UNIT 3 ESSENTIAL DRUGS - 3

Structure

3.0 INTRODUCTION

In the previous two units we have discussed about the pharmacology of some common drugs. There are many molecules which are used as medicines for treatment of various diseases. New drugs are being discovered regularly. It is important to have new drugs, as the pathogens which causes infectious diseases develops resistance to the old drugs due to indiscriminate use of antibiotics. But at the same time we should not discard or undervalue the time tested drugs. The proverb 'old is gold' is true in case of medicines

too. Many drugs which were discovered many decades ago are still being used to treat many dreaded diseases. It is repeated here that medicines, are active chemicals and should be used judiciously and should be prescribed by only those who have required qualification plus enough knowledge about its various aspects.

3.1 OBJECTIVES

At the end of the unit, you will be able to:

- explain the use of expectorant in day to day practice;
- explain the correct use of misoprostol as abortifacient and to control post-partum haemorrhage;
- counsel the eligible couple about the correct usage of oral contraceptive pills;
- list the common medications used for surface anaesthesia while treating minor injuries;
- enumerate drugs used to resuscitate individuals;
- discuss the harmful effects of regular usage of nasal decongestants and antibiotics with your clients; and
- explain the drugs used in various national health programmes.

3.2 EXPECTORANTS

A recurrent and chronic cough is an irritating symptom. It can affect one's work and sleep, and it can disturb others around the person having cough, too. Everyone wants to get rid of the cough as soon as possible. Expectorants are drugs that increase the airway secretion and enhance the expulsion of mucous by air passages of the lungs. This makes it is easier to cough up the phlegm or sputum. Expectorants are used in cough syrups and are used by someone who is having nagging cough. Often the term 'expectorant' is incorrectly extended to any cough syrup.

3.2.1 Difference between Expectorants and Mucolytics

A mucolytic agent is an agent which dissolves thick mucous and is usually used to help relieve respiratory difficulties. It does so by dissolving various chemical bonds within secretions, which in turn can lower the viscosity by altering the mucin-containing components. There is a difference in the terms 'expectorant' and 'mucolytic agent'. An expectorant increases bronchial secretions and mucolytics help loosen thick bronchial secretions.

3.2.2 Natural Remedies for Cough

Before prescribing someone with a cough syrup it is advisable to give him some natural expectorants to stop the cough. The natural remedies for stopping cough are honey and steam. Inhalation of soothing vapours of herbs like eucalyptus, peppermint, rosemary, and clove oil helps in forming a more productive cough. The vapour rubs available in the medicine stores usually contain a mixture of petroleum jelly and essential oils. Some replace petroleum with coconut oil or almond oil. These vapour rub or ointments can loosen mucous when they are rubbed onto the chest and neck. Drinking lots of warm liquids helps to thin mucous. Warm chicken soup is an effective and proven way for movement of mucous, providing relief.

3.2.3 A Word of Caution While Using Cough Syrups

There are cough syrups available in the market which contain a mix of cough suppressant or expectorant with medicines for other symptoms. That medicine may be an antihistaminic, a decongestantor a pain reliever. The mixture can be a good thing if the personhas a range of cold symptoms, like body aches, coughs, and congestion. The downside is that he may get a medicine which he does not need. So all cough syrups are not suitable for any type of cough.

However in day to day practice, most of the times, dry and irritating cough could be allergic or due to acid reflux. In these situations, you need to prescribe an appropriate antiallergic or a proton pump inhibitor/ H2 blocker as per the history and clinical impression. Also, the cough suppressants will be of immense use in non-specific dry cough especially associated with haemoptysis.

Check Your Progress 1

1) Define Expectorants.

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2) Explain natural remedies for cough.

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3) Explain cautions while using cough syrup.

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3.3 MISOPROSTOL

It is a synthetic prostaglandin E 1 analog. This is used for a variety of illnesses. Misoprostol is a medication used to start labour, cause an abortion, prevent, and treat postpartum bleeding due to poor contraction of the uterus. For abortions it is often used with mifepristone. By itself effectiveness of Misoprostol for abortion is between 66% and 90%. It is taken either by mouth, kept under the tongue, or placed in the vagina. Mifepristone 200 mg tablet 3 tablets orally followed by misoprostol 200 µg 2 tablets orally 2 days later is an effective way to terminate pregnancy of upto 49 days. The common side effects of the drug include diarrhoea and abdominal pain. Uterine rupture may occur if it is given as abortifacient without much consideration and the pregnant lady is not under medical supervision. Misoprostol is commonly used for labour induction. It causes uterine contractions and the ripening of the cervix. It is significantly less expensive than the other commonly used ripening agent. Misoprostol is also used to prevent and treat post-partum bleeding. Orally administered misoprostol is marginally less effective than oxytocin. The use of rectally administered misoprostol is optimal in cases of bleeding. Misoprostol is recommended due to its cost,

effectiveness, stability, and low rate of side effects. For post-partum haemorrhage oxytocin must also be given by injection, while misoprostol can be given orally or rectally. This strategy is very useful in areas where trained nurses and physicians are not available.

3.4 DRUGS FOR POSTPARTUM HAEMORRHAGE

Postpartum Haemorrhage (PPH) is commonly defined as a blood loss of 500 ml ormore within 24 hours after child birth. PPH is the leading cause of maternal mortality in low-income countries including India and the primary cause of nearly one quarter of all maternal deaths globally. Most deaths resulting from PPH occur during the first 24 hours afterbirth. The unfortunate part is that the majority of these deaths could be avoided through the use of prophylactic medications and by timely and appropriate management. The group of drugs which are used to control postpartum haemorrhage is known as uterotonics. These drugs stimulate contraction of the uterine muscle, helping to control PPH.These agents are useful in the treatment and prophylaxis of PPH. Following are the drugs which are commonly used during PPH.

3.4.1 Oxytocin

Oxytocin has variety of actions. It produces rhythmic uterine contractions, can stimulate the gravid uterus, and has vasopressive and antidiuretic effects. It is widely used to control postpartum bleeding. It can be used prophylactically in the third stage of labour.

3.4.2 Methylergonovine (Methergine)

It is an ergot alkaloid. Only the amine ergot alkaloid ergometrine (ergonovine) and its derivative methyl-ergometrine are used in obstetrics. It acts directly on uterine smooth muscle, causing a sustained tetanic uterotonic effect that reduces uterine bleeding and shortens the third stage of labour. It is administered intra-muscularly during puerperium, during delivery of placenta, or after delivering the anterior shoulder of the baby.Ergometrine is contraindicated in women with a history of hypertension, heart disease, preeclampsia, or eclampsia.

3.4.3 Syntometrine

It is a combination of 5 IU oxytocin plus 0.5 mg ergometrine. It controls PPH effectively by combined rapid action of oxytocin and sustained action of ergometrine.

3.4.4 Carboprost

It has a longer duration of action and produces myometrial contractions that induce haemostasis at the placental site, which reduces postpartum bleeding. It is given as 0.25 mg IM every 30–120 minutes for PPH.

Table 3.1: Common Drugs used to Control Post-partum haemorrhage

Name of Drug	Use	Dose	Side Effects	Contraindi-cations	Precautions
Oxytocin	Induction of labour, abortion, PPH	For PPH: 10 to 40 units IV infusion in 1000 mL at	Confusion, convulsions, difficulty in breathing,	Allergic, cephalopelvic disproportion	May interact with other drugs

Name of Drug	Use	Dose	Side Effects	Contraindi-cations	Precautions
		a rate suffi-cient to con-trol bleeding. 10 units IM after delivery of placenta.	dizziness fast or irregular heartbeat		
Ergometrine	PPH	0.2 mg IM; may repeat in 2-4 hr; not to exceed 5 doses total	Dizziness, headache, hypertension, nasal conges-tion, nausea and vomiting	Hyperten-sion, toxemia, pregnancy, hypersensi-tivity	IV only in emer-gency because of potential for hypertension and stroke
Syntometrine	Following the birth of the placenta, to prevent or treat PPH	IM injection of 1ml follo-wing expul-sion of the placenta, or when blee-ding occurs	Headache, dizziness, myocardial infarction, hypertension, vomiting, nausea, abd-ominal pain	Severe hypertension, pre-eclam-psia, eclam-psia, severe cardiac disorders	In breech presentations and other abnormal presentations, Syntometrine should not be given until after delivery of the child
Carboprost	Treatment of PPH due to uterine atony and refractory to conventio-nal methods of treatment with oxytocic agents and ergometrine	1 ml deep IM, may be repeated after an hour	Flushing, hot flush, chills, headache	Acute pelvic inflammatory disease, car-diac, pulmo-nary, renal, or hepatic disease.	should not be used for induc-tion of labor

3.4.5 Managing PPH

Uterine massage is recommended for the treatment of PPH as soon as it is diagnosed. Initial fluid resuscitation with isotonic crystalloids are recommended. The use of tranexamic acid is advised in cases of refractory atonic bleeding or persistent trauma-related bleeding. Bimanual uterine compression, external aortic compression, and the use of non-pneumatic anti-shock garments are recommended as temporary measures until substantive care is available. If bleeding persists despite treatment with uterotonic drugs and other conservative interventions, intervention radiology or surgical intervention should be used without further delay.

Box 3.1: Recommendations for the Prevention of PPH

- The use of uterotonics for the prevention of PPH during the third stage of labour is recommendedfor all births.
- Oxytocin (10 IU, IV/IM) is the recommended uterotonic drug for the prevention of PPH.

- If oxytocin is unavailable, we can use other injectable uterotonics (if appropriate, ergometrine/methylergometrine or the fixed drug combination of oxytocin and ergometrine) or oral misoprostol (600 mg).
- Community health care workers or lay health workers can use Tablet Misoprostol (600 mg PO) for the prevention of PPH if skilled birth attendants are not present and oxytocin is unavailable.
- Late cord clamping (performed after 1 to 3 minutes after birth) is recommended for all births while initiating simultaneous essential new-born care.
- Early cord clamping (<1 minute after birth) is not recommended unless the neonate is asphyxiated and needs to be moved immediately for resuscitation.
- Sustained uterine massage is not recommended as an intervention to prevent PPH in women who have received prophylactic oxytocin.
- Postpartum abdominal uterine tonus assessment for early identification of uterine atony is recommended for all women.
- Oxytocin (IV or IM) is the recommended uterotonic drug for the prevention of PPH in caesarean section.
- Controlled cord traction is the recommended method for removal of the placenta in caesarean section.

Box 3.2: Recommendations for the Treatment of PPH

- Intravenous oxytocin alone is the recommended uterotonic drug for the treatment of PPH.
- If intravenous oxytocin is unavailable, or if the bleeding does not respond to oxytocin, the use of intravenous ergometrine, oxytocin-ergometrine fixed dose, or a prostaglandin drug (including sublingual misoprostol, 800 ìg) is recommended.
- The use of isotonic crystalloids is recommended in preference to the use of colloids for the initial intravenous fluid resuscitation of women with PPH.
- The use of tranexamic acid is recommended for the treatment of PPH if oxytocin and other uterotonics fail to stop bleeding or if it is thought that the bleeding may be partly due totrauma.
- Uterine massage is recommended for the treatment of PPH.
- If women do not respond to treatment using uterotonics, or if uterotonics are unavailable, the use of intrauterine balloon tamponade is recommended for the treatment of PPH due to uterine atony.
- If bleeding does not stop in spite of treatment using uterotonics and other available conservative interventions (e.g. uterine massage, balloon tamponade), the use of surgical interventions is recommended.
- The use of bimanual uterine compression is recommended as a temporizing measure until appropriatecare is available for the treatment of PPH due to uterine atony after vaginal delivery.

- The use of external aortic compression for the treatment of PPH due to uterine atony after vaginal birth is recommended as a temporizing measure until appropriate care is available.
- The use of non-pneumatic anti-shock garments is recommended as a temporizing measure until appropriate care is available.
- The use of uterine packing is not recommended for the treatment of PPH due to uterine atony after vaginal birth.
- If the placenta is not expelled spontaneously, the use of IV/IM oxytocin (10 IU) in combination with controlled cord traction is recommended.
- The use of ergometrine for the management of retained placenta is not recommended as this may cause tetanic uterine contractions which may delay the expulsion of the placenta.
- The use of PGF2á (dinoprostone) for the management of retained placenta is not recommended.
- A single dose of antibiotics (ampicillin or first-generation cephalosporin) is recommended if manual removal of the placenta is practised.

Check Your Progress 2

1) List indications for misoprostol.

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2) Define Postpartum Haemorrhage (PPH).

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3) Define urotonics.

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4) List indications of Oxytocin injection.

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5) Enumerate drugs which control Postpartum Haemorrhage (PPH).

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3.5 ORAL CONTRACEPTIVES

Hormonal contraception is one of the most effective methods of reversible fertility control**.** These are classified further on the basis of components.

3.5.1 Combined Oral Contraceptives

Estrogen plus progestogen combinations are the most widely used hormonal contraceptives. They produce a contraceptive effect mainly by suppressing the hypothalamic-pituitary system resulting in prevention of ovulation; in addition, changes in the endometrium make it unreceptive to implantation. Ovulation usually resumes within three menstrual cycles after oral contraception has been discontinued; anovulation and amenorrhea persisting for six months or longer requires investigation and appropriate treatment if necessary. Potential non-contraceptive benefits of combined oral contraceptives include improved regularity of the menstrual cycle, decreased blood loss, less iron-deficiency anaemia and significant decrease in dysmenorrhoea.

Availability

Tablets:

1) Levonorgestrel + Ethinylestradiol

   0.15 mg + 0.03 mg

   0.25 mg + 0.05 mg

2) Levonorgestrel 0.15 mg + Ethinylestradiol 0.03 mg + Ferrous fumarate 60 mg.

3) Norethisterone + Ethinylestradiol

   0.5 mg + 0.03 mg

   1.0 mg + 0.03 mg

Dose

Adults- Contraception: 1 TAB (pill) daily for 21days; subsequent courses repeated after 7-daypill-free interval (during which withdrawal bleeding occurs). Each tablet (pill) should be taken at approximately the same time each day; if delayed by longer than 24 h contraceptive protection may be lost. It is important to bear in mind that the critical time for loss of protection is when a pill is omitted at the beginning or end of a cycle (which lengthens the pill-free interval).

Adverse effects

These are frequent, especially in the first 1–3 cycles and then disappear gradually.

Nausea and vomiting: Similar to morning sickness of pregnancy. Headache is generally mild; migraine may be precipitated or worsened. Breakthrough bleeding or spotting: Especially with progestin only preparations. Amenorrhoea may occur in few, or the cycles may get disrupted especially with injectable and maniple. Breast discomfort.These adverse effects appear later after several months of use. Weight gain, acne and increased body hair. Chloasma: pigmentation of cheeks, nose and forehead Pruritus vulvae. Carbohydrate intolerance and precipitation of diabetes. Mood swings, abdominal distention are occasional; especially reported with progesterone only contraceptives.

Serious complications

1) Leg vein or pulmonary thrombosis
2) Cerebral or coronary thrombosis leading to stroke or Myocardial infraction
3) Hypertension
4) Genital carcinoma
5) Dyslipidemia
6) Benign hepatoma
7) Gallstones

Contraindications

Thromboembolic, coronary and cerebrovascular disease or a history of it.Moderate-to-severe hypertension; hyperlipidemia. Active liver disease, hepatoma or history of jaundice during past pregnancy.Suspected/overt malignancy of genital and breast. Porphyria. Impending major surgery-to avoid operative thromboembolism.

3.5.2 Progesterone-only Contraceptives

Progestogen-only contraceptives, such as oral levonorgestrel may offer a suitable alternative when estrogens are contraindicated but the oral progestogen-only preparations do not prevent ovulation in all cycles and have a higher failure rate than combined estrogen-containing preparations. Progestogen only contraceptives carry less risk of thromboembolic and cardiovascular disease than combined oral contraceptives and are preferable for women at increased risk of such complications, for example smokers over 35 years. They can be used as an alternative to estrogen-containing combined preparations prior to major surgery. Oral progestogen-only contraceptives may be started 3 weeks after birth; lactation women should preferably start atleast 6 weeks after birth. Menstrual irregularities (oligomenorrhoea, menorrhagia, and amenorrhea) are common.

3.5.3 Non-steroidal Oral Contraceptive

Centchroman

It probably acts as an anti-implantation agent by inducing embryo-uterine asynchrony, accelerated tubal transport and suppression of decidualization. It prevents conception as long as taken, with return of fertility on withdrawal.

Availability

Tablet: 30 mg.

Dose

30 mg tablet. A single tablet should be taken twice a week (on a Sunday and a Wednesday) for the first three months and then weekly (every Sunday) thereafter.

Adverse Effects

Water retention; tender breasts; acne; heavy menstruation.

Contraindications

Medical history of liver disease, jaundice; ovarian disease (polycystic ovaries); cervical hyperplasia; cervicitis; chronic renal disorders.

3.5.4 Emergency Contraception

Levonorgestrel is used for emergency contraception.

Levonorgestre l1.5 mg should be taken as a single dose within 72 h of unprotected intercourse; alternatively, levonorgestrel 750 ìg can be taken within 72 h of unprotected intercourse followed 12 h later by another 750 mg. Under these circumstances levonorgestrel prevents about 86% of pregnancies that would have occurred if no treatment had been given.

Adverse effects

Nausea, vomiting, headache, dizziness, breast discomfort and menstrual irregularities. If vomiting occurs within 2–3 h of taking the tablet, replacement tablet can be given with an antiemetic.

Table 3.2: Common oral Contraceptive Pills

Name of Drug	Use	Dose	Side Effects	Contraindi-cations	Precautions
Estrogen progestin combination	Prevent pregnancy	Comes in 21 or 28 tablets packet. Take once daily	Nausea, breakthrough bleeding, skin colour changes, breast changes	Suspected pregnancy, genital bleeding, migraine, liver disease, breastfeed-ing, bleeding disorders, high blood pressure, breast cancer	Use with caution in women above 35 years of age
Progestin only pills	Prevent pregnancy	There are 28 pills in a pack of progestogen-only pills. Take once daily	Acne, breast tenderness and breast enlargement, mood changes, headache and migraine, nausea or vomiting	Heart disease, liver disease, breast cancer, ovarian cysts, unexplained vaginal bleeding	Take the progestogen-only pill at the same time each day
Emergency contraceptive pills	After unprotected intercourse	1.5 mg as soon as possible after unprotected intercourse	Nausea, vomiting, headache, feeling tired, fatigue, lower abdominal pain, vaginal bleeding, breast tenderness	Suspected pregnancy, hypersensiti-vity	Repeated ECP use is an indication that the woman requires further counselling on other contraceptive options. Frequently repeated ECP use may be harmful

Check Your Progress 3

1) List advantages of Oral contraceptives.

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2) List the importance of dose of contraception.

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3) Explain progesterone only contraceptives.

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4) Explain emergency contraception with dose.

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3.6 TOPICAL ANAESTHETIC AGENTS

A topical anaesthetic is a local anaesthetic that is used to numb the surface of a body part. They can be used to numb any area of the skin as well as the front of the eyeball, the inside of the nose, ear or throat, the anus and the genital area. Topical anaesthetics are available in creams, ointments, aerosols, sprays, lotions, and gels. Drugs include benzocaine, butamben, dibucaine, lidocaine, oxyethazaine, and tetracaine.

Many options to deliver anaesthesia have developed over the last several decades. Administration of topical anaesthetics to control pain associated with procedures such as laceration repair may avoid the need for infiltrative local anaesthesia injections and associated pain from the injections. Topical anaesthesia also avoids the risk of wound distortion that exists with infiltrative injection administration.

Mechanism of action

Topical anaesthetics reversibly block nerve conduction near their site of administration, thereby producing temporary loss of sensation in a limited area. Nerve impulse conduction is blocked by decreasing nerve cell membrane permeability to sodium ions, possibly by competing with calcium-binding sites that control sodium permeability.

Duration of topical anaesthetic

The duration of topical anaesthesia depends on the type and amount applied, but is usually about half an hour. Adequate anaesthesia is necessary for complete examination, cleansing and repair of wounds.

Usage of topical anaesthetics

Topical anaesthetics are used to relieve pain and itching caused by conditions such as sunburn or other minor burns, insect bites or stings, and minor cuts and scratches. Topical anaesthetic eye drops are used in ophthalmology to numb the surface of the eye to perform some tests for eye condition like glaucoma and also to remove foreign bodies and prior to surgeries of the eye. Topical anaesthetics finds its use in dentistry to numb oral tissue before performing any dental procedure. Some topical anaesthetics (e.g. oxybuprocaine) are also used in ENT setup.Topical anaesthetics are poorly absorbed through intact skin and hence are safe to use.

3.7 NASAL DECONGESTANTS

Nasal congestion happens when the blood vessels in the mucous membranes lining the nose become swollen, affecting breathing. For most people, a blocked nose is simply an annoyance, but for others, nasal congestion can affect their ears, their hearing and in severe cases, their sleep. In young babies who are being breast-fed or bottle-fed, nasal congestion can affect feeding, because babies need to breathe through their nose while they feed. A nasal decongestant is a type of drug that is used to relieve nasal congestion. The active ingredient in most decongestants is either pseudoephedrine or phenylephrine. Regular use of these agents for long periods should be avoided because mucosal ciliary function is impaired. Atrophic rhinitis and anosmia can occur due to persistent vasoconstriction. Decongestants can be absorbed from the nose via an inhaler and produce systemic effects, mainly CNS stimulation and rise in blood pressure. These drugs should be used cautiously in hypertensives and in those receiving some medications. Besides hypertension, common side-effects include sleeplessness, anxiety, dizziness, excitability, and nervousness.

Mechanism of action

The vast majority of decongestants act via enhancing norepinephrine and epinephrine, adrenergic activity. This induces vasoconstriction of the blood vessels in the nose, throat, and paranasal sinuses, which results in reduced inflammation (swelling) and mucous formation in these areas.

Warning

Topical nasal decongestants quickly develop tachyphylaxis (a rapid decrease in the response to a drug after repeated doses over a short period of time). Long-term use is not recommended, since these agents lose effectiveness after a few days. Medicated nasal decongestants should not be used in babies younger than 6 months, as rebound congestion may cause breathing difficulty. Decongestants containing pseudoephedrine, phenylephrine, oxymetazoline or xylometazoline should not be given to children younger than 6 years.

3.8 DRUGS USED IN SHOCK

A person in shock is an emergency condition. He needs advanced life support. Good quality cardio-pulmonary resuscitation (CPR) is the cornerstone of advanced life support. This includes delivery of chest compressions over the lower half of the sternum at a depth of atleast 5 cm, and at a rate of approximately 100–120 per minute, while minimising interruptions for compressions at all times. Some conditions may precipitate cardiac arrest or decrease the chances of successful resuscitation. These conditions

should be sought and, if present, corrected in every case. These conditions can be remembered as 4 Hs and 4 Ts (hypoxaemia, hypovolaemia, hyper/hypokalaemia and metabolic disorders, hypo/hyperthermia and Tension pneumothorax, Tamponade, Toxins / poisons / drugs, Thrombosis-pulmonary / coronary). Following drugs are commonly used as life saving measures in advanced life support.

Epinephrine: This is a first line drug. Epinephrine has combined α-adrenergic and β-adrenergic effects. The α-adrenergic effects may augment coronary diastolic pressure, thereby increasing sub-endocardial perfusion during chest compressions. Epinephrine also increases the likelihood of successful defibrillation.

Check Your Progress 4

1) Write meaning of topical anaesthetic agents.

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2) In which form are these drugs available.

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3) List uses of topical anaesthetic agents.

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4) Nasal decongestants need to be used with precautions in which group of patients.

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5) Name drugs used for treatment of shock.

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3.9 DRUGS USED IN VECTOR BORNE DISEASES

Let us now discuss the drugs used in vector born diseases under antimalarial and Kala-azar

3.9.1 Anti-malarial Drugs

Malaria is caused by a parasite called plasmodium. Its two species plasmodium vivax and plasmodium falciparum are prevalent in India. There are many drugs available for malaria. The first drug invented and still in use is quinine. Government of India regularly revises its national antimalarial drug policy because of the changing pattern of infection and growing resistance against the established antimalarials. In 1982, Ministry of Health and Family Welfare, Government of India formulated the first antimalarial drug policy. Initially chloroquine was the drug of choice to treat all malaria cases. Later when plasmodium developed resistance to chloroquine, the need of new drug arose.

Box 3.3: Currently registered antimalarial drugs in India

1) Amodiaquine
2) Artemether + Lumefantrine FDC
3) Arterolane + Piperaquine FDC
4) Artesunate + Amodiaquine FDC
5) Artesunate + Mefloquine blister pack and FDC
6) Artesunate + Sulphadoxine-Pyrimethamine blister pack
7) Chloroquine: Confirmed P. vivax cases should be treated with chloroquine in full therapeutic dose of 25 mg/kg as per the age-wise dosage schedule
8) Injectable artemisinin derivatives
9) Mefloquine
10) Primaquine: In some patients P. vivax may cause relapse. For its prevention, primaquine should be given at a dose of 0.25 mg/kg body weight daily for 14 days under supervision in all cases of plasmodium vivax infection except in pregnant women, infants and known G6PD deficient patients. Primaquine can lead to haemolysis in G6PD deficiency. Patient should be advised to stop primaquine immediately if he/she develops any of the following symptoms and should report to the physician immediately: dark coloured urine, yellow conjunctiva, bluish discolouration of lips, abdominal pain, nausea, vomiting, breathlessness, etc.
11) Proguanil
12) Pyrimethamine
13) Quinine
14) Sulphadoxine-Pyrimethamine

Artemisinin Combination Therapy (ACT): It should be given to all the confirmed P. falciparum cases found positive by microscopy or rapid diagnostic test (RDT). This is to be accompanied by single dose of primaquine (0.75 mg/kg body weight) on Day 2. ACT consists of an artemisinin derivative combined with a long acting antimalarial (amodiaquine, lumefantrine, mefloquine, piperaquine or sulfadoxine-pyrimethamine). The ACT recommended in the National Programme all over India except north-eastern states is artesunate (4 mg/kg body weight) daily for 3 days and

sulfadoxine (25 mg/kg body weight) -pyrimethamine (1.25 mg/kg body weight) on Day 0. In the north-eastern states due to the recent reports of late treatment failures to the current combination of AS+SP in P. falciparum malaria, the presently recommended ACT in national drug policy is fixed dose combination (FDC) of Artemether-lumefantrine (AL).

Table 3.3: Treatment of uncomplicated Malaria

Malaria	Drug Treatment
P. vivax	Chloroquine 10 mg base/kg stat. Followed by:10 mg/kg at 24 hour and 5 mg/kg at 48 hour and Primaquine 0.25 mg/kg body weight daily for14 days
P. falciparum (NE states)	Age-specificACT-AL (Artemether 20 mg and Lumefantrine 120 mg)for 3 days + primaquine 0.75 mg/kg body weight on day 2 single dose
P. falciparum (other states)	Artesunate 4 mg/kg body weight daily for 3 days Plus Sulfadoxine (25 mg/kg body weight) – Pyrimethamine (1.25 mg/kg body weight) on first day. Primaquine 0.75 mg/kg body weight on day 2.
Mixed infections (NE states)	Age-specific ACT-AL (Artemether 20 mg and Lumefantrine 120 mg) for 3 days +Primaquine 0.25 mg perkg body weight daily for14 days.
Mixed infections (other states)	Artesunate 4 mg/kg body weight daily for 3 days Plus Sulfadoxine (25 mg/kg body weight) – Pyrimethamine (1.25 mg/kg body weight) on first day+Primaquine 0.25 mg perkg body weight daily for14 days.

3.9.2 Drugs Used for Kala-azar

The Kala-azar is also known as Visceral leishmaniasis

Kala-azar is an intracellular protozoal infection caused by *Leishmania donovan*i and transmitted by phlebotomine sandflies.

The following drugs can be used in order of preference at all levels as shown in Table 3.4.

Table 3.4

Name of drug / Availabilty	Indications	Dose	Precautions	Contraindica-tions
Amphotericin B Availability Vials: 10, 25, 50 and 100 mg plain, 50 mg/vial (liposomal).	Life-threatening fungal infections Unresponsive to pentavalent anti-mony compounds; Severe meningitis, perioral candi-diasis	*Intravenous infusion (plain)* **Adults-** Systemic fungal infection: 250 µg/kg body weight daily, increase gradually 1 mg/kg body weight if tolerated (max 1.5 mg/kg body weight	Close medical super-vision throughout treat-ment; renal impairment; pregnancy; hepatic and renal function tests; blood counts and plasma electrolyte monitoring; corticoste-roid (avoid, except to	Toxic effects must be weighed against benefits. Regular kidney, liver func-tion tests and blood counts must be conducted; lacta-tion; antineoplastic therapy.

Name of drug / Availabilty	Indications	Dose	Precautions	Contraindications
		daily) or alternate days.**Children**- Same as for Adult based on body weight.*Intravenous (liposomal)* For fever in neutropenic patients: 3 mg/kg/day max. dose 5 mg/kg/day i.v. For cryptococcal meningitis: 3-4 mg/kg, max. 6 mg/kg, i.v. once daily. Visceral leismaniasis: Immunocompetent patients: 3 mg/kg.Immunocompromised patients: 4 mg/kg.	control reactions); lactation; avoid rapid infusion (risk of arrhythmias); geriatric use. Anaphylaxis occurs rarely, with intravenous Amphotericin B and a test dose is advisable before the first infusion. The patient should be observed for about 30 min after the test dose.	
2. Miltefosine Availability Capsule: 10 mg, 50 mg	As directly observed therapy (DOT) of visceral Leishmaniasis caused by Leishmania donovani.	**Dose** **Adults-** (>12 years): Weighing >25 kg: 100 mg/day, twice a day, after meals for 28 days. <25 kg: 50 mg/day, after meals for 28 days **Children** (2-11 years): 2.5 mg/kg daily after meals for 28 days, i.e., 50 mg once daily.	Avoid contact with eyes, kidney or liver impairment, may impair ability to drive or operate machinery.	**Contraindications** Children below 2 years, patients with HIV, newborns, and lactation.
3. Paramomycin Availability Injection 375 mg/ml		Dose **Adults:** 25-35 mg/kg daily in 3 divided doses for 5-10 days. **Children:** Same as adult dose	Patient with ulcerative bowel lesions. Prolonged use may result in overgrowth of non-susceptible organisms. Renal impairment. Pregnancy and lactation	**Contraindications** Hypersensitivity to Paramomycin and other aminoglycosides. Intestinal obstruction.

Let us discuss the adverse effects of the above mentioned drugs used for Kala-azar treatment as given below:

Adverse Effects of Amphotericin B

Fever, headache, anorexia, weight loss, nausea and vomiting, malaise, diarrhea, muscle and joint pain, dyspepsia and epigastric pain; renal function disturbances including hypokalaemia, hypomagnesaemia and renal toxicity; blood disorders; cardiovascular

toxicity (including arrhythmias); neurological disorders (including peripheral neuropathy);abnormal liver function (discontinue treatment); rash; anaphylactoid reactions (see above); pain and thrombophlebitis at injection site; respiratory failure. Store in a tightly closed container between 2 to 8 p C, protected from light.

Adverse Effects of Miltefosine

Nausea and vomiting, GI irritation, diarrhoea, constipation, ocular, hepatic, renal toxicity, skin rash, leukocytosis, thrombocytosis. Store in a cool place, protected from light and moisture.

Adverse Effect of Paramomycin

Ototoxicity, anorexia, nausea, vomiting, epigastric burning and pain, increased GI motility, abdominal cramps, diarrhoea, pruritus ani, hypocholesterolaemia, malabsorption of xylose and sucrose, abnormal fat metabolism, headache, vertigo, eosinophilia, exanthema, unexplained haematuria.

We have also discussed in details about other vecter borne diseases such as Japanese Excephalitis and Dengue, Chickunguniea alongwith primary management including medications in BNS-041, Block 3, Unit 2. You may refer that Block.

3.10 ANTI-TUBERCULAR DRUGS (ATDS)

Tuberculosis is caused an acid fast bacilli (AFB) named *Mycobacterium tuberculosis*. It can infect any organ or tissue of the body except nail, hair and teeth. TB of the lungs is the most common. In around 15% of all TB cases other organs like lymph nodes, CNS, bone is affected. These are known as extra-pulmonary TB cases. The investigation of choice for lung TB is sputum smear examination for AFB. Around half of all the pulmonary TB cases will have AFB in the sputum. These cases are known as smear-positive pulmonary TB patients. Other group of pulmonary TB cases in which AFB are not seen under microscope are labelled as smear-negative pulmonary TB patients. The main objectives of tuberculosis therapy are to cure the patients and to minimise the possibility of transmission of the bacillus to healthy individuals. There are many drugs available to treat tuberculosis. The first line drugs are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E) and Streptomycin (S).

The patient is categorised in either of the two groups based upon the previous intake of ATDs. The treatment duration of TB is long. New patients are defined as those who have no history of prior TB treatment or who received less than 1 month of anti-TB drugs (regardless of whether their smear results are positive or not). New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE/ 4HR. The drugs are given three times weekly dosing throughout therapy [2(HRZE)3/ 4(HR)3]. For previously treated, 8 months of treatment is required. The entire treatment duration is divided into phases: intensive and continuation. For smear-positive pulmonary TB patients treated with first-line drugs, sputum smear microscopy is performed at completion of the intensive phase of treatment. In new patients, if the specimen obtained at the end of the intensive phase (month 2) is smear-positive, sputum smear microscopy should be obtained at the end of the third month.In new patients, if the specimen obtained at the end of month 3 is smear-positive, sputum culture and drug susceptibility testing (DST) is performed. Similarly, in previously treated patients, if the specimen obtained at the end of the intensive phase (month 3) is smear-positive, sputum culture and drug susceptibility testing (DST) should be performed. Now-a-days drug resistant in TB is of wide importance. For diagnosing these drug resistant TB cases early, specimens for culture and drug susceptibility testing should be obtained from all

previously treated TB patients at or before the start of treatment. DST is performed for atleast isoniazid and rifampicin, two most important and most commonly used ATDs world over. ATB patient-wise box (PWB) contains the full course of treatment for a single patient and thus assures the TB patient that his or her medicines will be available throughout treatment. This helps limit confusion and wastage, and makes it easier to monitor the regularity of treatment; avoiding stock-outs and most important helps to maintain patient confidence in the health system. The patient may feel a sense of 'ownership' of the PWB and enhanced motivation to complete the full course of treatment – during visits to the health centre he or she can actually see the quantity of medicines that must be taken to achieve cure. It should be noted that the TB patient-wise box does not eliminate the need for directly observed treatment (DOT) which is the cornerstone of TB treatment. Standardised treatment is given to TB patients. This means that all patients in a defined group receive the same treatment regimen.

Previous TB treatment is a strong determinant of drug resistance, and previously treated patients comprise a significant proportion (13%) of the global TB notifications in 2007. Of all the forms of drug resistance, it is most critical to detect multidrug resistance (MDR) because it makes regimens with first-line drugs much less effective and resistance can be further amplified. Prompt identification of MDR and initiation of MDR treatment with second-line drugs gives a better chance of cure and prevents the development and spread of further resistance. At the global level, 15% of previously treated patients have MDR, which is five times higher than the global average of 3% in new patients.

3.10.1 Essential First-line Anti-Tuberculosis Drugs (ATDs)

Isoniazid: Isoniazid is highly bactericidal against replicating tubercle bacilli.

Streptomycin: Streptomycin is an aminoglycoside antibiotic derived from *Streptomyces griseus* that is used in the treatment of TB and sensitive Gram-negative infections.Streptomycin is not absorbed from the gastrointestinal tract but, after intramuscular administration, it diffuses readily into the extracellular component of most body tissues and attains bactericidal concentrations, particularly in tuberculous cavities. Streptomycin must be administered by deep intramuscular injection. Syringes and needles should be adequately sterilised to exclude any risk of transmitting pathogens. It is also available for intravenous administration. The doses is15 mg/kg (12–18 mg/kg) daily, or 2 or 3 times weekly; maximum daily dose is 1000 mg. Patients aged over 60 years and weighing less than 50 kg may not be able to tolerate more than 500–750 mg daily. The major contraindications are auditory nerve impairment, myasthenia gravis and pregnancy. Streptomycin should be used with caution in patients with renal insufficiency, because of the increased risk of nephrotoxicity and ototoxicity. Streptomycin injections are painful. Rash, induration, or sterile abscesses can form at injection sites.Numbness and tingling around the mouth occur immediately after injection.Cutaneous hypersensitivity reactions can occur. Impairment of vestibular function is uncommon with currently recommended doses. Hearing loss is less common than vertigo. Manifestations of damage to the 8th cranial (auditory) nerve include ringing in the ears, ataxia, vertigo and deafness.

Ethambutol: A synthetic congener of 1,2-ethanediamine, ethambutol is active against M. tuberculosis, M. bovis and some nonspecific mycobacteria. It is used in combination with other anti-TB drugs to prevent or delay the emergence of resistant strains.It is readily absorbed from the gastrointestinal tract. Ethambutol is administered orally. The dose is 15 mg/kg (15–20 mg/kg) daily or 30 mg/kg (25–35 mg/kg) 3 times weekly. The major contraindication is pre-existing optic neuritis from any cause. Patients should

be advised to discontinue treatment immediately and to report to a clinician if their sight or perception of colour deteriorates. Ocular examination is recommended before and during treatment. Whenever possible, renal function should be assessed before treatment. Dose-dependent optic neuritis can result in impairment of visual acuity and colour vision in one or both eyes. Early changes are usually reversible, but blindness can occur if treatment is not discontinued promptly. Ocular toxicity is rare when ethambutol is used for 2–3 months at recommended doses.Signs of peripheral neuritis occasionally develop in the legs.

Adverse effects of anti-tubercular drugs: Although the therapeutic regimens for tuberculosis are extremely effective, undesirable drug interactions can occur, as can adverse reactions of varying degrees of severity. Drug interactions can be defined as reciprocal reactions among drugs, resulting in undesirable or unexpected effects. Drug interactions can alter the serum concentrations of the drugs involved, thereby reducing their effectiveness. Adverse reactions to anti-tuberculosis drugs are related to various factors, and the principal determinants of such reactions are the dose and time of day at which the medication is administered, as well as patient age and nutritional status, together with the presence of pre-existing diseases or dysfunctions, such as alcoholism, impaired liver function, impaired kidney function, and HIV co infection. Minor adverse effects include nausea, vomiting, epigastric pain, abdominal pain, arthralgia, arthritis, peripheral neuropathy, cutaneous pruritus, headache, and changes in behaviour (insomnia, anxiety, decreased libido, and euphoria). Major adverse effects include exanthema, vertigo, psychosis, and hepatotoxicity.

Table 3.5: Category of TB Patients and their Treatment

Category	Treatment	Drugs
New (category I) New sputum smear-positive New sputum smear-negative New extrapulmonary tuberculosis	2 $H_3R_3Z_3E_3$ + $4H_3R_3$	H: Isoniazid (300 mg) Z: Pyrazinamide (1500 mg) S: Streptomycin (750 mg R: Rifampicin (450 mg) E: Ethambutol (1200 mg)
Previously treated (Category II) Sputum smear-positive relapse Sputum smear positive failure Sputum smear positive treatment after default	$2H_3R_3Z_3E_3S_3$ + $1H_3R_3Z_3E_3$ + $5H_3R_3E_3$	

Table 3.6: TB Drug Side Effects

Drug	Side Effects	Notes
Ethambutol	Rash, joint pain, gut upset, fever, headache, dizziness, eyesight problems	Check eyesight often
Isoniazid	Gut upset, loss of appetite, fever, rash, liver problems, peripheral neuropathy	Take on an empty stomach. Take pyridoxine (vitamin B6) to prevent peripheral

Drug	Side Effects	Notes
		neuropathy. Monitor liver function.
Pyrazinamide	Gut upset, fever, rash, joint pain, hepatitis, gout, light sensitivity	Monitor liver function.
Rifampicin	Gut upset, rash, fever, orange urine/tears/saliva, light sensitivity, liver problems, acute renal failure	Take on an empty stomach.

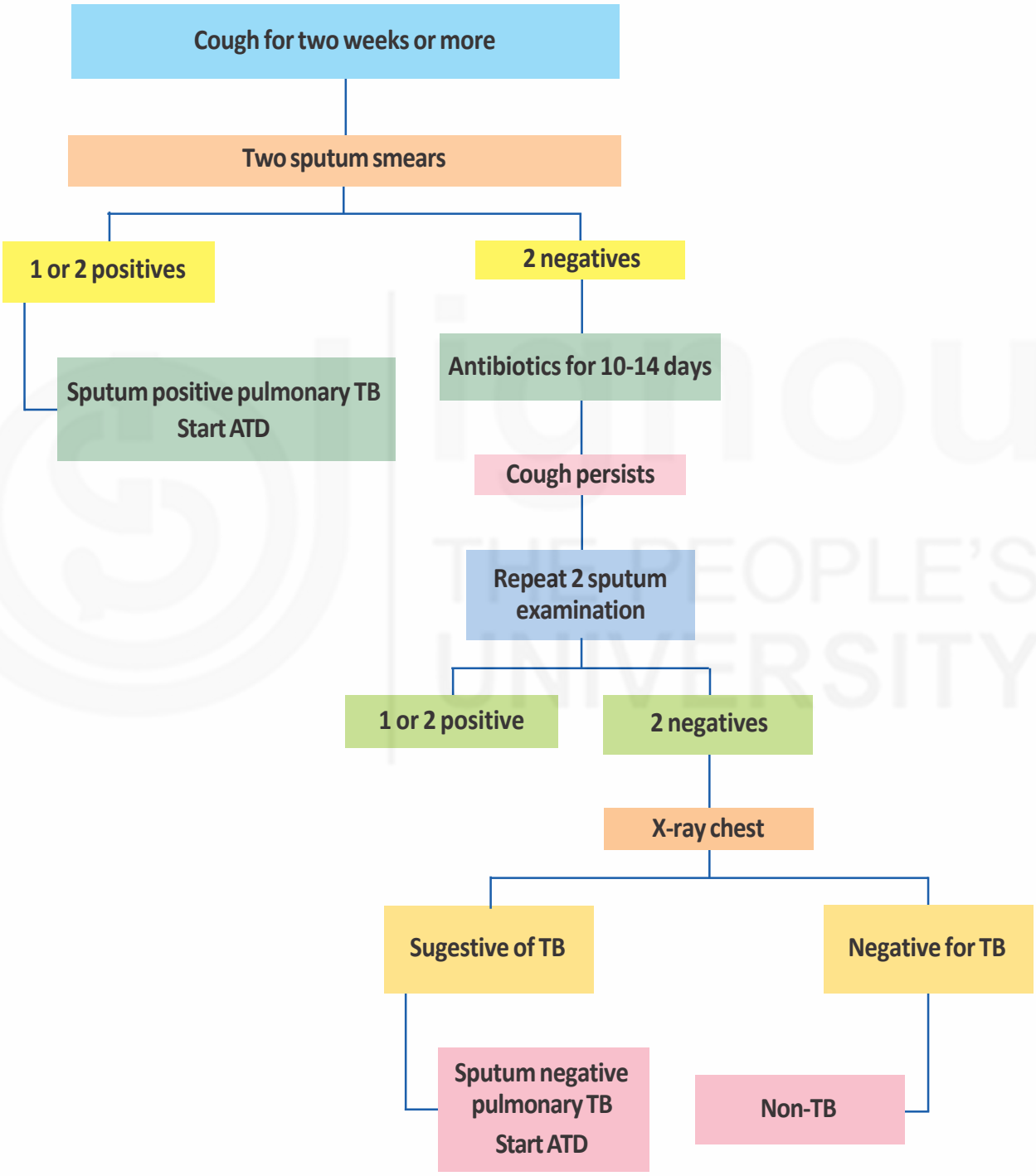

Fig. 3.1: Diagnostic algorithm for pulmonary tuberculosis

3.10.2 Treatment of MDR-TB

Multi-drug resistant tuberculosis is difficult to treat. There are different drugs used for them. These drugs are divided in these groups:

- Group 1 (First-line oral agents): Pyrazinamide (Z), Ethambutol (E), Rifabutin (Rfb)
- Group 2 (Injectable agents): Kanamycin (Km), Amikacin (Am), Capreomycin (Cm), Streptomycin (S)
- Group 3 (Fluoroquinolones): Levofloxacin (Lfx), Moxifloxacin (Mfx), Ofloxacin (Ofx)
- Group 4 (Oral bacteriostatic second-line agents): Para-aminosalicylic acid (PAS), Cycloserine (Cs), Terizidone (Trd), Ethionamide (Eto), Protionamide (Pto)
- Group 5 (Agents with unclear role in treatment of drug resistant-TB): Clofazimine (Cfz), Linezolid (Lzd), Amoxicillin/clavulanate (Amx/Clv), Thioacetazone (Thz), Imipenem/cilastatin (Ipm/Cln), High-dose isoniazid (high-dose H), Clarithromycin (Clr)

3.10.3 Treatment for Leprosy

(As per National Leprosy Eradication Programme)

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. And usually affects skin and peripheral nerves. It is classified as paucibacillaryleprosy in which 5 or less skin lesions are present and multibacillary leprosy, in which more than 5 or skin lesions are present.

6 month regimen for Paucibacillary (PB) Leprosy

	Dapsone	Rifampicin
Adults 50-70 kg	100 mg once daily	600 mg once monthly under supervision
Children 10-14 years	50 mg once daily	450 mg once monthly under supervision

12 month regimen for Multibacillary (MB) Leprosy

	Dapsone	Rifampicin	Clofazimine
Adults 50-70 kg	100 mg once daily	600 mg Once monthly under supervision	50 mg once daily & 300 mg once monthly under supervision
Children 10-14 years	50 mg once daily	450 mg once monthly. under supervision	50 mg every other day & 150 mg once monthly under supervision

Individual drugs used in the treatment of leprosy are given in the table below.

Medicine Name	Mechanism of Action	Dose	Adverse Effects
Dapsone	Inhibit folate synthesis	Paucibacillary and multibacillary (see the above table)	GT irritation, anaemia, peripheral neuropathy, haemolysis (G6PD deficient) and methaemoglobinaemia (dose-related), nephrotic syndrome, psychological changes, hepatitis
Rifampicin	Inhibit RNA polymerase	Paucibacillary and multibacillary (see the above table)	Facial flushing and itching, with or without a rash, flu-like syndrome characterised by episodes of fever, chills, headache, dizziness, bone pain, shortness of breath, and malaise, hepatitis, orange-red discolouration of the urine, faeces, sweat & other body fluids
Clofazimine	Interferes with template function of DNA	Paucibacillary and multibacillary (see the above table)	Red-brownish black discolouration of skin especially areas exposed to sunlight, hair, sweat, sputum, urine, faeces. Rash, pruritus, photosensitivity, diarrhoea, nausea, abdominal pain, vomiting, weight loss, headache, drowsiness, dizziness, taste disorders, dryness of the skin, ichthyosis, decreased tear and sweat production.

3.11 ANTI-RETROVIRAL DRUGS

Treatment with medicines against HIV is called antiretroviral therapy (ART). People on ART take a combination of HIV medicines every day. A person's initial HIV regimen generally includes three HIV medicines from atleast two different drug classes. ART is not a cure of HIV; they help people with HIV live longer, healthier lives. ART also reduce the risk of HIV transmission. The antiretroviral drug classes currently approved are:

- Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs/NtRTIs), also called nucleoside or nucleotide analogues:NRTIs block reverse transcriptase, an

enzyme HIV needs to make copies of itself: Abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovirdisoproxil fumarate, zidovudine

- Non-nucleoside reverse transcriptase inhibitors (NNRTIs): NNRTIs bind to and later alter reverse transcriptase, an enzyme HIV needs to make copies of itself: efavirenz, nevirapine, etravirine, rilpivirine
- Protease inhibitors (PIs):PIs block HIV protease, an enzyme HIV needs to make copies of itself: atazanavir, darunavir, fosamprenavir, ritonavir, saquinavir, tipranivir, nelfinavir, indinavir
- Integrase inhibitors:Integrase inhibitors block HIV integrase; an enzyme HIV needs to make copies of itself: dolutegravir, elvitegravir, raltegravir
- Fusion Inhibitors: Fusion inhibitors block HIV from entering the CD4 cells of the immune system: enfuvirtide
- Entry Inhibitors: Entry inhibitors block proteins on the CD4 cells that HIV needs to enter the cells: maraviroc
- Pharmacokinetic Enhancers: Pharmacokinetic enhancers are used in HIV treatment to increase the effectiveness of an HIV medicine included in an HIV regimen: cobicistat

Goals of ARV therapy:

- Clinical goals: Prolongation of life and improvement in quality of life
- Virologicalgoals: Greatest possible reduction in viral load for as long as possible
- Immunological goals: Immune reconstitution that is both quantitative and qualitative
- Therapeutic goals: Rational sequencing of drugs in a fashion that achieves clinical,virological and immunological goals while maintaining treatment options, limiting drug toxicity and facilitating adherence
- Reduction of HIV transmission in individuals: Reduction of HIV transmission by suppression of viral load

Table 3.7: Initiation of ART based on CD4 Count and WHO Clinical Staging

Classification of HIV-associated Clinical Disease	WHO Stage	CD4 not Available	CD4 Available
Asymptomatic	1	Do not treat	Treat if CD4 < 350
Mild symptoms	2	Do not treat	
Advanced symptoms	3	Treat	Consider treatment if CD4 < 350 and initiate ART before CD4 falls below 200
Severe/ advanced symptoms	4	Treat	Treat irrespective of CD4 count

Adverse effects: Each class and individual antiretroviral carries unique risks of adverse side effects.

- NRTIs: The NRTIs can interfere with mitochondrial DNA synthesis and lead to high levels of lactate and lactic acidosis, liver steatosis, peripheral neuropathy,

myopathy and lipoatrophy. Current first line NRTIs such as lamivudine/emtrictabine, tenofovir, and abacavir are less likely to cause mitochondrial dysfunction.

- NNRTIs: NNRTIs are generally safe and well tolerated. The main side effect is neuro-psychiatric effects including suicidal ideation. Other significant side effects are severe hepatotoxicity, especially in women with high CD4 counts.
- Protease inhibitors: They may cause lipodystrophy, elevated triglycerides and elevated risk of heart attack.
- Integrase inhibitors: Integrase inhibitors (INSTIs) are among the best tolerated of the antiretrovirals with excellent short and medium term outcomes. They are associated with an increase in creatinine kinase levels and rarely myopathy.

3.11 LET US SUM UP

In this unit we have learnt about some more medicines. We have also seen that there are non-pharmacological management available for cough. Correct use of oral contraceptive pills helps in planning the pregnancy better. Proper selection of client for OCPs will improve the compliance and decreases the unwanted effects of the pills. Emergency contraceptive is for emergency use only. It is not recommended to take ECs on regular basis. Misosprostol should be taken only on doctor's advice and woman should be under medical supervision while on Misoprostol as there is high chance of severe bleeding following its administration. PPH can be prevented if the third stage of labour is manged effectively. For the management of malaria, tuberculosis and HIV, government of India has very good guidelines and these should be used judiciously.

3.12 KEY WORDS

Abortifacient : A drug causing abortion.

Advanced Life Support : A set of life-saving protocols and skills that extend basic life support to further support the circulation and provide an open airway and adequate breathing.

Emergency contraceptive Pills : Also called emergency post-coital contraception or morning-after pill, are birth control measures that may be used after unprotected sexual intercourse to prevent pregnancy.

Patient-Wise box : A box containing the treatment of TB for entire duration.

Multi-drug Resistant Tuberculosis : A form of TB infection caused by bacteria that are resistant to treatment with at least two of the most powerful first-line anti-TB drugs, isoniazid and rifampicin.

Tachyphylaxis : A rapid decrease in the response to a drug after repeated doses over a short period of time.

Ventricular Fibrillation : A heart rhythm problem that occurs when the heart beats with rapid, erratic electrical impulses (irregularly irregular).

Ventricular Tachycardia : A type of rapid heartbeat that arises from improper electrical activity of the heart presenting as a rapid heart rhythm, that starts in the bottom chambers of the heart, called the ventricles.

3.13 MODEL ANSWERS

Check Your Progress 1

1) Expectorants are drugs that increase the airway secretion and enhance the expulsion of mucous by air passages of the lungs. This makes it is easier to cough up the phlegm or sputum.

2) The natural remedies for stopping cough are honey and steam. Inhalation of soothing vapours of herbs like eucalyptus, peppermint, rosemary, and clove oil helps in forming a more productive cough.

3) Medicine may be an antihistaminic, a decongestantor a pain reliever. The mixture can be a good thing if the person has a range of cold symptoms, like body aches, coughs, and congestion. The downside is that he may get a medicine which he does not need. So all cough syrups are not suitable for any type of cough.

Check Your Progress 2

1) Misoprostol is a medication used to start labor, cause an abortion, prevent, and treat postpartum bleeding due to poor contraction of the uterus.

2) Postpartum Haemorrhage (PPH) is commonly defined as a blood loss of 500 ml or more within 24 hours after child birth.

3) The group of drugs which are used to control postpartum haemorrhage is known as uterotonics. These drugs stimulate contraction of the uterine muscle, helping to control PPH. These agents are useful in the treatment and prophylaxis of PPH.

4) It produces rhythmic uterine contractions, can stimulate the gravid uterus, and has vasopressive and antidiuretic effects. It is widely used to control postpartum bleeding. It can be used prophylactically in the third stage of labour.

5) Drugs which control PPH

   a) Oxytocin

   b) Ergometrine

   c) Syntometrine

   d) Carboprost

Check Your Progress 3

1) Benefits of combined oral contraceptives include improved regularity of the menstrual cycle, decreased blood loss, less iron-deficiency anaemia and significant decrease in dysmenorrhoea.

2) Adults- Contraception: 1 TAB (pill) daily for 21days; subsequent courses repeated after 7-day pill-free interval (during which withdrawal bleeding occurs).Each tablet (pill) should be taken at approximately the same time each day; if delayed by longer than 24 h contraceptive protection may be lost. It is important to bear in

mind that the critical time for loss of protection is when a pill is omitted at the beginning or end of a cycle (which lengthens the pill-free interval).

3) Progestogen-only contraceptives, such as oral levonorgestrel may offer a suitable alternative when estrogens are contraindicated but the oral progestogen-only preparations do not prevent ovulation in all cycles and have a higher failure rate than combined estrogen-containing preparations. Progestogen only contraceptives carry less risk of thromboembolic and cardiovascular disease than combined oral contraceptives and are preferable for women at increased risk of such complications, for example smokers over 35 years. They can be used as an alternative to estrogen-containing combined preparations prior to major surgery. Oral progestogen-only contraceptives may be started 3 weeks after birth; lactation women should preferably start atleast 6 weeks after birth. Menstrual irregularities (oligomenorrhoea, menorrhagia, and amenorrhoea) are common.

4) Emergency contraception
Levonorgestrel is used for emergency contraception.
Levonorgestrel1.5 mg should be taken as a single dose within 72 h of unprotected intercourse; alternatively, levonorgestrel 750 ìg can be taken within 72 h of unprotected intercourse followed 12 h later by another 750 ìg. Under these circumstances levonorgestrel prevents about 86% of pregnancies that would have occurred if no treatment had been given.

Check Your Progress 4

1) A topical anaesthetic is a local anaesthetic that is used to numb the surface of a body part. They can be used to numb any area of the skin as well as the front of the eyeball, the inside of the nose, ear or throat, the anus and the genital area.

2) Topical anaesthetics are available in creams, ointments, aerosols, sprays, lotions, and gels. Drugs include benzocaine, butamben, dibucaine, lidocaine, oxyethazaine, and tetracaine.

3) Topical anaesthetics are used to relieve pain and itching caused by conditions such as sunburn or other minor burns, insect bites or stings, and minor cuts and scratches. Topical anaesthetic eye drops are used in ophthalmology to numb the surface of the eye to perform some tests for eye condition like glaucoma and also to remove foreign bodies and prior to surgeries of the eye. Topical anaesthetics finds its use in dentistry to numb oral tissue before performing any dental procedure. Some topical anaesthetics (e.g. oxybuprocaine) are also used in ENT setup. Topical anaesthetics are poorly absorbed through intact skin and hence are safe to use.

4) These drugs should be used cautiously in hypertensives and in those receiving some medications.

5) Epinephrine: This is a first line drug. Epinephrine has combined á-adrenergic and â-adrenergic effects. The á-adrenergic effects may augment coronary diastolic pressure, thereby increasing sub-endocardial perfusion during chest.

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