8

Fibers in medical healthcare

Fibers have always occupied a fundamental position in medical healthcare, by providing textiles, in the form of fibers, mono- and multi-filament yarns, woven, knitted, nonwoven and composite materials. The uses are many and varied, from the non-implantable materials such as bandages, dressings, etc., implantable materials such as sutures, vascular prostheses, hygiene products such as bedding, clothing, operating room garments, wipes, etc., to the more specialized items such as the artificial kidney. Most are disposable, but an increasing proportion of the products are reusable. In keeping with the objectives of this volume, some of the developing and possible future uses will be outlined.

8.1 Nonwoven

The official definition of nonwoven supported by the European Disposable and Nonwoven Association is:

> Nonwoven is manufactured sheet of directionally or randomly oriented fibers bonded by friction and/or cohesion and/or adhesion forces, excluding paper and products which are woven, knitted, tufted, stitch bonded incorporating binding yarns of filaments or felted by wet milling whether additionally needled or not. The fibers may be staple of continuous filament or be formed 'in situ'.

Traditional uses are for the many textile products used in operating rooms and hospital wards generally. Less obvious uses are:

Filtration

- Liquid, for example, blood, body fluids and water
- Air inwards and operating theatres
- Anaesthetic gases
- Odor removal, dressings, ostomy
- Anti-allergic bedding

Clothing
- Disposable gowns for patients
- Re-usable components of uniforms
- Components of shoes/footwear

Building
- Insulation for sound, heat
- Flame retardant materials
- Components of furniture
- Carpets

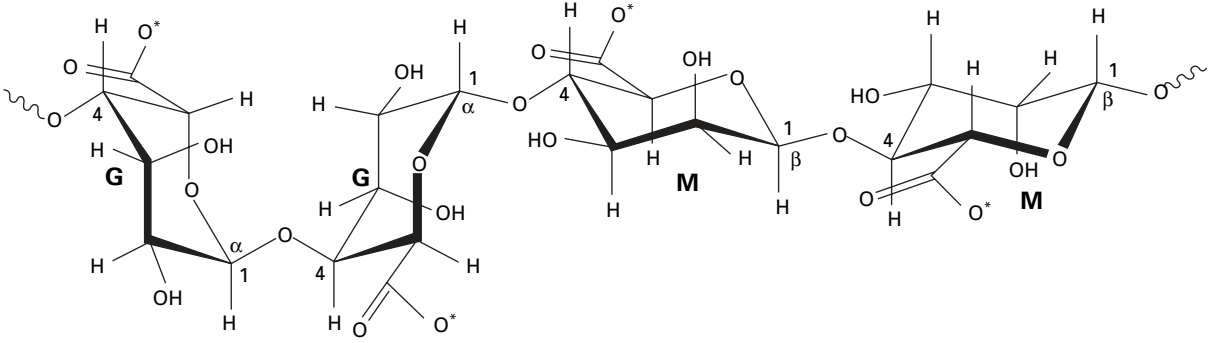
Their use is characterized by their ability to meet the huge variety of needs. Nonwoven technology allows for continuous production with minimal intermediate stages, whereas traditional textiles may require several distinct discontinuation batch processes, for example spinning, winding, beaming, sizing, before knitting or weaving.

The process for nonwoven is simple, productive, versatile, economic and innovative. It requires only the formation of the fibrous web and then binding together of the fibers. Their versatility will surely keep the nonwoven medical materials at the forefront well into the new millennium.

8.2 Alginate fibers

Alginate nonwoven dressings have many advantages over traditional dressings, particularly for moist wound dressings. Alginate is a hydrocolloid present in brown seaweed. The structure, shown in Fig. 8.1, is a polyelectrolyte made up of two building units: mannuronic acid (M) and guluronic acid (G). The counter ions are generally sodium or calcium fibers made from alginate either consisting of a high proportion of G or M units. In the high G alginate the calcium ions are firmly bound and consequently the fiber is slower to gel because of the slow rate of ion-exchange. High M alginate, on the other hand, gels more quickly because of the relative lower strength of binding of the calcium ions. To accommodate different dressing requirements, both high G and high M alginates are commercially available.

Alginates are indicated for all types of exuding wounds, although doubts have been expressed about their use on infected wounds. Their construction and availability in ribbons, ropes, and strips makes them suitable for many types of cavity wound. In the dental environment alginates are indicated as haemostat dressings. Most will require a secondary dressing to retain them in the wound. The England & Wales Drug Tariff (TSO) indicates they may be used on heavy exudate wounds, but it should be noted that the fluid handling capacity of some brands is lower than the foam dressings in terms of direct size comparison. However, their fast fluid uptake enables the alginates to cope with fast flowing wounds, at the cost of frequent dressing changes,



8.1 The structure and functional groups in alginate in the acid form.

where foams are sometimes overwhelmed. In this situation the use of a foam dressing as a secondary dressing can prove to be an effective, if expensive, solution. Data from Kings College Hospital London (Edmonds and Foster) suggests that foam dressings may be more appropriate for diabetic foot ulcers.

Alginate dressings are constructed from interwoven strands of calcium alginate mixed, in some brands, with varying proportions of sodium alginate. Normally they are presented as a flat sheet of a few mm thickness, although ribbons or ropes are available. Some brands may have a backing fixed to the alginate mass for structural strength.

On contact with wound exudate the fibres turn to a gel trapping moisture at the wound surface to create a moist environment. This also makes them easy to remove at dressing changes. This mode of action makes them unsuitable for dry or necrotic wounds, even when soaked with saline. Some concern has been expressed that under some conditions fibres that do not fully gel may act as a foreign body in the wound. This may increase the length of the inflammatory stage. Table 8.1 show the various commercial type of polysaccharide dressings available.

When gel is formed the fiber structure disintegrates and the dressings lose their strength. In many such situations a used alginate dressing cannot be removed in one piece. Thus reinforced wound dressings refer to the type of alginate dressings that contain a web of continuous non-gelling materials, which when wetted will act as a firm structure to the dressings to facilitate a complete and clean removal.

8.3 Superabsorbent fibers

The use of superabsorbent materials in fiber form have now become a commercial reality. A collaboration between Courtalds Fibres and Allied Colloids has produced a cross-linked copolymer of acrylic acid. It is marketed under the name OASIS. Their properties are given in Table 8.2.

Table 8.1 Various brands of commercial polysaccharide dressing

Brand	Type	Manufacturer
Algisite M		S+N
Algosteril		Biersdorff
Aquacel	Cellulose fiber	Convatec
Comfeel SeaSorb		Coloplast
Kaltostat	20% sodium alginate	Convatec
Kaltogel		Convatec
Melgisorb	Calcium/sodium mix	Molnlycke
Sorbsan		Maersk
Sorbsan Plus		Maersk
Tegagen		3M

Table 8.2 Properties of cross-linked acrylic acid co-polymers OASIS

Property	Saline (g/g)	Water (g/g)
Free swell absorbancy	40	80
Retention (0.5 psi)	30	60
Absorbancy under load (0.25 psi)	23	45

The advantages that fibers offer compared to powders is due to their physical form, or dimensions rather than their chemical nature. They will absorb many times their own weight, even when under pressure (Table 8.2). This is due to the small diameter of the fibers which is about 30μm, which gives a very high surface area for contact with the liquid. Also the fiber surface is not smooth. It has a crenulated structure with longitudinal grooves. These are beneficial in transporting moisture to the surface. The lubricant has also been selected to enhance this wetting effect and results in a very high rate of moisture absorption. Typically the fiber will absorb 95% of its ultimate capacity in 15 seconds. It is possible to process OASIS in blends with other fibers on most of the conventional nonwoven processing routes to produce fabrics suitable for medical products such as disposable incontinence products, wipes and absorbent pads, drapes, ostomy bags, and in wound care.

8.4 Wound healing and polysaccharide fibers

The process by which tissue repair takes place is termed wound healing and is comprised of a continuous sequence of inflammation and repair, in which epithelial, endothelial, inflammatory cells, platelets and fibroblasts briefly come together outside their normal domains, interact to restore a semblance of their usual discipline and having done so resume their normal function.

The process of wound repair differs little from one kind of tissue to another and is generally independent of the form of injury. Although the different elements of the wound healing process occur in a continuous, integrated manner, it is convenient to divide the overall process into three overlapping phases and several natural components for descriptive purposes.

Wound care management is an extremely complex medical operation and no single dressing can provide for all eventualities. The successful wound dressing must satisfy several criteria:

1. Seal the wound and prevent introduction of external stresses and loss of energy
2. Remove excess exudates and toxic components
3. Maintain a high humidity at the wound-dressing interface

4. Provide thermal insulation
5. Act as a barrier to microorganisms
6. Be free from particulates and toxic wound contaminants
7. Be removable without causing trauma at dressing changes.

Polysaccharide hydrocolloid systems have been devised to fulfill these criteria but they are seldom produced from a single polysaccharide. Commercial considerations protect the details of the various formulations.

Chitin (poly-1,4,2-acetamido-2-deoxy-β-D-glucose) is the second most abundant natural polymer, existing widely in the cell walls of fungi and crustacean shells. Chitin fibers has been suggested as a material which can accelerate wound healing, but due to its chemical and physical nature is very difficult to dissolve. New solvent systems have now been developed which allow fibers to be produced from chitin, but these have yet to make an impact on the market.

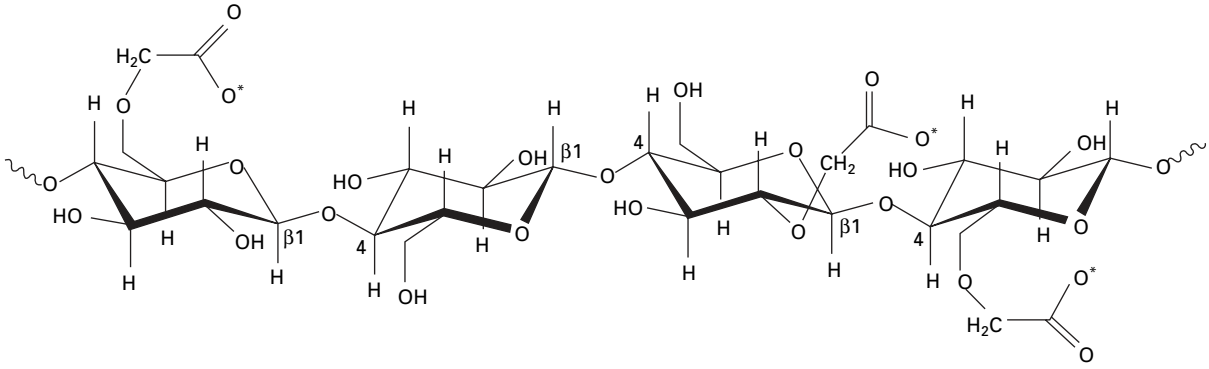
Another useful material is carboxymethyl cellulose (Fig. 8.2) which can be produced chemically from cellulose, the most abundant carbohydrate in nature. It has the merit that it can be produced in a variety of molecular weights and can then be integrated with other materials such as alginate to produce synergistic behavior in terms of physical properties.

8.4.1 Natural systems

Many natural systems containing polysaccharides have been suggested. One of these is the aloe vera leaf, which has polysaccharide in the parenchymal cells which is used by the plant for energy. When placed over a wound, the wound remains moist and does not dry up as dry wounds do. Epidermal and fibroblast growth factors come from the mucilage arising from the leaf and stimulate the fibroblast directly for growth and repair. The cells as a result migrate within the wound in a proper manner to increase wound healing. The occlusive nature of mucilage increases wound healing from a mechanical and endocrine viewpoint.

To follow up this observation, there has been further research and there is now a US patent covering this area, which claims the following:

> The present invention provides a rapid and efficient method for the preparation and isolation of biologically active polysaccharides from Aloe. The present invention includes the activated mixture of polysaccharides (referred to herein as ‘Inmuno-10’), produced by the methods of the invention. The invention also includes the use of the polysaccharides as immunostimulating, immunomodulating and wound healing agents. The resulting immunomodulatory complex has a higher activity and is more stable than bulk carbohydrates isolated using prior art alcohol precipitation schemes.



8.2 The structure of carboxymethyl cellulose.

Chemically the polysaccharide consists of:

- primarily (>95%) of polysaccharides derived from aloe having an average molecular weight of 70–80 kDa with a range between 50–200 kDa;
- D-galactose (approx. 5% or less), D-glucose (approx. 5% or less) and D-mannose (approximately 90%);
- monosaccharides having primarily β-1,4 linkages and
- highly acetylated, having approximately 1 acetyl group per monosaccharide, with the acetyl group on the 2, 3 or 6 position of the monosaccharide unit.

Another is CM101, an anti-pathoangiogenic polysaccharide derived from group B streptococcus, has been shown to inhibit inflammatory angiogenesis and accelerate wound healing in a mouse model and minimize scarring/gliosis following spinal cord injury.

8.4.2 Cellulosic membranes

Artificial kidney – Haemodialysis

Over the past 20 years cellulosic membranes have improved considerably, due to the ability to form:

- thinner membranes
- controlled pore size
- improvement of surface properties.

These are now the basis of the production of a range of artificial kidneys for the treatment of chronic renal failure, and for this purpose the membranes are made from cuprammonium solution and saponified cellulose triacetate. The world market for artificial haemodialysis is expanding at a rate of 5% per year and in 1988 the world consumption was 3×10^7 units. Of these 66% were cuproammonium, and 15% cellulose acetate membranes, with the remainder using synthetic polymers. The number of patients receiving monthly haemodialysis in Japan at the end of 1990 exceeded 100 000 and 77% used the cuprammomium membranes. By the mid-1980s new cuproammonium-regenerated cellulose membranes with controlled pores sizes (4–10 nm) were developed by Professor K. Kamide of the Asahi Chemical Industry, Japan.

Nowadays most cellulose membranes are of the hollow-fiber type and fall into two categories:

- conventional hollow fibers (AM-SD series)
- biocompatible artificial kidney with standard and middle flux range (AD-Bio series)

Virus removal filters for human blood

The porous cellulose membrane (BMM™) with mean pore diameter ranging from 10 to 100 nm and having a sharp pore radius distribution enables the exclusive removal of disease viruses, such as acquired immune deficiency syndrome (AIDS) virus, human immunodeficiency virus (HIV), and hepatitis C virus. The composition of the filtrate of human plasma, separated through BMM™ with mean pore size greater than 20 nm is very similar to that of the original plasma.

Plasma separation membranes can separate red cells (6–9.5 μm in diameter), white cells (6–20 μm in diameter) and platelets (2 μm in diameter) from plasma, mainly composed of proteins like albumin and γ-globulin.

Conclusion

Breakthroughs in cellulose membrane technology have arisen because the membrane formation mechanism is better understood and pore characteristics can now be controlled. The thermodynamics of membrane formation based on particle-growth concept and lattice theory is better understood with respect to the solvent-cast method (that is the phase separation method). The pore size distribution can be calculated numerically by the lattice theory. Breaking strength of membranes is explained by considering development of bonding between the secondary particles and the total number of contact between the nearest secondary particles per unit surface of the membrane. The three-dimensional multilayered structure derived from the concept is the most suitable model for progressing the pore characteristics of the membrane.

New cellulose haemodialysis membranes having a larger sieving coefficient for β_2–microglobulin can avoid chronic haemodialysis associated syndromes such as carpal tunnel syndrome. Furthermore, cellulose membranes have already been improved to suppress the activation of complement using the new techniques to decrease free OH groups on the surface. The progress of the cellulose membrane industry in the future looks extremely promising.

8.5 Hyaluronan – a new medical fiber

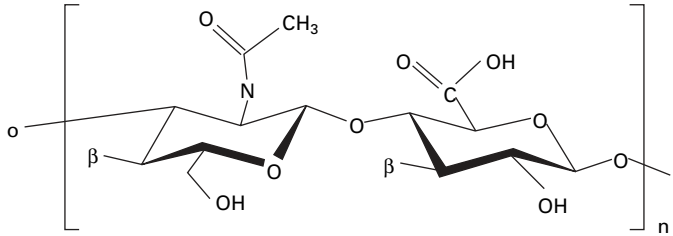
Once a scientific novelty, this connective tissue polysaccharide is now central to the understanding and treatment of many intractable diseases. Two major international conferences were organised in Wales (2003) and the the United States (2003). The books arising from these landmark meetings have shown how wide the medical interest is in this material, as detailed in the reference section to this chapter. Previously regarded as the matrix which acted as a shock absorber in the body, it has now been found to bind into cells via specific receptor sites, and to instruct the cell how to behave. It is, therefore, at the centre of normal and disease-related cell proliferation.

Among the reported new developments are its uses and potential in the following areas:

- breast cancer
- as a switch to control cell-cancer behavior
- as an anti-cancer material
- in corneal wound healing
- cartilage maintenance
- repair of lung injury
- healing of chronic wounds
- engineering of new tissues
- treatment of diabetic foot ulcers
- kidney diseases in relation to diabetes
- in the control of eye surgery

Hyaluronan (HA) is a linear polysaccharide, with a fiber structure, which consists of repeating disaccharide units of D-glucuronic and N acetyl-D-glucosamine residues (Fig. 8.3). The residues are both β-linked in the polymer, D-glucuronic acid being linked at carbon 1 and 4, the glucosamine residue at positions 1 and 3.

Hyaluronan occurs naturally in vitreous humor synovial fluid and umbilical cord and in many animal tissues in smaller concentrations. It has been reported that the molecular weight of naturally occuring hyaluronan varies within the range 10^5 to 10^7. Hyaluronan can be produced from biological sources such as bovine vitreous, umbilical cord and rooster comb. The highest molecular weight of hyaluronan produced from animal sources commercially available is about 5×10^6 and marketed under the trade name of Healon GV. Hyaluronan can also be produced from certain strains of *Streptococcus* bacteria, but the molecular weight of bacterial hyaluronan is lower, despite an easier production process of fermentation, extraction, and purification from the broth. The highest molecular weight produced by this method is about 2.5×10^6.



8.3 The component sugars and repeating disaccharide unit of hyaluronan fiber.

Balazs and co-workers have developed a family of cross-linked hyaluronan derivatives called hylans (HY) which can be produced either in water soluble form (hylan A) or as viscoelastic gels (hylan B). In the first procedure, formaldehyde is used at neutral pH to produce a permanent bond between the C-OH group of the polysaccharide and the amino group of a protein with relatively small molecular size and specific affinity to the hyaluronan chain. The protein forms a bridge between two polysaccharide chains. Under appropriate conditions, the cross-linking process will yield a molecular network consisting of permanent association of two to eight HA molecules. The average molecular weight of HY molecules is $6–24 \times 10^6$ with a protein content of 0.4–0.8% of the total polysaccharide weight. The second cross-linking process utilizes vinylsulfone. The HY molecules obtained from this technique are insoluble but are produced in the form of a viscoelastic gel. The two cross-linking procedures retain the biocompatibility and physical functionality of the unmodified hyaluronan, but physicochemical parameters such as molecular weight, molecular size and rheological properties, of the polymer solution or suspension, on hydration are substantially affected. Thus HY can be used in applications for which high molecular weights are needed such as viscosupplementation for the treatment of osteoarthritis of the knee joint.

The term *matrix engineering* was first used by Dr Endre A. Balazs (1971) to describe the use of natural and chemically modified biopolymers, derived from hyaluronan, to control, direct and augment tissue regeneration processes. Such biomaterials, therefore, can be regarded as a specialized type of non-inflammatory, biocompatible tissue graft, capable of a wide range of applications for the augmentation, protection and repair of human tissues. The base material, the glycosaminoglycan hyaluronan, is present in virtually every tissue in the human body and if the natural repeating structure and conformation are preserved and inflammatory fractions removed, the resulting biomaterial is not recognized as immunologically or otherwise foreign. This technically difficult task, achieved by Balazs, enabled the routine production of a highly purified, non-inflammatory hyaluronan fraction, known by its acronym, NIF-NaHA.

The first clinical studies with NIF-NaHA were initiated in 1968 using racehorses with traumatic osteoarthritis. In equine arthritis, the elastoviscosity of the synovial fluid in the joints decreased, and by using NIF-NaHA with an average molecular weight of $2–3 \times 10^6$, the pathological synovial fluid of low elastoviscosity was replaced with a fluid that had significantly higher elastoviscosity than the normal healthy synovial fluid. For this supplementation of the synovial fluid, the term *viscosupplementation* was coined. Since that time, it has become known that the medical benefits of a viscosupplement depend on its rheological properties, rather than on the chemical nature of the viscosupplement. The efficacy of the viscosupplement depends on the

elastoviscosity of the fluid or, at equal polymer concentrations, on the average molecular weight.

The first human clinical use of NIF-NaHA was reported by Balazs and coworkers in 1972 using this elastoviscous fluid as a viscosurgical tool during corneal transplantation and as a viscosupplement for the vitreus after retinal detachment surgery. The other clinical use of NIF-NaHA, at that time, was for the treatment of the painful osteoarthritic joints in humans.

In the early 1980s, after the introduction of intraocular lenses after cataract surgery became a widely used medical procedure, Healon® and viscosurgery found a new application. In a very short time, viscosurgery with Healon became routine in ophthalmic surgery, and provided elastoviscous protection for the corneal epithelium and the iris against mechanical damage due to instruments and implants. In viscosurgical procedures, the elastoviscous fluid also makes and maintains space for surgical manipulation, prevents tissue adhesion, controls bleeding by its barrier effect, and helps in the removal of tissue debris, such as pieces of cataractous lens. Today, in addition to Healon, at least ten different preparations are available worldwide for ophthalmic viscosurgery, but because of their lower molecular weight, none have the same high elastoviscous properties of Healon Viscosurgery. The use of 'viscoelastics' in ophthalmic surgery has been accepted internationally, and the International Standards Organization now provides standards for 'Ophthalmic Viscosurgical Devices for use in Anterior Segment'.

The first 'viscoelastic' used in medicine was marketed worldwide in the late 1970s and early 1980s by Pharmacia AB (Uppsala, Sweden, now Pharmacia & Upjohn Company). It was a 1% solution of NIF-NaHA with an average molecular weight of approximately 3 million and was used in ophthalmic viscosurgery (Healon®) and for the treatment of arthritis in horses and other animals (Hylartil®).

It was not until 1987 that the first hyaluronan (NIF-NaHA) viscosupplementation product became available to human patients in two countries for treatment of osteoarthritis. Two companies, Seikagaku in Japan, and Fidia in Italy, produced low molecular weight NIF-NaHA (average MW $0.5–0.8 \times 10^6$) and introduced it in their respective countries. The lower molecular weight and the lower elastoviscosity meant that these products required more injections (5–10 injections weekly) than the more elastoviscous NIF-NaHA tested decades earlier (2–3 weekly injections).

The need for a more elastoviscous hyaluronan product to produce a viscosity as close as possible to that of the synovial fluid of a healthy young adult human, and for strong, soluble and insoluble viscoelastic gels and solids, led to the development by Balazs and his coworkers at Biomatrix, Inc. (USA) of a new family of hyaluronan derivatives named hylans. Hylan is a generic term used to refer to a class of hyaluronan derivatives produced by cross-linking of the polysaccharide chains via hydroxyl groups of the hyaluronan,

leaving the carboxylate, the acetamido, and the reducing end groups unaltered. The retention of the carboxylate group is particularly important because it is this group that confers the polyanionic character to the molecule, which is critical to its physicochemical and biological properties. Hylan polymers are available in physical forms which range from highly elastoviscous solutions to viscoelastic gels and solids. This allows the physical properties and residence time of hyaluronan to be controlled without loss of biocompatibility.

The hylan polymers used in medical practice today are called hylan A and hylan B. Hylan A is produced *in situ* by treating hyaluronan-rich tissue sources with aldehydes before extraction. The aldehyde activates the hydroxyl groups of the hyaluronan, which interact with a small amount of specific protein, forming a covalent bond (protein content is ≤ 0.5% of polysaccharide) and resulting in soluble hyaluronan polymers with enhanced molecular weight. Hylan B is synthesized by treating hyaluronan or hylan A with divinyl sulphone under mild alkaline conditions. The reaction conditions can be varied to produce materials with properties which range from soft deformable elastic gels to solids of various shapes with long residence times in tissues.

Based on these two new biopolymers, a range of products has been developed and marketed worldwide. Synvisc® (hylan G-F 20) is a highly elastoviscous synovial fluid supplement with elastic and viscous properties similar to those of the synovial fluid of young, healthy humans used for the treatment of osteoarthritis. Hylaform® (hylan B) is a solid hydrated gel implanted into soft tissues for viscoaugmentation of facial wrinkles and depressed scars. Hylashield® (hylan A) is a dilute elastoviscous solution applied to the surface of the eye for comfort and protection from noxious environmental conditions (viscoprotection).

Tendon adhesion following injury or after surgical repair is a significant clinical problem. Ever-expanding procedures associated with tissue banking include the replacement of the cruciate ligament with human patellar allografts, spinal fusion, and revision hip surgery (using bone allografts) where this problem is frequently encountered. Dry sheets and high concentration NIF-NaHA solutions have been tested in various animal models of tendon regeneration and in primate tendon surgery since the early 1970s. Hylan B gels were used more recently as a viscoseparation device to reduce postsurgical tendon adhesion and scar formation.

Hylans have been used in percutaneous embolization to produce blood coagulation in vessels feeding arterial venous malformations in the brain or in facial tissue, and to alleviate arterial bleeding in the lung and other organs of the body. In this process, hylan B gel is used as a vehicle to deliver hemostatic agents with x-ray-opaque material to the target tissue, and blocking blood flow and causing the permanent blockage of the vessels by connective tissue formation.

Hylan A fluid and hylan B solids provide today the most biocompatible and most versatile intercellular matrix system to be used as a molecular framework alone or with other matrix molecules (collagen, elastin, proteoglycans) for cell populations to form artificial organs. The clinical use of medical devices made from hylans is well documented.

Matrix engineering introduced the concept of using elastoviscous fluids and viscoelastic solids as therapeutic agents in medicine. The various uses have been described as: *viscosurgery* for protection and manipulation of tissues during surgery, *viscoseparation* after surgery to prevent adhesion formation, *viscosupplementation* to replace or supplement dysfunctional tissues or tissue fluids, *viscoaugmentation* to add viscoelastic molecular matrices to augment and build up tissues, *viscoprotection* for coating of the tissue surfaces in order to protect them from environmental damage, and *viscoregulation* to regulate implants, tissue regeneration and new tissue and organ development with viscoelastic molecular matrices.

Hylan implants can be regarded as a new class of allografts because they are made from the molecules which exist in the human body and therefore fulfill non-definition of homeographs that originate from genetically not identical individuals of the same species. Matrix engineering can be redefined as the allogra use of molecular matrices made of building blocks of the body to be populated with homologous cells before or after grafting in order to replace tissues or regulate and stimulate their regeneration.

Hylans and their co-polymers, together with other glycosaminoglycans and a variety of molecular matrices and pharmacologically active agents, can be used as scaffolds, carriers and matrices of cells for implantation. Their unique biocompatibility and rheological properties combined with the greater resistance to free radical degradation and high water-binding properties of these new solid biopolymers, makes them an ideal material for tissue allografts for implantation and for control of tissue regeneration.

The interest in hyaluronan systems has been intense in respect to wound healing. Hydrogel dressings, based on hyalronan and another glycosaminoglycan from connective tissue (chondroitin sulphate), have been developed by University of Utah medical researchers. If the hydrogels work as well in people as they have in mice, millions of diabetics, elderly, burn victims and surgical patients may benefit from faster-healing diabetic ulcers, skin grafts, surgical incisions and other wounds. The researchers reported their findings in the journal *Biomaterials*.

The hydrogels look like a piece of clear, thin plastic when dry, but expand six times in volume and become pliable when wet. Trials with mice show hydrogel wound dressings accelerate healing in the epithelium – the outer layer of skin – in young, healthy mice by up to 33%, with complete healing of deep wounds in five to seven days. If the success in young, healthy mice is indicative, the researchers say the hydrogels would help older, less healthy mice, or people, even more profoundly.

The researchers hope to gain US Food and Drug Administration approval to begin human trials of the hydrogels. Conventional dressings and bandages serve mainly to keep moisture in and germs out as a wound heals. But hydrogel dressings slowly break down and reintegrate into the wound and extracellular matrix that surrounds human cells. According to Glen Prestwich, who led the project 'The hydrogel actually becomes integrated into the wound. It's a scaffolding that enhances healing.'

Hyaluronan and chondroitin sulphate were also mixed with a reactive version of a waxy polymer called polyethylene glycol (PEG). Within seconds of being mixed, the substances cross-linked – a chemical process akin to weaving cloth – and within minutes they became gels.

8.6 Other fibrous scaffolds for tissue engineering

The tissue engineering process starts with a scaffold and a supply of cells. The cells could be the patient's own cells, a donor's cell or taken from a tissue bank. These are seeded into a proposed scaffold. The cells themselves attach to the scaffold and are cultured within a mini bio-reactor. Tissue culture media provide nutrients for the cells and remove waste products. The cells increase in number and lay down the new extracellular matrix to form neo-tissue. If bio-resorbable fibers are used, then these will start to degrade. At the end of culturing the tissue engineered may require preservation and storage before used as an implant.

In addition to the polysaccharides the most important synthetic group which have application as bio-resorbable scaffolds are poly(glycolic acid) and poly(lactic acid). These have an established history as sutures or surgical devices. One such tissue engineered and now on the commercial market is Dermograft™, a joint venture between Advanced Tissue Services (USA) and Smith and Nephew, used for the treatment of diabetic foot ulcers. These wounds are difficult to heal and can often lead to serious complications. The scaffold is produced from multifilament yarn, a 90–10 co-polymer of poly(glycolic acid) and poly(lactic acid). Specially shaped scaffolds are produced for articular cartilage and meniscal cartilage.

8.7 Collagen: medical applications

Collagen is a major structural protein, forming molecular cables that strengthen the tendons and vast, resilient sheets that support the skin and internal organs. Bones and teeth are made by adding mineral crystals to collagen. Collagen provides structure to our bodies, protecting and supporting the softer tissues and connecting them with the skeleton. It is composed of three chains, wound together in a tight triple helix, each chain being over 1400 amino acids long. A repeated sequence of three amino acids forms this sturdy hydroxyproline

structure. Every third amino acid is glycine that fits perfectly inside the helix. The special amino acid sequence makes the tight collagen triple helix particularly stable. Every third amino acid is a glycine, and many of the remaining amino acids are proline or hydroxyproline.

The collagen molecule is a triple helix assembled from three individual protein chains. The triple helix is further assembled into larger structures known as fibers. The collagen fibers play an important role in binding platelets under conditions of blood flow. These 'type I' collagen molecules associate side-by-side, like fibers in a rope, to form tough fibrils. These fibrils criss-cross the space between nearly every one of our cells. These form a basement membrane (collagen-2), which forms a tough surface that supports the skin and many organs. A different collagen ('type IV') forms the structural basis of this membrane.

Collagen has found widespread medical uses. Urology, dermatology, orthopaedics, vascular and general surgery utilize collagen in various forms ranging from injectable solutions to sponge-like materials. In addition, collagens extracted from animal species, primarily bovine, are used in the preparation of a wide variety of commercial products including:

- biological dressings
- tissue culture applications
- dermal injectables.

Collagen is an ideal biomaterial for the development of medical and other commercial products because it is highly biocompatible, is readily available at high purity, and can be manufactured in such diverse forms as pastes, gels, films, sponges, and felt-like sheets using a variety of process methods. In cosmetic treatments it is able to:

- smooth facial lines and wrinkles
- add definition to lip line borders
- smooth smile lines
- improve 'marionette' lines
- decrease frown lines
- improve vertical lip lines
- fill shallow acne scars

The role of collagen in blood clotting is complex and multi-factorial. Platelet-collagen interactions have received considerable attention because collagen is considered to be the most thrombogenic constituent of the vessel wall. After injury, platelets exposed to collagen in the sub-endothelial layer adhere rapidly to the exposed collagen fibrils. Platelet binding to collagen can occur through a direct platelet-collagen interaction or can be mediated via von Willebrand factor forming a bridge between collagen and platelets. Platelets bind to collagen, aggregate, adsorb, and concentrate clotting factors.

Platelet-bound fibrinogen is converted to fibrin which forms a cross-linked network. The fibrin network which forms reinforces the otherwise friable platelet plug. The bound, activated platelets are completely degranulated, releasing ADP, thromboxane, and other secretory products which facilitate clotting. Since the discovery of the role of collagen in blood clotting, collagen obtained from animal skin and tendon has been processed into loose fibrillar forms and felt-like sheets or collagen fleece and used to stop bleeding in an increasing number of procedures including spleen repair, laparoscopy, oral surgery, and general surgery.

Collagen also plays an essential role in the wound healing process. Acting as a tissue scaffold, it is used as a carrier vehicle for cells in tissue engineered products for dermal wound repair and as a carrier vehicle for growth factors in bone repair. Collagen fibers are one of the best scaffolds for cell migration and proliferation. Collagen interacts with fibronectin and other adhesion proteins to promote cellular in-growth which speeds up wound healing. Type I collagen has been shown to attract fibroblasts in cell culture and appears to cause directed migration of cells. Drugs, cells, and growth factors use collagen as both the delivery vehicle and structural support for tissue development and in-growth.

8.8 Medical textiles

A Centre of Excellence for Medical Textiles is located in the Bolton Institute, in the United Kingdom, led by Professor Subhash Anand. Regular update conferences are organized in Bolton and as noted in the reference list the 1996 and 1999 Symposia have been published. Another excellent meeting was held in 2003 (MEDTEX 03) and the Proceedings will be incorporated into a new book due to be published in 2005. Some direct reference will be made here to a few contributions made at that meeting with details of the presenters of the papers for reference.

8.8.1 Textile medical sensors (Lieva van Langenhove and Carla Hertleer, Ghent University)

Textile materials cover a large surface area of the body. Consequently, they are an excellent measuring tool. Biosignals that are mentioned in literature are:

- temperature
- biopotentials: cardiogram, myography
- acoustic: heart, lungs, digestion, joints
- ultrasound: blood flow
- motion: respiration
- pressure: blood.

A significant breakthrough can only be achieved, however, when the sensors and all related components are entirely converted into 100% textile materials. This is a big challenge because, apart from technical considerations, concepts, materials, structures, and treatments must be focusing on the suitability for use in or as a textile material. This includes criteria like flexibility, water (laundry) resistance, durability against deformation, radiation, etc. As for real devices, ultimately most signals are being transformed into electrical ones. Electroconductive materials are consequently of utmost importance with respect to intelligent textiles.

One area of success is the Intellitex suit for measuring heart and respiration rate. Instead of using metal plates, the Intellitex suit uses a conductive textile as an electrode. To measure the heart rate and even an ECG, the Textrodes were developed. The Textrodes have a knitted structure and are made of stainless steel fibres (by Bekintex). They do not require any electrogel. This enables long-term monitoring but has an negative impact on the contact with the skin. For children, attractive design makes them want to wear the suit, and they can be monitored without disturbing them.

The Textrodes make direct contact with the skin. Test results have shown that the electrode's textile structure is an important parameter. When changing the structure, a different contact surface with the skin is obtained. Finer structures with more protruding fibres for instance will adapt more easily to the heterogeneous skin surface, which results in a more intense contact between the electrode and the skin. In turn, this results in a lower impedance of the skin electrode system. So a compromise has to be found between the sense of comfort and the intensity of the contact with the skin. A knitted structure has the advantage of being stretchable. Elasticity is a required property for close fitting of the suit around the thorax.

The Intellitex suit combines heart and respiration rate measurements in one garment. The respiration sensor is a knitted belt called 'Respibelt'. It is also made of a stainless steel yarn. The basic concept could also be used as a strain sensor, for instance to control tension applied in pressure bandages

8.8.2 Textiles in burns treatment (J. Edwards, Wythenshaw Hospital, Manchester)

The care of burns patients has made steady progress. Until the 1960s, even moderate burn injuries were usually fatal. The introduction of fluid resuscitation and the establishment of burns units have had a major impact on mortality. Burns patients have subsequently benefited from many developments, including the introduction of systemic and topical antimicrobial agents, progress in intensive care and nutritional support, changes in surgical philosophy, advances in wound care and methods of achieving skin cover, and the concentration of treatment of patients with serious burns in specialist care. Alongside these

improvements, the use of textiles in the patient's journey from injury to recovery has been crucial. Textile materials act as support surfaces, dressings, splinting, skin substitutes, pressure garments and silicone gels needed to enable a burns patient to travel the road from injury to recovery

The problem of hypothermia in burns has long been recognized. Plasticized Polyvinyl Chloride (PVC) is advocated by the Emergency Management of Severe Burns (EMSB) as a means of preventing hypothermia, reducing pain, and preventing desiccation and infection. The film is very thin and permeable to water vapor, oxygen, and carbon dioxide, easy to apply, and allows for visual inspection of the wound.

On admission, severely burned patients need to be nursed on specialized beds. These can either be air-fluidized beds or low air loss beds. Mattress coverings have developed greatly since the mid 1980s when regulatory changes were made to the flame retardancy requirements. These new coverings are water/moisture vapor permeable and have the ability to transmit water vapor molecules through itself, whilst at the same time remaining a complete barrier to liquid water. There are two main types of materials: microporous materials, and hydrophilic materials. Microporous materials are membranes made from special polymers that have tiny holes in them, e.g. Gore-Tex. Gore-Tex, is vapor permeable, it has pores 700 times larger than water molecules, which let water vapor pass through. This helps to eliminate moisture, friction, shear, infection, contamination, and heat. As burns have copious exudate during the first 24–48 hours, this function is important in a bed. Hydrophilic materials attract water into them and transmit the moisture through the coating by a chemical mechanism. They have no holes in them and are a complete barrier to liquid water. All polyurethanes are hydrophilic to some degree or other, and some can be formed into coatings that are tough, as well as being water vapor permeable. Polyurethane-coated fabrics provide greater patient comfort, are generally resistant to most cleaning agents, and complement carefully engineered support mechanisms.

Burns, after being dressed can be treated with a covering called Exu-Dry. Exu-Dry is a one-piece, multilayer, highly absorbent, non-adherent wound dressing. It incorporates a non-adherent wound contact layer, and an antishear layer, which helps to reduce friction. The absorbency of the product comes from the inner layer, which is highly absorbent. The outer layer is permeable and non-occlusive, allowing the wound to breathe. These dressings overcome many of the problems of traditional dressings of layered paraffin gauze, gauze and gamgee, which was time consuming and had problems of strike through. They also have a marked tendency to adhere to the surface of drying wounds. This is due in part to the exudate sticking the dressing to the wound as it dries and also if left in place long enough, the in-growth of capillary loops within the granulation tissue into the dressing. This in effect incorporates the dressing into the new tissue, which will inevitably be damaged when the

dressing is removed. Exu-Dry dressings come in body shapes such as arms, legs and chests, which enable even inexperienced nurses to dress extensive burns efficiently.

A useful alternative is a product called Telfa Clear, a non-adherent contact layer made from a Mylar perforated polyester (polyethylene terephthalate) film. The specially designed film is composed of hundreds of minute perforations that act as a selective membrane. The size of these holes allows the passage of wound fluid into the secondary dressing, but blocks the entrance of larger epithelial buds. Telfa Clear comes in large sizes and is used as a primary contact layer for the application of Flamazine, enabling large awkward areas to be dressed that are not perhaps covered by the use of Exu-Dry.

Regardless of the dressing type used, most dressings for major burns will require bandages to secure them. Bandages perform a number of functions including retention, support and compression. In burns patients the main functions are retention of the underlying dressings, and support to prevent oedema formation and provide joint support. The type of bandages used traditionally are crepe, which are made of a cotton fabric of plain weave with a characteristic appearance made from the crepe twisted cotton yarns (e.g. Elastocrepe, Elvic). More recently white knitted bandages have been used. These are made from a white knitted conformable fabric containing 93% viscose, 4% nylon and 3% elastomeric yarn (K Lite). This means that these bandages can give more support than traditional crepe bandages.

Having assessed and dressed the burns, the next most important area of care is splinting. Splinting is used for a number of reasons; to increase function, to prevent deformity, correct deformity, protect healing structures, restrict movement and allow tissue growth or remodeling. A number of splinting materials are used, but the majority are made from polycaprolactones (Polyform, Aquaplast). These are low temperature thermoplastic materials, which provide greater conformability and ease of splint fabrication.

8.8.3 Textile finishing for the production of new generation medical textiles (N. D. Oltargevskaya and G. E. Krichevsky, Educational Textile Institute, Russia)

A recent trend in textile chemistry has been the development of the theoretical technological and manufacturing principles for prolonged action textile-based materials for medical purposes. 'Koletex®' is an example of a prolonged action medical bandage, based on the technology used in printing and textiles.

The efficiency of medical bandages is determined by the choice of textile material type, type of a polymer – the medicine carrier (thickener), and medical properties depend on the chosen medical product introduced into a textile material together with the thickening. Printing technology allows the

obtaining on a base of bi-porous textile material a 'double depot', from which medical product can be released controllably and transported into a human organism (into a wound, through skin and into a malignant tumour as well) and performs a medical effect.

'Koletex'® bandages are widely used in Russia in medical practice: 20 types are in product in various areas of medicine for different purposes (surgery, neuralgia, stomatology, oncology, dermatology, gynecology, etc.).

8.8.4 Wound care dressings from chitin (K. Van de Velde, L. Szosland and I. Krucińska Department of Textiles, Ghent University and Department of Textile Metrology, Technical University of Łódź, Poland).

Chitin, a ubiquitous biopolymer found in the exoskeleton of insects and marine invertebrates, shows the extraordinary capability to promote the ordered healing of tissues and is well suited to use in wound dressings. However, chitin is insoluble in common organic solvents, therefore direct industrial applications of chitin are very difficult. Recently the synthesis of dibutyrylchitin (DBC), an ester of chitin, was developed. DBC is easily soluble in common organic solvents and has film- and fiber-forming properties. This invention opens the way for production of a wide assortment of novel functional biomaterials made from DBC and pure chitin regenerated (CR) from DBC, which would promote the wound healing process and can find other medical applications.

8.8.5 A spider silk supportive matrix used for cartilage regeneration (Kris Gellynck, Peter Verdonk, Fredrik Almqvist, Els Van Nimmen, Domir De Bakker, Lieva van Langenhove, Johan Mertens, Gust Verbruggen, Paul Kiekens, Ghent University)

Injured cartilage often decreases quality of life. Repair can be effected if the chondrocytes of the cartilage can be grown and implanted. The chondrocytes need an implanted support to bridge and recover the wound with extra-cellular matrix products forming fresh cartilage. Advances in cell biology and biomaterial research have lead to new possibilities in tissue engineering. Transplanted scaffolds, holding a 3D cell culture, should copy the cartilage characteristics. Strength and flexibility are important, but even more important is an adequate porosity, so the chondrocytes can migrate through the matrix, but are not able to float around.

Looking for regeneration and not a repair, the scaffold material should disappear while real cartilage is healing the wound. In this way the material and its hydrolysis products have to be biocompatible and harmless. In the case of synthetic polymers, the hydrolysis products are frequently toxic, but spider silk is a promising fibre for many applications. Completely made out of protein a possible biocompatibility has already been proven. The harmless amino acid hydrolysis products make the silk a good candidate for creating a bioresorbable textile scaffold.

The chondrocyte cells adhere quite well on the spider cocoon silk threads. Cocoons can be obtained each autumn in large numbers from the *Araneus diadematus* garden spider. The mechanical properties of the silk are more appropriate than polymeric gels, like hyaluronan, collagen, alginate, which proved to be successful in 3D immobilization and maintaining the differentiated phenotype of chondrocytes. The phenotypical products collagen II and aggrecan were also detected around the cells growing on the spider cocoon silk. A silk 3D textile could possibly be applied in combination with a polymer gel, probably alginate, in order to achieve some biomechanical stability. While biodegradation is occuring, the silk textile is overgrown with real cartilage and eventually the wound will recover without any definitive synthetic implants.

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