevent severe withdrawal signs, but not necessarily all signs. Higher doses may be required depending on the history of previous heroine abuse and tolerance. Higher doses should be given when physical signs of withdrawal are observed. Doses of 25–45 mg can produce unconsciousness if the person has not developed tolerance. After the appropriate dose has been established, it should be progressively reduced by not more than 20% each day.

BUPRENORPHINE SUBLINGUAL—Buprenorphine hydrochloride (Subutex) and buprenorphine hydrochloride plus naloxone hydrochloride (Suboxone) treat opiate dependence by preventing symptoms of withdrawal from heroin and other opiates. Administered sublingually, buprenorphine hydrochloride is intended for use at the beginning of treatment for opioid addiction. Naloxone in combination with sublingual buprenorphine is used for the maintenance period of treating opioid addiction. This combination is used to prohibit the abuse of intravenous buprenorphine.[54]

Buprenorphine sublingual formulations are the first narcotic drugs available for the treatment of opiate dependence that can be prescribed in a physician's office under the Drug Addiction Treatment Act (DATA) of 2000. Under this new law, medications for the treatment of opiate dependence that are subject to less restrictive controls than those of Schedule II can be prescribed in a doctor's office by specially trained physicians. This change is expected to provide patients greater access to needed treatment.

Role of the Pharmacist in Drug Abuse

Many pharmacists currently serve as specialists in addiction clinics and rehabilitation centers. Pharmacists' combined knowledge of medication therapy and the complex effects of illicit drugs make them a key resource in tailoring a patient's plan for recovery. As members of their community, hospital and retail pharmacists should create a list of substance abuse treatment resources, including the responsible contact person for each program or provider, and be able to refer individuals with addiction disorders for proper evaluation and treatment.

Curriculum Development

Education is the key to overcoming the many biases associated with addiction disorders. In the areas of assessment, intervention, and referral, pharmacists have the ability to assist in the early identification of individuals with addiction disorders by using standard screening instruments. Given this position, pharmacists should develop the skills needed to assume a greater role in substance abuse prevention, education, and treatment in organized health care settings and in the community. To achieve this, the professional pharmacy curriculum needs to address addiction disorders as it would other disease states. Pharmacists should be able to approach and treat substance abuse and addiction as they would any other chronic disease, without personal bias and judgment of the patient. Pharmacy curricula and continuing education programs need to aid in the development of communication skills so that pharmacists become confident in discussing substance use disorders with their patients.

In the area of treatment, pharmacists should be able to provide recommendations for the appropriate pharmacotherapeutic choices in individuals recovering from addiction disorders. Pharmacists can provide invaluable assistance in the development of treatment options for drug detoxification protocols used by health care providers. Pharmacists are aware of the different types of treatment modalities, their expected outcomes, and their cost-effectiveness. Pharmacists can also play an integral role in instructing drug abuse counselors and other health care professionals working in drug treatment programs on the pharmacology and mechanisms of action of abused substances and of medications used to treat substance use disorders.[7]

Finally, pharmacy school curricula should also focus on preventing the pharmacy candidate from developing problems with substance use. Pharmacy schools should develop policies to deal with and care for the student addict that are confidential and focus on aiding the student through a defined recovery process. Students should feel comfortable with their advisors and know that they are not alone; there is a place to turn when drug and alcohol problems develop during the education process.

The Addicted Pharmacist

Although health professionals have a similar rate of substance use disorders as the general population, patterns of abuse differ in this population. Health professionals tend to abuse alcohol and prescription drugs more often than illegal "street" drugs due to the accessibility of these substances. Pharmacists usually have stressful jobs where long hours and a great deal of responsibility are the norm (eg, ensuring the proper delivery of pharmaceutical care to patients).[55] Another reason for this problem of substance abuse is the pharmacist's close access to drugs and relatively comfortable income that allows easy access to alcohol and prescription drugs (ie, the "keys to the candy store" mentality).

Pharmacist Recovery Networks (PRNs) have been established in 47 states and are usually affiliated with state or local pharmacy organizations. PRNs serve as advocacy groups for pharmacists in all phases of recovery and often manage peers when they are going through recovery. Often, pharmacists who have been through the recovery process join the PRNs to give back and aid others in the profession who may need assistance; thus, new clients can draw upon the experience of those who have gone before them. PRNs meet on a regular basis as support groups and they also monitor laboratory testing for illicit drug use of those who are in the recovery process.

Clients are referred to a PRN by three methods. In the first scenario, a pharmacist will be ordered to enter into the PRN process by the state board of pharmacy. For example, a pharmacist who has been caught diverting medications or has been arrested for driving while intoxicated may have his/her license suspended and will be assigned to the PRN to undergo a supervised period of sobriety. Legal action may also be taken against the pharmacist depending on the nature of his/her offense. In most states, board of pharmacy meetings are public record, and the pharmacist runs the risk of his/her reputation being permanently scarred. The PRN is available to help the recovering pharmacist through this stressful period.

The second way in which a pharmacist can enter a PRN is through self-referral. This may occur after continued encouragement from friends, family, or peers. The pharmacist may also experience a close call, such as a medication error as a result of his/her impaired judgment, which may scare the pharmacist into joining the PRN. All activities of the self-referred client are kept confidential by the PRN and not reported to the board of pharmacy or the employer.

The final method of entry into a PRN is through an intervention. An intervention is a planned meeting involving the friends and family of the addicted pharmacist. A member of the PRN or an addiction specialist will coordinate this event. Interventions are designed to aid in getting the person into a recovery program immediately. Participants involved must be prepared for emotional outbursts, excuses, and physical struggles. The addicted pharmacist is often in denial about his/her problem and may have grandiose thoughts about overcoming the problem if given just one more chance. During the intervention, people close to the pharmacist will share ways in which the addiction has hurt them mentally and physically, and deficits in work performance may also be highlighted. These inequities are shared with love and compassion, and participants are trained not to lash out in anger. Interventions should not be attempted without careful planning and support from a trained expert.

Early intervention and referral into a recovery program is the key to assisting the addicted pharmacist. Many companies and hospitals have employee assistance programs that are confidential and covered through the employee's insurance plan. Every pharmacist should be familiar with his/her company's policies and procedures related to alcohol and drug addiction. All information related to the addiction disorder should remain confidential, and the employee should feel comfortable making inquiries without fear of being punished.

CONCLUSION

Substance use disorders range from ubiquitous tobacco use to illegal use of street drugs. The Transtheoretical Model for Change is a useful tool to help patients overcome their disease. Group therapy and individual counseling methods help to augment pharmacotherapeutic treatment methods for overcoming these disorders. Resources are available for individuals with tobacco, alcohol, or drug addictions. Pharmacists can play a vital role in detecting, intervening, and providing resources to patients who need assistance with recovery efforts. Help is also available through state support networks for pharmacists in need of help to overcome substance use disorders.

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CHAPTER 132

Complementary and Alternative Medical Health Care

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Most people would agree that during the 20th century there have been more changes and improvements in medical science than in almost all of the preceding years of recorded history. The germ theory of the 20th century enabled the eradication of most microbial infections through the use of antibiotics and antiviral drugs. Numerous advances in medical technology have brought rapid and accurate analysis of specific invading organisms, the determination of the status of the blood and immunological systems, and the kinds and levels of drugs to administer to patients.

The new high-tech machines including x-rays, the CAT scan (*c*omputerized *a*xial *t*omography), MRI (*m*agnetic *r*esonance *i*maging), ultrasound imaging, the PET scan (*p*ositron *e*mission *t*omography) and others have allowed the location and diagnosis of most major cellular and body organ malfunctions, so that appropriate therapy can be undertaken. There have also been rapid advances in medicinal chemistry, natural product chemistry, computational chemistry, genomics, proteomics, etc. which have allowed for the synthesis of more compounds which might be useful as drugs and a better understanding of the mechanisms of action of these compounds.

The rapidly emerging field of biotechnology has spawned a bewildering array of bioengineered enzymes, peptides, hormones, and the like, which have allowed the replacement of normal body substances that maintain health.

Similarly, ways have been found to bolster and increase levels of newly recognized immunological factors that strengthen our infection defense mechanisms. Hence, it is easy to understand why modern conventional or orthodox medicine (allopathy) has generally held the upper hand of *efficacious* therapy in most advanced societies. However, in recent years it has appeared to have reached its limits in the minds of many individuals. More and more people expect perfect and complete results every time they seek medical help. When modern medicine fails, this attitude often leads to the search for help in alternative or complementary medicine, which appears to offer hope in a more holistic mode.

THE RISE OF ALTERNATIVE MEDICINE—The past few decades have generated a rapidly growing interest and popularity in alternative or complementary medicine because of its perceived, either potentially beneficial or pernicious effects on individual health or society.

Many reasons have been given for the resurgence of nontraditional or holistic medicine. Some have blamed a loss of faith in science (many people believe science has caused pollution, depletion of ozone, drug misuse, and iatrogenesis); others feel that confidence in orthodox medicine has eroded because it has failed to meet continuously rising medical expectations. Some feel that high-tech medicine does not care about or pay attention to the patient's belief system.

There is little doubt that rising costs of medical care have not helped promote efficient use of all the major advancements in medical technology or given better attention to the patient. Worldwide, it has been acknowledged that modern health care in the US has become an uncontrolled "monster" that is difficult, if not impossible, to contain. The political upheaval being caused by current health-care reforms in the US serves as an example.

Medical costs have risen over 15-fold in the past 40 years, and yet only a little over 40% of the people are served with adequate medical care. The current medical costs have been rising faster than inflation, and insurance costs have been unaffordable to many individuals and industries. Over 30 years ago, forecasters predicted that neither decreasing or increasing amounts of money spent on health would have any further effect on how long one could expect to live.

Some have said that we have reached a state of diminishing returns in modern medicine. The truth is that we have finally identified all the major disorders for which there is no easy cure. Many of these are the normal consequences of aging. There is little doubt that we will probably never fully conquer the old age–related disorders of bronchitis, arthritis, rheumatism, heart disease, back pain, high blood pressure, and many others. These degenerative chronic diseases of old age simply do not respond well, even to the most modern treatments.

Another problem that exists is the profit-driven motive to design drugs simply to capture a fraction of established markets. This has led to more and more "*me too*" drugs that do not really promise important therapeutic gains. Because of the great expense involved in developing totally new drugs with unique pharmacological properties, many drug companies have shied away from the efforts.

With all these problems in mind, it is easy to understand why complementary 2nd alternative medicine has been summoned to *fill the gap* not met by modern medicine.

Since the 1960s more and more Americans have turned to self-awareness and self-controlled medical treatments. *Wellness* as a concept and *prevention* as a mode of life have become standard thinking for a significant percentage of the American population. Our increased trade and relations with Asia and better communication with the traditional medical practices of Asia, Europe, Africa, and South America have opened new doors of treatment for all ills.

From the 1970s and 1980s up to 2000 and beyond numerous articles on alternative medicine have appeared in the literature. At least one author has given 92 alternative therapies ranging from acupressure (Shiatsu) to yoga. Over 50 books also have appeared under the titles of natural or nature's therapies.

Many of these alternative systems are complex and possess variable standards of qualification, training, and registration. Indeed, many within alternative medicine do not even agree on definitions for the numerous specialities let alone on standardization of treatment modalities. Generally, many of the theories

on which alternative therapies are based are not in accord with current medical concepts. Nevertheless, many of these therapies have become popular and are in demand by the American public and should be understood by all health practitioners.

In 1990, the US population made an estimated 425 million visits to providers of nonconventional therapies at a cost of some $10 billion from their own pockets. Some of these therapies now are covered by health insurance, but many are not.

In November 1998, the *Journal of the American Medical Association (JAMA)* had as its major theme, alternative medicine. Statistics of the last few years have shown that 4 out of 10 Americans used alternative medical therapies in 1997. Further, the total visits to alternative medical practitioners increased by close to 50% from that in 1990 and in fact exceeded the patient visits for all US primary-care physicians. Monetarily, this population paid approximately $21.2 billion for services (an increase of 45%) provided by alternative medical practitioners. An updated survey by David M1. Eisenberg, MD, of Beth Israel Deaconess Medical Center in Boston, and his cohorts in 1997 showed that between 1990 and 1997, the prevalence of complementary/alternative medicine (CAM) increased by 25%, with the total number of visits increasing by 47% from an estimated 427 million in 1990 to 629 million in 1997. As mentioned above, the expenses for these services were about $21.2 billion, with $12.2 billion out-of-pocket, and exceeded the out-of-pocket expenses for *all hospitalizations* in 1997. This survey covered 16 CAM therapies, which included relaxation techniques, herbal medicine, massage, chiropractic, spiritual healing by others, megavitamins, self-help, imagery, commercial diet, folk, lifestyle diet, energy healing, homeopathy, hypnosis, biofeedback, and acupuncture.

Both the 1990 and 1997 surveys found that CAM was used most commonly for chronic conditions, which included back and neck problems, arthritis, headaches, and anxiety. An increase from 33.8% in 1990 to 42.1% in 1997 was seen in the use of at least 1 of the 16 CAM therapies. The largest increases were in the areas of use of herbal medicine, massage, megavitamins, self-help groups, folk remedies, energy healing, and homeopathy. Even though these data show increased use of CAM across the board, the level of patient disclosure of this to their physicians remained low at less than 40% in 1990 and 1997. Obviously, all health practitioners are concerned because at least 15 million Americans in 1997 took prescribed medications and herbal remedies concurrently. Since at least one in five patients who take prescription drugs also may take herbs, high-dose vitamins, and supplements, etc, investigators are concerned that millions of adults may be at risk for potential unintended herb or vitamin/drug interactions. They caution that the CAM market is continuing to grow, and that trend needs continuous monitoring based on scientific inquiry, clinical judgment, regulatory authority, and shared decision-making. They advise that the *don't ask* and *don't tell* approach to patient/physician communication must be discarded.

Further, interesting statistics from this study revealed that CAM was significantly more common among women (48.9%) than men (37.8) and less common among African-Americans (33.1%) than other racial groups (44.5%). Persons in the age range of 35 to 49 years reported higher rates of use (50.1%) than persons either older (39.1%) or younger (41.8%). CAM usage was higher among college-educated persons (50.6%) than persons with no college education (36.4%), and more common among those with annual incomes above $50,000 (48.1%) than those with lower incomes (42.6%). CAM usage was higher in the Western US (50.1%) than elsewhere in the US (42.1%). Surprisingly, the total out-of-pocket expenditures for CAM in 1997 (including professional service, herbals, vitamin diet products, books, and classes), were estimated conservatively to be about $27 billion. These studies also showed that 42% of all CAM use was attributable to the treatment of existing illness and/or health maintenance.

There is little doubt that all this concern led to Congress crafting legislation and establishing the National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH) in 1998. Congress empowered NCCAM to conduct basic and clinical research, train researchers and educate and communicate their findings to health professionals and the public, NCCAM leaders have stressed the importance at the dawn of the 21st century, of clarifying the lines between holism and reductionism. There is a strong desire to bring CAM into "integritive medicine" where the best of both philosophies are brought to bear in the medicine of the future. A few examples include studies into how accupuncture and meditation work and what lies behind the placebo effect. There is also the expectation of clarifying the basis for the effectiveness of selected herbal and nutritional supplements so that standardized preparations can be used with confidence for treating certain ailments.

During the latter part of the last decade (ca.1995–2004) there have been numerous programs and training courses on CAM in almost every medical, pharmacy, and nursing school in the US. While much relates to popular patient "pressure" for these treatments much also has related to their willingness to pay and to the increasing number of US insurance companies and managed-care organizations which also are willing to financially support unorthodox treatments.

In order to fully appreciate how quickly CAM has grown in the last decade, it is necessary to review the start with the Office of Alternative Medicine (OAM) in October of 1991 which led ultimately to NCCAM in 1998 and its continued growth up to 2004. Much of the history is covered in NCCAM's, Five Year Strategic Plan, 2001–2005, entitled, "Expanding Horizons of Healthcare." (Obtainable at their Web site: nccam.nih.gov). It is divided into 4 parts. Part I, The Case for Action, which covers advances in medical science in the 20th century, coupled with improvements, The Appeal of Nontraditional Approaches described Alternative Medical Systems, Mind-Body Interventions, Biologically based therapies, Energy therapies, CAM yesterday; Mainstream Healthcare Today, Resolving the Issue Responding to Public Demand.

Part II covers Future Directions including NCCAM's support of a broad portfolio of research, the clinical imperative. Contained in this part as well is, basic science research, NIH areas of emphasis, as well as collaboration and training, information and dissemination and integration topics.

Part III covers specifically NCCAM's Strategic Plan 2001–2005 which includes the confidence of Congress in authorizing NCCAM, their mission, their vision, the stakeholders, strategic areas, and specific goals. These goals include, investing in Research, training CAM investigators, expanding outreach programs, and facilitating the integration and the practice of responsible stewardship.

Part IV consists of several appendices consisting of major domains of CAM, important events in NCCAM history, a bio-

Table 132-1. Reasons for Popularity of Alternative/Complementary Medicine

Perceived and real limitations of allopathy.
Love (when it works) and hate (when it fails) relationships with *high-tech* medicine.
Lack of tender loving care. People complain about being seen as *problems* or interesting cases to solve rather than real persons.
Complaints of endless tests with ambiguous meanings.
Desire to be a partner in healing one's self.
Unhappy about being sent to various specialists.
Desire to have one physician who can treat whole person and not just a body part.
Desire to have a physician who listens, does not dictate therapies, and makes one a partner in recovery.
Desire to see the practitioner as a trusted friend and not an authority figure.
Desire to be empowered or given authority or trust over the manner of being healed and self-healing capabilities heeded.

graphical sketch of the director of NCCAM, the research and research training portfolio of NCCAM members, NCCAM outreach activities, evidence-based reviews, and the NCCAM Cancer Advisory Panel for CAM.

NCCAM also provides several publications on general information, consumer advisories, NCCAM fact sheets, cancer fact sheets, dietary supplements fact sheets, booklets and reports, and a newsletter.

DEFINITIONS—Table 132-1 provides a summary of reasons cited for why CAM has become popular in recent times. Table 132-2 provides criticisms and comments about CAM. Some organizations and health professionals have been against NCCAM since its inception. Sampon has in fact, published on the quackwatch web site a four page article on why NCCAM should be defunded (http://www.quackwatch.org/0.1quackeryrelatedtopics/nccam.html). He cites articles on the politics of CAM and gives his opinion on the waste of research dollars and the lack of proof of many CAM therapies. The Appendix provides a list of terms used in CAM as well as definitions for the numerous specialities. As with all listings of this sort there will be disagreements about reasons or definitions. However, these reasons and definitions should establish an understanding of the complex nature of the popularity and practice of complementary/alternative medical care.

The following practices in CAM are among the most popular in the US today. An attempt has been made to list and define all of these with minimal comments or judgments on efficacy, since there may be few hard data available. Most medical practitioners are aware that one out of three drugs or managements of disease may be successful regardless of true or known efficacy. It is with this thought that all practitioners should keep their minds open about all modalities of health care, as only time and science ultimately will show what is effective and what is not, in medicine. Studies & surveys on CAM in the U.S. reveal that 36% of adults are using some form of integrative medicine. If one includes megavitamin therapy and prayer specifically for health purposes, then the percentage of CAM users rises to 62%. Further, the surveys by NCCAM show that certain groups are more likely to use CAM and this includes more women than men, people of higher educational levels, people hospitalized in the past year, and former smokers. Generally, most practitioners have been in agreement that conventional medicine is best for the management of acute care.

Table 132-2. Comments and Criticisms about Complementary/Alternative Medicine

Many conventional practitioners and medical scientists believe these to be a modern form of quackery.
Some of the successes reported are *placebo* effects.
Most ailments treated successfully are self-limiting. Self-limiting disorders predominate in these areas of practice.
Many of the approaches lack scientific proof.
Relatively few studies are clinical, double-blind investigations.
Most references, books, and papers are not truly scientific publications, and many reports are anecdotal.

No attempt is made here to negate the necessity to handle emergencies in a hospital setting where all of the high-tech methods can usually solve severe traumatic medical problems. Conversely, many agree that numerous long-term health problems (aging, anxiety, arthritis, backaches, chronic pain, elevated blood pressure, headaches, ulcers, etc) often lend themselves to various complementary/alternative practices. Certainly, many of these can be treated less expensively and less invasively than with allopathy. The major caveat, of course, is that of providing care without causing harm or delay when allopathy clearly can do something that is efficacious. The ultimate choice must be made jointly by the patient and the practitioner, keeping in mind the limitations, advantages, and disadvantages of each medical practice.

Finally, it should be kept in mind that the preventative approach is of paramount importance in health. This is a major change in philosophy for the 21st century. More and more people have opted for the obvious and are protecting their future health with good nutrition, exercise, stress reduction, and cessation of smoking. Much of complementary and alternative medicine has moved in this direction or has practiced it for many years. Medical foods or *nutraceuticals* or functional foods also have been stressed recently and Tables 132-3 and 132-4 provide samples of foods and their contained active principles that may be preventative and curative for many medical problems, from appendicitis to ulcers.

For lack of a better place to cover an unusual "nutritional" or "food" product, it will be instructive to briefly mention shark cartilage because of its widespread continued promotion as a purported "cancer cure." In 1995 the annual world market for this and related products exceeded $30 million, although it has di-

Table 132-3. Examples of Foods with Purported Medical Properties

FOOD	CONSTITUENTS	PURPORTED MEDICAL PROPERTIES
Apple	Pectin, caffeic acid	Lowers cholesterol, blood pressure. Juice has antimicrobial, antidiarrheal properties. Possible protectant against cancer.
Banana and plantain	Fiber in unripe plantain, pectin	Prevents and heals ulcers, helps lower blood -cholesterol. Stimulates proliferation of cells in stomach lining and release of protective mucus.
Broccoli	Indoles, glucosinolates, dithiolthiones, carotenoids	Lowers risk of cancer.
Cabbage	Chlorophyll, dithiolthiones, flavonoids, indoles, isothiocyanates, phenolic caffeic & ferulic acids, vitamins E and C "growth factor" mucin-like substances	Lowers risk of colonic cancer, juice helps prevent and heal ulcers, stimulates immune system, kills microbes, is classed as desmutagen (cancer antagonist).
Chili pepper	Capsaicin, vitamin C	Increases mucous secretion in lung, acts as expectorant, alleviates chronic bronchitis and emphysema, decongestant, diminishes clot formation (fibrinolytic), topically effective analgesic used in cluster headaches, induces secretion of endorphin.
Spices, eg, cumin, cinnamon, ginger, mustard	Various active principles	Reduces cholesterol levels in animals.
Fenugreek	Various active principles, fiber	Helps control sugar levels in diabetics.

Table 132-4. Examples of Phytochemicals in Foods with Purported Medical Properties

PHYTOCHEMICALS	BOTANICAL SOURCE	PURPORTED PROPERTIES
Allicin, ajoene	Garlic	Stimulates biochemical pathways involving glutathione, which detoxifies foreign materials; intercepts activated carcinogensbefore they attach to DNA; inhibits prostaglandin E_2, which is linked to tumor promotion; has antimicrobial properties.
Flavonoids, phenolics, carotenoids, saponins, and triterpenoids	Citrus fruits	Enhance body's detoxification system; have antioxidant effects; regulate enzymes produced by cancer cells. Phenolics stimulate synthesis of glutathione, the body's detoxifier. Carotenoids quench damaging oxygen free radicals. Saponins and triterpenoids may block cell receptors for estrogen, which may protect against breast cancer. Inhibits prostaglandin E_2, which is linked to tumor promotion.
α-Linoleic acid, phenolic lignans	Flaxseed	These fatty acids diminish cholesterol formation; lignans have antiestrogenic activity, which may lower breast cancer risk. Inhibit prostaglandin E_2, which is linked to tumor promotion.
Glycyrrhizic acid, other related triterpenoids phenolics	Licorice	Antibiotic properties, phenolics inhibit key enzymes overproduced by cancer cells. Inhibit prostaglandin E_2, which is linked to tumor promotion.
Isoflavones	Soybeans	Inhibit activity of tyrosine kinases that are overproduced when normal cells are transformed into cancer cells.
Indoles, betacarbolenes	Cabbage-family members	Favor estrogen deactivation and excretion which minimizes tumor activation pathway.
Phenolic acids	Umbelliferous vegetables, eg, parsley, celery	Possible antiulcer properties.

minished in recent years for growing proof of lack of efficacy. At least two glycoproteins (sphyrnostatin 1 and 2) have been isolated from the cartilage of the hammerhead shark with early claims that these had strong antiangiogenic activity inhibiting tumor neovascularization. It was believed that this might be useful in human cancer therapy. Unfortunately, because macromolecules like this are not absorbed intestinally, high blood levels are not reached. To date, no controlled clinical studies have been published showing consistent significant efficacy for human cancer treatment. Preliminary results in a US trial showed 50% of cancer patients who took 100 mg of dried cartilage powder daily reported improvements in quality of life, appetite and relief of pain. However, later a more well documented study with sixty patients (various advanced cancers) showed no complete or even partial responses. These authors concluded that shark cartilage was inactive in advanced stage cancer and had no beneficial action in improving quallity of life.

All medical practices are beginning to pay a lot more attention to good and preventative aspects of nutrition as the US population ages and extends life well into the 70- to 90-year age potential.

Finally, it should be noted that money is now being spent in the academic and federal sectors to determine the veracity of alternative medicine as discussed earlier.

Temple University in Philadelphia developed a Center for Frontier Sciences for studying the mind/body connection as well as how electromagnetic fields may influence health. They also are looking into the potential of *soft* therapies in medicine, such as electroacupuncture and therapeutic touch. Almost all major universities have followed suit.

OAM AND NCCAM—Again in the latter part of 1992, in response to increasing public pressure, Congress established the Office of Alternative Medicine (OAM) within the Office of the Director of the National Institutes of Health (NIH) to facilitate the fair scientific evaluation of CAM and to establish an information clearinghouse. The OAM was designed primarily to encourage study and research in the many promising CAM approaches to determine which are potentially effective, safe, and economical as health-care practices. However with the passage of the fiscal year 1999 Omnibus appropriations bill, and the subsequent signing by the President on October 21, 1998, Congress established the National Center for Complementary and Alternative Medicine (NCCAM). With stronger support and money the center has been devoted to the conduct and support of basic and applied research and training, and has disseminated information on CAM to health practitioners and the public. It also has been set up to carry out related programs that one hopes will continue to advance the investigation and application of CAM methods that prove to be efficacious.

This Act has the legislative reference bill number S 2440, section 601, and is summarized in the the web site http://altmed.od.nih.gov/nccam/. These references provide the details on the OAM change to NCCAM, their address, toll-free phone number and fax number, history, purpose, mission, program advisory council charter, fiscal year budget, program areas, extramural affairs (grants), 10 specialty research centers, research database evaluation program, NCAAM clearinghouse and media relations, international and professional liaison program, research development and investigation program, intramural research training program, and relations with other government agencies (eg, Agency for Health Care Policy and Research, Department of Defense, Food and Drug Administration (FDA), Health Care Financing Administration Agency, and the Centers for Disease Control and Prevention). The NCAAM also holds regular meetings with the FDA to seek its help in reevaluating current rules and regulations that govern research on the use of new devices, acupuncture needles, herbs, and homeopathic remedies. NCAAM also continues to keep in touch with most of the CAM organizations to provide them with new information regarding research support and development.

The Web site has a *What's New* section that provides a running update on new bills, grants, requests for applications, annual meetings, CAM citation index, and results of new research in CAM. Scientific exploration in CAM has become vigorous enough for Congress to raise the status of CAM from an *office* to a *national center*. It has given NCAAM the authority to fund its own research projects.

Certainly, the big jump in annual funding ($117,752,000 in FY 2004) will go a long way in helping prove its promises. With recent studies showing that at least two out of five Americans use an alternative therapy, it certainly behooves reductionist science to determine the real efficacy of holistic medicine.

THE DSHEA ACT OF 1994—The Dietary Supplement Health and Education Act of 1994 (DSHEA) was passed after substantial negotiations between members of the House and Senate and their staffs, including representatives from the dietary supplement industry. The Act is intended to enable consumers to make informed choices about nutrient supplements and subjects these products to the same general labeling requirements that apply to foods. Basically, the Act came about through enormous public pressure to maintain the *All-American* freedom of choice in self-nutrition and *medication*. The Act generated more calls, letters, and faxes of support than any previous bill.

For several decades the FDA regulated dietary supplements as foods, mainly to ensure that they were safe and wholesome and that labeling on them was true and not misleading. One focus to ensure safety was the FDA's regulation of the safety of all new ingredients, even those used in dietary supplements under the older 1958 Food Additive Amendments to the Federal Food, Drug, and Cosmetic Act (FD&C Act). With the passage of DSHEA, Congress amended the FD&C Act to add several newer provisions that apply directly to dietary supplements and their ingredients. Because of the new provisions, ingredients in dietary supplements are no longer subject to the premarket safety evaluations required of other new food ingredients or new uses of old food ingredients. Now they must meet the requirements of other safety provisions. The specific areas of coverage of the DSHEA include definition of dietary supplement, safety, literature, nutrition support statements, ingredient and nutrition information labeling, new dietary ingredients, good manufacturing practices (GMPs), Commission on Dietary Supplements; Office of Dietary Supplements; and effective date.

The DSHEA defines a dietary supplement as any product (besides tobacco) that contains a vitamin, mineral, herb, or amino acid that is intended as a supplement to the normal diet. No proof of safety is required for dietary supplements marketed prior to Oct 15, 1994, to remain on the market. They are considered safe unless they "present a significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling or, if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use." In contrast to over-the-counter (OTC) and ethical drugs for which manufacturers are required to prove safety and efficacy before marketing, the *grandfathered* dietary supplements are deemed safe unless proven unsafe by the FDA. So it is obvious that DSHEA regulates herbals (as well as other dietary supplements) more like foods than drugs. The Act does, however, grant the secretary of Health and Human Services emergency powers to withdraw a supplement from the market if it poses an imminent health hazard. This happened with ephedra in 2004.

Unique to the act is the labeling requirement that allows warnings and dosage recommendations as well as substantiated *structure or function* claims. Before this time, such labeling would cause the product to be *misbranded* and removed from the market. Now this labeling is allowed with specific limitations, *viz,* all claims must be accompanied by a conspicuous notice that they have not been evaluated by the FDA and in fact must state on the label "This product is not intended to diagnose, treat, cure or prevent any disease." The label must also contain the term *dietary supplement* and give each ingredient by name, quantity, total weight, and identity of any plant parts from which the botanical ingredient is derived.

All statements on the label must be truthful and not misleading. Any claim to conform to an official reference (eg, *United States Pharmacopeia*) must meet all the specifications or be deemed misbranded. The USP has begun to establish new monographs on dietary supplements. Also new is the ability to provide information representing a balanced view of the scientific information on the botanical along with its sale. This literature must be truthful, cannot promote a specific brand of the herbal, and must be displayed physically separate from the product. The burden of proof that the information is false or misleading lies with the FDA. Before this time, such literature was considered an extension of the label, and any implied clinical efficacy claims were the basis for judging the product *misbranded*. The law further states that these requirements "shall not apply to or restrict a retailer or wholesaler of dietary supplements in any way whatsoever in the sale of books or other publications as a part of the business of such retailer or wholesaler."

DSHEA further created a Commission of Dietary Supplement Labels to make recommendations for the regulation of all claims and statements, with forthcoming reports on a timely basis. In addition, DSHEA created the Office of Dietary Supplements within the NIH. This agency is entrusted with promoting the scientific study of the usefulness of dietary supplements. The head of this office is specified as the principal advisor on dietary supplements to the Secretary of Health and Human Services, the FDA Commissioner, and other federal officials. All health professionals should expect that both the FDA and the entire supplement industry will be active for many years to come in establishing new and continuously changing rules. In particular, pharmacists should keep abreast of all legal changes, to provide proper patient counseling and evaluate all health advertising claims that appear for herbals.

To completely cover all aspects of this Act would be difficult in this overview. However, the Act may be summarized as follows:

Definitions (eg, a dietary supplement may be a vitamin, mineral, herb or other botanical, an amino acid, a supplement that can increase total dietary intake, and a concentrate, metabolite, constituent, extract or combination of these ingredients).

Information on adulteration (eg, a product is unsafe if it presents a significant or unreasonable risk of illness or injury under the label's suggested conditions of use).

Statements on allowable claims (eg, claims a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such diseases in the US).

Health claims (eg, a statement for a dietary supplement may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases).

Labeling exemptions (eg, the Act adds a new paragraph to exempt from *labeling* a third-party publication used in connection with the sale of dietary supplements if it is not false or misleading and does not promote a particular brand).

Misbranding (eg, the Act is amended and deems a supplement misbranded unless it lists each ingredient, the quantity, and total quantity of ingredients in proprietary blends; unless it is identified as a *dietary supplement;* and if it comes from a plant and does not identify the part of the plant from which it is derived).

Adds new labeling requirements (eg, 1); the nutrient information shall first list those ingredients that are present in the product in a significant amount and for which a recommended daily requirement has been established (dietary ingredient not present in significant amounts do not have to be listed) and shall list any other ingredient present and identified as having no recommendation for daily consumption).

Data on good manufacturing practices (eg, authorizes the Secretary to issue regulations for GMPs for dietary supplements, including for expiration date labeling, but prohibits imposition of standards for which there is no current and generally available analytical methodology).

Establishes a Commission on Dietary Supplement Labeling (eg, establishes a seven-member Commission as an independent agency within the Executive Branch to conduct a study and issue a report making recommendations, within 2 years of enactment, to the White House and Congress on regulation of label claims for dietary supplements and legislation, if appropriate).

Provides regulations (eg, within 90 days of the issuance of the Commission's report, the Secretary shall publish in the *Federal Register* a notice of any recommendations made by the Commission for changes in regulations and shall include with such notice of proposal a rule making an opportunity for public comment).

Establishes an Office of Dietary Supplements (eg, to conduct and coordinate scientific research on the extent to which dietary supplements can limit or reduce various conditions, such as heart disease, cancer, birth defects, osteoporosis, etc, and collect and compile the results of such research).

Table 132-5. The Five Domains of Complementary and Alternative Medicine as Defined by NCCAM

1. Alternative Medical Systems, eg, homeopathic and naturapathic medicine, Oriental medicine, Ayurvedic medicine
2. Mind-body Interventions, eg, meditation, cognitive-behavioral therapy
3. Biologically Based Therapies, eg, dietary supplements, herbs
4. Manipulative and Body-Based Methods, eg, chiropathic, massage
5. Energy Therapies (2 types)
   5A. Biofield therapies, eg, Reiki, Therapeutic Touch, qi gong
   5B. Bioelectromagnetic-based therapies, eg, magnet therapies

The complete details of DSHEA may be obtained by writing to NCCAM or accessing various web sites, eg, http://vm. cfsan.da.gov/dms/dietsupp.html. Finally, in effect, the DSHEA has resulted in a deregulation of the supplement industry. Now, unlike food additives or drugs, supplements do not require FDA approval prior to marketing. It is the manufacturers alone who decide whether their products are effective and safe. If a problem arises, the burden of proof falls on the FDA to prove that the supplement poses an unreasonable risk and should be recalled from the market. As might be expected, the $4-billion-a year supplement industry will strongly oppose any stringent regulations. For example, there are proposals to create new regulatory categories for some supplements as *nutraceuticals*.

While generally understood to be foods with health-promoting qualities, they are not yet defined legally or scientifically. In perspective, supplements (pills, powders, or other typical medicinal dosage forms) really make up only a relatively small percentage of the $77 billion nutraceutical market. The largest percentage obviously relates to foods, snacks, and drinks that purport to satisfy the consumers' desire for health through foods. For example, complete liquid meals, originally intended for those too ill to eat regularly, are now marketed as nutritionally complete and convenient *instant* meals for persons with active lifestyles or too busy to prepare meals. Often these products contain all the protein, vitamins, and minerals (and other *healthful* ingredients) in easy-to-swallow form. Even ideal ingredients such as *energy inducers,* herbal phytochemicals, and antioxidants are added to foods for long-term healthful benefits. Consumers easily can find products such as orange juice with added calcium, or peanut butter fortified with all the essential vitamins and minerals.

DSHEA has allowed the food industry to market readily any food or ingredient currently being investigated in biochemical nutrition research. For the most part nutraceutical advocates are now urging the FDA to "lighten up" on its criteria on health claims so that manufacturers can make exclusive claims based on their own research even without being required to reveal their studies in public. There is already much disagreement on health claims, labeling matters, proof of efficacy, and safety regarding nutraceuticals. It will take several decades to resolve these issues as the battle between holistic approaches and reductionist science continues.

Of the numerous complementary/alternative procedures in existence, the most widely accepted are acupuncture, aromatherapy, bodywork, chiropractic, faith healing, herbalism, homeopathy, hypnosis, iridology, mind/body connection, naturopathy, and reflexology. Table 132-5 gives the five general categories of alternative medicine as defined by NCCAM.

ACUPUNCTURE

This has been a primary practice of the health-care system of China for at least 2500 years. The Chinese systematized acupuncture and were the first to include it in a medical book—*The Yellow Emperor's Classic of Internal Medicine* (written between 300 and 100 BCE). Acupuncture and Chinese medicine spread to Japan in the 6th century and to France in the 17th century. It got the attention of the American medical scene in 1972 when James Reston, a *New York Times* columnist who was covering President Nixon's visit to China, wrote about his appendectomy, which was performed with acupuncture instead of pharmaceutical anesthesia.

Most recently, the NIH issued a statement supporting the integration of acupuncture into Western medicine's therapeutic regimens for certain conditions. The 12-member panel of experts who weighed the evidence that supported these recommendations, concluded that there is *clear evidence* of acupuncture's efficacy for treating postoperative and chemotherapy nausea and vomiting, the nausea of pregnancy, and postoperative dental pain. For a number of other conditions, the panel concluded that acupuncture may be an effective adjunctive therapy. Specific conditions cited are addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, low-back pain, carpal tunnel syndrome, and asthma.

The NIH panel of experts also explored what was known about the biological effects of acupuncture. Both human and animal studies were found to demonstrate that acupuncture can cause multiple biological responses. Some examples of these responses include release of opioid peptides during acupuncture and reversal of acupuncture-induced analgesic effects with naloxone administration, activation of the hypothalamus and the pituitary gland function, neurotransmitter and neurohormonal modulation, changes in the regulation of blood flow, and immune function alterations.

Questions regarding specificity of some of these biological changes have arisen because *sham* acupuncture point stimulation was found also sometimes to elicit biological effects. This makes research problematic, especially because nonspecific effects like the quality of the relationship between the clinician and the patient, trust, and expectations also are thought to account for a substantial proportion of acupuncture's effectiveness.

The system of healing for acupuncture is based on the fundamental concepts of Oriental medicine, which are strongly influenced by philosophical and metaphysical world views of Taoism, Confucianism, and Buddhism. The principle concepts of *yin* and *yang* harmony (balance of opposites), and the five phases or elements (represented by nature's elements: fire, earth, metal, water, and wood each of which correspond further to a color, emotion, Yin/Yang organ, sense organ, taste, season, tissue, sound, etc.) and the five substances (Qi, Jing, Shen, Blood, and Body Fluids are used to describe imbalances. Diagnostic procedures include physical examination similar to that in Western medicine but also include examination of pulse patterns in both wrists, tongue appearance, and abdominal and acupoint palpation. Often the practitioner will use herbal medicine, recommend exercise such as Qigong or Tai-Chi, and prescribe diets as adjuncts to acupuncture.

The therapeutic goal of acupuncture is to regulate the *Qi,* or *energy flow,* in the body through activating points on meridian pathways. Each meridian pathway is associated with specific organ systems that can be regulated by the stimulation of points on the skin surface or below. In classical Chinese texts at least 365 points are described, with a possible total of over 2000. In practice, a typical number of points a practitioner has in his or her repertory is 150. The acupuncturist may use needles, either inserted or held on the point, or may apply cupping, moxibustion, massage *(T'ui-na-Chinese, Shiatsu-Japanese),* or laser light to the point. Cupping involves inducing a vacuum in a small glass cup and immediately applying it to the skin surface at a meridian point. *Moxibustion* is a process in which small cones of the herb *Artemisia vulgaris L* (mugwort = *MOXA*) are placed on the needle or acupuncture point and then burned to produce a penetrating heat (thence removed before strong pain). Electrical stimulation also can be applied to inserted needles or to a meridian point directly for therapeutic effects.

Acupuncture needles are very fine (diameter, 0.12 to 0.34 mm) and may elicit a slight prick when inserted but do not, and should not, hurt once they are in place. The number of needles used in a treatment (usually 5 to 15), depth of needle insertion (usually 0.1 to 0.4 inches), diameter of needle used, and length of time the needle is kept in place vary in relation to the condition being treated. These parameters also will vary depending on the style (Chinese, Japanese, French) of acupuncture used; for instance, Japanese acupuncturists use finer needles more superficially. Finally, intradermal needles are used sometimes to engage a meridian point for longer periods of time.

Acupuncture needles have been made of bronze, gold, silver, copper, tin, and bamboo. Today, most acupuncturists use sterile, single-use, stainless-steel needles and are trained in *clean needle technique* guidelines and methods. The investigational label for acupuncture needles was removed in March 1996, when the FDA placed needles under Class 2 regulations, to ensure that reasonable safety would be maintained. A systematic review of the safety of acupuncture by Ernst and White (*American Journal of Medicine*, 2001), found the most common adverse events were needle pain (1–45%), tiredness (2–41%) and bleeding (0.03–38%). Uncommon side effects included a feeling of faintness or syncope (0–0.3% and phnemothorax was rare, occuring twice in nearly a quarter of a million treatments. Consumers who insure that their practitioner has adequate training and who use sterile disposable needles are unlikely to suffer adverse consequences from acupuncture treatments. Possible complications due to needle mishandling include organ puncture, infectious disease transmission, spinal cord injury, contact dermatitis, hematoma, and pain.

At least 300 programs are described nationally that use acupuncture, often combined with supportive counseling. Approximately 10,000 practitioners provide acupuncture to Americans today, of whom over 30% are MD or DO physicians. Licensing of acupuncturists varies from state to state and is designated by LAc, RAc, or CAc titles. It is obvious that anyone who wishes to be treated by acupuncture should be sure that the practitioner has attended an accredited acupuncture program (≥2 years), is licensed or registered in the state, or has passed the National Certification Commission for Acupuncture and Oriental Medicine examination for acupuncture. The American Association of Oriental Medicine has published a referral list of practitioners.

While the AMA has not officially sanctioned acupuncture, over 2000 of the US acupuncturists are MDs. Most feel it is difficult to understand and to accept the invisible energy-path or meridians theory of effectiveness. Many still claim a *placebo effect,* but even this has not held up to scientific testing. Some say that the distraction of the practice explained its efficacy. Most current research seems to indicate that the acupuncture stimulates the release of endorphins, enkephalins, and the natural anti-inflammatory agent, cortisol.

AROMATHERAPY

The basis of this form of therapy is aroma and the biochemical effects derived from the essential volatile oils of plant flowers and fruits. These fragrant extracts, when inhaled, allow patients to relax or bring about relief of pain. They also may induce a mild stimulation.

In most people, it is acknowledged that smell is undoubtedly the most acute of the five senses (at least 10,000 times more than any of the others). These volatile plant essential oils are inhaled and activate receptors in the nasal cavity. These, in turn, induce nerve impulses that travel rapidly from this olfactory bulb to the brain. The olfactory tract is connected directly to the limbic system, which is the control center in the brain for memory, emotions, and sexual arousal.

It has long been known that pleasant odors can mask offensive ones and that this perhaps was the basis for the use of incense in closed places wherever nonbathers congregated. In a like manner, almost all societies sought quiet refuge in pleasant odors and surroundings against the *smelly* world. Thus, in answer to the question "does aroma heal?", one can say that it will ease certain physical maladies such as headaches or colds as well as calm individuals who suffer from emotional irritability and nervousness. Recent studies show a usefulness in depression. The efficacy of aromatherapy in clinical situations has been tested widely in Europe.

Almost everyone acknowledges the powerful nudge of *smell memory* whenever their favorite food, perhaps originally from mother's kitchen, is sensed. Similarly, nearly everyone is repulsed by the odor of anything burning, probably a remnant of primitive instincts alerting one against potential danger.

In recent years, numerous studies have shown the usefulness of inhaled volatile oils to relieve bronchitis and sinusitis (eg, pine, thyme, peppermint, or eucalyptus), as a first-aid measure (eg, lavender for burns or tea tree for infections), and as massage oils to relax tense muscles (eg, rosemary or sage). The use of wintergreen oil is another example of a topically applied oil with a characteristic odor and aspirin-like analgesic qualities (viz Methyl Salicylate).

Aromatherapy long has been known and used in France, where René Gattefosse, a French chemist, coined the word in 1937. His personal experience of being healed after burning his hand and then plunging it into lavender oil to effect a cure led to its use in World War I to combat injuries. Today, many hospitals use essential oils to help relax patients and cleanse the air. Some have used aromas to help reduce the incidence of crime in subways, to increase worker productivity, and to increase students' concentration. World-wide research is being conducted to explain more fully how aromatherapy works, perhaps through the psychoneuroimmunology system, to promote both physical and emotional healing.

Aromatherapy encompasses a wide spectrum of use for essential oils, ranging from environmental fragrancing to body-mind therapy to internal medicine. In France, it is taught in medical schools; the oils are prescribed by a physician, prepared by a pharmacist, and taken internally. In many cases, essential oils (rosemary, mint) are incorporated into wellness programs because they are easy and pleasant to use and often mask malodorous facilities (eg, incontinence-related ammoniacal odors). Aromatherapy holds that pleasant aromas help maintain bodily balance and harmony and promote mental and emotional pleasantness. Most critics from allopathic medicine note the general lack of critical research on efficacy and the many unscientific pronouncements of its advocates. Even holistic practitioners fault aromatherapy because it promotes the use of the volatile oil and not the whole plant.

Finally, it should be cautioned that only very low doses or amounts of volatile oils are used in aromatherapy. Because they do represent the distilled essences of many pounds of flower parts and because they may contain pungent mixtures of terpenes, aldehydes, ketones, and esters, they are potentially powerful chemicals with pharmacological and toxicological effects. These should never be taken orally in a concentrated form. Several flavorful oils (wintergreen, cinnamon, mints) are used in highly diluted forms in mouthwashes, sprays, and the like for their topical antibacterial properties and refreshing taste.

There has recently been published a review summarizing all the randomized controlled trials (RCTs) testing the clinical efficacy of aromatherapy. It was found in twelve clinical trials, that six had no independent replication, and that six related to the relaxing qualities of various aromatic oils used topically in gentle massage. Those investigations suggest that aromatherapy massage does have a mild and transient anxiolytic effect. The authors concluded that while the effects are minimal, they may be of benefit for common patients by enhancing feelings of wellness. There have in recent years been several new tests and articles relating to aromatherapy.

AYURVEDIC MEDICINE

This system of medicine has its roots deep in the Indian philosophy of Asia. It emphasizes the use of a person's physical and mental abilities to reach harmony with the environment. The therapy here is composed of reaching a balance between diet, daily routine, and daily activities. Ayurveda literally means the *knowledge* or *science of life*. Many practice yoga (system or exercises) and meditation as part of Ayurveda. It has been described as an active or assertive program of prevention and can include a wide variety of things, including rising early in the morning, listening to parental advice, displaying consistent daily routine, basing exercise and activities on body type, drinking herbal teas, and having regular bowel movements.

There are many practices associated with Ayurvedic medicine including shirodara (pouring or dripping specially warm and prepared oils [eg, sesame oil] on the forehead for relief of tension and to bring on mental harmony); pulse reading (feeling for wave patterns, or *doshas*), which provides information on body types; taking histories on preference habits and dreams; physical exams of the body's *dhatus,* or tissues, and *srotases,* or passageways (exits of cleansing and elimination); cupping (using cups with a vacuum applied to the back) to lower blood pressure, increase circulation, or relieve muscle pain; sitting in a steam-filled sweatbox to cleanse the body; *panchakarma* (procedures to cleanse the body of accumulated wastes) using herbalized steam, oil massage, nasal flushing, laxatives, and medicated enemas.

Overall, Ayurveda is not a licensed practice in the US, but many health practitioners in related areas (nutritionists, chiropractors) do practice some aspects of it. At least several hundred physicians have trained in the US at Ayurvedic institutes. Basically, Ayurveda protects and sustains the body and does no harm. In India, physicians trained in this area complete a 5 1/2–year program of study, including a hospital residency.

Because Ayurvedic medicine uses nonstandard methods of diagnosis and treatment, conventional Western physicians often find it unsettling. However, those who have been trained in its practices (often Asian ethnic groups) use it to complement their conventional practices. Some have focused their criticism against the Maharishi ayurvedic system because of its perceived self-serving nature and great popularity in the US. Both traditional ayurvedic and Maharishi Ayurvedic therapies are being evaluated clinically at several localities, and one hopes time will reveal the good and bad aspects of the practices.

In 1999, an Ayurvedic college, The Center for Natural Medicine and Prevention, Maharishi University of Management, College of Maharishi Vedic Medicine in Fairfield, IA was granted a NIH/NCCAM Research Center Award to study cardiovascular disease and aging in African Americans. Ayurvedic medicine has been reviewed by the Agency for Healthcare Research and Quality (AHRQ) found on the NCCAM Website's health information page. According to AHRQ's review, the most common conditions for which studies of Ayurvedic therapies have been published were: diabetes mellitus, liver/hepatitis, infectious diseases, hypercholesterolemia, central nervous system disorders, (dementia/depression) and cardiovascular diseases. Herbal therapy was the most common subject published and no studies were found that tested Ayurvedic medicine as a whole system, and almost no studies were found on any other Ayurvedic modalities. The review found evidence to suggest that the single herbs *Coccinia indica,* holy basil, fenugreek, and *Gymnema sylvestre* and the herbal formulas Ayeesh-82 and D-400 have a glucose-lowering effect and deserve further study. For several other herbs, (*C. tamala, Eugenia jambolana* and *Momordica charantia*) less extensive evidence was found.

CHIROPRACTIC

As a result of searching for a uniform method of curing illness, Daniel David Palmer (1845–1913) devised a theory called chiropractic. A Greek word meaning laying of the hands. He based his treatment mainly on the manipulation of the spinal vertebrae. He, along with his son B.J., developed this treatment technique and started the first school in the world to teach chiropractic in Davenport, IA. As his practice gained a foothold, he refined the original basic theory that disease is caused by vertebra pressing on the spinal nerves. These blockages were referred to as subluxations, and he felt that dispatching these quick thrusts or adjustments would restore normal function to muscles, organs, joints, and other tissues.

Chiropractor physicians or practitioners take a complete medical history, perform an examination, and may take x-rays to find problems elated to what is called the vertebral subluxation complex. Attempts are made to locate muscle strength or weaknesses, extent of spinal mobility, skeletal deformities, or bad posture. Some practitioners attempt to evaluate the electrical activity of muscles and nerves, so that a baseline can be obtained to monitor any progress in treatments. If pathologies (fractures, tumors) are located, these are referred to appropriate allopathic practitioners.

The most common adjustment procedures are referred to as high-velocity, low force recoil thrust and/or rotational thrust. In the former procedure, the patient is placed in the prone position on a specially designed segmented table that can be raised or lowered so that the appropriate adjustments can be made. In the latter procedure, the patient is placed so that the upper body is twisted counter to the pelvis. Then, the spine is rotated to its normal limit while the chiropractor uses a short, fast thrust to the spine to realign it.

Today, many chiropractors fall into two groups, those who adhere strictly to Palmer's philosophy of adjustments to get rid of subluxations (straight chiropractors) or those who use the original technique coupled with exercises, treatments involving heat, and nutritional counseling (mixer chiropractors). Many of today's chiropractors treat neuromusculoskeletal ailments of the spine which include, but not limited to, lower back pain, sciatic pain, neck pain, headaches, shoulder pain, golfers and/or tennis elbow, wrist, hand, leg and foot pain.

While some orthodox allopathic practitioners doubt the claims of effectiveness, chiropractic devotees abound, usually swearing that regular medical practice provided no relief for their problems. At one time the AMA labeled chiropractic an unscientific cult, but now they are licensed in all 50 states and throughout Canada. In both countries, treatment is covered by many private health-insurance plans and all similar government agencies. During the 1970s up to the 2000s, chiropractic has moved from being considered unusual and dangerous to a place where it is accepted relatively well by both the lay and medical communities. It now ranks as the third largest primary-care profession in the Western world, with only medicine and dentistry exceeding it.

Some 60,000 licensed chiropractors and 16 accredited schools may be found in the US. They offer a four-year post-graduate curriculum covering much of what is given in the average medical school. Upon graduation, a Doctor of Chiropractic degree is earned. The scope of practice of chiropractic licensure in most states does not include surgery or the prescribing of medication. The basic philosophy of chiropractic is that the body has an innate ability to heal itself.

Numerous articles abound in the medical literature on the positive and negative aspects of chiropractic treatments. A 1996 systematic overview of conservative treatments for neck pain and headache failed to demonstrate convincingly that chiropractic is more effective than other interventions. Another meta-analysis of chiropractic for low back pain published in 1992 suggested that it is effective for acute low back pain. Yet another more recent and rigorous systematic review concluded that, "the available randomised clinical trials provided no convincing evidence of the effectiveness of chiropractic for acute or chronic low back pain." Nonetheless, a substantial number of studies have found chiropractic to be as effective as conventional therapy for various conditions. Certainly more research is indicated and the chiropractic profession is actively engaging in the research process.

HERBALISM

It is well known that herbs have been used in medicine by all cultures from the beginning of time. Almost every modern drug owes its origin to some medicinal plant. Of the numerous potent phytopharmaceuticals that have been used in US medicine, one can cite morphine (opium poppy), digitoxin (foxglove), diosgenin (Mexican yam), atropine (nightshade), colchicine (autumn crocus), quinine (cinchona trees), reserpine (Indian snakeroot), vincristine (periwinkle plant), podophyllin (mayapple), castor oil (castor-oil plant), anthraquinones (cascara), artemesinin (artemisia), taxol (Pacific yew), and the numerous antibiotics.

For centuries, right up to the 19th century, herbs were the major source of drugs and were kept in glass jars or as alcoholic extracts for long shelf-life or convenience of use. While they were put aside with the rapid advances in synthetic organic chemistry of the past 50 years, they still occupy an important place in medicine. For the most part, the reasons for their being left aside in the last 40 years included difficulty in identification and extraction, difficulty in patentability (in the US, products from nature cannot be patented), and abuses in the early 1900s when spurious plant mixtures were sold as cures for everything. [For the latter reason alone, plants have been considered quack cures by the medical establishment and the FDA and efforts in the US generally are aimed at keeping their use at a minimum.] There is little doubt that some reasons for this attitude exist, because modern medicine wishes that all herbals be standardized and show efficacy in the same way that single-entity synthetic drugs do. However, because of costs involved (up to several hundred million dollars) to do this, few companies have an incentive to produce drugs from natural products, patent problems notwithstanding.

So, currently, we are in an era when many herbals in the US (once standardized and common in pharmacies up to the 1960s) are now widely available in health-food stores and offered as *foods* with active ingredients not being appropriately standardized. With the upswing in consumer interest in CAM since the 1960s, high demand has been seen for these, to the extent that health foods and herbals have become a several billion dollar per year business. Part of this has been due to an international rise in the interest in herbals or because many countries never let them go as part of their traditional and cultural medical practices. Similarly, efforts of the NIH, through the cancer-screening program have uncovered numerous leads to potential drugs that currently are being used (eg, camptothecin, taxol).

Phytomedicinals (eg, garlic, ginkgo, ginger) from international traditions are being adopted for use by many Americans and presently are being investigated by medical researchers in the United States. However, Chinese, Ayurveda, and Tibetan herbalists, among others, usually use combinations of herbs in their prescriptions. Combinations of herbs are used by these herbalists because they believe that illness is attributed to an imbalance in the total person (including emotional and spiritual elements) and that an environment inhospitable to disease can be established by combining herbs with specific properties.

A Chinese herbalist would rarely, if ever, use one herb by itself and might include other ingredients such as zoological (eg, insects, reptiles) and mineral derivatives in their prescriptions. Chinese herbalists use four different categories of herbs in their prescriptions. The chief herb(s) support(s) the main therapeutic direction of the formula; the deputy herb(s) assist(s) the chief herb; the assistant or adjunctive herb(s) moderate(s) and support(s) the actions of the chief and deputy herbs; and the envoy herb(s) harmonize(s) and distribute(s) the actions of the other herbs. Chinese herbal medicine is based on a tradition that has developed over thousands of years. It stands as the most experienced of all the herbal *traditions*. Some English translations of Chinese herbal materia medicas and herbal therapeutics are available. While these can be useful to pharmacists, they are often difficult to interpret because plant activities and applications are given in Chinese medical terminology. For example, herbs may be indicated for their Exterior-resolving, Heat-clearing, Qi-rectifying, or Blood-rectifying properties.

Practitioners of Chinese herbal medicine frequently use acupuncture with herbs, and herbs are taken for periods between acupuncture sessions. A formally trained practitioner would have a degree in Oriental medicine (OMD). Three states in the US, Nevada, New Mexico, and Texas require NCCAOM exams in acupuncture and Chinese herbology for acupuncture licensure (www.nccaom.org/states.html). This site also lists CA as having its own test but no mention is made of herbal medicine being required. Several companies are marketing Chinese herbal combinations in the US that have been derived from ancient recipes. One should be cautious about buying combination products from companies or stores that can not ensure that proper procurement or manufacturing procedures have been practiced in the preparation of the medicine, as there have been many reports in the medical literature of heavy-metal contamination, adulteration with prescription medications, and inclusion of misidentified plant materials.

Concomitantly, many of the crude forms of herbs have made it into this country via the various ethnic connections in the United States (eg, Japan and India on the West Coast and Mexico in the Southwest) and are being used in various cultural groups. So, while the use of herbs is moving rapidly to the mainstream, it behooves pharmacists and consumers to locate reliable information available in books and periodicals, in colleges of pharmacy (scientifically reliable), and in health-food stores (advocacy literature) with the view in mind that appropriate authors and articles in the valid scientific literature be stressed.

The powerful green wave of interest in phytopharmaceuticals (plant medicine) has prompted the FDA to develop labeling requirements for supplements, which include herbs, vitamins, minerals, and amino acids. The labeling requirements are found in the DSHEA, which was published first in September 1977. Under these regulations herbs will be considered dietary supplements, not food or drugs. After March 1999, all herbal products must be labeled with a *Supplement Facts* box. Many high-quality manufacturers of herbs began to include it on their products in 1998. The information on the product label includes nutrient content, health claims, and statements of nutritional support. Ingredients on the market as of October 1994 are *grandfathered.* New ingredients require submission of information to the FDA before marketing, but formal FDA approval is not required before marketing. The FDA published notice of proposed rulemaking for GMPs in February 1997 and will publish a final ruling upon thorough evaluation of the matter.

At least 60 to 100 other herbs that have been used for minor ailments are used in the US and elsewhere, eg, basil, thyme, rosemary, aloe, anise, boneset, buckthorn, cayenne pepper, chamomile, cranberry, echinacea, eucalyptus, evening primrose, feverfew, garlic, ginger, ginkgo, ginseng, goldenseal, hawthorn, juniper, licorice, milk thistle, peppermint, psyllium, senna, valerian, wintergreen, witch hazel, and yarrow. All of these have known active principles and a specific regulatory status in the US and other various countries, eg, GRAS, OTC, Commission E (Germany).

It also should be mentioned that perfectly acceptable nonpharmacologically active herbal teas have established themselves in the US popular drink marketplace. Where once we had only regular tea, there are now numerous varities (with citrus flavors, cinnamon, fruit flavors), as well as mixtures of lemon tea, ginger tea, wintergreen, peppermint, blueberry, and many others.

As with Chinese medicine, one should be careful of sources, because different species may be used in different countries or may be adulterated accidently or purposefully.

As far as reliable dosage forms are concerned, tinctures (alcoholic extracts) and freeze-dried herbs are usually best. Dried (oven or sunlight) herbs sold in bulk, whole or powdered, or encapsulated forms may lose potency rapidly because of air oxidation.

Table 132-6. Selected Drug Interactions with Herbs

MEDICATION(S)	HERBS WITH POSSIBLE SYNERGISTIC OR ANTAGONISTIC EFFECTS
Anticoagulant and antiplatelet drugs	Alfalfa, astragalus, bilberry, evening primrose oil, garlic, ginger, ginkgo, ginseng, gugulipid, feverfew, scullcap
CNS stimulants	Guarana, kola, ephedra, St John's wort, yohimbe
CNS depressants	Hawthorn, skullcap, valerian
Antidepressants	Ginseng, ephedra, passion flower, St John's wort, yohimbe
Diabetes	Garlic, ginger, ginseng, hawthorn, ephedra, nettle
Hypertension	Devil's claw, ginseng, goldenseal, hawthorn, licorice, ephedra, squill, yohimbe

As far as dosage is concerned, one should start with the lowest recommended amount and work upward. Unless these herbs are standardized, there is little choice to obtain the active dose. Certainly, overdosing with herbs can have deleterious effects. One also should be careful of potential herb-drug interactions. These also can occur, so it is advisable to check with the experts (pharmacists, physicians, pharmacognosists, herbalists) before use. It is likewise imperative to monitor one's reactions, being careful to observe that desired effects are obtained and undesired effects (eg, rash) are avoided.

Many people in the US are turning to herbal medicine to treat their ills, and pharmacists are in a position that requires them to have resources to answer patients' questions and monitor for possible adverse effects. While no one reference is available that covers it all and information regarding drug interactions is especially lacking, there are some good resources available. See the *Bibliography* for suggestions for building a reference library on herbal medicine. The pharmacist has the opportunity to help build the database that is needed to use herbs safely. For many of the most popular herbs used by Americans today, some important drug interactions are known. See Table 132-6 for examples. Herbs without known drug interactions should be treated like any new prescription product that comes on to the market. Here too, pharmacists are called upon to participate in collection and management of drug interactions manifested. Unlike prescription drugs however, with herbal medicine, the patient is more likely to be taking herbs without the support of a conventional medical doctor. This puts the pharmacist in a more direct role with the patient in making sure that herbs taken with conventional prescription drugs are documented and monitored.

Regardless of the potential usefulness of herbal therapy, critics note the widespread availability of spurious data on them via advocacy literature. Even though the DSHEA Act of 1994 delimits OTC herbals from legally labeling them efficacious in treating diseases, much promotional literature is sold (books) or provided free as handouts alongside herbs, on or near the store shelves. Occasionally, dangerous herbs may be recommended, particularly in older books or references. Some *new age* publications promote herbs as having mystical or magical powers. Some also rightly point out that the rapid rise in herbal popularity has made it difficult to list them adequately for efficacy via the usual rigid pharmaceutical standards. Of course, the major reason for this is the cost (often millions of dollars) and lack of ability to patent natural products easily in the United States. Beyond this, it will always remain difficult to test the entire herbal product for the major active ingredient(s), which may take years to identify and characterize adequately. There are more reasons requiring adequately trained health personnel to advise patients on which herbs are safe and which may or may not be potentially useful for various health conditions.

Overall, in herbal therapy it is impossible to define the major active principle(s). Hence the clinical properties of these herbal products may not be known with certainty. This is because the herbs often contain several active components which may vary considerably from batch to batch of the herbal. It certainly is very expensive and time consuming to follow the conventional wisdom of isolation and assay directed identification of active compounds.

Several Asian traditions (eg, Chinese Traditional Medicine, Ayurvedic medicine, etc.) employ complex, often individualized mixtures of many (often 10–20) different herbs in each single prescription. Fortunately, most of the modern herbal products in the US consist of a single herb. Quite a few of these (eg, St. John's wort, *Ginkgo biloba*) have been subjected to a fair number of clinical studies. These have undergone fairly systematic reviews or meta-analyses. Obviously each herbal has to be evaluated on its own merit and experience in any traditional usage. One cannot simply state that all uses are justified, safe and consistently efficacious.

Several other herbal products have uncertain efficacy. A case in point is mistletoe (*Viscum album*) which has been recommended in Europe as a cancer treatment. Its popularity has prompted such use in Australia and in the US. Mistletoe proponents claim that it can arrest or delay tumor progression and improve quality of life. The lectins in the plant have been shown to possess antineoplastic activity. Unfortunately, a systematic review of all eleven controlled clinical trials demonstrated disappointing results. It was revealed that the average methodological quality of the primary studies was rather poor. While the results of most trials showed mistletoe to be favorable, the most vigorous one did not show good efficacy. To quote the authors, they "cannot recommend the use of mistletoe extracts in the treatment of cancer patients with an exception for patients involved in clinical trials." Since this study, several other new investigations have brought the overall conclusion that it is not effective for this purpose

Table 132-7 displays examples of herbal medicinal products for which systematic reviews and meta-analyses have been published. There are found in a text entitled Herbal medicine, a concise overview for professionals (Oxford Butterworth Heinemann Press, 2000.)

Finally, it should be remembered that herbs usually should be used for minor ills only. One should avoid self-medication for serious ailments or injuries. Certainly, the very young or old, pregnant or lactating women, and persons already on certain medications should not take herbal remedies without consulting with their physician.

Many ethnobotanical studies are continuing in the rain forests and elsewhere to ferret out any new potential leads to phytopharmaceuticals. Almost every plant or animal drug has dozens of potentially active constituents, and the potential pharmacological activity of each needs to be evaluated thoroughly. Several recent successes for newer medicines derived from plants via the FDA OTC and prescription drug development route are taxol, artemesinin, calanolide A, etoposide, and *Ginkgo biloba.* Hopefully, some of the CAM practices involving herbs will yield more phytopharmaceuticals in the near future.

HOMEOPATHY

Homeopathy is a system of medicine that has its own principles of practice and pharmacopoeia that differs from both phytopharmacy and conventional medicine. A homeopathic medication is often referred to as a "remedy", but herbalists may also use this term for herbal medications. Thus, the pharmacist must be careful when interpreting literature describing the use of botanical medications to distinguish if an herbal or homeopathic dosage form is being described. While it is difficult to define homeopathy specifically, because of cultural and historical perspectives, one may begin with a description provided by homeopaths:

Homeopathy is a therapeutic method. It clinically applies the Law of Similars (like cures like) and uses medically active substances at weak or infinitesimal doses.

Table 132-7. Examples of Herbal Medicinal Products for which Systematic Reviews and Meta-Analyses have been Published

COMMON NAME OF PLANT	INDICATION	EVIDENCE FOR EFFECTIVENESS
Aloe vera	Various	Poor
Artichoke	Hyperlipoproteinaemia	Poor
Feverfew	Prevention of migraine	Encouraging
Ginger	Nausea/vomiting	Encouraging
Ginkgo biloba	Dementia	Good
Ginkgo biloba	Intermittent claudication	Good
Ginkgo biloba	Tinnitus	Encouraging
Ginseng	Various	Poor
Horsechestnut	Chronic venous insufficiency	Good
Kava	Anxiety	Very good
Mistletoe	Cancer	Poor
Peppermint	Irritable bowel syndrome	Encouraging
St John's wort	Mild/moderate depression	Very good
Valerian	Insomnia	Encouraging

This assessment is based on an overview of systematic reviews. By Ernst (Year 2000)

Homeopaths believe that body is not reduced easily to the sum of its parts; therefore, they assess all the person's physical, mental, and emotional aspects in the course of finding the correct homeopathic medication.

The first basic principle, the *Law of Similars*, is that a substance that causes symptoms in a person may cure an illness that manifests those same symptoms. Hence, a homeopathic medication that mimics disease symptoms can be given to stimulate a person's body to fight against the symptoms depicted by the illness. The second basic principle *(Law of Infinitesimals)* and most controversial is the concept that the lower the concentration of a substance (derived from a botanical, animal, mineral source) in a properly manufactured homeopathic medication, the greater the effectiveness. However, for illnesses of a physical nature low potency (less diluted) homeopathic medications are used while more emotional or psychological-based conditions require the higher potency medications.

Further, even when so diluted that no more drug can be found, homeopaths believe that the preparation still is effective. The father of homeopathy, Hahnemann, taught his followers to use a single medicine at a time. However, in modern times, with the complexity of causes, eg, stress or cellular toxicities, many practitioners employ a pluralistic approach, termed *homeovitics*. Combinations of single homeopathic medications are also available for self-limiting illnesses, eg, colds and flu, seasonal allergies, headaches, and teething, etc., for which most people experience the same symptoms.

Generally, homeopaths found which drugs to prescribe through a process of placebo-controlled trials, which are referred to as *provings*. Guidelines for provings can be found in the current *Homeopathic Pharmacopoeia of the United States* (www.hpus.com/eligibil.html). These data are recorded in homeopathic materia medica texts and repertories. These books give symptoms and the drugs that have been observed to effect cures. For the most part, while these are guidelines, homeopaths emphasize individual uniqueness, and drug regimens must be tailored to individual needs.

Usually practitioners of homeopathy deal with such chronic disorders as allergies, arthritis, asthma, colitis, headaches, high blood pressure, and weight control. Certain deficiencies (anemia), hormonal imbalance, and some infections also are treated. Most practitioners of this field acknowledge the need for antibiotics for severe infections and the importance of conventional treatments for severe injuries or management of emergency situations.

Homeopathy is displaying a rebirth of popularity, even though for several decades it had been predicted that it would almost certainly disappear in the light of modern medicine. It is for this reason that pharmacists and other health professionals should be aware of the current status of this field. Finally, homeopathy is *not* herbal medicine even though both practices use botanical substances.

POPULARITY—Homeopathy reached its peak of popularity in the early 1900s. Today, there is a resurgence of the popularity of this old medical method. The FDA recently referred to a 100% increase in homeopathic drug products. Concern about this rapid influx of homeopathic drug products into the American marketplace led to the issuance in May 1988 of the FDA Compliance Policy Guide 7132.15 entitled *Conditions under Which Homeopathic Drug Products May Be Marketed.*

In December 1988, the Homeopathic Pharmacopoeia Convention of the United States (HPUS) issued the first volume of its *Homeopathic Pharmacopoeia Revision Service (HPRS)*. Along with its allopathic counterpart, the USP, the HPUS was adopted by Congress as an official compendium in 1938. Substances monographed in the HPUS are recognized as official drugs in the current FD&C Act and the *Code of Federal Regulations*. The HPUS updates manufacturing methods, provides guidelines for Rx-OTC status, and publishes monographs for all official homeopathic drug products. The 2000 year edition of the HPUS contains 1286 monographs of individual homeopathic medications.

Today, there are over 3000 recognized practitioners in the US whose practice is mostly homeopathic according to the National Center for Homeopathy in Alexandria, VA. Homeopathy has become a favorite of many dentists and veterinarians and is a integral part of naturopathic medical curriculums.

From 1994 to 1999, homeopathic drug sales were estimated to represent 0.26% of the US drug market and consumer sales increased by $30 million dollars. In the US, there are at least 40 schools although these programs are not yet recognized by the Department of Education as being accredited; however, the Council on Homeopathic Education is currently taking steps to establish professional standards of homeopathic education that will be submitted for accreditation status in the future. Currently, there are four homeopathic journals published in the US (*Homeopathy Today* [National Center for Homeopathy], the *Simillimum* [Homeopathic Academy of Naturopathic Physicians], *The American Homeopath* [North American Society of Homeopaths], *American Journal of Homeopathic Medicine* [American Institute of Homeopathy]).

In the health care systems of many countries around the world homeopathy plays a major role in their health care systems. In France, the Netherlands, Belgium, and Germany an estimated one third of conventional doctors use homeopathy or refer patients to a homeopath. Homeopaths are officially recognized in India and Germany and between 15% and 56% of the European population make use of homeopathy along with conventional treatment for a wide range of illnesses. The English royal family traditionally has been treated homeopathically and is one of its most famous proponents. In the United Kingdom homeopathy has been integrated within the national health care system for almost 50 years and currently has five homeopathy hospitals and a university offering a degree in homeopathy health sciences. In Russia, at least 20% of the med-

ical care is homeopathic. Homeopathy also has a strong following Italy, and South America and traditionally has had a strong following in poorer countries. Because of homeopathy's strength and business success in foreign countries, there are many homeopathic pharmaceutical firms and homeopathic drug products coming into the US.

MODERN HISTORY—At the present time people in Europe (and to some extent here in the United States) who are disillusioned by allopathy have turned again to homeopathy. France and England show a remarkable upturn in homeopathy now under the relatively new umbrella of alternative or complementary medicine. Both French and English homeopaths have developed research centers for *in vitro* and clinical studies of homeopathic medicines. Doing research with homeopathy is complicated. One of the challenges involved with individualizing drug therapy is that many patients with the same chief complaint will required different drugs from a homeopath, based on the etiology and specific symptoms, as well as aspects of the patient's temperament. Therefore, an RCT, which tests a single homeopathic drug for a particular diagnostic category, is likely to fail because that drug will match the symptoms of only a small percentage of patients. In addition, the homeopathic drug must be administered in a potency and dosage schedule likely to be effective in that condition. The correct drug may have no apparent action if the potency is too low (given the individual needs or characteristics of a patient) or given too late to be effective.

Different approaches have been implemented to surmount this obstacle. One approach is to give patients a drug agreed on by two professional homeopaths, rather than a predetermined trial drug. A set of active and placebo drugs for each remedy likely to be effective for the disease state being tested is set up by a pharmacy who selects which agent a patient receives based on a randomization. Another approach involves performing the study on a diagnostic category for which a single homeopathic drug is likely to be effective in which patients are only accepted for the trial if their symptoms matched that of the remedy. Given the need to use the correct potency and dosage regimen for optimal therapeutic results, outcome research provides perhaps the most realistic evidence of homeopathy's effectiveness and reflects the results of homeopathy used in everyday practice by experienced homeopaths.

While there continue to be pro and con articles on the efficacy of homeopathy, two recent articles serve to summarize opposing reviews and difficulties in proof methodology. A meta-analysis of placebo-controlled trials in homeopathy (Linde K *et al,* 1997) reviewed 156 trials and identified 119 that met their inclusion criteria. At least 89 had adequate data for meta-analysis, and two sets of trials were used to assess reproducibility. The two reviewers assumed study quality using two scales and obtained data for information on clinical condition, homeopathy type, dilution, remedy, population, and outcomes. They found, after analysis, that their meta-analysis was *not* compatible with the hypothesis that the clinical effects of homeopathy are due completely to placebo. Further, however, they reported that they found insufficient evidence from their study that homeopathy is clearly efficacious for any single clinical condition. They recommend further research on homeopathy, particularly if it is rigorous and systematic.

A later review (Dean M, 1998) stated some objections to this study; it was felt that the meta-analysis may well have overestimated the positive effects of homeopathy and that the placebo question is not resolved. The authors suggested that different models are needed to answer different questions and that results would be more valid if based on a comprehensive literature search, appropriate classification of primary studies, clear discrimination between clinical effectiveness and placebo questions, more sound and transparent review methods, and a reliable and unconfounded clinical treatment model for testing the ultramolecular hypothesis.

A model for a possible mechanism of action of homeopathic medications is being researched with the premise that each original drug substance, when diluted and succussed in water, stimulates water's capacity to record patterns of energy shifts leading to the formation of a unique icelike crystalline structures in water called by various investigators as calthratos (Anagnostatos 1998) or I_E crystals (Lo and Bonavida 198). As more kinetic energy is added to the system by further succussions, more water molecules are attracted into the pattern, and more information is thus stored in the water. One research team (Anagnostatos 1998) used depolarization thermocurrent and differential scanning calorimetry measurements while another (Lo and Bonavida 1998) had used transmission electron micrography, fluorescence spectrophotometry, and ultraviolet (UV) spectroscopy to detect evidence of the crystalline structures identified. Using nuclear magnetic resonance (NMR) imaging, changes in potentized drug water have also been measured (Smith and Boricke, 1996).

The interested reader can find more detailed information on research discussed in this section and other models that are being investigated to explain a mechanism of action for homeopathic drugs in publications by Bellavite and Signorini and Gray, as well as on the National Center for Homeopathy Web site and the National Center for Complimentary and Alternative Medicine Web site at nccam.nih.gov/health/homeopathy/index.htm.

MEDICINES—Homeopathy uses a wide variety of pharmacologically active natural substances such as plants, animals, zoological specimens, and minerals in its repertoire. Most of these materials are used to prepare *Mother Tinctures* by maceration in alcohol according to conditions strictly defined by the HPUS. Using these tinctures as starting materials, they are subjected to successive dilutions according to the decimal or centesmal scale. Decimal dilutions are based on a 1:10 ratio represented by the Roman numeral X or D, and centesmal based on a 1:100 ratio by the Roman letter C. Hence, a 1X homeopathic dosage is a 10-fold dilution, 2X is a 100-fold dilution, 3X is a 1000-fold dilution, etc. The 1C represents a 100-fold dilution, 2C is a 10,000-fold dilution and 3C is a 1,000,000-fold dilution, etc. Most homeopathic over the counter remedies range from 6X and 6C to 30X and 30C. Professional homeopathic practitioners also use higher potencies of 200C, 1M (equal to 1000C) or higher M potencies in their practice. A dilution that Hahnemann developed in his later years (published in the 6th ed of the Organon), called LM, is made using a complicated procedure which uses trituration and succussion lending to a dilution factor of 1:50,000 of the final product which is commonly dispensed as a liquid. Currently, this potency is not found on the general market as OTC products. This potency is gaining popularity in the US as it allows the homeopathic practitioner to titrate the patient's dose more effectively than with X or C potencies.

It should be mentioned here that according to the laws of chemistry, there is a point at which a substance can be diluted so that no more original substance remains. The limit is referred to as Avogadro's number, which closely corresponds to the homeopathic dosage of 24X or 12 C (or one part in 10^{-24}). Even Hahnemann recognized that in all likelihood, extreme dilutions would not contain a single molecule of the original material. However, homeopaths believe that vigorous shaking (succussion) or pulverizing of a solution between dilutions releases into the solution or diluent a mysterious *essence* or *imprint* or *resonance* of the medicine as discussed previously. This message is purported to be of sufficient magnitude to stimulate the *vital force,* which mitigates illness. In the case of insoluble starting materials, the initial dilutions of the medicine are carried out by trituration (mixing and rubbing together in lactose).

While it is impossible to list all of the hundreds of homeopathic products available, it is instructive to list a few of the common drugs available and why they are used.

***Arnica montana*—**A mountain herb widely used in homeopathic medications for bruises, sports injuries (soft tissue trauma), and aches, pains, and stiffness following excess physical activity.

***Allium cepa*—**A product of the red onion, widely used in the treatment of colds, allergies, and hay fever. It also is suggested

for patients who have congestive symptoms (nasal discharge, tearing eyes) in a warm room that improve in a cooler room.

Apis—A preparation made from whole crushed bees, used for inflammations accompanied by burning, stinging, and pain, such as in hives, insect bites, and tonsillitis, particularly when these maladies improve with cold compresses and are worsened by heat.

Arsenicum album—A product made from white arsenic and used for diarrhea or indigestion encountered during travel and for general food poisoning.

***Atropa belladonna* (Deadly nightshade)—**A plant product used in homeopathy for a range of conditions including childhood fevers and throbbing headaches (with accompanying sensitivity to motion, noise, and light).

Rhus toxicodendron *(Toxicondendron radicans)*—A preparation made from the poison ivy plant, used homeopathically for sprains and strains of the arthritic type in which continued motion lessens the pain and improves range of motion.

***Urtica urens*—**A medicine made from the stinging nettle plant and used for utricaria and pruritus aggravated by cold water.

Homeopathic products initially were once marketed exclusively through pharmacies; however, the current market is mostly in natural or health-food stores and pharmacies that specialize in natural products. This will probably change as pharmacies respond to their customers, and some studies may show effectiveness and safety of homeopathic drug products. A recent request to FDA for reports of adverse reactions to homeopathic drug products produced no substantiated reports. Recent studies and scientific articles in *Lancet, Nature,* the *British Medical Journal,* and other respected medical journals attest to the reliability and safety of homeopathically prepared substances in infinitesimal doses. However, controversy about their efficacy remains.

FDA ATTITUDES—As is well known in medicine, testimonials are easy to come by, but scientific proof is not. The FDA has long recognized homeopathic remedies as drugs, mainly as a way of controlling quality and use. The FDA has not subjected any of these remedies to premarket screenings for safety and effectiveness as with normal or conventional drugs. Homeopathic medications have NDC numbers listed on their packaging and can be designated as OTC or prescription drugs depending on the substance used and the indicated condition it treats.

DRUG SAFETY—Homeopathic drug products are well known for their safety. The current Homeopathic Pharmacopoeial Convention of the United States, which publishes *HPUS* and *HPRS,* has placed a high priority on ensuring the safety of official homeopathic drug products in the marketplace. Recent requests to the FDA for information on homeopathic drug products produced no confirmed reports of side effects or toxicity or adverse reactions regarding homeopathic drug products.

LABELING—Official homeopathic drug products must be identified properly on the label by using *HPUS* after the compendial name, eg, Arnica mont. 12X HPUS. The 12X indicates the potency or degree of dilution. Potencies are either indicated as numeral followed by an X, C, or D, etc. The number indicates the number of dilution steps taken to make the medicine, while the letters indicate the dilution scale used in the process.

OTC homeopathic drug products have no known side effects but must carry all of the customary warnings regarding pregnancy, nursing mothers, and tamper-evident features. Homeopathics are relieved of the obligation to bear an expiration date but otherwise must meet all provisions of the FDA and CFR, although many homeopathic manufacturers put expiration dates on their products. Homeopathics usually bear a legend which recommends that the consumer should discontinue use if the treated condition does not improve within a specified period of time or becomes worse. Homeopathics generally are marketed for conditions that are considered OTC by the FDA Scientific Advisory Panels. On single homeopathic products usually only 2 of the remedy's indications are listed and the consumer and pharmacist should be aware that product has other indications as well. The pharmacist or consumer can check a materia medica to find all the indications of a particular homeopathic drug.

HOW HOMEOPATHY MAY WORK—Homeopathics possibly work by stimulating the body's own forces in the direction of cure. They are, therefore, most effective in children, when these forces are most active. Children's remedies are a most successful segment of the homeopathic drug market. One can safely advise a patient that there are no side effects or contraindications for OTC homeopathic drug products, especially if potencies of 12C or 24X are utilized.

Homeopathic drugs do not cover up or mask symptoms; they are claimed to stimulate the reactive processes of the body to overcome and correct the problem. Therefore, they may not provide instantaneous relief. While the patient may start to feel better in a short time, complete lasting relief may not occur for several days. Such relief may be lost by discarding a remedy as ineffective after a few hours. Generally, the longer a symptom has gone untreated, the longer it will take the homeopathic medicine to bring relief.

With a few exceptions, substances prepared according to the specifications of the HPUS, which are stored in a cool, dry place, out of direct sunlight and protected from contamination, retain their therapeutic effectiveness indefinitely.

If the patient fails to respond to an OTC homeopathic remedy in the stated period of time or if the symptoms worsen or new symptoms develop, the patient should discontinue use and seek the advice of a health professional.

HOMEOPATHIC PRESCRIBING—The homeopathic prescriber studies the patient *(takes the case)* in great detail. The aim is to know and treat the whole person, not just a single organ or set of symptoms. The patient's history is, by necessity, more detailed than that taken by an allopathic physician. After a careful consideration of the background and current symptoms, the prescriber usually is able to select the precise drug for the individual.

In some cases, when symptoms are acute (come on suddenly) and self-limiting, the patient can study a case to choose a single remedy or use a combination of three or four remedies that have been proved individually to apply to symptoms similar to those observed. The combination has the advantage of improving the probability of successful prescription; however, it is difficult to determine which individual remedy was responsible for clearing the symptoms. It should be remembered, though, that when the illness has persisted for years and has become chronic, it may take more time to achieve results and these cases are best treated by a experienced homeopath.

The homeopathic medical method is a specialty of many medical doctors, osteopaths, naturopaths, and other complementary and alternative practitioners. Four organizations in the US currently certify practitioners: The American Board of Homeotherapeutics, the Homeopathic Academy of Naturopathic Physicians (DHANP), the Council for Homeopathic Certification (CCH), and the National Board of Homeopathic Examiners (DNBHE). Certification ensures that the practitioner has had documented educational and experiential training and has passed a rigorous board examination. The National Center for Homeopathy has links to all the above organizations and a listing of practitioners on their web site which consumers and pharmacists can use to identify practitioners practicing in their area.

HOMEOPATHY AND ALTERNATIVE HEALTH PRACTICES IN MODERN MEDICINE—The main premise claimed for an increase in interest in homeopathy in the US is the recognition that diseases of the immune system have increased (eg, AIDS), the number of persons suffering from incurable viral conditions is increasing, bacterial infections are becoming resistant to commonly used antibiotics, allergies to foods and other common substances are becoming more prevalent, chronic disability is affecting persons more frequently at younger ages, and mental disease is affecting more and more persons.

There is also reference to futurists who believe that 21st century medicine will have both a *high-tech* and a *high-touch* component, with significantly greater reliance on self-care prac-

tices; wellness programs; therapeutic, nutritional, and fitness regimens; and other alternative or complementary practices. Also cited is a greater emphasis on more fully integrated concepts of how a person's psychological state affects various physiological processes. Homeopathy may fit some of these needs.

One major important facet of homeopathy is the extensive use of mineral, plant, and animal substances in therapy. An important scientific question should be one of testing whether high dilutions of these materials can in fact stimulate the immune system or the bodies vital force. While there have been a number of clinical trials in Europe, none have definitely shown a specific effect that can be duplicated under controlled conditions.

If homeopathy is to succeed scientifically, it needs verification. Thus far, it has survived on historical, and perhaps a placebo medicine, basis. There is ample evidence that numerous plant principles can stimulate the immune system. Seminal studies by Wagner and others have shown that there are multitudes of nonmicrobial compounds with potential homoeopathic immunostimulating activity in plants and fungi. He lists dozens of plants that contain immunostimulant alkaloids, terpenoids, phenols, quinones, lipids, lectins, polysaccharides, peptides, and proteins. Skeptics maintain the idea that a substance can cure by releasing energy, which puts homeopathy in the realm of metaphysics.

Another set of recent meta-analysis of 123 randomized or placebo-controlled investigations found that the clinical efficacy of homeopathy are not entirely due to placebo. This study has been criticized for pulling together data relating to all types of indications and remedies. Hence, it may important to assess defined disorders and remedies in order to see what evidence pro or con homeopathy emerges. One homeopathic product which has been studied more than any other is *Arnica montana*, often used for alleviating bruising and trauma. Two independent systematic reviews of all studies of homeopathic arnica gave no conclusive proof that it is clinically more effective than placebo. Similarly, studies of delayed-onset muscle soreness with homeopathic remedies produced no convincing evidence of any greater efficacy than placebo. Again in reviewing studies on alleviating asthma or headache via homeopathy means, there was no proven efficacy. Many homeopaths would claim that their approach can alleviate symptoms related to certain cancers and hence a role in supportive or fallestive care. Thus far, evidence in proving these claims is lacking.

On the brighter side, as discussed before, it is obvious that highly diluted homeopathic preparations are devoid of adverse side effects on drug interactions. However some homeopaths claim that about 20% of all patients may demonstrate an acute clinical deterioration (labelled "homeopathic aggravation") if the optimal remedy has been administered. This obviously is a safety issue for the higher doses remedies. There are also some homeopaths who advise their patients against vaccinations, which itself may be a hazard of neglect in certain situations.

HYDROTHERAPY

Hydrotherapy or balneotherapy or water treatments for medical purposes is probably as old as 'mankind'. As a matter of fact, hot water spas for pain relief (back pain, arthritis, injuries, etc.) were fairly common up to the last century. However, these practises declined in the Western world with the advent of hot showers, effective analgesics and the recent development of disposable "hot-pacs" for muscular pain relief. Electric pads for back and arthritic pain have and continue to be used as well, although not strictly considered hydrotherapy but simply heat therapy for local pain relief and in low and upper circulation problems of various kinds. Because of lack of effectiveness over time, unwanted side-effects of drugs and recent interest in exercise coupled with heat hydrotherapy of various kinds has resurfaced in treating some conditions. These include osteoarthritis, rheumatoid arthritis, chronic heart failure, peripheral neuropathy, poor circulation, back pain, consipation, stress and anxiety control and pregnancy and labor. Overall, hydrotherapy does offer a relatively safe and inexpensive and generally effective and useful alternative to the treatment of these and other related conditions. However, several articles have pointed out that the various methodological difficulties and lack of research funding, as well as great variation in types of medical conditions have precluded controlled trials to fully evaluate their true effectiveness.

Many studies which involved exercise regimens in hot-tubs or warm water pools, showed functional gains in patient's conditions. Others showed some possible dangers where some association was seen between the use of a hot tub or whirlpool during early pregnancy and the risk of miscarriage. Another study on the other hand, showed that hydrotherapy is a safe, nonpharmacological alternative for women to use during labor and delivery, infections from the use of commercial hot tubs have been reported. These also is considerable popular interest in colonic hydrotherapy, and one study in England concluded that it is practiced widely in the UK (as well as the US) with an estimated 5600 procedures carried out by different practitioners monthly. Many of these users appear to be well trained and a proportion have medical backgrounds. Clients who are frequently dissatisfied with orthodox medicine seem satisfied enough with the practice of colonic hydrotherapy to undergo regular purging by this method. Few serious effects were noted. Practitioners appear to do well financially in this practice.

HYPNOSIS

Hypnosis is a focused concentration somewhere between sleep or unconsciousness and awareness, usually brought on by a trained hypnotist. The hypnotized person shuts out distractions and pays strong attention to a particular object or subject, emotion, or memory. While once dismissed as quackery, hypnosis has gained new respect as a viable therapeutic modality for treating everything from fear to pain.

Although hypnosis is a current orthodox medicine, caution is still important, and one should have a proper diagnosis before submitting to it. It certainly does not make sense to use it as a possible coverup for some serious underlying medical problem. For this reason, the hypnotist should work with the primary physician, or the primary physician already has certified training in the discipline.

Many states now have local societies of clinical hypnosis. Among the strongest factors supporting hypnosis is the recognition that it can be a valuable adjunct to standard therapy. It has proved to be an excellent technique for managing chronic pain, particularly when standard treatment fails. However, it also is described as a coping mechanism and not a cure.

Hypnosis has proved able to allow persons to gain insight into their experience, which is completely separate from conscious awareness. Hence, it can be viewed as enabling unconscious awareness. It has been applied successfully to dealing with fear of flying, decreasing drug dependence for chronic pain, lowering dosages of analgesics and anesthetics, influencing the immune system, promoting healing, and regulating addictions.

A form of self-hypnosis referred to as *autogenic training* has been used by itself or in conjunction with biofeedback to induce relaxation in individuals. It has been in use for at least 60 years and was introduced by a German psychiatrist, Johannes Schultz. He studied how hypnosis affected the brain, nervous system, and the body and through experimentation was able to develop a series of exercises that led to the ability of patients to self-induce deep relaxation.

Considerable disagreement exists over how autogenic training works, but brain-wave changes and related physiological effects reveal that it somehow modifies the bodily response to acute stress. Perhaps it reduces stimuli from reaching regions of the brain under autonomic control. This form of self-hypnosis has been applied in helping to control anxieties, depression, allergies, and migraine headaches.

A recent review of the medical literature reveals numerous references to the application of hypnosis in several kinds of medical problems. Some of these include the potential usefulness of

hypnosis for reducing hot flashes in breast cancer survivors, a systematic review of psychological therapies for nonulcer dsypepsia, psychological treatments for posttraumatic stress disorder, usefulness in treating nocturnal enuresis, management of labor pain during childbirth, reduction of procedural pain and distress in pediatric oncology, childhood habit cough, applying hypnosis in dermatology (eg, urticaria) general management in pain, usefulness in smoking cessation, and helping diminish anxiety and pain. Many of these articles are positive in nature but universally call for more clinically relevant studies. Admittedly, clinical double-blind cross-over studies involving hypnosis maybe difficult or impossible to conduct.

IRIDOLOGY

This is a system that attempts to correlate changes in the texture and color of the iris with various mental and physical illnesses. Practitioners further claim that iridology may identify dietary deficiencies and even locate accumulation of toxic substances in the body. The concept was devised by Ignatz von Peczely, a Hungarian physician of the 19th century. It was further developed by Bernard Jensen, an American chiropractor in the 1950s.

These practitioners divided the iris into six zones or concentric rings that they related to the body's systems. For example, the innermost zone related to the stomach, the next to the intestines, the third to the lymph and blood systems, the fourth to glands and organs, the fifth to skeleton and muscles, and the sixth to skin and elimination.

By attempting to *read* the degrees of light and darkness in the iris, clues could be obtained regarding a patient's health. While conventional medicine does examine the eyes for diagnostic reasons, the iridology procedures have not been widely accepted medically. Most orthodox physicians reject the theory that the iris can be used to give reliable and extensive information about the status of health or disease.

Relatively few legitimate medical articles exist on iridology based on a recent literature review. Almost all place this purported diagnostic procedure in the unproven category. One review by E. Ernst at the University of Exeter, UK., undertook a systematic review of all interpretable tests of the validity of iridology as a diagnostic tool and found it wanting. Three independent literature searches were performed to identify all blinded tests. The data were extracted in a predefined, standardized fashion. They found four case-control studies, the majority of which suggested that iridology is not a valid diagnostic method. They reported that patients and therapists should be discouraged from using this procedure. Several other studies have come to the same conclusions.

MANUAL HEALING—MASSAGE/BODYWORK

Manual healing is synonymous with the terms bodywork and massage. Therapeutic massage methods used by therapists today originate from Eastern and Western traditions. The Eastern traditions can be traced back to the folk medicine of China and the Ayurvedic medicine of India (1000 BCE). Western traditions can be traced back to Hippocrates, the ancient Greek physician, who wrote, "the physician must be experienced in many things, but most assuredly in rubbing. For rubbing can bind a joint that is too loose, and loose a joint that is too tight."

There are three main premises or paradigms that underlie these therapies, namely, relaxation, remediation, and holistic modifications. Relaxation is based on the well-documented human biological need for nonthreatening, nurturing touch, relaxing, pleasurable, sensual (not sexual), and stress-reducing. Remediation encompasses all of the hands-on healing approaches that seek the correction of dysfunction and alleviation of pain. Skills in assessment and evaluation of the patient's condition are applied to relaxation principles. The holistic paradigm considers enhancing the body/mind/spirit's natural tendency to seek a higher order of functioning and well-being. Although these paradigms are distinct, they often overlap in practice. The massage/bodywork approaches can be divided into five categories:

1. Traditional massage.
2. Contemporary Western massage/bodywork.
3. Structural/functional/movement integration.
4. Oriental bodywork.
5. Energetic bodywork.

Before discussing specific examples of these practices, it is important to understand the regulatory systems that apply to massage/bodywork in the US. The Commission on Massage Therapy Accreditation (COMTA) sets the curriculum requirements for quality education and training of therapists. Minimum requirements include 500 hr of in-class supervised instruction; 100 hr of anatomy and physiology; 300 hr of massage theory, technique, and practice; 100 hr of instruction covering contraindications, business practice, history, ethics, and legalities; and successful completion of first aid and CPR training. In 1992, a national certification program for the broad range of massage/bodywork therapists was established. The National Certification Board for Therapeutic Massage and Bodywork (NCBTMB) awards this certification after the candidate passes the National Certification examination process.

The American Massage Therapy Association (AMTA) supported the creation of the NCBTMB and is the oldest and largest international member-driven organization representing the massage/bodywork therapy profession. It was founded in 1943 and in 1998 had nearly 24,000 members in over 20 different countries, with chapters in all 50 states, the District of Columbia, and the US Virgin Inlands. The COMTA was established to uphold AMTA's principles of ethics and professionalism in all phases of career training and professional development.

Government regulation of massage/bodywork varies widely from state to state; however, states are increasingly awarding licensure to practitioners who successfully complete a COMTA-accredited program and have attained National Certification from the NCBTMB.

A brief review of the current medical literature of the past few years reveals literally hundreds of articles dealing with the successful application of various types of massage in numerous medical conditions including muscle problems, body pain in the elderly, massage as an adjunct to analgesics in cancer treatment, asthma and allergy, dermatitis, labor pain, tennis elbow, depression, excessive exertion, and pediatric conditions. Few if any of these are done in clinical and double blind types of studies.

SPECIFIC THERAPEUTIC CATEGORIES

Traditional Massage

This is a form of bodywork that uses five basic strokes (effleurage/stroking, petrissage/kneading, friction, tapontemont/tapping, and vibration), developed by Johann Metzger of Amsterdam in the late 19th century. In the US this work was merged with Pehr Heinrik Ling's along with several adjunct modalities to become the well-known *Swedish massage* of the 20th century. This massage primarily works on the soft tissue and more-superficial layers of the muscles and implements active and passive movements of the joints. It promotes deep relaxation, which reduces tension, stress, spasm, and pain; soothes injured muscles; and stimulates blood and lymphatic circulation.

Sports massage therapy uses Swedish massage techniques as a supplement to the athlete's warmup routine by enhancing circulation and reducing excess muscle and mental tension before competition. Postevent massage is geared toward reducing the trauma that occurs after the cessation of vigorous exercise and can help break up scar tissue and lessen fibrosis and adhesion that develops as a result of injury and immobilization.

The Touch Research Institute at the University of Miami School of Medicine has established formal review of studies sup-

porting the positive effects of massage on anorexia, lower back pain, hypertension, migraine headache, multiple sclerosis, premenstrual symptoms, burns, infant health, and sleep disorders.

Contemporary Western Massage/Bodyworks

This system uses a wide variety of manipulative techniques. The approach is based on the Western sciences of neuromuscular massage, myofacial release, and positional release to relieve somatic pain or dysfunction. They are distinguished from the next category reviewed because emphasis is placed more on the patients' affected part(s) or symptoms rather than on the whole person. Myotherapy is an example of this kind of therapy. Myotherapy (Trigger Point Therapy) is a technique popularized by physical fitness and exercise expert Bonnie Prudden. It was developed by Dr. Janet Travell (Myotherapy, 2 vols.by Travell & Simons). Trigger points are tender or irritable spots in the muscles that produce pain in the body directly or indirectly (referred pain). Muscles pick up trigger points or become *armored* when the body encounters a traumatic event. The practitioner identifies trigger points by taking a detailed history of the patient's birth and early childhood experiences, accidents, operations, occupations, and other life incidents that might have caused physical/emotional distress. After the point(s) is (are) identified and located, pressure and massage are applied to the point and surrounding area, and the patient also is assigned stretching exercises to retrain the muscles. This therapy can be considered for patients who have recurrent pain from injuries in the past, and it can decrease or eliminate the need for analgesics.

Structural/Functional/Movement Integration Practitioners

These practitioners use a wide variety of manipulative techniques. Alexander Technique, Feldenkrais methods, Rubenfeld Synergy Method, Rosen method, and Trager Method feature movement to affect physiological structure and function along with education and awareness to change or enhance physiological functioning. Practices such as Rolfing use pressure or deep friction to alter the muscular and soft tissue structures. Breathing and emotional expression also are used to eliminate tension and change physiological functioning.

Frederick Matthias Alexander (a Shakespearean actor) developed his therapy by correcting periodic losses of his own voice. Experiments conducted by Frank Pierce Jones at Tufts University concluded that Alexander's methods effectively could interrupt or inhibit habitual and learned responses in body posture that interfere with proper body functioning. The practice restores poor or inhibited use of the body contributing to diseases including debilitation curvatures of the spine, rheumatism, arthritis, and a variety of GI and breathing disorders.

Moche Feldenkrais, a Russian-born Israeli physicist, like Alexander, developed his program by healing himself of a sports-related injury. He applied his experience of martial arts, physiology, anatomy, psychology, and neurology to develop two approaches: Awareness through Movement, which implements group awareness, and Functional Integration, which focuses on individualized hands-on touch and movement. The methods are useful for those who have limitations of movement brought on by stress, accidents, back problems, and other physically debilitating diseases. Performers and athletes use Feldenkrais to improve their level of performance and for enhanced personal growth.

The Ilana Rubenfeld (former musician and conductor) technique is a mixture of Alexander, Feldenkrais, and Gestalt psychotherapy. She combined gentle touch coupled with subtle movements and adjustments and emotional relaxation to achieve results. A caring presence that helps clients tap long-repressed memories and express deep feelings helps them release tensions and achieve physical comfort.

In the Rosen method, the practitioner focuses on gentle and deep pressure to relax the client. By paying attention to what is said and felt during the session, the practitioner helps the person deal with any repressed feelings and ultimately brings them relief.

The *light-touch* approach of Milton Trager, MD, in the Trager Psychophysical Integration Technique, pays attention to the subconscious roots of muscle weakness or tension. This school of thought believes that everyone develops mental and physical patterns that may limit movement or lead to pain and tension. Typical sessions include gentle, rhythmic rocking and other movements to teach the client that free movement and relaxation are possible and to promote a sensation of lightness, looseness, and well-being. Simple exercise *(mentastics)* performed at home helps clients to maintain good health through integrated and coordinated movements.

Bioenergetics was developed by psychiatrist Alexander Lowen, who was strongly influenced by Wilhelm Reich, MD, who coined the term *body armor*. The therapy is based on the idea that rigidity and tension in the body (body armor) leads to psychological problems or *vice versa*. Sessions involve a variety of positions that allow detection of tension areas. These then are relieved by a combination of talk therapy, deep breathing, massage, and bioenergetic exercises. When appropriate, the clients are allowed to kick, scream, strike objects, etc, to relieve tension. Hence, persons who react to life's various traumas by developing a tension pattern early in their lives, which leads to physical conditions such as ulcers, colitis, or arthritis, may be helped by this technique.

Rolfing, also called structural integration, was developed by Ida Rolf, who was a PhD biochemist from Columbia University. The technique involves applying deep, hands-on pressure to loosen the fascia (connective tissue surrounding and penetrating the muscles), thereby enabling the body to properly restructure itself. This intense and usually painful bodywork loosens the tightened muscles that serve to form a wall (armoring) protecting the patient from remembering painful life experiences. Some patients use Rolfing as an adjunct to psychotherapy, as a way to work with their bodies as well as their emotions.

Oriental Body Work

This comprises all the different styles of Oriental body work, originally developed throughout Asia. Shiatsu is an example of this kind of therapy. Reflexology is derived from oriental body work philosophy. Shiatsu, or Japanese acupressure, considers the client's symptoms as an expression of the condition of the whole person and focuses on relieving pain and discomfort by applying firm rhythmic pressure (usually with the fingers) on specific points along the meridians for 3 to 10 sec. Meridians are invisible channels of energy flow in the body, and the technique is designed to awaken the meridians. Once the proper energy flow is restored the body can function normally, and tensions and toxicities can be eliminated before they develop into illnesses. Acupressure massage techniques and practices also use rubbing, kneading, percussion, and vibration to improve circulation and to stimulate stale blood and lymph from tissues. Many books are available on self-acupressure techniques for the treatment of a variety of complaints. A popular item found in many stores today, including pharmacies, is a bracelet that fits over the acupressure points for the treatment of nausea.

Reflexology is an American refinement of Oriental wisdom. Dr William Fitzgerald first introduced the concept of Reflexology as Zone Therapy in 1913, and it was further refined in the 1940s by Eunice Ingham. The technique consists of stroking and applying gentle pressure to the feet (sometimes hands) to effect changes in other parts of the body, relax muscles, and stimulate the body's own natural ability to heal itself. Each part of the foot corresponds to different parts of the body. For example, the toes relate to the head and neck, the arch to the internal organs, the ball of the foot to the lungs and chest, and the heel to the pelvic

area and sciatic nerve. Theoretically, reflexology stimulates sensory receptors in the nerve fibers of the foot, which produces energy (Indian *prana* or Chinese *qi*) that travels to the spinal cord from which it is dispersed throughout the nervous system. Other theories hold that the procedure relaxes the body and lessens any constricted blood vessels to improve circulation. Reflexology has been applied to the treatment of chronic conditions such as asthma, headaches/migraines, hypertension, constipation, sinus trouble, and stress/anxiety. Elaborate procedures by various practitioners are available, as well as self-reflexology or foot/hand massage.

Energetic Bodywork

This is represented by terms such as biofield, subtle energy, and energetic systems. These therapies help balance energy in the body and engender enhanced health and well-being. Therapeutic Touch and Reiki are well-known practices in America today. While many practitioners use these techniques free-standing, it is more common for therapists to incorporate this work into their massage or bodywork therapy. The idea behind energy work is that a life force flows through the body and psyche and can be redirected by various mind-body techniques. Therapeutic Touch, developed by Dolores Krieger, PhD, RN, and Dora Kunz is a contemporary application of many healing practices, such as visualization, laying on of hands, and aura therapy. With this method there is generally no physical contact between the client and practitioner. Therapists begin by entering a centered or calm state, then they place their hands 2 to 6 inches away from the client and with rhythmic and slow hand motions, detect blockages in the client's energy field. Once the blocked energy flow is detected, practitioners consciously direct or sensitively modulate human energies through their hands and balance any misalignment of the energy flow. The client may experience a range of experiences, from a discharge of previously suppressed emotions to a quiet, gentle sense of well-being. The technique primarily is known for its ability to relieve pain and reduce stress and anxiety. In Dr Krieger's latest book she also suggests that the practice may help reduce headache pain, calm crying babies, ease asthmatic breathing, reduce pain in postoperative patients, and reduce fever and inflammation.

Reiki is a Japanese word derived from *ray (divine wisdom)* and *ke (life force energy)*. The practice also is called Radiance Technique by the American International Reiki Association (AIRA), and this organization collects case studies to document uses and publishes a journal. According to Reiki philosophy, life-force energy is the essential source of direction and nourishment for the cells and organs of the body. Reiki practitioners can be trained to achieve proficiency at different levels. First-degree training or attunement is for physical healing, second degree is for mental healing, and higher levels (up to seven) allow the practitioner to heal at long distance. Imbalances in the living field of energy, or aura, are thought to be the cause of illness. As in Therapeutic Touch the practitioner does not make physical contact with the client. The therapist acts as a medium by channeling life-force energy through his or her hands at 12 positions on the body or within the aura of the client. Reiki proponents promote energy work as a complement to a long list of other traditional and modern health-care systems.

THE MIND-BODY CONNECTION

Almost all practitioners of medicine have acknowledged the importance of the mind and emotions in health. Only relatively recently, however, has research given us a glimpse of the possible mechanisms.

A whole new area of research has arisen that focuses on this, entitled psychoneuroimmunology (PNI). Basically, it is helping uncover the interconnecting neural pathways between the brain, and endocrine and immune systems. For the most part, it is accepted that molecular messages (hormones, etc) allow communication between cells of these organs. Their unique shape or chemical architecture determines their destination and function. They head toward another cell that has receptors (lock) uniquely shaped to accept them. As the agonist reaches the receptor, it binds with it and brings about a particular action.

Specifically, PNI researchers have located white blood cells that make hormones that fit receptors of certain brain cells. This may help the brain sense or detect infective organisms. The same biochemicals also may influence the mind by altering mood and behavior. Similarly, immune functions could be enhanced or depressed by variations in emotions. The major feature of understanding this process is the possibility that we may be able to gain conscious control over our own biochemistry. Already, it is accepted that people can deal with stress in constructive and even preventive ways.

Research has uncovered the fact that under long periods of stress, the adrenal glands increase the production of corticosteroids that are capable of depressing immune function. All of this can lead to a greater degree of vulnerability to illness. Many have learned how to mitigate these stress responses by using biofeedback, meditation, and related techniques.

Some investigators in PNI have speculated that because the brain and immune system possess a type of memory that can recall previous microbial encounters, it may be possible to tap into it as needed. Various procedures such as visualization, guided imagery, and self-hypnosis may allow this kind of conditioning.

In guided imagery, through suggestion or hypnosis, one is led to imagine a warrior leading an attack through the body to kill all of the diseased cells. There are over 15,000 cancer patients who have found solace in various free community wellness programs that have provided services that include new cancer therapies, seminars on nutrition, classes in guided imagery, and support groups. They provide no direct medical services, opting for the belief in fighting disease and freedom from stress through mental vigor and strength.

Some have thought that the well-known *placebo response* may be explained on this basis. Also, the widely recognized phenomenon of the *belief system* of the patient may play a part in the success or failure of medications, treatments, and other procedures used by health practitioners.

All of these may relate to PNI phenomena. All of these certainly recognize that heightened anxiety can lead to hypermotility in the intestine, ulcers, colitis, etc. Similarly, anger can raise blood pressure through the autonomic nervous system. Studies have revealed that depressed people are more vulnerable to physical ills than those who are not depressed.

Epidemiological data show that 5 years after a spouse dies, the death rates for widows and widowers are significantly greater than for those still married. Happily married women have a greater level of certain immune cells than unhappily married women. It has been shown that relaxation, exercise, and overall stress management can increase the number of T cells (up to 10%) in a group of men who have HIV.

A higher percentage of highly stressed than relaxed persons got sick when exposed to cold germs. This also may help to explain why laughter can mitigate an illness such as arthritis. It is part of the concept that positive thinking has medical power, as espoused by writers like Norman Cousins. Physicians in California such as Dr Dean Ornish have received grants from insurance companies to study how heart disease can be reversed through changes in diet and lifestyle (exercise, meditation, etc). Thus far, quite a good response has been elicited by these methods.

Many hospitals now are studying the relaxation response and Buddhist meditation to treat people with chronic pain, stress, and other related disorders. Similarly, transcendental meditation (TM) of the type espoused by Maharishi Mahesh Yogi has shown the ability to diminish stress and hypertension. Research in TM has demonstrated 56% lower hospitalization rates than normal for such treatments as reducing alcohol and drug abuse, diminishing muscle pain, and asthma attacks. Most major cities have programs (TM Centers) in leading hospitals.

In an overall summary of the strengths and weaknesses of mind/body therapies, one must keep in mind that while they generally may improve the quality of life and even prolong it, the right attitude cannot cure everything. Many people who have been taught that they can think themselves well may be prone to feeling like failures if the disease progresses. This can be a dreadful psychological burden. Nevertheless, sufficient successes, in many areas, promote the study and use of these methods.

NATUROPATHY

Natural therapies are the major modalities of general practitioners in the field of naturopathic medicine. There are three accredited colleges and a fourth which has candidate status in this discipline in the United States (Washington, Oregon, Arizona, Connecticut) today. Presently, 13 states (Alaska, Arizona, California, Connecticut, Hawaii, Kansas, Maine, Montana, New Hampshire, Oregon, Utah, Vermont, and Washington), as well as Washington DC, Puerto Rico, the Virgin Islands, and several Canadian provinces, license naturopaths. To obtain licensure, as a naturopathic physician (N.D.), the candidate must graduate from an accredited naturopathic college (4-5 year program) and pass a comprehensive physicians licensing examination (NPLEX). The scope of practice varies according to each state and some states (AZ, WA) even allow licensed naturopathic practitioners to prescribe allopathic medications with some restrictions.

Curricula in the graduate schools of naturopathy include medical training similar to MD's and OD's in the first two years. Botanical medicine, homeopathy, nutritional sciences, laboratory and clinical diagnosis, minor surgery, counseling, traditional Chinese medicine, and various aspects of physical medicine, eg, manipulative therapy, hydrotherapy, and physiotherapy are also included in the curriculum. Bastyr University also offers a program in Naturopathic Midwifery and this college as well as National College of Naturopathic Medicine and University of Bridgeport College of Naturopathic Medicine offers Master of Science in Acupuncture degree. The interested reader can find a chart comparing curricula of naturopathic medical schools with conventional schools of medicine on the American Association of Naturopathic Physicians web page. Generally, the NDs are trained as a primary care providers for all aspects of family health and wellness using diverse techniques that include modern and traditional scientific and empirical methods.

The dynamic philosophy of naturopathic medicine rests on six fundamental principles. The first involves the healing power of nature and a trust in the body's inherent wisdom to heal itself. Identifying and treating the causes of illness is a primary focal point and naturopaths are trained to look beyond the most apparent symptoms to find the underlying cause. Another important philosophy, one that naturopaths share with their allopathic medical colleagues, is to do no harm. Naturopaths strive to use the most natural, least invasive and toxic therapies in their management of patients. Naturopaths firmly believe that they are responsible for educating their patients to achieve and maintain health and spend considerable time to ensure this goal is met. Treating the whole person is a philosophy that allows the naturopath to view the body as an integrated whole in all its physical and spiritual dimensions. Finally, and most importantly, prevention of illness is the ultimate goal of every naturopath. With this philosophical base naturopathic physicians are unique in providing treatment and diagnosis that bridges both allopathic and natural medicine perspectives which combines scientific research with healing powers of nature.

Most allopaths criticize naturopathy as being overly vague with too much emphasis on nutritional counseling and untested herbal remedies. They simply feel that some of these modalities might be useful but really have not been subjected to modern scientific methods of experimentation and peer review. The naturopathic profession has recognized the need to answer these criticisms and over the past several years has increased their efforts to engage in science-based research. A review of NIH/NCCAM grants awarded in the last three years shows Bastyr University in particular has obtained several grants including most recently, a grant (North American Naturopathic Medical Research Consortium) to develop a research agenda for the naturopathic profession.

The American public continues to demonstrate a growing interest in preventing illness, and using more natural means to fight the illnesses they have developed. In the U.S. today there is perhaps no better-trained practitioner to meet his or her needs than a licensed naturopathic physician. The consumer and pharmacist should be cautious however because the term naturopathy is often used in association with practitioners who use natural healing methods and have not received the rigorous training of a licensed naturopathic physician. The consumer or pharmacist should check the credentials of a naturopathic physician before accepting treatment from them and can find listed practitioners in their area by checking the American Association of Naturopathic Physicians web site.

A brief review of the current literature through the Pubmed web site reveals a number of recent artistic dealing with naturopathy. These include its application in the treatment of menopausal symptoms, chronic facial pain, oncologists' and naturopath's nutrition beliefs and practices, the application of speleotherapy (the use of subterranean environments) as a therapeutic measure in the treatment of chronic obstructive airways diseases, various naturopathic procedures in German, Australia, and other countries, naturopathic applications in treating breast cancer, nutraceuticals in the management of cardiovascular diseases, cataract and naturopathic remedies, naturopathy applications in clinical practicing gynecology and obstetrics in Germany, the various naturopathic treatments for ear pain in children, the use of bioactive natural compounds for the treatment of gastrointestinal disorders, and a recent critical appraisal of naturopathy.

OZONE THERAPY

In recent years, various procedures for administering ozone have been promoted as treatments for cancer. So called, "optimal" techniques are applied via the exposure *ex vivo* of up to 300 mL of freshly drawn blood to a gas mixture of ozone and oxygen. This is followed by reinfusing this blood back into the patient. Various modes of action are claimed for support of ozone therapy in these treatments. For the most part, however, very few real rigorous clinical trials of the procedure exist. Among those which have been published, no good evidence of effect have been demonstrated. The proponents have played down any risks, yet some studies suggest serious complications, eg, hepatitis, and at least five fatalities have been reported. It is obvious that this procedure should be avoided until true safety and efficacy can been proven.

CONCLUSION: ATTITUDES AND CAVEATS

Some authors have listed over 50 common illnesses that may be alleviated by various natural therapies. Table 132-8 lists some of these along with their conventional treatments and alternative or complementary approaches to healing. But, before any of these are attempted, it is obviously important to obtain an accurate diagnosis of the problem by a qualified physician. Once this has been done, there should be an understanding of which method(s) may or may not really help, coupled with an involvement in the treatment selected. As discussed before, the belief-system of the patient is paramount in the success of most - management modalities. This is one of the major variables in any clinical double blind studies.

It is also imperative to know what constitutes an emergency problem, for which high-technology conventional medicine most likely will do the most good. These include moving-vehicle

Table 132-8. Various Illnesses and Treatment Options

ILLNESS	COMMON SENSE	CONVENTIONAL MEDICINE	ALTERNATIVE/COMPLEMENTARY MEDICINE
Acne	Keep face and hair clean. Use water-based cosmetics.	OTC agents, eg, benzoyl peroxide, tetracycline, isotretinoin.	Homeopathy, naturopathy, diet, shiatsu, vitamins and minerals
Allergies	Avoid allergic materials, *viz,* foods, plants, animals, drugs, dust, etc. Use air-conditioning dehumidifiers	Antihistamines, cromolyn sodium, steroids	Acupuncture, homeovitics, homeopathy, hypnotherapy, naturopathy, osteopathy, vitamins and minerals
Arthritis	Regular exercise. Warm baths	OTC acetaminophen, aspirin, ibuprofen	Acupuncture, bodywork, homeopathy, homeovitics, hypnotherapy, massage, naturopathy, yoga
Back pain	Practice good posture. Learn how to lift properly. Use firm seat with adequate back support. Rest	Exercises, corset or brace, surgery, drugs for pain relief and muscle relaxation.	Acupuncture, bodywork, chiropractic, homeopathy, massage, yoga
High blood pressure	Diet and exercise. Weight control. Low salt diet.	Antihypertensives (eg, beta-blockers, diuretics, calcium channel blockers)	Acupuncture, homeovitics, massage, naturopathy, shiatsu, yoga

accidents, shootings, explosions, severe trauma, burns, and broken bones and when heatstroke, poisoning, or related dramatic health-threatening events have occurred. Signs include difficult breathing, shortness of breath, severe wheezing, serious persistent diarrhea and/or vomiting, serious bleeding from any source, sudden strong pain in the chest or abdomen, rapid dizziness or vision impairment, loss of speech or slurred speech, and numbness or tingling in the extremities.

One should avoid self-diagnosis for any persistent problem. Often people try to treat bruises superficially when the real problem may be a broken bone. There are also warnings regarding adult's versus children's treatments. Healthy adults do have occasional diarrhea problems, but these can be serious for young children or the elderly, and appropriate treatments are needed. Similarly, pregnant and lactating women are more sensitive to drugs, herbals, certain foods, and certain alternative or complementary therapies. These all must be taken into account.

The Sep-Oct 1998 issue (updated periodically) of the *FDA Consumer* published an article entitled "An FDA Guide to Dietary Supplements," which provides background data on the 1994 DSHEA Act and FDA's current rules of regulation on these. Suggestions are provided for general safety and efficacy concerns; however, these are understandably incomplete because of the general lack of scientific knowledge about many of these products. Hence, it is important for consumers to do their homework on which CAM is appropriate, particularly in concert with an informed health professional. As mentioned earlier in this chapter, a number of important articles appeared during 1998–2004 that cover such areas as doubting the true existence of alternative medicine (Fontanarosa P *et al*) ; a national survey (US) focusing on the reasons for alternative medicine usage (Astin JA); *JAMA* publishing an entire issue on alternative medicine (Grady D); a new study on the growth of alternative medicine (Eisenberg D *et al*); and a review on cardiovascular herbs (Mashour N *et al*). There is little doubt that alternative medicine studies will continue unabated for some time yet, well into the next decade. A continued growing number of CAM sites on the Web has well attested to this fact and shows little sign of decreasing at this date.

Both conventional and alternative or complementary approaches to healing need to heed the following general guidelines:

Treat the whole person and not just the symptoms.
Promote preventative medicine, healthy lifestyle, and a wellness philosophy.
Gray areas in conventional medicine may be treated better by alternative or complementary medicine management.
Pay more attention to psychosocial and related disorders.
Give attention to personal factors and belief systems.
Most minor ailments are self-limiting. One out of three get relief in whatever they believe in.
Always be an active participant in the healing process (individual volition).
All natural products (plant- or animal-derived drugs) should be identified properly, standardized and analyzed, and appropriately dosed.
Both conventional and alternative or complementary medical practitioners should have open minds and cooperate in mutual research.

Finally, it is imperative that proper advice be given to patients seeking information on complementary and alternative medical therapies. Eisenberg (1998) has provided guidance on this matter by proposing a process for managing alternative therapy (after medical evaluation has been completed and conventional options have been offered), which includes a weekly plan coupled with patient monitoring over a 13-week time course. He also covers legal issues in alternative medicine (liability experience of alternative-care practitioners) and laws governing patient referral and delivery. Elion (1997) has published an article relating to the important issue of CAM and HIV infection. He concludes that the conventional scientific community harbors a significant prejudice against CAM, which limits the responsible evaluation of its safety and efficacy. His proposal here is focused on working toward an open scientific dialog that eventually will help solve such intractable disorders.

WEB SITES

[http://www.altmed.od.nih.gov/nccam]
HerbalGram [http://www.herbalgram.org/abcmission.html]
Herbnet [http://www.herbnet.con/associations.html]
Napralert [http://www.pmmp.uic.edu]
Herb Research Foundation [http://www.herbs.org]
Acupuncture [http://www.acupuncture.com]
Homeopathy [http://www.homeopathyhome.com]
Homeopathie Internationale, click on English icon on homepage [http://www.homeoint.org]
Homeopathic Educational Services [http://www.homeopathic.com]
http://onemedicine.com/aboutus/presummitsurvey.asp
http://www.chiro.org/alt.med_abstracts/index.shtml
http://www.mja.com.au/public/issues/170_02_15010/erns/ernst.html

ORGANIZATIONS

American Association of Oriental Medicine, Catasauqua, PA. Phone: 888-500-7999
American-International Reiki Association, 2201 Wilshire Boulevard, Suite 831, Santa Monica, CA 90403
American Massage Therapy Association, 820 Davis Street, Suite 100, Evanston, IL 60201

International Center for Reiki Training. Web site—http://www.reiki.org
National Certification Board for Therapeutic Massage and Bodywork, 8201 Greensboro Drive, Suite 300, McLean, VA 22102. Web site—http://www.ncbtmb.com
National Certification Commission for Acupuncture and Oriental Medicine, Washington, DC. Phone: 202-232-1404; Web site—http://www.nccaom.org
Touch Research Institute, University of Miami School of Medicine, Dept of Pediatrics, P.O. Box 016820, Miami, FL 33101. Web site—http://www.miami.edu/touch-research
National Center for Homeopathy, 801 N. Fairfax #306, Alexandria, VA 22314. Phone: 703-548-7790. Web site—http://www. homeopathic. org
American Association of Homeopathic Pharmacists, P.O. Box 80178, Valley forge, PA 19484. Phone: 610-735-5124. Web site—http://www.homeopathicpharmacy.org
American Association of Naturopathic Medical Colleges. Web site—http://www.aanmc.org
American Association of Naturopathic Physicians, 3201 New Mexico Avenue, NW Suite 350, Washington, DC 20016. Phone: 1-866-538-2267 (toll free). Web site—http://www.naturopathic.org.

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DEFINITIONS OF TERMS AND SPECIALITIES OF COMPLEMENTARY/ALTERNATIVE MEDICINE

Acupressure—The application of fingertip pressure on different parts of the body to treat specific symptoms or disorders.

Acupuncture—An ancient Chinese healing art that employs fine needles inserted at various locations (ca 2000) in the body to restore *the smooth flow of qi (energy).* Each location along a meridian is associated with specific organs, and every acupuncture point is considered to have a particular therapeutic effect.

Adaptogen—Agent (usually from plants such as ginseng) that helps or adapts the body or protects it from stress.

Allopathy—A system of medical treatment using remedies that produce effects upon the body differing from those produced by disease; now generally used to refer to standard or orthodox medical practice.

Alternative Medicine—Almost any form of therapy that is outside the purview of conventional modern medicine. Examples include homeopathy, chiropractic, and naturopathy. The name suggests a method other than the more conventional treatment.

Aromatherapy—The treatment of diseases through the use of various aromatic herbs, volatile oils, and similar preparations.

Ayurvedic Medicine—A system of medicine derived from an ancient Indian philosophy and the practice of which emphasizes the use of one's physical and mental abilities to achieve harmony with the environment. Therapy consists of maintaining a balance between diet, daily routine, and activities. Foods and herbs are used to modify these three basic life forces (doshas).

Belief-System—The belief or faith that the patient holds as his or her innermost cultural, spiritual, and psychological resource for healing. For modern man the healer may be a physician or priest, for Native Americans and Mexicans it is the *curandero* or *shaman,* for Alaskan Eskimos it is an *angakok,* and so forth. Each concept has its own specific practices that help the person with faith to be healed. The key to faith healing is belief. All healers must understand the patient-belief system, to achieve success in treating most disorders.

Bioenergetics—A combination of psychotherapy with bodywork (a wide range of massage-like therapies). It involves a combination of deep breathing, talk therapy, bioenergetic exercises, and massage to relieve tension and release confined emotions.

Chiropractic—A system of therapies based upon the theory that disease is caused by abnormal function of the nervous system. It attempts to restore normal function by manipulation and treatment of the structures of the body, especially those of the spinal column.

Colonic Irrigation—The flushing of the intestines with water or soapy solutions via a rectal enema for therapeutic, diagnostic, or nutritive purposes.

Complementary Medicine—This term often is used synonymously with alternative medicine. However, this name suggests that the procedures complement those that are considered to be conventional.

Faith Healing—The system or practice of treating disease by religious faith and prayer.

Folk Medicine—Therapy based on different cultures (eg, Indian folk medicine). It usually involves specific cultures, belief in chosen cures, and remedies based on plants, charms, and rituals unique to the specific folk culture.

Health Foods—Foods purported to be produced without the use of chemical fertilizers, herbicides, or pesticide sprays and sold without the addition of chemical additives (preservatives, fillers, artificial flavoring, or coloring agents). Many are claimed to be *natural* (ie, not containing added chemicals) and are purported to be healthier than the usual foods.

Herbs—Plants used for their medicinal, flavor, odor, or nutritive principles.

Holistic Medicine—Therapies that treat the whole person—mind and body—as opposed to just the part of the body where symptoms occur.

Homeopathy—A therapeutic method developed by Dr Samuel Hahnemann in the early 19th century. It clinically applies the law of Similar (like cures like) and uses medically active, potentized substances at weak or infinitesimal doses.

Homeovitics—A contemporary approach to homeopathy. It uses complex, pluralistic formulations in treating chronic diseases associated with toxicities by clearing, cellular detoxification, and regeneration.

Homeostasis—The maintenance of steady states (well or healthy states) in the organism by coordinated physiological processes.

Hypnosis—A state of altered consciousness, sleep, or trance induced artificially in a subject by means of verbal suggestion by the hypnotist or by the subject concentrating upon some object. The degree of hypnotic state may vary from mild, increased suggestibility to that comparable to surgical anesthesia.

Informed Skepticism—A stance in which one is kept informed about a new idea and doesn't necessarily believe it until it is proven scientifically.

Iridology—A diagnostic tool that purports to correlate changes in the color and texture of the iris with mental and physical disorders.

Macrobiotics—A branch of Zen philosophy that advocates a diet in which *Yin* (negative) and *Yang* (positive) foods are balanced to overcome disease and keep in good health. From the Greek roots *makros* (long) and *bios* (life). Certain foods are considered yin (eg, sugar or honey), while others are yang (eg, eggs or meat). Brown rice and other grains are in the middle, and diets are planned around these grains, with a balance of yin and yang foods accompanying them. Some food faddists have taken macrobiotics to an extreme, eliminating all foods except brown rice and thereby suffering nutritional deprivation.

Mind-Body Connection—Currently taken to refer to psychoneuroimmunology (PNI), the study of the connections between the brain and endocrine and immune neural pathway connections.

Naturopathy—Healing by the exclusive use of natural remedies (eg, light, heat, cold, water, vegetables, and fruits). No drugs or surgery are used.

Nutraceutical—The term used by some to promote health and healing through the use of foods as pharmaceuticals (eg, the increased consumption of garlic—allicin; ajoene—for antimicrobial, blood-thinning and cholesterol-lowering properties; or the cabbage-family members—indoles, beta-carbolenes—for anticancer properties, etc).

Natural—A method of healing or a product from natural sources used in medical treatment. A difficult term to define because it can mean different things to different people. See *Organic*.

Orthomolecular Medicine—The treatment or prevention of diseases by altering body concentrations of certain normally occurring substances (eg, vitamins) given in high doses.

Organic or Natural—In alternative medicine this usually means materials obtained from nature without the use of chemical fertilizers or pesticides.

Orthodox—Usually meaning the prevailing and most widely accepted procedures or medications.

Osteopathy—A school of healing that teaches that the body is a vital mechanical organism with coordinate and interdependent structural and functional integrity; the abnormality of either constitutes disease. It uses manipulation but also medicine, surgery, and other specialities.

Placebo Effect—A real physiological effect caused by an inactive drug.

Psychoneuroimmunology (PNI)—The newly emerging field of study that focuses on the series of neural pathways that interconnect the brain, endocrine, and immune systems. These pathways are felt to constitute a communications network between the mind and body that enables them to influence each other.

Quackery—The practice of medicine by a pretender to medical skill. Also referred to as a medical charlatan or quack.

Reflexology (Reflexotherapy)—Treatment by irritation of an area of the body distant from the lesion. It usually consists of using the hands to apply gentle pressure to the feet to ease pain, relieve tension, and restore energy. The term also can be applied to the technique of applying pressure to specific points on the hands and ears.

Risk/Benefit Ratio—Weighing the good effects of a drug or treatment against its bad effects.

Shamanism—In its potential medical applications, this term has been used to describe a way of achieving a kind of spiritual or emotional healing through the practice of ancient rituals (chanting, visualization, drumming). It has been used to treat pain, stress, anxiety, etc.

Shiatsu—A Japanese term for finger pressure or manual massage and pressure to stimulate and free energy pathways within the body.

Tea or Tisane—Any vegetable infusion or decoction used as a beverage.

Therapeutic Massage/Touch—A healing technique that combines traditional laying on of hands with certain Eastern theories of energy flow. It is based on the concept of unblocking *fields of energy* in the body to relieve pain or disease (backache, tension, headache).

Traditional Medicine—A term generally used to describe the native therapies of a certain region (eg, the traditional medicine of China) or the medical traditions of a particular culture.

Wellness—The concept of practicing all the things that keep one well. It involves maintaining good nutrition, exercise, stress-control, and good personal and familial social relationships.

CHAPTER 133

Chronic Wound Care

Mathew Thambi, PharmD, BCPS
Robert W Martin III, M.D.

The prevention and care of wounds are pertinent aspects of caring for patients in diverse settings including the disabled elderly at home, non-ambulatory hospitalized patients, and those who have undergone surgery. Unfortunately, wound care is often neglected in health care, but remains a unique area in which pharmacists can play a vital role in a multidisciplinary approach. Pharmacists can aid in the selection of cost-effective topical and systemic therapies and dressings and help maintain the vigilance that is required for preventing and treating wounds.

The provision of wound care incurs an excessive burden to society, the health care system, and its patients. With respect to chronic skin ulcers, currently it is estimated that there are 1.7 million patients with pressure ulcers, over 1 million with venous ulcers, and 0.6 million with diabetic ulcers.[1,2] Each of these wounds requires a great deal of time and finances to change dressings, apply topical therapies, and provide in-patient surgical and medical therapy as needed. In 1995, the cost of caring for diabetic lower extremity ulcers to the Medicare system accounted for $1.5 billion.[1] Chronic wounds have also been shown to reduce significantly the quality of life in affected patients.[3,4] Despite these figures, there remains a need for increased attention to the subject of wound care by the medical literature and clinicians.[5]

ASSESSMENT

There are several types of wounds (Table 133-1). The most common chronic wounds include pressure, vascular, and diabetic ulcers. Acute wounds include those caused by surgery, trauma, and burns and are beyond the scope of this chapter. Each assessment of a wound should include etiology, location, size, depth, duration, characteristics of surrounding tissue, color, viability, characteristics of any drainage or exudate, pain, and temperature.[6] Follow-up assessments should be performed frequently and systematically to determine the effects of any efforts that have been made. A validated, standardized monitoring form should be used for this purpose rather than attempting to rely on memory or inconsistent descriptions in the patients' charts.[7] Two popular monitoring forms for pressure ulcers can be adapted to monitor other wounds as well. These are the Pressure Sore Status Tool (PSST) and the Pressure Ulcer Scale for Healing (PUSH).[8,9] Photographs of the wound adjacent to a ruler showing its size can also facilitate documentation of the wound healing process.

CHRONIC WOUND MANAGEMENT BY WOUND TYPE

Pressure Ulcers

Pressure ulcers were first described in 1593, by Fabricius Hildanus.[10] A pressure ulcer is an area of localized tissue destruction caused by the compression of the skin over a bony site for a prolonged duration. This compression interferes with tissue blood supply, leading to tissue anoxia and eventually cell death.[11] The incidence of pressure ulcers varies widely from 0.4% to 38.0% in hospitals to 2.2% to 23.9% in long-term care settings, each with an estimated cost of treatment of $500 to $40,000.[12] Pressure ulcers have also been associated with a four-fold increase in mortality in the geriatric population and can lead to pain, osteomyelitis, and sepsis.[13–15]

Because pressure ulcers are often considered preventable wounds, their development is increasingly used as an indicator of the quality of care that a patient receives from an institution.[12,16] Also, although sometimes unfair, the development or worsening of pressure ulcers can be viewed as neglect of the patient.[17] As a result, there is increased litigation related to failure to prevent the development or worsening of pressure ulcers.[18]

Pressure ulcers are classified according to the degree of tissue damage observed (Table 133-2) and can be first noticed in any of these stages. The tissue in the ulcer can range from viable tissue to nonviable or necrotic tissue.[11]

Pressure ulcers develop quickly in the presence of risk factors. Therefore, prevention is directed at avoiding, identifying, and reducing these factors as early as possible. Risk factors include immobility, incontinence, inadequate nutritional intake or absorption, reduced sensory perception, and diminished mental status. The Agency for Healthcare Research and Quality (AHRQ) recommends that a validated risk assessment tool, such as the Braden or Norton Scale, be used to encourage the routine, systematic assessment of these risks.[19]

The following have been adapted from the AHRQ guidelines for the prevention of pressure ulcers and should be implemented immediately in those with any risk factors.[7]

1. Any patient with a risk factor should undergo a daily systematic skin inspection with special attention to areas over bony prominences.
2. Frequent repositioning is a natural and an effective way of preventing pressure ulcers. Patients that are unable to reposition themselves adequately should be repositioned by nursing staff

Table 133-1. Types of Wounds

- Traumatic
  - Decubitus ulcers
  - Self-induced ulcers
    - Lesch-Nyhan Syndorme
    - Factitial
- Vasuclar
  - Venous
    - Stasis ulcers
    - Postphlebitic syndrome
    - Arterovenous shunts
  - Arterial
    - Large vessel
      - Ateriosclerosis obliterans
      - Thromoangitis obliterans
      - Temporal arteritis
      - Polyarteritis nodosum
    - Small vessel
      - Raynauds phenomenon
      - Vasculitis
        - Wegener's disease
        - Churg and Strauss disease
      - Atherosclerotic emboli
  - Hypertensive ulcers
- Neuropathic ulcers
  - Diabetes (Mal perforans of the sole)
  - Trigeminal Trophic syndrome
  - Spinal cord lesions
  - Neuropathies (variety of causes)
- Neoplasm
  - Basal cell cancer
  - Squamous cell cancer/ Keratoacanthoma
  - Melanoma
  - Cutaneous metastasis
  - Cutaneous lymphoma
- Autoimmune
  - Pyoderma gangrenosum
  - Crohn's disease of the skin
- Hematologic
  - Sickle cell disease
  - Thalessemia
- Infectious
  - Bacterial
    - Erytrhasma
    - Malignant pyoderma
    - Ecthyma gangrenosum of *Pseudomonas* spp
    - Anthrax
    - Tularemia
    - Blastomycosis-like pyoderma (staphylococcal)
  - Fungal/ Yeast
    - Blastomycosis
    - Sporotrichosis
    - Actinomycosis, Nnocardiosis
    - Candida Septicemia
  - Viral
    - Herpesvirus infection in the immunosuppressed patient
  - Protozoan infection
    - Leishmaniasis
    - Amebiasis
  - Mycobacterial infection (especially M. *marinum*)
- Spider bite with necrosis (especially brown recluse spider)
- Congenital/ Hereditary
  - Prolidase deficiency
  - Developmenta (congenital) sinus
  - Aplasia cutis congenital
  - Bart's syndrome
  - Focal dermal hypoplasia
- Panniculitis

every 2 hours. Physical rehabilitation is also an excellent method of promoting repositioning by the patients themselves.

3. Episodes of incontinence, perspiration, or wound drainage should be cleaned promptly due to the macerating effects of these wastes on healthy skin. Incontinence should also be treated appropriately and moisture absorbing adult diapers can be used to keep the skin dry. The patient's hygiene should be maintained with routine skin cleansing using a mild soap and minimal pressure.
4. Excessively dry skin should be treated with a moisturizer to prevent skin cracking.
5. A nutritional assessment of the patient's caloric, protein, and fat needs is required to help determine his/her risk of ulcer development.
6. To reduce the amount of friction and shear that occurs with movement, protective dressings, such as hydrocolloids, can be used on the elbows and heels. Oftentimes, when patients are sitting or have the heads of their beds elevated, they tend to slide slowly down their chair or bed. This sliding pulls at the skin and can lead to ulcer development. Maintaining the head of the bed as horizontal as possible will reduce these shear forces. Appropriate moving techniques that avoid dragging the patient across the bed linens will also reduce friction and shear injuries.
7. Pillows or foam can be used to relieve pressure on bony prominences from one another or from the bed. This is particularly important on the heels of immobile patients. A pillow under the lower leg can allow suspension of the heel. Foam heel protectors can also be used. For immobile patients at high risk, pressure reducing beds (eg, foam, air, gel, or water) should be used. Doughnut-type devices should not be used because evidence demonstrates that these are more likely to cause ulcers than prevent them.[20]
8. Spasticity, as it occurs in patients with spinal cord injury, causes shearing and increases the risk of pressure-ulcer development. Treatment includes administration of antispasmodics (eg, baclofen, benzodiazepines) to minimize spasms and decrease shearing.[11]

Once a pressure ulcer develops, the presence of necrotic tissue and infection must be managed as discussed under *General Treatment Considerations*. Preventive measures should also be continued to allow for healing of the pressure ulcer and to prevent the development of new pressure ulcers.

Vascular Ulcers

Vascular ulcers are divided into venous and arterial forms. Both forms occur primarily on the extremities, especially the legs.

VENOUS ULCERS

STASIS DERMATITIS/ STASIS ULCERS—Usually, venous ulcers develop over the inner ankle and are often associated with lower extremity edema that worsens with prolonged standing. They usually appear shallow, irregularly shaped, oozing, and bright red with granulation tissue. Unlike pressure and arterial ulcers, necrotic tissue is rarely present. In general, venous ulcers are much less painful than other types of ulcers but can vary widely in the degree of associated pain. The pathophysiology of these ulcers remains controversial but involves venous hypertension and dysfunction of venous valves.[21] This leads to an increased escape of fluid and various substances from capillaries into the interstitial space that eventually leads to tissue breakdown and ulcerations. Risk factors include the presence of obesity, edema, varicose veins, inactive or sedentary life-style, and a history of leg injury, phlebitis, or deep venous thrombosis. Reducing lower extremity edema is a mainstay of treating venous ulcers.[25]

The most noninvasive method of reducing edema is by supine leg elevation. The legs should be raised above the level of the heart several times a day for a total of 2 hours and during sleep. This relieves the swelling and venous hypertension that underlies the development and chronic nature of these ulcers. The time demands of this method make adherence difficult, especially in those patients with jobs that require prolonged periods of standing.[25]

Another option is compression therapy which is considered to be the standard of care for venous stasis ulcers by the United States Food and Drug Administration (FDA) because it has been shown to improve ulcer healing rates. Continued use after healing also prevents re-ulceration.[25] The methods of compres-

Table 133-2. Staging System and Nomenclature of Pressure Ulcers

STAGE	DEFINITION
I	The skin is intact but erythema, warmth, edema, induration, or hardness is present. In individuals with darker skin, erythema may present more discretely as subtle shades of red, blue, or purple.
II	The skin has been broken and may appear as an abrasion, blister, or shallow crater. Also referred to as a superficial ulcer.
III	There is a loss of skin at the wound site that may extend to, but not through, the fascia. This will appear as a deep crater.Also referred to as a partial-thickness ulcer.
IV	Full thickness skin loss with extensive destruction, tissue necrosis, or damage to muscle, bone, adipose, or supporting structures. Also referred to as a full-thickness ulcer.

Adapted from Bergsrtom N, Allman R, Alvarez OM, et al. Treatment of Pressure Ulcers. Clinical Practice Guideline, No. 15. AHRQ Publication No. 95-0652. Rockville, MD: U.S. Department of Health and Human Services, The Agency for Health Care Policy and Research; December 1994.

sion include inelastic, elastic, and sequential therapy.[27] The traditionally used inelastic bandage is the Unna boot, which is a type of cast. Before applying the boot, the local edema can be reduced by wrapping the foot in an elastic Ace bandage. When the swelling has been reduced as much as possible, layers of bandages are applied to the wound and foot. These bandages are moistened with zinc oxide and hardening compounds to harden the bandages into a cast or boot. As the edema begins to recur, the hard boot will compress the tissues at a pressure consistent with the degree of edema. The boot needs to be changed at least weekly or when drainage from the wound penetrates the boot. To keep the boot dry, patients will have to bathe rather than shower. So, if an Unna boot is to be used at home, it is important to determine whether the patient has a bath tub or shower stall. Elastic compression is achieved with elastic stockings that are applied like a sock or with bandages that are wrapped around the affected extremity. There are several types available that vary in size, area of coverage, and degree of compression. These should be washed and replaced as per the manufacturer instructions. Generally, sequential compression is used for prevention of deep vein thrombosis of the lower extremities. However, it is also used to reduce edema and heal chronic venous ulcers. It consists of a sleeve that is placed around the affected extremity that inflates in a sequential manner starting at the ankle and ending at the upper leg. Significant peripheral arterial disease is a contraindication to any type of compression therapy as this will worsen blood supply to already deficient tissues. Compression therapy can also exacerbate severe congestive heart failure by increasing preload pressures. Despite compression therapy, 30–60% of venous ulcers remain unhealed.[26–28]

An oral drug that has been studied for the treatment of venous ulcers is pentoxifylline. Pentoxifylline inhibits neutrophil adhesion, reduces the viscosity of blood by increasing the flexibility of erythrocytes, and has weak fibrinolytic activity. The largest randomized, placebo-controlled study to date included 200 subjects with "pure" venous ulcers that were confirmed to have venous disease without significant arterial disease.[29] Patients were treated until complete healing occurred or for 24 weeks, whichever happened first. The intervention consisted of pentoxifylline 400 mg by mouth three times daily or an identical placebo with both groups receiving compression therapy. Complete healing occurred in 64% of subjects receiving pentoxifylline and 53% of those receiving placebo. This difference was not statistically significant, but this could have been due to a lack of power.[30] Other, smaller trials yielded conflicting results. Therefore, a systematic review was performed to combine these results.[31] When only the outcome of "complete healing" was used, the relative risk of healing was significantly higher for the pentoxifylline treated group at 1.30 (CI 1.10–1.54). Side effects were uncommon and included gastrointestinal disturbances, dizziness, and headache. Pentoxifylline can be considered a safe and effective adjunct to compression therapy. Although cost-effectiveness studies are still required, its current role should be for chronic venous ulcers that fail to heal with compression therapy alone. The dose is 400 mg three times a day with meals. If gastrointestinal disturbances develop, the dose can be reduced to twice daily, although this may not be as effective. Pentoxifylline can increase levels of theophylline so theophylline levels should be closely monitored when these agents are taken together.[33]

ARTERIAL ULCERS, SMALL VESSEL ULCERS

ATHEROSCLEROSIS—Ischemic ulcers occur most often in elderly patients suffering from hyperlipidemia or diabetes mellitus. They are usually the result of atherosclerotic occlusion of arterial vessels in which cholesterol-containing plaques rupture and occlude vessels.[34] Even with excellent local care, frequently, an ischemic ulcer will not heal until surgical revascularization is accomplished.

Color duplex scanning of the arterial system or diagnostic arteriography may be necessary to define the underlying arterial abnormality. Angioplasty is the treatment of choice because bypass grafting in patients with ulcers carries an increased risk of wound or graft infection. For patients in whom angioplasty is not possible, some form of bypass operation, preferably using the saphenous vein, should be attempted.[35]

SMALL VESSEL VASCULITIS—The most common causes of vasculitic ulcers are rheumatoid arthritis, systemic lupus, and polyarteritis nodosa. The blood dyscrasias that most commonly lead to leg ulceration are sickle cell disease, thalassemia, thrombocythemia, and polycythemia rubra vera.[36]

HYPERTENSIVE ULCERS—Hypertensive ischemia due to high vascular resistance from arteriolar sclerosis results in interference with the compensatory relaxation that would normally occur distal to arterial narrowing resulting in poor tissue perfusion and subsequent ulcer formation. Clinically, a painful, lateral lower calf/ankle ulcer results in elderly women.[37]

Neuropathic Ulcers

DIABETIC FOOT ULCERS—Foot wounds are the most common cause of hospitalization for patients with diabetes.[38] A total of 15% of those with diabetes will develop a lower extremity ulcer at some time in their lives with 14–24% of them ultimately requiring an amputation.[39] Once diabetic foot ulcers develop, it can be very difficult for them to heal due to angiopathy, neuropathy, and immunopathy that frequently exist in these patients. Unfortunately, many of these ulcers progress toward the need for amputation. It is thought that relatively simple and inexpensive measures for ulcer prevention can reduce amputation rates by as much as 85%.[40]

As with pressure ulcers, it is important to determine first which diabetics are at higher risk for lower-extremity ulcers. Because foot ulcers precede most amputations in diabetics, the risk factors for foot ulcers are considered to be the same as those for leg amputations.[39,41]

The American Diabetes Association (ADA) stratifies patients with diabetes into high- and low-risk groups for diabetic foot ulcers. The presence of any of the following risk factors will place this patient type into the high risk group: loss of protective sensation (neuropathy), evidence of increased plantar pressure, limited joint mobility, peripheral vascular disease, current or past foot ulcer, bony deformity, or amputation. Those that are without any of these risk factors are classified as being at low risk. The ADA recommends that all patients with diabetes have a comprehensive annual examination of their feet along with extensive patient education. Those in the high-risk groups should be seen by a clinician every 3–6 months for the characteristic(s) that placed them at high risk.[39]

The following methods of preventing foot ulcers should be considered for all patients with diabetes.[39]

1. Lower extremity neuropathy is one of the most important predictors of ulcer formation and amputation.[42] Tight glycemic control has been shown to delay and reduce neuropathy significantly and should be attempted when appropriate.[43]
2. If neuropathy is present, plantar pressure should be reduced as much as possible with the use of shoes with cushioned soles or inserts and adequate room for the toes.
3. If bony deformities are present, such as bunions or Charcot foot, therapeutic footwear should be fitted by an expert.
4. Thickened, painful, mycotic, or ingrown toenails should be treated by a podiatrist.
5. Callus formation can increase plantar pressure and lead to ulcer formation. The use of shoes with cushioned soles or inserts can help prevent their formation. If significant calluses are present under the forefoot, debridement by a specialist can help relieve plantar pressure.
6. The risk of peripheral vascular disease can be reduced by the same methods of risk prevention as for cardiovascular disease (eg, smoking cessation, exercise, healthy diet, lipid management).

7. Patients with significant peripheral vascular disease should be seen by a vascular surgeon for possible medical, surgical, or radiographic intervention.
8. Skin should be kept supple with emollients, but these products should not be applied between the toes for fear of tissue breakdown.
9. Tinea pedis should be treated appropriately.
10. All patients should be educated on proper diabetic foot self-care (Table 133-3).

TRIGEMINAL TROPHIC SYNDROME—Trigeminal trophic syndrome is a rare complication of sensory denervation of the fifth cranial nerve caused by infarction, degeneration, tumor, or artificial destruction resulting in neurotrophic ulcerations of the nose and paranasal areas in elderly, mentally impaired women. Affected individuals usually have a prior history of trigeminal neuralgia and subsequent therapeutic intervention. There is a latent period of weeks to years between the initial trigeminal injury and the subsequent development of ulceration. The severity of the ulcer is directly proportional to the degree of analgesia in the corresponding area. Management is often unsuccessful. The use of protective devices, transcutaneous electrical stimulation, antibiotics, surgical repair, ipsilateral cervical sympathectomy, ionizing irradiation, analgesics, antihistamines, nerve blockade, iontophoresis have given variable results.[44,45]

Hematologic Ulcers

Patients with red blood cell membrane disorders or hemoglobinopathies (eg, sickle cell disease) have blood flow abnormalities due to erythrocyte sludging and resultant vascular occlusion and ulceration in 50–75% of patients with sickle cell disease.[46] Clinically, sickle cell leg ulcers occur as unilateral "punched out" medial malleoli ulceration in the second and third decades. Following healing of cutaneous ulcers, the tissue scarring impairs blood supply to the skin promoting ischemia, sickling, and recurrent ulceration with persistence for months to years. Management involves folate and zinc supplementation, hyperbaric oxygen therapy, or exchange transfusions.

Autoimmune Ulcers

PYODERMA GANGRENOSUM—Pyoderma gangrenosum is an autoimmune disease resulting in rapidly progressive ulcers. These begin as an innocuous pustule on a red base or as a red nodule rapidly (in a few days) enlarging to an ulcer with a liquefying center without eschar formation, a purple undermined boggy border, which may be covered by hemorrhagic blisters, and a peripheral red border. The lesions occur most commonly on the legs, although they may develop on virtually any part of the body. Approximately one-half of these patients will have an associated chronic inflammatory disease, such as rheumatoid arthritis, inflammatory bowel disease, chronic active hepatitis, sarcoid, a leukemia, myelofibrosis, or gammopathy. Systemic steroids are the mainstay of therapy and must be instituted rapidly and in very high doses. Other therapy that has been reported to be effective includes dapsone, cyclophosphamide, topical cromolyn sodium, minocycline intralesional steroids, clofazimine and cyclosporine.[47] Concomitant gentle debridement by daily whirlpool baths and silver sulfadiazine dressings are appropriate.

Table 133-3. Patient Education on the Prevention of Diabetic Foot Ulcers

1. Understand that damage that can cause foot ulcers may not be felt.
2. Maintain good foot hygiene by washing feet daily and drying them well.
3. Trim toenails regularly and file rough edges.
4. Do not soak feet for prolonged periods of time. This can lead to maceration of skin and increase susceptibility to damage.
5. Use skin moisturizers to avoid dryness and cracking of the skin; however, moisturizers should not routinely be used between the toes.
6. Select well-fitted socks and shoes and inspect shoes for foreign objects or irregularities before placing them on.
7. Avoid foot trauma by wearing proper footwear at all times.
8. Do not attempt to warm feet in hot water or next to radiators or space heaters.
9. Inspect feet daily including the plantar aspects and between the toes. Those unable to examine the soles of their feet should be taught how to use a mirror to do this. If loss of vision is significant, inspect feet by touch or ideally, have a caregiver visually inspect them.
10. Consult medical care in the presence of maceration, fissures, erythema, or edema.

Congenital/ Hereditary Syndromes with Ulceration of Skin

HYPOGONADISM—Hypogonadism secondary to pituitary abnormalities (ie, diabetes insipidus) or chromosomal defects (ie, Klinefelter's syndrome) has been associated with recurrent lower leg ulcerations.[48,49]

PROLIDASE DEFICIENCY—Prolidase deficiency is an autosomal recessive disease that results in distinct facial characteristics (ie, low hair line, frontal bossing, far apart eyes, narrow eyelid openings, tiny eyes, saddle nose, thick lips and high-arched palate), deafness, hyperextensible joints, protruding abdomen, mental retardation, short stature, and splenomegaly. Multiple, recurrent, chronic leg ulcers are a common finding. Prolidase deficiency should be suspected in patients who develop leg ulcerations at an early age and who have a family history of leg ulcers.[50]

LESCH-NYHAN SYNDROME—Lesch-Nyhan syndrome is a sex-linked recessive disorder characterized by aggressive self-mutilating behavior, apparent mental retardation, and spastic cerebral palsy. Following the eruption of teeth, the patients begin to bite themselves. Partial or total destruction of peri-oral tissues, particularly the lower lip, results. Partial or complete amputation of the fingers, nose, and tongue may also occur.[51] Decreased red blood cell hypoxanthine-guanine phosphoribosyltransferase activity confirms the diagnosis.

Neoplastic Ulcers

A variety of neoplasms can affect the skin. The possibility of malignancy, particularly in ulcers that do not heal after adequate treatment, should always be borne in mind. The most common malignancies are basal cell carcinoma, squamous cell carcinoma, and melanoma.[35] Although any site can be potentially affected, exposure of the extremities to the sun is commonly involved. The lesion presents as an asymptomatic ulcer with raised edges above the skin level. Pigmentation may indicate a melanoma. Raised pearly borders with overlying telangiectasias suggest basal cell carcinoma. A biopsy of the border of any non-healing ulcer should be obtained to rule out malignancy.

GENERAL TREATMENT CONSIDERATIONS

Although improving, evidence for therapies promoting wound healing or treating wound infections have been lacking. In 2001, the FDA Wound Healing Clinical Focus Group published "guidance" for future trials of new products in this field. An important aspect of this document was its description of appropriate outcomes for clinical trials. The document suggested that complete wound closure should be the primary

endpoint of most clinical trials investigating a product's ability to improve wound healing.[52]

Wounds with Necrotic Tissue

For reasons beyond the scope of this chapter, the tissues within several types of wounds can begin to die. These include pressure, diabetic foot, and vascular ulcers along with surgical and traumatic wounds. Eventually, the necrotic tissue can dry into black, hard, mummified tissue, called *eschar*, or moisten into a yellow, gray, or green, malodorous, stringy tissue, called *slough*. The presence of this necrotic tissue impedes the clinician's ability to assess the wound and can hinder the healing process significantly. It also provides a medium for bacterial growth that can spread infection to healthy adjacent tissues of the skin, bone, and blood. Ideally, for healing to progress and infection to be prevented, this dead tissue should be removed from the wound bed without damaging the underlying healthy tissue. This process of removal is called debridement. Debridement is the mainstay of managing chronic pressure, diabetic foot, and arterial ulcers and many non-healing surgical and traumatic wounds.[53]

There are several methods of debridement: sharp, mechanical, enzymatic, and autolytic. Methods that selectively remove devitalized tissue without affecting healthy tissue are preferred over nonselective techniques. Other criteria for selection include the desired speed of debridement, degree of associated pain, quantity of exudate, presence of infection, and cost.[54]

Sharp debridement should be performed by an experienced clinician in accordance to state practice laws. Sharp debridement involves the use of a scalpel or scissors to remove necrotic tissue. It is the fastest method of debridement and the method of choice when there is an urgent need to remove a source of infection (eg, advancing cellulites, sepsis).[54] A drawback of sharp debridement is the significant degree of pain it can cause. The associated pain can also limit the amount of necrotic tissue that can be removed before the pain becomes unbearable. When planning sharp debridement, especially at the bedside, clinicians should administer pain medications and allow sufficient time for the onset of pain relief before debridement is attempted. An agent with a fast onset and time-honored effectiveness is intravenous morphine. Usually, its duration of action lasts long enough to cover the painful post-debridement period. The dose will depend on the patient's degree of pain, prior opiate use, and level of tolerance. Repeated doses should be given as needed during the procedure. Sharp debridement should be used with caution in patients who are receiving an anticoagulant or have hemophilia.

Mechanical debridement of devitalized tissue is performed with wet-to-dry dressings, whirlpool, or pulsed lavage. The wet-to-dry dressings consist of applying wet gauze primary dressings to the wound and securing it in place with a dry secondary dressing for about 8 hours. After this time, the dressings are pulled from the wound along with the tissue that has dried and adhered to it. This can be a very painful process for patients and premedication as described for sharp debridement is required unless significant loss of sensation is present. It may be tempting to wet the dressing before removal but this will defeat the purpose of the dressing because the tissue will no longer be removed along with the dressing. Whirlpool debridement involves submerging the wounded anatomy in a whirlpool bath. This method combines soaking, mechanical debridement (from the water pressure), and heat to loosen and remove the tissue. Further, the heat is thought to promote blood flow to the wound to improve healing and reduce infection. This method is nonselective, time-consuming, and may increase the risk of waterborne infections with *Pseudomonas aeruginosa*.[55] Pulsed lavage involves irrigating the wound with pressurized water from a variety of devices including irrigation syringes, squeeze bottles, and shower heads. The pressure should be between 4 and 15 psi to effectively remove devitalized tissue while minimizing harm to healthy tissue.[19] All methods of mechanical debridement are nonselective and can remove healthy, healing tissue along with dead tissue. For this reason, these should be used only when attempting to remove infected tissue.

Enzymatic debriding ointments break down proteins, fibrin, elastin, and collagen within necrotic tissues. This helps to loosen and separate the devitalized tissue from the base of the wound for easier removal. This method is usually slower than sharp or mechanical debridement, but is selective for removing devitalized tissue. Enzymatic ointments can be applied as often as the dressing needs to be changed, generally once or twice a day.[56–58] When used for hard eschar, the eschar should be cross-hatched or scored with a scalpel before the agent is applied to allow deeper penetration of the enzymatic ointment. Despite this technique, enzymatic ointments do not work as well for hard eschar. The active ingredients of commercially available products in the US include papain, urea, and collagenase marketed in various combinations: papain and urea; papain, urea, and chlorophyllin; and collagenase (Table 133-4). For some products, chlorophyllin is added to reduce inflammation and odor. All of these agents, and even combination of agents, were developed in response to the great need for debriding agents during World War II with the first published study in 1940 by Glasser.[59,60] Unfortunately, no large, placebo-controlled clinical trials have been published on these agents to allow objective evaluation of their safety and effectiveness.[61] Patients should be warned that a transient burning sensation can occur with the application of these agents.

Autolytic debridement is a method of debridement that involves the application of an occlusive, moisture retentive dressing that takes advantage of the body's own enzymes to break down devitalized tissue. There are over 100 of these dressings available. To relieve confusion, these have been broadly subcategorized as transparent films, foams, hydrogels, hydrocolloids, alginates, and collagens (Table 133-5). Unfortunately, occlusive dressings are usually referred to in practice by their brand names, so it is important to know the brand names of each type used at one's institution (Table 133-6). These dressings keep wound fluid within the wound allowing the macrophages and neutrophils to digest necrotic tissue. In addition, these cover and protect the wound from bacteria and trauma. This tends to take the longest of the various methods of debridement. However, it is selective, non-invasive, painless, and less labor intensive than other methods. The dressing can also be left in place for several days as long as there is no leakage of wound fluid or infection. After the dressing is removed, the wound should be irrigated with normal saline to remove the liquefied, devitalized slough before the new dressing is applied. The disadvantages of this method include the time to achieve a clean wound, the associated foul odor, and unpleasant appearance of the slough when the dressing is removed. This malodorous slough is often mistaken as pus or infection, causing clinicians or patients sometimes to abandon this method prematurely. These dressings are also more expensive than traditional gauze dressings.

Some general considerations before selecting a dressing should be made as outlined by AHCPR guidelines. First, most wounds should be kept continuously moist. Wet-to-dry dressings with gauze are not considered moisture retaining dressings and

Table 133-4. Enzymatic Debriding Ointments

PRODUCTS	BRAND NAMES	COMPANY
Collagenase	Santyl	Smith & Nephew, Inc.
Papain-Urea	Accuzyme	Healthpoint
	Ethezyme	Ethex
	Kovia	Stratus Pharmaceuticals
Papain-Urea-Chlorophyllin	Panafil-	Healthpoint
	Panafil-White	Healthpoint
	Ziox	Stratus Pharmaceuticals

Table 133-5. General Characteristics of Wound Dressing by Category

	GAUZE	HYDROGELS	POLYURETHANE FOAMS	HYDROCOLLOIDS	ALGINATES	TRANSPARENT FILMS	COLLAGENS
Properties	• Permeable • Use for wet-to-dry mechanical debridement • Absorbent	• Available as a gel or impregnated dressing or sheet • Primarily composed of water • Some types are absorptive • Semi-permeable • Semi-occlusive	• Permeable to vapor • Semi-occlusive	• Impermeable to vapor • Occlusive • Forms a moist gel as it absorbs exudate • Waterproof	• Forms a moist gel when in contact with the wound • Very absorbent	• One side is adhesive • Impermeable to liquid • Permeable to vapor	• Derived from animal sources
Indications	• Moderate to heavy drainage • Infected wounds • As secondary dressings • As packing for tunneled wounds or sinuses	• Dry wounds • Stage II to IV pressure ulcers • Wounds with exposed bone, muscle, or tendon	• Mild to moderate drainage • Stage I to IV pressure ulcers • Deep cavity wounds	• Thin hydrocolloids: dry to light drainage • Thick hydrocolloids: moderate to heavy drainage • Stage I to IV pressure ulcers	• Heavy drainage • Wounds with exposed bone or tendon	• Dry to mild drainage • Stage I pressure ulcers • Lacerations • As secondary dressings • Prophylaxis for areas of high friction / shear forces	• Heavy drainage • Stage IV ulcers
Advantages	• Can be used with infected wounds	• Keep dry wounds moist • Non-irritating upon removal	• Absorptive • Easy to apply and remove • Conforms to the contour of the anatomy	• Self-adhesive • Absorbent • Minimal irritation upon removal • Conforms to the contours of the anatomy	• Permeable • Non-occlusive • Highly absorbent • Conforms to the contours of the anatomy	• Allows visibility of the wound without removal • Reduces infection rates	• Promotes deposition of collagen and granulation tissue
Disadvantages	• Can damage healthy tissue and cause pain upon removal	• Most require secondary dressings	• Require secondary dressings	• Can only be used for smaller wounds in which one piece can cover	• Require secondary dressings to secure • Can be drying if low volume of drainage present	• Not absorbent • Have the potential of causing skin tears if removed improperly	• High cost • Current evidence does not show benefit over hydrocolloids for stage II and III pressure ulcers
Contraindications	• Do not use for healthy, granulating wounds • Wounds with exposed bone or tendon		• Wounds with exposed muscle, tendon, or bone		• Dry eschar	• Fragile skin	• Allergy to bovine products

Data from Lyder CH. Pressure ulcer prevention and management. *JAMA* 2003; 289(2):223; Wound Care Information Network. Available at: http://www.medicaledu.com. Accessed July 23, 2003; Helfman T, Ovington L, Falanga V. Occlusive dressing and wound healing. *Clin Dermatol* 1994;12:121; Fleck CA. Wound care dressings. *Extended Care Product News* 2002; 6;4–7.

Table 133-6. Trade Names of Occlusive Dressings

TRANSPARENT FILMS	COMPANY
Acu-Derm	Acme United
Bioclusive	Johnson & Johnson
Blister Film	Tyco Healthcare / Kendall
CarraFilm	Carrington
Hi / Moist Transparent	Catalina Biomedical
Omniderm	Doak
Opsite	Smith & Nephew United
Polyskin II	Tyco Healthcare / Kendall
SureSite	Medline Industries
Tegaderm	3M
Transite Exudate Transfer Film	Smith & Nephew United
Transparent Adhesive	Baxter Healthcare
Uniflex	Smith & Nephew United
Vari / Moist Modifiable	Catalina Biomedical
Visi Derm II by Medline	WTS

FOAMS	COMPANY
Allevyn Hydrophilic Polymer	Smith & Nephew United
Biopatch	Beiersdorf
Cutinova Plus Foam Gel Film	Beiersdorf
Epi-Lock Synthetic	Calgon Vestal
Flexzan	Convatec
Hydrasorb	Convatec
Lyofoam	Ferris
Mitraflex Dressing with Adhesive	Calgon Vestal

GELS AND HYDROGELS	COMPANY
Biolex Wound Gel	Catalina Biomedical
Carrasyn	Carrington
Carrington Wound Dressing Gel	Carrington
Clearsite by NDM	WTS
Elasto-Gel	Southwest Tech
Flexderm	Dow B. Hickam
Intrasite Gel Hydrogel	Smith & Nephew
Nu-Gel	Johnson & Johnson
Replicare hydrocolloid	Smith & Nephew
Restore	Hollister
Saf-Gel	Convatec
2nd Skin Dressing	Spenso
SoloSite	Smith & Nephew
Tegagel	3M
TenderWet	Medline Industries, Inc.
TransiGel	Smith & Nephew
Vigilon	Bard Home Health

HYDROCOLLOIDS	COMPANY
CombiDerm ACD	Convatec
Comfeel Ulcer Care Dressing	Coloplast Inc
Cutinova Hydro	Beiersdorf Inc
Duoderm	Convatec
Exuderm	Medline
Hydrapad	Beiersdorf Inc
Hydrocol	Bertek
Intact	Baxter Healthcare
Intrasite Wound Dressing	Smith & Nephew, Inc.
J & J Ulcer Dressing	Johnson & Johnson
Orahesive	Convatec
Replicare	Smith & Nephew
Restore Wound Care Dressing	Hollister Inc
SignaDress Sterile	Convatec
Sween-A-Peel	Sween Corporation
Tegasorb Ulcer Dressing	3M
Triad	Coloplast
Ultec	Tyco Healthcare / Kendall

CALCIUM ALGINATES	COMPANY
Algisite M	Smith & Nephew
Algosteril	Johnson & Johnson
Curasorb	Tyco Healthcare / Kendall
Fibracol Collagen	Johnson & Johnson
Kaltostat	Convatec
Sorbsan Absorbent	Dow B. Hickam
Tegagen HI	3M
Ultec Pro	Tyco Healthcare / Kendall

COLLAGENS	COMPANY
Fibracol Plus	Johnson & Johnson
Promogran	Johnson & Johnson

SILVER DRESSINGS	COMPANY
Arglaes Film and Powder	Medline Industries
SilvaSorb Sustained Release Super Absorbent	
Acticoat	Smith & Nephew

ODOR ABSORBERS	COMPANY
Actisorb Plus	Johnson & Johnson
Carboflex	Convatec
Carbonet	Smith & Nephew

Data from Postsurgical wound care. U.S. Pharmacist Continuing Education. January, 2002; and Wound Care Information Network. Available at: http://www.medicaledu.com. Accessed July 23, 2003.

act by mechanical debridement rather than autolytic.[62] Second, studies do not demonstrate any significant differences among various non-gauze dressings in clinical outcomes.[19,63–65] Clinical judgment should be used to select them (see Table 133-5). Third, the dressing should keep the tissue surrounding the wound dry to avoid maceration. Wounds with excess exudate should be dressed with absorptive dressings to prevent "spilling over." Fourth, dressings should be easy to apply and should remain in place once applied. Fifth, wounds that track or tunnel into tissues causing cavities should be packed with dressings to avoid premature closure and abscess formation.[19]

If autolytic debridement is selected as a method of debridement, the specific dressing category should be based on the stage of the ulcer, amount of drainage (ie, exudate), presence of infection, and cost (see Table 133-5). For wounds that generate copious amounts of exudate, a highly absorbent dressing should be used including thick hydrocolloids or alginates. For mild to moderately draining wounds, hydrocolloid, hydrogel or foam dressings can be used. Dry or minimally draining, superficial wounds, can be dressed with transparent film or thin hydrocolloid dressings. For wounds that extend to underlying tissues, such as muscle, tendon, or bone, it is important to prevent desiccation of these tissues with a dressing, such as a hydrogel, that will assuredly maintain a moist wound environment. Although collagen dressings are generally the most expensive type, they have not been proven to be superior. Each dressing is different and once a general category is selected, product information and cost of individual dressings within the selected category should be compared.

Another method of debridement is the application of sterile maggots, or *Lucilia sericata*, to the wound that will selectively digest necrotic tissue. Their benefits have been anecdotally published; it may be the fastest method of debridement after that of the scalpel. The main disadvantages are the high cost and the sensation felt by the movement of the maggots.[66,67]

Infection

All open wounds are colonized by bacteria from the surrounding environment. The presence of foul odor, purulence, or surrounding cellulitis are strong indicators of infection and should be treated with antibiotics. Appropriate systemic antibiotics should be used for immunocompromised or diabetic patients or patients that have cellulitis or systemic signs of infection (eg, fever, leukocytosis, tachycardia, hypotension). Oth-

erwise, infections that are localized can be treated with topical antibiotics. In addition, infected wounds should be debrided of necrotic tissues that serve as reservoirs for bacterial growth. As described earlier, debridement can be accomplished by mechanical means except when associated with advancing cellulitis or sepsis when sharp debridement should be performed.

When obvious signs of infection are not present, the distinction between colonization and infection is difficult and controversial. Culturing swabs of an open wound is not recommended because this may represent superficial bacteria that are not invading the tissues. Also, the presence of slough in the wound can mimic that of purulent, infected tissue making it difficult to determine visually whether infection is present. To address this problem, recommendations are based on the principle that the greater the quantity of bacteria within the wound, the more likely the bacteria are to invade tissues and inhibit wound healing. The AHCPR recommends that if topical, broad-spectrum antibiotics (ie, silver sulfadiazine, triple antibiotic ointment) fail to reduce exudate or improve healing, quantitative cultures of a soft tissue biopsy should be performed. A quantitative culture with a bacterial count greater than 100,000 (10^5) organisms per gram of tissue (or mL of exudate) was defined as being sufficient enough to inhibit wound healing.[68] These wounds should probably be treated with systemic antibiotics. The AHCPR also recommends avoiding the use of topical antiseptics to reduce the bacterial burden of a wound due to the toxic effects of these substances on wound-healing cells.[19]

Nutrition

Nutrition plays a role in preventing wounds and healing existing wounds. A nutritional assessment, mentioned earlier in this textbook (ie, Chapter 107), should be performed routinely in patients that are at risk for wounds (eg, pressure ulcers, elective surgery) or who have existing wounds (eg, postoperative, traumatic, ulcers).

Malnutrition, as determined by nutritional parameters, is associated consistently with the development of pressure ulcers. These nutritional parameters include low body mass index,[69] recent weight loss,[70,71] reduced anthropometric measures, dehydration,[58] low prealbumin,[59] low albumin (<3.5),[72] reduced appetite,[73] lymphopenia ($<1.50 \times 10^9$/L),[60] and low dietary intake.[74,75]

Supplemental nutrition consists of nutrient-rich fluids given orally, enterally, or parenterally in addition to meals (see Chapter 107 for further discussion). Because malnutrition is associated with pressure ulcer development, it is tempting to assume that providing supplemental nutrition to malnourished patients would reduce the rate of pressure ulcer development or improve their healing rates. However, the published randomized, clinical trials to date show no benefit of supplemental nutrition on the prevention or healing of wounds to balance the risks inherent to supplemental nutrition (reviewed elsewhere in this text).[76–82] It is unknown whether this is due to limited sample sizes of the studies or a lack of effect. It should be kept in mind that supplemental nutrition could even worsen wound care in incontinent patients by increasing urine and fecal output. These issues will remain until larger, well-randomized, comparative trials are conducted.

In the absence of firm evidence for or against supplemental nutrition, most clinicians will encourage and request assisted oral intake in nutritionally deficient patients. It is oftentimes possible to increase intake by determining from the patient and his/her family what foods the patient prefers. If these are not available at the institution, family members should be allowed to bring outside food to the patient. Also, dividing meals into smaller, more frequent schedules can allow better tolerance of them. In those who are unable to eat, supplemental nutritional should be based on the risks and benefits unrelated to wound care. The patient and family should be included in this decision.[83,84]

Growth Factors

Growth factors are proteins excreted from platelets, macrophages, fibroblasts, and endothelial cells that orchestrate a complex series of events involved in healing. There have been many attempts to synthesize these growth factors to promote healing.[85] The only approved growth factor to date, however, is becaplermin, a recombinant human platelet-derived growth factor BB (PDGF-BB). It was approved in December 1997 for the treatment of non-ischemic diabetic ulcers that extend into or past the subcutaneous tissue.[86] Becaplermin is thought to promote the chemotaxis and proliferation of cells involved in wound healing and the formation of granulation tissue. The largest study published to date of the approved strength of becaplermin for use on diabetic ulcers was a randomized, double-blind, placebo-controlled, clinical trial.[87] The primary end point was the proportion of subjects with complete wound healing within the 20-week treatment period. Patients were randomized to beclapermin 30 mcg/g, 100 mcg/g, or placebo with 127, 132, and 123 subjects in each arm, respectively. Treatment with the 100 mcg/g strength significantly improved the incidence of complete healing *versus* placebo (50% versus 35%). The incidence of complete healing with the 30 mcg/g formulation was similar to placebo. Becaplermin is non-irritating and undergoes negligible absorption so that side effects are similar to those of placebo. It is applied once a day, but should be removed gently with water after 12 hours. Any infection present should be treated to resolution before becaplermin is applied. The major disadvantages of this agent are that it must be stored in the refrigerator and it is very expensive. One 15 g tube currently costs $452.98 and will usually last approximately 2 weeks depending on the size of the wound.[88]

Pharmacy Involvement in Wound Care

As clinical pharmacists increasingly round with medical teams, they are able to see the daily management of chronic wounds as a part of the health care team. Many times when physicians and nurses apply topical creams and ointments to these wounds, they look toward the clinical pharmacist to determine the appropriate type and method of application. This will be most pharmacists' initial foray into the field of wound care. With knowledge of a field few are familiar with, a pharmacist can be increasingly relied upon for recommendations not only for topical creams and ointments but also for assessments, antibiotics, dressings, and other wound care products as well.

SUMMARY AND CONCLUSIONS

The focus of this review was on the most common types of chronic wounds: pressure, vascular, and diabetic ulcers. Many, less common types were also briefly reviewed. The prevention of these types of wounds varies with the type but the treatment will generally depend on the clinical presentation of the wound. The presence of necrotic tissue necessitates debridement to prevent infection and allow healing to progress. The methods of debridement include sharp, mechanical, enzymatic, and autolytic. The method chosen should be based on the need for selectivity, presence of infection, amount of associated pain, amount of drainage, available resources, and other patient specific factors. The distinction between infection and colonization is currently based on clinical signs and symptoms and colony counts. When infection is present, it should be treated appropriately. Despite an association between the development of wounds and poor wound healing with poor nutritional parameters, the role of supplemental nutrition remains unclear until further studies are done. Most clinicians, however, will prescribe supplemental nutrition to those with poor nutritional parameters if concern

of poor wound healing or development of pressure ulcers exists. Growth factors show modest improvements in healing chronic wounds but at a significant cost.

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METALS

PERIOD ▼ / GROUP ▶ †	I A	II A	III B	IV B	V B	VI B	VII B	VIII	VIII	VIII
1	1 g 1 **H** 1.00794[a] 1 Hydrogen									
2	2 1 3 **Li** 6.94[1][a,b,c] 1 Lithium	2 2 4 **Be** 9.012182 2 Beryllium								
3	2 8 1 11 **Na** 22.989768 1 Sodium	2 8 2 12 **Mg** 24.305[b] 2 Magnesium								
4	2 8 8 1 19 **K** 39.098[3] 1 Potassium	2 8 8 2 20 **Ca** 40.078[b] 2 Calcium	2 8 9 2 21 **Sc** 44.95591 3 Scandium	2 8 10 2 22 **Ti** 47.88 2, 3, 4 Titanium	2 8 11 2 23 **V** 50.9415 2, 3, 4, 5 Vanadium	2 8 13 1 24 **Cr** 51.9961 2, 3, 6 Chromium	2 8 13 2 25 **Mn** 54.93805 2, 3, 4, 6, 7 Manganese	2 8 14 2 26 **Fe** 55.84[7] 2, 3 Iron	2 8 15 2 27 **Co** 58.9332 2, 3 Cobalt
5	2 8 18 8 1 37 **Rb** 85.467[3][b] 1 Rubidium	2 8 18 8 2 38 **Sr** 87.62[b] 2 Strontium	2 8 18 9 2 39 **Y** 88.90585 3 Yttrium	2 8 18 10 2 40 **Zr** 91.224[b] 4 Zirconium	2 8 18 12 1 41 **Nb** 92.90638 3, 5 Niobium	2 8 18 13 1 42 **Mo** 95.94 2, 3, 4, 5, 6 Molybdenum	2 8 18 13 2 43 Tc (97.9072) 6, 7 Technetium	2 8 18 15 1 44 **Ru** 101.0[7][b] 2, 3, 4, 6, 8 Ruthenium	2 8 18 16 1 45 **Rh** 102.9055 2, 3, 4 Rhodium
6	2 8 18 18 8 1 55 **Cs** 132.90543 1 Cesium	2 8 18 18 8 2 56 **Ba** 137.327[b] 2 Barium	57–71 See Lanthanide Series	2 8 18 32 10 2 72 **Hf** 178.4[9] 4 Hafnium	2 8 18 32 11 2 73 **Ta** 180.947[9] 5 Tantalum	2 8 18 32 12 2 74 **W** 183.8[5] 2, 3, 4, 5, 6 Tungsten	2 8 18 32 13 2 75 **Re** 186.207 3, 4, 5, 6, 7 Rhenium	2 8 18 32 14 2 76 **Os** 190.2[b] 2, 3, 4, 6, 8 Osmium	2 8 18 32 17 2 77 **Ir** 192.2[2] 2, 3, 4 Iridium
7	2 8 18 32 18 8 1 87 **Fr** (223.0197) 1 Francium	2 8 18 32 18 8 2 88 **Ra** 226.0254[b,d] 2 Radium	89–103 See Actinide Series	104 **(Unq)** (261.11) (Unnil-quadium)§	105 **(Unp)** (262.114) (Unnil-pentium)§	106 **(Unh)** (263.118) (Unnil-hexium)§	107 **Uns** (262.12) (Unnil-septium)§			

Lanthanide Series (Rare Earth Elements)	2 8 18 18 9 2 57 **La** 138.905[8][b] 3 Lanthanum	2 8 18 19 9 2 58 **Ce** 140.115[b] 3, 4 Cerium	2 8 18 20 9 2 59 **Pr** 140.90765 3, 4 Praseodymium	2 8 18 22 8 2 60 **Nd** 144.2[4][b] 3 Neodymium	2 8 18 23 8 2 61 Pm (144.9127) 3 Promethium	2 8 18 24 8 2 62 **Sm** 150.36 2, 3 Samarium	2 8 18 25 8 2 63 **Eu** 151.965[b] 2, 3 Europium		
Actinide Series	2 8 18 32 18 9 2 89 **Ac** 227.0278[d] 3 Actinium	2 8 18 32 19 9 2 90 **Th** 232.0381[b,d] 4 Thorium	2 8 18 32 20 9 2 91 **Pa** 231.0359[d] 5 Protactinium	2 8 18 32 21 9 2 92 **U** 238.0289[b,c] 3, 4, 5, 6 Uranium	2 8 18 32 22 9 2 93 Np 237.0482[d] 3, 4, 5, 6 Neptunium	2 8 18 32 23 9 2 94 Pu (244.0642) 3, 4, 5, 6 Plutonium	2 8 18 32 24 9 2 95 Am (243.0614) 3, 4, 5, 6 Americium		

KEY

Electron population of orbits

K L M N O P Q

At No
Symbol
At Wt
Valence
Name

State at 30°C if other than solid: g = gas; l = liquid

Outline letters represent elements known only through synthesis.

On the scale $^{12}C = 12$*

Characteristic values

* Atomic weight is an alternative term for 'relative atomic mass of an element', A_r(E). The IUPAC values given here are scaled to $A_r(^{12}C) = 12$ and apply to elements as they exist in materials of terrestrial origin and to certain artificial elements. When used with due regard to the footnotes they are considered reliable to ±1 in the last digit or ±3 if that digit is subscript. Values in parentheses are for radioactive elements whose atomic weights cannot be quoted precisely without knowledge of the origin of the elements; the value given is the atomic mass number of the isotope of that element of longest known half-life.

† Beginning with Group III, authors differ in their presentation of the "A" and "B" groups of elements.

‡ Expected value from theoretical considerations. § Names and symbols provisionally suggested by IUPAC.

			NON-METALS				INERT GASES
						VII A	ZERO
						1 g 1 **H** 1.00794[a] −1 Hydrogen	2 g 2 **He** 4.002602[b] 0 Helium
			III A	IV A	V A	VI A	
			2 3 5 **B** 10.811[a,c] 3 Boron	2 4 6 **C** 12.011[a] −4; 2, 4 Carbon	2 5 g 7 **N** 14.00674 −3; 3, 5 Nitrogen	2 6 g 8 **O** 15.999$_4$[a] −2 Oxygen	2 7 g 9 **F** 18.9984032 −1 Fluorine	2 8 g 10 **Ne** 20.1797[c] 0 Neon
			2 8 3 13 **Al** 26.981539 3 Aluminum	2 8 4 14 **Si** 28.085$_5$ −4; 4 Silicon	2 8 5 15 **P** 30.973762 −3; 3, 5 Phosphorus	2 8 6 16 **S** 32.066[a] −2; 2, 4, 6 Sulfur	2 8 7 g 17 **Cl** 35.4527 −1; 1, 3, 5, 7 Chlorine	2 8 8 g 18 **Ar** 39.94$_8$[a,b] 0 Argon
	I B	II B						
2 8 16 2 28 **Ni** 58.69 2, 3 Nickel	2 8 18 1 29 **Cu** 63.54$_6$[a] 1, 2 Copper	2 8 18 2 30 **Zn** 65.39 2 Zinc	2 8 18 3 l 31 **Ga** 69.723 3 Gallium	2 8 18 4 32 **Ge** 72.61 4 Germanium	2 8 18 5 33 **As** 74.92159 −3; 3, 5 Arsenic	2 8 18 6 34 **Se** 78.9$_6$ −2; 4, 6 Selenium	2 8 18 7 l 35 **Br** 79.904 −1; 1, 3, 5, 7 Bromine	2 8 18 8 g 36 **Kr** 83.80[b,c] 0 Krypton
2 8 18 18 46 **Pd** 106.42[b] 2, 4 Palladium	2 8 18 18 1 47 **Ag** 107.868$_2$[b] 1 Silver	2 8 18 18 2 48 **Cd** 112.411[b] 2 Cadmium	2 8 18 18 3 49 **In** 114.82[b] 3 Indium	2 8 18 18 4 50 **Sn** 118.71 2, 4 Tin	2 8 18 18 5 51 **Sb** 121.7$_6$ −3; 3, 5 Antimony	2 8 18 18 6 52 **Te** 127.6$_0$[b] −2; 4, 6 Tellurium	2 8 18 18 7 53 **I** 126.90447 −1; 1, 3, 5, 7 Iodine	2 8 18 18 8 g 54 **Xe** 131.29[b,c] 0 Xenon
2 8 18 32 17 1 78 **Pt** 195.0$_8$ 2, 4 Platinum	2 8 18 32 18 1 79 **Au** 196.96654 1, 3 Gold	2 8 18 32 18 2 l 80 **Hg** 200.5$_9$ 1, 2 Mercury	2 8 18 32 18 3 81 **Tl** 204.3833 1, 3 Thallium	2 8 18 32 18 4 82 **Pb** 207.2[a,b] 2, 4 Lead	2 8 18 32 18 5 83 **Bi** 208.980437 3, 5 Bismuth	2 8 18 32 18 6 84 **Po** (208.9824) 2, 4 Polonium	2 8 18 32 18 7 85 **At** (209.9871) 1, 3, 5, 7‡ Astatine	2 8 18 32 18 8 g 86 **Rn** (222.0176) 0 Radon

2 8 18 25 9 2 64 **Gd** 157.2$_5$[b] 3 Gadolinium	2 8 18 26 9 2 65 **Tb** 158.92534 3, 4 Terbium	2 8 18 28 8 2 66 **Dy** 162.5$_0$ 3 Dysprosium	2 8 18 29 8 2 67 **Ho** 164.93032 3 Holmium	2 8 18 30 8 2 68 **Er** 167.2$_6$ 3 Erbium	2 8 18 31 8 2 69 **Tm** 168.93421 3 Thulium	2 8 18 32 8 2 70 **Yb** 173.0$_4$ 2, 3 Ytterbium	2 8 18 32 9 2 71 **Lu** 174.96$_7$ 3 Lutetium
2 8 18 32 25 9 2 96 **Cm** (247.0703) 3 Curium	2 8 18 32 26 9 2 97 **Bk** (247.0703) 3, 4 Berkelium	2 8 18 32 27 9 2 98 **Cf** (251.0796) 3 Californium	2 8 18 32 28 9 2 99 **Es** (252.083) 3‡ Einsteinium	2 8 18 32 29 9 2 100 **Fm** (257.0951) 3‡ Fermium	2 8 18 32 30 9 2 101 **Md** (258.10) 3‡ Mendelevium	2 8 18 32 31 9 2 102 **No** (259.1009) 3‡ Nobelium	2 8 18 32 32 9 2 103 **Lr** (262.11) 3‡ Lawrencium

Element for which known variations in isotopic composition in normal terrestrial material prevent a more precise atomic weight being given; A_r(E) values should be applicable to any 'normal' material. [b]Element for which geological specimens are known in which the element has an anomalous isotopic composition, such that the difference between the atomic weight of the element in such specimens and that given in the table may exceed considerably the implied uncertainty. [c]Element for which substantial variations in A_r from the value given can occur in commercially available material because of inadvertent or undisclosed change of isotopic composition. [d]Element for which the value of A_r is that of the radioisotope of longest half-life.

Table of Logarithms

Natural Numbers	0	1	2	3	4	5	6	7	8	9	Proportional Parts 1	2	3	4	5	6	7	8	9
10	0000	0043	0086	0128	0170	0212	0253	0294	0334	0374	4	8	12	17	21	25	29	33	37
11	0414	0453	0492	0531	0569	0607	0645	0682	0719	0755	4	8	11	15	19	23	26	30	34
12	0792	0828	0864	0899	0934	0969	1004	1038	1072	1106	3	7	10	14	17	21	24	28	31
13	1139	1173	1206	1239	1271	1303	1335	1367	1399	1430	3	6	10	13	16	19	23	26	29
14	1461	1492	1523	1553	1584	1614	1644	1673	1703	1732	3	6	9	12	15	18	21	24	27
15	1761	1790	1818	1847	1875	1903	1931	1959	1987	2014	3	6	8	11	14	17	20	22	25
16	2041	2068	2095	2122	2148	2175	2201	2227	2253	2279	3	5	8	11	13	16	18	21	24
17	2304	2330	2355	2380	2405	2430	2455	2480	2504	2529	2	5	7	10	12	15	17	20	22
18	2553	2577	2601	2625	2648	2672	2695	2718	2742	2765	2	5	7	9	12	14	16	19	21
19	2788	2810	2833	2856	2878	2900	2923	2945	2967	2989	2	4	7	9	11	13	16	18	20
20	3010	3032	3054	3075	3096	3118	3139	3160	3181	3201	2	4	6	8	11	13	15	17	19
21	3222	3243	3263	3284	3304	3324	3345	3365	3385	3404	2	4	6	8	10	12	14	16	18
22	3424	3444	3464	3483	3502	3522	3541	3560	3579	3598	2	4	6	8	10	12	14	15	17
23	3617	3636	3655	3674	3692	3711	3729	3747	3766	3784	2	4	6	7	9	11	13	15	17
24	3802	3820	3838	3856	3874	3892	3909	3927	3945	3962	2	4	5	7	9	11	12	14	16
25	3979	3997	4014	4031	4048	4065	4082	4099	4116	4133	2	3	5	7	9	10	12	14	15
26	4150	4166	4183	4200	4216	4232	4249	4265	4281	4298	2	3	5	7	8	10	11	13	15
27	4314	4330	4346	4362	4378	4393	4409	4425	4440	4456	2	3	5	6	8	9	11	13	14
28	4472	4487	4502	4518	4533	4548	4564	4579	4594	4609	2	3	5	6	8	9	11	12	14
29	4624	4639	4654	4669	4683	4698	4713	4728	4742	4757	1	3	4	6	7	9	10	12	13
30	4771	4786	4800	4814	4829	4843	4857	4871	4886	4900	1	3	4	6	7	9	10	11	13
31	4914	4928	4942	4955	4969	4983	4997	5011	5024	5038	1	3	4	6	7	8	10	11	12
32	5051	5065	5079	5092	5105	5119	5132	5145	5159	5172	1	3	4	5	7	8	9	11	12
33	5185	5198	5211	5224	5237	5250	5263	5276	5289	5302	1	3	4	5	6	8	9	10	12
34	5315	5328	5340	5353	5366	5378	5391	5403	5416	5428	1	3	4	5	6	8	9	10	11
35	5441	5453	5465	5478	5490	5502	5514	5527	5539	5551	1	2	4	5	6	7	9	10	11
36	5563	5575	5587	5599	5611	5623	5635	5647	5658	5670	1	2	4	5	6	7	8	10	11
37	5682	5694	5705	5717	5729	5740	5752	5763	5775	5786	1	2	3	5	6	7	8	9	10
38	5798	5809	5821	5832	5843	5855	5866	5877	5888	5899	1	2	3	5	6	7	8	9	10
39	5911	5922	5933	5944	5955	5966	5977	5988	5999	6010	1	2	3	4	5	7	8	9	10
40	6021	6031	6042	6053	6064	6075	6085	6096	6107	6117	1	2	3	4	5	6	8	9	10
41	6128	6138	6149	6160	6170	6180	6191	6201	6212	6222	1	2	3	4	5	6	7	8	9
42	6232	6243	6253	6263	6274	6284	6294	6304	6314	6325	1	2	3	4	5	6	7	8	9
43	6335	6345	6355	6365	6375	6385	6395	6405	6415	6425	1	2	3	4	5	6	7	8	9
44	6435	6444	6454	6464	6474	6484	6493	6503	6513	6522	1	2	3	4	5	6	7	8	9
45	6532	6542	6551	6561	6571	6580	6590	6599	6609	6618	1	2	3	4	5	6	7	8	9
46	6628	6637	6646	6656	6665	6675	6684	6693	6702	6712	1	2	3	4	5	6	7	7	8
47	6721	6730	6739	6749	6758	6767	6776	6785	6794	6803	1	2	3	4	5	5	6	7	8
48	6812	6821	6830	6839	6848	6857	6866	6875	6884	6893	1	2	3	4	4	5	6	7	8
49	6902	6911	6920	6928	6937	6946	6955	6964	6972	6981	1	2	3	4	4	5	6	7	8
50	6990	6998	7007	7016	7024	7033	7042	7050	7059	7067	1	2	3	3	4	5	6	7	8
51	7076	7084	7093	7101	7110	7118	7126	7135	7143	7152	1	2	3	3	4	5	6	7	8
52	7160	7168	7177	7185	7193	7202	7210	7218	7226	7235	1	2	2	3	4	5	6	7	7
53	7243	7251	7259	7267	7275	7284	7292	7300	7308	7316	1	2	2	3	4	5	6	6	7
54	7324	7332	7340	7348	7356	7364	7372	7380	7388	7396	1	2	2	3	4	5	6	6	7
55	7404	7412	7419	7427	7435	7443	7451	7459	7466	7474	1	2	2	3	4	5	5	6	7
56	7482	7490	7497	7505	7513	7520	7528	7536	7543	7551	1	2	2	3	4	5	5	6	7
57	7559	7566	7574	7582	7589	7597	7604	7612	7619	7627	1	2	2	3	4	5	5	6	7
58	7634	7642	7649	7657	7664	7672	7679	7686	7694	7701	1	1	2	3	4	4	5	6	7
59	7709	7716	7723	7731	7738	7745	7752	7760	7767	7774	1	1	2	3	4	4	5	6	7
60	7782	7789	7796	7803	7810	7818	7825	7832	7839	7846	1	1	2	3	4	4	5	6	6
61	7853	7860	7868	7875	7882	7889	7896	7903	7910	7917	1	1	2	3	4	4	5	6	6
62	7924	7931	7938	7945	7952	7959	7966	7973	7980	7987	1	1	2	3	3	4	5	6	6
63	7993	8000	8007	8014	8021	8028	8035	8041	8048	8055	1	1	2	3	3	4	5	5	6
64	8062	8069	8075	8082	8089	8096	8102	8109	8116	8122	1	1	2	3	3	4	5	5	6
65	8129	8136	8142	8149	8156	8162	8169	8176	8182	8189	1	1	2	3	3	4	5	5	6
66	8195	8202	8209	8215	8222	8228	8235	8241	8248	8254	1	1	2	3	3	4	5	5	6
67	8261	8267	8274	8280	8287	8293	8299	8306	8312	8319	1	1	2	3	3	4	5	5	6
68	8325	8331	8338	8344	8351	8357	8363	8370	8376	8382	1	1	2	3	3	4	4	5	6
69	8388	8395	8401	8407	8414	8420	8426	8432	8439	8445	1	1	2	2	3	4	4	5	6
70	8451	8457	8463	8470	8476	8482	8488	8494	8500	8506	1	1	2	2	3	4	4	5	6
71	8513	8519	8525	8531	8537	8543	8549	8555	8561	8567	1	1	2	2	3	4	4	5	5
72	8573	8579	8585	8591	8597	8603	8609	8615	8621	8627	1	1	2	2	3	4	4	5	5
73	8633	8639	8645	8651	8657	8663	8669	8675	8681	8686	1	1	2	2	3	4	4	5	5
74	8692	8698	8704	8710	8716	8722	8727	8733	8739	8745	1	1	2	2	3	4	4	5	5
75	8751	8756	8762	8768	8774	8779	8785	8791	8797	8802	1	1	2	2	3	3	4	5	5
76	8808	8814	8820	8825	8831	8837	8842	8848	8854	8859	1	1	2	2	3	3	4	5	5
77	8865	8871	8876	8882	8887	8893	8899	8904	8910	8915	1	1	2	2	3	3	4	4	5
78	8921	8927	8932	8938	8943	8949	8954	8960	8965	8971	1	1	2	2	3	3	4	4	5
79	8976	8982	8987	8993	8998	9004	9009	9015	9020	9026	1	1	2	2	3	3	4	4	5
80	9031	9036	9042	9047	9053	9058	9063	9069	9074	9079	1	1	2	2	3	3	4	4	5
81	9085	9090	9096	9101	9106	9112	9117	9122	9128	9133	1	1	2	2	3	3	4	4	5
82	9138	9143	9149	9154	9159	9165	9170	9175	9180	9186	1	1	2	2	3	3	4	4	5
83	9191	9196	9201	9206	9212	9217	9222	9227	9232	9238	1	1	2	2	3	3	4	4	5
84	9243	9248	9253	9258	9263	9269	9274	9279	9284	9289	1	1	2	2	3	3	4	4	5
85	9294	9299	9304	9309	9315	9320	9325	9330	9335	9340	1	1	2	2	3	3	4	4	5
86	9345	9350	9355	9360	9365	9370	9375	9380	9385	9390	1	1	2	2	3	3	4	4	5
87	9395	9400	9405	9410	9415	9420	9425	9430	9435	9440	0	1	1	2	2	3	3	4	4
88	9445	9450	9455	9460	9465	9469	9474	9479	9484	9489	0	1	1	2	2	3	3	4	4
89	9494	9499	9504	9509	9513	9518	9523	9528	9533	9538	0	1	1	2	2	3	3	4	4
90	9542	9547	9552	9557	9562	9566	9571	9576	9581	9586	0	1	1	2	2	3	3	4	4
91	9590	9595	9600	9605	9609	9614	9619	9624	9628	9633	0	1	1	2	2	3	3	4	4
92	9638	9643	9647	9652	9657	9661	9666	9671	9675	9680	0	1	1	2	2	3	3	4	4
93	9685	9689	9694	9699	9703	9708	9713	9717	9722	9727	0	1	1	2	2	3	3	4	4
94	9731	9736	9741	9745	9750	9754	9759	9763	9768	9773	0	1	1	2	2	3	3	4	4
95	9777	9782	9786	9791	9795	9800	9805	9809	9814	9818	0	1	1	2	2	3	3	4	4
96	9823	9827	9832	9836	9841	9845	9850	9854	9859	9863	0	1	1	2	2	3	3	4	4
97	9808	9872	9877	9881	9886	9890	9894	9899	9903	9908	0	1	1	2	2	3	3	4	4
98	9912	9917	9921	9926	9930	9934	9939	9943	9948	9952	0	1	1	2	2	3	3	4	4
99	9956	9961	9965	9969	9974	9978	9983	9987	9991	9996	0	1	1	2	2	3	3	3	4

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Glossary

A

AA	atomic absorption, Alcoholics Anonymous
AACP	American Association of Colleges of Pharmacy
AAFP	American Academy of Family Practice
AAGR	average annual growth
AAP	American Academy of Pediatrics
AAPCC	American Association of Poison Control Centers
AAPS	American Association of Pharmaceutical Scientists
AARP	American Association of Retired Persons
ABAT	American Board of Applied Toxicology
ABC	ATP binding casette
ABG	arterial blood gas
ABMS	American Board of Medical Specialties
ACA	American College of Apothecaries
ACD	acid-citrate-dextrose
ACE	angiotensin converting enzyme
ACEI	angiotensin converting enzyme inhibitor
ACCP	American College of Clinical Pharmacy, American College of Clinical Pharmacists
ACF	Administration for Children and Families
Ach	acetylcholine
ACh	acetylcholinesterase
ACHC	Accreditation Committee for Health Care
ACIP	American Committee on Immunization Practices, Immunization Practices Advisory Committee
ACP	American College of Physicians, acyl carrier protein
ACPE	Accreditation Council for Pharmaceutical Education
ACTH	corticotropin (adrenocorticotropic hormone)
AD	Alzheimer's disease, Alzheimer's dementia
ADA	American Dental Association, American Dietetic Association, adenosine deaminase, American Diabetes Association
ADCC	antibody-dependent cell-mediated cytotoxicity
ADE	adverse drug event, adverse drug experience
ADEPT	antibody directed enzyme prodrug therapy
ADH	antidiuretic hormone
ADL	activity of daily living
ADME	absorption, distribution, metabolism, and excretion
ADP	adenosine diphosphate
ADR	adverse drug reaction
AEC	Atomic Energy Commission
AERS	Adverse Event Reporting System
AES	Auger electron spectrometry
AF	atrial fibrillation
AFMS	Air Force Medical Service
AFP	α-1-fetoprotein
A/G	albumin-globulin ratio
AGD	agar gel diffusion
AHA	American Hospital Association, American Heart Association
AHCPR	Agency for Health Care Policy Research
AHF	antihemophilic factor
AHFS	American Hospital Formulary System
AHG	antihemophilic globulin
AHRQ	Agency for Healthcare Research and Quality
AI	adequate intake, aortic insufficiency
AIDS	acquired immunodeficiency syndrome
AIMS	abnormal involuntary movement scale
AIRA	American International Reiki Association
AL	allergy unit
ALARA	as low as reasonably achievable
ALF	American Liver Foundation
ALL	acute lymphoblastic leukemia
ALT	alanine aminotransferase
AMA	American Medical Association
AMC	Army Medical Center
AMCP	Academy of Managed Care Pharmacists
AMD	age-related macular degeneration
AMDA	American Medical Director's Association
AMI	acute myocardial infarction
AMTA	American Massage Therapy Association
ANA	antinuclear antibodies
ANC	acid neutralizing capacity
ANDA	abbreviated new drug application
ANF	atrial natriuretic factor
ANN	artificial neural network
ANOVA	analysis of variance
ANS	autonomic nervous system
AO	atomic orbital
AOA	American Osteopathic Association
AoA	Administration on Aging
APAP	acetaminophen
APC	antigen-presenting cell, ambulatory patient classification
APCI	atmospheric pressure chemical ionization
APHA	American Public Health Association
APhA	American Pharmacists Association
API	active pharmaceutical ingredient, atmospheric pressure ionization
APP	alternating pressure pad
APPM	Academy of Pharmacy Practice and Management
APRS	Academy of Pharmaceutical Research and Science
APSF	Anesthesia Patient Safety Foundation
APTT	activated partial thromboplastin time
ARB	angiotensin receptor blocker
ARDS	adult respiratory distress syndrome
ASA	acetylsalicylic acid, American Society for Anesthesia
ASCP	American Society of Consultant Pharmacists
ASHP	American Society of Health-System Pharmacists
ASNN	associate neural network
ASO	administrative service organization
ASP	Academy of Students of Pharmacy
ASPEN	American Society of Parenteral and Enteral Nutrition
ASRS	Aviation Safety and Reporting System
AST	aspartase aminotransferase
ATC	around-the-clock
ATCC	American *Type Culture* Collection
ATM	automated teller machine
ATN	acute tubular necrosis
ATP	adenosine triphosphate
ATPase	adenosine triphosphatase
ATSDR	Agency for Toxic Substances and Disease Registry
AUC	area under the curve
AV	atrioventricular
AZT	zidovudine

B

BAC	blood alcohol concentration
BAL	British anti-Lewisite, bioequivalent allergy unit
BBB	blood-brain barrier
BCE	before the Christian era
BCG	Bacillus Calmette Guerin
BCMA	Bar Code Medication Administration System
BCNP	Board Certified Nuclear Pharmacist
BCPS	Board Certified Pharmacotherapy Specialist
BCS	Biopharmaceutical Classification System
BET	bacterial endotoxin test
bFGF	basic fibroblast growth factor
BI	biological indicator
BIA	bacteria inhibition assay
BJA	Basic Journal Abstracts
BM	bowel movement
BMD	Bureau of Medical Devices, bone mineral density
BMI	body mass index
BMJ	British Medical Journal
BMS	between mean square
BMT	bone marrow transplantation
BOC	Board for Arthotists/Prosthetist Certification
BOP	Bureau of Prisons
BP	British Pharmacopeia
BPC	bulk pharmaceutical chemical
BPH	benign prostatic hypertrophy
BPS	Board of Pharmaceutical Specialties
BRH	Bureau of Radiologic Health
BSA	bovine serum albumin
BSC	Biomedical Service Corps
BSE	breast self-examination, bovine spongiform encephalopathy
BSS	between sum-of-squares, balanced salt solution
BUN	blood urea nitrogen
BWFI	bacteriostatic water for injection

C

CAD	coronary artery disease
CADD	computer-assisted drug design
CAGE	cut down, annoyed, guilty, eye opener
CAM	cell adhesion molecule, complimentary/alternative medicine
cAMP	cyclic adenosine monophosphate, cyclic adenosine-3′,5′-monophosphate
CARF	Commission on Accreditation of Rehab Facilities
CARTI	community-acquired respiratory tract infection

CAS Chemical Abstracts Service, composite adherence score
CAT cellulose acetate trimellitate, computer-aided tomography
CBAC Chemical-Biological Activities
CBC complete blood count
CBA cost-benefit analysis
CBER Center for Biologics Evaluation and Research
CCB calcium channel blockers
CCD countercurrent distribution
CCP Council on Credentialing in Pharmacy
CCRF Commissioned Corps Readiness Force
CD circular dichroism
CDA chiral derivatizing agent
CDC Centers for Disease Control and Prevention
CDER Center for Drug Evaluation and Research
CDM certified disease management
CDRH Center for Devices and Radiologic Health
CD-ROM compact disk-read only memory
CE capillary electrophoresis
CEA carcinoembryonic antigen, cost-effectiveness analysis
CEC capillary electrochromatography
CEO chief executive officer
CEP counterelectrophoresis
CF complement fixation
CFC chlorofluorocarbon
CFR Code of Federal Regulations
CFSAN Center for Food Safety and Applied Nutrition
CFTR cystic fibrosis transmembrane regulator
CFU colony-forming unit
CGD chronic granulomatous disease
cGMP cyclic guanosine-3′,5′-monophosphate, current good manufacturing practice
CHAP Commission on Health Accreditation Programs
CHD coronary heart disease
CHF congestive heart failure
CHO Chinese hamster ovary
CI confidence interval, chemical ionization
CIMS chemical ionization mass spectrometry, chemical ionization mass spectroscopy
CIOMS Council for International Organization of Medical Sciences
CIP clean-in-place
CI-PDED chlorine-selective pulsed discharge emission detector
CK creatinine kinase
CLIA Clinical Laboratory Improvement Amendments
CLL chronic lymphoblastic leukemia
CLT Central Limit Theorem
CMC comprehensive medical chemistry, critical micelle concentration
CME cystoid macular edema
CMI cell-mediated immunity
CML chronic myeloid leukemia
CMN certificate of medical necessity
CMOP Consolidated Mail Outpatient Pharmacies
$CMRO_2$ cerebral metabolic rate for oxygen
CMS Centers for Medicare and Medicaid Services
CMV cytomegalovirus
CN Crigler-Najjar syndrome
CNS central nervous system
CO communication objective, carbon monoxide
COHgB carboxyhemoglobin
COMTA Commission on Massage Therapy Accreditation
CONSORT Consolidated Standards of Reporting Trials
COPD chronic obstructive pulmonary disease
COSTEP Commissioned Officer Student Training and Externship Program
COSY correlation spectroscopy
COX cyclo-oxygenase
CPC Council on Pharmacy and Chemistry, centrifugal partition chromatography
CPD citrate-phosphate-dextrose
CPG FDA's Compliance Policy Guide
CPI consumer price index
CPMP Committee for Proprietary Medicinal Products
CPOE computerized physician order entry, computerized prescriber order entry
CPPDE calcium pyrophosphate deposition disease
CPR cardiopulmonary resuscitation
CPS Compendium of Pharmaceutical Specialties
CPSC Consumer Product Safety Commission
CPT current procedural terms
CQI continuous quality improvement
CREST calcinosis, Reynaud's phenomenon, esophageal involvement, sclerodactyly, and telangiectasis
CRF chronic renal failure
CRH critical relative humidity, corticotropic releasing hormone
CRO contract research organization
CRP C-reactive protein
CRT controlled-release tablet
CSA Comprehensive Drug Abuse Prevention and Control Act of 1970, Controlled Substances Act
CSF cerebrospinal fluid, colony stimulating factor
CSH combat support hospitals
CSP chiral stationary phase, compounding sterile preparations
CT charge-transfer, compressed tablet, computerized tomography, computed tomography
CTL cytotoxic T-lymphocyte
CTS compressed tablet for solution
CTZ chemoreceptor trigger zone
CUA cost utility analysis
CV coefficient of variation
CVD cardiovascular disease
CVID common variable immunodeficiency
CW continuous wave

D

DEA Drug Enforcement Administration
DAEA diethylaminoethyl
D&C drug and cosmetic
DATA Drug Addiction Treatment Act
DBP diastolic blood pressure
DC direct current
DCBE double contrast barium exam
DCCT Diabetes Complications and Control Trial
DDMAC FDA's Drug Marketing Advertising and Communications
DEA Drug Enforcement Administration, Drug Enforcement Agency
DEET diethyltoluamide
DF degrees of freedom
DFV daily food value
DHHS Department of Health and Human Services
DI diabetes insipidus
DIC disseminated intravascular coagulation
DIP desquamative interstitial pneumonitis
DIP distal interphalangeal
DISCUS dyskinesia identification system-condensed use scale
DJD degenerative joint disease
DLBCL diffuse large B-cell lymphoma
DLVO Derjaguin-Landau-Verwey-Overbeek
DM dermatomyositis
DMAA Disease Management Association of America
DMSO dimethyl sulfoxide
DMT dimethyltryptamine
DNA deoxyribonucleic acid
DNR do not resuscitate
DOD Department of Defense
DOT directly observed treatment, Department of Transportation
DPCPTRA Drug Price Competition and Patent Term Restoration Act
DPPC dipalmitoylphosphatidylcholine
DPSV differential pulse stripping voltammetry
DRE drug response element, digital rectal examination
DRG diagnosis-related group
DRI dietary reference intake
DRP drug-related problem
DRR drug regimen review
DRV daily reference value
DS degree of substitution
DSC differential scanning calorimetry
DSHEA Dietary Supplement Health and Education Act
DSMB Drug Safety and Monitoring Board
DSM disease state management
DSMT diabetes self-management training
DT dispensing tablet
DTA differential thermal analysis
DTAP diphtheria and tetanus toxoids and acellular pertussis
DTAW drug therapy assessment worksheet
DTP diphtheria, tetaus and pertussis
DTPL drug therapy problem list
DTwP diphtheria and tetnus toxoids and whole-cell pertussis
DUE drug utilization evaluation, drug usage evaluation
DUR drug utilization review, drug use review
DV daily value
DVA Department of Veterans Affairs
DVD digital video disk
DVT deep venous thrombosis
DXA dual energy x-ray absorptimometry

E

E&M evaluation and management
EAR estimated average requirement

EBM	evidence-based medicine
EBV	Epstein-Barr virus
EC	ethics committee, effective concentration
ECD	electron capture detector
ECF	extracellular fluid
ECF-A	eosinophil chemotactic factor of anaphylaxis
ECG	electrocardiogram
ECL	enterochromaffin-like
ECT	enteric-coated tablet
ED	emergency department
EDA	electron donor-acceptor
ED_{50}	50% effective dose
EDI	electronic data interchange
EDRF	endothelium-derived relaxing factor
EDTA	ethylenediaminetetraacetic acid
EDV	end diastolic volume
EEG	electroencephalogram
EES	exfoliative erythroderma syndrome
EI	electron impact
EIA	enzyme immunoassay
EKG	electrocardiogram
ELISA	enzyme-linked immunosorbent assay
ELS	evaporative light scattering
ELSI	ethical, legal, and social implication
EM	electromagnetic, emergency medicine
EMIT	enzyme-mediated immunologic technique
EMS	error mean square
EN	enteral nutrition
ENTOMA	Entomological Society of America
ENZ-Aux	enzyme auxotroph bacterial assay
EOF	electro-osmotic flow
EP	European Pharmacopeia
EPA	Environmental Protection Agency
EPMA	electron probe microanalysis
EPS	extrapyramidal symptom
EPT	enzyme prodrug therapy
Eq	equivalent, equation
ERM	electrochemical relaxation measurements
ESCA	electron spectroscopy chemical analysis
ESI	electrospray ionization
E-Sign	Electronic Signatures in Global and National Commerce Act
ESR	electron spin resonance, erythrocyte sedimentation rate
ESRD	end stage renal disease
ET	enterostomal therapist
EU	endotoxin unit

F

FAA	Federal Aviation Administration
FAB	fast-atom bombardment
FAO	Food and Agriculture Organization
FBI	Federal Bureau of Investigation
FCT	film-coated tablet
F-D	force-displacement
FDA	Food and Drug Administration
FDAMA	FDA Modernization Act
FD&C	Food, Drug and Cosmetic
FDP	fibrinogen degradation products
FEF	forced expiratory flow
FEPCA	Federal Environmental Pesticide Control Act
FEV	forced expiratory volume
FFA	free fatty acid
FFT	fast Fourier transform
FH	field hospital, familial hypercholesterolemia
FHD	first human dose
FIA	flow injection analysis
FID	flame ionization detector, free induction decay
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FIR	far infrared
FLP	fragment length polymorphism
FMEA	failure mode and effects analysis
FOBT	fecal occult blood test
FODA	fiber-optic Doppler anemometer
FPD	flame photometric detector
FPIA	fluorescence polarization immunoassay
FRC	functional residual capacity
FSH	follicle-stimulating hormone
FT	Fourier transformation
FTA	fluorescent treponemal antibody
FTC	Federal Trade Commission
FT-IR	Fourier transform infrared spectrometry
FTMS	Fourier transform mass spectrometry
FT-NMR	Fourier transform nuclear magnetic resonance
FVC	forced vital capacity

G

GABA	gamma-aminobutyric acid
GAD	generalized anxiety disorder
GAO	General Accounting Office
GAP	good aseptic practice
GC	gas chromatography
G-cells	gastrin-producing cells
GCP	Good Clinical Practices, Good Compounding Practices
GC-MS	gas chromatography/mass spectrometry
GCP	Good Compounding Practices
G-CSF	granulocyte colony-stimulating factor
GDEPT	gene-directed EPT
GDP	gross domestic product
GERD	gastroesophageal reflux disease
GFR	glomerular filtration rate
GH	growth hormone
GI	gastrointestinal
GLC	gas-liquid chromatography
GLP	good laboratory practice
GLUT	glucose transporter
GMP	good manufacturing practice
Gn-RH	gonadotropin-releasing hormone
GN	glomerulonephritis
GNDF	glial cell line-derived neurotrophic factor
GPCR	guanine nucleotide-coupled receptor
GRAS	generally recognized as safe
GSC	gas-solid chromatography
G6P	glucose 6-phosphate
G6PD	glucose 6-phosphate dehydrogenase
GVHD	graft vs host disease
GYN	gynecology

H

HA	hemagglutination
HAA	hepatitis-associated antigen
HAART	highly active antiretroviral therapy
HACEK	haemophilus, actinobacillus, cardiobacterium, eikenella, kingella
HACCP	hazard analysis and critical control point
HBIG	hepatitis B immune globulin
HBP	high blood pressure
HbS	hemoglobin S
HBV	hepatitis B virus
HC	hydrocarbon
HCA	hierarchical cluster analysis
HCFA	Health Care Financing Administration
HCFC	hydrochlorofluorocarbons
HCG	human chorionic gonadotropin
HCM	health collaboration model
HCP	home care pharmaceutical
HCPCS	HCFA Common Procedure Coding System
HCPS	home-care pharmaceuticals
HCR	health care representative
HCTZ	hydrochlorothiazide
HCV	hepatitis C virus
HDL	high-density lipoprotein
HDPE	high-density polyethylene
HEDIS	health employer data and information set
HEPA	high-efficiency particulate air
HepB	hepatitis B
HETP	height equivalent to a theoretical plate
HFA	hydrofluoroalkane
HFC	hydrofluorocarbons
HFMEA	health care failure modes and effects analysis
HGF	hyperglycemic factor
hGH	human growth hormone
HHS	Health and Human Services
Hib	*Haemophilus influenza* type b
HIC	hydrophobic interaction chromatography
HIMA	Health Industry Manufacturers Association
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HLA-DR	human leukocyte antigen (locus) DR
HLB	hydrophile-lipophile balance
HLH	human luteinizing hormone
HME	home medical equipment
HMO	health maintenance organization
HOCA	high osmolality contrast agents
HOPE	Heart Outcomes Prevention Evaluation, Women's Health, Osteoporosis, Progestin, Estrogen Trial
HPDP	health promotion and disease prevention
HPA	hypothalamic-pituitary-adrenal
HPL	human placental lactogen
HPLC	high-performance liquid chromatography
HPLC/MS	high-performance liquid chromatography/mass spectrometry
HPRS	Homeopathic Pharmacopoeia Revision Service
HPUS	Homeopathic Pharmacopoeia of the United States
HPV	human papillomavirus
HRSA	Health Resource and Services Administration
HRT	hormone replacement therapy
HSA	human serum albumin
HSAB	hard and soft acid-base
HSV	herpes simplex virus
HT	hypodermic tablet
HTS	high-throughput screen
HUS	hemolytic-uremic syndrome
HVAC	heating, ventilating, and air conditioning
HWD	hot wire detector

I

I electric current
IBD inflammatory bowel disease
IBW ideal body weight
IC ion chromatography
ICD International Classification of Diseases
ICF intracellular fluid, intermediate care facility
ICH International Committee on Harmonization
ICP inductively coupled argon plasma, intercostals position
ICR ion cyclotron resonance
ICSH interstitial cell-stimulating hormone
ICU intensive care unit
ID intradermal
IDDM insulin dependent diabetes mellitus
IDIS Iowa Drug Information Service
IDU injection drug user
IEC institution ethics committee
IFN interferon
Ig immunoglobulin
IGIM immune globulin intramuscular
IGIV immune globulin intravenous
IGT impaired glucose tolerance
IHD ischemic heart disease
IHGFC International Human Genome Sequencing Consortium
IHI Institute for Healthcare Improvement
IHS Indian Health Service
IL interleukin
ILP inductive logic programming
IM intramuscular
IMA Individual Mobilization Augmentee
IN intranasal
INADEQUATE incredible natural abundance double quantum transition experiment
IND Investigational New Drug
INEPT insensitive nucleus enhancement by polarization transfer
INN International Nonproprietary Names
INR International Normalized Ratio
IOL intraocular lens
IOM Institute of Medicine
IOP intraocular pressure
IPA International Pharmaceutical Abstracts, isopropyl alcohol
IPE introductory practice experiences
IPM integrated pest management
IPV inactivated polio virus
IR infrared
IRB institutional review board
IRR Individual Ready Reserve
IS information sciences
ISE ion-sensitive electrode
ISF interstitial fluid
ISI Institute for Scientific Information
ISMP Institute for Safe Medication Practices
ISO International Standardization Organization
ISP internet service provider
ISPE International Society for Pharmaceutical Engineering
ISS ion-scattering spectroscopy
ITA intention to treat analysis
ITP idiopathic thrombocytopenic purpura, immune thrombocytopenia purpura
IUD intra-uterine device
IUPAC International Union of Pure and Applied Chemistry
IV intravenous
IVD *in-vitro* diagnostic
IVF intravascular fluid
IVIV *in vitro—in vivo*

J

JAMA Journal of the American Medical Association
JCAH Joint Commission on Accrediation of Hospitals
JCAHO Joint Commission on Accrediation of Healthcare Organizations
JNC Joint National Committee
JP Japanese Pharmacopeia

K

KS ketosteroid, Kaposi's sarcoma
kGy kilogray
KVO keeping the vein open

L

LAFW laminar airflow workbench
LAIV live attenuated influenza vaccine
LAL limulus amebocyte lysate
LC liquid chromatography
LC-FTIR liquid chromatography-Fourier transform infrared
LC-MS liquid chromatography
LCST lower critical solution temperature
LDL low-density lipoprotein
LDPE low-density polyethylene
LED light-emitting diode
LF laminar flow
LH luteinizing hormone
LLDPE linear low-density polyethylene
LLE liquid-liquid extraction
LOCA lower osmolality contrast agents
LPL lipoprotein lipase gene
L/S least square, lecithin to sphingomyelin ratio
LSD lysergic acid diethylamide
LT leukotriene
LTCF long term care facility
LTH luteotropin
LVEDP left ventricular end diastolic pressure
LVI large-volume injection
LVP large-volume parenteral

M

MAb monoclonal antibody
MAC maximum allowable cost, minimum alveolar concentration
MALDI matrix-assisted laser desorption ionization
MALT mucosa-associated lymphoid tissue
MAOI monoamine oxidase inhibitor
MAP maximum *a posteriori*
MAS magic angle spinning
MASH mobile army surgical hospital
MAT mean absorption time
MAUT multi-atribute utility theory
MBC minimum bactericidal concentration
MBNQ Malcolm Baldrige National Quality Program
MCH mean corpuscular hemoglobin
MCHC mean corpuscular hemoglobin concentration
MCO managed care organization
MCP metacarpophalangeal
MCT multiple compressed tablet
MCV mean corpuscular volume
MDI metered-dose inhaler
MDR multidrug resistance
MDS minimum data set
MEC minimum effective concentration
MECC micellar electrokinetic capillary chromatography
MedDRA Medical Dictionary for Drug Regulatory Affairs
MEKC micellar electrokinetic chromatography
MEMS medication event monitoring system
mEq millieqivalent
MER medication errors reporting
MERP medication error reduction program
MHHP Minnesota Hospital and Healthcare Partnership
MHC major histocompatibility complex
Mho reciprocal ohm
MI mitral insufficiency, myocardial infarction
MIA metabolite bacterial inhibition assay
MIC minimum inhibitory concentration
MIL-STD military standard
MKT mean kinetic temperature
MLV multilamellar vesicle
MMR measles, mumps, and rubella
MMWR Morbidity and Mortality Weekly Report
MNT medical nutrition therapy
MO molecular orbital
MPBR master production batch record
MPD minimum pyrogenic dose
MPJE Multistate Pharmacy Jurisprudence Exam
MQ-NMR multiple quantum technique nuclear magnetic resonance
MR mental retardation, mentally retarded
MRC medical research council
MRFIT Multiple Risk Factor Intervention Trial
MRI magnetic resonance imaging
MRIP Model Rules for Institutional Pharmacy
mRNA messenger RNA
MRS magnetic resonance spectroscopy
MRT mean residence time
MS mass spectrometry, mass spectroscopy, multiple sclerosis, mitral stenosis
MSC Medical Service Corps
MSD mass spectral detector
MS/MS mass spectrometry/mass spectrometry
MSPPA Model State Pharmacy Practice Act
MSUD maple syrup urine disease
MTC minimum toxic concentration
MTP metatarsophalangeal
MTT mean transit time
MTX methotrexate
MUE medication-use evaluation
MW molecular weight
MWQ minimum weighable quantity

N

NABP National Association of Boards of Pharmacy
NACDS National Association of Chain Drug Stores
NADPH nicotinamide-adenine-dinucleotide phosphate
NAG ASPEN's National Advisory Group
NAMS North American Menopause Society
NARD National Association of Retail Druggists
NASA National Aeronautics and Space Administration
NASHP National Academy for State Health Policy
NCBTMB National Certification Board for Therapeutic Massage and Bodywork

NCCAM National Center for Complimentary and Alternative Medicine
NCCAOM National Center for Complimentary and Alternative Oriental Medicine
NCCLS National Committee for Clinical Laboratory Standards
NCC MERP National Coordinating Council for Medication Error Reporting and Prevention
NCE new chemical entity
NCEP National Cholesterol Education Program
NCF-A neutrophil chemotactic factor of anaphylaxis
NCHC National Coalition on Health Care
NCI negative-ion chemical ionization, National Cancer Institute
NCPA National Community Pharmacists Association
NCPDP National Council for Prescription Drug Programs
NCPIE National Council on Patient Information and Education
NCPS National Center for Patient Safety
NCQA National Committee for Quality Assurance
NDA New Drug Application
NDC National Drug Code
NDMS National Disaster Medical System
NEPM non-parametric population modeling
NGC National Guideline Clearinghouse
NHANES National Health and Nutrition Examination Survey
NHGRI National Human Genome Research Institute
NIDA National Institute on Drug Abuse
NIDDM non-insulin dependent diabetes mellitus
NIH National Institutes of Health
NIMH National Institute for Mental Health
NIOSH National Institute for Occupational Safety and Health
NIR near infrared
NISPC National Institute for Standards in Pharmacist Credentialing
NIST National Institute of Standards and Technology
NKC natural killer cell
NMR nuclear magnetic resonance
NOE nuclear Overhauser effect
NPD nitrogen phosphorus detector
NPH neutral protamine Hagedorn
NPLEX Naturopathic Physician Licensing Examination
NPN nonprotein nitrogen
NPR National Public Radio
NPSF National Patient Safety Foundation
NPSG National Patient Safety Goals
NQF National Quality Forum
NQMC National Quality Measures Clearinghouse
NRC Nuclear Regulatory Committee, Nuclear Regulatory Commission
NRT nicotine-replacement therapy
NSABP National Surgical Adjuvant Breast and Bowel Project
NSAID nonsteroidal anti-inflammatory drug
NSF National Science Foundation
NTI narrow therapeutic index

O

OA "open access," osteoarthritis
OAM Office of Alternate Medicine
OASI Old-Age and Survivors Insurance
OB obstetrics
OBDIV operational division
OBRA Omnibus Budget Reconciliation Act
OCD obsessive-compulsive disorder
OCP oral contraceptive pill
OD outside diameter
ODT orally disintegrating tablet
OEF Operation Enduring Freedom
OIF Operation Iraqi Freedom
OLV oligolamellar vesicles
OMD Oriental medicine degree
OPV oral polio vaccine
OR operating room
ORD optical rotatory dispersion
OSHA Occupational Safety and Health Administration
OT old tuberculin
OTC over-the-counter, ornithine transcarbamylase
O/W oil-in-water

P

PAD premature atrial depolarization
PADE potential adverse drug event
PAGE polyacrylamide gel electrophoresis
P&P policies and procedures
P&T pharmacy and therapeutics
PANSS positive and negative syndrome scale
PAO peak acid output
PAW pulmonary arterial wedge
Pb phenobarbital
PBE proton-balance equation
PBI protein-bound iodine
PBM pharmacy benefit management, pharmacy benefit manager
PBP penicillin-binding protein
PBR production batch record
PC personal computer, percutaneous
PCA patient-controlled analgesia, principal component analysis
PCCF pharmacist care claim form
PCP phencyclidine, *pneumocystis carinii* pneumonia
PCR polymerase chain reaction
PCV pneumococcal conjugate vaccine
PDA Parenteral Drug Association, personal digital assistant
PDCA Plan-Do-Check-Act
PDGF platelet-derived growth factor
PDMA Prescription Drug Marketing Act
PDR Physicians' Desk Reference
PDSA Plan-Do-Study Act
PDUFA Prescription Drug User Fee Act
PE pulmonary embolism
PEG polyethylene glycol, percutaneous endoscopic gastrostomy
PEPI Postmenopausal Estrogen/Progestin Interventions
PEPT1 plasma membrane peptide transporter
PET positron emission tomography, positron emission test
PFG pulsed field gradients
PFM peak flow meter
PFR peak flow rate
PGDB Prevention Guidelines Database
PGE prostaglandin E
PHI personal health information, protected health information
PhRMA Pharmaceutical Research and Manufacturers Association
PHS US Public Health Service
PHSA Public Health Service Act
PICVI plasma impulse chemical vapor deposition
PID photo-ionization detector, pelvic inflammatory disease
PIP proximal interphalangeal
PIT phase inversion temperature
PKC protein kinase C
PKU phenylketonuria
PL Public Law
PLAN Pharmacists' Learning Assistance Network
PLC programmable logic controllers, phospholipase C
PLM polarized light microscopy
PM polymyositis
PMA Pharmaceutical Manufacturers Association
PMMA polymethylmethacrylate, (methacrylic acid)
PMN polymorphonuclear leukocyte
PMS post-marketing surveillance
PN parenteral nutrition
PND paroxysmal nocturnal dyspnea
PNI psychoneuroimmunology
PNS peripheral nervous system
PNSU probability of nonsterile unit
PNU protein nitrogen unit
POA durable power of attorney
POC point-of-care
POMR problem-oriented medical record
POST Polymer Science and Technology
PP protein precipitation
PPA phenylpropanolamine
PPAC pharmacy practice activity classification
PPD purified protein derivative
PPI proton pump inhibitor, patient package insert
PPLO pleuropneumonia-like organism
ppm parts per million
PPO preferred provider organization, poly(propylene oxide)
PPPA Poison Prevention Packaging Act
PPS professional pharmacy services
Prl prolactin
PRN as needed, Pharmacist Recovery Network
PRO professional review organization
PSA prostate specific antigen
PSC Program Support Center, pluripotent stem cell
PSE porto-systemic encephalopathy
PSIT Pennsylvania Smell Identification Test
PSP phenolsulfonthalein
PSST pressure sore status tool
PST pocket smell test
PSVT paroxysmal supraventicular tachycardia
PT prothrombin time
PTA plasma thromboplastin antecedent
PTC plasma thromboplastin component
PTCB Pharmacy Technician Certification Board
PTFE polytetrafluorethylene
PTH parathyroid hormone
PT/INR prothrombin time/international normalized ratio

PTSD	post-traumatic stress disorder
PTT	partial thromboplastin time
P2C2	professionals and patients for customized care
PUSH	pressure ulcer scale for healing
PVC	premature ventricular contraction
PVD	premature ventricular depolarization
PVP	polyvinylpyrrolidone
PWDT	pharmacist's workup of drug therapy

Q

Q	coulomb
QA	quality assurance
QALY	quality-adjusted life years
QC	quality control
QOL	quality of life

R

RA	rheumatoid arthritis
RAM	random access memory
R&D	research and development
RAP	resident assessment protocol
RBC	red blood cell
RBRVS	resource-based relative value scale
RCA	root cause analysis
RCC	renal cell carcinoma
RCT	randomized controlled trial
RDA	recommended daily allowance, recommended dietary allowance
rDNA	recombinant DNA
RDI	reference daily intake
REM	rapid eye movement
RES	reticuloendothelial system
RF	rheumatoid factor
RFLP	restriction fragment length polymorphism
RH	relative humidity
Rh	rhesus blood factor/group
rhGM	recombinant granulocyte-macrophage
RI	refractive index
RIA	radioimmunoassay
RIBA	recombinant immunoblot assay
RMP	risk management program
RNA	ribonucleic acid
RNAi	RNA interference
RNase	ribonuclease
RO	reverse osmosis
ROI	return on investment
rPA	recombinant plasminogen activator
RPC	reverse-phase chromatography
RPN	risk priority number
RPR	rapid plasma reagin
RPS	Remington's Pharmaceutical Sciences
RSD	relative standard deviation
RSE	reference standard endotoxin
RSV	respiratory syncytial virus
RV	residual volume
RVU	relative value unit
Rx	prescription

S

SA	sinoatrial
SAD	sunlight affective disorder
SADR	suspected adverse drug reaction
SAE	serious adverse event
SAL	sterility assurance level
SAMHSA	Substance Abuse and Mental Health Services
SAP	sterility assurance probability
SARA	Superfund Amendment and Reauthorization Act
SARS	severe acute respiratory syndrome
SBP	systolic blood pressure
SC	subcutaneous
SCD	soybean casein digest
SCID	severe combined immunodeficiency
SCOT	support-coated open tubular
SCT	sugar-coated tablet
SD	standard deviation
SDO	standards development organization
SDS	special delivery system
SEC	size-exclusion chromatography, soft elastic capsule
SERM	selective estrogen-receptor modulator
SFC	supercritical fluid chromatography
SI	International System of Units
SIADH	syndrome of inappropriate antidiuretic hormone secretion
SIDS	sudden infant death syndrome
SIMS	secondary ion mass spectrometry
siRNA	small interfering RNA
SLE	systemic lupus erythematosus
SMBGP	self-monitoring blood glucose product
SMILES	Simplified Molecular Line Entry Specification
SMU EC	Safe Medication Use Expert Committee
SNDA	supplemental new drug application
SNP	single nucleotide polymorphism
SOAP	subjective, objective, assessment, and plan
SOP	standard operating procedure
SPE	solid phase extraction
SPF	sun protective factor
SRM	selected reaction monitoring
SSA	Social Security Act
SSRI	selective serotonin reuptake inhibitor
STA	slit-to-agar
STD	sexully transmitted disease
STH	somatotrophic hormone
STP	standard temperature and pressure
SUPAC	scale-up and post-approval changes
SUV	small unilamellar vesicles
SVI	small-volume injection
SVM	support vector machine
SVP	small-volume parenteral
SWI	sterile water for injection
SWOT	strengths, weaknesses, opportunities, and threats

T

T_3	triiodothyronine
T_4	thyroxine
TAP	total available pool
TB	tuberculosis
TBG	thyroxine-binding globulin
TBPA	thyroxine-binding prealbumin
TC	total cholesterol
TCD	thermal conductivity conductor
TCGF	T-cell growth factor
TCR	T-cell receptor
TD	toxicodynamic, tetanus and diphtheria
TDD	telecommunication device for the deaf
TDDS	transdermal drug-delivery system
TESS	toxic exposure and surveillance system
TG	triglyceride
TGA	thermogravimetric analysis
TH	T helper
TIA	transient ischemic attack
TIBC	total iron binding capacity
TIV	trivalent inactivated influenza vaccine
TK	toxicokinetic
TLC	thin-layer chromatography, therapeutic life-style change
TM	transcendental meditation
TMA	thermomechanical analysis
TMP-SMZ	trimethoprim-sulfamethoxazole
TNA	total nutrient admixture
TNF	tissue necrosis factor
TOC	total organic carbon
TOPS	Take Off Pounds Sensibly
tPA	tissue plasminogen activator
TPC	total pharmacy care
TPN	total parenteral nutrition
TPO	treatment, payment and health care operations
TPU	Troop Program Unit
TPQ	total product quality
TQM	total quality management
TRH	thyrotropin-releasing hormone
TRIP	turning research into practice
T.R.U.E.	thin-layer rapid use epicutaneous
TS	test solution
TSD	thermionic specific detector
TSH	thyroid-stimulating hormone
TT	tablet triturate
TTP	thrombotic thrombocytopenic purpura
TV	tidal volume
2D-NMR	two-dimensional nuclear magnetic resonance

U

UCC	Uniform Commercial Code
UCR	usual, customary and reasonable
UL	tolerable upper intake level
ULV	unilamellar vesicles, ultralow-volume
UPIN	unique provider identification number
URI	upper respiratory infection
URL	Uniform Resource Locater
USAF	United States Air Force
USAN	United States Adopted Names
U.S.C.	United States Code
USDA	United States Department of Agriculture
USNS	United States Naval Ship
USP	United States Pharmacopeia
USP DI	USP Drug Information
USP/NF	United States Pharmacopeia/National Formulary
USPSTF	United States Preventive Services Task Force
UTI	urinary tract infection
UV	ultraviolet

V

V	volt
VA	Veterans Affairs
VC	vital capacity
VDRL	Venereal Disease Research Laboratory
VEGF	vascular endothelial growth factor
VHA	Veterans Health Administration
VIP	vasoactive intestinal polypeptide
VIPPS	verified internet pharmacy practice sites
Vis	visible
VLCD	very low calorie diet
VLDL	very low-density lipoprotein
VOC	volatile organic compound
VTE	venous thromboembolism
VNTR	variable number of tandem repeats

v/v percent volume in volume
VWD von Willebrand's disease
VWF von Willebrand factor

W

W watt
WA wide awake
WAP wireless application protocol
WAS Wiskott-Aldrich syndrome
WAVE Women's Angiographic Vitamin and Estrogen
WBC white blood cell
WCOT wall-coated open tubular
WFI water for injection
WHA World Health Assembly
WHIMS Women's Health Initiative Memory Study
WHO World Health Organization
WIC Special Supplemental Program for Women, Infants, and Children
W/O water-in-oil
w/v percent weight in volume
w/w percent weight in weight

X

X-LA X-linked agammaglobulinemia
XML extensible markup language
XRD X-ray diffraction
XRPD X-ray powder diffraction

Y

Z

Z atomic number
ZE Zollinger-Ellison syndrome
ZSR zeta sedimentation ratio