Chapter 6
OBSTETRICS, GYNAECOLOGY AND GENITO-URINARY TRACT DISORDERS

For hormone therapy of gynaecological disorders *see section 5.4.1* (female sex hormones), *section 5.5.1 & 5.4.2.3* (hypothalamic, anterior pitutary hormones and antioestrogens) and *section 14.3.4.2* (gonadorelin analogues).

6.1 DRUGS USED IN OBSTETRICS

6.1.1 OXYTOCICS AND PROSTAGLANDINS

Oxytocics and prostaglandins are known to increase myometrial activity and can be used to stimulate (induce or augment) labour, to minimize blood loss from placental site and to induce abortion. They include oxytocin, ergometrine and the prostaglandins. All induce uterine contraction with varying degrees of pain according to the strength of contractions induced.

INDUCTION OR AUGMENTION OF LABOUR: **Oxytocin** is administered by slow intravenous infusion preferably using infusion pump to induce or augment labour, usually in conjunction with amoniotomy. Uterine activity must be monitored carefully and hyperstimulation avoided. Large doses of oxytocin

may result in excessive fluid retention due to its vasopressin like action, though it may not occur with presently available synthetic products (e.g. Syntocinon).

PREVENTION AND TREATMENT OF HAEMORRHAGE: Bleeding due to incomplete abortion can be controlled with **Ergometrine** and **Oxytocin**. Usually given intramuscularly (or intravenously), the dose is adjusted according to the patient's condition and blood loss. This is used prior to surgical evacuation of uterus, particularly when surgery is delayed or after evacuation. Ergometrine acts better in first trimester, but later oxytocin and ergometrine combined are more effective than either drug alone.

For active management of third stage of labour inj. oxytocin 10 units is given by intramuscular injection immediately after delivery of baby. & after excluding the presence of additional babies. In case of home delivery where oxytocin is not available tab. Misoprostol 3 tab taken orally can be a good alternative.

In high risk cases where there is increase risk of PPH, intravenous infusion of oxytocin 10-20 unit in 500 ml of normal saline can be given after delivery as a measure of prevention and/or treatment of postpartum haemorrhage, particularly when the uterus is atonic. Excessive bleeding also has to be controlled with inj. Ergometrine and tab. prostaglandin.

ERGOMETRINE MALEATE [ED]

Indications: *see notes above*

Cautions: cardiac disease; hypertension; hepatic and renal impairment; multiple pregnancy (it can be given after the delivery of last baby)

Contraindications: induction of labour, first and second stages of labour, vascular disease, severe cardiac disease, impaired pulmonary function, severe hepatic and renal impairment, sepsis, severe hypertension, eclampsia

Interactions: *see Appendix-2*

Side-effects: nausea, vomiting, headache, dizziness, tinnitus, abdominal pain, palpitation, dyspepsia, bradycardia, transient hypertension, vasoconstriction; stroke, myocardial infarction and pulmonary oedema also reported.

Dose: *see notes above*

Proprietary Preparations
G-Ergometrine *(Gonoshasthaya),* Inj. 0.2mg/ml, Tk. 3.90/Amp.; Tab. 125 microgram, Tk. 0.55/Tab.
Urgotin *(Chemist),* Inj. 0.2mg/ml,, Tk. 30.00/ Amp.

OXYTOCIN [ED]

Indications : *see under dose and notes above*

Cautions: particular caution needed when given for induction or enhancement of labour in presence of borderline cephalopelvic disproportion; mild to moderate pregnancy induced hypertension or cardiac disease; history of lower uterine segment Caesarean section *(see also under Contraindications)*; if foetal death in utero or meconium stained amniotic fluid, avoid tumultuous labour (may cause amniotic fluid embolism); avoid large infusion volumes and restrict fluid intake by mouth (to prevent water intoxication and hyponatreamia); caudal block anaesthesia (may enhance hypertensive effects of sympathomimetic vasopressors);

Contraindications : hypertonic uterine contraction, mechanical obstruction to delivery, fetal distress; any condition where spontaneous labour or vaginal delivery is inadvisable (e.g. significant cephalopelvic disproportion, malpresentation, placenta praevia, vasa praevia, placental abruption, cord presentation or prolapse, predisposition to uterine rupture as in multiple pregnancy, polyhydramnios, grand multiparity and presence of uterine scar from major surgery including Caesarean section); avoid prolonged administration in oxytocin-resistant uterine inertia, severe

pre-eclampsia or severe cardiovascular disease.

Interactions : *see Appendix-2*

Side-effects: uterine spasm (may occur even at low doses), uterine hyperstimulation (usually with excessive doses may causes fetal distress, asphyxia and death, or may lead to hypertonicity, tetanic contractions, soft tissue damage or uterine rupture); water intoxication and hyponatraemia associated with high doses with large infusion volumes of electrolyte-free fluid *(see also under Dose below)*; also nausea, vomiting, arrhythmias, rashes and anaphylactic reactions (with dyspnoea, hypertension or shock) reported; placental abruption and amniotic fluid embolism also reported on overdose

Dose : induction of labour for medical reasons or stimulation of labor in hypotonic uterine inertia by intravenous infusion 0.001-0.004 units/minute until labour pattern established similar to normal (usually less than 0.01 units/ minute for pregnancy at term); maximum recommended rate 0.02 unit/minute (use solution containing 10 units/500 ml if higher rate required); (may be repeated the following day starting again at 0.001-0.004 units/minute)

IMPORTANT: Careful monitoring of fetal heart rate and uterine contraction by trained personnel essential to allow dose titration according to response (never give direct intravenous injection); discontinue immediately in uterine hyperactivity or fetal distress. Caesarian section: *by slow intravenous injection* immediately after delivery, 5-10 units. Prevention of postpartum haemorrhage after delivery of placenta: *by slow intravenous injection* 5-10 units (if infusion used for induction or enhancement of labour, increase rate during third stage and for next few hours). May be given in a dose of 5-10 units by intramuscular injection instead of oxytocin with ergometrine (*see notes above)*. Treatment of postpartum haemorrhage: by slow intravenous injection 5-10 units followed in severe cases by intravenous infusion of 5-20 units in 500 ml of non hydrating diluent (e.g. glucose 5% solution) at a rate sufficient to control uterine atony. Avoid rapid intravenous injection (may cause short-lasting drop in blood pressure); prolonged administration, see warning below. Incomplete, inevitable or missed abortion: by slow intravenous injection 5 units, followed if necessary by intravenous infusion of 0.02-0.04 units/ minute or faster

WARNING. Prolonged intravenous administration at high dose with large volume of fluid (as possible in inevitable or missed abortion or postpartum haemorrhage) may cause water intoxication with hyponatraemia. To avoid: use electrolyte-containing diluent (i.e not glucose), increase oxytocin concentration to reduce fluid, restrict fluid intake by mouth; monitor fluid and electrolytes

Proprietary Preparations

Linda-SDS *(Nuvista),* Inj., 10 IU/ml , Tk. 20.63/Vial
Ocin *(Opsonin),* Inj., 5 IU/ml, Tk. 7.93/Vial
Oxyton *(Renata),* Inj., 5 IU/ml, Tk. 10.00/Vial
Pitocin *(Chemist),* Inj., 10 IU, Tk. 15/Amp.; 5 IU, Tk. 8.35/Amp.
Syntocin *(Techno),* Inj., 5 IU/ml, Tk. 7.50/Vial

6.1.2 DUCTUS ARTERIOSUS

Alprostadil (Prostaglandin E_1) is used to maintain patency of the ductus arteriosus in neonates with congenital heart defects, prior to corrective surgery in centres where intensive care is immediately available. Prostaglandin E_1 maintains the patency of the ductus arteriosus; **Indomethacin** is believed to close it by inhibiting prostaglandin synthesis.

6.1.3 MIFEPRISTONE

Indications: medical termination of intrauterine pregnancies of up to 49 days gestation .It is used in combination with **gemeprost** for termination of pregnancies between 13 and 24 weeks gestation;can also be used in smaller doses as an emergency

contraceptive;used in combination with misoprostol for the termination of intrauterine pregnancy through day 49 of the pregnancy
Contraindications: presence of an intrauterine device, ectopic pregnancy, adrenal failure, hemorrhagic disorders and anticoagulant or long-term corticosteroid therapy
Side effects: vaginal bleeding, cramping, nausea, vomiting, diarrhea, dizziness, back pain, and tiredness
Dose: It is given by mouth for the termination of pregnancy up to 63 days duration. Single dose of 600 mg of mifepristone followed by gemeprost 1 mg vaginally or misoprostol 400 micrograms by mouth 36-48 hours later if the abortion has not been completed. Lower doses of mifepristone and other prostaglandins have also been used for medical termination of pregnancy

Note. Treatment with mifepristone and misoprostol requires three separate office visits.

Day 1: Three 200 mg tablets (600 mg) of mifepristone are taken as a single dose.

Day 3: 400 microgram of misoprostol is given orally unless abortion has been confirmed.

Day 14: No medication administered. Patient returns for a post-treatment examination to confirm that a complete termination of pregnancy has occurred.

Proprietary Preparations
Mifeston *(Incepta),*Tab., 200mg,Tk.175/Tab.
Mprix *(Sharif),* Tab., 200 mg, Tk. 240/Tab.
Mifton *(Ziska),* Tab., 200 mg, Tk. 240/Tab.

Misoprostol 0.20mg and Mifepristone 200mg Tablet
MTP Kit *(Sharif),*Tk 300.00/Kit
MM Kit *(Ziska)*, Tk. 280.00/Kit

6.1.4 MYOMETRIAL RELAXANTS

$Beta_2$-adrenoceptor stimulants ($beta_2$ sympathomimetics) relax uterine muscle and are used in selected cases in an attempt to inhibit premature delivery. Their main purpose is to permit a delay in delivery of at least 48 hours; not statistically significant effect on perinatal mortality has as yet been observed. The greatest benefit is gained by using the delay to administer corticosteroid therapy (with care to avoid fluid overload) or to implement other measures known to improve perinatal health (including transfer to a unit with neonatal intensive care facility). They are indicated for the inhibition of uncomplicated premature labour between 24 and 33 weeks of gestation. Prolonged therapy should be avoided since risks to the mother increase after 48 hours, and further more myometrial response is reduced. Oral therapy following initial parenteral treatment is not therefore recommended.**Ritodrine hydrochloride** has been used (by mouth or by injection) as a myometrial relaxant. **Salbutamol** has also been used in uncomplicated premature labour orally or by injection (intramuscular or intravenous).
***Note*.** The incidence of neonatal respiratory distress syndrome, necrotizing enterocolitis and interventicular haemorrage is low in patients treated with **Nifidipine**
(*see section 4.1.1 for other products.)*

NIFIDIPINE[ED]

Indication: premature labour
Caution: should not be combined with magnesium sulphate or beta 2 agonists .
Dose: It is given in the dose of 3 tab. Stat followed by 2 tab. after 30 min. & then 1-2 tab. every 6-8 hourly for 48 hours until the dose of inj. **Dexamethasone** for lung maturity has been completed. Pretreatment with fluids before infusion reduce hypotension and uteroplacental perfusion.

Proprietary Preparations
(see section 3.3.2)

RITODRINE HYDROCHLORIDE

Indication : uncomplicated premature labour *(see notes above)*

Cautions : suspected cardiac disease (physician experienced in cardiology to assess), hypertension, hyperthyroidism, hypokalaemia (special risk with potassium depleting diuretics), diabetes mellitus (closely monitor blood glucose during intravenous treatment); mild to moderate preclampsia (avoid if severe, *see Contraindications*), monitor blood pressure and pulse rate (should not exceed 135-140 beats per minute) and avoid over hydration *(see section-16).*

IMPORTANT: Closely monitor state of hydration (discontinue immediately and institute diuretic therapy if pulmonary oedema occurs); beta blockers (effect antagonized may be used to reverse increased tendency to uterine bleeding following caesarian section); drugs likely to enhance sympathomimetic side effect or induce arrhythmias.

Contraindications: cardiac disease, eclampsia, severe preeclampsia, intrauterine infection, intra uterine fetal death, antipartum heamorrhage (requires immediate delivery) placenta praevia (requires immediate delivery), cord compression; not for use in first or second trimesters

Interactions:*see Appendix-2*

Side-effects: nausea, vomiting, flushing, sweating, tremor, hypokalaemia, tachycardia, palpitations and hypertension (left lateral position throughout infusion to minimize risk); increased tendency to uterine bleeding *(see cautions)*, pulmonary edema *(see below and under cautions)*; chest pain or tightness (with or without ECG changes) and arrhythmias; salivary gland enlargement; on prolonged administration (several weeks) leucopenia and agranulocytosis reported; liver function abnormalities (including increa-sed transaminase level and hepatitis) reported

Proprietary Preparation
Ritopar *(ACI),* Tab. 10 mg, Tk. 8.00/Tab.; Inj. 50 mg/5 ml, Tk. 70.00/Vial

SALBUTAMOL [ED]

Indications: uncomplicated premature labour *(see notes above)*; asthma *(see section 4.1.1)*

Cautions; Contraindications; Side-effects: *see under Ritodrine Hydrochloride*

Dose: *by intravenous infusion*, 10 micrograms/minute gradually increased to max. of 45 micrograms/minute until con-traction have ceased, then gradually reduced; or *by intravenous or intramuscular injection,* 100-250 micrograms repeated according to response; then *by mouth (but see notes above)*, 4 mg every 6-8 hours

Proprietary Preparation
see section 4.1.1

6.2 TREATMENT OF VAGINAL AND VULVAL CONDITIONS

6.2.1 PREPARATION FOR VAGINAL ATROPHY.
6.2.2 ANTI-INFECTIVE DRUGS FOR COMMON VAGINAL CONDITIONS

Symptoms are preliminarily referred to the vulva, but infections almost invariably involve the vagina which should also be treated. Applications to the vulva alone are likely to give only symptomatic relief without cure. Aqueous medicated douches may disturb normal vaginal acidity and bacterial flora. Topical anaesthetic agents give only symptomatic relief and may cause sensitivity reactions. They are indicated only in cases of pruritus where specific local causes have been excluded. Systemic drugs are required in the treatment of infections such as gonorrhea and syphilis

6.2.1 PREPARATION FOR VAGINAL ATROPHY

Application of an oestrogen containing cream may be used on a short-term

basis to improve the quality of the vaginal epithelium in menopausal atrophic vaginitis. It is important to bear in mind that topical oestrogen should be used in the minimum effective amount to minimize absorption of the oestrogen; if they are used on a long-term basis, some require oral progestogen for 10-14 days of each month to combat endometrial hyperplasia *(for details see under preparations below)*. **Topical oestrogen** are also used prior to vaginal surgery in postmenopausal women, e.g. in prolapse when there is epithelial atrophy.

TOPICAL OESTROGENS

Indications: *see notes above*

Cautions; Contraindications; Side-effects: *see Oestrogen for HRT (section 5.4.1.1);* contraindicated in pregnancy and lactation. Examine patients periodically to assess the need for further treatment

Proprietary Preparations

Ovestin(l) *(Organon),* Intravaginal cream, oestriol 0.1%; 1 applicator-dose to be inserted daily for 2-3 weeks, before retiring at night, then reduce to twice a week dose (discontinue every 2-3 months for 2 weeks to assess the need of further treatment; vaginal surgery, 1 applicator dose daily for 2 weeks before surgery resuming 2 weeks after surgery; 1 application (with calibrated applicator filled up to ring mark) contains 0.5 mg ovestin cream which corresponds to 0.5 mg oestriol. Tk. 1114.00/15g tube

Premarin(l) *(Pfizer),* Vaginal cream, conjugated oestrogens (equine) 0.625 mg in 1 g non-liquidifying cream; insert 1-2 daily, starting on day 5 of cycle for 3 weeks followed by one weak interval; if therapy is long term in women with intact uterus, oral progesterone needs to be given for 10-14 days at end of each cycle. Tk. 801.03/14 gmTube

6.2.2 ANTI-INFECTIVE DRUGS FOR COMMON VAGINAL CONDITIONS

Effective specific treatments are available for common vaginal infections.

FUNGAL INFECTIONS

(see section1.2)

Candidal vulvitis can be treated locally with cream but is almost invariably associated with vaginal infection which should also be treated. Vaginal candiasis is treated primarily with antifungal pessaries or cream inserted high into the vagina (including during menstrual). Imidazole drugs (**clotrimazole, econazole fenticonazol, isoconazole** and **miconazole, ticonazole**) are effective in short course of 3 to 14 days according to the preparation used; single dose prepar-ations offer an advantage when compliance is a problem. Vaginal applications may be supplemented with antifungal cream for vulvitis and to treat other superficial sites of infection. **Nystatin** is a well established treatment (but stains clothings yellow). One or two pessaries are inserted for 14 to 28 nights; they may be supplemented with cream for vulvitis and to treat other superficial sites to infection. Oral treatment with **Fluconazole** or **Itraconazole** *(see section 12.2.2)* is also effective; oral **ketoconazole** *(see section 12.2.2)* has been associated with fatal hepatotoxicity.

Recurrence is common if the full course of treatment is not completed and particularly if there are predisposing factors such as antibiotic therapy, oral contraceptive use, pregnancy or diabetes mellitus. Possible reservoirs of infection may also lead to recontamination and should be treated. These include other skin sites such as digits, nail beds and umbilicus as well as the gastrointestinal tract and the bladder. The partner may also be the source of re-infection and should be treated with cream at the same time.

CLOTRIMAZOLE

(see also section 12.2.2)

Indications: *see notes above*

Dose: *see notes above .*

Pessary (with applicator), clotrimazole 500 mg; 1 to be inserted at night as a single dose

Note: Treatment should be timed to avoid menstrual period. Effect on latex condoms and diaphragms is not yet known

Proprietary Preparations
Afun *(Square),* Vaginal Tab.,100 mg, Tk. 10.04/Tab.; Vaginal Tab.,200 mg, Tk. 20/Tab.; Vaginal Tab., 500 mg, Tk. 60/Tab.
Clotrim *(Acme),* Vaginal Supp., 200 mg, Tk. 20.07/Supp.;Vaginal Tab., 200 mg, Tk.20.07/Tab.
Clozol VT *(Chemist),* Vaginal Tab.,200 mg, Tk. 60/Tab.
Dermasim *(ACI),* Vaginal Tab., 500 mg , Tk. 60.23/Tab.
Neosten *(Beximco),* Vaginal Tab., 200 mg, Tk. 20/Tab.

ECONAZOLE

Indications : *same as that of clotrimazole*
Dose: insert one tablet high in vagina for 3 consecutive nights regardless of any intervening menses.
Note: Econazole vaginal preparations are known to damage latex condoms and diaphragms.

Proprietary Preparations
Econate VT *(Incepta),* Vaginal Tab.,150 mg, Tk. 23.33/Tab.
Ecoren *(ACI),* Vaginal Tab., 150 mg, Tk. 24.09/Tab.
Ecozol *(Opsonin),* Vaginal cream, 1%,Tk. 70.26/30gm; Tk.32.12/10g
Ecozol-VT *(Opsonin),* Vaginal Tab. 150 mg Tk. 23.42/Tab.

NYSTATIN[ED]

Indications: vulvitis, perineal pruritis, dyspereunia and dysuria due to fungal infection

Side-effects: local irritation and burning sensation; stains clothing yellow

Proprietary Preparation
Nystat VT *(Acme),* Vaginal tablet 5 Lac IU,, insert 1-2 tablets daily and continue for 2 weeks; may be continued during menstruation. Tk. 1.95/Tab.

TIOCONAZOLE

Indications: vaginal yeast infections.; reduces vaginal burning, itching.
Side-effects: *same as that of Nystatin*

Proprietary Preparation
Tycon *(Acme),* Vaginal Supp., 300 mg Tk. 60.22/Supp.

OTHER INFECTIONS

Vaginal preparations intended to restore normal acidity may prevent recurrence of vaginal infections and permit the re-establishment of the normal vaginal flora. Trichomonal infections commonly involve the lower urinary tract as well as the genital system and need systemic treatment with **metroindazole** or **tinidazole** Bacterial infections are particularly common in association with gynaecological operat-ions and trauma. **Metronidazole** is effective against certain Gram-negative organisms, especially *Bacteroides* may be used prophylactically in gynaeco-logical surgery (for systemic prepara-tions of **Metronidazole**, (*see section 1.1.9)*. In case of trichomonal infection, the male partner should be treated concurrently with metronidazole 200 mg orally twice daily for 10 days.

Topical vaginal products containing **povidone iodine** may be used to treat vaginitis due to candidal, trichomonal, non-specific or mixed infections; they are also used for the pre-operative preparation of the vagina. **Clindamycin** cream and **metronidazole** gel are also indicated for bacterial vaginosis. Anti-bacterial and antifungal combination products are also available for mixed infections.

The antiviral drugs **aciclovir, famci-clovir** and **valaciclovir** may be used in the treatment of genital infection due to herpes simplex virus, the HSV type 2

being a major cause of genital ulceration. They have a beneficial effect on virus shedding and healing generally giving relief from pain and other symptoms. For antiviral drugs, *see section 1.4 for systemic preparations* and *section 12.2.3 for topical preparations*.
Note: avoid in impaired renal function

PREPARATIONS FOR OTHER VAGINAL INFECTIONS

Proprietary Preparations
Flamyd *(Incepta),* Gel, metrinidazole 0.75%, Tk. 50/30 gm
Povisep *(Jayson),* Gel, povidone iodine 10%, Tk.80/30 gm
Clindax(Opsonin),Vaginal cream, clindamycin 2%, Tk. 70.26/20 gm

Neomycin sulphate 35,000 IU polymyxin B sulphate 35,000 IU, nystatin 1,00,000 IU and metronidazole 200 mg
Gynoril *(Opsonin),* Vaginal suppository insert 1 suppository; insert high up in vagina for 12 nights; Tk.24.09./Supp.
Gynomix *(Drug Intl)*,Vaginal soft gelatin cap., IU.Tk.25/ capsule
V Cap*(Renata),* Vaginal soft gelatin cap Tk.25/Cap

Metronidazole200mg+NeomycinSulphate35,000 IU+Po lymyxin BSulphate35,000 IU + Nystatin1,00,000 IU
Gynepro *(Square)* Vaginal Suppository, Tk.24.00/Tab

6.3 CONTRACEPTIVES

The criteria by which contraceptives methods should be judged are effectiveness, acceptability and freedom from side effects. Hormonal contraception is the most effective method of fertility control, but has unwanted major and minor side-effects especially for certain groups of women. Intra-uterine devices have a high use-effectiveness but may produce undesirable side-effects especially menorrhagia, or be otherwise unsuitable in a significant proportion of women; their use is generally inadvisable in nulliparus women because of the increased risk of pelvic sepsis and infertility. Barrier methods alone (condoms, diaphragms and caps) are less effective but can be very reliable for well-motivated couples if used in conjunction with a spermicide. Condoms are useful in preventing reproductive tract infection and/or sexually transmitted diseases. Occasionally sensitivity reactions to latex may occur. Female condom is also now available; it is prelubricated but does not contain a spermicide.

6.3.1 COMBINED ORAL CONTRACEPTIVES

Oral contraceptives containing an oestrogen and a progestogen are the most effective preparation for general use. Their advantages include: reliability; reduction of dysmenorrhoea; less iron deficiency anaemia; less pre-menstrual tension; less benign breast disease; significant protection against endometrial and ovarian cancer; and protection against pelvic inflammatory disease.
The oestrogen content ranges from 30 to 50 micrograms and generally a preparation with the lowest oestrogen and progestogen content, which gives good cycle control and minimal side-effect in the individual woman is chosen. The choices include:

Low dose preparations (containing ethinyloestradiol 20 micrograms) are particularly appropriate for obese or older women provided a combined oral contraceptive is otherwise suitable. It is

recommended that the combined oral contraceptive is not continued beyond 50 years of age since there are more suitable alternatives. Switching from low dose to high dose pill or from high dose to low dose pill does not cause any major problem.They are particularly appropriate for obese or older women.The latest 4th generation OCP contains ethinyloestradiol 0.030 mg. and 4th generation progesterone Drospirenone 3 mg.

Standard dose preparations (containing ethinyloestradiol 30 or 35 micrograms) are appropriate for standard use in the case of those also containing levonorgestrel or norethisterone (but in the case of those also containing desogestrel or gestodene, *see advice below*).

High dose preparations (containing either ethinyloestradiol 50 micrograms or mestranol 50 micrograms) provide greater contraceptive security but with an increase in the possibility of side-effects. These are used mainly in circumstances of reduced bioavailability (e.g. during long term use of enzyme inducing antiepileptics, *see under Interactions below*).

The progestogens desogestrel, gestodene and norgestimate in combination with ethinyloestradiol have been reported to have less adverse effects on lipids than ethynodiol, levonorgestrel and norethisterone in combination with ethinyloestradiol. Desogestrel and gestodene may be given to women who experience side-effects (such as acne, headache, depression, weight gain, breast symptoms and breakthrough bleeding) with other progestogens. However, women should be advised that desogestrel and gestodene have also been associated with an increased risk of venous thromboembolism *(see below)*.

RISK OF VENOUS THRMBOEMBOLISM: Studies indicate venous thromboembolic risks associated with oral contraceptives containing levonorgestrel, norethisterone or ethynodiol (excess risk around 5 to 10 cases per 1,00,000 women per annum). Studies further indicate that combined oral contraceptives containing desogestrel and gestodene are associated with around a two fold increase in the risk, compared with those containing other progestogens. There is insufficient information to know whether there is any increased risk of thromboembolism associated with combined oral contraceptives containing norgestimate. It is, therefore, advised that combined oral contraceptives containing gestodene or desogestrel should not be used by women with risk factors for venous thromboembolism including obesity (body mass index greater than 30 kg/m^2), varicose veins or a previous history or thrombosis from any cause. Combined oral contraceptives containing desogestrel or gestodene should only be used by women who are intolerant of other combined oral contraceptives and are prepared to accept an increased risk of thromboembolism. Any personal history of venous or arterial thrombosis is a contraindication to any combined oral contraceptive.

MISSED PILL: The following advice is now recommended by family planning directorate: 'If you forget one pill, take it as soon as you remember and the next one at normal time, so that 2 pills are to be taken on that particular day. If you forget two pills, take 2 pills as soon as you remember, take another 2 pills on the next day. Take one pill daily and use condom, till you finish rest of the pills. When the pills are finished and menstruation starts, start a new packet. If you forget three pills, pills will no more work; stop pills and use condom. Probably menstruation will start; start the next packet at the first day of menses.

DIARRHOEA AND VOMITING: Vomiting and severe diarrhoea can interfere with absorption and limit the effectiveness. Additional precautions (use condom) should therefore be used during and for 7 days after recovery. If vomiting and diarrhoea occurs during the last 7 tablets, the next pill-free interval should be omitted; in the case of Every Day

(ED) pills, the inactive ones should be omitted.

Interactions: The effectiveness of both combined and progestogen only oral contraceptives may be considerably reduced by interaction with drugs that induce hepatic enzyme activity (e.g. carbamazepine, griseofulvin, phenytoin, phenobar-bitone, primidone, topiramate and above all, the rifamycins (rifabutin and rifampicin). Additional contraceptive precautions should be taken whilst taking the enzyme inducing drug and for at least 7 days after stopping it; if these 7 days run beyond the end of a packet the new packet should started immediately without a break (in the case of ED pills, the inactive ones should be omitted). It should be noted that rifampicin is such a potent enzyme inducing drug that even if a course lasts for less than 7 days the additional contraceptive precautions should be continued for at least 4 weeks after stopping it.

Some broad-spectrum antibiotics (e.g. ampicillin) may reduce the efficacy of combined oral contraceptives by impairing the bacterial flora responsible for recycling of ethinyloestradiol form the large bowel. Additional contraceptive precautions should be taken whilst taking a short course of a broad-spectrum antibiotic and for 7 days after stopping. If these 7 days run beyond the end of a packet the next packet should be started immediately without a break (in the case of ED pills, the inactive ones should be omitted). If the course exceeds 2 weeks, the bacterial flora develops antibiotic resistance and addi-tional precautions become unnecessary.

SURGERY: Oestrogen containing oral contraceptives should be discontinued (and adequate alternative contraceptive arrangements made) 4 weeks before major elective surgery (requiring at least one week of bed rest) and all surgery to the legs. They should normally be recommended at the first menses occurring at least 2 weeks after full mobilization. A depot injection of a progestogen only contraceptive may be given, if required, until the oestrogen containing contraceptive can be reinstated. When discontinuation of an oestrogen containing contraceptive is not possible (e.g. after trauma or if by oversight), and a patient admitted for an elective procedure is still on an oestrogen containing oral contraceptive, some consideration should be given to subcutaneous heparin prophylaxis against thromboembolism. These recommendation do not apply to minor surgery with short duration of anaesthesia, e.g. laparoscopic sterilization or tooth extraction or to women taking oestrogen free hormonal contraceptives (whether by mouth or by injection).

WHEN TO STOP IMMEDIATELY: Com-bined oral contraceptives should be stopped (pending investigation and treatment), if any of the following occur:

- Sudden severe chest pain (whether or not radiating to the left arm);
- Sudden breathlessness (or cough with blood stained sputum);
- Severe stomach pain;
- Unusual severe, prolonged head-ache-especially if first time or getting progressively worse, sudden partial or complete loss of vision, diplopia, sudden disturbance of hearing or other perceptual disor-ders, dysphasia, vertigo, bad fainting attack or collapse increase in number of epiletpic seizures, weakness or very marked numb-ness suddenly affecting one side or one part of body, motor disturbances;
- Hepatitis, jaundice, generalized itching, liver enlargement;
- Severe depression;
- Blood pressure above systolic 160 mmHg and diastolic 95 mm Hg;
- Detection of a risk factor-see Cautions and Contraindications under Combined Oral Contraceptives.

COMBINED ORAL CONTRACEPTIVES (COC) [ED]

Indications: contraception; menstrual symptoms
(section 5.4.2.2, Progesterone)

Contraindications : pregnancy; severe or multiple risk factors for arterial disease *(see above)*; risk factors for venous thromboembolism *(see above)*; valvular heart disease associated with pulmonary hypertension or risk of mural thrombi, ischaemic heart disease; transient cerebral ischaemic attacks without headaches; migraine; liver diseases including disorders of hepatic excretion (e.g. Dubin-Johnson or Rotor syndromes), infective hepatitis (until liver function returns to normal); systemic lupus erythematosus; prophyria *(section 9.8.2)*; liver adenoma, gallstones; after evacuation of hydatidiform mole (until return to normal of urine and plasma gonadotrophin concentration); history of haemolytic uraemic syndrome or history of pruritus or cholestatic jaundice during pregnancy, pemphigoid gestationis, chorea or deterioration of otosclerosis, breast or gastrointestinal tract carcinoma; undiagnosed vaginal bleeding; breast feeding (until weaning or for 6 months after birth)

Interactions: *see above and also Appendix-2 (contraceptives, oral)*

Cautions: risk factors for venous thromboembolism, arterial disease and migraine, *see below and also notes above*; hyperprolactinaemia (seek specialist advice); severe depression, sickl-ecell disease, inflammatory bowel disease including Crohn's disease

RISK FACTORS FOR VENOUS THROMBOEMBOLISM: Use with caution if any of following factors present: Family history of venous thromboembolism in first degree relative aged under 45 years (avoid if prothrombotic coagulation abnormality e.g. factor V Leiden or antiphospholipid antibodies (including lupus anticoa-gulant); obesity (avoid if body mass index exceeds 39 kg/m^2; Long-term immobilization e.g. in a wheelchair (avoid if confined to bed or leg in plaster cast); Varicose veins, avoid during sclerosing treatment or where definite history of thrombosis exists.

RISK FACTORS FOR ARTERIAL DISEASE: Use with caution if any one of following factors present but avoid if two or more factors present; family history of arterial disease in first degree relative aged under 45 years (avoid if atherogenic lipid profile); diabetes mellitus (avoid if diabetes complication present); hypertension (avoid if blood pressure is above systolic 160 mmHg and diastolic 95 mm/Hg); smoking (avoid if smoking 40 or more cigarettes daily); age over 35 years (avoid if over 50 years); obesity (avoid if body mass index exceeds 39 kg/m^2); migraine, subject should report any increase in headache frequency or onset of focal symptoms (discontinue immediately and refer urgently to neurology expert if focal neurological symptoms not typical of aura persist for more than 1 hour, *see also notes above)*

Side-effects: nausea, vomiting, headache, breast tenderness, changes in body weight, fluid retention, thrombosis (more common when factor V present or in blood groups A, B and AB) (see notes above); changes in libido, depression, chorea, skin reactions, chloasma, hypertension, contact lenses may irritate impairment of liver function, hepatic tumours, reduced menstrual loss, spotting in early cycles absence of withdrawal bleeding rarely photosensitivity

BREAST CANCER: There is a small increase in the risk of having breast cancer diagnosed in women taking the combined oral contraceptive pills; this relative risk may wholly or partly be due to earlier diagnosis. In users of combined oral contraceptive pills, the cancers are more likely to be localized to the breast. The most important risk factors appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by

10 years. A small increase in the risk of breast cancer should be weighed against the benefits and evidence of the protective effect against cancers of the ovary and endometrium

Dose: *by mouth* every day combined (mono-phasic) preparations (30-tablets packet; each tablet should be taken at approximately same time each day; if delayed by longer than 12 hours contraceptive protection may be lost. Always start with the first tablet, follow the arrow/finger and swallow from the first tablet 21 tablets in 21 days. After finishing the white tablets similarly take one brown tablet a day for the next 7 days. Irrespective of starting of menstrual bleeding, after finishing the 7 brown tablets, start taking the first white tablet from a new packet

Pills showed be swallowed with water, take tablet same time each day. Best time is after meal at night or at bed time. If for any reason husband is out of home for few days pills have to be continued. After starting taking pills some clients may experience minor side effects (e.g. nausea, spotting) but nothing to be worried. It corrects itself after 3-4 months of continuing taking pills. If these are matter of concern/anxiety client should contact family planning clinics. Pills should be kept in dry place and out reach of the children. During each follow up visit clients should bring the rest of the pills. During taking any other health related services a client should always mention that she is taking oral contraceptive pills.

21-day combined (monophasic) preparations (21 tablets packet); 1 tablet daily for 21 days; subsequent course repeated after a 7-day interval (during which withdrawal bleeding occurs). First course usually started on 1st day of cycle; if starting on 4th day of cycle or later, additional precautions (barrier methods) necessary during first 7 days.

Biphasic and triphasic preparations: as instructed under individual preparations.

CHANGING TO COMBINED PREPARATION CONTAINING DIFFERENT PROGESTOGEN: Every day (ED) combined preparations; start the new brand (the first active tablet of the ED preparation) the day after taking the last active tablet of previous brand (omitting the inactive tablets). If not possible to avoid talking the inactive tablets of an ED preparation, additional precautions (barrier methods) necessary during first 14 days of taking the new brand. 21-day combined preparations: continue current pack until last tablet and start first tablet of new brand the next day. If a 7-day break is taken before starting new brand additional precautions (barrier methods) should be used during first 7 days of taking the new brand.

CHANGING FROM PROGESTOGEN-ONLY TABLET: Start on first day of menstruation, or any day if amenorrhoea is present and pregnancy has been excluded.

SECONDARY AMENORRHOEA (exclude pregnancy): Start any day, additional precautions (barrier methods) necessary during first 7 days.

AFTER CHILDBRITH (not breast-feeding): Start 3 weeks postpartum (increased risk of thrombosis if started earlier): later than 3 weeks postpartum additional precautions (barrier methods) necessary for first 7 days. Not recommended if woman is breast-feeding (oral progestogen only contraceptive is to be given).

AFTER ABORTION OR MISCARRIAGE OR MENSTRUAL REGULATION (MR): Start on the same day.

COUNSELING: Clients must be counselled before giving oral contraceptive pills (OCP). The subject of discussion should include all other available methods of contraception, previous experience, superstitions and actual information's on OCP. If the clients decides on using oral contraceptive pills, give proper information on how OCP acts; advantage and disadvantage; probable side effects (nausea vomiting; headache; inter-menstrual bleeding). If a woman is nervous she may stop taking pills

management. Inform on common side effects, how to take pills and what to do for missing pill; danger signs and for follow up visits. Resupply should be ensured before the pervious supply is finished. In follow-up visits clients should be asked about proper use of OCP, problems encountered in taking the pills, detection of side effects, and treatment. Encourage using of condom in case of missing pill and stoppage of use of OCP due to side effect.

Note : under the national family planning programme the Govt. is supplying in the brand name of **Shukhi** the standard preparation of oral contraceptive.

Shukhi White tablets levonorgestrel 150 micrograms, ethinyloestradiol 30 microgram; brown tablets, ferrous fumerate 75 mg; Govt. supply. **Dose:** 1 white tablet (active) daily from 1st day of menstruation for 21 days followed by 7 brown (inactive) tablets; withdrawal bleeding usually occurs during taking of the brown tablets; brown tablets to be continued during bleeding; the 1st white tablet from the next packet should be started from the next day after finishing the brown tablets irrespective of occurrence of withdrawal bleeding.

Proprietary Preparations

Levonorgestrel 0.15mg + Ethinyl Estradiol0.03mg & Ferrous Fumarate75mg
Mini 28 *(ACI),* Tab. Tk. 1.38/Tab.
Lyta 28 Pill*(Incepta),* Tab. Tk. 0.84/Tab.
Levopill *(Popular),* Tab. Tk. 1.38/Tab
Dose: *as Shukhi above*.

Desogestrel 0.15mg + Ethinylestradiol 0.03mg
Desolon *(Renata),* Tab. Tk. 4.05/Tab.
Marvelon *(Organon)*, Tab.Tk. 5.09/Tab
Dose: 1 tab daily from 1st day of menstruation for 21 days followed by 7 days tab-free interval (during which withdrawal bleeding occurs).
Gestodene 0.30mg & Ethinylestradiol 0.075mg
Gestop *(Incepta),*Tab.,Tk.3.56/Tab

Other Proprietary Preparations
High Dose Pills

Lynes (*Nuvista),* Tab. lynestrenol 2.5 mg with ethinyloestradiol 50 micrograms; **Dose:** 1 tab daily from 1st day of menstruation for 22 days followed by 6 tab-free days (during which withdrawal bleeding occurs). Tk. 5.35/Tab.

Ovostat Gold *(Nuvista),* Tab. ethinyloestradiol 0.0375mg + lynestrenol 0.75 mg.Tk. 3/Tab

Drospirenone 3mg + Ethinylestradiol 0.03mg
Novelon *(Renata),* Tab. Tk. 19.00/Tab.
Rosen *(Incepta),* Tab., Tk. 14.25/Tab.

6.3.2 PROGESTOGEN-ONLY CONTRACEPTIVES

6.3.2.1 ORAL PROGESTOGEN-ONLY CONTRACEPTIVES
6.3.2.2 PERENTERAL PROGESTOGEN-ONLY CONTRACEPTIVES

6.3.2.1 ORAL PROGESTOGEN ONLY CONTRACEPTIVES

Oral progestogen only preparations offer a suitable alternative when oestrogens are contraindicated (including patients with venous thrombosis or a past history or predisposition to venous thrombosis), but have a higher failure rate than combined preparations. They are suitable for older women, for heavy smokers and for those with hypertension, valvular heart disease, diabetes mellitus and migraine. Menstrual irregularities (oligomeno-rrhoea, menorrhagia) are more common but tend to resolve on long-term treatment. Effectiveness of oral progestogen-only preparations is not affected by board spectrum antibiotics but is reduced by enzyme inducing drugs *(see Appendix-2)*. All progestogen only contraceptives (including those given by injection) are suitable for use as an alternative to combined oral contracep-tives before major elective surgery.

STARTING ROUTINE: 1 tablet daily on a continuous basis, starting on 1st day of cycle and taken at the same time each day (if delayed by longer than 3 hours contraceptives protection may be lost). Additional contraceptive precautions are not necessary when initiating treatment. Changing from a combined oral contraceptive: start on the day following completion of the combined oral contraceptive course without a break (or in the case of ED tablets omitting the inactive ones). After childbirth: start any

time after 3 weeks postpartum (increased risk of breakthrough bleeding if started earlier); lactation is not affected.

ADVICE ON MISSED PILL: If a pill is forgotten, take it as soon you remember and carry on with the next pill at the right time. If the pill was more than three hours overdue you are not protected. Continue normal pill taking but you must also use another method, such as the condom, for the next 7 days.

ORAL PROGESTOGEN-ONLY CONTRTACEPTIVES

(Progestogen-only pill, 'POP')

Indications:contraception; for use in Emergency Contraception, *see section 6.3.5*

Cautions: heart disease, sex-steroid dependent cancer, past ectopic pregnancy, malabsorption syndromes, functional ovarian cysts, active liver disease, recurrent cholestatic jaundice, history of jaundice in pregnancy, uncontrolled diabetes mellitus. Advised caution in patients with history of thromb-oembolism, hypertension, diabetes and migraine

Contraindications: pregnancy, undiag-nosed vaginal bleeding; severe arterial disease; live adenoma, porphyria; after evacuation of hydatidiform mole (until return to normal urine and plasma gonadotrophin values), lump in breast or breast cancer

Interactions: *see Appendix-2*

Side-effects: menstrual irregularities; nausea, vomiting, headache, dizziness, breast discomfort, depression, skin diso-rders, disturbance of appetite, weight changes, changes in libido. Vomiting and severe diarrhoea can interfere with absorption and limit effectiveness; additional precautions should be used during and for 7 days after recovery

BREAST CANCER: There is a small increase in the risk of having breast-cancer diagnosed in women using, or who have recently used, a progestogen only contraceptive pill; this relative risk may wholly or partly be due to an earlier diagnosis. The most important risk factor appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by 10 years. The small increase in the risk of breast cancer is to be weighed against potential benefits

Dose: Levorgestel;1.5mg as a single dose as soon as possible after coitus,preferably within 12 hours but no later than after72 hours; 750 micrograms to be taken within 72 hours (3 days) of unprotected inter-course, followed by another tablet to be taken after 12

Proprietary Preparations

Levonoregestrel

I-Pill *(Popular),* Tab., 750 microgram, Tk. 22.50/Tab.
Norpill 1 *(Square),* Tab. , 1.5 mg , Tk. 70.00/Tab.
E-Plan *(ACI),* Tab. , 750 microgram , Tk. 22.89/Tab.
Emcon *(Renata),* Tab. ,1.5 mg, Tk. 60.00/Tab.; 750 microgram , Tk. 30.00/Tab.

Desogestrel

Pop-D *(Incepta),* Tab. , 75 microgram, Tk. 2.15/Tab.
Bredicon *(Renata),* Tab. , 75 microgram, Tk. 2.15/Tab

Medroxyprogesterone

Medrogest *(Renata),* Tab., 5 mg, Tk. 5.38/Tab.; 10 mg, Tk. 10.00/Tab.
Movera *(ACI),* Tab., 5 mg, Tk. 5.38/Tab.; 10 mg , Tk. 10.00/Tab.
Medrina *(Beacon),* Tab., 5 mg, Tk. 4.70/Tab.
Medroxy *(Popular),* Tab., 5 mg, Tk. 5.38/Tab.; 10 mg, Tk. 10.04/Tab.
Medora*(Nuvista),* Tab., 5 mg, Tk. 4.78/Tab.; 10 mg, Tk. 8.89/Tab.
Provenor *(Eskayef),* Tab, 5 mg, Tk. 5.00/Tab.; 10 mg, Tk. 10.00/Tab.
Perlutex(I) *(Leo*) Tab 5 mg. Tk. 8.53/Tab

6.3.2.2 PARENTERAL PROGESTOGEN-ONLY CONTRACEPTIVES

Medroxyprogesterone acetate is a long-acting progestogen when given by intra-muscular injection. It is as effective as the combined oral preparations but because of its prolonged action should

never be given without full counseling backed by the manufacturer's approved leaflet. It may be used as a short-term or long-term contraceptive for women who have been appropriately counseled concerning the likelihood of menstrual disturbance and the potential for a delay in return to full fertility. Delayed return of fertility and irregular cycles may occur after discontinuation of treatment but there is no evidence of permanent infertility. Heavy bleeding has been reported in patients given medroxyprogesterone acetate in the immediate puerperium (the first dose is best delayed until 5 to 6 weeks postpartum). If the woman is breast-feeding, the first injecttion may be given within 5 days postpartum (she should be warned that the risk of heavy or prolonged bleeding may be increased). Reduction in bone mineral density has also been reported. **Norethisterone enanthate** is a long-acting progestogen given as an oily injection, which provides contraception for 8 weeks to provide short-term interim contraception e.g. before vasectomy becomes effective.

The cautions and contra-indications of oral progestogen only contraceptives apply except that since the injection also inhibits ovulation, it protects against ectopic pregnancy and functional ovarian cysts. Clients who have PID or are high risk for PID and cannot take IUD are suitable candidates for receiving parenteral progestogen only contraceptives; these can also be used for endometriosis (monthly injections).

Levonorgestrel-releasing implant system is also available. Its efficacy is comparable to that of injected medroxyprogesterone acetate but lasts for 5 years. The cautions and contraindications are again as for oral preparations, but irregular and prolonged bleeding and amenorrhoea are common; unlike the injectable preparations the method is almost immediately reversible on removal of the implants. The risk of ectopic pregnancy is believed to be reduced overall but the proportion of ectopic to intrauterine pregnancies is increased among the very few pregnancies that do occur; since functional ovarian cysts may also be more common they need to be distinguished from ectopic pregnancy. Health personnel administering (or removing) the system should be fully trained in the technique and should provide full counseling backed by the manufacturer's approved leaflet.

PARENTERAL PROGESTOGEN-ONLY CONTRACEPTIVES

MEDROXYPROGESTERONE ACETATE

Indications: contraception for women who have at least one living child; endometriosis; see also notes above and under preparations

Cautions; Contraindications; Side-effects: *see notes above and under preparations*

Interactions: effectiveness is not affected by broad-spectrum antibiotics but may be reduced by enzyme including drugs; the interval between injections of medroxyprogesterone acetate should be reduced from 12 weeks to 10 weeks; *see Appendix-2 (progestogens)*

Dose: *by deep intramuscular injection*, 150 mg within first 5 days of cycle or within first 5 days after parturition (delay until 6 weeks after parturition if breast-feeding); for long-term contraception, repeated every 12 weeks (if interval greater than 12 weeks and 5 days, exclude pregnancy before next injection and advise patient to use additional contraceptive measures (e.g. barrier) for 14 days after the injection). It should be started immediately after abortion or MR. To be started immediately after stopping other contraceptive methods. During Ramadan, Muslim ladies will not take injection during daytime, so the injection can be given 14 days earlier/later or at night. During rainy season or flood doses of injections can be given 14 days earlier/later.

Note: Injection (aqueous suspension), medroxyprogesterone acetate 150mg/ml

available free of change under the national family planning prog-ramme.

Proprietary Preparations
Medroxy *(Popular),* Inj., 150 mg/ml, Tk. 38.00/Vial
Provera *(Techno),* Inj., 150 mg/ml, Tk. 43.40/Vial

6.3.2.3 INTRA-UTERINE PROGESTOGEN-ONLY CONTRACEPTIVE

Levonorgestrel is released directly in to the uterine cavity from an intrauterine system. Effects are therefore mainly local and hormonal including prevention of proliferation of the endometrium, thickening of cervical mucus, and suppression of ovulation in some women (in some cycles): the physical presence of the system in the uterus may also make a minor contribution to the overall contracep-tive effect. Return of fertility after removal is rapid and appears to be complete. Advantages over copper intra-uterine devices are that there may be an improvement in any dysmenorrhoea and a reduction in blood loss; there is also evidence that the frequency of pelvic inflammatory disease may be reduced (particularly in the youngest age groups who are most at risk).

Cautions and contra-indications are as for standard intra-uterine devices *(section 6.3.4)* but the risk of ectopic pregnancy is considerably reduced and pre-existing heavy menses and anaemia may be alleviated. Moreover, since the progestogen is released close to the site of the main contraceptive action (on cervical mucus and endometrium) progesto-genic side-effects and interactions are less likely to be a problem in particular, enzyme inducing drugs are unlikely to have much influence on the contraceptive effect. Initially changes in the pattern and duration of menstrual bleeding (spotting or prolonged bleeding) are common and full counseling should be undertaken before insertion. Improvement usually occurs a few months after insertion and bleeding may often become scanty or absent; this may therefore be a method of choice for women who have excessively heavy menses. Functional ovarian cysts (usually asymptomatic) may occur and usually resolve spontaneously (ultrasound monitoring recommended).

Indications : contraception

Cautions; Contraindications; Side-effects: *see notes above*; avoid in severe liver impairment. Insert into uterine cavity within 7 days of onset of menstruation (any time if replacement) or immediately after first-trimaster termination by curattage; post-partum insertions should be delayed until 6 weeks after delivery; effective for 5 years

Interactions: *see notes above and Appendix-2*

6.3.3 SPERMICIDAL CONTRACEPTIVES

Spermicidal contraceptives based on nonoxinol (**delfen, double Check, durage**l, etc.) are useful additional safeguards but do not give adequate protection if used alone; they are suitable for use with barrier methods. However, no such drug preparation is registered in Bangladesh.

6.3.4 CONTRACEPTIVE DEVICES

INTRA-UTERINE DEVICES

The intra-uterine device (IUD) is suitable for older parous women but should be a last-resort contraceptive for young nulliparous women because of the increased risk of pelvic inflammatory disease and infertility. In recent times, smaller devices have been introduced to minimise side-effects; these consist of a plastic carrier wound with copper wire or fitted with copper bands; some also have a central core of silver to prevent fragmentation of the copper. Family planning services now recommend that the replacement time for these devices

should be 5 years. IUDs are also useful for emergency contraception *(see section 6.3.5)*.

The timing and technique of fitting an IUD are critical for its subsequent performance and call for proper training and experience. Devices should not be fitted during the heavy days of the period; they are best fitted after the end of menstruation and before the calculated time of implantation. The main excess risk of infection occurs in the first 20 days after insertion and is believed to be related to existing carriage of a sexually transmitted disease. Therefore, pre-screening (at least for chlamydia) should ideally be performed. The woman should be advised to attend an emergency if she experiences sustained pain during the next 20 days.

An intra-uterine device should not be removed in midcycle unless an additional contraceptive was used for the previous 7 days. If removal is essential (e.g. to treat severe pelvic infection), post-coital contraception should be considered. If an intrauterine device fails and the woman wishes to continue to full-term the device should be removed in the first trimester if possible.

INTRA-UTERINE CONTRACEPTIVE DEVICES (IUDs)

Indications: contraception; secondary amenorrhoea due to Asherman's syndrome; *see notes above*

Cautions: anemia, heavy menses, endometrosis, severe primary dysmenor-rhoea, history of pelvic inflammatory disease, history of ectopic pregnancy or tubal surgery, diabetes, fertility problems, nulliparity and young age, severely scarred uterus (including after endome-trial resection) or severe cervical steno-sis, valvular heart disease (antibiotic cover needed), avoid if proshetic valve or past attack of infective endocarditis; HIV infection or immunosuppresive therapy (avoid if immunosuppression); joint and other prostheses; epilepsy; increased risk of expulsion if inserted before uterine involution ; anti coagulant therapy (avoid if possible); remove if pregnancy occurs (if pregnancy occurs, increased likelihood that it may be ectopic). Gynaecology examination advised before insertion, 6 weeks after (or sooner if there is a problem), then after 6 months and then yearly

Contraindications : pregnancy, severe anaemia, recent sexually transmitted infection (if not fully investigated and treated), unexplained uterine/vaginal bleeding, distorted or small uterine cavity, genital malignancy, trophoblastic disease, pelvic inflammatory disease, chronic cervicitis, erosion, polyp; history of vaginal discharge and ectopic pregnancy; established or marked immuneeosuppression; copper devices: copper allergy, Wilson's disease, medical diathermy

Side-effects: uterine or cervical perforation, displacement, pelvic infection may be exacerbated, heavy menses, dysmenorrhoea, allergy on insertion: some pain (helped by giving buprofen 30 minutes before insertion); and bleeding; occasionally epileptic seizure, vasovagal attack

COUNSELING: inform the patient about all available contraceptive methods in a friendly environment. IUD is a suitable method of contraceptive for couple with one or more children and who want contraceptive measures for longer time. If a client chooses IUD as her contraceptive method she should be informed on what can happen during and after its insertion; she should be also informed about the side-effects, and that though there are some side-effects, the method suits most women who fulfill selection criteria. Use a checklist during counseling and take feedback. Provide a card to the client with her name, date of insertion, date of removal and date of follow up. Clients should be shown how to feel the thread and asked to feel it. She should also be informed about danger signs and return of fertility after removal of IUD

CuT 380. Intrauterine device, copper wire surface area 320 mm^2 wound on

vertical stem of T-shaped plastic carrier (impregnated with radio opaque substance), plastic thread attached to base of vertical stem and copper collar surface 30 mm^2 on distal portions of each arm; replacement time 5 years. Available free of charge in family planing clinics *(Green Umbrella)* under the national family planning programme.

CuT 200B, Intrauterine device, copper wire surface area 200 mm^2 wound on vertical stem of T-shaped plastic carrier (impregnated with radio opaque substance), plastic thread attached to base of vertical stem; replacement time 3 years. Available free of charge in family planning clinics *(Green Umbrella)* under the national family planning programme.

BARRIER METHODS

CONDOMS[ED]

A condom is a sheath or covering made to fit over a man's erect penis usually made of thin latex rubber. Condoms help prevent both pregnancy and sexually transmitted diseases (STDs), ensures male participation in contraception, are safe, easily available and inexpensive and almost devoid of any side-effect. Additional advantages include prevention of premature ejaculation and over-coming of dryness during intercourse; prevention of STDs and Reproductive Tract Infections (RTIs). It also prevents anti sperm antibody formation.

Contraindication: practically nil; only medical contraindication is allergy to latex which is very rare (recommend non-latex condom in that case)

INSTRUCTIONS FOR USE: Put the condom on the erect penis before penis touches the vagina. Hold the pack at its edge and open by tearing from a ribbed edge. Hold the condom so that the rolled rim is facing up, away from the penis. Pull the foreskin back if the penis is uncircumcised. Place the condom on the tip of the penis and unroll it all the way to the base of the penis. The condom should unroll easily; if it does not, it is probably placed backwards; turn it over and try again. If using the condom to avoid passing an STD, throw away the condom that was on backwards and start over with a new one.

Any lubricant used should be water based. Water can also be used. Good lubricants include spermicides, glycerine and other specially made products. They help keep condoms from tearing during intercourse. Natural vaginal secretions also act as a lubricant. Do not use lubricants made with oil because most oils damage condoms. Never use cooking oil, baby oil, coconut oil, hair oil, mineral oil, petroleum jelly, vaseline, skin lotions, suntan lotions, cold cream, butter, cocoa butter or margarine.

After ejaculation, hold the rim of the condom to the base of the penis so that it does not slip off. It is advisable that the penis be withdrawn out of the vagina before completely losing its erection. Take off the condom without spilling semen on the vaginal opening. Throw the condom into a pit latrine, bury it, burn it or dispose of it in some other way; do not leave it where children can find it and play with it. Do not use a condom more than once. If a condom breaks while it is being used: immediately insert a spermicide into the vagina, if a spermicide is available. Washing both penis and vagina with soap and water may reduce the risk of STDs and pregnancy to some extent. Some client may want to use emergency oral contraception to prevent pregnancy *(see below)*.

Various brands of condoms are available in the market. *Raja, Panther* and *Sensation* are some of the popular brands which are available both in family planning clinics and also in most pharmacies.

6.3.5 EMERGENCY CONTRACEPTIVES

Emergency contraception refers to contraceptive methods that can be used

by women in the first few days following unprotected intercourse to prevent an unwanted pregnancy. The hormonal (Yuzpe) method is suitable for emergency use (2% failure) but it is less effective than insertion of an intra-uterine device (1% failure). Emergency contraception is indicated to prevent pregnancy within 3 days (72 hours) of unprotected sexual intercourse or a contraceptive accident or misuse (e.g. condom rupture, slippage, or misuse; failed coitus interruptus; IUD expulsion; in cases of sexual assault, etc.). Emergency contraception is not suitable as a regular method of contraception.

HORMONAL METHOD. Two regimens can be used: the standard regimen consists of 'combined' pills containing ethinyloestradiol and levonorgestrel or comparable formulations (for instance, those containing norgestrel instead of levonorgestrel). When high-dose pills containing ethinylestradiol 50 micrograms and levonorgestrel 250 micrograms (or norgestrel 500 micrograms) are available : two pills should be taken as the first dose as soon as convenient (but no later than 72 hours after unprotected inter-course), followed 12 hours later by another two pills. When only low-dose pills containing ethinylestradiol 30 micrograms and levonorgestrel 150 micrograms (or norgestrel 300 micrograms) are available (e.g. *Shukhi,*.), four pills should be taken as the first dose as soon as convenient (but no later than 72 hours after unprotected intercourse), followed 12 hours later by another four pills. Alternate hormonal regimen consists of high dose progestogen-only pills. One pill contai-ning 750 micrograms of levonorgestrel should be taken as soon as convenient but no later than 3 days (72 hours) after unprotected intercourse. This should be followed by another pill 12 hours later. Side-effects of hormonal methods include nausea, vomiting, headache, dizziness, breast discomfort and menstrual irregularities.

IUD METHOD. Insertion of an IUD is a more effective emergency contraceptive method than the hormonal method. Copper based IUDs may be appropriate for some women who meet the strict screening requirements for IUD use and who wish to retain the IUD for long-term contraception. Inserted within five days (120 hours) of unprotected intercourse, IUDs provide a highly effective method of emergency contraception.

Tablet Ulipristal Acetate- 30 mg.

It is the USFDA approved drug for use within 5 days of unprotected intercourse but should be taken as soon as possible.

Proprietary Preparation
(see section 6.3.2)
Ulipristal Acetate
Peuli *(Ziska),* Tab. 30 mg, Tk. 195.00/Tab.s
Tulip *(Square),* Tab. 30mg, Tk. 485.00/Tab.

6.4 DRUGS FOR GENITO-URINARY DISORDERS

For individual drugs used in the treatment of urinary tract infection, *see section 1.1*

6.4.1 DRUGS FOR URINARY RETENTION

Acute retention is painful and is treated by catheterisation. Chronic retention is painless and often long standing; catheterisation is not needed unless there is deterioration of renal function. After the cause has initially been established and treated, drugs may be required to increase detrusor muscle tone. Benign prostatic hyperplasia is treated either surgically or medically with alpha-blockers *(see below)* or with the anti-androgen **Finasteride** *(section 12.8.2)*.

ALPHA-BLOCKERS

(see also section 3.2.3)

The selective alpha-blockers **alfazosin, doxazosin, indoramin, prazosin, tamsulosin** and **terazosin** relax smooth muscle in benign prostatic hyperplasia producing an increase in urinary flow rate and an improvement in obstructive symptoms. Side-effects of selective alpha blockers include sedation, dizziness and hypotension (notably postural hypotension particularly after the first dose); other side-effects associated with this group of drugs include drowsiness, weakness and lack of energy, depression, headache, dry mouth, nausea, urinary frequency and incontinence, tachycardia and palpitations. They should be avoided in patients with a history of orthostatic hypotension and micturition syncope; special care (and reduced dosage) is needed when initiating them in the elderly and in renal and possibly hepatic impairment. Since selective alpha-blockers are also anti hypertensive, patients receiving antihypotensive treatment require reduced dosage and specialist supervision (as do those with cardiac disorders). Selective alpha-blockers may cause drowsiness and so affect ability to drive or operate machinery. For interactions, *see Appendix-2 (alpha-blockers)*.

Note: FIRST DOSE EFFECT: First dose may cause collapse due to hypotensive effect (therefore should be taken on retiring to bed). Patient should be warned to lie down if symptoms such as dizziness, fatigue or sweating develop and to remain lying down until they pass off completely

ALFAZOSIN

Indications; Cautions; Contraindications; Side-effects: *see notes above*;
Dose : benign prostatic hyperplasia 10 mg once daily. Acute urinary retention associated with benign prostatic hyperplasia in men over 65 years, 10 mg once daily for 2–3 days during catheterisation and for one day after removal; max. 4 days

Proprietary Preparations
Alfasin *(Incepta),* Tab. 10 mg, Tk. 10.00/Tab.
Alfumax*(Unimed),* Tab. 10 mg, Tk. 10.00/Tab.
Uriten *(Square),* Tab. 10 mg, Tk. 10.04/Tab.
Zatral *(Eskayef),* Tab. 10 mg, Tk. 10.00/Tab.

PRAZOSIN HYDROCHLORIDE

Indications: benign prostatic hyperplasia; *see notes above; hypertension; also see section 3.2.3*

Cautions; Contraindications; Side-effects: *see notes above and also section 3.2.3*

Dose : initially 500 micrograms twice daily for 3-7 days, subsequently adjusted according to response; usual maintenance (and maximum) 2 mg twice daily. ELDERLY: initiate with lowest possible dose

Proprietary Preparations
Alphapress *(Renata),* Tab.1 mg, Tk. 4.00/Tab;Tab. 2 mg, Tk. 6.00/Tab.
Prazopress *(Unimed),*Tab. 1 mg, Tk. 4.00/Tab;Tab. 2 mg, Tk. 6.00/Tab.

TAMSULOSIN HYDROCHLORIDE

Indications; Cautions; Contraindications; Side-effects: *see notes above*; avoid in severe liver impairment

Dose: 400 micrograms daily after breakfast

Proprietary Preparations
Maxflou *(Rangs),* Cap., 400 microgram, Tk. 10.00/Cap.
Maxrin *(Square),* Cap. 400 microgram, Tk. 10.04/Cap.;
Prostam *(Drug Int.),* Cap. 400 microgram, Tk. 10.00/Cap.
Prostanil *(Aristo),* MR Cap. 400 microgram, Tk. 10.00/Cap.
Sasolin *(ACI),* MR Cap. 400 microgram, Tk. 10.04/Cap.
Tamisol *(Healthcare),* MR. Cap., 400 microgram, Tk. 10.00/Cap.
Tamlosin *(Orion),* Tab. 400 microgram, Tk. 10.04/Tab.

Tamsin *(Delta),* Cap. 400 microgram, Tk. 10.00/Cap.
Tamsule *(Sharif),* SR Cap. 400 microgram, Tk. 10.00/Cap.
Tamurin *(Globe),* Cap., 400 microgram, Tk. 10.00/Cap.
Urinom *(Opsonin),* Tab.400 microgram, Tk. 7.55/Tab.;Cap. 400 microgram, Tk. 7.52/Tab.
Urocap *(Ibn Sina),* Cap. 400 microgram, Tk. 10.00/Cap.
Uroflo *(Beximco),* Cap. 400 microgram, Tk. 10.00/Cap.
Urolosin *(General),* Tab. 400 microgram, Tk. 10.04/Tab.
Uromax *(Unimed),* Cap. 400 microgram, Tk. 10.00/Cap.
Uropass *(Acme),* Cap.400 microgram, Tk. 10.04/Cap.
Urosin *(Eskayef),* Cap. 400 microgram, Tk. 10.00/Cap.
Urotam *(Navana),* Cap.400 microgram, Tk. 10.00/Cap.

Tamsulosin HCl + Dutasteride
Tamsin D *(Delta),* Cap., 400 microgram + 500 microgram, Tk. 20.00/Cap.
Uromax-D *(Unimed),* Cap., , 400 microgram + 500 microgram,, Tk. 20.00/Cap.

TERAZOSIN

Indications; Cautions; Contraindications; Side-effects : *see notes above* and *also section 3.2.3*

Dose: initially 1 mg at bedtime; dose may be doubled at weekly intervals according to response to maximum 10 mg once daily; usual maintenance 5-10 mg daily

FIRST DOSE EFFECT: First dose may cause collapse due to hypotensive effect (therefore should be taken on retiring to bed). Patient should be warned to lie down if symptoms such as dizziness, fatigue or sweating develop and to remain lying down until they pass off completely

Proprietary Preparation
Terazon *(Incepta)*, Tab. 2 mg, Tk. 5.00/Tab.; 5mg, Tk. 8.00/Tab.

PARASYMPATHOMIMETICS

Parasympathomimetics produce the effect of parasympathetic nerve stimulation: they possess the muscarinic rather than the nicotinic effect of acetylcholine and improve voiding efficiency by increasing detrusor muscle contraction. In the absence of obstruction to bladder outlet they have a limited role in relieving urinary retention. Generalised parasympathomimetic side effects such as sweating, bradycardia and intestinal colic may occur, particularly in the elderly. Use of parasympathomimetics is now limited because they do not give clinical benefit to patients as might be expected. Their use has largely been replaced by intermittent catheterisation, especially in cases of areflexia. **Carbachol** and **Bethanechol** are choline esters that have been used in postoperative urinary retention. Bethanehol has a more selective action on the bladder than carbachol but the use of both has now been superseded by catherterisation.

Distigmine inhibits the breakdown of acetylcholine. It may help patients with an upper motor neurone neurogenic bladder. No drug preparation containing carbachol, bethanechol or distigmine is presently registered in Bangladesh.

6.4.2 DRUGS FOR URINARY INCONTINENCE AND NOCTURNAL ENURESIS

URINARY INCONTINENCE: Antimuscarinic drugs such as **oxybutynin** and **flavoxate** are used to treat urinary frequency; they increase bladder capacity by diminishing unstable detrusor contractions. The dosage needs to be carefully assessed, particularly in the elderly. **Flavoxate** has less marked side effects but is also less effective. **tolterodine** and **propiverine** are also antimuscarinic drugs used for urinary frequency, urgency and incontinence.
Propantheline was formerly widely used in urinary incontinence but had a low response rate with a high incidence of side-effects; it is now primarily indicated in adult enuresis. The **Tricyclic antidepressants** *(see section 7.3)* such as **imipramin, amitriptyline, and nortriptylin** *(see section 7.3)* are sometimes effective in the management

of unstable bladder because of their antimuscarinic properties.

NOCTURNAL ENURESIS: Nocturnal enuresis is a normal occurrence in young children but persists in about 5% by 10 years of age. In the absence of urinary-tract infection simple measures such as bladder training or the use of an alarm system may be successful. Drug therapy not usually appropriate for children under 7 years of age and should be reserved for cases when alternative measures have failed, and preferably on a short term basis to cover period away from home. The possible side effects of the drugs should be borne in mind when they are prescribed. **Desmopressin** *(see section 5.3.3),* an analogue of vasopressin, is used or nocturnal enuresis; particular care is needed to avoid fluid overload and treatment should not be continued for longer than 3 months without stopping for a week for full reassessment. Tricyclic antidepressants *(see section 7.3)* such as amitriptyline, imipramine, and less often nortriptyline, are also used but behavior disturbances may occur and relapse is common after withdrawal. Treatment should not normally exceed 3 months unless a full physical examination (including ECG) is given and the child is fully reassessed; toxicity following over dosage with tricyclics is of particular concern.

Darifenacin, fesoterodine, propive-rine, solifenacin, and trospium are newer anti-muscarinic drugs indicated for urinary frequency, urgency, andincontinence.

DARIFENACIN

Indications, Cautions, Contraindications & side-effect: *see notes above*

Proprietary Preparations
Darilax *(Incepta),* ER Tab.,15 mg, Tk. 40/Tab.; ER Tab., 7.5 mg, Tk. 22/Tab.
Darifen *(Acme),* ER Tab., 7.5 mg, Tk. 22/Tab.

FLAVOXATE HYDROCHLORIDE

Indications: urinary frequency and incontinence, dysuria, urgency, bladder spasm due to catherterization

Cautions; Contraindications: *see under oxybutynin hydrochloride* (antimu-scarinic effect considerably less marked)

Side-effects: antimuscarinic side-effects; *see also notes above*

Dose: 200 mg 3 times daily; for CHILD under 12 years, not recommended

Proprietary Preparations
Flavox *(Somatec),*Tab.100 mg, Tk. 7.03/Tab.; 200 mg, Tk. 13.05/Tab.
Urilax *(Incepta),* Tab. 100 mg, Tk. 10.00/Tab.; 200 mg, Tk. 18.00/Tab.

OXYBUTYNIN HYDROCHLORIDE

Indications: urinary frequency, urgency and incontinence; neurogenic bladder instability and nocturnal enuresis

Cautions: frail elderly; hepatic and renal impairment; neoropathy; hyperthy-roidism; cardiac disease where increase in heart rate undesirable; prostatic hypertrophy; hiatus hernia with reflex oesophagitis; pregnancy, breast feeding; porphyria

Contraindications: intestinal obstru-cttion or atony; severe ulcerative colitis or toxic megacolon; significant bladder outflow obstruction; glaucoma; myasthe-nia gravis

Side-effects: dry mouth, constipation, blurred vision, nausea, abdominal discomfort, facial flushing (more marked in children), difficulty in micturition (less commonly urinary retention), also head-ache, dizziness, drowsiness, dry skin, rashes, angioedema, photosensitivity, diarrhoea, arrhythmia, restlessness, disorientation, hallucination (children higher risk of excitatory effects); convulsions

Dose: 5 mg 2-3 times daily increased if necessary to max. 500 mg 4 times daily. ELDERLY, 2.5-3 mg twice daily initially, increased to 5 mg twice daily according

to response and tolerance. CHILD, over 5 years, neurogenic bladder instability, 2.5-3 mg twice daily increased to 5 mg 3 times daily, max. 5 mg 3 times daily; nocturnal enuresis (preferably over 7 years), 2.5-3 mg twice daily increased to 5 mg 2-3 times daily (last dose before bedtime)

Proprietary Preparation
Uricon *(Beximco),* Tab. 5mg, Tk.6/Tab.

PROPANTHELINE BROMIDE

Indications: adult enuresis, *see notes above*; *see also section 2.2.*
Cautions; Contraindications: *see under oxybutynin hydrochloride.*
Side-effects: antimuscarinic side-effects; *see also notes above*
Dose: 15-30 mg 2-3 times daily one hour before meals

Proprietary Preparation
see section 2.2.

SOLIFENACIN SUCCINATE

Indications: urinary frequency, urgency and urgeincontinence
Cautions: see notes above; neurogenic bladder disorder
Contra-indications: *see notes above*; hepatic impairment;renal impairment; pregnancy:
Side-effects: see notes above; also chest pain, peripheral oedema; sinusitis, bronchitis; paraesthesia

Proprietary Preparations
Solifen *(Aristo),* Tab. 5mg, Tk. 20/Tab.
Utrobin *(Unimed),* Cap. 10 mg,Tk. 30/Cap; 5mg,Tk.15/Cap.

TOLTERODINE TARTRATE

Indications: urinary frequency, urgency and incontinence
Cautions: significant bladder outflow obstruction; gastro-intestinal obstruction; hiatus hernia; neuropathy; liver impairment; renal impairment
Contraindications: urinary retention, uncontrolled angle-closure glaucoma; myasthenia gravis; severe ulcerative colitis or toxic megacolon
Side-effects: dry mouth, dyspepsia, constipation, abdominal pain, flatulence, vomiting, headache; paraesthesia; less commonly blurred vision, chest pain; rarely urinary retention, confusion
Dose: 2 mg twice daily; reduce to 1 mg twice daily if necessary to minimise side-effects; review after 6 months
Not recommended for CHILDREN

Proprietary Preparations
Detrisom LA *(Unimed),* ER Cap., 2 mg, Tk. 8.00/Cap; ER Cap. 4 mg, Tk. 15.00/Cap.
Tolorin *(General),* Tab. 2 mg, Tk. 3.01/Tab.
Tolter *(Renata),* Tab. 1 mg, Tk. 2.00/Tab.; 2mg, Tk. 3.00/Tab.
Toltrex *(Incepta),* Tab. 2 mg, Tk. 3.00/Tab.
Ucol *(Square),* Tab. 2 mg, Tk. 3.01/Tab.

6.4.3 DRUGS USED IN UROLOGICAL PAIN

The acute pain of ureteric colic may be relieved with **pethidine** *(see section 7.5.1)*. **Diclofenac** by injection or as suppositories *(see section 9.1.1)* is also effective and compares favorably with pethidine; other non-steroidal antiinflammatory drugs are occasionally given by injection. **Lignocaine gel** is a useful topical application in urethral pain or to relieve the discomfort of catheterization *(see section 8.2)*.

6.4.4 DRUG FOR ERECTILE DYSFUNCTION

Erectile disorders are treated with drugs given by mouth which increase the blood flow to the penis. Drugs should be used with caution if the penis is Deformed.

SILDENAFIL

Indications: erectile dysfunction, pulmonary arterial hypertension and for the prevention and treatment of high-altitude pulmonary edema.
Cautions: angina, heart failure, hypotension, dehydration, priapism. *It is taken not more than once per day*

between 30 minutes and 4 hours prior to sexual intercourse.

Contraindications: taking organic nitrites and nitrates, men having cardiovascular risk factors, hepatic impairment ,impairment in renal function, recent stroke or heart attack

Side-effects: headache, flushing, dyspepsia, nasal congestion and impaired vision,

Note: Rare but serious adverse effects found through post marketing surveillance include priapism, severe hypotension, myocardial infarction (heart attack), ventricular arrhythmias, stroke, increased intraocular pressure, and sudden hearing loss

Dose: ADULT over 18 years initially 50mg approx. 1 hour before sexual activity, subsequent doses adjusted according to response to 25–100mg as a single dose as needed; max. 1 dose in 24 hours (max. single dose 100 mg)

Proprietary Preparations

Acmegra *(Acme),* Tab.100 mg, Tk. 50/Tab.; 25 mg, Tk. 20/Tab.**;** 50 mg, Tk. 30.00/Tab.
Activa *(Pacific),* Tab.100 mg, Tk. 30.08/Tab.; 50 mg, Tk.18.80/Tab.
Adegra *(ACI),* Tab., 100 mg, Tk. 50.00/Tab.; 25 mg, Tk. 20.00/Tab.; 50 mg, Tk. 30.00/Tab.
Aggra *(Eskayef),* Tab., 100 mg, Tk. 50.00/Tab.; 50 mg, Tk. 30.00/Tab.
Danafil *(Nipro JMI),* Tab., 50 mg, Tk. 30.00/Tab.
Edegra *(Sun),* Tab. 100 mg, Tk. 50.00/Tab.; 50 mg, Tk. 30.00/Tab.
Enegra *(Beximco),* Tab., 100 mg, Tk. 50.00/Tab.; 50 mg, Tk. 30.00/Tab.
Enjofil *(Navana),* Tab., 100 mg, Tk. 50.00/Tab.; 25 mg, Tk. 15.00/Tab.; 50 mg, Tk. 50.00/Tab.
Erecta *(Renata),* Tab., 100 mg, Tk. 50.00/Tab.; 50 mg, Tk. 30.00/Tab.
Fulfeel *(Orion),* Tab., 50 mg, Tk. 30.00/Tab.
Immense *(Biopharma),* Tab., 25 mg, Tk. 18.00/Tab.; 50 mg, Tk. 25.00/Tab.
Kx *(Kemiko),* Tab.100 mg, Tk. 50.00/Tab.; 50 mg, Tk.30/Tab.
Niagra *(Delta),* Tab., 100 mg, Tk. 40.00/Tab.; 25 mg, Tk.15/Tab.; 50 mg, Tk. 25.00/Tab.
Peak *(General),* Tab., 100 mg, Tk. 50/Tab.; 50 mg, Tk.30/Tab.
Powergra *(Albion),* Tab.100 mg, Tk. 50.00/Tab. ; 50 mg, Tk. 30.00/Tab.
Silagra *(Incepta),* Tab., 100 mg, Tk. 50.00/Tab.; 50 mg, Tk. 30.00/Tab.
Silfil *(Organic),* Tab., 100 mg, Tk. 50.00/Tab.;50 mg, Tk. 30.00/Tab.
Veagra *(Astra),* Tab., 100 mg, Tk. 50.00/Tab.; 50 mg, Tk. 30.00/Tab.
V-gra *(Aristo),* Tab., 100 g, Tk. 50.00/Tab.; 25 mg, Tk. 16.00/Tab. ;50 g, Tk. 30.00/Tab.
Viamax *(Unimed),* Tab., 100 mg, Tk. 50.00/Tab.; 25 mg, Tk. 20.00/Tab.; 50 mg, Tk. 30.00/Tab.
Viax *(Opsonin),* Tab., 100 mg, Tk. 37.59/Tab.; 50 mg, Tk. 22.56/Tab.
Vigorex *(Square),* Tab., 100 mg, Tk. 50.00/Tab.; 25 mg, Tk. 20.00/Tab.; Tab., 50 mg, Tk. 30.00/Tab.
Visagra *(Sharif),* Tab., 50 mg, Tk.30/Tab.
X-cite *(Alco),* Tab., 100 mg, Tk. 50/Tab.; Tab., 50 mg, Tk. 30/Tab.
Yogra*(White Horse),*Tab.,100 mg,Tk.50/Tab.
Vigorex *(Square),* Tab., 50 mg, Tk. 30/Tab.

TADALAFIL

Indications: erectile dysfunction, pulmonary hypertension, benign prostetic hyperplasia with erectile dysfunction.

Caution and Contraindications: same as that of sildenafil

Side-effects: headache, stomach discomfort or pain, indigestion, burping, acid reflux, back pain, muscle aches, flushing, and stuffy or runny nose.

Dose: For BPH, or BPH and erectile dysfunction is 5 mg daily taken about the same time each day. Tadalafil may be taken with or without food since food does not affect its absorption from the intestine.

Proprietary Preparations

Adafil *(Beximco),* Tab., 10 mg, Tk.35/Tab.; 20 mg, Tk.60/Tab.
Celeste *(General),* Tab., 10 mg, Tk.35/Tab.; 20 mg, Tk.60/Tab.; 5 mg, Tk.18/Tab.
Ciafil *(Navana),* Tab., 10 mg, Tk.35.00/Tab.; 20 mg, Tk.55.00/Tab.;Tab. , 5 mg, Tk.18.00/Tab.
Cialix *(Nipro JMI),* Tab., 10 mg, Tk. 35/Tab.
Ciaton *(ACI),* Tab., 10 mg, Tk.35/Tab. ; Tab., 20 mg , Tk.60/Tab.;, 5 mg, Tk.18/Tab.
Edysta *(Unimed),* Tab.,10 mg, Tk.35.00/Tab.; 20 mg, Tk.60.00/Tab.;Tab. , 5 mg, Tk.18.00/Tab.
Intimate *(Square),* Tab.,10 mg, Tk. 35/Tab. 20 mg, Tk.60/Tab.; 5 mg, Tk.18/Tab.
Ktx *(Kemiko),* Tab., 10 mg, Tk.35.00/Tab.; 20 mg, Tk. 60.00/Tab.
Megafil *(Acme),* Tab., 10 mg, Tk.35.00/Tab.; 20 mg, Tk.60.00/Tab.

Pawar *(Aristo),* Tab. , 10 mg, Tk.35.00/Tab.; 20 mg, Tk.60.00/Tab. **;** 5 mg, Tk.18.00/Tab.
Penfil *(Biopharma),* Tab. , 10 mg, Tk.30.00/Tab. ; 20 mg, Tk.55.00/Tab.
Prolonga *(Pacific),* Tab. , 10 mg, Tk.18.80/Tab.; 20 mg, Tk.30.08/Tab., 40 mg, Tk.45.11/Tab.
Refeel *(Orion),* Tab., 10 mg, Tk.30/Tab.; 20 mg, Tk. 50/Tab.
Tadafil *(Astra),* Tab., 10 mg, Tk.35.00/Tab.;Tab., 5 mg, Tk.18.00/Tab.
Tadalafil *(Albion),* Tab., 20 mg, Tk.60/Tab.
Tadalis *(Incepta),* Tab., 10 mg, Tk. 35/Tab.
Tafil *(Sharif),* Tab. , 10 mg, Tk.35.00/Tab.
Tealis *(Opsonin),* Tab. , 10 mg, Tk.26.32/Tab.; 5 mg, Tk.13.53/Tab.
Tiagra *(Ziska),* Tab., 10mg, Tk. 30/Tab.; 20mg, Tk. 50/Tab.; 5mg, Tk. 18/Tab.
Viev *(Alco),* Tab.,10 mg, Tk.35.00/Tab. ; 20mg, Tk.60.00/Tab.

6.4.5 ALKALINISATION AND ACIDIFICATION OF URINE

Alkalinisation of urine may be undertaken with **potassium citrate**.
The alkalinising action may relieve the discomfort of cystitis caused by lower urinary tract infections. Sodium bicarbonate and sodium citrate are also used as urinary alkalinising agents for relief of discomfort in mild urinary tract infections.
Acidification of urine has been undertaken with **ascorbic acid** but it is not always reliable. Large doses may cause gastrointestinal disturbances including diarrhoea. Special pH-modifying solutions are necessary for the maintenance of indwelling urinary catheters.

Urological surgery

Endoscopic surgery within the urinary tract requires an isotonic irrigant since there is a high risk of fluid absorption; if this occurs in excess, hypervolaemia, haemolysis, and renal failure may result. **Glycine Irrigation Solution (1.5%)** is the irrigant of choice for transurethral resection of the prostrate gland and bladder tumours. **Sterile sodium chloride solution 0.9%** (physiological saline) is used for percutaneous renal surgery.

ASCORBIC ACID[ED]

Indications: acidification of urine but *see notes above*; prevention and treatment of scurvy *(see section 16.2.4.3)*
Dose: *by mouth* 4 g daily in divided doses

Proprietary Preparation
see section 16.2.3.3

GLYCINE

Indications: bladder irrigation during urological surgery; *see notes above*
Cautions; Side-effects: *see notes above*

Generic Preparations
Irrigation Solution 1.5%
Glycine *(Opso Saline),* Tk. 60.15/1000 ml
Irigon *(Beximco),* Tk. 70.80/1000 ml
Sterisol *(Popular),* Tk.165.00/2000 ml

POTASSIUM CITRATE

Indications: relief of discomfort in mild urinary tract infections; alkalinisation of urine; stone prophylaxis
Cautions: renal impairment, cardiac disease; elderly; for interactions, *see Appendix-2 (Potassium salts)*
Side-effects: hyperkalaemia on prolonged high dosage, mild diuresis
Potassium Citrate Mixture BP: Oral solution, potassium citrate 30%, citric acid monohydrate 5% in a suitable vehicle with a lemon flavour. Preparations should be freshly prepared; contains about 28 mmol k^+/10 ml
Dose: 10 ml (well diluted with water) 3 times daily

Proprietary Preparation
Urokit *(Easkayef)*, Tab.,1080mg, Tk.10/Tab.

SODIUM BICARBONATE

Indications: relief of discomfort in mild urinary tract infections; alkalinisation of urine
Cautions; Side-effects: caution in elderly; *see also section 1.1.2*

Dose: 3 gm in water every 2 hours until urinary pH exceeds 7; for maintenance of alkaline urine 5-10 gm daily

Proprietary Preparations
Sodinate *(Opsonin),* Tab., 600mg, Tk.4.53/Tab.
Sodicarb *(Popular),* Tab., 600 mg, Tk.6.02/Tab.
Sodium Bi Carbonate *(Opso Saline),* Inj., (IV Infusion) 7.5%, 75mg/ml, Tk. 5.29/25 ml

6.5 HORMONE THERAPY OF GYNAECOLOGICAL DISORDERS

6.5.1 BROMOCRIPTINE

Bromocriptine is a stimulant of dopamine receptors in the brain. It also inhibits release of prolactin by the pituitary. It is used in the treatment of galactorrhoea and cyclic benign breast disease, and for treatment of prolactinomas (when it reduces both serum prolactin and tumour size). Bromocriptine also inhibits the release of growth hormone and is sometimes used in treatment of acromegaly. Other dopamine-receptor stimulants are cabergoline and quinagolide. Bromocriptine and other dopaminereceptor stimulants are *not recommended for routine suppression of lactation* or for the relief of postpartum pain and engorgement of the breasts, which can be adequately treated with simple analgesics and breast support.

BROMOCRIPTINE MESYLATE

Indication: prevention and suppression of lactation *(see notes above),* hypogonadism, galactorrhoea, infertility, cyclical benign breast disease, acromegaly, prolactinoma; *see also under Dose.* Use in children under 15, not recommended
Cautions: pituitary enlargement, particularly during pregnancy; peptic ulcer in acromegalic patients; oral contraceptives may increase prolactin concentrations; caution in patients with serious mental or psychotic disorders or with cardio-vascular disease or Raynaud's syndrome (monitor for retroperitoneal fibrosis); hepatic and renal impairment; porphyria; hypotensive reactions (may be disturbing in some patients during the first few days of treatment); caution with antihypertensive therapy and avoid other ergot alkaloids. *Should be dispensed under prescription only*
Contraindications: hypersensitivity to bromocriptine or other ergot alkaloids; toxaemia of pregnancy and hypertension in post-partum women or in puerperium; advise women not to breast-feed if lactation prevention fails. Should not be used in postpartum or in puerperium in women with high blood pressure, coronary artery disease or with symptoms (or history) of serious mental disorder. Discontinue immediately if hypertension, unremitting headache or signs of CNS toxicity develop
Interactions : *see Appendix-2*
Side-effects: nausea, vomiting, indigestion, constipation, headache, fatigue, dizziness, insomnia, nasal congestion, postural hypotension, vasospasm of fingers and toes particularly in patients with Raynaud's syndrome. With high doses, confusions, psychomotor excitation, hallucination, dyskinesia, dry mouth, leg cramps, pleural effusions, retroperitoneal fibrosis (needs monitoring)
Dose: prevention/suppression of lactation 2.5 mg on first day (prevention) or daily for 2–3 days (suppression); then 2.5 mg twice daily for 14 days. Hypogonadism/galactorrhoea, infertility, initially 1.25 mg at bed time increased gradually; usual dose 7.5 mg daily in divided doses; increased if necessary to a maximum of 30 mg daily; usual dose in infertility without hyperprolactinemia, 2.5 mg twice daily. Cyclical benign breast disease and cyclical menstrual disorders with pain, 1.25 mg at bed time, increased gradually; usual dose 2.5 mg twice daily. Acromegaly, initially 1.25 mg at bedtime, increased gradually to 5 mg

every 6 hours. Prolactinoma, initially 1.25 mg at bedtime, increased gradually to 5 mg every 6 hours

Proprietary Preparations
Bromergon *(Novartis),* Tab. 2.5 mg, Tk.14/Tab.
Bromodel *(Opsonin),* Tab.2.5 mg, Tk.7.55/Tab.
Bromolac *(Square),* Tab. 2.5 mg, Tk.12/Tab.
Criptine *(Renata),* Tab. 2.5 mg, Tk.12/Tab.

6.5.2 DANAZOL

Danazol inhibits pituitary gonadotropins; it has androgenic, antioestrogenic and antiprogestogenic properties. It is used in the treatment of endometriosis and also in mammary dysplasia and gynaecomastia where other measures have proved unsatisfactory; it has been used in menorrhagia and other menstrual disorders but in view of its side-effects, treatment with other drugs may be preferable. It may be effective in the long-term in management of hereditary angioedema. Another less common drug Gestrinone, has general action similar to those of danazol and has also been used in the treatment of endometriosis.
Indications : *see notes above and under dose*
Cautions: cardiac, renal and hepatic impairment (avoid if severe); elderly : polycythaemia, epilepsy, diabetes mellitus, hypertension, migraine, lipoprotein disorders, history of thrombosis; withdraw if signs virilisation appear; nonhormonal contraception should be used
Contraindications: pregnancy (ensure that patient with amenorrhoea are not pregnant); breast-feeding; severe renal, cardiac and hepatic impairment; thromboembolic disease; undiagnosed vaginal bleeding; androgen dependent tumours; porphyria
Interactions: *see Appendix-2*
Side-effects: nausea, headache, dizziness, rashes, backache, nervousness, weight gain; menstrual disturbances, flashing, reduction in breast size; skeletal muscle spasm, hair loss; androgenic effects like- acne, oily skin, oedema, hirsutism, voice changes and clitoral hypertrophy; insulin resistance; leucopenia, thrombocytopenia; benign intracranial hypertension and visual disturbance reported
Dose : usual range 200-800 mg daily in up to 4 divided dose; all dose should start during menstruation, preferably on first day of cycle. Endometriosis: initially 400 mg daily up to 4 divided doses, adjust according to response, usually for 6 months. Menorrhagia: 200 mg daily, usually for 3 months. Severe cyclical mastalgia: 200-300 mg daily, usually for 3–6 months. Benign breast cysts: 300 mg daily, usually for 3-6 months. Gynaecomastia: 400 mg daily in divided doses for 6 months (adolescents 200 mg daily, increased to 400 mg daily if response after 2 months). Pre-operative thinning of endometrium: 400–800 mg daily for 3–6 weeks

Proprietary Preparations
Danamet *(Eskayef),* Cap.,100 mg, Tk.20/Cap.; 200 mg , Tk. 38.00/Cap.
Danzol *(Renata),* Cap., 100 mg, Tk. 20/Cap.; 200 mg, Tk. 38.00/Cap.
Lozana *(Incepta),* Cap., 100 mg, Tk.20/Cap.; 200 mg, Tk. 38.00/Cap.

6.5.3 CETRORELIX

Indications: combination with gonadotropins used in the treatment of female infertility (under fertility specialist supervision)
Contraindications: pregnancy, breast-feeding, moderate renal impairment, moderate hepatic impairment
Side effects: nausea, hedache, injection site reaction, rarely hypersensitivity reactions
Dose: 0.25 mg/ml (250 microgram) by subcutaneous injection into the lower abdominal wall to be administered daily in the morning on day 5 or 6of ovarian stimulation with gonadotropins continue throughout administration of gonadotropins

Proprietary Preparation
Cetrotide$^{(U)}$ *(Serono),* Inj. 0.25mg, Tk.3,592.90/Vial