

**FOOD, MEDICINE AND HEALTH CARE ADMINISTRATION AND CONTROL AUTHORITY**

# STANDARD TREATMENT GUIDELINES FOR GENERAL HOSPITALS

**Third Edition, 2014**

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# ACRONYMS

| | |
|---|---|
| ACD | Allergic contact dermatitis |

| | |
|---|---|
| ACEIs | Angiotensin converting enzyme inhibitors |
| ACS | Acute Coronary Syndrome |
| ADL | Acute adenolymphangitis |
| ADRs | Adverse Medicine Reactions |
| AFB | Acid fast Bacilli |
| AIVR | Accelerated Idioventricular Rhythm |
| AKI | Acute kidney Injury |
| ALF | Acute liver failure |
| ARBs | Angiotensin receptor blockers |
| ART | anti-retroviral therapy |
| AV | Atrio ventricular |
| BID | Twice a day |
| BMI | body mass index |
| C/Is | Contraindications |
| CBC | Complete blood count |
| CDAD | Clostridium Difficille Associated Disease |
| CKD | Chronic kidney Injury |
| CL | Cutaneous leishmaniasis |
| CLL | Chronic lymphocytic leukemia |
| CML | Chronic Myelogenous Leukemia |
| CNS | Central nervous system |
| COPD | Chronic Obstructive Pulmonary Disease |
| CPR | Cardiopulmonary resuscitation |
| CRP | C-reactive protein |
| CSF | Cerebrospinal fluid |
| D/Is | Medicine interactions |
| D/S | Dextrose in Saline solution |
| D/W | Dextrose in water solution |
| DBS | Dry Blood Spot |
| DEC | Diethylcarbamazine citrate |
| DKA | Diabetic Ketoacidosis |
| DLA | Dermatolymphangioadenitis |
| DMARD | Disease-modifying anti-rheumatic medicines |

| | |
|---|---|
| DST | Medicine Susceptibility Testing |
| DVT | deep vein thrombosis, |
| ECG | electrocardiogram |
| ENL | Erythema Nodosum Leprosum |
| ENT | Ear, Nose and Throat |
| ESR | erythrocyte sedimentation rate |
| ESRD | End Stage Renal Disease |
| FH | Fulminant hepatitis |
| FMHACA | Food, Medicine and Health Care Administration and Control Authority |
| FPG | Fasting plasma glucose |
| G | Gram |
| GDM | Gestational Diabetes Mellitus |
| GERD | Gastro Esophageal Reflux Disease |
| GFR | Glomerular Filtration rate |
| GI | Gastrointestinal |
| GTD | Gestational Trophblastic diseases |
| GTN | Gestational Trophoblastic Neoplasia |
| HDL | high-density lipoprotein cholesterol |
| HHS | Hyperglycemic Hyperosmolar State |
| Hrs | Hours |
| ICD | Irritant Contact Dermatitis |
| IDU | Intravenous Medicine Use |
| IHCP | Intra-hepatic cholestasis pregnancy |
| IM | Intramuascular |
| IOP | Intra-ocular pressure |
| IRIS | Immune Reconstitution Immune Syndrome |
| ITP | Immune Thrombocytopenic Purpura |
| IU | International Unit |
| IUGR | Intrauterine growth restriction |
| IV | Intravenous |
| IVDA | intravenous medicine abuse endocarditic |
| LDL | low-density lipoprotein cholesterol |

| | |
|---|---|
| MAT | Multifocal Atrial Tachycardia |
| MDR | Multi Medicine Resistance |
| MDT | Multi-medicine therapy |
| Ml | Milliliter |
| MNT | Medical Nutrition Therapy |
| MOH | Ministry of Health |
| MSH | Management Sciences for Health |
| N/S | Normal saline solution |
| NNRTI | Nucleoside Reverse Transcriptase Inhibitors |
| NRTIs | Nucleoside Reverse Transcriptase Inhibitors |
| NSVT | Non sustained ventricular tachycardia |
| NVE | native valve endocarditic |
| OGTT | Oral Glucose Tolerance Test |
| P.O | Per Os (mouth) |
| P/Cs | Precautions |
| PCP | Pneumocystis Carinni Pneumonia |
| PEP | Post-exposure prophylaxis |
| PI | Protease Inhibitors |
| PKDL | Post kala-azar Dermal Leishmaniasis |
| PMTCT | Prevention of mother-to-child transmission |
| PPH | Post-Partum Haemorrhage |
| PRN | As required |
| PROM | Premature Rupture Of Membranes |
| PSVT | Paroxysmal supra-ventricular tachycardia |
| PTE | Pulmonary thrombo-embolism |
| PTT | Placental trophoblastic tumour |
| PVE | Prosthetic Valve Endocarditits |
| QD | Once a day |
| QID | Four times a day |
| RA | Rheumatoid Arthritis |
| RBC | Reduction in red blood cell |
| RDT | Rapid Diagnostic Tests |

| | |
|---|---|
| RUTF | Ready to use therapeutic feeding |
| SBGM | Self-blood glucose monitoring |
| SBP | Prophylaxis for spontaneous bacterial peritonitis |
| SSIs | Surgical site infections |
| STG | Standard Treatment Guideline |
| STI | Sexually transmitted infections |
| TID | Three times a day |
| VT | Ventricular Tachycardia |
| VTE | Venous thromboembolism |
| WBC | White blood cell count |
| WPW | Wolff-Parkinson-White |

## PREFACE

In a healthcare system where multiple treatment optionsare available, the development and implementation of standard treatment guidelines (STGs) is a crucial strategy for ensuring effective and safe use of medicines, containing health care costs, and preventing antimicrobial resistance.

STGs promote therapeutically effective and economic use of medicinesat different levels of health facilities, as they give clear guidance and recommendations about the treatment and management of each clinical condition. When properly developed and implemented, treatment guidelines enhance rational medicine use and improve the quality of care. These guidelines provide up-to-date informationrelevant to theprevention, diagnosis and treatment of common diseases in Ethiopia which helps to achieve provision of quality care to patients.

These STGs provide greater consistency and standards of care, improve diagnostic accuracy, and promote effective and safe use of medicines, and serves as a basis for improvingtreatment outcomes. It is also important to supply chain managers in improving the predictability of demand, and provide a standardized basis for forecasting, ordering, and purchasing of medicines. Health policy makers, health insurance agencies and planners will benefit from these STGs as it serves as an effective way to contain the cost of treatment for both patients and the health sector.

This3rd edition includes a package of evidence based information on diseases conditions, clinical features, methods of investigations, treatment options and referral to the next level of care.Special emphasis is giventoprimary healthcare so as to addressimportantpublic health needs in the country.EFMHACA has officially approved this treatment guidelines to be used as a guide for prescribers, dispensers and other health care providers operating at the level General Hospital. Accordingly, health care providers shall comply with these guidelines unless there is aproven and specific treatment need for a patient that is supported by adequate evidence.

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**January 2014**

# INTRODUCTION

Irrational use of drugs has been one of the major problems in the Ethiopian health care system for a long time. Among the strategies devised to improve the situation, Medicine, Food and Healthcare Administration and Control Authority (FMHACA) of Ethiopia, was involved in the preparation and distribution of Standard Treatment Guidelines (STGs) for the different levels of health institutions in the country.

The 1st edition of the STGs was published in January 2004 after wide consultation withrelevant stakeholders. There has been continuous demand since then for copies of the STGs, calling for several reprints and revisions. The 2nd edition of the guidelines was published in 2010. The demand fort hese guidelines are increasing, perhaps because STGs are also being used as an alternative to fillthe gap in reference materials. Following the changes made to the national list of drugs and an increasing demand for incorporating new developments in diagnosis and treatment, it wasfound important to revise the 2nd edition of STGs. Accordingly, the 2nd edition of STGs was thoroughly revised by a panel of experts through contracting out to Bethel Teaching General Hospitalwith technical and financial support from USAID/SIAPS.

This third edition addresses common health problems in Ethiopia and it includes several new diseases as well as brief description of the diseases condition, clinical features, methods of investigation and non-pharmacologic and pharmacologic treatment options.Information on dosing, dosage forms, course of treatment, adverse reactions, contraindications and drug interactions are given for the first line and alternative drugs whenever applicable. Diseases have been classified into cardiovascular disorders, endocrine disorders, gastrointestinal tract and liver disorders, hematologic disorders, infectious diseases, kidney and genitourinary tract disorders, musculoskeletal disorders, neurological disorders, oncology, psychiatric disorders, respiratory disorders, emergency conditions, pediatric disorders, gynecology and obstetrics, dermatological disorders, sexually transmitted infections, ophthalmological disorders and ear, nose and throat disorders.

EFMHACA believes that utmost care has been made by the panel of experts to ensure that the recommendations given are evidence-based. In addition, the draft STGs documentswere reviewed in a national consultative workshop where relevant experts are involved. Above all, this document will undergo continuous improvement through the inputs of users including

prescribers, dispensers, academia and researchers, supply chain managers, policy makers and other relevant stakeholders. Users are, therefore, encouraged to send their feedbacks, supporting it with scientific evidences, to the following address:


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# CHAPTER I: GOOD PRESCRIBING AND DISPENSING PRACTICES

## General

The prescription is the link between the prescriber, the pharmacist (or dispenser) and the patient so it is important for the successful management of the presenting medical condition. Fill the diagnosis or ICD code for proper communication with the dispenser and choice of the medicine among the available generic options. Readers are kindly requested to read "Ethiopian Medicines Good Prescribing Practices (GPP)" and Medicines Good Dispensing Practice guideline/manual.

Rational use of medicines is a mechanism through which safe, effective and economic medication is provided. It is promoted through the collaborative efforts of prescribers, dispensers, patient and policymakers. Rational prescribing ensures adherence to treatment and protects medicine consumers from unnecessary adverse medicine reactions. The prescriber could be a physician, a nurse or health officer Or any health professional authorized to prescribe . Rational dispensing, on the other hand, promotes the safe, effective and economic use of medicines. The dispenser could be a pharmacist, Medicinegist and pharmacy technician. Prior to prescribing or dispensing any Medicines, the prescriber or dispenser should make sure that it is within his/her scope of practice.

Medicines should only be prescribed when necessary, and the benefit-risk ratio of administering the medicine should always be considered prior to prescribing. Irrational prescribing leads to ineffective, unsafe and uneconomical treatment. Thus it is very important that steps are taken to promote rational medicine use in order to effectively promote the health of the public especially given limited resources. One way of promoting rational medicine use is throught the development and use of standard treatment guidelines.

Rational approaches to therapeutics requires careful evaluation of health problems and selecting appropriate therapeutic strategies. Making the right diagnosis is the cornerstone for choosing the right kinds of therapy. Based on the diagnosis, health workers may select more

than one treatment and the patient should agree with the selected treatment. The treatment could be non-pharmacologic or pharmacologic. It is important to consider the total cost of treatment in the selection process. The process should also consider efficacy, safety and suitability. Medicine treatment should be individualized to the needs of each patient as much as possible. The concept of good clinical practice has to be incorporated within rational prescribing.

**Prescription writing**

A prescription is a written therapeutic transaction between the prescriber and dispenser. It is a written order by the prescriber to the dispenser on how the medicine should be dispensed. It serves as a means of communication among the prescriber, dispenser and medicine consumer, pertaining to treatment or prophylaxis.

A prescription should be written on a blank standard prescription legibly and clearly in ink and using generic names of the medicine(s).

A prescription should contain:

- Name, address, age body weight of the medicine consumer and Date of the prescription;
- Diagnosis; Generic name, dosage form and strength and directions for use of the medcines. The pharmaceutical form (for example ‘tablet’, ‘oral solution’, ‘eye ointment’) should also be stated.
- The strength of the drug should be stated in standard units using abbreviations that are consistent with the Systéme Internationale (SI). ‘Microgram’ and ‘nanogram’ should not, however, be abbreviated. Also, ‘units’ should not be abbreviated. Avoid decimals whenever possible. If unavoidable, a zero should be written infront of the decimal point.

- prescriber’s name, signature and address.
- **See Annex 17 for Standard Prescription form**

**Directions for use:**

Directions specifying the route, dose and frequency should be clear and explicit; use of phrases such as ‘take as directed’ or ‘take as before’ should be avoided. For preparations which are to be taken on an ‘as required’ basis, the minimum dose interval should be stated together with, where relevant, the maximum daily dose. It is good practice to qualify such prescriptions with the purpose of the medication (for example ‘every 6 hours as required for pain’, ‘at night as required to sleep’). It is good practice to explain the directions to the patient; these directions will then be reinforced by the label on the medicinal product and possibly by appropriate counseling by the dispenser. It may be worthwhile giving a written note for complicated regimens although it must be borne in mind that the patient may lose the separate note.

**Good Dispesing Practice**

Good dispensing practices ensure that the correct medicine is delivered to the right patient, in the required dosage and quantities, with clear information, and in package that maintains an acceptable potency and quality of the medicine. Dispensing includes all the activities that occur between the times the prescription or oral request of the patient or care provider is presented and the medicine is issued. This process may take place in health institutions and community drug retail outlets. It is often carried out by pharmacy professionals. No matter where dispensing takes place or who does it, any error or failure in the dispensing process can seriously affect the care of the patient mainly with health and economic consequences. Therefore, the dispenser plays a crucial role in the therapeutic process. The quality of dispensing may be determined by the training and supervision the dispenser has received. During medcines dispensing and counseling the information mentioned under prescribing above, the“Medicines Good Dispensing Practices” manual 2012 edition and also medicines dispensing and counseling guides are good resources to use. Finally, an application of the professional code of ethics by pharmacy professionals is an important issue that needs due consideration particularly with respect to confidentiality of patient data, withholding therapeutic interventions and varying cost of drug.

**Patient adherence**

Patient compliance is the extent to which the patient follows the prescribed medicine regime, while adherence is participation of patients in their care plan resulting in understanding, consent and partnership with the provider. There are different factors which contribute to patients' non-adherence. These factors include:

- Nature of treatment, which in turn depends on:
    - the complexity of the regime (increases with the frequency of administration and number of medicines prescribed)
    - adverse effects
- Characteristics of the patient, such as:
    - forgetfulness about taking the medication
    - inability to finish as they feel better
    - lack of understanding the prescription
    - fear of dependence
    - social or physical problems to go to pharmacies
    - inability to pay prescription charges
    - inconvenience of taking medicines everyday
- Type of illness, like schizophrenia
- The health care system (long waiting times, uncaring staff, uncomfortable environment, exhausted medicine supply, inaccessibility of health institutions)
- Behaviour of prescribers and dispensors:
    - not able to gain confidence from patients
    - irrational prescribing and dispensing
    - giving inadequate information on the treatment
    - poor attitude towards patients
    - negligence
    - poor perception to team work
    - absence or ineffective care plan

Patient adherence can be improved by supervising medicine administration; simplifying the therapeutic regime; educating patients on the importance of adhering to the prescribed medication and improving the attitudes of prescribers.

**Adverse Drugs/ medicine reactions**

Adverse Drugs/medicine reactions (ADRs) are unwanted effects that occur at certain therapeutic doses. They could be mild (where no intervention is required), moderate (where switching to another medicine is necessary), severe (where an antidote should be employed to alleviate the situation), or lethal. They could also be predicatable (extensions of pharmacological effects) or unpredictable (bizarre reactions which are not expected in all patients taking the medicine, such as hypersensitivity and idiosyncratic reactions). ADRs are different from toxic reactions for the latter occur at doses higher than therapeutics. They are also different from side effects as this is a broader concept, i.e., including both beneficial and all unwanted effects which may not necessarily be noxious. The two extreme age groups, i.e., pediatric and geriatric patients, are more susceptible to ADRs due to physiological and pathological factors. Special precaution should be taken for coexisting illnesses, such as kidney and liver diseases, as they could contribute to ADRs.

**Monitoring ADRs**

Pre-marketing clinical trials cannot be exhaustive as far as detection of all ADRs is concerned due to:

- Recruitment of small populations (often < 2500 patients)
- Low chance of low incidence reactions being picked up before marketing
- Shorter duration of assessment
- Exclusion of patients who may take the medicine post-marketing

Only the most common ADRs could be detected during pre-marketing trials. It is therefore, important to devise methods for quickly detecting ADRs. This could be carried out by post-marketing surveillance, i.e., ADR monitoring. All health professionals have the responsibility to report any unique ADR observed to Food, Medicine and Health Care Control and Administration Agency (FMHACA).

**Drug/ Medicine Interactions**

Although some medicine interactions could be beneficial, most are harmful. Hence, it is always important to note the possible medicine interactions prior to concomitant medicine/food or drink administration.

Drug/ Medicine interactions could occur at different levels, including:

- Pharmaceutics, which are physicochemical interactions in an IV infusion or in the same solution;
- Pharmacokinetics, which may take place at the level of absorption, distribution, biotransformation or excretion;
- Pharmacodynamics, which could occur directly at receptor level, or indirectly, where a medicine alters the response to another medicine.

Drug/Medicine interactions could be additive (the effect is simple algebraic sum), synergism (the total effect is more than the algebraic sum) potentiation (the effect of one medicine increases by the presence of another medicine), or antagonism (the effect of the agonist is blocked by the antagonist when given together). Medicine interactions are some of the most common causes of adverse reactions. As medicine reactions could also occur between a medicine and food or a medicine and drink. We should always inform our patients the type of food or drink which they have to avoid while taking the medicine.

Medicines should not be added to blood, amino acid solutions or fat emulsions. Some medicines, when added to IV fluids, may be inactivated due to changes in pH, precipitate formation or chemical reactions. For example, benzylepenicillin and ampicillin lose potency after 6-8 hours if added to dextrose solutions, due to the acidity of the solutions. Some medicines, such as diazepam and insulin, bind to plastic containers and tubing. Aminoglycosides are incompatible with penicillins and heparin. Hydrocortisone is incompatible with heparin, tetracycline and chloramphenicol.

**Prescribing for pregnant women**

The kinetics of a medicine is altered during pregnancy: the rate of absorption decreases, while volume of distribution, metabolism and glomerular filtration rate increase. The embryonic period, where, organogesis takes place, is the most susceptible period to medicine effects. Administration of medicines, except those proved safe, in the first trimester, is therefore not generally recommended. It is advisable not to prescribe any medicine during any stage of pregnancy if possible. This, however, should not preclude the importance of prescribing in life-threatening conditions of the mother. Prior to prescribing any medicine for pregnant women, the benefit risk ratio of prescribing should be considered.

**Prescribing for breast feeding women**

Most medicines administered are detectable in breast milk. The concentration, however, is low. If the woman has to take a relatively safe medicine, she should do so optimally 30-60 minutes after breast feeding and 3-4 hours before the next feeding in order to allow time for medicines to be cleared from the blood, and concentration in the breast milk is relatively low. Medicines for which no safety data are available during lactation should be avoided, or breast feeding discontinued while they are adminstered. Most antibiotics taken by breast feeding mothers can be detected in breast milk. e.g., tetracycline and chloramphenichol. Similarly, most sedative hypnotics and opioids are easily absorbed in breast milk. Antineoplastic medicines are contraindicated in breast feeding.

**Prescribing for infants/children**

Physiologic processes that influence medicine kinetics in infants change significantly in the first year of life, especially the first few months, while there is not much difference in the dynamics. All the four parameters of kinetics are, therefore, affect children. Gastric acid secretion begins soon after birth and increases gradually over several hours in full term infants. In premature infants, however, secretion is slower, with the highest concentration occurring on the fourth day. So medicines, which are partially or totally inactivated by the low pH of gastric content should not be administered orally. GI enzymes are lower in neonates than in adults. Neonates have less bile acids such that lipid soluble medicines is absorbed less. Gastric emptying time is prolonged in the first day. Thus, medicines that are

absorbed primarily in the stomach may be more fully absorbed. For medicines absorbed in the small intestine, therapeutic effects may be delayed. Peristalsis in neonates is slow. More medicines, therefore, will get absorbed from the small intestine. The volume of distribution is low in children, and medicine metabolizing enzymes are not well developed. The glomerular filtration rate is slower than in adults (30-40%), such that the clearance of medicines is slower in children than in adults. This definitely demands dose adjustment for these age groups.

**Dose adjustment in pediatrics**

The most reliable pediatric doses are those given by the manufacturer. If no such information is given, the dose can be calculated using formulae based on age, weight or surface area. Calculations of doses based on age or weight are conservative and tend to underestimate the required dose. Doses based on surface area are more likely to be correct. Pediatric doses can be calculated as follows:

Dose calculations based on age:

Dose = adult dose*(age in years/(age+12))

Dose calculations based on weight:

Dose = adult dose*(weight in kg/70)

**Prescribing for elderly patients**

There is no major alteration in medicine absorption in elderly patients. However, conditions associated with age may alter the rate of absorption of some medicines. Such conditions include altered nutritional habits; alteration in gastric emptying (which is often slower); and the concurrent administration of other medicines. Aged people have reduced lean body mass, reduced body water and an increase in fat as a percentage of body mass. There is a decrease in serum albumin, and the ratio of bound to free medicine is significantly changed. Phase I reactions affect elderly patients more than phase II reactions. There is a decline with age of the liver's ability to recover from injury. Diseases that affect hepatic function like congestive cardiac failure and nutritional deficiencies are more common in the elderly. Creatinine clearance declines in the elderly leading to marked prolongation of the half life of medicines. The increased incidence of active pulmonary disease in the elderly could compromise medicine elimination through exhalation.

There is also a change in the sensitivities of receptors to medicines in elderly people. The quality and quantity of life for elderly patients can be improved through the careful use of medicines. Adherence to the doses is absolutely required in these patients. Unfortunately patient nonadherence in the elderly is common because of forgetfulness, confusion, deliberate skipping of doses and physical disabilities.

**Prescribing in renal failure**

Many medicines are excreted through the kidneys and impairment of renal function alters the excretion of these medicines, resulting in renal as well as non-renal toxicity unless doses are adjusted accordingly. There are two principal pathways for medicine excretion by the kidneys; glomerular filtration and tubular excretion. Glomerular filtration plays a major role in the excretion of small, non-protein bound molecules whereas protein bound molecules that are excreted in urine are eliminated by secretion into the proximal tubules.

For dose adjustment in renal failure it may occasionally be necessary to measure medicine levels and adjust doses accordingly, but generally, doses are adjusted on the basis of the estimated glomerular filtration rate (GFR). Among the various formulae used to estimate the GFR from the serum creatinine, the Cockcroft Gault formula is the easiest to use (although not the most accurate). The GFR in the CG formula is calculated as follows:

$$GFR = \frac{(140-age) \times \text{lean body weight(kg)}}{\text{Serum creatinine (mg/dl)} \times 72}$$

The value is multiplied by 0.85 in women to account for smaller muscle mass.

Factors that potentiate renal dysfunction and contribute to the nephrotoxic potential of renally excreted medicines include: i) intravascular volume depletion either due to external losses or fluid sequestration (as in ascites or edema) and ii)concomitant use of 2 or more nephrotoxic agents e.g. Nonsteroidal anti-inflammatory agents, aminoglycosides, radio contrast agents. To avoid worsening renal dysfunction in the presence of renal impairment:

1. Avoid potentially nephrotoxic medicines and use alternative medicines that are excreted through other routes;

2. If there are no alternatives, calculate the GFR and adjust the dose on the basis of the estimated GFR (many textbooks, formularies have tables showing dose adjustment on the basis of estimated GFR). Dose adjustment may be accomplished in three different ways: i) decreasing each individual dose and maintaining the same dose frequency; ii) maintaining the same individual dose but administering each dose less frequently; and iii) modifying both individual doses and the frequency of administration, which is a combination method;

3. Avoid concomitant use of 2 or more potentially nephrotoxic agents;

4. Insure that the patient is adequately hydrated;

5. If the patient is on dialysis check if the medicine is eliminated by the specific dialysis modality and consider administering a supplemental dose at the end of the dialysis session;

6. Serially monitor kidney function.

**Prescribing in liver disease**

The liver is a site for the metabolism and elimination of many medicines but it is only with severe liver disease that changes in medicine metabolism occur. Unfortunately, routine determination of liver enzymes and other tests of liver function cannot predict the extent to which the metabolism of a certain medicine may be impaired in an individual patient.

In general terms medicine prescription should be kept to a minimum in all patients with severe liver disease as it may alter the response to medicines in several ways. Major problems occur in patients with advanced liver disease who have ascites, jaundice or hepatic encephalopathy:

- The hypoproteinemia in patients with severe liver disease is associated with reduced protein binding and increased toxicity when highly protein bound medicines are used.

- One must exercise caution in the use of some medicines like sedatives, opioids and diuretics which may precipitate hepatic encephalopathy in patients with advanced liver disease.

It is always advisable to consult tables in standard textbooks or medicine formularies before prescribing medicines for patients with severe liver disease.

**Prescribing and pain management in Palliative Care**

Palliative care is the active total care of patients whose disease is not responsive to curative treatment. Focus lies in four main domains: 1) control of pain and other physical symptoms; 2) mental or psychological symptoms; 3) social needs; and 4) spiritual needs. This requires careful assessment of the symptoms and needs of the patient by a multidisciplinary team. The family should be included in the care of terminally ill patients.

The number of medicines should be as few as possible. Oral medications are usually satisfactory unless there is severe nausea and vomiting, dysphagia, weakness, or coma, in which case parenteral medications may be necessary. The most common medicine classes used in palliative care are strong opioids, nonopioids, corticosteroids, laxatives, antiemetics, gastric protection agents, neuroleptics, sedatives/anxiolytics, antidepressants and diuretics.

Interventions for pain must be tailored to each individual with the goal of preempting chronic pain and relieving breakthrough pain. Pain relief in palliative care may require nonpharmacologic interventions such as radiotherapy or neurosurgical procedures such as peripheral nerve blocks. Pharmacologic interventions follow the World Health Organization three-step approach involving nonopiod analgesics, mild opioids and strong opioids with or without adjuvants.

Analgesics are more effective in preventing pain than in relieving established pain; it is important that they are given regularly. Nonopioid analgesics, especially nonsteroidal anti-inflammatory medicines, are the initial management for mild pain. Ibuprofen, up to 1600mg/day, has minimal risk of gastrointestinal bleeding and renal impairment and is a good initial choice. If nonopioid analgesics are insufficient, then weak opiods such as Codeine should be used. However, if weak opioids are escalated but fail to relieve pain, then strong opioids such as Morphine should be used. When using opiods, start with short acting formulations and once pain relief is obtained, switch to extended release preparations. Opioids have no ceiling dose-the appropriate dose is one required to achieve pain relief. When using opioids, side effects like constipation, nausea and vomiting have to be anticipated and treated preemptively.

Constipation is another physical symptom that may require pharmacologic management and one may use stimulant laxatives such as Bisacodyl or osmotic laxatives, such as Lactulose or Magnesium Hydroxide.

**General guidelines for use of topical steroids**

- Absorption from the skin depends on the sites (high at axilla, face and scalp; medium at limbs and trunk; and low at palm, elbow and knee) and nature of lesion (high in exfoliative dermatitis and low in hyperkeratinised skin)
- Strong preparations should be avoided at highly absorption sites and on acute lesions. They may, however, be used for chronic lesions.
- Lotions/creams are better for exudative lesions as they allow evaporation, have cooling, drying and antipruritic effects
- Sprays and gels are good for hairy regions
- Ointments from occlusive film and are good for chronic scaly conditions
- Occlusive dressing enhances steroid absorption, retains moisture and results in maceration of horny layer
- Absorption is greater in pediatric patients, hence milder preparations should be used
- Do not use strong steroids routinely
- Strong preparations should be restricted for short term use only
- Sudden withdrawal should be avoided
- Upon improvement, milder preparations should be substituted
- Twice a day application is enough: do not exceed three times a day

**Narcotics and controlled substances**

The prescribing of a medicine that is liable to abuse requires special attention and may be subject to specific legal requirements. Authorized health workers must use these medicines responsibly. The strength, directions and quantity of the controlled substance to be dispensed should be stated clearly. Required details must be filled in the prescription form carefully to avoid alteration and abuse.

**Antimicrobial prophylaxis**

Postoperative wound infections are the major source of infectious morbidity in the surgical patient. Surgical site infections (SSIs) are associated with prolonged hospital stays and increase cost. The use of antimicrobial prophylaxis has become an essential component of care standards in virtually all surgical procedures and has resulted in reduced risk of postoperative infection when sound and appropriate principles of prophylaxis are applied. These include the following:

- Probable risk of infection in the absence of a prophylactic agent;
- Knowledge of the probable contaminating flora associated with the operative wound or organ site;
- Activity of the chosen prophylactic agent should encompass the majority of pathogens likely to contaminate the wound or operative site;
- When more than one choice is given as a prophylactic agent, the agents selected should be based on the most likely contaminating organisms;
- Single antimicrobial agent is preferable;
- The prophylactic agent must be administered in a dose which provides an effective tissue concentration prior to intra-operative bacterial contamination. **Administration must occur 30-45 minutes prior to incision** (usually with the induction of anesthesia);
- The effective dose should be governed by the patient's weight;
- In procedures lasting 3 hour or less, a single prophylactic dose is usually sufficient. **Procedures lasting longer than three hours require an additional effective dose.** Procedures in which there is rapid blood loss and/or fluid administration will dictate more frequent prophylactic dosing. Under no circumstance should any prophylactic agent be given on-call because it often results in less than effective tissue levels at the time of incision. Postoperative prophylaxis is strongly discouraged except under bioprosthetic insertion in which case 2 or 3 additional prophylactic doses may be deemed sufficient (warning: there are no standard rules on prophylaxis following prosthetic insertion and clinical experience strongly dictates practice);
- Vancomycin may be used for patients with severe penicillin/cephalosporin allergy;

- An effective and thoughtful prophylactic regimen is no substitute for exquisite surgical technique and competent postsurgical management.

## Table 1 - Antimicrobial prophylaxis in selected surgeries

| Type of procedure | Agent | Route | Dosage | Time of administration | Rationale (likely infective agent) |
|---|---|---|---|---|---|
| **I. Clean surgery**<br>a. Insertion of synthetic biomaterial device/prosthesis<br>b. Patients with impaired immunity | Cefazolin<br>Or<br>Cefuroxime | IV | 750mg | 30-45min before skin incision, 2nd dose if procedure lasts > 3hrs | Gm positive cocci (*S. aureus* and epidermidis), aerobic coliforms (*E. coli)* |
| **II. Upper GIT and elective bowel surgeries** (stomach, small bowel, pancreas, hepatobilliary etc) | Ciprofloxacin<br>Or<br>Cefazolin<br>Plus<br>Metronidazole | IV<br><br>IV<br>IV | 400mg<br><br>750gm<br><br>500mg | 30-45min before skin incision | Coliforms > Enterococcus > Streptococci>Aerobic> Clostridia>Pepto-Streptococci Bacteriodes > Prevotella |
| **III. Large bowel resection** | Bisacodyl<br><br>Neomycin<br>Plus<br>Erythromycin<br>Cefazolin<br>Or<br>Ceftetan | PO<br><br>PO<br><br>PO<br>IV<br><br>IV | 2tablets<br><br>500mg<br><br>500mg<br>1-2gm<br><br>1-2gm | 2days before surgery 1pm,2pm and 10pm before surgery<br>30-45min before skin incision, 2nd dose if procedure lasts>3hrs | Coliforms, enterococci, Bacteriodes, peptostreptococci, Clostridia |
| **IV. Acute appendicitis** (Non-perforated)<br>NB: In perforated or gangrenous cases treatment should continue as clinically indicated | Cefazolin<br>Plus<br>Metronidazole | IV<br><br>IV | 1gm<br><br>500mg | 30-45min before skin incision | Coliforms, anaerobes |
| **V. Trauma surgery** (penetrating abdominal trauma) | Ampicillin<br>Or<br>Cefazolin<br>Plus<br>metronidazole | IV<br><br>IV<br>IV | 3gm<br><br>1-2gm<br><br>500mg | 30-45min before skin incision, 2nd dose if surgery lasts> 3hrs | Coliforms and anaerobes(gm positive and negative) |
| **VI. Gynecology and Obstetrics**<br>a. Vaginal and abdominal hysterectomy including radical hysterectomy<br>b. Ceasarean section/hysterectomy | Ceftizoxime<br>Or<br>Cefazolin<br><br>Ceftizoxime<br>Or<br>Cefazolin | IV | 1gm<br><br>1gm<br><br>1gm | 30-45min before skin incision,<br>In high risk patients 2gm may be used after clamping the umbilical | Coliforms, enterococci, streprococci, clostridia, bacteroides |

| Type of procedure | Agent | Route | Dosage | Time of administration | Rationale (likely infective agent) |
|---|---|---|---|---|---|
| | | | | | |
| **VII. Urology**<br>Prostatectomy | Cefazolin<br>Or<br>Ciprofloxacin | IV | 1gm<br><br>400mg | cord<br>30-45min before skin incision | Coliforms, staphylococci, Pseudomonads |
| **VIII. Head and neck surgery**<br>**a.** Clean procedure (skin incision and dissection)<br>**b.** Mandibular fracture | Cefazolin<br>Or<br>Pencillin G<br>Pencillin G | IV<br><br><br>IV | 1gm<br><br>2-4MU<br>2-4MU | | <br><br>Staphylococci |
| **IX. Orthopedics** (Traumatic open fractures) | Cefazolin<br>Or<br>Ceftizoxime | IV | 2gms | 30-45min before skin incision | Staphylococci |
| **X. Neurosurgery** | Cefazolin | IV | 1gm | 30-45min before skin incision | Staphylococ |

## Antimicrobial resistance

Infectious diseases are those which are caused by microorganisms like bacteria, protozoa, viruses and fungi. These diseases are threats to all societies irrespective of age, gender, ethnicity, education and socioeconomic status. Unexpected outbreaks of infectious disease can occur at any time and at any place resulting in high morbidity and mortality. Their treatment imposes a huge financial burden to societies, especially developing ones. A very good example is the cost incurred for the treatment of HIV with ARVs which are expensive: a lot of money is spent for the development of better medicines and vaccines. On top of these problems, resistance can easily emerge through microorganisms in medicines used for the treatment of infectious diseases, known as antimicrobials.

Currently, antimicrobials are irrationally used for the treatment, prophylaxis and growth promotion of food for animals in order to decrease the percentage of fat and increase protein content in the meat. Furthermore they are also used inappropriately to control zoonotic

pathogens, such as salmonella and campylobacter. These improper uses exacerbate antimicrobial resistance.

Antimicrobial resistance is the ability of microorganisms to survive and/or multiply in the presence of tolerable doses of antimicrobial medicines. Antimicrobial resistance may be natural when it occurs spontaneously as a result of gene mutation, or may be acquired due to inappropriate exposure to antimicrobials.

**Biological Mechanisms for antimicrobial resistance**

There are several mechanisms by which microorganisms develop antimicrobial resistance. These include

1. Inability of antimicrobials to concentrate on their targets by
    a. Denying access to their sites of action, e.g., Resistance to cephalosporins
    b. Increasing their efflux e.g., Resistance to tetracycline,
2. Inactivation of antimicrobials, through
    a. Production of degrading enzymes like β lactamases which hydrolyze β lactams, e.g. resistance to penicillins ; and medicine biotransforming enzymes, e.g., resistance to chloramphenicol.
    b. Inducing bacterial failure to convert a pro-medicine to active metabolites, e.g., resistance to INH.
3. Alteration of targets, due to:
    a. Target modification, e.g., macrolide resistance
    b. Substitution with a resistant target to the native agent e.g., methicillin resistance
    c. Use of alternate metabolic pathways, e.g., sulfonamides resistance
    d. Mutation of the natural target, e.g., fluoroquinolone resistance

**Types of antimicrobial resistance**

There are different types of antimicrobial resistance. These include

- Multi Medicine Resistance (MDR) (resistance to two or more medicines)
- Cross-resistance, (resistance that occurs among two different antimicrobials)
- Co-resistance, (more than one mechanism of resistance is involved by the same organism for a given antimicrobial)

**Factors which contribute to antimicrobial resistance**

There are a number of factors responsible for resistance to emergence. These include:

- Natural disaster due to climatic and weather changes which result in spread of resistant microorganisms
- Poverty, lack of education, poor sanitation, malnutrition, lack of diagnostic facilities and poor access to medicines
- Over population, which leads to overcrowding and spreading of resistant MOs
- Irrational antimicrobial consumption owing to self-medication, non-compliance, misinformation, beliefs
- Economic problems leading to premature cessation or sharing of antimicrobials
- Irrational prescribing (see section on rational prescribing)
- Irrational dispensing (see section on rational dispensing)
- Manufacturers' pressure impacting both prescribers and consumers
- Problems in medicine procurement
- Inappropriate health service providing center catering for patients with acute or chronic infection (who are reservoirs of highly resistant pathogens)
- Environmental contamination with antimicrobials from human, animal, agricultural/pharmaceutical spillovers
- Use of antimicrobials in animal feed

**Threats of antimicrobial resistance**

Many important medicine options for the treatment of common infectious diseases are becoming limited, expensive or cease to exist. Today, nearly all *Staph. aureus* strains are

resistant to penicillin and many even to methicillin. Resistance to vancomycin is also increasingly observed. If it is not possible to limit emergence and/or spread of antimicrobial resistance, infections may become untreatable. Antimicrobials are the most misused medicines in many developing countries like Ethiopia. They are available not only over the counter (OTC) in pharmacies but also in open markets. Studies indicate the most common medicines used for self-medication are antibacterials.

Antimicrobial resistance has several economic and health impacts. They cause prolonged illness, absence from work and reduced productivity. Antimicrobial resistance can also contribute towards longer hospital stay which increases cost. Antimicrobial resistance prolongs the period of infectiousness resulting in spread of infection, ultimately impacting mortality rates.

Strategies for antimicrobial containment include:

- Keeping track of a resistance profile to help identify the most prevalent pathogens, status of resistance, and appropriate choices of treatment
- Keeping public health officials on alert to new pathogens
- Implementation of control policies
- Preparing Guidelines for antimicrobial use
- Optimizing AM prophylaxis for surgery
- Optimizing choice and duration of empirical therapy
- Improving prescribing/dispensing patterns
- Controlling hospital infections
- Improving diagnostic quality
- Improving laboratory facilities, together with skills of technicians
- Introducing efficient recording/reporting systems
- Improving public health
- Adhering to principles of chemotherapy during prescribing, which includes the identification of underlined causative agent/s; testing for medicine sensitivity;

consideration of the nature of the medicine (static/cidal); potential toxicity; age of patient/presence of concomitant diseases; previous exposure to medicines; cost of therapy; “Reserve antimicrobials”; rational antibacterial prophylaxis; limiting duration of antimicrobial use and avoiding indiscriminate use of broad-spectrum AMs.

**Differential Diagnosis**

Differential diagnosis is a systematic diagnostic method used to identify the presence of an entity where multiple alternatives are possible (the process may also be termed differential diagnostic procedure), and may also refer to any of the included candidate alternatives (which may also be termed candidate condition). This method is essentially a process of elimination, or at least of obtaining information, that shrinks the "probabilities" of candidate conditions to negligible levels.

The differential diagnostic procedure is generally based on the idea that one begins by considering the most common diagnosis: for example, flu versus meningitis, in someone presenting with a headache.As a reminder, medical students are taught the adage, "When you hear hoofbeats, look for horses, not zebras," which means to look for the simplest, most common explanation first. Only after the simplest diagnosis has been ruled out should the clinician consider more complex diagnoses.

Differential diagnosis has four steps. First, the physician/health worker should gather all available information on the patient (from their history to physical examinations) and create a list of possibilities. Second, the physician/health worker should make a list of all possible causes (also termed "candidate conditions") of the symptoms and physical signs. Third, the physician/health worker should prioritize the list by placing at the top of the list the most likely explanation for the given symptoms. Fourth, the physician/health worker should rule out causes by beginning with the most likely condition and working his or her way down the list. "Rule out" practically means to use tests and other scientific methods to render a condition of clinically negligible probability as being the cause. In the differential diagnostic process the physician/health worker will need to use various sources of information (in addition to the history and physical examination obtained from the patient) including the

epidemiology of the condition/s under consideration and results of laboratory tests and/or imaging studies to narrow down the list. The physician/health worker may sometimes be confronted with incomplete information, particularly in emergencies. Treatment for the most likely condition according to the differential diagnosis procedure will then be acceptable clinical practice.

***Note: The information presented in these guidelines conforms to the current medical, nursing and pharmaceutical practice. Contributors and editors cannot be held responsible for errors, individual responses to drugs /medicines and other consequences.***

## CHAPTER II: CARDIOVASCULAR DISORDERS

### 1. Acute Cardiogenic Pulmonary Edema

Acute cardiogenic pulmonary edema is a life threatening medical emergency resulting from either systolic and/or diastolic left ventricular dysfunction, arrhythmias or preload after load mismatch. It could result from acute Heart Failure or an acute decompensation of chronic Heart Failure . The etiology of Heart Failure can be any cause of acute or chronic Heart Failure such as valvular heart disease, cardiomyopathies, ischemic heart disease, hypertensive heart disease, tachyarryhymias.

**Clinical features**

- Rapid onset of dyspnea at rest, marked orthopnea
- Cough with frothy sputum, hemoptysis
- Tachypnea and severe hypoxemia
- Pulmonary crepitations and wheezing
- S3 gallop
- Hypertension or hypotension
- Other features of Heart Failure -raised JVP, hepatomegaly, peripheral edema
- Findings which suggest the specific cause of the Heart Failure

**Investigations**

Investigations should not cause any delay in the management of acute cardiogenic pulmonary edema

- Chest X-ray, ECG, echocardiography
- Cardiac biomarkers-troponin and/or CK-MB (creatinine kinase myocardial isoenzyme)
- Kidney function test and serum electrolytes-creatinine, BUN, potassium, sodium
- Complete blood count (CBC)
- Blood sugar
- PT and PTT-when there is a plan to anticoagulate

**Treatment**

**Objectives**

- Relieve symptoms
- Stabilize haemodynamic state
- Shorten hospital stay
- Minimize medication adverse effects

**Non pharmacologic**

- Maintain open airway
- Bed rest in sitting position, unless hypotensive or comatose
- Oxygen via nasal catheter or face mask
- If hypoxemia persists despite all efforts endotracheal intubation and mechanical ventilation should be considered
- Continuous ECG monitoring
- Frequent monitoring of vital signs
- Identify and treat precipitating factor

**Pharmacologic**

**First Line-intravenous loop diuretics**

**Furosemide** 40 mg, IV bolus. The dose can be repeated or doubled after 30 minutes-one hour depending on response.

- After the initial bolus continuous infusion can be given at a dose of 10-40mg/hr.
- Start higher dose (80 mg) in patients with chronic diuretic use and chronic kidney disease
- Titrate dose based on response
- When there is resistance to furosemide add **Hydrochlorothiazide 25 mg** once or twice a day, to be given 30 minutes before the furosemide.

**ADRs:** hypovolemia, hypokalemia, ototoxicity, hypersensitivity reactions

**C/Is:** hypersensitivity to sulfa medicines, hypotension, uncorrected hypokalemia

**Dosage forms:** Furosemide Tablet, 40mg, 80mg; injection. 2ml ampoule, 10mg/ml

**Additional**

**Nitrates**

**Nitroglycerin**-Sublingual nitroglycerin 0.4mg every 5 min, maximum of three doses. If pulmonary edema persists in the absence of hypotension, it will be followed by IV nitroglycerin-starting dose 10μg/minute, may increase by 10-20μg/minute every 10-20 minutes based on response, maximum dose is 400 μg/minute.

**ADRs:** headache, hypotension, flushing, lightheadedness, anaphylactoid reaction

**Dosage forms:** Sublingual tablet 0.3mg, 0.4mg, 0.5mg, 0.6mg.
Sublingual spray 0.4mg/dose
Infusion-0.1mg/ml, 0.2mg/ml, 0.4mg/ml. Injection-5mg/ml

**Morphine** 1 to 2mg IV, bolus, slowly. Dose may be repeated two to three times, if pulmonary edema persists.

**ADRs:** Hypotension, respiratory depression, seizure, coma, cardiac arrest, anaphylaxis

**Dosage forms:** Injection**,** 10mg/ml, 20mg/ml, 30mg/ml in 1ml ampoule

**ACE inhibitors** start low dose of a short acting ACEI in patients who have high blood pressure. Escalate the dose gradually**.**

**Enalapril** 2.5 to 5mg, P.O., BID.

**Captopril** 6.25mg to 12.5mg P.O., TID.

**ADRs:** Hypotension, Hyperkalemia, Acute kidney injury, Cough, Angioedema

**Dosage forms:** Captopril Tablet, 12.5mg, 25mg, 50mg, 100mg
Enalapril Tablet, 2.5mg, 5mg, 10mg, 20mg

## 2. Arrhythmias (Cardiac)

These are disorders of cardiac rate, rhythm and conduction. Based on the heart rate, they are classified into bradyarrhythmias, when the heart rate is less than 60 per minute; and tachyarrhythmias, when the heart rate is greater than 100 per minute.

Bradyarrhythmias include sinus bradycardia, sinus pauses and atrioventricular blocks. The tachyarrhythmias can further be classified into supraventricular and ventricular arrhythmias, based on their site of origin. Supraventricular tachyarrhythmias includes atrial fibrillation, atrial flutter, paroxysmal supraventricular tachycardia and multifocal atrial tachycardia. Ventricular tachyarrhythmias include ventricular tachycardia and ventricular fibrillation.The etiologies for arrhythmias are structural heart disease (valvular heart disease, cardiomyopathies, coronary artery disease), thyrotoxicosis, electrolyte abnormalities, ingestion of stimulants, side effects of some medicines (digoxin, antiarrhythmic medicines), post cardiac surgery.

**Clinical features**

- Palpitation, Shortness of breath, Dizziness/syncope
- Sensation of a pause in the heart beat
- Chest discomfort that mimics symptoms of myocardial ischemia(angina)
- Development of Heart Failure or decompensation of previously existing Heart Failure
- Sudden death
- Rapid or slow pulse rate
- Regular pulse rate (sinus tachycardia/bradycardia, AV block, paroxysmal atrial tachycardia)
- Irregularly irregular (atrial fibrillation, atrial flutter, frequent, sick sinus syndrome)
- Pulse deficit (apical rate faster than radial pulse rate)

**Investigations**

- 12 lead surface ECG, Chest X-ray, Echocardiography, Ambulatory ECG (Holter)
- Serum electrolytes, thyroid function tests, haemoglobin

Prior to treatment of any suspected arrhythmia the diagnosis should be confirmed with ECG. It is dangerous to give any antiarrhythmic medicine without doing ECG!

**Supra ventricular tachyarrhythmias**

**Atrial Fibrillation or Atrial flutter**

Atrial fibrillation is marked by disorganized, rapid, and irregular atrial activation which results in irregular ventricular response. The ventricular rate is usually rapid. The ECG in Atrial Fibrillation is characterised by the lack of P-waves, irregularly irregular ventricular response and narrow QRS.

Atrial flutter is characterised by regular rapid atrial rate of 260–300 beats per minute, which usually results in a regular ventricular response in a 2:1 ratio resulting in a heart rate of 130–150 beats per minute. The ventricular response can sometimes be in 3:1, 4:1, irregular or rarely 1:1 ratio. The typical ECG finding is of saw-tooth appearance of the baseline mainly on inferior leads (II,III,AVF) with rapid, regular and narrow QRS. When a 2:1 conduction happens it can be mistatken for sinus tachycardia.

**Treatment**

**Objectives**

- Controlling ventricular rate
- Prevention of thromboembolic events
- Identification and treatment of the cause
- Identification, prevention and treatment of precipitating factors

**Non pharmacologic**

- **Immediate electrical cardio-version**-associated with haemodynamic instability (cardiogenic shock) due to a rapid ventricular rate. If hypotension occurs at ventricular rate <130 beats/min, other causes of hypotension should be investigated. The energy requirement is usually 100 to 200 joules; it should be synchronized.
- Avoid stimulants (e.g. Caffeine, Khat) and alcohol intake.

**Pharmacologic**

1. **Acute ventricular rate control**

**First line**

**Metoprolol**, 2.5-5mg, IV, over 3–5 min, to maximum total dose 15mg over 10-15 minutes

**Dosage forms:** 5ml ampoule of 1 mg/ml, 5mg/ml

**Alternative**

**Digoxin**, 0.25mg, IV, q2h until 1 mg total (digoxin is the first line medicine if atrial fibrillation is associated with severe left Ventricular dysfunction)

**ADRs:** lower stomach pain, diarrhoea, weakness, blurred or yellow vision, drowsiness, confusion, mental depression, headache and hallucinations, arrythmias, hypotension, AV block.

**C/Is:** hypersensitivity to digoxin or digitoxin, ventricular fibrillations, hypertrophic obstructive cardiomyopathy

**D/Is:** amiodarone, beta-adrenergic blocking agents, (including atenolol, carvedilol, verapamil, furosemide, propafenone, quinidine or quinine, sympathomimetics

**P/Cs:** patients with recent myocardial infarction, sick sinus syndrome, hyporthyroidism, severe pulmonary disease; elderly patients and in patients with renal function impairment where dosage adjustment is necessary; breast-feeding; electrolyte disturbances;

**Dosage forms:** Elixir, 0.05mg/ml
Injection, 0.1mg/ml in 1 ml ampoule; 0.25mg/ml in 2 ml ampoule
Tablet, 0.25mg

2. **Chronic ventricular rate control**

**First line**

**Beta blockers**

**Metoprolol**, preferred beta blocker in patients with Heart Failure with depressed LV(left ventricle) systolic function.

Immediate release: 25-100mg twice daily

Extended release: 25-200mg/day

*OR*

**Atenolol**, 25-100mg P.O., daily

**Dosage forms:** Tablets, 50mg, 100mg

*OR*

**Propranolol**, 10-40mg P.O., 3-4 times daily.

**Alternatives**

**Digoxin**, 0.125 – 0.25mg P.O., daily. Digoxin can be added to beta blocker when the ventricular rate control is suboptimal. It is the preferred agent when Heart Failure due to LV systolic dysfunction is not well controlled

*OR*

**Verapamil**, 40-80mg P.O., 2-3 times daily. Apply caution when beta blockers are combined with verapamil.

3. **Anticoagulation or antiplatelet treatment**

**Warfarin**, starting dose, 2.5-5mg/day, dose titrated to achieve INR of 2.0-3.0. Indications of warfarin in patients with atrial fibrillation

- All patients with valvular heart disease
- Previous ischemic stroke or transient ischemic attack
- Presence of intra cardiac thrombus on echocardiography
- For patients with non valvular heart disease and with two or more of the following- Heart Failure , hypertension, diabetes mellitus, age $\geq$ 75 years

**ADRs:** haemorrhage, hypersensitivity, rash, alopecia, diarrhoea, unexplained drop in haematocrit, jaundice, hepatic dysfunction

**C/Is:** Hypersensitivity to warfarin, haemorrhagic tendencies

**D/Is:** acetylsalicylic acid, alcohol, allopurinol, amoxicillin, ampicillin

**P/Cs:** hepatic or renal failure, recent surgery, breastfeeding

**Dosage forms:** Tablets, 2mg,5 mg, 10mg

**Warfarin should never be started if INR/PT cannot be followed regularly.**

**Aspirin**, 75-162mg/day-for patients with atrial fibrillation who are not on warfarin either due to lack of indication or lack of access for INR follow up.

**Paroxysmal supra-ventricular tachycardia (PSVT)**

Paroxysmal supra-ventricular tachycardia (PSVT) is an intermittent narrow complex tachyarrhythmia other than AF, atrial flutter, and MAT (Multifocal Atrial Tachycardia). PSVTs are often caused by reentry (AV nodal or atrioventricular). PSVT usually occurs in

individuals without underlying structural heart disease. ECG shows regular narrow QRS tachycardia. P wave may be seen preceding or following or superimposed on QRS complex or may not be seen.

**Objectives**

- Control ventricular rate
- Identify and treat the cause.
- Identify, prevent and treat precipitating factors

**Non pharmacologic**

1. **Vagal maneuvers**-maneuvers which increase vagal activity can terminate episodes of PSVT. ECG and blood pressure monitoring is required during the procedure.

**Carotid sinus massage**-supine position with the neck extended. The carotid sinus is located inferior to the angle of the jaw at the level of the thyroid cartilage. Steady pressure is applied to one carotid sinus for 5 to 10 seconds. If no response, repeat it in the contralateral side after 1-2 minutes.

**Carotid massage should not be attempted in patients with carotid bruit/stenosis or ischemic stroke. Both carotid sinuses should never be massaged simultaneously.**

**Valsalva maneuver-**while in the supine position the patient is instructed to exhale forcefully against a closed glottis with closed mouth and nose for 10 seconds. Adequacy indicated by neck vein distension, and increased tone in the abdominal wall muscles.

2. **Synchronized electrical Cardioversion-**required rarely for haemodynamically unstable patients. The energy needed is 150 to 200 joules for monophasic defibrillators.

**Pharmacologic**

1. **Termination of acute episode**

**First line**

**Adenosine**, I.V, very rapidly (over 1-2 seconds): Initial: 6mg; if not effective within 1-2 minutes, 12mg may be given; may repeat 12mg bolus if needed. Follow each dose with 20mL very rapid Normal saline flush.

| | |
|---|---|
| **ADRs:** | Transient new arrhythmia, facial flushing, headache, dizziness/lightheadedness, GI discomfort, chest pressure/discomfort, dyspnea, bronchospasm |
| **C/Is:** | Hypersensitivity to adenosine, bradycardia, Wolff-Parkinson-White (WPW) syndrome |
| **Dosage forms:** | Injection, 3mg/ml |

**Alternatives**

**Verapamil**, I.V, 2.5-5mg over 2 minutes; second dose of 5-10mg may be given after 15-30 minutes; maximum total dose: 20-30mg

**Metoprolol**, IV, 2.5-5mg every 2-5 minutes (maximum total dose: 15mg over a 10-15 minute period).

**Digoxin**, 0.5 to 1mg IV over a period of 10 to 15 min followed by 0.25mg every 2-4 hours with a total dose less than 1.5mg with in 24-hour period

2. **Prevention of recurrence (chronic therapy)**

**First line – beta blockers**

**Metoprolol**, Extended release: 25-200mg/day, P.O.

**Atenolol**, 25-100mg/day, P.O. or

**Propranolol** 10-40mg P.O. 3-4 times daily

**Alternatives**

**Verapamil**, immediate release 40-120mg, P.O.TID or extended release 180-360mg/day

**Ventricular tachyarrhythmias**

Ventricular tachycardias are wide QRS tachychyarrhythmias that originate in the myocardium. They are commonly associated with some form of structural heart disease. Based on their clinical significance, they can be divided in to two:

1. Malignant (potentially lethal) arrhythmias-sustained ventricular tachycardia (VT) and Ventricular fibrillation.
2. Non sustained (haemodynamically tolerated) arrhythmias-premature ventricular contactions (PVCs), non sustained ventricular tachycardia (NSVT), and accelerated idioventricular rhythm (AIVR).

A ventricular tachycardia which stays for more than 30 seconds is labeled **sustained**.

**All Wide QRS (> 120 ms) tachycardias are considered and treated as ventricular tachyarrhythmias until proved otherwise.**

**Treatment**

**Objectives**

- Prevent degeneration of ventricular tachycardia to ventricular fibrillation.
- Reverse cardiac arrest

**Non pharmacologic**

- CPR should be provided to patients with sustained VT with **cardiac arrest** (the victim is unresponsive, pulseless and not breathing)
- $O_2$ via face mask or nasal catheter
- Continuous ECG monitor
- Suction device and endotracheal intubation set should be ready
- Correct electrolyte disorders
- Reassure patients with non sustained ventricular tachycardia
- Defibrillation:

1. **Sustained polymorphic VT, ventricular flutter, or ventricular fibrillation**

Emergency defibrillation (without synchronization), with ≥200 Joules (monophasic), increase the energy to the maximum if arrhythmia persists.

2. **Sustained monomorphic VT** – synchronized with ≥200 Joules (monophaisc). If the haemodynamic status allows conscious sedation should be provided.

**Pharmacologic**

1. DC cardioversion is first line therapy for sustained wide QRS tachycardias. Pharmacologic treatment may be an acceptable option in haemodynamically stable monomorphic VT with no Heart Failure .
2. Never give intravenous verapamil to patients with a wide QRS tachycardia

**First line-Intravenous Amiodarone**

**Stable VT regimen**:

Step 1: 150mg over first 10 minutes (dilute in 100mL D5W)

Step 2: 360mg over next 6 hours (dilute 500mL D5W): 1 mg/minute

Step 3: 540mg (dilute in 500 to 1000ml D5W) over next 18 hours: 0.5mg/minute

**Pulseless VT (cardiac arrest) regimen**: If unresponsive to defibrillation attempts and CPR **Amiodarone**, I.V push, 300mg (**undiluted**), if VT or VF recurs, administer supplemental dose of 150mg and continue CPR.

| | |
|---|---|
| **ADRs:** | asystole, cardiac arrest, electromechanical dissociation, ventricular tachycardia, shock, photosensitivity, hypothyroidism or hyperthyroidism, photosensitivity, slate blue skin discoloration |
| **C/Is:** | Hypersensitivity to amiodarone, bradycardia causing syncope |
| **D/Is:** | Oral anticoagulants, other antiarrythmics, digoxin, phenytoin; beta blockers, cimetidine and ritonavir |
| **P/Cs:** | Heart Failure and impaired liver function, avoid exposure to sunlight. Arrhytmias, Hepatotoxicity, Proarrhytmic effects, Pulmonary toxicity |
| **Dosage forms:** | Injection, 50mg/ml |

**Alternative-Intravenous lidocaine**

**Both stable VT and Pulseless VT(cardiac arrest) regimen**:

**Lidocaine**, I.V, 1-1.5mg/kg; repeat with 0.5-0.75mg/kg every 5-10 minutes if no response. (maximum cumulative dose: 3mg/kg).

- Follow with continuous infusion of 1-4mg/minute
- Preparation for continuous infusion infusion: 2g of lidocaine/250mL D5W
- Rate of infusion: 1mg/min = 7.5ml/hour, 2mg/min =15ml/hour, 3mg/min= 22.5ml/hr, 4mg/min= 30ml/min

| | |
|---|---|
| **ADRs:** | Respiratory depression, depression of mental status, hallucinations, psychosis convulsion, hypotension, arrhythmia, bradycardia, arterial spasms, cardiovascular collapse, defibrillator threshold increased ; rarely hypersensitivity |

**1. Prevention of recurrence**

**Non-pharmacologic**

- Standard treatment of the underlying cause is the main stay of treatment for preventing recurrent VT. (e.g. treatment of acute coronary syndrome)
- Correct precipitating causes(e.g. hypoxia, hypo/hyperkalemia, acidosis, pulmonary embolism)
- Discontinue arrhythmogenic medicines-digoxin, antiarrhythmic medicines.

**Pharmacologic**

**First line**

**Amiodarone**, P.O., 800-1600mg/day in 2 divided doses for 1-3 weeks, when adequate arrhythmia control is achieved, decrease to 600-800mg/day in 1-2 doses for 1 month. Maintenance: 400mg/day

| | |
|---|---|
| **ADRs:** | Photosensitivity, slate blue skin discoloration, hypothyroidism/hyperthyroidism, constipation, corneal microdeposits,visual disturbance, hepatitis, pulmonary toxicity, abnormal oral smell |
| **C/Is:** | Severe bradycardia, 2nd or 3rd degree AV block, hypersensitivity to Amiodarone or its components e.g. iodine |
| **D/Is:** | Indinavir, Nelfinavir, Saquinavir,thioridazine, quinolones, beta blockers, digoxin |
| **Dosage forms:** | Amiodarone tablet 100mg, 200mg, 400mg |

**Alternative or additional to Amiodarone-Beta blockers**

**Metoprolol**, extended release: P.O.,25-200mg/day

**Atenolol**, 25-100mg daily

**Propranolo**l, 10-40mg P.O., 3-4 times daily

**3. Atrioventricular (AV) Block**

AV block describes a delay/block of atrial impulses at the atrioventricular node of varying severity. When severe it results in symptomatic bradycardia which can manifest as easy fatigability, Heart Failure , syncope, seizures and bradycardia associated ventricular tachycardias. It is caused by structural heart diseases (mainly ischemic heart disease,

cardiomyopathies, congenital heart disease), medicines (beta blockers, verapamil, digoxin), electrolyte abnormalities, hypothyroidism and cardiac surgery.

ECG is the diagnostic of AV block.

**First degree AV block**-Characterised by prolonged PR interval (> 0.20 seconds)

**Second degree AV block**: Some atrial impulses fail to be conducted to the ventricles

**Type 1:** progressive prolongation of the PR interval before block of an atrial impulse

**Type 2**: conduction fails suddenly without preceding change in PR interval

**3rd degree AV block:** No atrial impulse propagates to the ventricles resulting in atrioventricular dissociation

**Treatment**

**Objectives**

- Prevent syncope and sudden death in those with higher degrees of AV block

**Non pharmacologic**

- Bed rest
- Look for reversible causes and manage accordingly(discontinuation of medicines which can cause/worsen AV block, management of Acute coronary syndrome, correction of severe electrolyte abnormalities, management of myxedema)

**The main stay of management for persistent symptomatic advanced AV block is permanent pacemaker implantation**

**Pharmacologic**

**For Acute termination**

**First line**

**Isoproterenol**, Continuous I.V. infusion: 2-10 µg/minute; titrate to patient response

**ADRs:** Angina, palpitation, flushing, tachyarrhythmia, tremor, restlessness, headache, blurred vision, headache, dizziness, dyspnea, hypokalemia

**C/Is:** Angina, pre-existing ventricular tachyarrhythmias, digoxin toxicity

**Dosage forms:** Injection, 0.02mg/ml, 0.2mg/ml

**Alternatives**

1. **Adrenaline,** I.V, infusion, 2-10 µg/minute

| | |
|---|---|
| **ADRs:** | tachyarrhythmia, hypertension, tremor, anxiety, sweating, nausea, vomiting, angina, dizziness, pulmonary edema, headache, peripheral vasoconstriction |
| **C/Is:** | asymmetric septal hypertrophy, pheochromacytoma, tachyarrhytmias |
| **DIs:** | beta blockers, digoxin, theophylline, tricycluc antidepressants, MAO inhibitors |
| **P/Cs:** | hyperthyroidism, hypertension, diabetes mellitus, ischaemic heart disease, arrhythmias, cerebrovascular disease, and elderly, cerebral arteriosclerosis, pankinson's |
| **Dosage forms:** | Injection, 0.1%, 1:1000 1mg/ml |

2. **Dopamine**, IV, infusion, 2-10 µg/Kg/minute

## 4. Endocarditis (Infective Endocarditis)

It is an infection of the endocardial surface of the heart, which may include one or more heart valves, the mural endocardium, or a septal defect. Endocarditis can be broken down into the following categories: 1)native valve endocarditis (NVE), acute and subacute; 2)prosthetic valve endocarditits (PVE), early and late; and 3) intravenous medicine abuse (IVDA) endocarditis. *Streptococcus viridans* causes the majority of cases of subacute bacterial endocarditis; the rest are due to organisms like *Entetrococci*, *Staphylococci* and others. A number of factors predispose to the development of SBE. These include structural heart disease, prosthetic heart valves, and intravenous medicine use (IDU).

**Clinical features**

- Fever, chills and sweating
- Reddish/tea colored urine
- Worsening of Heart Failure symptoms
- Anorexia, weight loss, malaise, arthralgia
- Features of anaemia, Petechial rashes
- Physical findins-Rash, splenomegaly,clubbing, worsening or new onset regurgitant murmurs, arterial embolic events. Peripheral manifestations suchas Osler's nodes, subungual haemorrhages, Janeway lesions and Roth's spots may occasionaly be found

**Investigations**

- CBC, ESR or CRP, Rheumatoid factor
- Urine examination (for microscopic hematuria and proteinuria)
- Blood culture-**three blood culture sets** (each with two bottles), separated from one another by at least 1hr, should be obtained from different venipuncture sites over 24h. If the cultures remain negative after 48–72 hours and empiric antibiotic are not started, two or three additional blood culture sets should be obtained
- Echocardiography
- RFT

**N.B-Precise clinical and microbiologic diagnosis is mandatory in order to guide therapy. The Modified Duke Criteria is used to make the diagnosis infective endocarditis.**

**Modified Duke Criteria for the diagnosis of Infective Endocarditis** (adapted from: Li, JS, Sexton, DJ, Mick, N, et al. Clin Infect Dis 2000)

**Major Criteria**

1. **Positive blood culture –** either of the following (A to C) are considered as positive

A. **Typical** microorganism for infective endocarditis from **two** separate blood cultures
   - Viridans streptococci, Streptococcus gallolyticus, HACEK group, Staphylococcus aureus, or ommunity-acquired enterococci are the typical organisms

***OR***

B. **Persistently positive** blood culture, defined as recovery of a microorganism consistent with infective endocarditis from:
   - Blood cultures drawn >12 h apart

     or
   - All of 3 or a majority of 4 blood cultures, with first and last drawn at least 1hr apart

***OR***

C. **Single** positive blood culture for Coxiella burnetii or IgG antibody titer of >1:800

**2**. **Evidence of endocardial involvement –** either of the following two (A or B) are considered as evidence of endocardial involvement

A. **Positive echocardiography**
   - **Oscillating intracardiac mass in the absence of an alternative explanation**-on valve/s or supporting structures or implanted material or in the path of regurgitant jets

***OR***

- **Abscess**

***OR***

- **New partial dehiscence of prosthetic valve**

B. **New valvular regurgitation** (increase or change in preexisting murmur **not sufficient**)

---

**Minor Criteria**

1. **Predisposition**: predisposing heart condition or injection medicine user
2. **Fever** -38.0°C
3. **Vascular phenomena**: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages, Janeway lesions
4. **Immunologic phenomena**: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor
5. **Microbiologic evidence**: positive blood culture not meeting major criterion or serologic evidence of active infection with organism consistent with infective endocarditis

- **Definite endocarditis = 2 major criteria OR 1 major & 3 minor criteria, or 5 minor criteria**
- **Possible IE = 1 major &1 minor criteria or 3 minor criteria**

**Rejecting the diagnosis of Infective Endocarditis (IE**) – the diagnosis of IE can be rejected if one of the following are meet:

- Firm **alternate diagnosis** for manifestations of endocarditis
- **Resolution** of manifestations of endocarditis, with antibiotic therapy **for four days or fewer**
- Does not meet the modified Duke's criteria for possible infective endocarditis

**Treatment**

**Objectives**

- Treat the infection and prevent further valve damage
- Treatment of Heart Failure

**Non pharmacologic**

- Treatment of fever
- Surgical intervention – in patients with severe CHF or haemodynamic instability unresponsive to medical therapy, persistent bactermia despite optimal antibiotics, lack of effective antiobiotic

**Pharmaclogic**

1. Blood culture should be taken before the start of antiobiotics in all patients suspected of having IE including those haemodynamically unstable. As blood culture results usually arrive in 48-72 hours, antiobitic intiation can be awaited till results arrive, unless the patient is hemodymically unstable
2. If blood culture result is negative after 48-72 hrs, two to three sets of blood culture should be taken again. The laboratory should be communicated about the quality of blood culture

1. **Empiric antiobiotic therapy**

**Table 2 - Empiric treatment of "community acquired" Native Valve SBE**

| Antibioics – regimen options | Dosage and route | Duration in weeks | Comments |
|---|---|---|---|
| **Ceftriaxone** | 2g, IV, once per day | 4-6 | |
| PLUS **Gentamicin** | 3mg/kg, IV once per day OR 1mg/kg/dose, IV, TID | 2 | Dose should be adjusted to creatinine clearance. Creatinine should be monitored. |
| **Crystalline Penicillin G** | 4 million U, IV,Q 4hr | 4-6 weeks | |
| PLUS **Gentamicin** | 3mg/kg, IV once per day OR 1mg/kg/dose, IV, TID | 2 | See above |
| **Vancomycin** PLUS | 15mg/kg/dose, IV, BID | 4 | For patients patients with severe or immediate **beta-lactam allergy.** Do not exceed 2g per day Adjust dose to creatinine clearance. |
| **Gentamicin** | 3mg/kg, IV once per day OR1mg/kg/dose, IV, TID | 2 | See above |

*Treatment should be modified based on culture and sensitivity results as well as clinical judgement of response, risk factors and expected oraganisms.

**Table 3 - Empiric treatment of health care–associated and IV medicine users endocarditis**

| Antibioic-regimen | Dosage and route | Duration in weeks | Comments |
|---|---|---|---|
| **Vancomycin** | 15mg/kg/dose, IV, BID | 4 | -Do not exceed 2g per day<br>-Adjust dose to creatinine clearance. |
| PLUS<br>**Gentamicin** | 3mg/kg, IV once a day<br>OR<br>1mg/kg/dose, IV, TID | 2 | See the table above |

**Organisim specific antibiotic therapy**

A. **Penicillin susceptible and relatively penicillin resistant streptococci-**Treat with the emperic treatment regimen for "community acquired" Native Valve SBE (see table)

B. **Moderately penicillin-resistant streptococci and nutritionally variant organisms-**treat with the empiric regimen for"community acquired" Native Valve SBE (see table) with the following modifications:

- Prolong the duration crystalline penicillin G to 6 wks and increase dose to 4-5million U, Q4hr
- Prolong the duration of ceftriaxone to 6 weeks
- Prolong the duration of gentamicin for 6 weeks with close renal monitoring
- Vancomycin based regimen (if available and affordable) is preferable

**Table 4 - Methicillin–suceptible Staphylococcal endocarditis with out prosthetic material**

| Antibioics- options | Dosage and route | Duration in weeks | Comments |
|---|---|---|---|
| **Cloxacillin** | 2 g, IV, q4h | 4-6 | |
| **Vancomycin** | 15mg/kg/dose, IV, BID | 4 – 6 | See the table above for comment |

**Table 5 - Methicillin–Resistant Staphylococcal endocarditis with out prosthetic material**

| Antibioics- options | Dosage and route | Duration in weeks | Comments |
|---|---|---|---|
| **Vancomycin** | 15mg/kg/dose, IV, BID | 4 – 6 | See the table above for comment |

**Table 6 - Enterococcal Infective Endocarditis**

| Antibioics – regimen | Dosage and route | Duration in weeks | Comments |
|---|---|---|---|

| | | | |
|---|---|---|---|
| **options** | | | |
| **Crystalline Penicillin G**<br>PLUS<br>**Gentamicin** | 4-5 million U, IV,Q 4hr | 4-6 | |
| | 3mg/kg, IV once per day<br>OR<br>1mg/kg/dose, IV, TID | 4-6 | Dose should be adjusted to creatinine clearance.<br>Creatinine should be monitored. |
| **Ampicillin**<br>PLUS<br>**Gentamicin** | 2 gm, IV,Q 4hr | 4-6 | |
| | 3mg/kg, IV once per day<br>OR<br>1mg/kg/dose, IV, TID | 4-6 | See above |
| **Vancomycin**<br>PLUS<br>**Gentamicin** | 15mg/kg/dose, IV, BID | 4-6 | For patients with severe or immediate **beta-lactam allergy** |
| | 3mg/kg, IV once per day<br>OR<br>1mg/kg/dose, IV, TID | 4-6 | See above |

## 5. Heart Failure

Heart Failure is an abnormality of cardiac structure or function leading to failure of the cardiac output to meet the body's metabolic requirements despite normal filling pressures. Clinically it is a syndrome consisting of typical symptoms (shortness of breath, fatigue, orthopnea, ankle swelling) and signs (raised JVP, pulmonary crackles, displaced apex beat, edema). It might predominantly involve the left ventricle or the right ventricle. More commonly, however, both left and right ventricular dysfunctions co-exist. It could result from systolic or diastolic dysfunction or both. Identification of the underlying cause of the Heart Failure is central to diagnosis. It could result from valvular disease, ischemic heart disease, hypertension, cardiomyopathies, thyrotoxicosis, congenital heart disease, etc.

The functional classification of Heart Failure using the New York Heart Association (NYHA) Classification is described in the table below:

**Table 7 - New York Heart Association (NYHA) functional Classification for Heart Failure**

| | |
|---|---|
| **NYHA I** | No limitation of physical activity. |
| **NYHA II** | Slight limitation of physical activity-comfortable at rest, but ordinary physical activity results in fatigue, palpitation or dyspnea. |
| **NYHA III** | Marked limitation of physical activity-comfortable at rest, light activity causes fatigue, palpitation or dyspnea. |
| **NYHA IV** | Symptomatic at rest |

**Clinical features**

- Breathlessness on exertion, Breathlessness on lying flat (orthopnea)
- Intermittent breathlessness at night (paroxysmal nocturnal dyspnea)
- Night cough, Tachypnea, Frothy blood-stained sputum, Lower chest crepitations
- Swelling of the feet and lower extremities, Abdominal distention and discomfort
- Pitting pedal edema, Ascites, Tender hepatomegaly
- Tachycardia, S3 gallop, Cardiac murmurs, Displaced apex beat
- Raised jugular venous pressure

**Investigations**

- ECG, Chest X-ray, Echocardiography
- CBC, BUN, Creatinine and Electrolytes, LFT
- FBS, lipid profile
- Thyroid function tests

**Treatment**

**Objectives**

- Relieve symptoms and improve quality of life
- Improve survival
- Treat the precipitating cause
- Prevent complications
- Treat the precipitating cause

**Non pharmacologic**

- Reduce salt intake, avoid salt intake of >6g/day
- Avoid "salt replacement" tablets due to their high potassium content.
- Encourage patients to weigh themselves
- Reduction of weight in overweight and obese individuals
- Refraining from excessive alcohol consumption
- Avoid smoking. Patients should be offered smoking cessation advice and support.
- Encourage low intensity physical activity amongst patients with stable Heart Failure
- Bed rest in hospitalized patients.

**Pharmacologic**

**Caution!**
**Heart Failure is a pathophysiologic state caused by different etiologies such as valvular heart disease, hypertensive heart disease, coronary artery disease and cardiomyopathies. Treatment needs to be tailored to the specific causes. The main stay of treatment in symptomatic valvular heart disease is surgical correction; the use of ACE inhibitors or beta blockers is not well studied in valvular heart disease. ACEI use in stenotic valvular heart diseases is deleterious.**

A. **Initial therapy of mild Heart Failure (NYHA CLASS I-II) due to systolic dysfunction**

1.**ACE inhibitors or Angiotensin receptor blockers (ARBs) –** start with lower dose and increase the dose gradually. See options below**:**

**ACE inhibitors**:

**Enalapril** ,start with 2.5mg once to twice per day. Escalate dose to target of 10-20mg, BID

**Dosage forms:** Tablet, 2.5mg, 5mg, 10mg, 20mg, 40mg

OR

**Lisinopril**, start with 2.5-5mg,once daily. Increase dose to target of 20 – 40mg once daily

**Dosage forms:** Tablet 2.5mg, 5mg, 10mg, 20mg

OR

**Captopril**, start with, 6.25-12.5mg 3 times/dayp P.O.,. Increase dose to target 50mg, TID

**Dosage forms:** Tablet, 12.5mg, 25mg, 50mg

**ADRs:** cough, angio-edema, hyperkalemia, rash, loss of taste, leukopenia

**C/Is:** life threatening side effects during earlier exposure (angio-edemia, anuria, renal failure), pregnancy, hypotension, hyperkalemia, acute kidney injury

**P/C:** should be used with caution in systolic blood pressure < 80mmHg, bilateral renal artery stenosis

*OR*

**ARBS:**

**Valsartan**,start with 40mg, BID; titrate to 80-160 mg, BID, maximum dose-320mg/day

**Dosage forms:** Tablet, 40mg, 80mg, 160mg, 320mg,

OR

**Candesartan-**start with 4 mg/day; increase dose as tolerated, target dose is 32mg/day

**Dosage forms:** Tablet, 4mg, 8mg, 16mg

**Losartan** ,start with 12.5 to 25 mg/day, increase dose gradually, target dose is 50mg/day

**Dosage forms:** Tablet 25mg, 50mg, 100mg

**ADRs:** hypotension, dizziness, hyperkalemia, renal dysfunction, rarely cough

**C/Is:** pregnancy, hypotension, hyperkalemia, acute kidney injury

**P/C:** systolic blood pressure < 80mmHg, bilateral renal artery stenosis

2. **Beta blockers –** start low dose and increase dose gradually (≥2 weeks). See options below:

**Metoprolol**,starting dose 25 – 50mg, BID. Increase dose to target of 200-400mg/day

**Dosage forms:** Tablet, 50 mg, 100mg, 200mg (s/r)

OR

**Carvedilol**, starting dose 3.125mg, BID. Increase dose to target of 25-50mg/day

**Dosage forms:** Tablet, 3.125mg, 6.25mg, 12.5mg, 20mg, 25mg

**ADRs:** Hypotension, bradycardia, AV block, worsening CHF, dizziness, fatigue, depression, confusion, decreased libido, worsening diabetes control, bronchospasm, pruritis

**C/Is:** Severe bradycardia, second-and third degree heart block, hypotension, decompensated Heart Failure , sick sinus syndrome, active bronchospasm, phechromocytoma without α-blockade.

**D/Is:** Inhalation anesthetic agents,Calcium channel blockers (nondihydropyridines), CYP2D6 inhibitors (eg,chlorpromazine, cimetidine, diphenhydramine, hydroxychloroquine, fluoxetine, thioridazine) concurrent use in CYP2D6 may increase plasma concentrations of Metoprolol

**P/Cs:** sinus bradycardia and partial heart block

3. **Furosemide**, 40mg-80mg/day in two divided doses when there is evidence of fluid overload with Spironolactone 25 to50mg/day or KCl 600 to 1200mg, BID

**Dosage forms:** Tablet, 40mg, 80mg

B. **Initial therapy of moderate Heart Failure (NYHA CLASS III) due to systolic dysfunction**

1. **Furosemide**, 40-80mg, P.O., BID

2. **ACE inhibitors/Angiotensin receptor blockers (ARBs)**

ACE inhibitors: see intial doses and dose escalation above

**Enalapril** ,start with 2.5mg 1 to 2 times/day. Escalate dose to target of 10-20mg, BID, OR

**Lisinopril**,start with 2.5-5mg,once daily. Increase dose to target of 20 – 40mg /day,OR

**Captopril**,start with,6.25-12.5mg 3 times/day P.O. Increase dose to target 50mg, TID

*OR*

**ARBs**:

**Valsartan**,start with 40mg, BID; titrate to 80-160 mg, BID, maximum dose-320 mg/day, OR

**Candesartan**,start with 4mg/day; increase dose as tolerated, target dose is 32 mg/day, OR

**Losartan**,start with 12.5 to 25mg/day, increase dose gradually, target dose is 50mg/day

3. **Beta blockers** – Should not be started before adequate diuresis, ACEI/ARB and patient is in good clinical state. start low dose and increase dose gradually(>2 weeks):

**Metoprolol**,starting dose 25 – 50mg, BID. Increase dose to target of 200-400mg/day, OR
**Carvedilol** ,starting dose 3.125mg, BID. Increase dose to target of 200-400mg/day

4. **Spironolactone**, 25-50mg,P.O.,daily

| | |
|---|---|
| **ADRs:** | Gynecomastia in men, breast pain, hyperkalemia, hypotension, AKI |
| **C/Is:** | hyperkalemia, acute renal failure |
| **Dosage forms:** | Tablet, 25mg, 50mg |

- **Do not give potassium sparing diuretics such as spironolactone and Potassium**
- **Chloride supplements together.**

5. **Digoxin**, 0.125 mg once, P.O., daily

| | |
|---|---|
| **ADRs:** | diarrhoea, weakness, arrythmias, AV block. |
| **C/Is:** | hypersensitivity to digoxin, ventrivular arrhythmia, hypertrophic obstructive cardiomyopathy, severe hypokalemia |
| **Dosage forms:** | Tablet 0.25mg |

C. **Initial therapy of severe Heart Failure (NYHA CLASS IV)**

**Non pharmacologic**

- Admit patient
- Prop up position
- Oxygen, by nasal cannula or face mask

**Pharmacologic**

**Furosemide**, IV, 40mg, repeat after 30 minutes if necessary. Increase the dose of furosemide if response is inadequate, then IV, 40-80 mg 12 hourly as standing dose. Change it to oral before discharge. Add **KCl** 600mg, 1-2 tabs, twice per day or **Spironolactone** 25-50mg, BID, if there is no renal impairment or hyperkalemia

**ACE inhibtors or ARBS**-see options and dosing above

**N.B**. Do not start ACE inhibitors/Angiotensin Receptor Blockers until the patient is haemodynamically stable. For patients with Left ventricular systolic dysfunction. Start with low dose and increase gradually.

**Beta blockers – see options and dosing** above

**N.B.** Beta blockers – should not be started in the acute management of decompensated Heart Failure . After patient stabilization, beta blockers can be started **during discharge or as an out patient management**. Start with low dose and escalate gradually.

**Digoxin**, 0.125 mg once, P.O, daily

If there is cardiogenic shock – start inotopic support

**Dopamine**, I.V infusion 1-5 µg /kg/minute up to 50 µg /kg/minute; increase by 1-4mcg/kg/minute at 10-to 30-minute intervals until optimal response is obtained

| | |
|---|---|
| **ADRs:** | Ectopic beats, tachycardia and tachyarrhythmia, anginal pain, palpitation, vasoconstriction and gangrene at high dose, headache, anxiety. |
| **C/Is:** | Hypersensitivity to sulfites, Pheochromocytoma,Tachyarrhythmia |
| **D/Is:** | Sympathomimetics, alogenated hydrocarbon anesthetics |
| **Dosage forms:** | Injection, 40mg/ml |

*OR*

**Dobutamine**, I.V. infusion: 2.5-20 µg/kg/minute; maximum: 40 mcg/kg/minute, titrate to desired response

| | |
|---|---|
| **ADRs:** | Ectopic beats, tachyarrhythmia, anginal pain, palpitation, hypertension, leg cramp |
| **C/Is:** | Hypersensitivity to sulfites, idiopathic hypertrophic subaortic stenosis (IHSS) |
| **D/Is:** | Sympathomimetics, calcium salts |
| **Dosage forms:** | powder for injection 250mg |

**Venous thromboembolism prophylaxis-** if not already on anticoagulant

**Unfractionated Heparin**, 5,000 IU, SC, BID

*OR*

**Enoxaparin**, 40mg, SC, daily

**Pharmacologic treatment of chronic Heart Failure with depressed left ventricular systolic function**

- Diuretics
- ACEI or ARBS +/- } Spironolactone and Digoxin
- Beta blockers

**Table 8 - Medicines for the treatment of Chronic Systolic Heart Failure**

| – Medicines | – Initial dose | – Maximum dose | – Comments |
|---|---|---|---|
| – **Diuretics** | | | |
| – Furosemide | 20–40 mg qd or bid | 400 mg/d | - Dose depends on fluid overload<br>- Followfor hypokalemia |
| **Angiotensin-Converting Enzyme Inhibitors (ACEI)** | | | |
| Captopril | 6.25 mg tid | 50 mg tid | - Increase dose to target gradually<br>- Follow RFT and serum $K^+$ |
| Enalapril | 2.5 mg bid | 10 mg bid | |
| Lisinopril | 2.5–5 mg qd | 20–35 mg qd | |
| **Angiotensin Receptor Blockers(ARBs)-alternative to ACEI** | | | |
| Valsartan | 40 mg bid | 160 mg bid | - Increase dose to target gradually<br>- Follow RFT and serum $K^+$ |
| Candesartan | 4 mg qd | 32 mg qd | |
| Losartan | 12.5 mg qd | 50 mg qd | |

| | | | |
|---|---|---|---|
| | | | - Do not combine with ACEI |
| **Beta Blockers** | | | |
| Carvedilol | 3.125 mg bid | 25–50 mg bid | -Start when patient is stable<br>-Increase dose gradually(≥ 2wks) |
| Metoprolol succinate CR | 12.5–25 mg qd | Target dose 200 mg qd | |
| **Additional Therapies** | | | |
| Spironolactone | 12.5–25 mg qd | 25–50 mg qd | To be added if HF remains poorly controlled despite optimal therapy with the above class of medicines |
| Digoxin | 0.125 mg qd | 0.25 mg qd | |

**6. Hypertension**

Hypertension is a state of elevated systemic blood pressure that causes marked increment of cardiovascular risk. It is one of the major, but preventable, risk factors of coronary artery disease, haemorrhagic and ischemic stroke, Heart Failure and chronic kidney disease. In 90-95% of cases, the cause is unknown – this is called essential hypertension. Secondary hypertension refers to hypertension caused by other systemic illness as part of their manifestation. The common causes are renal parenchymal disease (e.g. glomerulonephritis, chronic kidney disease of any cause), renovascular disease (renal artery stenosis), endocrine (e.g. Cushing syndrome, primary hyperaldosteronism, Pheochromocytoma), coarctation of the aorta, obstructive sleep apnea and medicine induced (e.g. corticosteroid, oral contraceptive pills).

Although the risk of cardiovascular and renal disease continuously rises over the entire range of blood pressure; based on the level of blood of blood pressure hypertension is defined a systolic blood pressure ≥ 140mmHg and/or diastolic blood pressure ≥ 90mmHg.

**Clinical features**

- Hypertension is generally **ASYMPTOMATIC**

- Clinical evaluation (history and physical examination) should focus on proper blood pressure measurement, looking for other cardiovascular risk factors (Diabetes Mellitus, Dyslipidemia, Obesity, Smoking and family history of coronary heart disease), looking for evidence of end organ damage and searching for possible secondary causes.

**Table 9 - Category of blood pressure according to the USA Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7)**

| **Blood pressure in mm Hg** | | | |
|---|---|---|---|
| **Category** | **Systolic** | | **Diastolic** |
| Normal | <120 | AND | <80 |
| Prehypertension | 120-139 | OR | 80-89 |
| Hypertension | ≥140 | OR | ≥90 |

**Table 10 - Category of stage of hypertension according to the USA Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7)**

| **Stage of hypertension** | **Systolic** | | **Diastolic** |
|---|---|---|---|
| **Stage 1** | 140-159 | OR | 90-99 |
| **Stage 2** | ≥160 | OR | ≥100 |

**N.B.** These definitions apply to adults who are not on antihypertensive treatment and not acutely ill. If there is a disparity between systolic and diastolic pressures, the higher value determines the severity of hypertension.

**Hypertensive Crisis**: there are two major forms:

1. **Hypertensive Emergencies-**are acute, life-threatening, and usually associated with marked increases in blood pressure (BP), generally ≥180/120mmHg. These are situations that require immediate (within minutes) blood pressure reduction to prevent or limit target organ damage.

Conditions include hypertensive encephalopathy, intracranial haemorrhage, unstable angina, acute myocardial infarction, acute kidney injury, pulmonary edema and dissecting aortic aneurysm, and eclampsia.

2. **Hypertensive Urgency**-is a situation in which there is asymptomatic severe hypertension with no target organ damage. The goal is to reduce the blood pressure to ≤160/100mmHg over several **hours to days, not rapidly.** This is based on the adverse effects observed with faster correction and/or lower achieved blood pressure.

**Investigations**

- Urinalysis
- Blood chemistry potassium, sodium, creatinine/estimated glomerular filtration rate
- Fasting blood glucose
- Fasting total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides
- Standard 12 lead electrocardiogram (ECG)

**Treatment**

**Objectives**

- Detection and management of other cardiovascular risk factors
- Detection and management of target organ damage
- Prevention of target organ damage
- Decrease the side effects of medications
- Achieve target blood pressure (< 140/90mmHg, in patients having diabetes with proteinuria and chronic kidney disease (< 130/80 mmHg)

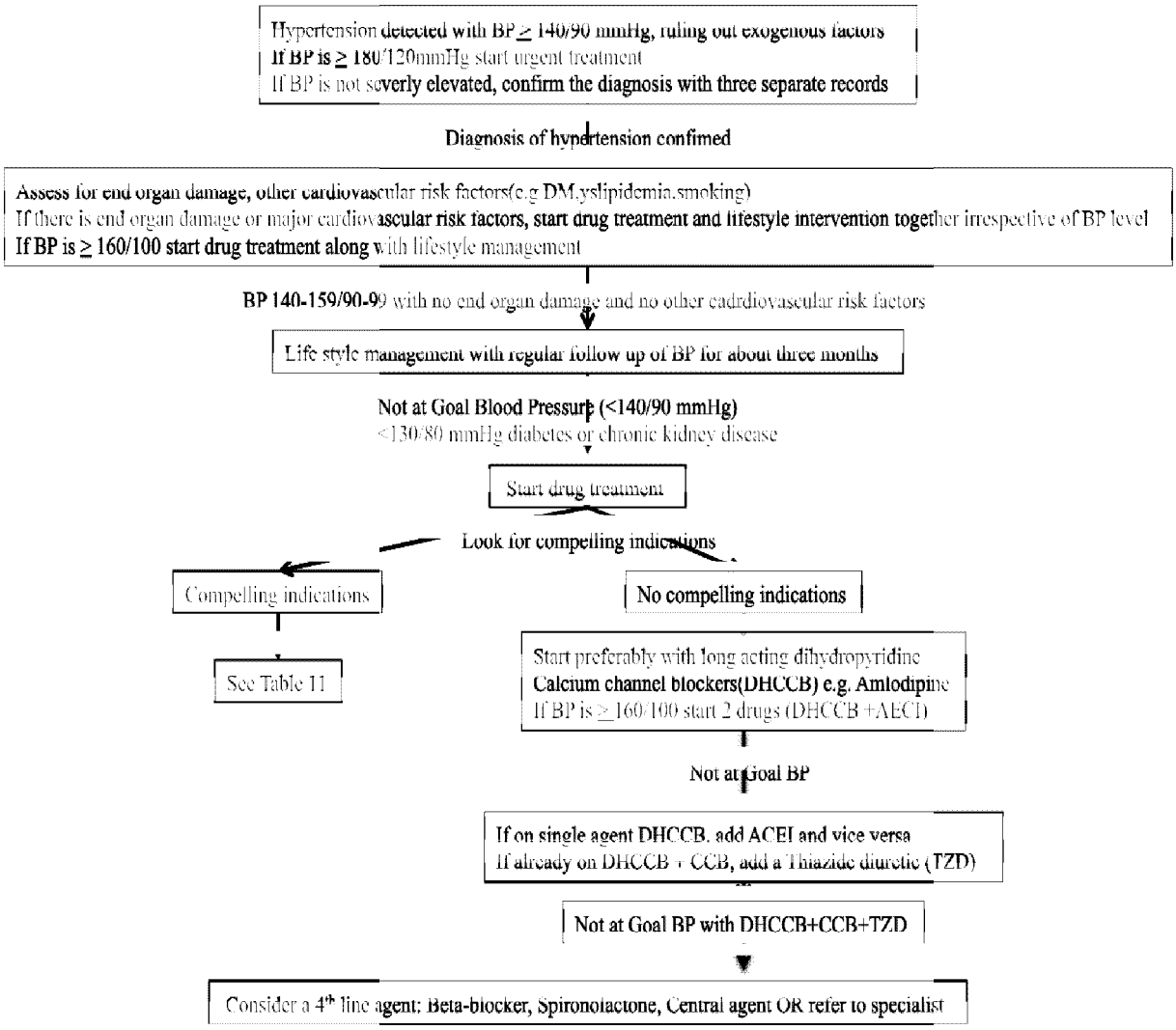
**Non pharmacologic**

- **Smoking cessation**: Complete cessation of smoking
- **Physical activity**: At least 30 minutes of moderate intensity activity 5-7 days per week
- **Weight reduction**: BMI 18-24kg/$m^2$, waist circumference < 102cm men, < 88cm women
- **Dietary recommendations**: emphasize fruits, vegetables, low-fat dairy products, fibre, wholegrains, and protein sources that are reduced in saturated fats and cholesterol

- **Reduce salt intake**: about1 tsp of table salt. Do not forget hidden salt in home prepared spices
- **Alcohol consumption**: limited to two drinks or less per day **(one standard drink)**
- 1 bottle (341 mL) of 5% beer or,
- 1 glass (150 mL) of 12% wine or,
- 1.5 oz (45 mL) of 40% spirits

**Pharmacologic**

- The first-line medicines are roughly equally effective as monotherapy although there is inter-patient variability
- Beta blockers are not considered as first line in the absence of a compelling indication
- Start with a single agent among the first lines; two medicines can be started at the beginning in stage 2 hypertension if the BP is higher than 20/10 mmHg from the target
- If BP target is not achieved by a single agent add a second agent rather than increasing the dose of the first medicine to maximum dose
- If two medicine combinations are started, start with a long acting ACEI (e.g Lisinopril) and long acting dihydropyridine calcium channel blocker(e.g Amlodipine)




**Non-Emergency conditions**

**First line** (in the absence of compelling indications**)**

**Calcium channel blockers-**Amlodipine, Nifedipine (extended or slow release), Felodipine

**ACE inhibitors-**Lisinopril, Enalapril and Captopril

**Thiazide diuretics**-Hydrochlorothiazide

**Angiotensin receptor blockers (ARBs)** – Candesartan, Valsartan, Losartan

**Alternatives**

**Beta blockers**-Atenolol, Metoprolol, Carvedilol, Propranolol

**Central alpha-2 agonist** – methyldopa

**Table 11 - Dose and frequency of antihypertensive medications available**

| Class | Medicine | Dose range (mg/d) | Frequency (Per day) | Common side effects |
|---|---|---|---|---|
| ACEI | Enalapril | 5-40 | 1-2 | Dry cough, hyperkalemia, AKI, angioedema |
| | Lisinopril | 10-40 | 1 | |
| | Captopril | 25-100 | 2-3 | |
| Thiazide diuretics | Hydrochlorothiazide | 12.5-25 | 1 | Frequent urination, hyperglycemia, hyperlipidemia, hyperuricemia |
| Dihydropyrdine CCB | Amlodipine | 2.5-10 | 1 | Pedal edema and headache |
| | Nifedipine(extended release) | 20-120 | 1-2 | |
| | Felodipine | 2.5-20 | 1 | |
| Beta blockers | Atenolol | 25-100 | 1 | Fatigue, bronchospasm,bradycardia, AV block hyperglycemia, sexual dysfunction |
| | Propranolol | 40-160 | 2-3 | |
| | Metoprolol succinate | 25-100 | 1 | |
| | Carvedilol | 12.5-50 | 2 | |
| ARBS | Candesartan | 8-32 | 1 | Hyperkalemia and AKI |
| | Valsartan | 80-320 | 1-2 | |
| | Losartan | 25-100 | 1-2 | |
| Non-dihydropyrdine CCB | Verapamil | 120–360 | 1-2 | Constipation (verapamil), headache (diltiazem), bradyacrdia |
| | Diltiazem | 180-420 | 1 | |
| Central α agonists | Methyl dopa | 250-1000 | 2 | Sedation, dry mouth, rebound hypertension, sexual dysfunction |

**Table 12 - Compelling indication/co-morbidities in hypertension treatment**

| Compelling condition | First line | Second line |
|---|---|---|
| Coronary heart disease | ACE inhibitors/ARB<br>Beta blockers | Calcium channel blocker |
| Heart Failure | ACE inhibitor/ARB<br>Metoprolol/Carvedilol | Diuretics |
| Diabetes with proteinuria | ACE inhibitor/ARB | Thiazide<br>Calcium channel blockers |
| Left ventricular hypertrophy | ACE inhibitor/ARB | Thiazide |
| Chronic kidney disease | ACE inhibitor/ARB | Loop diuretics, cacium channel blocker |

## I. Treatment of Hypertensive Emergencies:

Optimal therapy varies with the type of hypertensive emergency. Hydralazine, 5-10 mg initial dose, repeated every 20 to 30 minutes (with maximum dose of 20 mg) should be given until the mean arterial blood pressure is reduced by 25% (within minutes to 2 hours), then towards 160/100 mm Hg within 2-6 hours.

## II. Hypertensive Urgency

- **For previously treated patients**-adjust existing medication regimen, or reinstitute medications (if nonadherent)
- **For previously untreated patients** – start either a low dose of a calcium channel blocker (Nifedipine slow release 30) or ACE inhibitor (captopril or Enalapril) or Beta blocker
- **Furosemide 20-40mg** (PO or IV) can be added to the above agents
- If patient is reliable follow up can be made every one to two days. If not reliable, admit.
- Avoid rapid drop in blood pressure

**Table 13 - Medicines used in the treatment of hypertensive emergency**

| Medicine | Route | Initial dose | Dose Range | Onset peak Effects | Duration |
|---|---|---|---|---|---|
| Nitroprusside | I.V | 0.5 μg/kg /min | 0.5 to 10 μg/kg /min | 1 to 2 min | 2 to 3 min |
| Nitroglycerin | IV | 5 μg/min IV infusion | 5–100 μg/min IV infusion | 2–5 min | 5–10 min |
| Hydralazine | I.V | 5-10 mg | 5 to 20 mg | 5 to 15min | 2 to 6 hr |
| Captopril | P.O | 6.25 to 12.5 mg | 12.5-50 mg, TID | 30 to 90 min | 4 to 6 hr |

## 7. Ischaemic Heart Disease

Clinically, Ischemic Heart Disease comprises stable angina pectoris, acute coronary syndromes and ischemic cardiomyopathy.

**Stable angina pectoris**

Stable angina pectoris refers to recurrent characteristic/atypical chest pain induced by physical activity or emotional stress and is relieved by rest or nitrates. The key cause is Atherosclerosis, with narrowing of the coronary blood vessels leading to reduction in blood supply to the myocardium. One main risk factor of stable angina is atherosclerotic vascular disease, while other major risk factors include: diabetes mellitus, hypertension, cigarette smoking, dyslipidemia, obesity, a family history of ischemic heart disease or sudden death, old age, male gender and elevated markers of inflammation such as C-reactive protein.

**Clinical features**

- Central/retrosternal or precordial squeezing chest pain or heaviness on the chest which may radiate into the left arm, neck or jaw, and is relieved by rest or nitrates
- The pain usually happens during physical activity
- No typical signs are found in patients with stable angina
- Physical findings which indicate the presence of risk factors may be observed: hypertension, obesity, xanthelasmata, evidence of peripheral arterial disease

**Investigations**

- ECG-resting and/or exercise/stress ECG
- Echocardiography
- Fasting blood glucose and/or Haemoglobin A1C, Lipid profile

**Treatment**

**Objectives**

- Decrease the severity and frequency of symptoms
- Improve quality of life/functional status
- Decrease risk of acute coronary events
- Decrease present modifiable risk factors

**Non pharmacologic**

- Initiate and/or maintain lifestyle modifications-weight control; increased physical activity; moderation of alcohol consumption, diet high in fresh fruits, vegetables, and low-fat dairy products
- Smoking cessation and avoidance of exposure to environmental tobacco smoke at work and home
- Taking rest during symptoms

**Pharmacologic**

**During episodes of chest pain**

**Sublingual Nitroglycerin (glyceryl trinitrate)**, 0.3mg to 0.5mg or 0.4mg sublingual spray (repeat every 5 min as needed) for maximum of 3 doses

**Long-term Treatment**

**Anti angina therapy**, beta blocker, calcium channel blocker or long acting nitrate OR combination of two or more of these agents

1. **Beta blockers – options**

**Metoprolol**, Initial: 25mg P.O., BID; usual dosage: 50-200mg BID; maximum: 400mg/day

**Atenolol**, 50-100mg, P.O., daily.

**Propranolol**, 80-320mg/day P.O., in doses divided 2-4 times/day.

**N.B.** Beta blockers-are initial therapy of choice in the absence of contraindication in the management of stable angina.

**2. Calcium channel blockers-Dihydropyridine or Non-dihydropyridine**

**Verapamil**, Extended release: Initial: 180mg – 480mg/day; Immediate realse Initial: 80-160 mg, P.O., TID

**Amlodipine**, 5-10mg/day P.O.,daily

**Felodipine,** 2.5-10mg/day P.O.

**Nifedipine slow release**, 20-180mg/day P.O.

**Do not combine verapamil or diltiazem with beta blockers**

3. **Long acting Nitrate**

**Isosorbide Dinitrate**, 10mg, 8-12 hourly P.O

**ADRs:** headache, lightheadedness, postural hypotension, tachycardia, flushing, peripheral, tolerance to nitrate edema

**C/Is:** Hypersensitivity to nitrates, concurrent use with phosphodiesterase-5 (PDE-5) inhibitors (e.g. sildenafil, vardenafil), angle-closure glaucoma, severe anaemia

**Dosage forms:** Tablet, oral: 5 mg, 10 mg, 20 mg or extended release capsule, 40mg

**Antiplatelet therapy**

**Aspirin**, 75 to 162 mg, P.O. daily

**ADRs:** GI irritation, bleeding, skin reaction and broncho-spasm

**C/Is:** Active bleeding, history of GI bleeding associated with Aspirin, allergy to Aspirin

**Dosage forms:** Tablet, 75mg, 81mg,100mg

**Alternative**-When Aspirin is contraindicated or not tolerated

**Clopidogrel**, 75mg, P.O, daily

**Statins (HMG CoA reductase inhibitors**)-options

**Simvastatin**, P.O, 10-40mg/day

**Atorvastatin**, P.O., 10-80mg/day

**Rosuvastatin**,P.O., 5-20mg/day

**Lovastatin**,P.O., 20-80 mg/day

## 8. Acute Coronary Syndrome (ACS)

ACS describes a group of clinical entities that are characterised by severe, acute myocardial ischemia or infarction resulting from thrombotic occlusion of coronary artery/ies as a result of

atherosclerotic plaque erosion/rupture. Rarely, the ischemia could be due to coronary artery spasm. ACS is a medical emergency and should be managed in the intensive care unit.

ACS comprises the following three clinical entities:

1. **ST-segment elevation myocardial infarction (STEMI**) – Significant ST elevation or new left bundle branch block (LBBB) on ECG, elevated cardiac enzymes (Troponin and/or CKMB) and symptoms of myocardial ischemia (typical or atypical).
2. **Non-ST-segment elevation myocardial infarction (NSTEMI**) – No ST elevation on ECG (other ECG evidence of ischemia may or may not be present), elevated cardiac enzymes and symptoms of myocardial ischemia (typical or atypical).
3. **Unstable angina-**symptoms of myocardial ischemia (typical or atypical) but no elevation in cardiac enzymes, with or without ECG changes indicative of ischemia.
   Unstable angina is considered to be present in the following circumstances:
   - Rest angina >20 minutes in duration
   - New onset angina
   - Increasing angina- more frequent or longer in duration, or occurs with less exertion than previous angina.

**Clinical features**

Chest pain of:

- Acute onset but not very sudden
- Diffuse and usually difficult to localize. Localization of the site with a single finger makes the ischemia to be less likely. Retrosternal, precordial
- Varying degree but often severe. The intensity may wax and wane
- Described as tightness, heaviness or constrictive in nature
- Persisting for more than 20 minutes
- Not relieved by rest or nitroglycerin
- May radiate to the arm/s, the neck or jaw, the upper abdomen (epigastrium), the back (inter scapular region)

**Other symptoms include sudden onset of the following:**

- Nausea
- Vomiting
- Sweating
- Shortness of breath or fatigue

- Collapse

**Some patients with ACS present without chest pain. These presentations include dyspnea alone, nausea and/or vomiting, palpitations, syncope and cardiac arrest. Elderly, diabetic and female patients are more likely to present with painless ACS.**

**Physical findings may include:**

- Excessive sweating, respiratory distress
- Pulse: Tachycardic or bradycardic or normal. It can irregular or regular, feeble or full
- Blood pressure: low/unrecordable, high or normal
- Bilateral crepitations in the chest when there is left ventricular failure
- Presence of a third or fourth heart sound

**Investigations**

- Standard 12 lead ECG-should be done and interpreted immediately, ECG needs to be done serially if the initial one is normal or there is ongoing/recurrent chest pain
- Cardiac enzymes: CK-MB, troponins
- BUN and creatinine, electrolytes
- Random blood sugar
- Serum lipid profile
- Random blood glucose
- CBC
- Chest X-ray
- Echocardiography

**N.B-Patients should not be moved outside the critical care unit for the sake of investigations such as Chest X-ray and Echocardiography**.

**Treatment**

**Objectives**

- Relieve distress and pain
- Limit infarct size

- Prevent re-infarction
- Prevent as well as treat electrical and mechanical complications i.e. Arrhythmias and Heart Failure
- Prevent embolic complications
- Halt cardiac remodeling

**Non pharmacologic**

- Insert intravenous cannula for medications. Avoid intravenous fluid administration unless specifically indicated e.g. Right ventricular infarction with hypotension
- Reassure patient and encourage strict bed rest for at least 12 hrs. Patients can be seated after 24hrs, walk in the room after 48-72 hrs if there are no complications or ongoing pain
- Put the patient NPO or only clear liquids by mouth for the first 6–12hrs
- Encourage cessation of smoking
- Ensure weight reduction (in overweight and obese individuals)

**Pharmacologic**

**Immediate treatment –** All of the following:

1. **Oxygen** via nasal cannula or face mask if the patient $SPO_2$ is < 90% or in respiratory distress
2. **Nitroglycerin**, sublingual, 0.4 to 0.5mg every 05 minutes for a maximum of three doses
3. **Morphine**, IV, 2 to 4mg, with increments of 2 to 8mg repeated at 5 to 15 minute intervals, should be given for the relief of chest pain or anxiety
4. **Aspirin**, (chew or disperse if dispersible), 300mg stat P.O. then 75-162mg, oral, daily
5. **Clopidogrel**, Loading dose of 300-600mg followed by 75mg/d P.O
6. **Anticoagulation – unfractionated heparin or low molecular weight heparin**

**Unfractionated Heparin (UFH)**, Bolus 60 U/kg (maximum 5,000 U) IV, followed by infusion of 12 U/kg per/h (imaximum 1,000 U/h) titrated to a PTT 50 –70s

**ADRs:** immune-mediated thrombocytopenia, haemorrhage, skin necrosis, hypersensitivity reactions, osteoporosis after prolonged use and rarely alopecia

**C/Is:** Hypersensitivity to heparin, severe thrombocytopenia;

**D/Is:** Aspirin, captopril and ibuprofen, nitroglycerin, omega-3 fatty acids

**P/Cs:** hepatic impairment and renal failure; spinal or epidural anaesthesia

**Dosage forms:** Injection (solution for injection) 1000U/ml, 5000 U/ml, 10,000U/ml, 12,500 U/ml, 25,000U/ml, Injection, 1000IU in 500ml Normal saline.

*OR*

**Enoxaparin**, 1 mg/kg SC every 12 h; the first dose may be preceded by a 30mg IV bolus

**Dosage forms:** Injection, 20mg/0.2ml, 40mg/0.4ml, 60mg/0.6ml, 80mg/0.8ml

**Warfarin** is indiacted for patients with anterior STEMI or mural thrombus only and continued for three months only.

**Metoprolol**, 5mg, I.V, every 5 minutes for 3 doses; thereafter 50 mg, P.O., QID, beginning 15 minutes after last I.V dose. After 48 hours give a maintenance dose of 100mg P.O.,BID.

**If Metoprolol is not available do not hesistate to use other beta blockers(e.g. Atenolol, Propranolol).**

**Avoid beta blockers if the patient has significant pulmonary congestion or hypotension**.

**ACEI/ARBs**, If there is pulmonary congestion, depressed LV ejection fraction(< 40%), anterior STEMI). Start within 24 hours, if there is no hypotension. Start with low dose and increase gradually.

**Enalapril**, 2.5mg-10mg P.O., BID

**Lisinopril**, 5-20mg P.O., daily

**Captopril**, 6.25-25mg P.O., TID

**Statins**-Give high dose statin to all patients irrespective of lipid levels

**First line statin**: **Atorvastatin**, 80mg P.O.,. daily

**Alterantive statins**: **Rosuvastatin** 20mg/day, **Simvastatin** 40mg/day

**Thrombolytics**

**Indication**-any patient with **STEMI** who presents within 12 hours of symptom onset and has no contraindications for fibrinolysis.

**Contraindications**

- A history of cerebrovascular haemorrhage at any time
- A nonhaemorrhagic stroke or other cerebrovascular event within the past year
- Marked hypertension (SBP>180mmHg and/or DBP >110mmHg) at any time during the acute presentation
- Suspicion of aortic dissection
- Active internal bleeding (excluding menses)

**Relative contraindications**- risk:benefit ratio should be considered

- Current use of anticoagulants (INR of 2)
- A recent (<2 weeks) invasive or surgical procedure
- Prolonged (>10 min) cardiopulmonary resuscitation
- Known bleeding diathesis
- Pregnancy
- Haemorrhagic ophthalmic condition (e.g. haemorrhagic diabetic retinopathy)
- Active peptic ulcer disease
- History of severe hypertension that is currently adequately controlled

**Table 14 - Dosage regimens of Fibrinolytics**

| Medicine | Recommended IV regimen | Advantages and limitations |
|---|---|---|
| **Streptokinase** | 1.5 million units over 30 to 60 minutes | Generally less costly but outcomes inferior |
| **Alteplase** | 15mg bolus<br>then<br>0.75 mg/kg (maximum 50 mg) over 30 minutes<br>then<br>0.5mg/kg (maximum 35 mg) over the next 60 minutes | More expensive and more difficult to administer because of short half-life |
| **Reteplase** | 10 U over two minutes<br>then | Similar outcomes as alteplase but easier to administer |

| | | |
|---|---|---|
| | Repeat 10 U bolus at 30 minutes | |
| **Tenecteplase** | Single IV bolus over 5-10 minutes<br>60kg = 30mg 60-69kg = 35mg<br>70-79kg = 40mg 80-89kg = 45mg<br>≥90kg = 50mg | Less noncerebral bleeding and less need for transfusion<br>Easier to administer |

**Doasge forms:**

| | |
|---|---|
| Alteplase | Powder for injection, 50mg, 100mg |
| Reteplase | Powder for injection, 10.4Unit |
| Tenecteplase | Powder for injection, 50mg |

**Refer:** All patients with suspected ACS to specialized center with coronary ICU care facility and/or coronary interventions if proper ambulance transport is available. It should be possible to notify the center and reach within 30 minutes to 2hrs**.**

### 9. Rheumatic Fever

Rheumatic fever is a systemic illness in which there is inflammation of several organs. It occurs as non-suppurative complication of group A streptococcus pharyngitis and may consist of arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules. The onset of symptoms occurs 1-3 weeks after the throat infection. Damage to cardiac valves is the most serious complication and is usually progressive. In developing countries, it is a major cause of permanent damage to the heart. The disease occurs mainly in children of school age.

**The major manifestations are:**

- Migratory arthritis (predominantly involving the large joints)
- Carditis and valvulitis (eg, pancarditis)
- Central nervous system involvement (eg, Sydenham chorea)
- Erythema marginatum
- Subcutaneous nodules

**The minor manifestations are:**

- Arthralgia, Fever
- Elevated acute phase reactants [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)]
- Prolonged PR interval

**Supporting evidence of preceding streptococcal infection**-Elevated or rising ASO titre, positive throat culture

Diagnosis – requires the presence of supporting evidence for preceding streptococcal infection and the following:

1. Primary episode of Rheumatic Fever or recurrence without established rheumatic heart disease-Two major, or one major and two minor manifestations.
2. Recurrent attack of Rheumatic fever with established rheumatic heart disease-two minor manifestations.
3. Rheumatic chorea or insidious onset carditis-neither evidence of preceding streptococcal infection nor other major manifestation needed.

**Investigations**

- CBC
- ESR/CRP
    - Throat swab for culture
    - Antistreptolysin O(ASO) titre
    - Electrocardiogram
    - Echocardiogram
- Chest X-ray

**Treatment**

**Objectives**

- Eradicate streptococcal throat infection
- Prevent recurrent episodes of rheumatic fever and further valvular damage
- Treat Heart Failure , if co-existent
- Control inflammation and relive symptoms of arthritis

**Non-pharmacologic**

- Bed rest if the patient has severe rheumatic carditis or arthritis/arthralgia only.
- Salt restriction if there is associated Heart Failure

**Pharmacologic**

1.**Antibiotic (primary prevention**)

2.**Conventional therapy for Heart Failure**

3.**Anti-inflammatory**

**First line**

**Aspirin**, 4-8 grams per day P.O. in 4 divided doses

Add a GI prophylaxis – PPI (e.g. Omeprazole 20mg, P.O., BID)

**Alternative**

**Prednisolone** (consider its use in severe carditis only), 1–2mg/kg per day (maximum, 80mg) only required for a few days or up to a maximum of 3 weeks.

4.**Prevention of recurrent rheumatic fever (secondary prevention**)

**First line**

**Benzathine penicillin**, 1.2 million units or 600,000 units if <30 kg, every 4 weeks. It can be given every 3 weeks, to persons considered to be at particularly high risk.

**Alternative** (if penicillin allergic)

**Erythromycin**, 250mg, P.O. BID

*OR*

**Sulfadiazine**, 1gm, P.O., QD

**Table 15 - Duration of secondary prophylaxis**

| **Category of Patient** | **Duration of Prophylaxis** |
|---|---|
| Rheumatic fever without carditis | For 5 years after the last attack or 18 years of age (whichever is longer) |
| Rheumatic fever with carditis with no residual valvular disease or mild mitral regurigitation | For 10 years after the last attack, or 25 years of age (whichever is longer) |
| Rheumatic fever with persistent valvular disease or after valve surgery | Life long |

## CHAPTER III : ENDOCRINE DISORDERS

### 1. Adrenal Insufficiency

Adrenal insufficiency is a clinical condition where the amount of cortisol is insufficient to meet the body's needs. The condition is associated with fluid and electrolyte imbalance and may result in acute circulatory collapse, in a state commonly referred to as adrenal crisis. Adrenal crisis is a medical emergency.

Destruction of the adrenal gland by auto-antibodies (Addison's disease) or infectious conditions involving the gland (e.g. tuberculosis, HIV, meningococcemia), sudden cessation of corticosteroid therapy after prolonged use, pituitary failure from severe postpartum haemorrhage, pituitary surgery or tumour are the major causes of adrenal insufficiency. Stress (e.g. infection, severe trauma, surgery, and dental procedures) precipitates adrenal crisis.

**Clinical features**

- Easily fatigued
- Vague abdominal complaints/abdominal pain
- Nausea, vomiting, diarrhoea, collapse, dehydration, craving for salt
- Low blood pressure (postural drop in blood pressure)
- Darkening of oral mucosa, gums, skin, palms and soles in some patients

**Investigations**

- CBC
- Urine and blood cultures, if indicated
- Blood urea and electrolytes
- Blood glucose
- CXR, Abdominal ultrasound
- Plasma cortisol-morning sample
- ACTH stimulation test-refer to specialist

**Treatment**

**Objectives**

- Correct the fluid and electrolyte imbalance
- Replace corticosteroids
- Identify cause and treat any precipitating factor

**Non pharmacologic**

- Encourage fluid and salt intake

**Pharmacologic**

**Acute therapy**

- Intravenous fluid replacement 0.9% Sodium Chloride in 5% Glucose (Dextrose in Saline), IV, 1 litre 4-6 hourly
- Hydrocortisone, IV, 200 mg stat, followed by 100 mg, IV, 6 hourly until condition is stable

**Adjunct treatment**

- Treat infection, if present or suspected,with appropriate medication.

**N.B. The IV hydrocortisone therapy may be required for days. Do not rush to change to maintenance therapy. Start maintenance oral therapy when patient is stable.**

**Maintenance therapy**

**For patients with previous or newly diagnosed adrenal or pituitary disease**

**Prednisolone**, oral, 5 mg morning and 2.5 mg evening each day

- Patients on corticosteroids should report to a hospital if they become ill.
- Patients SHOULD NOT stop treatment if they become ill. Rather double the regular doses of corticosteroids where required.
- Revert to hydrocortisone, IV for even minor surgical procedures including labor and delivery

## 2. Cushing's Syndrome

This condition results from high levels of cortisol in the blood and is associated with various changes in the body including the development of obesity, hypertension, diabetes and osteoporosis. It is commonly caused by pituitary tumour/adenoma, adrenal tumour or prolonged and excessive intake or abuse of corticosteroids.

**Clinical features**

- Weight gain, truncal obesity, prominent supraclavicular fat pad, rounded or 'moon' face
- Easy bruising of skin, striae (purplish stretch marks), excess facial and body hair

- Menstrual irregularity and sub-fertility
- Weakness of the thigh muscles
- Rounded or 'moon' face
- Hypertension

**Investigations**

- Blood sugar, Fasting lipid profile
- Serum electrolytes
- Serum basal cortisol
- 24 hour urinary cortisol, and
- Low-dose dexamethasone suppression test – to differentiate patients with Cushing's syndrome those who do not have Cushing's syndrome
- High-dose dexamethasone suppression test-to distinguish patients with Cushing's disease (Cushing's syndrome caused by pituitary hypersecretion of ACTH) from patients with the ectopic ACTH
- Imaging for localization i.e. pituitary MRI and or abdominal CT-should be requested by specialist after biochemical confirmation of the presence of hypercortisolism.

**N.B.**The diagnostic studies should be ordered and interpreted by an experienced specialist.

**Treatment**

**Objectives**

- Normalize plasma level of cortisol
- Correct electrolyte imbalance
- Correct plasma glucose
- Correct blood pressure
- Prevent complications of excess plasma cortisol

**Non pharmacologic**

Pituitary or adrenal surgery respectively when tumours in the pitutary or adrenal glands have been diagnosed.

**Pharmacologic**

Manage hypertension and diabetes **as per the standared treatment guidelines** and refer patient for definitive treatment.

**Ketoconazole**-treatment needs expert opinion. Refer patients to experienced specilalist.

### 3. Diabetes Mellitus

Diabetes mellitus describes a group of disorders which are phenotypically characterised by persistently high blood glucose levels. Diabetes is a major cause of cardiovascular disease, chronic kidney disease, visual loss and amputations.

**Current diagnostic criteria for the diagnosis of diabetes mellitus**:

1. Fasting plasma glucose (FPG) ≥126 mg/dl
2. Haemoglobin A1C ≥6.5%
3. A random plasma glucose ≥200mg/dl, in patients with classic symptoms of hyperglycemia or hyperglycemic crisis
4. Two-hour plasma glucose ≥200mg/dl during an oral glucose oral tolerance test

**The classification of diabetes includes four clinical classes**

1. **Type 1 diabetes**- results from β-cell destruction (immune mediated or idiopathic), leading to absolute insulin deficiency
2. **Type 2 diabetes**-results from a progressive insulin secretory defect on the background of insulin resistance
3. **Other specific types of diabetes** e.g. genetic defects in β-cell function, genetic defects in insulin action, diseases of the exocrine pancreas, and medicine-induced diabetes
4. **Gestational diabetes mellitus (GDM)**-diabetes diagnosed during pregnancy in previously non-diabetic woman.

**Clinical features**

- No recognizable symptoms in many individuals particularly in type 2 diabetes
- Large amounts of urine (polyuria)
- Thirst and excessive drinking of water
- Unexplained weight loss

- Blurred vision
- Recurrent skin infections
- Recurrent itching of the vulva
- Symptoms related to chronic complications
- Abnormal sensory/motor neurologic findings on extremities
- Foot abnormalities (various deformities, ulcers, ischemia)
- Visual impairment

**Investigations**

Newly diagnosed patient:

- Fasting or random blood glucose
- Glycated haemoglobin (HbA1c)
- Urine ketones
- Urine protein
- Blood urea, electrolytes and creatinine
- Fasting lipid profile
- ECG (adults)

**N.B.** In the absence of severe hyperglycemia, the diagnosis of diabetes mellitus should be confirmed with repeat fasting blood sugar determination.

**Treatment**

**Objectives**

- Relieve symptoms
- Prevent acute hyperglycemic complications
- Prevent chronic complications of diabetes
- Prevent treatment-related hypoglycemia
- Achieve and maintain appropriate glycemic targets

- Ensure weight reduction in overweight and obese individuals

**Treatment of type-2 diabetes mellitus is not just treatment of hyperglycemia. It includes management of all cardiovascular risk factors (hypertension, dyslipidemia and obesity, smoking)**

**Treatment of Type-2 Diabetes Mellitus**

**Non pharmacologic**

1. **Medical Nutrition Therapy (MNT)**

   - Avoid refined sugars as in soft drinks, or adding to their teas/other drinks.
   - Be encouraged to have complex carbohydrates
   - Low in animal fat
   - Increase in the amount of fibre e.g. vegetables, fruits and cereals

2. **Exercise**

   - Regular moderate-intensity aerobic physical activity for at least 30 minutes at least 5 days a week or at least 150 min/week.
   - Encourage resistance training three times per week

3. **Self-blood glucose monitoring (SBGM)**

4. **Screening and treatment of micro and macro vascular complications**

**Table 16 - Glycemic Targets for Non-Pregnant Adults with Diabetes**

| | |
|---|---|
| Fasting plasma glucose (capillary) | **70-130 mg/dl** |
| Postprandial (1–2 hrs after the beginning of the meal) plasma glucose | **< 180 mg/dl** |
| Haemoglobin A1C | **< 7%** |

**CAUTION!**

**For older adults, for those with reduced life expectancy, higher cardiovascular disease burden and advanced chronic kidney disease glycemic targets should be high (less ambitious). Avoidance of hypoglycemia, decreasing extreme hyperglycemia and medicine safety should be the focus.**

**Pharmacologic**

1. **Oral blood glucose lowering medicines**

**Metformin**

- the first line medicine for initiation of therapy
- if intolerant to metformin or have a contraindication to it, sulfonylureas can be the initial treatment medicine.

**Metformin**, 500mg, P.O.daily with meals.Titrate dose slowly depending on blood glucose levels or HbA1C to a maximum dose 2000-2500mg.

**ADRs:** abdominal discomfort and diarrhoea, lactic acidosis

**C/Is:** Serum creatinine >1.5 mg/dL (men) >1.4 mg/dL (women), CHF, radiographic contrast studies, seriously ill patients, acidosis, hepatic failure

**Dosage forms**: Tablet, 500mg, 850mg,1000mg

If blood sugar targets are not achieved,

**ADD**

**Sulfonylureas**

**Glibenclamide**, 2.5mg-5mg, P.O.daily 30 minutes before breakfast.

- Titrate dose slowly depending on HbA1c and/or fasting blood glucose levels to 15mg daily.
- When 7.5mg per day is needed, divide the total daily dose into 2, with the larger dose in the morning.
- Avoid in the elderly and patients with renal impairment.

**ADRs:** anorexia, nausea, vomiting, abdominal discomfort and diarrhoea;

**C/Is:** renal diseases, hepatic disease, alcoholism.

**Dosage forms:** Tablet, 5 mg.

*OR*

**Glimepiride**, 1-2mg P.O. QD, administered with breakfast or the first main meal

- Titrate dose slowly depending on HbA1c and/or fasting blood glucose levels.
- Allow several days between dose titrations
- usual maintenance dose: 1-4mg once daily; maximum dose of 8mg once daily

**ADRs:** dizziness, headache, hypoglycemia, weakness, heartburn, vomiting

**C/Is:** hypersensitivity to sulfonyl ureas or sulfonamides, breast feeding, DKA

**D/Is:** ketoconazole, NSAIDs, beta blockers, chloramphenicol, cimetidine, fluconazole, salicylates, sulfonamides,

**P/Cs:** pregnancy, hypoglycemia may be produced during use.

**Dosage form:** Tablet 1mg, 2mg, 4mg

**Insulin therapy in type 2 diabetes mellitus**

Indications for insulin therapy:

- Failure to control blood glucose with oral medicines
- Temporary use for major stress, e.g. surgery, medical illness
- Severe kidney or liver failure
- Pregnancy
- Initial therapy for a patients presenting with HbA1C >10%, fasting blood glucose >250 mg/dl, random glucose consistently >300 mg/dl, or ketonuria
- In patients in whom it is difficult to distinguish type 1 from type 2 diabetes

**Table 17 - Insulin initiation and dose increment in type-2 diabetes**

| Regimen | Insulin type | Starting dose | Increment | Alternative dosing |
|---|---|---|---|---|
| **Add on**-to oral agent | NPH (intermediate to long acting) | 10 units before bedtime | 2–4 units in 3-7 days | Higher dose may be started in patients with severe |

| | | | | |
|---|---|---|---|---|
| | | | | hyperglycemia |
| **Substitution** Therapy (Insulin substituting all oral agents) | NPH | 15 units<br>• 10 units, 30 minutes before breakfast<br>• 5 units, 30 minutes before supper | 4 units in 3-7 days | Higher dose may be started in patients with severe hyperglycemia |

**N.B.** If postprandial hyperglycemia remains high with good fasting blood sugar while patient is on basal insulin regimen as depicted above; pre meal short acting agents can be added.

**ADRs:** hypoglycemia, hypersensitivity, hypokalemia

**C/Is:** hypoglycemia, hypersensitivity to NPH or any component of the formulation

**Dosage forms:** Injection, 100u/ml

**Management of other cardiovascular risks**

**Aspirin**, 75–162mg, P.O., once/day

Indications:

- Increased cardiovascular risk (10-year risk >10%)
- Men >50 years of age or women >60 years of age who have at least one additional major risk factor (Hypertension, Smoking, Dyslipidemia, Albuminuria and family history of CVD)

**Statins**

Indications:

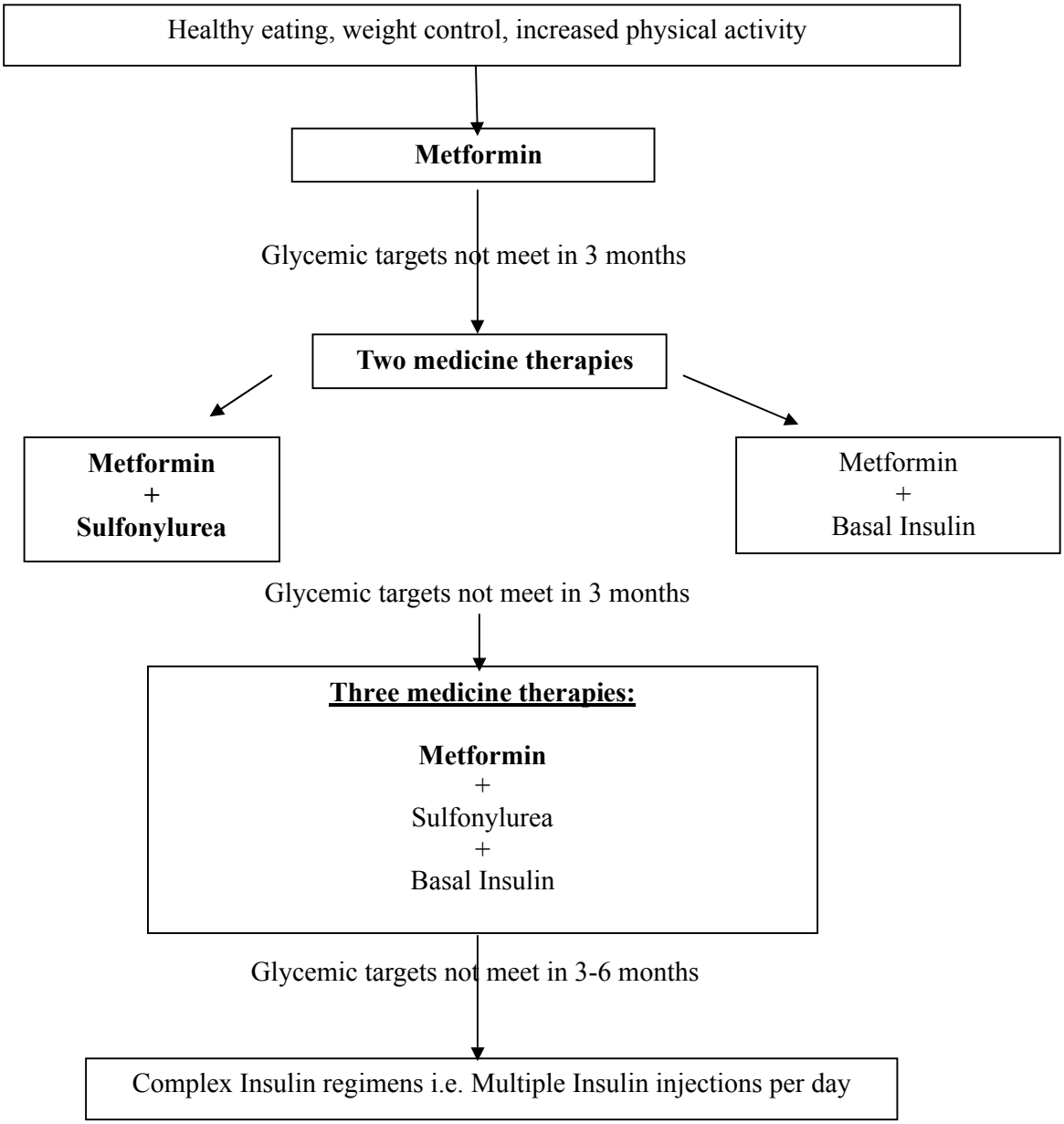
- Overt CVD , >40 years of age and have one or more other CVD risk factors
- Without CVD and <40 years- if LDL cholesterol remains >100mg/dl or have multiple CVD risk factors**,**

**Options**

- **Simvastatin**, 10-40mg, P.O. daily
- **Atorvastatin,** 10-40mg, P.O. daily

- **Rosuvastatin** 5-20mg P.O. daily
- **Lovastatin** 20-80mg P.O. daily
- **Antihypertensives (See treatment of hypertension)**-ACE inhibitors or ARBS are the medicines of choice

**Figure 1 - Sequential therapy in Type 2 Diabetes (modified from Diabetes Care Diabetologia.19 April 2012)**



**Treatment of Type 1 Diabetes Mellitus**

**Non pharmacologic**

See type 2 Diabetes

**Pharmacologic**

Insulin

**Insulin regimen in type 1 Diabetes Mellitus**

1. **Conventional insulin therapy**-describes simpler non-physiologic insulin regimens, such as single daily injections, or two injections per day (including a combination of regular or short-acting and NPH insulin)

2. **Intensive insulin therapy**-describes treatment with **three or more injections per day** or with continuous insulin infusion with an insulin pump.

   Intensive insulin therapy requires:

   - Monitoring blood sugar before breakfast (fasting), before lunch, before dinner & before bed.
   - Counting and recording carbohydrates.
   - Adjusting insulin doses in response to given glucose patterns.
   - Coordinating diet, exercise, and insulin therapy.
   - Responding appropriately to hypoglycemia

**Designing insulin therapy**

**Total insulin dose per day**

**Initiation**, 0.2 to 0.4 units/kg/day

**Maintenance – highly variable** roughly 0.6 to 0.7 units/kg/day

**Regimen options-with NPH and regular insulin (commonly available in Ethiopian setting)**

1. **NPH** twice daily injection – before breakfast and at bed time **and Regular Insulin** twice daily injection-before breakfast and before supper

2. **70/30 (**70% **NPH** & 30% **regular)** twice daily injection-before breakfast and before supper

3. **NPH** twice daily injections – before breakfast and before bedtime

**Table 18-Properties of common insulin preparations and insulin analogues**

| Preparation | Onset(hr) | Peak(hr) | Effective Duration(hr) |
|---|---|---|---|
| **Short acting** | | | |
| Aspart,Glulisine, Lispro | 0.25 | 0.5–1.5 | 3–4 |
| – Regular (more intermediate than short acting) | 0.5–1.0 | 2–3 | 4–6 |
| **Long acting** | | | |
| Detemir, Glargine | 1–4 | minimal | Up to 24 |
| NPH | 1–4 | 6–10 | 10–16 |
| **Mixed** | | | |
| 70/30 = 70% NPH + 30% regular | 0.5–1.0 | Dual peak (as regular + as NPH) | 10-16 |

## 4. Diabetic Ketoacidosis (DKA) And Hyperglycemic Hyperosmolar State (HHS)

Diabetic ketoacidosis (DKA) is a condition in which there is a severe deficiency of insulin resulting in very high blood glucose. Fat is therefore broken down as an alternative source of energy with ketones/ketoacids as a by-product. This state of severe hyperglycemia and ketone body production results in severe metabolic, fluid and electrolyte abnormalities.

It often occurs in type 1 diabetes patients but may also occur in type 2 diabetes. The most common settings in which DKA occurs include:

- Previously undiagnosed and untreated diabetes

- Interruption therapy
- Stress of intercurrent illness (e.g. infection, myocardial infarction, stroke, surgery, complicated pregnancy etc.)

Hyperglycemic hyperosmolar state (HHS) is a hyperglycemic emregncy that occurs in type 2 DM due to relative insulin deficiency and inadequate fluid intake. Apart from acidosis the manifesations, risk factors and management of HHS is similar to DKA

**Clinical features**

- Excessive urination
- Excessive thirst and drinking of water
- Nausea, vomiting
- Abdominal pain
- Alteration in sensorium or collapse
- Symptoms of infection or other underlying condition
- Dehydration with dry skin, reduced skin turgor or sunken eyes
- Deep and fast breathing
- Low blood pressure
- Fast and weak pulse
- 'Fruity' breath (smell of acetone)
- Confusion, stupor or unconsciousness
- Evidence of infection, recent surgery, stroke etc.

**Investigations**

- Random blood glucose (usually >300mg/dl)
- Urine glucose (usually >3+)
- Urine ketones (usually >2+)

- BUN and Creatinine
- Electrolytes
- Blood film for malaria parasites
- CBC
- Blood and urine cultures if indicated
- Chest X-ray-for pneumonia or tuberculosis
- Electrocardiogram in older patients to exclude acute myocardialinfarction as a precipitating factor

**Treatment**

**Objectives**

- Replace fluid losses
- Replace electrolyte losses and restore acid-base balance
- Replace deficient insulin
- Seek the precipitating cause and treat appropriately

**Non Pharmacologic**

- Admit to intensive care unit (or a ward patient can be very closely observed)
- Closely monitor fluid input and urine output

**Pharmacologic**

– See the following table

**Table 19 - Management of DKA or HHS**

1.**Replace fluids**:

2–3L of 0.9% NS in 1–3 hrs; the reduce to 250–500 mL/h; change to 5% glucose when plasma glucose reaches 250 mg/dl in DKA and 300mg/dl in HHS. HHS requires more fluid. Assess hydration status, BP and urine output frequently

2. **Administer short-acting insulin**:

Regular Insulin 10units IV and 10 units IM, stat, then 0.1 units/kg per hour by continuous IV infusion OR 5 units, I.V boluses every hour.

If serum glucose does not fall by 50 to 70 mg/dL from the initial value in **the 2-3 hours**, the insulin infusion rate should be doubled every hour until a steady decline in serum glucose is achieved

3.**Potassium**

All patients with DKA have potassium depletion irrespective of the serum K+ level.-

- If the initial serum K+ is <3.3 mmol/L, do not administer insulin until the K+ is corrected.
- If the initial serum K + is >5.3 mmol/L, do not supplement K+ until the level reaches < 5.3.
- If K+ determination is not possible delay intiation of K+ replacement until there is a reasonable urine put(>50 ml/hr)
- The serum potassium should be maintained between 4.0 and 5.0 meq/l
    - Add 40–60 meq/l of IV fluid when serum $K^+$ < 3.7 meq/L
    - Add 20-40meq/l of IV fluid when serum K+ < 3.8-5.2 meq/l

4.**Precipitant identification and treatment**-noncompliance, infection, trauma, infarction. Initiate appropriate workup for precipitating event (cultures, CXR, ECG)

5.**Follow up of response-** Blood glucose every 1–2hrs, Urine ketones every 4hr,electrolytes (especially K+) every 6 h for first 24 h.

6.**Continuation of treatment** – the above treatment should continue until the patient is stable, ketone free.

7.**Transition**-Insulin infusion may be decreased to 0.05–0.1 units/kg per hour or 2-3 units,IV, hourly.

Overlap in insulin infusion and SC insulin injection for about 3-5hrs

8.**SC long acting Insulin** – start SC NPH as soon as the patient eats. Monitor bloog glucose evry 4-6 hour and give correctional doses of regular insulin when needed. DO NOT USE SLIDING SCALE

## 5. Gout

This condition results from the deposition of microcrystals of uric acid in the joints and peri-articular tissues of the affected joints. It is often, but not invariably, associated with elevated blood uric acid levels. This implies that gout may be present even when the level of uric acid in the blood is normal, while patients with high levels of uric acid may not necessarily have attacks of gout. Acute symptoms are often precipitated by the consumption of alcohol and foods rich in purines e.g. red meat, sea foods, as well as trauma, surgery, starvation and infection. Persistent hyperuricemia may be associated with uric acid crystal deposition in subcutaneous tissues (tophus) and in other tissues such as the kidneys and tendons.

Gout can be a manifestation or complication of other diseases such as metabolic syndrome, hematological malignancies, chronic kidney disease and medicines like thiazide and loop diuretics, cytotoxic medicines and pyrazinamide

The three classic stages in the natural history of progressive urate crystal deposition disease (gout) are:

- Acute gouty arthritis
- Intercritical (or interval) gout
- Chronic recurrent and tophaceous gout

**Clinical features**

The clinical manifestations include one or more of the following:

- Recurrent attacks of acute inflammatory arthritis
- Chronic arthropathy
- Accumulation of urate crystals in the form of tophaceous deposits
- Uric acid nephrolithiasis
- A chronic nephropathy that in gouty patients is most often due to comorbid states

**Typical acute attack**

- Excruciating pain, redness, swelling, and disability.
- Maximal severity of the attack is usually reached within 12 to 24 hours.

- 80% of initial attacks involve a single joint, most often at the base of the great toe (known as **podagra**), or the knee
- Affected joint is inflamed, swollen and tender

**Investigations**

- CBC, ESR,BUN, creatinine, Serum uric acid, Blood glucose, Serum lipids
- X-ray of affected joint

**Treatment**

**Objectives**

- Relieve pain immediately
- Reduce joint inflammation
- Prevent recurrent attacks and joint damage
- Prevent uric acid crystal deposition in soft tissues

**Non Pharmacologic**

- Rest affected joint
- Identify and manage underlying or predisposing factors
- Weight reduction in obese or overweight individuals
- Dietary modification (low purine diet)

**Pharmacologic**

1. **Acute Gout**

**NSAIDS**

**Ibuprofen**, 800mg P.O.TID with meals. If not tolerated: 400 mg 8 hourly

An extra **night-time** dose of a NSAID may be added in some patients with severe nocturnal pain/morning stiffness

*OR*

**Diclofenac**, Immediate or delayed release tablet: 150-200mg/day P.O., in 2-4 divided doses. Rectal suppository, Insert 50mg or 100mg rectally as single dose to substitute for final daily dose (maximum combined dose [rectal and oral]: 150mg/day)

*OR*

**Indomethacin,** 25-50mg P.O. BID or TID; maximum dose: 200mg/day **or** Rectal suppository, 100mg, BID or once at bed time

**Alternative** (when NSAIDS are not tolerated or contraindicated)

**Prednisolone**, 20-40mg P.O. for one to two wks and tapered over another one to two wks

**Do not give allopurinol in the acute phase. It may worsen or prolong the attack. Start it only when pain is under control i.e. after approximately 2 weeks. NSAIDs are not to be given as maintenance or prophylaxis**

## 2. Chronic gout

- If possible, avoid known precipitants
- Treat secondary causes when possible
- Assess renal function and blood uric acid level

**Uric acid lowering therapy**

Indicated for

- >2 acute attacks per year
- chronic tophaceous gout
- Uric acid renal stones
- urate nephropathy

**Allopurinol**, 100 mg P.O. daily.

- Increase monthly by 100mg according to uric acid blood levels and eGFR.
- Most patients will be controlled with a dose of 300 mg daily

**N.B.** Do not stop uric acid lowering medicines during an acute attack

## 6. Hypothyroidism

The body requires thyroid hormones for normal metabolism and growth. Hypothyroidism is a condition in which there is a reduction in thyroid hormone production. In adults, it may be the cause of a slow metabolic rate, systemic problems and dementia. Antibody-related thyroid gland destruction, surgical removal of the thyroid, pituitary lesions or surgery, congenital, severe iodine deficiency are the major causes. Myxedema coma describes the most severe state of hypothyroidism and is a medical emergency.

**Clinical features**

- Intolerance to cold environments, constipation, weight gain, hair loss, dry skin
- Hoarse voice, lethargy, memory loss, depressed reflexes, dementia
- Abnormal menstrual periods and sub-fertility (in adult females)
- Puffy face, pallor, slow pulse (usually <60 per minute)
- Goitre may be present

**Investigations**

- Thyroid function tests-free T3, free T4, TSH

**Treatment**

**Objectives**

- Correct level of thyroid hormones
- Improve symptoms
- Prevent complications

**Non Pharmacologic**

None

**Pharmacologic**

**Levothyroxine**, oral, 25-200microgram daily (start with a low dose and adjust according to TSH levels)

| | |
|---|---|
| **ADRs:** | anginal pain, arrhythmias, palpitations, tachycardia, skeletal muscle cramps, diarrhoea, vomiting, tremors, restlessness, excitability, insomnia, headache, flushing, sweating, excessive loss of weight and muscular weakness. |
| **C/Is:** | thyrotoxicosis, cholestyramine or colestipol, sympathomimetics |
| **D/Is:** | warfarin |
| **P/Cs:** | hypopituitarism or predisposition to adrenal insufficiency; elderly, long-standing hypothyroidism, diabetes insipidus, diabetes mellitus; pregnancy; breast feeding. |
| **Dosage Forms***:* | Tablet, 0.05mg, 0.1mg |

**7. Thyrotoxicosis**

Excess thyroid hormone in the blood results in thyrotoxicosis. If left untreated, significant weight loss and cardiac complications, including Heart Failure , may occur. The major causes are toxic multi-nodular goiter, Grave's disease and hyper-functioning solitary adenoma.

**Clinical features**

- Weight loss despite increased appetite, Excessive sweating, Heat intolerance
- Tremors, Nervousness and irritability, Tremors, Moist palms
- Menstrual irregularity and sub-fertility

- Staring or protruding eyes
- Heart Failure , Rapid pulse rate which may be irregular
- Goitre often present but not always
- Smooth and diffuse goitre in Grave's disease
- Irregular goitre in toxic multi-nodular goiter

**Investigations**

- Thyroid function tests free T3, free T4, TSH
- Thyroid ultrasound scan

**Treatment**

**Objectives**

- Improve symptoms
- Prevent or treat complications e.g. Heart Failure , ophthalmopathy

**Non pharmacologic**

- Avoid stimulants e.g. Caffeine
- Partial thyroidectomy – should only be done after a state of euthyroidism is achieved with medical therapy
- Radioiodine ablation

**Pharmacologic**

**First line**

**Carbimazole,** P.O., Initial dose 15-60mg/day divided in 2-3 doses until euthyroid state is achieved. Maintenance dosage can vary from patient to patient in the range 5-15mg/day

**ADRs:** allergy, arthraigia, hepatitis, medicine fever and agrahennulocytosis

**C/Is:** impaired liver function

**Dosage forms:** Tablet 5mg, 20mg

**Alternative**

**Propylthiouracil**, Initial: 300 to 400mg/day in 3 divided doses ; until euthyroid state is achieved. Maintenance dosage can vary from patient to patient in the range 100-150mg/day

**ADRs:** Leukopenia, allergy, **agranulocytosis, hepatitis**, medicine fever, arthralgia;

**C/Is:** impaired liver function

**Dosage forms:** Tablet 25mg, 50mg,100mg

**N.B.** Duration of treatment depends on the specific cause of the hyperthyroidism. In Grave's disease, PTU can be stopped after 1-2 years of treatment. In case of toxic nodular goiter, treatment with PTU should be continued almost indefinitely unless surgically removed.

**Adjunct treatment**

**Beta blockers –** until euthyroid state is achieved**.** See options below

- **Propranolol**, 20-40mg, P.O, 8 hourly
- **Atenolol** 25-100mg, P.O., daily
- **Metoprolol** 25-100mg, P.O,daily

## CHAPTER IV : GASTROINTESTINAL TRACT AND LIVER DISORDERS

### 1. Constipation

Constipation is difficult to define. In general it may be defined as infrequent passage of stool. It may be caused by either organic or functional disorders. A new onset of constipation should be taken as an alarm sign for possible colorectal malignancy, hence investigation for the underlying cause should be performed before resorting to symptomatic treatment.

**Clinical features**

- Complaint of persistent, difficult, or infrequent, or seemingly incomplete defecation

**Investigation**

- Diagnosis is mainly clinical

**Treatment**

**Objectives**

- Improve symptoms
- Prevent large bowel obstruction

**Non pharmacologic**

- Removal of the underlying cause
- More fibre diet intake
- High residue diet intake
- Increased fluid intake

**Pharmacologic**

**I. Short term relief of severe constipation**

**Magnesium Sulphate**, 10-20mg P.O. in a glass of water, preferably before breakfast.

**ADRs**: colic

**C/Is:** acute gastro-intestinal conditions

**Dosage forms:** Magnesium sulphate crystals in sachets

**II. For chronic constipation**

**Treating constipation with laxatives of any type for long period of time is not advisable.**
**All patients with more than acute constipation should be evaluated for colonic malignancy.**
**The presence of exweight loss, anaemia, anorexia are strong indicators of malignancy.**

**First line**

**Bisacodyl**, 5 – 10mg, P.O. at night OR 10mg rectally in the morning

**ADRs:** mild

**C/Is:** insignificant

**Dosage forms:** Tablet, 5mg; suppository, 5mg, 10mg

**Alternatives**

**Cascara,** 40mg, P.O. at night.

**ADRs**: mild

**C/Is:** insignificant

**Dosage forms:** tablet, 125mg

*OR*

**Glycerin**, gm, rectally at night after moistening with water

**ADRs**: loose stool

**C/Is**: insignificant

**Dosage forms:** suppository, 1g, 1.36g, 2g, 2.76g

*OR*

**Liquid paraffin**, 10ml, P.O. every 8-12 hrs as required

**ADRs**: loose stool

**C/I:** insignificant

**Dosage forms:** semi-liquid preparation

## 2. Dyspepsia and Peptic Ulcer Disease

Dyspepsia describes a wide and common clinical entity which presents in one of the three ways:

1. Epigastric pain/burning (epigastric pain syndrome)
2. Postprandial fullness
3. Early satiety

Dyspepsia is caused by a number of disorders. The most common cause is functional (non-ulcer) dyspepsia followed by peptic ulcer disease. Gastro esophageal reflux disease (GERD), gastric cancer, medicine induced dyspepsia, biliary pain, chronic abdominal wall pain and pancreatitis are other possible causes.

**Clinical features**

Depending on the type of dyspeptic syndrome patients may present with predominant epigastric burning sensation/pain/discomfort, postprandial discomfort and fullness or be unable to finish a regular meal.

ALARM INDICATORS

| | |
|---|---|
| Advanced age (>55years) | previous gastric surgery |
| Unintended weight loss | Persistent vomiting |
| Progressive dysphagia/Odynophagia | Otherwise unexplained anaemia |
| Hematemesis | Palpable abdominal mass |
| Lymphadenopathy | Jaundice |

**Investigations**

- H. Pylori test-IgG serology or stool antigen or 13C-urea test
- Haemoglobin/hematocrit, stool for occult blood-when indicated
- Upper GI endoscopy or barium meal-when indicated

*H. Pylori* test needs to be done for patients with long standing dyspepsia younger than age 55 and no alarm symptoms after excluding the history of medicines (NSAIDS) and features of GERD (Gastro Esophageal Reflux Disease). "Test and treat" for H. Pylori can be practiced in these group of individuals

**Caution!**

**Serology test for H. Pylori should not be used as a test of cure/eradication. As a serology test could remain positive for a very long period of time despite eradication, patients should never be treated repeatedly with eradication regimen.**

**Treatment**

**Objectives**

- Decrease symptoms/improve quality of life
- Prevent development of complications

**Non pharmacologic**

- Avoid offensive substance intake

**Pharmacologic**

**I. *H. Pylori* negative**

**First line-Proton pump inhibitors, see options below**

**Omeprazole**, 20mg P.O., twice per day for 4-8 weeks

**Dosage forms:** Capsule, 20 mg

**Esomeprazole**, 40mg P.O., daily for 4-8 weeks

**Dosage forms**: Capsule, 20mg, Tablet (e/c), 20mg, 40mg

**Pantoprazole**, 40mg P.O., BID for 4-8 weeks

(For ADRs, C/Is D/Is and P/Cs see under omeprazole)

**Dosage forms:** Capsule, 15mg, 30mg, Tablet, 15mg, 30mg

**ADRs:** GI disturbances

**C/I:** pregnancy, lactation

**D/Is:** may enhance the effect of medicines like warfarin and phenytoin

**Alternatives-$H_2$ receptor blockers, see options below**

**Cimetidine**, 400mg P.O., BID for 4-8 weeks

**ADRs:** galactorrhea, Gynacomastia, impotence

**C/Is:** insignificant

**D/Is:** may enhance the effect of medicines like warfarin, phenytoin, and lidocaine

**Dosage forms:** Tablet, 200mg, 400mg, 800mg; chewable tablet, 200mg;

**Ranitidine**, 150mg P.O. BID

**ADRs:** GI disturbances

**C/I:** insignificant

**Dosage forms:** Tablet, 150mg

**Famotidine,** 20-40mg P.O. daily

**ADRs:** GI disturbances

**C/Is:** insignificant

**Dosage forms:** Tablet, 20mg, and 40mg

**II. *H. Pylori* positive-H.pylori eradiaction therapy**

**First line therapy**

All medicides below for 7-14 days

**Amoxicillin,** 1g, P.O. BID

*PLUS*

**Clarithromycin,** 500mg, P. O., BID

*PLUS*

**PPI**

**Alternative (for penicillin allergic patients). This regiemen has a higher failure rate.**

All medicides below for 7-14 days

**Clarithromycin,** 500mg P.O. BID

*PLUS*

**Metronidazole,** 500mg, P.O. BID

*PLUS*

**PPI**

**III. Symptomatic relief**

**Aluminium hydroxide + Magnesium trisilicate**, 10-30ml PRN P.O.

**ADRs:** rare and mild

**C/I:** insignificant

**Dosage forms:** Suspension, 310mg + 620mg in 5ml; tablet (chewable), 125mg + 250mg; 250mg + 500mg

*OR*

**Magnesium hydroxide + Almuninium hydroxide**, 10-30ml P.O.

**ADRs:** rare and mild

**C/I:** insignificant

**Dosage forms:** Tablet (chewable) tablet, 400mg+400 mg, 195mg+220mg in 5ml

*OR*

**Magnesium trisilicate**, 100-200mg, P.O. between meals PRN

**ADRs:** rare and mild

**C/I:** insignificant

**Dosage forms:** Tablet (chewable). 500mg

*OR*

**Magnesium hydroxide**, 10-30ml OR 600+622mg to 1200+1244mg, P.O between meals PRN

**ADRs:** rare and mild

**C/I:** insignificant

**Dosage forms:** Tablet (chewable), 300mg + 311mg; Mixture, 375mg/5ml, 7.75%

### 3. Haemorrhoids

Haemorrhoids are the enlargement of veins of the hemorrohidal plexus in the submucosal space of the anal canal. Haemorrhoids can be external or internal depending on whether it is the internal or external plexus that is enlarged.

**Clinical features**

- Internal Haemorrhoids are painless and often manifest with bright red rectal bleeding (usually with or following bowel movements)
- Prolapse with defecation or other straining activities can also occur
- External haemorrhoids are quite often painful and manifest with a tender swelling at the anal verge

**Internal haemorrhoids are graded as follows:**

| | |
|---|---|
| Grade I | Visualised on anoscopy |
| Grade II | Prolapse with defecation or with straining but reduce spontaneously |
| Grade III | Require the patient to reduce them into their normal position |
| Grade IV | Irreducible and may strangulate |

**Investigations**

- Diagnosis is usually clinical but confirmation needs anoscopy
- Haemoglobin/hematocrit

**Treatment**

**Objectives**

- Relief of symptoms
- Decrease bleeding and prolapse
- Prevent strangulation

**Non pharmacologic**

– Fluid and fibre rich diet

- Sitz bath
- Avoid constipation
- The main stay of treatment for refractory and significantly relapsing haemorrhoids is surgical

**Pharmacologic**

**First line**

**Bismuth subgallate**, insert one suppository in the rectum BID, OR topical application, BID for five days

*OR*

**Bismuth Subgallate + Bismuth Oxide + Peru Balsam+ Zinc oxide + Hydrocortisone acetate + Benzyl benzoate**, one suppository in the rectum or topical application, BID for five days

| | |
|---|---|
| **ADRs:** | worsening of untreated infection, and thinning of the skin structure on prolonged use |
| **C/Is:** | known hypersensitivity to the preparation, untreated infection |
| **P/Cs:** | Same as Bismuth Subgallate Compound. Avoid this preparation in the presence of and infection in the rectal area |
| **Dosage forms:** | Ointment, 2.25% + 0.875% + 1.875% +10.75% + 0.25% +1.25% Suppository, 59mg + 24mg + 49mg +296mg + 10mg + 33mg |

**Alternative**

**Lidocaine + Aluminium acetate + Zinc oxide + Hydrocortisone acetate**, rectal suppository, once per day OR topical application BID for five days.

| | |
|---|---|
| **Dosage forms:** | Ointment, 50mg + 35mg + 180mg + 2.5mg<br>Suppository, 60mg + 50mg + 500mg + 5mg |

## 4. Hepatitis

Hepatitis is an inflammation of the liver with multiple etiologies. It presents as an acute illness with jaundice and altered liver function tests or chronically with progressive liver dysfunction.

When symptoms, signs or laboratory abnormalities persist for more than 6 months it is considered as chronic. Common causes include viruses (Hepatitis A, B, C, D and E, EBV etc.), medicines (e.g. anti Tb medicines, ARVs, anti convulsant, paracetamol and herbal medicines), autoimmune disease (autoimmune hepatitis), deposition disease (e.g. Hemochromatosis, Wison's disease).

**Clinical features**

- Right upper quadrant abdominal pain
- Fever
- Fatigue, malaise, anorexia, nausea and vomiting
- Yellow or dark coloured urine and pale stools
- Physical findings include jaundice, right upper quadrant tenderness, hepatomegaly, ascites, edema, astrexis and mental status change

**Investigations**

- AST,ALT, alkaline phosphatase, serum bilirubin, serum albumin, PT or INR
- Hepatitis viral markers-HBSAg, anti HCV antibody, HAV Igm
- Autoimmune markers-ANA
- Abdominal Ultrasound

**Treatment**

**Objectives**

- Identify and treat cause
- Idnentify and treat precipitants
- Relieve symptoms

**Non-pharmacological treatment-**mainly supportive

- Withdrawal of hepatoxic medicines or herbal preparation
- Bed rest or hospitalization (if patient has poor oral intake, siginificant vomiting, signs of encephalopathy)
- High calorie fluids-glucose drinks, fruit juices, light porridge
- Intravenous dextrose (5-10%) infusion – when patient's oral intake is poor or if there is vomiting
- Decrease protein intake-if there is risk of encephalopathy
- Avoid constipation
- Avoid alcohol

**Pharmacological treatment – depends on the cause.** Refer patients to progressive hepatits specialist

## 5. Acute Liver Failure And Fulminant Hepatitis

**Acute liver failure (ALF)** refers to the rapid development of severe acute liver injury with impaired synthetic liver function and hepatic encephalopathy in a person who previously had a normal liver or well-compensated liver disease.

**Fulminant hepatitis (FH)** refers to the development of hepatic encephalopathy within eight weeks of the onset of symptoms in a patient with a previously healthy liver or the appearance of encephalopathy within two weeks of developing jaundice. Causes of ALF or FH are similar to that of acute hepatitis.

**Clinical features**

- Jaundice
- Bleeding
- Ascites and edema
- Hepatic encephalopathy-depressed mental status, restlessness
- Decreased urine out put

**Investigations-**see acute hepatitis

**Treatment-**Patients should be treated in an ICU setting. Secure air way, IV line, correct hypoglycemia and hypotension, insert NG tube if unconscious, Cathterize the urinary bladder and refer to a center with ICU care.

## 6. Liver Cirrhosis

Cirrhosis represents a late stage of progressive hepatic fibrosis with distortion of the architecture of the liver with formation of regenerative nodules. It can result from any cause of chronic liver disease e.g. chronic viral hepatitis, alcoholic liver disease. Patients with cirrhosis develop a variety of complications which cause marked morbidity and mortality. The common complications include ascites, spontaneous bacterial peritonitis, variceal bleeding, hepatic encephalopathy, hepatorenal syndrome and hepatocellular carcinoma.

**Clinical features**

- Symptoms are generally nonspecific (fatigue, poor appetite, weight loss)
- Symptoms of complication e.g. body swelling, hematemesis or melena
- Liver and spleen may be enlarged

- Scleral icterus
- Parotid gland enlargement
- Palmar erythema, spider angiomas
- Pubic and axillar hair loss
- Ascites and edema
- Sleep disturbance, behavioural or mental status changes in patients with encephalopathy

**Investigations**

- CBC, Transaminases, Alkaline phosphatase/GGT, Bilirubin, Prothrombin time, serum Albumin, Creatinine, Urea, Serum electrolytes
- HBSAg, anti-HCV antibody
- Abdominal ultrasound
- Upper GI endoscopy

**Treatment**

**Objectives**

- Reduce complication rates

**Non pharmacologic**

- Salt restriction (< 2 g/day)-for ascites
- Monitor weight regularly
- Bed rest
- Low protein diet-for encephalopathy
- Endoscopic sclerotherapy and/or banding-for variceal bleeding

**Pharmacologic**

**For ascites/edema**

**First line**

**Spironolactone**, 50–200mg P.O. daily. Titrate to higher dosages with caution. Maximum dose: 400 mg daily.

**ADRs:** gynecomastia

**C/Is:** hyperkalemia, acute renal failure

**Dosage forms:** Tablet, 25mg, 100mg

If there is no response to spironolactone or if there is gross fluid retention:

*PLUS*

**Furosemide**, 20–40mg P.O. BID. Titrate carefully to desired effect as rapid fluid shift may precipitate hepatic encephalopathy.

**ADRs:** hypovolamia, hypokalemia, ototoxicity, hypersensitivity reactions

**C/Is:** hypersensitivity to sulfa medicines, hypotension, uncorrected hypokalemia

**Dosage forms:** Tablet, 40mg, 80mg; injection, 10mg/ml in 2 ml ampoule; elixir, 10mg/ml

Keep **10:4** proportion of Spironolactone to furosemide dosage to prevent hypokalemia and maximize response.

**A. Encephalopathy**

**First line**

**Lactulose**, 10–30mL P.O., 8 hourly. Aim for 2 soft stools /day and no diarrhoea

**ADRs:** flatulence, cramps, and abdominal discomfort

**C/Is:** as for bisacodyl; galactosaemia, intestinal obstruction, hypersensitivity to lactulose

**P/Cs:** lactose intolerance, diabetic patients (presence of some free galactose and lactose)

**Dosage forms:** Enema, Syrup

**Alternative**

**Bisacodyl**, 5 – 10mg P.O. BID

**Magnesium Sulphate**, 10-20 mg P.O. in a glass of water, preferably before breakfast

*PLUS*

**Metronidazole,** 250mg P.O. TID

**B. Esophageal varices-prevention of variceal bleeding**

**Propranolol**, 20mg – 40mg P.O., two-three times daily start low dose and escalate gradually.

## C. Spontaneous bacterial peritonitis

**Treatment of Spontaneous bacterial peritonitis**

**First line**

**Ceftriaxone**, 1000mg, IV, BID for 7-10 days

**Alternative**

**Ciprofloxacin**, 200mg, IV, BID for for 7-10 days

*OR*

**Amoxicillin/clavulinic acid**, 1/0.2g, IV, TID for 7-10days

**Prophylaxis for spontaneous bacterial peritonitis (SBP)**

**Indications**

- Patients who recover from an episode of SBP
- Severe liver disease with ascitic fluid protein lower than 1.5 g/dl without prior SBP
- In patients with gastrointestinal bleeding and severe liver disease

**First line**

**Norfloxacin**, 400mg, P.O. daily

**Alternative**

**Ciprofloxacin**, 750mg P.O once weekly

*OR*

**Cotrimoxazole**, 800/160mg= 960mg P.O. daily

## CHAPTER V: HEMATOLOGIC DISORDERS

### 1. Anaemia

Anaemia is defined as reduction in red blood cell (RBC) mass which will be measured in the laboratory by reduction in haemoglobin concentration or hematocrit or RBC count. WHO criteria for anaemia in men and women are haemoglobin values <13 and <12 g/dl, respectively.

Anaemia is not a single disease entity, it is rather a manifestation of several pathologies. The causes of anaemia can be divided in to two broad categories:

1. Anaemia due to increased RBC loss or destruction-Haemorrhage or hemolysis

Anaemia due to defective or decreased RBC production –e.g. Iron deficiency anaemia, B12 or folate deficiency, anaemia of chronic disease/chronic renal failure/hypothyroidism, aplastic anaemia, bone marrow infiltration, chemotherapy induced anaemia

**Clinical features**

- Fatigue/dyspnea/palpitation/syncope
- Headache, lightheadedness, tinnitus, vertigo, difficulty of concentration
- Anorexia/nausea/indigestion
- Pallor /tachycardia/wide pulse pressure /ejection systolic murmur
- Signs of Heart Failure (raised JVP, S3, hepatomegaly, edema)
- Features of the underlying disease e.g. Melena in GI bleeding

**Investigation**

- CBC
- RBC indices
- Peripheral blood smear
- Reticulocyte count

Further investigation will depend on the suspected cause/s of anaemia based on the above tests, history and physical examination findings. Suspected iron deficiency anaemia-iron studies (serum iron, ferritin, TIBC), stool for occult blood, stool microscopy for hookworm infestation. GI endoscopy might also be needed.

**Treatment**

**Objectives**

- Improve the functional status of anaemia
- Prevent development of complications such as Heart Failure
- Treatment of the underlying cause

**Non pharmacologic**

- Packed RBC or whole blood transfusion (when there is Heart Failure , severe hypoxic symptoms, acute ongoing bleeding)
- Nutritional support
- Non pharmacologic treatment pertinent to the underlying cause

**Pharmacologic**

- There is no universal pharmacologic treatment for all causes of anaemia

**Hematinics (Iron, folate and vitamin B12) should not be routinely administered to patients with anaemia without a definitive diagnosis of the cause**

A. **Pharmacologic treatment of iron deficiency anaemia-Oral iron replacement**

N.B. The cause of the iron deficiency state should be identified and treated

**First line**

**Ferrous sulphate,** 325mg (65mg elemental iron), OR 60mg elemental iron, TID between meals for at least 3 months following correction of the anaemia

**ADRs:** abdominal cramps and dyspeptic symptoms, diarrhoea

**D/Is:** Antacids, tetracyclines, chloramphenicol, and quinolone antibiotics interfere with the absorption and metabolism of iron

**Dosage forms:** Capsule Drop, Tablet (enteric coated)

**N.B.** For patients who do not tolerate ferrous sulfate tablets, they may be advised to take it with meals, or to take a smaller dose, or to change the brand to ferrous gluconate or fumarate tablets or elixir forms.

*OR*

**Ferrous gluconate**, 325mg P.O. (39mg elemental iron), 1-2tabs, TID

*OR*

**Ferrous fumarate**, 325mg P.O., (107 elemental iron), one tab, daily to twice per day

B. **Pharmacologic treatment of megaloblastic anaemia – cobalamin (Vitamin B12) deficiency**

**Cobalamin,** 1000micrograms (1mg), IM, every day for one week, every week for four weeks and then, **if the underlying disorder persists**, 1mg every month for the remainder of the patient's life.

C. **Pharmacologic treatment of megaloblastic anaemia-Folate deficiency**

**Folic acid**, 1 to 5mg P.O., daily for 1-4 months, or until complete hematologic recovery.

Folic acid can partially reverse the hematologic abnormalities of Cobalamin (B12) deficiency BUT neurologic manifestations will progress. Thus, it is important to rule out cobalamin deficiency before treating a patient with megaloblastic anaemia with folic acid alone.

**2. Immune Thrombocytopenic Purpura (ITP)**

Immune thrombocytopenic purpura (ITP) or idiopathic thrombocytopenic purpura is a common acquired bleeding disorder. It is characterised by isolated thrombocytopenia while the complete blood count is entirely normal, unless other coincidental abnormalities are present, such as iron deficiency.

Clinically apparent associated conditions (e.g. systemic lupus erythematosus, chronic lymphocytic leukemia) should be excluded to diagnose ITP. Patients with these associated conditions are described as having secondary immune thrombocytopenia. The incidence of ITP is higher in children than adults. Preceding viral infections are common precipitants.

**Clinical features**

- Petechiae, purpura, and easy bruising
- Epistaxis, gingival bleeding, and menorrhagia
- Gastrointestinal bleeding and gross hematuria
- Intracranial haemorrhage
- The bleeding of thrombocytopenia is mucocutaneous, as opposed to the delayed, deep seated hematomas characteristic of coagulation disorders such as hemophilia

- The clinical manifestations of thrombocytopenia vary with age. Older patients may have more severe bleeding manifestations, such as gastrointestinal bleeding and possibly intracranial haemorrhage because of comorbidities such as hypertension

**Investigations**

- CBC
- Peripheral blood smear(to exclude other causes of thrombocytopenia)
- Serology for HIV, HCV (hepatitis C Virus) and ANA (antinuclear antibody test)
- Bone marrow aspiration or biopsy indicated in old patients and refractory ITP only

**Treatment**

**Objectives**

- Increase the platelet count to a safe level to prevent major bleeding rather than bringing it to normal

**Non pharmacologic**

**Emergent platelet transfusion** – indicated when there is life-threatening bleeding only and it should be combined with rapidly-acting conventional interventions (e.g. intravenous steroids).

**Hospitalization**, Patients with wet purpura and retinal haemorrhages (impending CNS bleeding) for observation and expectant treatment

**Splenectomy**, in patients who fail treatment with glucocorticoids or require ongoing glucocorticoids ($\geq$ 15mg/day) to maintain an adequate platelet count.

**Pharmacologic**

**First line**

**Prednisolone**, 1mg/kg, oral, daily. The tapering and duration of treatment is determined by the platelet count response. There is no standard regimen for tapering. After achieving a normal platelet count it can be tapered and discontinued over four to six weeks.

**Alternative**

**Dexamethasone**, 40mg, oral, daily for 04 consecutive days. Repeat each four day doses every 2-4 weeks. Refractory cases should be referred to specialist for decision on further management.

| |
|---|
| N.B. The diagnosis of ITP does not necessarily mean that treatment must be instituted. Treatment should not be started in all patients unless symptomatic with moderate or severe thrombocytopenia. |

### 3. Venous Thrombo Embolism

Venous thromboembolism (VTE) is a condition in which a blood clot (a thrombus) forms in a vein, most commonly in the deep veins of the legs or pelvis. This is known as deep vein thrombosis, or DVT. The thrombus can dislodge and travel in the blood, particularly to the pulmonary arteries. This is known as pulmonary embolism, or PE. The term 'VTE' includes both DVT and PE. Venous thromboembolic diseases cover a spectrum ranging from asymptomatic calf vein thrombosis to symptomatic DVT. They can be fatal if they lead to PE. Non-fatal VTE can cause serious long-term complications such as post-thrombotic (post phlebitic) syndrome.

**Risk factors for VTE are**

- Immobility
- Previous PE or DVT
- Major surgery, e.g. orthopedic, abdominal and pelvic surgery
- Trauma especially involving the pelvis and lower limbs
- Pregnancy and postpartum state
- Contraceptive pill use, hormone replacement therapy (HRT)
- Medical conditions, e.g. CHF, nephrotic syndrome, SLE, IBD
- Malignancy
- Inherited disorders causing hypercoagulability

**Clinical features**

- Swelling calf or thigh (usually unilateral)
- Pain in the affected limb
- Occasionally tenderness in the limb
- Breathlessness (may be intermittent)
- Dizziness, fainting or collapse

- Sharp chest pain
- Blood stained sputum
- Tachypnea /Tachycardia
- Hypotension
- Pleural effusion
- Low oxygen saturation on pulse oximetry <90%

**Investigations**

- CBC, Chest X-ray, ECG
- Doppler ultrasound of leg and pelvic veins
- Echocardiography
- APTT, INR /PT as baseline
- CT scan of the chest with contrast (CT pulmonary angiography)

**Treatment**

**Objectives**

- Prevent further clot formation and embolization
- Relieve symptoms
- Prevent death from PE
- Prevent recurrence of DVT/PE and development of pulmonary hypertension/post phlebitis syndrome

**Non pharmacologic**

- Elastic compression stockings after anticoagulation
- Early ambulation after proper anticoagulation

**Pharmacologic**

I. **Acute treatment**

**First line**

**Unfractionated heparin (UFH)**, 5000 U, IV, bolus then 250 U/Kg/dose,BID

or 17,500U SC, BID (for an average adult) until two consecutive INR values become therapeutic (2-3)

*OR*

**Enoxaparin**, 1mg/kg, SC, BID, until two consecutive INR values become therapeutic (2-3)

*PLUS*

**Warfarin** (starting simultaneously with heparin), 5 mg P.O., daily with regular dose adjustment and monitoring of INR until target of 2.0-3.0 is attained

Note: Heparin and warfarin therapy should overlap for 5-7 days until two consecutive INR values are therapeutic i.e. 2 to 3

II. **Chronic treatment**

**Warfarin,** dose adjusted to achieve target INR of 2.0-3.0

| | |
|---|---|
| **ADRs:** | haemorrhage, hypersensitivity, rash, alopecia, diarrhoea, unexplained drop in haematocrit, 'purple toes', skin necrosis, jaundice, hepatic dysfunction, and pancreatitis. |
| **C/Is:** | Hypersensitivity; haemorrhagic tendencies; blood dyscrasias; severe uncontrolled or malignant hypertension; pericarditis or pericardial effusion; bacterial endocarditis;; eclampsia/pre-eclampsia, threatened abortion, pregnancy |
| **D/Is:** | acetylsalicylic acid, alcohol, allopurinol, amoxicillin, ampicillin, azathioprine, carbamazepine, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, ciprofloxacin, contraceptives, dexamethasone, |
| **P/Cs:** | hepatic or renal failure, recent surgery, breastfeeding. |
| **Dosage forms:** | Tablets, 2mg, 5mg, 10mg |

**Duration of anticoagulation**

- Patients with VTE due to a reversible/time-limited risk factor (eg surgery) for 3-6 months.
- Patients with first episode of idiopathic/unprovoked VTE for 3-6 months
- Most patients with advanced malignancy should be treated indefinitely or until the cancer resolve
- Patients with recurrent idiopathic/unprovoked VTE– indefinitely

III. **Prophylaxis**

Prophylaxis is indicated for many **medical and surgical patients who are hospitalized.** For those who are assessed to have high risk give VTE prophylaxis

**Table 20- VTE risk categories in surgical patients**

**Low risk patients** — < 40 yrs + no patient-related or surgery-related risk factors and require general anaesthesia for < 30 minutes

**Moderate risk patients** —

- Minor surgery + additional risk factors
- Age 40 – 60yr + general anaesthesia for > 30 minutes But no additional patient-or surgery-related risk factors

**High risk patients** —

- >60 years of age undergoing major surgical procedures

**High risk surgeries**

- Cancer surgery
- Major vascular surgery
- Major gynecologic surgery
- Major urologic procedures
- Major thoracic surgery
- Hip or knee arthroplasty
- Pelvic or hip fracture surgery
- Major trauma & spinal cord injury

**Patient related risk factores**

- Malignancy
- Presence of a central venous catheter

- Trauma
- Immobilization
- Antiphospholipid antibody syndrome
- Inflammatory bowel disease
- Tamoxifen, Thalidomide, Lenalidomide
- Inherited thrombophilic disorders
- Pregnancy/Oral contraceptives/HRT
- CHF
- Myeloproliferative disorders
- Nephrotic syndrome

**Risk stratification in medical patients-**VTE prophylaxis is considered reasonable for medical patients > 40 years + limited mobility for ≥3 days + one thrombotic risk factor

All patients admitted to intensive care units are considered high risk for VTE

**Non pharmacologic prophylaxis**

- Encourage patients to ambulate
- Intermittent pneumatic compression
- Graduated compression stocking

**Pharmacologic prophylaxis-**for moderate and severe surgical risk categories and for medical patients as mentioned above

**Unfractionated heparin**, SC, 5 000 units 12 hourly
*OR*

**Enoxaparin,** SC, 40 mg once daily

## CHAPTER VI: INFECTIOUS DISEASES

### 1. Acquired Immunodeficiency Syndrome (AIDS)

AIDS is a chronic infectious disease caused by the *Human Immuno-deficiency Virus* types 1 and 2. It is transmitted largely by sexual contact. Other important means of transmission are direct contact to contaminated blood and blood products and from infected mother to child. It is essentially a disease of the immune system, which results in progressive immunodeficiency state. This immunodeficiency fails to control various types of infections progressing into diseases and the development of malignancies.

**Human Immuno-deficiency Virus (HIV)** infection targets the immune system and weakens a person's surveillance and defense systems against infections and some types of cancer. The virus destroys and impairs the function of immune cells; hence HIV infected individuals gradually become immunodeficient. Immunodeficiency results in increased susceptibility to a wide range of infections and diseases that people with healthy immune systems can fight off.

The most advanced stage of HIV infection is called **Acquired Immunodeficiency Syndrome (AIDS)**. AIDS is defined by the development of certain cancers, infections, or other severe clinical manifestations.

Causitive organisms

- HIV 1
- HIV 2

**Clinical features**

The clinical manifestations are variable depending on the degree of immunodeficiency which determines the clinical stage of the disease. The first few weeks after initial infection, individuals may experience no symptoms or an influenza-like illness including fever, headache, rash or sore throat. At advanced immunodeificiency, patients are at a very high risk of being infected with less virulent organisms (opportunistic infections). Refer below for a list of clinical conditions in the four WHO stages of HIV.

**Investigations**

- Demonstration of antibodies to HIV by Rapid test using the National HIV test algorisim

- HIV antigen detection
- Direct detection of the virus using PCR

**Table 1: Clinical Stages of HIV Disease as per World Health Organization Classification**

**Clinical Stage 1**

1. Asymptomatic infection
2. Persistent generalized lymphadenopathy
3. Acute Retroviral (HIV) Syndrome

**Performace Status 1: asymptomatic, normal activity**

**Clinical Stage 2**

1. Unintentional weight loss < 10% body weight
2. Minor mucocutaneous manifestations (e.g., PPE seborrhicdermatitis, prurigo, fungal nail infections, angular cheilitis)
3. Herpes zoster within previous 5 years
4. Recurrent upper respiratory tract infections

**Performance Status 2: symptoms, but nearly fully ambulatory**

**Clinical Stage 3**

1. Unintentional weight loss > 10% body weight
2. Chronic diarrhoea > 1 month
3. Prolonged fever > 1 month (constant or intermittent)
4. Oral candidiasis
5. Oral hairy leukoplakia
6. Pulmonary tuberculosis within the previous 2 years
7. Severe bacterial infections
8. Vulvovaginal candidiasis
9. Unexplained Anaemia, Neutropenia or chronic thrombocytopenia

**Performance Status 3: in bed more than normal but < 50% of normal daytime during the previous month**

**Clinical Stage 4**

1. HIV wasting syndrome
2. Pneumocystis carinii pneumonia
3. Toxoplasmosis of the brain
4. Crytosporidiosis with diarrhoea > 1 month
5. Isosporiasis with diarrhoea > 1 month

6. Cryptococcosis, extrapulmonary
7. Cytomegalovirus disease of an organ other than liver, spleen or lymph node
8. Herpes simplex virus infection, mucocutaneous
9. Progressive multifocal leukoencephalopathy
10. Any disseminated endemic mycosis (e.g., histoplasmosis)
11. Candidiasis of the esophagus, trachea, bronchi, or lung
12. Atypical mycobacteriosis, disseminated
13. Non-typhoid Salmonella septicemia
14. Extrapulmonary tuberculosis
15. Lymphoma
16. Kaposi's sarcoma
17. HIV encephalopathy
18. Viseral Leishmaniasis
19. HIV –associated cardiomyopathy
20. HIV-associated nephropathy

**Performance Status 4: in bed > 50% of normal daytime during previous month**

**Treatment**

**Objective**

- Suppress viral replication to undetectable levels
- Prevent opportunistic infections
- Rehabiliate the patient and allow full function

**Non pharmacologic**

- Counseling and psychological support
- Nutritional support
- Socio-economic support

**Pharmacologic**

Management of HIV disease includes prevention and treatment of opportunistic infections (OIs) and controlling viral replication with Anti Retroviral Medicines (ARVDs) as Highly Active Antiretroviral Therapy (HAART).

**Indications for initiation of ART**

**General Considerations for Anti-Retroviral Therapy (ART)**:

The goal of anti-retroviral therapy (ART) is to attain maximal and durable suppression of the viral replication. Effective ART should restore and/or preserve immunologic function. The effectiveness of ART is assessed by clinical observations, CD4 cell count and determination of plasma viral load. ART initiation should be timed appropriately and not delayed until the immune system is irreversibly damaged. Consideration of the stage of the HIV disease and the degree of immune damage determine the timing of initiation of ART. For ART naïve patients, treatment is initiated with a combination of 3 medicines (**Triple Therapy**); consisting of two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and a third medicine from the Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) or Protease Inhibitors (PI).

**When to start treatment**

- All adolescents and adults with HIV infection with CD4 count ≤500cells/$mm^3$ should be started on HAART irrespective of WHO clinical stage
- All adolescents and adults with HIV infection and WHO clinical stage 3 and 4 should be started on HAART irrespective of CD4 cell count
- HIV infection and Active TB disease should be started on HAART irrespective of CD4 cell count
- Obtain CD4 cell count every six months for all patients with WHO stage 1 and 2 HIV infections until CD4 Count is $\underline{\leq}$ 500cells/$mm^3$ to start ART

**Medicine regimens**

First-line regimens for adults and adolescents

First line regimen is the combination of ARVs started for treatment naive patient for the first time.

**Table 21-Recommended first line antiretroviral regimens in adults and adolescents**

| **Recommended ARV Regimens for Adults and Adolescents: One of the following should be used unless there are contraindications:** |
|---|
| ***Preferred***<br>• TDF+FTC+EFV = triple Fixed Medicine Combination (FDC)<br>***Alternatives***<br>• TDF/3TC/NVP<br>• ZDV+3TC+EFV<br>• ZDV+3TC+NVP |
| ***Others***<br>• ABC/3TC/NVP<br>• ABC/3TC/EFV<br>• ABC/3TC/ZDV = double FDC + ABC |

**Second-line ARV combination regimens for adults and adolescents**

Second line regimen is the combination of ARVs given for a patient who has been taking ART and developed treatment failure, or severe side effects

**Table 22-First and Second-Line ARV Regimens in Adolescents and Adults**

| **First-line Regimen** | **Second-line Regimen (*during treatment failure*)** |
|---|---|
| TDF+FTC or 3TC +EFV or NVP | ZDV ±3TC +LPV/r or ATV/r<br>Or ZDV+ABC+LPV/r or ATV/r |
| ZDV +3TC+EFV or NVP | TDF+3TC±ZDV+LPV/r or ATV/r<br>Or ABC + ddI[a] +LPV/r[b] or ATV/r |
| ABC + 3TC + ZDV | EFV or NVP + LPV/r or ATV/r |

[a] Didanosine alone must be taken on an empty stomach, at least one hour before or at least 2 hours after (<50% absorbed after) a meal. Tablets should be dissolved in at least 30 ml of water; no other liquids may be used to dissolve the tablets. The enteric coated version will not need to be dissolved.

[b] LPV/r use the heat stable tablet (200/50mg).

- Atazanavir/ritonavir has equivalent efficacy to LPV/r and has advantage of being given once a day and in patients with dyslipidemia.

- If TDF and ABC have been used in the first-line regimen, patients may be referred to experienced physicians for selection of the second-line medicines
- Medicine hypersensitivity and high-level cross-resistance to long term use of thymidine analogues (ZDV) are concerns when using ABC
- TDF can be compromised by multiple nucleoside analogue mutations (NAMs) but often retains activity against nucleoside-resistant viral strains. It is attractive in that, like ddI, it is administered once daily

**Table 23-Dose regimens of anti-retroviral medicines for adults and adolescents[a]**

| **Medicine class/Medicine** | **Dose** |
|---|---|
| **Nucleoside & Nucleotide RTI's** | |
| Zidovudine (ZDV) | 300mg twice daily |
| Lamivudine (3TC) | 150mg twice daily |
| Didanosine (ddl) | 400mg once daily (250 mg once daily if < 60 kg) |
| Abacavir (ABC)<br>Tenofovir (TDF)<br>Emtricitabine(FTC) | 300mg twice daily<br>300mg daily<br>200mg daily |
| **Non-Nucleoside RTI's** | |
| Efavirenz (EFZ) | 600mg once daily |
| Nevirapine (NVP) | 200mg once daily for 14 days, then 200mg twice daily |
| **Protease inhibitors** | |
| Lopinavir/ritonavir (LPV/r) | 400mg/100mg twice daily (533mg/133mg twice daily when combined with EfZ or NVP) |
| Atazanavir/ritonavir (ATV/r) | 300mg/100mg once daily |

These dosages are in common clinical use. The dosages featured in this table were selected based on the best available clinical evidence. Dosages that can be given on a once or twice daily basis were preferred in order to enhance adherence to therapy. The doses listed are those for individuals with normal renal and hepatic function. Product specific information should be consulted for dose adjustments that may be indicated with renal or hepatic dysfunction or for potential medicine interactions with other HIV and non-HIV medications.

**Monitoring ARV Treatment**

**Treatment Adherence**

- Patient and attendant or family education and counseling before initiation of therapy is mandatory to maximize future adherence.
- Ongoing attention and counseling is crucial to enforce adherence throughout the entire course of treatment.
- Strategies to enhance adherence include:
    - Minimizing pill counts and dosage frequencies, preferentially using combination pills on a once or twice daily basis.
    - Enlisting the assistance of family or community members to support patients in taking their medications.
    - Tackling psychosocial issues that can contribute to low adherence to therapy.
- WHO recommends that innovative approaches to enhance adherence to ART be developed and used.
- It is advisable for patients on triple therapy to be seen:
    - Bi-monthly; particularly at the initiation of treatment. Once stabilized, patients may then be seen every three months.
    - At each visit, side effects and adherence to the treatment should be discussed in depth.

**Baseline Clinical assessment:**

It should include the following:

- Documentation of past medical history (including major illnesses, tuberculosis, hospitalizations and surgeries)
- Length of time since the diagnosis of HIV
- Current medications
- Identification of co-existing medical conditions that may influence choice of therapy (such as TB or pregnancy)
- Current symptoms or physical signs
    - This clinical assessment should be supplemented with review of the expected benefits and potential side-effects of regimen to be chosen, possible medicine interactions (e.g. with contraceptives, ant-tuberculosis medicines), patient-caregiver partnership, commitment to long-term treatment and adherence to medicine therapy, any perceived side-effects, and maintenance of safe sexual practices.

- **Once on ART**: first follow-up visit will be two weeks after initiation of treatment and every one to two months thereafter. The visits should be combined with medicine dispensing, and should be used also as an opportunity to reinforce adherence. During each visit, patient should be evaluated for new symptoms that may be related to medicine side effects, the disease progression, and clinical improvements/deterioration, development of OIs or recurrent problems that may exist.

**Monitoring for toxicity of ART**

**Clinical monitoring for toxicity of ART**

- All patients require clinical evaluation every month in the first 6 months for ARV related toxicity. Subsquent followup can be done every 3months.

**Laboratory monitoring for toxicity of ART:**

- **Baseline:** Haemoglobin/hematocrit, white blood cell count and differential, serum alanine aminotransferase, serum creatinine and/or blood urea nitrogen, serum glucose, pregnancy test. ***Resources permitting:*** serum bilirubin, amylase, triglycerides, and cholesterol.

- **Follow-up:** The above investigations need to be repeated bi-monthly, particularly at the start of treatment. Once stabilized, investigations may then be performed every three months and at any time when they are indicated.

**Table 24 - Major ADRs, contraindications and dosage forms of Antiretroviral medicines**

| Medicine | Major ADRs | C/Is | Dosage forms |
|---|---|---|---|
| **NRTIs/ NTRTIs** | | | |
| Zidovudine | Anaemia, hperpigmentation | Severe anaemia | Tablet, 150mg, 300mg; Capsule, 100mg,250mg; Syrup, 50mg/ml; I.V. infusion, 10mg/ml |
| Didanosine | Pancratitis, neuropathy | | Tablet, 25mg, 150mg; chewable/dispersable, 100mg |
| Lamivudine | GI disturbances | | Tablet, 150mg; Oral solution, 100mg/ml |
| Abacavir | Hypersensitivity | Hyper-sensitive to it | Tablet, 300mg |
| Emitricitabin | Headache, diarrhoea, rash | | Tablet 100mg |
| Tenofovir | GI disturbances | | Tablet 300mg |
| | | **NNRTIs** | |
| Efavirenz | Skin rashes | | Capsule Capsule 50mg, 100mg, 200mg |
| Nevirapine | Hepatitis, rash, fever, artraligia, myalgia | | Tablet, 200mg; Oral suspension, 50mg/5ml |
| | | **PIs** | |
| Lopinavir | Hyperglycaemia, asthenia, rhythm, disturbance, GI disturbances | | tablet, 200mg, 400mg |
| Ritonavir | Parasthesia, GI disturbances, hyperlipedemia, liver damage | | Capsule, 100mg; Oral solution, 80mg/ml |
| Atazanivir | Headache, diarrhoea, rash, itching, swelling | hypersensi-tvity | Tablet, 100mg, 150mg, 200mg |
| | | **Fixed Dose Combinations** | |
| Emitricitabin e+Tenofovir | The combination of individual S/Is | | Tablet, 200mg+300mg |

| | | |
|---|---|---|
| Lopinavir+ Ritonavir | The combination of individual S/Is | Capsule, 133.33mg+33.33mg; Tablet, 200mg+50mg ; Oral suspension, 80mg+20mg/5ml |
| Efavirenz+ Emiticitabine +Tenofovir | The combination of individual S/Is | Tablet, 600mg+200mg+300mg |
| Atazanavir+ Ritonavir | The combination of individual medicine ADR | Tablets 300mg + 100mg |
| Lamivudine+ Zidovudine+ Nevirapine | The combination of individual S/Is | Tablet, 150mg+300mg+200mg |

**Monitoring Effectiveness of ART**

Response to ART is monitored using both clinical and laboratory parameters.

**Laboratory parameters**

**a. The concentration of HIV - RNA in plasma (the "viral load")**

- The desirable **"virologic" endpoint** is a plasma viral load that is: "below the limits of detection", within 3 to 4 months of starting treatment, and
- The achievement of a minimum decline from the baseline viral load of 1.5-2.0log by the end of the first month of treatment
- The plasma viral load is checked at baseline then after one month of initiating therapy and two-monthly thereafter until the virologic goal of therapy is achieved. Following this, plasma viral load may be checked every 3 to 4 months

**N.B.** In patients with higher baseline plasma viral loads (e.g. above 100,000 copies/ml by RT-PCR) maximal suppression of viral replication may take a longer time

**b. CD4+ cell count**

- When optimal therapy is achieved, the median CD4+ cell rise is 50-100 cells within the first year.
- The CD4+ cell response may lag behind the “virologic response” in timing and at times the two responses may even be discordant

- In general CD4+ count, is checked at baseline, thereafter it may be checked every 3 month in the 1st year every 6 month in the 2nd year and every 12 months
- In places where CD4+ count cannot be done, total lymphocyte count can be used

**Clinical Parameters**

- An increase in body weight
- Decrease in frequency and severity of OIs
- Decrease in frequency and severity of HIV related malignancies

**Table 25-Definitions of treatment failure in adults and adolescents**

| | Definition |
|---|---|
| **Clinical Failure** [a] | New or recurrent WHO stage 4 condition [b c] |
| **Immunologic Failure** [d] | • Fall of CD4 count to pre-therapy baseline (or below);<br>• 50% fall from the on-treatment peak value (if known);<br>• Persistent CD4 levels below 100 cells/$mm^3$ |
| **Virological Failure** | Plasma viral load above 5,000 copies/ml in duplicates after six months on ART |

a. Should be differentiated from Immune Reconstitution Inflammatory Syndrome (IRIS).
b. Certain WHO clinical conditions (e.g. pulmonary TB, severe bacterial infections), may indicate treatment failure and should be investigated
c. Some WHO clinical stage 4 conditions (lymph node TB, uncomplicated TB pleural disease, oesophageal candidiasis, recurrent bacterial pneumonia) may not be indicators of treatment failure and thus do not require consideration of second-line therapy.
d. Without concomitant infection to cause transient CD4 cell decrease. If patient is asymptomatic and treatment failure is being defined by decreased CD4 cell criteria alone, consideration should be given to performing a repeat CD4 cell count before establishing diagnosis of treatment failure.

**Post-exposure prophylaxis (PEP)**

Universal precaution is the most effective way of protecting individuals from accidental transmission of HIV and other blood borne pathogens. Special attention should, therefore, be given to training health care givers on prevention methods and to provide them with necessary safe materials and protective equipment.

**Assessment of risk of exposure**

**Low risk exposure**

- Exposure to a small volume of blood or blood contaminated with fluids from asymptomatic HIV positive patients.
- Following an injury with a solid needle.
- Any superficial injury or muco-cutaneous exposure.

**High risk exposure**

- Exposure to a large volume of blood or other potentially infectious fluid
- Exposure to a large volume of blood or blood contaminated with fluids from a patient with clinical AIDS or early sero-conversion phase of HIV
- Injury with a hollow needle
- Deep and extensive injuries

**Timing of initiation of treatment**

- Should be given in the shortest time possible (within the first 1-4 hours of exposure)
- Do not consider PEP beyond **72 hours**

**N.B**. Doses for post exposure prophylaxis are given below

**Table 26- Post exposure prophylaxis**

| Risk Category | ARV Prophylaxis | Duration |
|---|---|---|
| Low risk (2 medicine regimen) | ZDV 300 mg BID + 3TC 150 mg BID or<br>ZDV + 3TC 1 tab BID | For 28 days |
| High risk (3 medicine regimen) | ZDV 300 mg BIT +3TC 150 mg bid + EFZ600 mg daily<br>Lopinavir/ritonavir (LPV/r) can be used as alternative to EFZ if available (LPV/r) 400/100mg | For 28 days |

## 2. Amoebiasis

Amoebiasis results from infection with the non-invasive Entamoeba dispar or the invasive Entamoeba histolytica, and is the third most common cause of death from parasitic disease. It is most commonly contracted through ingestion of live cysts found with faecally contaminated water, food, or hands. Foodborne infection is caused by faecally contaminated soil or water used for growing vegetables. It is endemic in most developing countries including Ethiopia.

**Clinical features**

- Gradual development of lower abdominal pain and mild diarrhoea
- Malaise, weight loss, and diffuse lower abdominal or back pain
- If caecum is involved, signs and symptoms will mimic those of appendicitis (right lower quadrant pain)
- Full dysentery develops in some patients with passage of 10–12 stools per day
- Stools are mostly blood and mucoid

Complications or unusual presentations: amoebic liver abscess, amoebic colitis can be confused with inflammatory bowel disease, and amoeboma (tender abdominal mass)

**Investigations**

- Stool examination: Fresh stools specimens must be examined for trophozoites typical of *E. hemolytica*. Cysts of both entamoeba species
- Entamoeba dispar or the invasive Entamoeba histolytica are very similar therefore trophozoites that have ingested red blood cells are diagnostic of E. hemolytica

**Treatment**

**Objectives**

- Eradicate the invasive disease and subsequently to eradicate cysts to prevent relapses.

**Non pharmacologic**

Hydration is impotant in patients who have severe dysentry

**Pharmacologic**

Treatment of invasive disease:

**First line**

**Metronidazole**, 500-750mg P.O., TID for 5-7 days. For children: 7.5mg/kg P.O., TID for 5-7 days.

**ADRs:** unpleasant metallic test, furred tongue and gastrointestinal disturbances; rarely headache, drowsiness, dizziness

**C/Is:** chronic alcohol dependence

**P/Cs:** disulfiram like reaction with alcohol; hepatic impairment and hepatic encephalopathy, pregnancy; breastfeeding

**D/Is:** phenytoin, cumarine or indandion derivative anticoagulant, warfarin, disulfiram, alcohol

**Dosage forms:** Tablet, 250mg, Intravenous infusion, 5mg/ml in 100ml
Cream, 0.75%, 1%

**Alternative**

**Tinidazole**, 2g P.O. QD for 3 consecutive days. For children: 50-60mg/kg daily for 3 days.

**Dosage forms:** Tablet, 250mg, 500mg

Eradication of cysts:

**First line**

**Diloxanide Furoate**, Adult 500mg 3 times daily P.O., for 10 days. Child over 25kg, 20mg/kg daily in 3 divided doses for 10 days; course may be repeated if necessary.

**ADRs:** flatulence, urticaria, pruritus

**Dosage forms:** Tablet, 500mg

**Alternative**

**Paromomycin**, 25–35mg/kg/day P.O., divided in 3 daily doses for 7 days

### 3. Amoebic Liver Abscess

Amoebic liver abscess is caused by an often delayed extra-intestinal infection by E. histolytica. It is the most common extra-intestinal manifestations of amoebiasis. It is 7 to 10 times more common in adult men.

**Clinical features**

- In symptomatic patients, fever and right upper quadrant pain are the usual manifestations
- Point tenderness over the liver with or without right side pleural effusion is also common Amoebic liver abscess is not usually associated with diarrhoea (although the source is always the colon)
- In endemic areas, the course is often subacute with hepatomegaly and weight loss. Ten to fifteen percent of patients with amoebic liver abscess present with only fever
- It may be complicated by pleuro-pulmonary involvement when the abscess extends from the liver into the lung area

**Investigations**

- CBC-About 75% of patients will have WBC more than 10 000 cells/µl
- Liver enzymes are often normal or only mildly elevated. Alkaline phosphatase levels are often elevated and can remain so for months
- A negative stool examination for amoebic cysts or trophozoites does not exclude an amoebic liver abscess. An ultrasound of the liver can show abscesses
- Aspiration of the abscess with Gram staining (and culture if available) may be useful to differentiate the amoebic abscess from a pyogenic abscess
- Trophozoites are rare in liver aspirates (since they are in the capsule of the abscess and not in the aspirated necrotic centre)
- Serology: positive serology for anti-amoebal antibody means invasive amoebiasis and generally will revert to negative after 6–12 months

**Treatment**

**Objectives**

- Rapid defervescence
- Prevent rupture and other complications

**Non pharmacologic**

Ultrasound guided aspiration of the liver abscess is indicated in the following situations:

- no other causes of abscess
- no clinical response after 3–5 days
- threatment of imminent rupture of the abscess (superficial abscess)
- prevention of left lobe abscess rupture into pericardium (very rare)

**Pharmacologic**

**First line**

**Metronidazole**, 500-750mg, P.O. TID or 500mg IV QID for 10 days. For children: 7.5mg/kg, P.O., TID for 5 days

Most patients will respond well to treatment with metronidazole, with a decrease in fever within 72 hours. The advantage of metronidazole is that if the etiology of the liver abscess is bacterial, this treatment will generally still work (if the bacteria is sensitive)

**Alternative**

**Tinidazole**, 2g P.O. QD for 3 consecutive days. For Children: 50-60mg/kg daily for 3 days.

**Dosage forms:** Tablet, 250mg, 500mg

**4. Anthrax**

Anthrax is an infection caused by a bacterium called *B. anthracis*, a gram-positive, rod-shaped bacteria that exists in the environment as a spore and can remain viable in the soil for decades. Spores ingested by grazing herbivores germinate within the animal to produce the virulent vegetative forms that replicate and eventually kill the host. Products (e.g., meat or hides) from infected animals serve as a reservoir for human disease. Germination from spore to vegetative organism is thought to occur inside host macrophages and after germination occurs, three factors appear key to the pathogenesis of anthrax: a capsule, the production of two toxins (i.e., lethal and edema), and the bacteria's ability to achieve high concentrations in infected hosts.

Anthrax was known to typically occur as one of three syndromes related to entry site of (i.e., cutaneous, gastrointestinal, or inhalational). The estimated mortalities of cutaneous, gastrointestinal, and inhalational, anthrax are 1%, 25 to 60%, and 46%. Ninety-five percent of

reported anthrax cases globally are cutaneous, and most occur in developing countries around the world where animal and worker vaccination is limited. It is estimated that there are approximately 2,000 cases annually worldwide. Characteristics of anthrax in Ethiopia include a known exposure to diseased animals, occurrence within families, frequent treatment by local healers, and high morbidity and mortality.

**Clinical features**

- The initial skin lesion is a painless or pruritic papule associated with a disproportionate amount of edema and which progresses to a vesicular form (1–2 cm)
- Fever and regional lymphadenopathy can occur
- The vesicle then ruptures and forms an ulcer and black scar, which sloughs in 2 to 3 weeks
- Purulence is only seen with secondary non anthrax infection. Edema with face or neck infection may produce airway compromise

**Investigations**

- Gram stain and culture from blood or other biologic samples (blood, skin lesion exudates, cerebrospinal fluid, pleural fluid, sputum, and feces) prior initiation of antimicrobial therapy

**Treatment**

**Objectives**

- Treat infection

**Non pharmacologic**

Use standard barrier precautions. Use contact isolation precautions for patients with draining anthrax lesions.

**Pharmacologic**

**Treatment of cutaneous anthrax without systemic illness**

**First line**

**Ciprofloxacin,** 500mg P.O., twice daily for 7-10 days. Treatment is extended to 60 days if concomitant inhalation exposure is possible.

| | |
|---|---|
| **ADRs:** | dyspepsia, abdominal pain, diarrhoea, headache, dizziness, weakness, sleep disorders, rash, and pruritus |
| **C/Is:** | known allergy, Pregnancy and lactation, patients with history of tender disorder, children under 18 yrs old |
| **P/Cs:** | epilepsy, G6PD deficiency, myasthenia gravis |

**D/Is:** Quinolones, analgesics, anticoagulants, and theophylline

**Dosage forms:** Tablet (as hydrochloride), 250mg, 500mg, 1000mg Capsule, 500mg, 1000mg, Injection Infusion (as lactate), 2 mg/ml in 50 ml and 100 ml bottle

**Alternative**

**Doxycycline**, 100 mg P.O., twice daily for 7-10days

**ADRs:** diarrhoea, erythema, headache, visual disturbance, hepatotoxicity, pancreatitis, pseudomembrane colitis, discolouration of infants and children's teeth, photosensitivity

**C/Is:** pregnancy, and breast-feeding, in infants and children up to 8 years of age

**P/Cs:** hepatic impairment

**D/Is:** antacids, carbamazepine, oral contraceptives, ferrous salts, phenobarbital, phenytoin, rifampicin and warfarin

**Dosage forms:** Tablet, 100mg, Capsule, 100mg

**Treatment of cutaneus anthrax with systemic illness or extensive edema involving face or neck and gastrointestinal or inhalational anthrax**

**First line**

**Ciprofloxacin,** 400mg IV every 8 h 10-14 days

*OR*

**Doxycycline**, 100mg IV every 12h 10-14days

(in children >8 years and >45 kg: 100mg twice daily; in children >8 yrs and ≤ 45 kg: 2.2mg/kg twice daily [not to exceed 100mg/dose]; or <8 years: 2.2mg/kg twice daily [not to exceed 100mg/dose])

*OR*

**Penicillin G**, 4 MU IV every 4–6 h 10-14days

*PLUS*

**Clindamycin**, 600 mg-900mg IV every 8 hour 10-14days

(for children: 7.5mg/kg IV Q6hrs)

**ADRs:** abdominal discomfort, rashes, urticaria, jaundice

**C/Is:** hypersensitivity

**P/Cs:** hepatic and renal impairment, neonates and infants; elderly; pregnancy; breast feeding

**D/Is:** alcuronium, neostigmine, pyridostigmine, vecuronium

**Dosage forms:** Capsule, 75mg, 150mg; Injection, 150mg/ml in ampoule; Oral solution, 15mg/ml

When intravenous courses of antibiotics is completed, switch to P.O., antibiotics and treat as follows to complete a course of 60days:

**Ciprofloxacin**, 500mg P.O., every 12h

*OR*

**Doxycycline**, 100mg P.O., every 12h

*PLUS*

**Clindamycin**, 450mg P.O., every 8h

*OR*

**Rifampicin**, 300mg P.O., every 12h

### 5. Bacillary Dysentery

Bacillary dysentery is diarrhoeal disease caused by bacteria, which invade and destroy the intestinal epithelium. It is often caused by Shigella spp. Other less important causes are Campylobacter species, non-typhoidal Salmonella species and entero-invasive Escherichia coli. Transmission occurs via contaminated water or food.

**Clinical features**

- Common clinical manifestations include severe abdominal cramps, fever, watery, mucoid or bloody diarrhoea with tensmus.

**Investigations**

- Direct stool examination which mostly reveals abundance of leukocytes (pus cells)
- Stool culture

**Treatment**

**Objective**

- Prevent dehydration
- Replace lost fluid
- Eradicate the infecting organism

**Supportive treatment**

Correct dehydration with **ORS** or IV fluids

Relieve pain and fever if necessary

**Pharmacologic**

**First line**

**Ciprofloxacin,** 500mg P.O., BID for 3-5days.

**Alternatives**

**Sulfamethoxazole+trimethoprim**, 800mg/160mg P.O., BID for 5-7 days. For children 6 weeks–5 months; 100/20mg; 6 months – 5 yrs, 200/40mg; 6 – 12 yrs, 400/80mg BID.

| | |
|---|---|
| **ADRs:** | hypersensitivity, photosensitivity, blood disorders, peeling of the skin, GIT disturbance |
| **C/Is:** | infants up to two months of age, hypersensitivity |
| **P/Cs:** | elderly, renal and hepatic function impairment, photosensitivity, Glucose-6-phosphate dehydrogenase deficiency, predisposition to folate deficiency; asthma; pregnancy; breastfeeding |
| **D/Is:** | oral hypoglycemics, oral anticoagulants, penytoin, methotrexate, folate antagonists |
| **Dosage forms:** | Tablet (pediatric), 100mg + 20mg; (adult), 400mg + 80mg, 800mg+160mg, Mixture, 200mg + 40mg in each 5ml, Injection, 400mg + 80mg in each 5ml ampoule |

**N.B.** Avoid in blood disorders and discontinue immediately if blood disorder develops, adequate fluid intake to avoid crystalluria, monitor blood counts; rash – discontinue immediately;

OR

**Ceftriaxone**, 1-2g stat or 2 divided doses IM or slow IV. For children: 20-50mg/kg/day as a single dose or 2 divided doses IM or slow IV.

| | |
|---|---|
| **ADRs:** | GI disturbances, headache, colitis, allergic reactions, transient hepatitis and cholestatic jaundice, blood disorders, reversible nephritis, rarely prolongation of prothrombin time, pancreatitis |
| **C/Is:** | cephalosporin hypersensitivity, porphyria, neonates with jaundice, hypoalbuminaemia, acidosis or impaired bilirubin binding |
| **P/Cs:** | penicillin sensitivity; renal and hepatic impairment, pregnancy and breast feeding |
| **D/Is:** | furosemide and warfarin. Do not admix with aminoglycosides in ame bottle/bag |
| **Dosage forms:** | Injection, 0.25g, 0.5g, 1g, 2g in vial |

**N.B.** As it precipitates in urine or in gall bladder, consider discontinuation if symptomatic Antidiarrhoeals are best avoided in the treatment of patients with bacillary dysentery as they may slow the clearance of the organisms and may increase the risk of toxic megacolon.)

## 6. Brucellosis

Brucellosis is a zoonotic infection caused by different species of the gram negative bacteria, *Brucella species. B. melitensis* is the most virulent and invasive. Transmission to humans occurs through direct contact, through broken skin, with infected animal tissue, inhalation of infectious aerosols, or ingestion of infectious milk or dairy products. Brucellosis is predominantly an occupational disease. Sporadic cases and sometimes large outbreaks occur after consumption of raw milk and milk products. Animals involved are cows, sheep, goats, swine, and occasionally dogs. Brucellosis is endemic in Ethiopia and the Mediterranean countries, North and East Africa, the Middle East, South and Central Asia, and South and Central America. Brucellosis is often unrecognized and frequently unreported.

**Clinical features**

- Brucellosis has a long incubation period of 1-8 weeks and the most common symptoms are prolonged fever classically referred to as 'undulating' fever, chronic fatigue and arthralgia
- Osteomyelitis of the vertebrae is commonly seen
- Mortality, though rare, is due to neurologic complications (e.g.meningoencephalitis) or infective endocarditis

**Investigations**

The major confusion in a patient with brucellosis is to tell whether the patient has Tuberculosis. The following can be used to confirm diagnosis of brucellosis in a patient who is suspected to have the disease clinically:

1. Isolation of Brucella from blood, bone marrow, pus, or other tissues:
    - Blood culture – requires special technique and long incubation period, and is often negative in long-standing disease
    - PCR for Brucella;-Not Routinely avaialble
    - Both of the tests above are not widely available in Ethiopia

2. Serological tests for Brucella antibodies in blood or other tissue:

- Combine Rose Bengal test for agglutinating antibodies (IgM, IgG, IgA) with a test for non-agglutinating antibodies
- IGG (ELISA-IgG). Antibody Titers of 1:160 or higher are very highly suggestive of the diagnosis of brucellosis

3. X-rays to demonstrate joint disease (blurred joint margins, widened sacroiliac space, destruction of vertebrae)

**Treatment**

**Objectives**

- Eradicate the infection
- Prevent long term sequelae

**Non pharmacologic**

- Surgical intervention e.g. abscess drainage, joint replacement will be needed for focal infections

**Pharmacologic**

- The principle here is to use two or more antibiotics in combination to ensure success
- Treatment depends on the presence or abscence of focal disease

A**. No focal Disease:**

**First line**

**Doxycycline**, 100mg P.O., BID for 6weeks

*PLUS*

**Gentamycin**, 5mg/kg once daily for the first 7days

**Alternative**

**Doxycycline,** 100mg P.O., BID for 6weeks

*PLUS*

**Rifampicin**, 600-900mg/day P.O., once daily for 6 weeks

The relapse rate is 10-20%.

B. **Spondylitis, Sacroillitis:**

**First line**

**Doxycycline**, 100mg P.O., BID for at least 3months

*PLUS*

**Gentamycin,** 5mg/kg once daily for 3months

*PLUS*

**Rifampicin**, 600-900mg/day P.O., once daily for at least 3months

**Alternative**

**Ciprofloxacin**, 750mg P.O., BID for at least 3months

*PLUS*

**Rifampicin**, 600-900mg/day P.O., once daily for at least 3months

C. **Neurobrucellois:** Most cases will have meningitis but it is a rare event

**First Line**:

**Doxycycline**, 100mg P.O., BID

*PLUS*

**Rifampicin,** 600-900mg/day P.O., once daily

*PLUS*

**Sulphamethoxazole-Trimethoprim,** 5mg/kg of the Trimethoprim component P.O., BID

*Treatment duration is determined by the clearance of CSF. Give treatment until CSF analysis findings return to normal.

D. **Endocarditis**

This condition is a rare, but most common cause of death in patients with brucellosis. The treatment needs surgical intervention and antimicrobial therapy for a long duration of time upto 6 months. Patients suspected with these conditions need referal to be evalauated in specialized hospitals

## 7. Candidiasis

Candidiasis is a disease caused by fungi of *Candida species*. The most common causative agent is *C.albicans.* These fungi are parts of the normal human flora and found in the mouth, vagina, and gastrointestinal tract. Candidiasis can be limited to mucous membranes or can occasionally spread through the blood or be deeply invasive. Predisposing factors that can lead to infection are: wide-spectrum antibiotic use, diabetes mellitus, HIV, pregnancy, skin maceration, or a break in the natural skin or mucosal barrier.

**Clinical features**

**Oral candidiasis:**

- Difficulty with swallowing and white deposits that adhere to the mucosa in the mouth. Persistent oral candida in an HIV patient is a WHO stage 3 condition

**Skin infection:**

- Red macerated skin if infection occurs in skin folds under breasts or around the anus; usually associated with itching.

**Vaginal candidiasis:**

- White itchy discharge; sometimes associated with pain on urination.

**Oesophageal candidiasis:**

- This can be asymptomatic but is often associated with chest pain and difficulty swallowing.
- Oesophageal candidiasis (and candida of trachea, bronchi, or lungs) in an HIV infected patient is a WHO stage 4 condition

**Diseminated Candida/Invasive disease:**

- Fungemia can occur mainly through infection of intravenous devices or urinary catheters and can spread throughout the whole body..
- There are a few organs that are very prone to be invaded after bloodstream infections.
- These are the eyes, causing blurred vision and showing white cotton ball lesions on fundoscopy, and the liver and spleen, particularly in patients recovering from very low WBC. These situations require specific treatment

**Investigations**

- A wet smear can identify the fungus with pseudo-hyphae (branching structures).
- Since Candida species are one of the easier fungi to culture, a culture of the likely source will often yield a positive result.

**Treatment**

**Objectives**

- Depend on the site of infection from symptom control to eradication of the organism from the site.

Approaches to management depend on the location and the severity of the infection.

**Oral candidiasis:**

**First line**

**Miconazole oral gel**, 60mg 4 times daily for 7 days

**ADRs:** GI disturbances; allergic reactions

**C/Is:** hepatic impairment

**P/Cs**: pregnancy and breast feeding; avoid in porphyria, monitor haematocrit, haemoglobin and serum electrolytes and lipids

**D/Is:** oral anticoagulants, sulphonylurea hypoglycaemic medicines, phenytoin; amphotericin

**Dosage forms:** Tablet, 250mg; Oral Gel, 25mg /ml; Intravenous infusion, 10 mg/ml in 20ml

**Alternatives**

**Nystatin,**

Adult: One tablet 500,000 IU 4 times daily; tablets should be sucked and retained in the mouth for as long as possible; therapy should be continued for at least 48 hours after symptoms have resolved

Child: 100,000 units 4 times daily prophylaxis, 1 million units once daily.

Neonate: 100,000 units once daily

**ADRs:** GI disturbances; Steven Johnson syndrome, irritation.

**Dosage forms:** Tablet, 500,000IU; Oral suspension, 100,000units/ml

*OR*

**Clotrimazole troche,** (dissolving tablet) P.O., twice daily for 7 days;

**ADRs:** local irritation, hypersensitivity reactions

**C/Is:** Known hypersensitivity reactions

**P/Cs:** Pregnancy, contact with eyes and mucous membranes should be avoided.

**D/I:** Benzodiazepines, calcium channel blockers, ergot derivatives, mesoridazole, mirtazapine, nateglinide, nefazodone, pimozide, quinidine, thioridazine

**Dosage forms:** Powder, 1%; Mouth paint, 1%

*OR*

**Fluconazole,** 100 to 200mg P.O., for 7 to 14 days for recurrent oral candidiasis

**ADRs:** GI disturbances, headache, rash, abnormalities of liver enzymes, angioedema, dizziness, seizures

**C/Is:** hypersensitivity to other azole antifungals

**P/Cs:** renal, hepatic impairment

**D/Is:** Rifampicin, hydrochlorthiazide, phenytoin, sulphonylureas, hypoglycemic agents, nortriptyline, and zidovudine, terfenadine, oral anticoagulants and theophylline

**Dosage forms:** Capsule/tablet, 50mg, 100mg, and 200mg;
Oral Suspension, 50mg /5ml, 200mg /5ml

**Skin infection:** Use measures to reduce wetness or moisture and decrease friction. If needed topical application of an antifungal cream such as nystatin, cotrimazole, terbinafine, or miconazole cream for 5 to 7 days is effective.

**Vaginal** (see Section in STIs)

**Oesophageal candidiasis:**

**Fluconazole**, 100mg or 200mg P.O., daily for 14 to 21 days;

*OR*

**Itraconazole**, 200mg P.O., daily, can be increased to a maximum of 400mg daily,for 10–14 days; the capsules should be taken with food or an acid drink (such as a cola) to increase their bioavailability;

**ADRs:** skin rash, gastrointestinal disturbances, headache; transient increase in liver enzymes and rarely, hepatitis

**C/Is:** hypersensitivity to any azole antifungal

**P/Cs:** hepatic disease

**D/Is**: antacids, sucralfate, cimetidine, didanosine, carbamazepine, phenytoin, rifampicin, terfenadine, digoxin, indinavir, ritonavir, midazolam, triazolam, warfarin

**Dosage forms:** Capsule, 100mg, 200mg ;Oral solution, 10mg/ml

*OR*

**Ketoconazole**, 200 to 400mg P.O., daily if fluconazole is not available, until remission is obtained.

**ADRs:** gastro intestinal disturbance, gynaecomastia, impotence, menstural irregularities, hepatotoxicity

**C/Is:** pre-existing liver disease, pregnancy; hypersensitivity to azole antifungals

**P/Cs:** breast-feeding, pediatrics and geriatrics patients, alchlorhydria, hypochlorhydria, alcoholism, renal function impairment

**D/Is:** antimuscarinic agents, antacids, $H_2$ -receptors antagonists; rifampicin, isoniazid, phenytoin, astemizole, terfenadine,

corticosteroids, oral anticoagulants, alcohol, oral contraceptives, tolbutamide, didanosine, digoxin, indinavir, nevirapine

**Dosage forms***:* Tablet, 200mg; Syrup, 20mg /5ml

**N.B.** When administered with lopinavir/r, the dose of ketoconazole should not exceed 200 mg daily.

**Disseminated disease:** Removal of prosthetic devices including catheters is recommended for the management of invasive candida infections.

**Fluconazole,** 400mg daily (orally or IV if patient cannot swallow) for 14 days after the last fever.

## 8. Cholera

Cholera is an acute diarrhoeal disease that can cause severe dehydration and death in a few hours. It is caused by *Vibrio cholera* and often occurs as epidemics under conditions of poor hygiene.

**Clinical features**

- Sudden onset of explosive diarrhoea is the hallmark of the disease.
- The diarrhoea is classically voluminous, non-offensive, and somewhat looks gray or "rice water". Fever is absent.

**Investigations**

- It is often diagnosed based on clinical grounds.
- If possible stool culture.

**Treatment**

**Objectives**

- Replace volume deficit and ongoing losses
- Decrease duration of diarrhoea

**Prevention:** The promotion of adequate hygienic conditions in the community is important to prevent an outbreak and spread of the disease.

**Non pharmacologic**

- Advise patients to take fluid
- Symptomatic/Supportive Treatment

For dehydration in mild cases give ORS, PRN; for children: < 2yrs: 50-100ml; 2-10 years: 100-200ml after each loose stool. For severe cases Ringer lactate IV infusion (alternatively Normal saline) should be given 50-100ml/min until shock is reversed; thereafter, according to fluid loss. KCl solution 20-40mmol/litre may be added as required.

In the absence of IV infusion aggressive rehydration with ORS is vital.

**Pharmacologic**

**First line**

**Doxycycline**, 100mg, P.O., BID for 3 days. For children: 6mg/kg daily for 3 days.

**Alternatives**

**Tetracycline,** 500mg P.O., QID for 3-5 days.

*OR*

**Sulfamethoxazole+trimethoprim**,

children 6 weeks – 5 months: 100/20mg

children 6 months – 5 yrs: 200/40mg

children 6 – 12 yrs: 400/80mg BID for 5 days

adults: 800mg/160mg P.O., BID for 5 days.

*OR*

**Ciprofloxacin***,* 500mg P.O., BID, for 3-5 days

## 9. Clostridium Difficille Associated Disease (CDAD)

*Clostridium difficile* associted disease results from a disturbance of the normal bacterial flora of the colon, colonization by *C difficile,* and the release of toxins that cause mucosal inflammation and damage. Antibiotic therapy is the key factor that alters the colonic flora. *C difficile* infection primarily occurs in hospitalized patients. While recent antibiotic use is the strongest risk factor for the development of CDAD, the following have also been implicated as a risk factor: elderly age, kidney failure, burn patients, abdominal surgery, chemotherapy, immune-compromised and ICU patients. All classes of antibiotics have been associated with CDAD, including the penicillins, cephalosporins, macrolides, lincosamides, and aminoglycosides. Symptoms may occur while patients are receiving antibiotics, usually after 5 to 10 days of therapy, or can occur 2 to 10 weeks after antibiotic therapy has been completed.

**Clinical features**

Symptoms of *C difficile* colitis often include the following:

- mild to moderate watery diarrhoea that is rarely bloody
- cramping abdominal pain, anorexia, malaise.

Physical examination may reveal:

- fever(specially in more severe cases)
- dehydration
- lower abdominal tenderness
- rebound tenderness(raises the possibility of colonic perforation and peritonitis)

**A mild case** may be defined as having 5 to 10 watery bowel movements per day, no significant fever, and only mild abdominal cramps. Blood tests may show a mild rise in the white blood cell count (WBC) upto15,000.

**Severe cases** may experience more than 10 watery stools per day, nausea, vomiting, high fever (upto 40 degree Celsius), rectal bleeding, severe abdominal pain with much tenderness, abdominal distention, and a high white blood count of 15-40,000.

**Investigations**

- WBC count: leucocytosis expected.
- Stool exam: shows pus cells and may be heme positive.
- Detection of toxin(enzyme immunoassays for rapid detection of TcdA and TcdB.
- Stool culture: presence of ofganisms in the stool does not necessarily indicate CDAD.

**Treatment**

**Objectives**

- Arrest diarrhoea and to prevent recurrence of diarrhoea.
- Educate patients and health professionals on judicious use of antibiotics.

**Non Pharmacologic**

- Discontinue offending agent. This may be the only treatment required in mild cases.
- Replace fluids and electrolytes.

**Pharmacologic**

If non-pharmacologic measures are not effective or practical, specific therapy with:

**First line**

**Oral Metronidazole**, 250mg four times per day for 10 days should be initiated.

**Alternative**

**Oral Vancomycin**, 125mg four times daily for 10 days should be reserved for patients with severe disease.

**ADRs:** hypotension, palpitations, urticaria

**C/Is:** patients with hearing problem

**Dosage forms:** Injection, 500mg in vial.

*OR*

**Metronidazole**, 500 mg Intravenously every 8 hours in the patient who is unable to take oral medications. Intravenous vancomycin fails to achieve significant intraluminal bowel concentrations and is not recommended.

First-time recurrences should be treated with the same regimen used to treat the initial episode. Cure rates of 95% have been reported with the use of this agent.

**N.B.** Avoid antiperistaltic agents as they may cause toxic megacolon

## 10. Cryptococcosis

This infection is most commonly caused by a fungus called *Cryptococcus neoformans*, particularly in HIV-positive patients with advanced immunodeficiency (CD4 cell count generally <100/mm3). However, patients who have been on long-term steroid therapy, as well as other immunosuppressive medicines, are also at risk. Typically, infection is acquired by inhalation of the fungus into the lungs. Cryptococcus is found in most areas with a relatively warm climate, and is not restricted to the tropics.

Cryptococcal meningitis or meningo-encephalitis is the most common presentation in HIV-positive patients, and is associated with a universal mortality without treatment. Non-meningeal presentations of cryptococcosis include pneumonia, skin lesions, and lymphadenitis.

**Clinical features**

Sub-acute meningitis:

- Headache increasing over days to weeks, fever, photophobia, nausea, seizures, confusion, irritability, blurred vision, sixth cranial nerve palsy, papilloedema on retinal exam are common.
- Nuchal rigidity is often not marked. Coma, or a reduced level of consciousness are associated with a poor prognosis.

Lung infections:

- Chest pain and cough in a minority of patients, but often no fever.

Skin lesions:

- Disseminated disease is associated with papular lesions with an umbilicated, centrally depressed area (similar appearance to molluscum contagiosum), which can become ulcerated.

**Complications**

- Intracranial pressure can become raised (increasing headache, vomiting,cranial nerve palsy). Hydrocephalus, blindness, dementia, and personality change can occur as permanent sequelae.
- Cryptococcomas can develop in the brain, more commonly in patients who are not immunocompromised. Coma, cerebral oedema, and death follow if it is untreated, usually due to elevated intracranial pressure.

**Investigations**

- CSF examination:
    - Opening pressure, cell count,glucose and protein
    - Tests to detect the organism with India Ink,antigen tests or culture
- Serology for cryptococcal antigens
- Chest X ray to demonstrate the organism

**Treatment**

**Objectives**

- Suppress fungal growth
- Prevent sequelae related to increased intracranial pressure

**Non Pharmacologic**

- Control of raised intracranial pressure (ICP): daily lumbar puncture with withdrawal of 20-30ml of CSF

- Coma care (including NG tube feeding) if the patient is unconsious

**Pharmacologic**

**Induction and Consolidation treatments**:

**First line**

If amphotericin, laboratory monitoring, pre-hydration, and flucytosine available:

**Amphotericin B**, 0.7 to 1mg/kg

*PLUS*

**Flucytosine**, 100mg/kg for 14 days, followed by oral **fluconazole** 400mg daily for 8 weeks.

**Alternatives**

If amphotericin, laboratory monitoring, and pre-hydration available, but not flucytosine:

**Amphotericin B**, (as above)

*PLUS*

Oral **fluconazole**, 800mg for 14 days followed by **fluconazole** 400mg for 8 weeks.

*OR*

If laboratory monitoring unavailable:

Intravenous **Amphotericin B**, (as above) for 5-7 days

*PLUS*

Oral **fluconazole** 800mg for 14 days followed by **fluconazole** 800mg for 8 weeks.

*OR*

If amphotericin, lab monitoring and pre-hydration NOT available:

Oral **fluconazole,** 800–1200mg for 14 days followed by **fluconazole** 400mg for 10 weeks.

**N.B.** If the patient has meningitis or pneumonia, treatment with a regimen containing amphotericin is preferred provided that facilities allow appropriate monitoring (kidney function and electrolytes).

**Secondary prophylaxis:**

**Fluconazole**, 200mg P.O.. daily until the patient is successfully on ART and the CD4 count is maintained above 200cells/mm3 (two measurements 6 months apart).

**Minimize acute infusion reactions when amphoterecin is given (e.g. fever, chills, headache, hypotension):**

- Infuse the initial dose slowly over 3–6 hours.

- Prophylactic antipyretics or hydrocortisone should only be used in patients who have previously experienced acute infusion reactions (and in whom continued treatment with amphotericin is essential).

**Delay initiation of ART**

Due to the high risk of IRIS with CNS disease, which may be life-threatening, in HIV infected adults, adolescents and children with a recent diagnosis of cryptococcal meningitis, ART initiation should be deferred until there is evidence of a sustained clinical response to antifungal therapy. This depends on the type of regimen used in the induction and consolidation:

After 2-4 weeks of induction and consolidation treatment with amphotericin B-containing regimens combined with flucytosine or fluconazole (two weeks with non-meningeal disease);
*OR*
After 4-6 weeks of induction and consolidation treatment treatment with a high-dose oral fluconazole regimen (four weeks with non-meningeal disease).

## 11.Filariasis, Lymphatic (Elephantiasis)

The term filariasis refers generally to disease caused by the lymphatic-dwelling filarial worms *Wucheria bancrofti, Brugia malayi, and Brugia timori*. *Wuchereria bancrofti* is the most common cause of lymohatic flariasis in the Tropics including Ethiopia. The infection is transmitted by mosquitoes. Filarial parasites exhibit a daily periodicity in the concentration of microfilariae in the peripheral blood of the host. They have a nocturnal or diurnal periodicity. This diseases should be differentiated with podoconiosis ("non-filarial elephanthiasis") a non-communicale diseases which is common in some areas of Ethiopia.

**Clinical Features**

**Progressive filariasis:** In progressive filariasis, the clinical features depend on the clinical stage.

1. **Asymptomatic amicrofilariaemic stage: No clinical symptom**
2. **Asymptomatic microfilariaemic stage: No clinical symptoms but microfilariae detectable**
3. **Stage of acute manifestations**:

In the initial months and years following infection, patients may have recurrent episodes of acute inflammation in the lymph nodes or vessels of the limb and scrotum.These are generally related to bacterial and fungal superinfections of tissue compromised by reduced lymphatic function. Clinical manifestations: Filarial fever (ADL-DLA)

- Acute adenolymphangitis (ADL): high fever, lymphatic enlargement in the area where the adult worm resides, transient local oedema, tenderness and redness of overlying skin. Ulceration can occur.
- Dermatolymphangioadenitis (DLA): high fever, chills, muscle aches, and headache with inflammatory skin changes in the area of infection.
- Lymphangitis
- Lymphadenitis
- Epididimo-orchitis

4. **Stage of obstructive (chronic) lesions:**

These take 5–15 years to develop. They result from permanent damage to lymph vessels by the adult worms. Recurrent inflammatory reactions to the worms cause dilation of the lymph vessels, which results in oedema. In clinical surveys, leg lymphoedemas are commonly classified as grade I: pitting lymphoedema spontaneously reversible on elevation; grade II: non-pitting lymphoedema, loss of skin elasticity; and grade III: evident elephantiasis with skin folds and papules. A more detailed classification with stages of lymphoedema are outlined below.

**Table 27-Stages of lymphoedema**

| | Swelling | Skin folds | Apearance |
|---|---|---|---|
| **Stage I** | Reversible at night | Absent | Smooth, normal |
| **Stage II** | Not reversible at night | Absent | Smooth, normal |
| **Stage III** | Not reversible at night | Shallow | Smooth, normal |
| **Stage IV** | Not reversible at night | Shallow | Irregular, occasional knobs or nodules |
| **Stage V** | Not reversible at night | Deep | Smooth or irregular |
| **Stage VI** | Not reversible at night | Shallow or deep | Wart-like lesions on foot or toes |

| | | | |
|---|---|---|---|
| **Stage VII** | Not reversible at night | Deep | Irregular;needs help with daily activities; dependent |

**Occult or cryptic filariasis, presenting as tropical pulmonary eosinophilic (TPE) syndrome:**

Occult filariasis results from hyperresponsiveness to filarial antigens. It occurs more commonly in males and the classic manifestations are: paroxysmal cough and wheeze, scanty sputum, occasional haemoptysis, adenopathy, chronic interstitial lung disease, recurrent low-grade fever, and weight loss.

**Investigations**

- CBC: extremely high eosinophil count.
- Blood film to demonstrate the organisms
- Immuno-chromatographic (card) test to demonstrate filarial antigens
- Diethylcarbamazine (DEC) provocative test (2mg/kg). After taking DEC, microfilariae enter the peripheral blood within 15 minutes
- Ultrasonography: organisms may be visualised ih the lymphatics of the female breast or male scrotum
- Chest X ray
- Diagnosis is clinical in late disease

**Treatment**

**Objectives**

- Eradicate the filaria
- Prevent complications

**Non pharmacologic**

1. Supportive treatment and prevention of acute ADL attacks:
    - hydration and rest
    - antipyretics and analgesics

2. Treatment and prevention of lymphoedema:

Hygiene measures for the affected limb:

- wash twice daily with soap and clean water and dry well
- keep nails short and clean
- elevate the affected limb at night
- wear comfortable footwear
- prevent and treat entry lesions

- Frequent exercise of the affected limb to promote lymph flow:
  - standing on toes, flexing and circling ankles while sitting
- Use of antibiotic or antifungal agents:
  - antiseptic, antibiotic, and antifungal creams for small wounds and abrasions
  - systemic antibiotics or antifungals in severe cases
- Surgical treatment of hydrocele

**Pharmacologic**

Recommended regimen for lymphatic filariasis in clinical settings:

**Diethylcarbamazine citrate (DEC)**, 6mg/kg P.O.daily for 12 days

*OR*

**Diethylcarbamazine citrate**, 6 mg/kgp. P.O., plus **albendazole** 400mg P.O., as single dose.

**N.B.** DEC should not be used in patients with onchocerciasis, due to possible severe adverse reactions. Patients should be examined for co-infection before using DEC. In co-infected patients, the following alternative regimen should be used:

**Ivermectin**, 200-400micrograms/kg P.O., plus **albendazole** 400mg P.O. as single dose

**N.B.** Ivermectin should not be used in patients with loiasis.

**Recommended regimen for lymphatic filariasis in public health interventions:**

Current public health strategies for lymphatic filariasis elimination rely on preventive chemotherapy with the aim of interrupting transmission of the infection. WHO currently recommends mass medicine administration as an annual single dose of DEC 6mg/kg plus albendazole 400 mg, yearly for 4-6 years in areas where onchocerciasis is not co-endemic with filariasis. In areas where onchocerciasis is present but loiasis is absent, an annual single dose of ivermectin 200-400 micrograms/kg plus albendazole 400 mg, yearly for 4-6years, is recommended.

## 12. Giardiasis

*Giardia lamblia* is a ubiquitous gastrointestinal protozoa that results in clinical pictures ranging from asymptomatic colonization to acute or chronic diarrhoeal illness. It can occur both sporadically and in epidemics. *Giardia lamblia* infects humans through ingestion of as

few as 10 cysts. The infection is more prevalent in children than adults. Asymptomatic infection occurs in approximately 60% of people exposed to Giardia. The most common presentation is diarrhoea which is foul-smelling with fatty stools (steatorrhea), flatulece, weight loss, crampy abdominal pain with bloating and failure to thrive.

**Clinical features**

- Abdominal cramps, bloating and diarrhoea.

**Investigations**

- Established by identifying *Giardia lamblia* trophozoite or cyst from fecal or duodenal samples.

**Treatment**

**Objectives**

- Prevent and treat dehydration
- Stop diarrhoea as promptly as possible

**Medicine Treatment**

**First Lline**

**Tinidazole**, single oral dose of 2g. For children, 50-75mg/kg as a single dose (may be repeated once if necessary)

**Alternative**

**Metronidazole**, 250-500mg P.O., TID for five days

**13. Intestinal Helminthic Infestations**

These are infections caused by intestinal worms (nematodes and cestodes), which are commonly associated with poor personal and environmental hygiene. Although they may not be fatal, they contribute to malnutrition and diminished work capacity.

**Clinical features**

- Include abdominal cramps, nausea, bloating, anorexia, Anaemia, passage of adult worms

**Investigations**

- Mainly by direct stool microscopy

**Treatment**

**Objectives**

- Reduce symptoms
- Break the cycle of transmission

**Non pharmacologic**

- Personal hygiene

**Pharmacologic** (See table below)

**Table 28-Treatment of common intestinal helminthic parasitic infestations**

| NAME OFINFECTIONETIOLOGY; MODE OF TRANSMISSION | TREATMENT | REMARK |
|---|---|---|
| **Ascariasis**<br><br>***Ascaris lambricoids***<br><br>Ingestion of the larvae of the parasite together with food | **First line-options**<br>**Albendazole,** 400mg P.O. as a single dose, for children:<br>1 – 2 years, 200mg as a single dose.<br>**Mebendazole,** 100mg P.O.BID for 3 days or 500mg, once<br>**Alternative (pregnant women)**<br>**Pyrantel pamoate**, 700mg P.O. as a single dose | Presence of migrating larvae in the lungs can provoke pneumonia |
| **Enterobiasis**<br><br>***Enterobius Vermicularis***<br><br>Ingestion of the eggs of the parasite together with food | **First line-options**<br>**Mebendazole,** 100mg P.O. BID for 3 days OR<br>**Albendazole,** 400mg P.O. as a single dose,<br>Alternative<br>**Piperazine,** 4g in a single dose. | Common in children and auto infection may occur |
| **Hookworm infestation**<br>***Necator americanus or Ancylostoma duodenale***<br>Penetration of the larvae of the parasite through skin | **First line**-options<br>**Mebendazole,** 100mg P.O. BID for 3 days or 500mg stat OR<br>**Albendazole,** 400mg P.O. as a single dose mg as a single dose.<br>**Alternatives:**<br>**Pyrantel pamoate**, 700mg P.O. as a single dose | |
| **Strongyloidiasis**<br><br>***Strongloidexs stercolaries***<br><br>Penetration of the larvae of the parasite through skin | **First line**<br>**Ivermectin,** 200mg/kg daily for 2 days. For disseminated strongyloidiasis, treatment with ivermectin should be extended for at least 5–7 days or until the parasites are eradicated.<br>**Alternatives-**options<br>**Albendazol**e 400mg P.O.BID for three consecutive days. OR<br>**Thiabendazole,** 1500mg, P.O. BID, for children: 25mg/kg p.o. for three consecutive days. | Larvae migrate to the lungs where they cause tissue destruction and bleeding.<br>Treat concomitant anaemia if any |
| Trichuriasis<br>***T.tricura*** | **First line-options**<br>**Mebendazole**, 500mg P.O., single dose OR<br>**Albendazole,** 400mg,P.O. for three days | Heavy infestation leads to bloody diarrhoea, bleeding and weakness |

| | | |
|---|---|---|
| Taeniasis<br>***T.saginata***<br>***T.solium*** | **First line-Intestinal infestation**<br>**Praziquantel** P.O. 600mg or 10mg/Kg, single dose<br>**Alternative**<br>**Niclosamide,** 2g in a single dose P.O.<br>**Treatment ofneurocysticercosis**<br>**Albendazole** P.O. 15mg/kg per day for 8–28 days<br>**or**<br>**Praziquantel** 50–100mg/kg daily in three divided doses for 15–30 days**.**<br>Longer courses are often needed in patients with multiple subarachnoid cysticerci<br>**PLUS**<br>-High-dose glucocorticoids<br>-Anti epileptics (if there is seizure) | *T. solium* (pork tapeworm) may cause fatal cysticercosis |
| ***Hymenolepis nana*** | **First line**<br>**Praziquantel**, 25mg/kg or 1800mg P.O. single dose<br>**Alternatives**<br>**Niclosamide,** 2g P.O. on the first day followed by 1g QD for 6 days | |

## 14. Leishmaniasis

Leishmaniasis is a zoonotic disease caused by protozoa, which belong to the genus *Leishmania*. Mode of transmission is by the bite of phlebotomites (sand flies) from animals to humans. It has two major clinical forms: **cutaneous** and **Visceral leishmaniasis**.

**Cutaneous Leishmaniasis**

This form is characterised by the development of single or multiple firm, erythematouos papules which occur on the exposed parts of the body. The papules may ulcerate later in the course of the illness.

**Post kala-azar Dermal Leishmaniasis (PKDL)**

VL due to *L. donovani* occurs with a post treatment complication called PKDL. PKDL is characterised by the occurrence of painless skin lesions relatively common towards the end of treatment (more common in Sudan with about 50% of the cases) or shortly *after treatment*. PKDL is rare in Ethiopian VL patients but it is relatively common in *Leishmania* HIV co-infection. PKDL patients harbor Leishmania parasites in the skin lesions and these can be potential sources of infection and disease transmission. Patients should be advised to seek medical attention and use impregnated bed nets if they develop skin rash following treatment.

Depending on the severity of the lesion, PKDL can be graded which will facilitate treatment decisions. Occasionally, PKDL may occur prior to the VL (Pre-*kala azar* dermal Leishmaniasis) or concomitantly (para-*kala azar* dermal Leishmaniasis) to the active VL disease.

## 15. Visceral Leishmaniasis (Kalazar)

The two *Leishmania* species usually considered as responsible for VL are *L. donovani* and *L. infantum.* The commonest species causing Visceral leishmanisasis in Ethiopia *is L. donovani.* The epidemiology of visceral leishmaniasis in Ethiopia is closely related to travel history to the North, North west and south west parts of the country particularly areas closer to the Ethio-Sudanese border. The disease is more prevalent in males and HIV infected adults.

**Clinical features**

- Its cardinal manifestations include fever, marked weight loss, splenomegally and features of pancytopenia.

**Investigations**

Diagnosis is established by the clinical presentation in endemic areas and the demonstration of the organisms in smears.

a. Non-Leishmanial Tests: CBC

b. Parasite Detection-Visualization of the amastigote form of the parasite by microscopic examination of aspirates from lymph nodes, bone marrow or spleen aspiration. *Culture improves the detection of the parasites. However, this technique remains restricted to referral hospitals or research centers.

c. Antibody Detection-DAT and rK39 have been extensively evaluated and used for the diagnosis of VL in the field and in laboratory settings.

d. Antigen Detection Test-It is more specific than the antibody-based immunodiagnostic test. Evaluation of the performance of A urine latex agglutination (KATEX) at the Indian subcontinent and East Africa has shown that this test has a good specificity but only a low to moderate sensitivity.

e. Molecular Techniques-Compared to the other diagnostic techniques available, the molecular approaches remain expensive and technically highly demanding. Their applicability in the endemic areas is highly questionable.

**Treatment**

**Objectives**

- Reduce the parasite burden
- Prevent medicine resistance
- Avoid toxic medicine effects, and
- Improve the clinical condition of patients and to manage complications (anaemia, malnutrition and secondary infections)

**Non pharmacologic**

- Supportive care including proper hydration and nutritional therapy before and during the VL treatment
- Correct severe anaemia with blood transfusion
- Closely monitor patient for cardiovascular toxicities of VL treatment

**Pharmacologic**

**First line**

A. **Combination Therapy: Sodium Stibogluconate (SSG) and Paromomycin**

**Sodium stibogluconate**, 20mg/kg body weight/day IM daily for 17d

| | |
|---|---|
| **ADRs:** | abdominal pain; muscle pain, joint stiffness |
| **C/Is:** | significant renal impairment, breast-feeding |
| **Dosage forms:** | Injection, 33% w/v in 2 and 6ml ampoules and 100ml vials. SSG 100mg/ml |

*PLUS*

**Paromomycin**, 15mg/kg body weight/day IM daily for 17d

| | |
|---|---|
| **ADRs:** | Hearthburn, abdominal cramps, diarrhoea |
| **C/Is:** | Intestinal obstruction and previous hypersensitivity reactions to the medicine |
| **P/Cs:** | Peptic Ulcer disease, pregnancy |
| **D/Is:** | Digoxin (increased toxicity), quinidine, amikacin, amiodarone, amphotericin b deoxycholate, cisplatin, clarithromycin, clotrimazole, felodipine, ketoconazole, loratadine, nifedipine, |

phenobarbital, phenytoin, Rifampicin, ritonavir, sirolimus, spironolactone, tacrolimus, warfarin

**Dosage forms:** Solution for Intramuscular (IM) Injection (375mg/mL)

B. **Sodium Stibogluconate or Meglumin Antimoniate (Monotherapy)*** In the absence of or in case of stock ruptures of Paromomycin, Pentavalent antimonials can be used in monotherapy.

**Sodium stibogluconate,** 20 mg/Kg/day given IV (slow infusion obver 5min) OR IM in a single dose for 30 consecutive days.

**Dosage forms**: Injection, 33% w/v in 2 and 6-ml ampoules and 100ml vials. SSG 100mg/ml or Meglumin Antimoniate(Glucantime) 81mg/ml

C. **Liposomal Amphotericin B (LAmB),** 5mg/kg/day over a period of 6days (i.e. 30mg/kg in total)

**N.B.** Liposomal Amphotericin B is recommended in those patients with pregnancy, HIV-coinfection, severe illness, severe anaemia, severe malnutrition and extremes of age (below 2 years or above 45 years). In special situations with severe risk factors for death at the patient's admission, antimonials toxicity has proved to be very high and, therefore, LAmB is preferable if available for these patients.

It is administered by reconstitution with 5% D/W with a volume of 100ml of D/W for 50mg of LAmB (for 100mg or 2 vials of LAmB 200ml of D/W, for 3 or more vials use all the 500ml D/W). It is advised to use whole vials to avoid wastage but the medicine should be discarded after 24 hours of reconstitution. The infusion can run over 30 to 60 minutes.

*OR*

**Miltefosine**, 2-3mg/kg P.O., per day (100mg/day for patients weighting more than 25kg) for 28 days.

**ADRs:** diarrhoea; increased liver enzymes

**C/Is:** Hypersensitivity to the active substance or any of the excipients. Pre-existing severe damage of liver or kidney function, Sjögren-Larsson-Syndrome, Pregnancy and women of childbearing potential who do not use a reliable contraception during and up to 3 months after treatment

**P/Cs:** mild and moderate impairment of liver and kidney function

**D/Is:** Not significant

**Dosage forms:** Capsules of 10mg, 50mg

*Evaluation of cure:* Cure is best defined as the absence of clinical features of the disease after completion of the recommended dose and duration of treatment for VL in addition to a negative parasitological test for LD bodies. Detailed evaluation of response to treatment of VL is not within the scope of this guideline and should be refered from the latest National Guideline for diagnosis, treatment and prevention of leishmaniasis in Ethiopia. 2013.

NB: Patients with treatment failure or relapse of VL should be sent to referal hospitals or specialized leishmania treatment centers for better investgation, treatment and followup.

## 16. Cutaneous Leishmaniasis (Oriental leishmaniasis, Oriental Sore, Leishmaniasis Tropica)

Cutaneous Leshmaniasis in Ethiopia is caused by *Leishmania tropica or Leishmania aetiopica*, which is transmitted by phlebotomus. Before ulceration occurs, there appears dermal infiltrates consisting of large histiocytes filled with many leishman-donovan (L-D) bodies, while during ulceration an influx of neutrophils occurs. Older lesions develop a tuberculoid infiltrate and at this stage either the organisms are scant or absent.

**Clinical features**

Cutaneous leishmaniasis (CL) is a disease of the skin and mucous membranes. There are different clinical forms of CL: localized CL, diffuse CL, and mucosal leishmaniasis. The typical features of each are outlined below.

**Cutaneous lesions**

- Occur mainly on exposed body parts (face, neck, arms, legs)
- May be single or multiple with regional lymph node enlargement
- Are usually painless
- If secondarily infected, they can be painful and itchy

**Localized cutaneous leishmaniasis**

- Papule at the site of the bite (like an insect bite)
- If papule persists, it develops into either:
- A small nodule
- An ulcer with a fl at base and raised border
- The nodulo-ulcerative form (broad-based ulcer with crust)

- Leishmaniasis recidivans is localized CL that is characterised by a chronic solitary lesion that expands slowly and often reoccurs. The lesion can continue for many years, causing severe disfigurement.

**Diffuse cutaneous leishmaniasis**

- Coalescence of papules and nodules to form plaques
- Chronic and very difficult to treat

**Mucosal leishmaniasis**

- Is the most severe form of CL, causing severe disfigurement and mutilation of the face
- Nasal lesions cause discharge, bleeding, obstruction, deformity, and destruction of cartilage with collapse of the nose
- Oropharyngeal lesions: difficulty chewing and swallowing, bleeding gums, toothache, loose teeth, perforation of the hard palate
- Involvement of mucosa can follow:
    - primary infection (with L. major or L. donovani); OR
    - dissemination of cutaneous leishmaniasis; OR
    - treatment for visceral leishmaniasis (post-kala-azar dermal leishmaniasis).

**Investigations**

Demonstration of the parasite:

- microscopic identification of intracellular amastigote in Giemsa-stained specimens from lesions
- culture of extracellular promastigote on specialized media

**Useful in established disease**;

- PCR on a skin biopsy-only available in the research setting.

Diagnosis is established by the clinical presentation in endemic areas, and the demonstration of the organisms in smears.

**N.B.**Leishmanian skin test and serology tests are of little use in the diagnosis of Cutaneous leishmaniasis.

**Treatment**

**Objectives**

- kill the parasite and control its spread, especially in the mucosal disease, to accelerate healing and to reduce scarring, especially in cosmetic sites

- Prevent disfigurement**.**

**Non pharmacologic**

Thermotherapy (1 or 2 applications of localized heat (55°C during 5 minutes) using a thermal device), with or without cryotherapy with liquid nitrogen (-195°C) applied to the lesion once or twice weekly up to 6 weeks.

**Pharmacologic**

- Spontaneous healing is mainly observed in old world CL after several months (L.major: 40-70% after 3 months, 100% after 12 months; *L. tropica*: 1-10% after 3 months, 68% after 12 months, close to 100% after 3 years);
- The decision to treat is based on the species, the potential for dissemination, as well as the location, number, and size of the lesions, and previous treatment used if any. With the exception of L.major, CL of the old World is commonly treated with local treatment (for exceptions see below). Because of the risk of developing mucocutaneous leishmaniasis, CL of the New World is commonly treated with systemic treatment.
- Arrange referral to designated leishmaniasis treatment centres if possible.

**Local treatment**

- This needs to be adapted according to species, and the clinical characteristics – site, size, number of lesions, whether open or nodular, whether superinfected, and the immune status of patients.
- Local infiltration (1 to 5 intralesional injections, every few days or weekly) with **Sodium stibogluconate**, with or without cryotherapy

**Systemic treatment**

- This is indicated for MCL and DCL

**First Line**

**Paromomycin**, 14–15mg (sulphate) /kg IM once daily for 20–30 days.

**Alternatives**

**Miltefosine and Liposomal Amphotericin B,** Miltefosine and Liposomal Amphotericin B are effective in the treatment of CL in several countries, but have not yet been used for *L. aethiopica* infections.

*OR*

**Pentavalent Antimony Compounds (SSG) or Meglumine Antimoniate (MA)** 20mg Sb/kg/day IM or IV for 4–8 weeks.

**Response to Treatment:** The signs of therapeutic response or natural healing are flattening followed by re-epithelization of the lesion. Clinical reactivation usually begins at the margins of the old lesions. The response is generally poor in HIV co-infections resulting in high rates of recurrence, treatment failure and relapse.

## 17. Leprosy (Hansen's Disease)

Leprosy is a chronic infectious disease mainly affecting the skin and peripheral nerves, although other tissues, such as the eye, mucosa of the upper respiratory tract, joints and testis can also be involved. Leprosy is considered to be transmitted from person to person through the nasal mucosa from droplet infection from untreated leprosy patient to individuals living in the same household and/or in frequent contact with the index case. The disease has a long incubation period, averaging 3 to 5 years, occurring usually in people in the age group between 15 and 45 years. If not properly treated, leprosy can cause severe disability, mainly as a result of peripheral nerve damage. Among communicable diseases, leprosy is the leading cause of permanent physical disability. It is caused by *Mycobaterium leprae.*

**Clinical features**

The earliest clinically detectable lesion usually occurs in the skin. Patients may present with a history of any of the following complaints:

- Pale or reddish patches on the skin with loss of, or decreased sensation on the skin
- Painless swelling or lumps on the face and earlobes
- Numbness or tingling of the hands and/or the feet
- Weakness of eyelids, hands or feet
- Difficulty closing the eyes
- Burning sensation in the skin
- Dry palms
- Skin cracks on palms and soles with sensation loss
- Painless wounds or burns on the hands or feet

- Decreased vision
- History of close contact with a leprosy patient

**The most common & early symptom of Leprosy is pale or reddish discoloration of the skin.**

On physical examination, any of the following signs may exist

- Hypo-pigmented or erythematous skin lesions
- Loss of, or decreased sensation on the skin patches when touched with a wisp of cotton
- Enlarged/thickned peripheral nerves
- Painful and/or tender nerves on palpation
- Loss of muscle strength or paralysis of muscles of the eyes, hands and feet
- Sensory loss on the soles of he feet and/or palm of the hands when examined with ball point pain
- Corneal anesthesia with loss of corneal reflex
- Cracks on palms and soles with sensation loss
- Wounds, ulcer on palms and soles with sensation loss
- Clawed fingers and toes
- Foot drop
- Wrist drop
- Shortening and scarring of fingers and toes

**Investigation**

- Skin slit smear microscopy

Leprosy cases can be diagnosed on clinical grounds. Laboratory investigation is indicated for confirmation in doubtful cases. Diagnosis of leprosy is confirmed when one of the three cardinal signs of leprosy present.

The **cardinal signs** of leprosy are:

1. Definite loss of sensation in a pale (hypo-pigmented) or reddish skin lesion.
2. Thickened or enlarged peripheral nerve/s with or without tenderness
3. Presence of the acid-fast bacilli *Mycobacterium leprae* in slit skin smears from skin lesions.

**Presence of one or more of the three cardinal signs of Leprosy is a definite diagnosis or confirmation of a leprosy case.**

A case of leprosy is classified as multi-bacilary or pauci-bacilary leprosy depending on the number of skin lesion and/or skin smear microscopy result.

1. **Multibacillary Leprosy**:

   - Usually presents with multiple (>5) poorly defined, hypopigmented or erythematous lesions associated with hypoesthesia.
   - Six or more skin lesions. Or
   - Slit skin smear result positive for AFB, irrespective of the number of skin lesion.or
   - If there is involvement (enlargement) of more than one nerve.

2. **Paucibacillary leprosy**:

   - Presents with one or few (usually <5) hypopigmented and hypoesthetic lesions.
   - Only one nerve trunk enlarged and
   - Slit skin smear negative for AFB.

**Pure neural leprosy**

These are patients who do not have any skin lesion, but who have clearly thickened nerves with or without signs of nerve damage. Patients with pure neural leprosy should be reported and treated as a MB case

**Treatment**

**Objectives**

- Cure leprosy by rapidly eliminating the bacilli
- Prevent the emergence of medicine resistance
- Prevent relapse
- Prevent disability

**Non pharmacologic**

- Counseling and Psychological support
- Socio-economic support

**Pharmacologic**

Leprosy is treated with a combination of two or more medicines in the form of Multi-Medicine Therapy (MDT). **Multi-medicine therapy (MDT)** is a combination of Rifampacin, Clofazimine and/or Dapsone. MDT medicines are provided in blister calendar packs each containing a four week (one month) supply.

**Treatment of Multibacillary Leprosy**:

Use three medicines as below to be taken for 12 months (to be completed within 15-month period) in all multi-bacillary cases. Treatment should be given for one year only (12 MDT blister packs).

**Rifampicin,** 10mg per kilogram body weight **(**600mg P.O., for adults), once-monthly, supervised for 12 months.

**ADRs:** abdominal pain, itching, skin rash, urticaria, Skin rashes, hepatoxicity, jaundice, Shock, purpura and renal failure

**C/Is:** hepatic dysfuncion, known hypersensitivity to rifampicin

**Dosage forms:** Capsule, 150mg, 300mg, and 600mg.

*PLUS*

**Dapsone,** 2 mg/kg (100 mg P.O., for adults), daily self-administered for 12 months

**ADRs:** insomnia, Skin rashes, severe itching and urticaria (pale red, raised itchy bumps), hemolytic anaemia (may occur in individual with G6PD-deficiency), jaundice

**C/Is:** Hypersensitivity reactions to sulphonamides

**Dosage forms:** Tablet, 25mg, 50mg, 100mg

*PLUS*

**Clofazimine,** 6mg/kg (300mg P.O., for adults) monthly, supervised and 1mg/kg (50mg for adults) daily, self-administered for 12 months.

**ADRs:** nausea, vomiting, abdominal pain, rash, pruritis, elevation of blood sugar, Brown discoloration of skin lesions and pigmentation of the conjunctiva; photosensitivity; hepatic and renal impairment, Dryness of the skin and ichthiosis (thick, rough and scaly skin).

**Dosage forms:** capsule, 100mg.

**Table 29-Dose regimens of medicines use for treatment of multibacillary leprosy**

| Medicines | 0-5 yrs old | 6-14 yrs old | ≥ 15 yrs old |
|---|---|---|---|
| Rifampicin(4-weekly supervised) | 300 mg | 450 mg | 600 mg |
| Clofazimine (4-weekly supervised) | 100 mg | 150 mg | 300 mg |
| Clofazimine (unsupervised) | 50 mg twice a week | 50 mg every other day | 50 mg daily |

| | | | |
|---|---|---|---|
| Dapsone(daily, unsupervised) | 25 mg | 50 mg | 100 mg |

**Treatment of Paucibacillary leprosy**

Use two medicines as below to be taken for 6 months (to be completed within 9-month period) in all pauci-bacillary cases. Treatment should be given for 6 months only (6 MDT blister packs).

**Rifampicin,** 10mg per kilogram body weight **(**600mg P.O., for adults), once-monthly, supervised for 6 months

*PLUS*

**Dapsone** 2 mg/kg (100mg P.O., for adults), daily self-administered for 6 months

**Table 30-Dose regimens of medicines use for treatment of Paucibavillary leprosy**

| Medicines | 0-5 yrs old | 6-14 yrs old | ≥ 15 yrs old |
|---|---|---|---|
| Rifampicin (4-weekly supervised) | 300 mg | 450 mg | 600 mg |
| Dapsone (daily, unsupervised) | 25 mg | 50 mg | 100 mg |

**Table 31-Symptom based approach to the Management of Adverse effects of MDT**

| ADRs | | Responsible Medicine (s) | Action |
|---|---|---|---|
| Minor | Itching and skin rash | Rifampicin | Reassurance |
| | Loss of appetite, nausea and abdominal pain | Rifampicin | Give medicines with food |
| | Orange/red urine, faeces, saliva and sputum | Rifampicin | Reassurance (harmless and will disappear after cessation of MDT) |
| | Brown discoloration of skin lesions and pigmentation of the conjunctiva | Clofazimine | Reassurance (harmless and will disappear after cessation of MDT) |
| | Dryness of the skin and ichthiosis (thick, rough and scaly skin) | Clofazimine | Apply Vaseline ointment |
| | Insomnia (sleeping difficulties and disturbances) | Dapsone | Give the medicine in the morning |
| | Anaemia | Dapsone | Give iron and folic acid |
| Major | Jaundice (Yellowish discoloration of the sclera, skin and mucous membranes) | Rifampicine<br>Dapsone | Stop treatment and refer |
| | Skin rashes, severe itching and urticaria (pale red, raised itchy bumps) | Dapsone & Rifampicin | Stop treatment and refer |

**Precautions in leprosy treatment**

**Patients co-infected with TB**

Patients suffering from both TB and leprosy require standard TB treatment in addition to the standard MDT. Hence, skip the monthly dose of the rifampicin in the leprosy MDT regimen. Once the TB treatment is completed, the patient should continue his/her MDT, or the other way round.

**Pregnancy and breast-feeding**

The standard MDT regimens are safe, both for the mother, the unborn child and the child and therefore can be administered during pregnancy and breast-feeding.

**Treatment Monitoring and Follow-up**

- Leprosy Patients on MDT must collect medicines from the clinic every month on regular bases.
- During every clinic visit patients must be educated about the importance of regularly taking the medications, the major side effects of the medicines and signs and

symptoms of reactions/neuritis and on the need to report immediately to the nearby treatment center whenever any problem occurs.

- Nerve function tests (VMT and ST of the eyes, hands and feet) must be carried out to detect nerve function impairment early and to prevent the occurrence of disability.
- A patient who has missed MDT dose for more than 3 months in total should be recorded as default.

**Leprosy complications (reaction in leprosy)**

Complications of leprosy may occur or may have already occurred at the time of diagnosis/during treatment. One of the most common complications in leprosy is reaction. Leprosy reaction is an immunological response to the bacilli, presenting as acute inflammatory episodes. It is the sudden appearance of symptoms and signs of inflammation on the skin, eyes and peripheral nerves. The long-term problems related to leprosy (deformity and disability) are due to nerve damage from leprosy reactions. **There are two types of leprosy reactions:**

1. Reversal Reaction (or Type 1 reaction)
2. Erythema Nodosum Leprosum (ENL) or Type 2 reaction

Both types of leprosy reactions can occur before the start of treatment, during treatment and after completion of treatment.

**Mild reaction**

Usually occurs in type 1 reaction and characterised by the presence of oedema and erythema of skin lesions only (excluding the face and overlying peripheral nerves)

**Clinical features**

- Oedema and erythema of skin lesions (excluding the face and overlying nerve trunk).
- Redness, swelling and sometimes tenderness of skin lesions.

**Investigations**

- Blood sugar
- Stool examination
- CBC

**Treatment of mild reaction**

**Objectives**

- Relieve the patient from pain and restore quality of life and productivity
- Reduce symptoms

**Non pharmacologic**

- Rest
- Reassurance
- Psychological support and counseling
- Patient education on early recognition of signs of severe reaction

**Pharmacologic**

**First line**

**Aspirin,** 600mg to 1200mg P.O., is given 4 to 6 times daily until the reaction is controlled and then the dose decreased gradually.

**ADRs:** GI irritation; skin reaction; broncho-spasm.

**C/Is:** GI ulceration; hemophilia; children under the age of 12.

**Dosage forms:** Tablet, 75 mg, 100mg (soluble), 300mg, 500mg (enteric coated), 324 (microfined)

**Alternative**

**Paracetamol**,

Children: 3 months-1 year 60-125mg, 1-5 years 120-250mg, 6-12 years 250-500mg these doses may be repeated every 4-6 hours if necessary (maximum 4 doses in 24 hours)

Adults: 0.5 to 1g P.O. every 4-6 hours, maximum 4g daily

**ADRs:** Allergic reactions such as skin rashes, neutropenia and thrombocytopenia may occur rarely.

**P/Cs:** caution in alcoholics, and in patients with hepatic diseases, and severe renal function impairment, anaemia and other disorders of the haemopoietic system.

**D/Is:** avoid simultaneous use of single toxic doses or long-term high doses of paracetamol with alcohol, or phenobarbitone; oral anticoagulants.

**C/Is:** severe hepatic or renal disease.

**Dosage forms:** Tablet, 100mg, 500mg; Suppository, 125mg, 250mg; Syrup, 120mg/5ml, 250mg/5ml; Drops, 100mg/ml

**Severe reactions**

Usually occurs in type 2 reaction but sometimes it can also occur in type 1 reaction. All type 2 reaction are severe

**Clinical features**

- Appearance of tender redish lesions with ulceration
- Painful eyes, with redness around the limbus cornea, increased lacrimation, fixed narrowing (constriction) of the pupil and diminishing vision (irido-cyclitis)
- Painful swollen fingers (dactylitis)
- Swelling of hands or feet
- Painful testicular swelling (orchitis)
- Weakness of muscles of the eyes, hands and feet
- Numbness or tingling of the hands and/or the feet
- Weakness of eyelids, hands or feet
- Difficulty of closing the eyes
- Burning sensation in the skin and Dryness of he palms
- Skin cracks on palms and soles with sensation loss
- Painless wounds or burns on the hands or feet
- A raised, red swollen patch overlying a nerve trunk or around the eye/s
- Red, raised and ulcerating skin lesions
- Oedema of hands or feet
- Erythematous Sub-cutaneous Nodular Lesions with ulceration (ulcerating ENL) –hallmark of type 2 severe reaction
- Tenderness of eyes, with redness around the limbus cornea, increased lacrimation, fixed narrowing (constriction) of the pupil and diminishing vision (irido-cyclitis)
- tender nerves on palpation
- Corneal anesthesia with loss of corneal reflex

- Loss of muscle strength and/or loss of sensation in eyes, hands or feet, for less than 6 months
- Change in VMT (including eye closure) of less than six months duration. The change can be from strong to weak, from weak to paralysis, or from strong to paralysis
- Change in Sensory Testing of less than six months duration. A change is considered to be significant when any hand or foot has increased loss of sensation at two or more points
- Tender testicular swelling (orchitis)
- Marked arthritis or lymphadenitis

**Investigations**

- Blood sugar
- Stool examination
- CBC
- Sputum for AFB examination to exclude tuberculosis

**Treatment of severe reactions**

**Objectives**

- Prevent nerve damage
- Prevent disabilities
- Relieve the patient from pain and restore quality of life and productivity

**Non pharmacologic**

- Complete rest to the affected nerve
- Immobilize the affected limb with a splint
- Physical rehabilitation
- Physiotherapy
- Health education on self care

**Pharmacologic**

**Type 1 severe reaction**

**Prednisone**, 1 mg/kg body weight/day (40-60mg daily), according to severity and starting high dose should be reduced to 40mg after a few days. Thereafter, the dose is reduced by 5-10mg every 2-4 weeks, ending with 10mg every 2-4 weeks (see table below).

**ADRs:** Abdominal discomfort, peptic ulceration; hypertension, diabetes, osteoporosis; myopathy;

**C/Is:** Peptic ulcer, diabetes, Cushing's disease.

**Dosage form:** Tablet, 1mg, 5mg, 40mg prednipac.

**Table 32-Ambulatory treatment of severe reversal reaction with Prednisolone**

| **Duration of treatment** | | **Daily dose of prednisolone (do not exceed 1 mg per kg body weight)** |
|---|---|---|
| **MB** | **PB** | |
| 4 weeks | 2 weeks | 40 mg |
| 4 weeks | 2 weeks | 30 mg |
| 4 weeks | 2 weeks | 20 mg |
| 4 weeks | 2 weeks | 15 mg |
| 4 weeks | 2 weeks | 10 mg |
| 4 weeks | 2 weeks | 5 mg |
| **Total 24 weeks** | **Total 12 weeks** | **Stop** |

**Table 33-Hospital treatment with Prednisolone of severe type 1 reaction**

| | |
|---|---|
| 60 mg daily (12 tablets of 5mg prednisolone) | 1 week |
| 50 mg daily (10 tablets of 5mg prednisolone) | 1 week |
| 40 mg daily ( 8 tablets of 5mg prednisolone) | 2 weeks |
| 30 mg daily ( 6 tablets of 5mg prednisolone) | 2 weeks |
| 20 mg daily ( 4 tablets of 5mg prednisolone) | 12 weeks |
| 15 mg daily ( 3 tablets of 5mg prednisolone) | 2 weeks |
| 10 mg daily ( 2 tablets of 5mg prednisolone) | 2 weeks |
| 5 mg daily ( 1 tablet of 5mg prednisolone) | 2 weeks |
| **Total** | **24 weeks** |

**Erythema Nodosum Leprosum (ENL) or Type 2 reaction**

It is often better to start treatment with a higher dose of prednisolone and then taper more quickly. Preferrably, these patients are better referred to specilaied leprosy hospitals and managed by dermato-venerologist and/or leprologists. A higher dose of prednisolone usually helps to suppress the immune reaction and restore the nerve function. However, ENL has a tendency to recur, much more so than type 1 reactions. The course can be re-prescribed up to three times. If the condition then still recurs, it can be treated along the guidelines described below for recurrent ENL. ENL is better managed by dermato-venorologist at hospital level, not necessarily specialized leprosy center. A sample four week long prednisolone course is shown in the table below:

**Prednisone**, 1 mg/kg body weight/day (60-80 mg daily) for a maximum duration of 12 weeks

**Table 34-Four week prednisolone treatment course for ENL**

| | **Day 1** | **Day 2** | **Day 3** | **Day 4** | **Day 5** | **Day 6** | **Day 7** |
|---|---|---|---|---|---|---|---|
| **Week 1** | 60 mg | 60 mg | 60 mg | 60 mg | 50 mg | 50 mg | 50 mg |
| **Week 2** | 50 mg | 40 mg | 40 mg | 40 mg | 40 mg | 30 mg | 30 mg |
| **Week 3** | 30 mg | 30 mg | 20 mg | 20 mg | 20 mg | 20 mg | 10 mg |
| **Week 4** | 10 mg | 10 mg | 10 mg | 5 mg | 5 mg | 5 mg | 5mg |

**P/Cs**: Prednisolone may worsen pre-existing conditions such as hypertension, diabetes, latent tuberculosis or any other existing

infection. It is therefore important to exclude (or treat) tuberculosis.

Treat existing infections:

- Diarrhoea, with blood and/or mucus
- Fungal infections
- Scabies
- Worm infestations
- Epigastric pain (gastritis/peptic ulcer disease)
- Conjunctivitis and trachoma

- Treatment for the above conditions should be started immediately but one does not need to wait until the treatment is completed before starting prednisolone.
- Diabetes should be controlled with oral hypoglycemic medications.
- Prednisolone can mask fevers; even if there is only a suspicion of malaria treat with anti-malarials.
- Follow up patients on prednisolone treatment (for reaction) every 2 weeks and assess the patient condition and do VMT and ST at each visit

**Referral:** Indication for referral and admission to hospital during severe reaction

- ENL reaction
- Deep ulcer(s)
- Red and/or painful eye
- Pregnancy
- Younger than 12 years of age
- Severe peptic ulcer disease
- Diabetes
- General illness with fever
- Patient who improved during previous courses, but who develops a reaction for the 3$^{rd}$ time
- Severe depression or psychosis
- Suspected relapse

**Treatment of Recurrent ENL**

A few patients get recurrent episodes of ENL as soon as the dose of prednisolone dips below 20 or 15 mg per day. This is called chronic or recurrent ENL. It carries the risk of prednisolone dependence and thus increases also the risks of prednisolone side effects. Such patients are better co-managed with clofazimine.

Patients with Recurrent ENL are better referred to specilaied leprosy hospitals and managed by dermato-venerologist and/or leprologists as follows.

**Clofazimine** is indicated for patients who cannot be weaned off corticosteroids or in those who are troubled by continuous erythema nodosum leprosum (ENL), and also in those in whom thalidomide is contraindicated.

**Clofazimine,** initially 300 mg P.O., given daily in three divided doses for 2 weeks, reducing to 200 mg QD for a month or two and then to 100 mg QD according to response. Start tapering the prednisolone one month after starting with clofazimine at a rate of 5 mg every two to four weeks

**Table 16: Treatment of recurrent ENL with clofazimine**

| Duration (Months) | Dose of Clofazimine |
|---|---|
| 1 – 3 months | 1 capsule of 100mg three times daily |
| 3 – 6 months | 1 capsule of 100mg two times daily |
| 6 – 12 months | 1 capsule of 100mg once daily |

**Prevention of leprosy**

**Chemoprophylaxis**

- Unlike Tuberculosis, there is no indication for chemoprophylaxis for leprosy.

BCG

- BCG vaccination has a documented and substantial effect in preventing leprosy and is therefore considered as an important tool for prevention of leprosy

**18. Malaria**

Malaria is a major public health problem in Ethiopia and has been consistently reported as one of the leading cause of morbidity and mortality. Malaria is a parasitic infection caused by plasmodium species known to affect humans. The most serious and life-threatening disease

occurs from *Plasmodium Falciparum* infection. Prompt diagnosis and treatment is essential even in mild cases to prevent complications.

**Causes**: the commonest causes of Malaria in Ethiopia are

- P. Falciparum
- P. vivax

**Clinical feature: uncomplicated malaria**

- Fever, Chills, Rigors, Sweating, Severe Headache, Generalized body and joint pain
- Nausea and or vomiting, Loss of appetite, Abdominal pain (especially in children)
- Irritability and refusal to feed (in infants), flu-like symptoms, fever above 38°C
- Splenomegaly, Pallor

**Investigations**

- Microscopy-thick and thin blood films for malaria parasites, CBC
- Rapid diagnostic tests (RDT)-if microscopy is unavailable

The diagnosis of malaria can be confirmed when malaria parasites are demonstrated in the blood films (thick or thin) or with Rapid Diagnostic Test (RDT). Blood film is also helpful to estimate the degree of parasitemia, which is extremely useful not only to predict severity but gauge response to treatment as well. If neither microscopy nor rapid tests are available, diagnosis should be made on the basis of clinical symptoms.

**N.B.** Clinical diagnosis of malaria is made in a patient who has fever or history of fever in the last 48 hours and lives in malaria-endemic areas or has a history of travel within the last 30 days to malaria-endemic areas. Malaria treatment based on clinical diagnosis must be the last option when there is no RDT or blood film microscopy

**Treatment**

**Objectives**

- Treat the patient and restore quality of life and productivity
- Prevent uncomplicated malaria from progressing to severe and fatal illness
- Prevent death from malaria complication
- Prevent the development and transmission of medicine resistance
- Decrease malaria transmission to others

**Non pharmacologic**

- Apply tepid sponging or fanning to reduce body temperature
- Admit severe complicated cases

**Pharmacologic**

**1. Treatment of uncomplicated P. Falciparum malaia**

**First line**

**Artemether + Lumefantrine**, 20mg + 120mg in a fixed dose combination

**ADRs:** dizziness and fatigue, abdominal pain, palpitations, myalgia, sleep disorders, arthralgia, headache and rash

**C/Is:** previous history of reaction after using the medicine;
Pregnant women in the first trimester and
infants less than 5 kg;
severe and complicated malaria should not be treated with oral medications

**Dosage forms**: **Artemether (20mg) + Lumefantrine (120mg)** FDC Tablet

**N.B.** Artemether-lumefantrine should not be used as malaria prophylaxis either alone or in combination;

**Table 35-Dose regimens of artemether-lumfantrine**

| Weight (KG) | Age | Dose |
|---|---|---|
| 5-14 kg | From 4 months to 2 years | 1 tablet bid for 3 days |
| 15-24 kg | From 3 years to 7 years | 2 tablets bid for 3 days |
| 25-34 kg | From 8 years to 10 years | 3 tablets bid for 3 days |
| >35 kg | 10 years & above | 4 tablets bid for 3 days |

**P/Cs:** It should be stored at temperatures below 30°C
It should not be removed from the blister if it is not going to be used immediately
It is not recommended for infants weighing <5KG and pregnant mothers in the first trimester
It should preferably be taken with food or fluids; fatty meal or milk improves absorption of the medicine

**Dosage forms:** tablet containing 20mg of Artemether and 120mg of lumefantrine

**Alternative**

**Quinine dihydrochloride**, 10mg quinine sulphate salt/kg TID for 7 days.

**ADRs:** Cinchonism, including tinnitus, headache, nausea, abdominal pain, rashes, visual disturbances, confusion, blood disorders (including thrombocytopenia and intra-vascular coagulation), acute renal failure, and hypoglycemia may be caused by quinine

**C/Is:** Haemoglobinuria, optic neuritis

**Dosage forms:** Tablet (dihydrochloride or sulphate), 300mg and 600mg; injection, 300mg/ml in 1 ml ampoule.

**2. Treatment of uncomplicated P. Vivax malaria**

**First line**

**Chloroquine phosphate,** 1 g, then 500mg in 6 hours followed by 500mg P.O., QD for 2 days, or 1g at 0 and 24 hrs followed by 0.5g at 48 hrs P.O.,

**ADRs:** gastro-intestinal disturbances, headache, also convulsions, visual disturbances

**P/Cs:** Avoid alcoholic beverages

**D/Is:** Carbamazepine, digoxin, ethosuximide, mefloquine, phenytoin and valproic acid

**Dosage forms:** Tablets, 250mg, 500mg (equivalent to 150mg, 300mg chloroquine base); Syrup, 50mg/5ml ; Injection, 50mg/ml; (equivalent to 40 mg chloroquine base)

***Followed by***

**Primaquine,** 15mg base P.O., QD for 14 days.

**ADRs:** hemolytic anaemia, especially in patients with G6PD deficiency.

**P/Cs:** In patients with G6PD deficiency; systemic diseases associated with granulocytopenia, e,g. rheumatoid arthritis, and pregnancy and breast feeding)

It is recommended for patients with limited risk of malaria infection in the future; for patients who are not living in malaria endemic areas.

**Dosage forms:** Tablet, 7.5mg base, 15mg base

**Alternatives**

**Artemether + Lumefantrine**, 20mg + 120mg in a fixed dose combination

*OR*

**Quinine dihydrochloride**, 10mg quinine sulphate salt/kg TID for 7 days

### 3. Treatment of uncomplicated Mixed infection (Multi-species RDT positive for P.falciparum and P.vivax)

**First line**

**Artemether + Lumefantrine,** 20mg + 120mg in a fixed dose combination

**P/C:** do not treat a patient with confirmed mixed infection with both AL and chloroquine

**Alternative**

Quinine dihydrochloride, 10mg quinine sulphate salt/kg TID for 7 days

**Complicated P.falciparum malaria**

Delay in diagnosis or inappropriate treatment of uncomplicated malaria can lead to the rapid development of severe or "complicated malaria". It mostly occurs in children under 5 years of age, pregnant women and non-immune individuals. Severe malaria may lead to death unless it is diagnosed early and appropriately managed.

**Clinical features**

- Inability to take in fluids (or breast milk in children)
- Repeated profuse vomiting
- Dark or 'cola-coloured' urine
- Passing of very little urine
- Difficulty in breathing
- Generalised weakness, inability to walk or sit without assistance
- Sleepiness, change of behaviour
- Repeated generalized convulsions
- Altered consciousness, confusion, delirium, convulsions, coma
- Tachypnoea, respiratory distress and/or cyanosis
- Oliguria, renal failure

- repeated vomiting
- hypoglycaemia
- severe anaemia (Hb < 6 g/dL)
- Hyperpyrexia (axillary temperature >38.5°C)
- Extreme pallor (severe anaemia)
- Circulatory collapse or shock (cold limbs, weak rapid pulse)
- Crepitations on chest examination
- Haemoglobinuria (dark or 'cola-coloured' urine)
- Spontaneous unexplained heavy bleeding (disseminated intravascular coagulation)

**Investigations**

- Microscopy-thick and thin blood films for malaria parasites
- Rapid diagnostic test (RDT)-if microscopy is unavailable
- CBC
- RBS
- Blood grouping and cross-matching
- BUN and creatinine
- Lumbar puncture to exclude meningitis or cover with appropriate antibiotic.

The diagnosis of severe malaria is based on clinical features and confirmed with laboratory testing. While confirmation of the diagnosis is necessary treatment must be started promptly and not withheld while confirming the diagnosis

**Treatment of Severe and complicated *P. falciparum* malaria**

**Objectives**

- Administer medicines parenterally to ensure adequate blood-serum concentrations of the medicine and rapid clearance of parasitaemia

- Provide urgent treatment for life threatening problems e.g. convulsions, hypooglycaemia, dehydration, renal impairment
- Prevent death from malaria

**Non pharmacologic**

- Clear and maintain the airway.
- Position semi-prone or on side.
- Weigh the patient and calculate dosage.
- Make rapid clinical assessment.
- Exclude or treat hypoglycemia (more so in pregnant women).
- Assess state of hydration.
- Measure and monitor urine output.
- If necessary insert urethral catheter.
- Measure urine specific gravity.
- Open IV line for 8 hours of intravenous fluids including diluents for anti-malarial medicine, glucose therapy and blood transfusion.
- If rectal temperature exceeds 39°C, remove patient's clothes, use tepid sponge,
- Consider other infections.
- Consider need for anti-convulsant treatment

**Pharmacologic**

**First line**

**Artesunate**, 2.4mg/Kg IV or IM given on admission (time = 0), then repeat at 12 hours, and 24 hours, then once a day for up to 5 days.

Artesunate is dispensed as a powder of Artesunic acid. From 60mg vials, artesunate must be reconstituted in two steps: initially with sodium bicarbonate solution (Provided), then with 5ml of 5% glucose (D5W) solution. Full reconstitution results in either 6ml (intravenous concentration 10mg/ml) or 3ml (for intramuscular injection concentration 20mg/ml) of injectable artesunate dosed by weight.

**Table 36-Dose Regime of Artesunate IV, IM**

| Weight (kg) (approximate) | IV 10mg/ml | IM 20mg/ml |
|---|---|---|
| **0-8** | 1ml | 0.5ml |
| **9 to 12** | 2ml | 1ml |
| **13-16** | 3ml | 1.5ml |
| **17-18** | 4ml | 2ml |
| **19-21** | 5ml | 2.5ml |
| **22-25** | 6ml | 3ml |
| **26-29*** | 7ml | 3.5ml |
| **30-33*** | 8ml | 4ml |
| **34-37*** | 9ml | 4.5ml |
| **38-41*** | 10ml | 5ml |
| **42-46*** | 11ml | 5.5ml |
| **47+*** | 12ml | 6ml |

* for persons weighing more than 25 kg, a second artesunate vial must be completely reconstituted as above for each dose, and then each dose administered determined by the chart.

**ADRs:** dizziness, tinnitus, neutropenia, elevated liver enzymes, ECG abnormalities, type 1 hypersensitivity reaction

**P/Cs:** The solution should be prepared for each administration and should not be stored.

**N.B.** Give parentral Antimalarials in the treatment of severe malaria for a minimum of 24 hours, once started (irrespective of the patient's ability to tolerate oral medication earlier)

**Dosage forms:** ampoules for IV/IM injection 6omg anhydrous Artesunic acid + a separate ampoule of 5% sodium bicarbonate solution; Tablets 50mg or 200mg sodium artesunate, Rectal capsule 100mg or 400mg

**Alternatives**

**Artemether**, IM 3.2mg/kg loading dose on the first day followed by 1.6mg/kg daily for five days

**ADRs:** dizziness, tinnitus, ECG abnormality, neutropenia, type 1 hypersensitivity reaction

**P/Cs:** the medicine should only be used during the first trimester of pregnancy when both IV/IM artesunate and IV/IM Quinine are unavailable

**Dosage forms:** capsules 40mg; Tablets 50mg; ampoules for injectable solutions (IM) 80mg in 1ml for adults or 40mg in 1ml of children

*OR*

**Quinine dihydrochloride: Loading dose**: 20mg/kg in 500ml of isotonic saline or 5% dextrose over 4 hours (4ml/minute). The pediatric dose is the same but the fluid replacement must be based on body weight.

**Maintenance dose**: should be given 8 hours after the loading dose at a dose of 10mg /kg and it should be given 8 hourly diluted in 500 ml of isotonic saline or 5% dextrose over 4 hours.

**Table 37-Dose regimens of Quinine**

| Route | Loading dose over 4 hours | Rest for next 8 hours | Maintenance dose over 4 hours (12 hours after start of loading Dose) | Rest for 4 hours | Maintenance dose over 4 hours 8 hourly |
|---|---|---|---|---|---|
| IV | 20 mg/kg in 500 ml of isotonic saline or 5 % dextrose over 4 hours (4ml/minute) | Give N/Saline or Ringers lactate to keep vein open and maintain fluid balance | 10 mg salt/kg body weight in 500 ml of 5 % dextrose over 4 hours | Give N/Saline or Ringers lactate to keep vein open and maintain fluid balance | 10 mg salt/kg body weight in 500 ml of 5 % dextrose over 4 hours |
| | Loading dose | | Rest for next 4 hours | Maintenance dose 8 hourly | |
| IM | 20mg/kg body weight divided into 2 site (one in each thigh) | | | 10 mg salt/kg body weight IM into thigh | |

The parenteral treatment should be changed to P.O., only after 24 hours and as soon as the patient‘s condition improves and if there is no vomiting.

Oral treatment should be given with ***Artemether + Lumefantrine*** in the doses as indicated above. However, if a patient has a history of intake of ***Artemether + Lumefantrine*** before complications developed, give **Quinine** tablets 10 mg salt per kg TID to complete 7 days treatment.

**ADRs**: Cinchonism, including tinnitus, headache, nausea, abdominal pain, rashes, visual disturbances, confusion, blood disorders (including thrombocytopenia and intra-vascular coagulation), acute renal failure, and Hypoglycemia may be caused by quinine

**C/Is:** Haemoglobinuria, optic neuritis

**Dosage forms:** Tablet (dihydrochloride or sulphate), 300mg, and 600mg; injection, 300mg/ml in 1 ml ampoule.

**Prevention of malaria**

**Chemo-prophylaxis**

*P. Falciparum*

**First line**

**Mefloquine**, 5mg base per kg weekly (1tablet for adults >50kg, begin ≥ 2weeks before travel to malariuos area, take weekly on the same day while in the area and for 4 weeks after leaving the area.

**Table 38-dose regimen of Mefloquine as prophylaxis; 5 mg /kg mefloquine (250 mg salt) once weekly**

| Weight (Kg) | Age (approx.) | Number of tablets per week |
|---|---|---|
| <9 | < 3 months | 5mg/kg salt |
| 9 – 19 | 3 – 23 months | ¼ tablet |
| 20 – 30 | 2 – 7 year | ½ |
| 31 – 45 | 8 – 10 year | ¾ |
| 36 – 50+ | 11 – 14+ | 1 |

**ADRs:** Dizziness, abdominal pain and diarhorrea

**C/Is:** Persons with known hypersensitivity;
Persons with a history of severe neurospsychiatric disease;
Pregnant women in the first trimester;
Infant less than 3 months;

Persons who have received treatment with mefloquine in the previous 4 weeks;
Persons performing activities requiring fine coordination and spatial discrimination

**Dosage form:** Tablet, 250mg

**Alternatives**

**Atovaquone/Proguanil:** 250mg/100mg P.O., daily for adults; begin 1-2 days before travel to malarous area and daily while in the areas and for 7 days after leaving the area.

**Table 39-Dose regimen of Atovaquone-proguanil chemoprophylaxis**

| Weight (kg) | Atovaquone/Proguanil HCl Dosage form | Dosage Regimen |
|---|---|---|
| **5-8** | 62.5mg/25mg (pediatric tablet) | ½ Pediatric Tablet daily |
| **>8-10** | 62.5mg/25mg | ¾ Pediatric Tablet daily |
| **11-20** | 62.5mg/25mg | 1 Pediatric Tablet daily |
| **21-30** | 62.5mg/25mg | 2 Pediatric Tablets as a single dose daily |
| **31-40** | 62.5mg/25mg | 3 Pediatric Tablets as a single dose daily |
| **>40** | 250mg/100mg (adult tablet) | 1 Tablet (adult strength) as a single dose daily |

**ADRs:** renal impairment

**C/I:** severe renal impairment**,** children<5Kg body weight, prergnant women

**P/C:** the medicine should be taken with food or a milky drink, medicine should be taken daily at the same tme each day

**Dosage forms:** adult tablets 250mg atovaquone/100mg Proguanil; pediatric tablet 62.5mg atovaquone/25mg proguanil**.**

*OR*

**Doxycycline,** 100mg daily for adults; 2.2mg/kg daily for children >8yrs; begin 1-2 days before travel to malarious areas, to be taken daily while at the area and for 4 weeks after leaving the area.

**ADRs:** visual disturbance, hepatotoxicity, pancreatitis, pseudomembrane colitis, discolouration of infants and children's teeth, photosensitivity

**C/Is:** pregnancy, breast-feeding, children up to 8 years of age.

**D/Is:** antacids, carbamazepine, oral contraceptives, ferrous salts, phenobarbital, phenytoin, rifampicin and warfarin

**Dosage forms:** Tablet, 100mg; capsule, 100mg

**For *P. vivax***

**Primaquine phosphate**, 15mg base P.O., QD for 14 days after travel.

**19. Neutropenic Fever**

Nowadays, many patients with Cancer (either solid tumours or hematologic malignancies) receive treatment with different cytotoxic medications. Cytotoxic agents exert their effects on both malignant cells and normally replicating progenitor cells and thus also cause major toxicity to normal tissues with high turnover (i.e. bone marrow and mucous membranes) resulting in myelosuppression and alteration of physiologic barriers. Neutropenia is one of the commonest complications of cancer chemotherapy.

During neutropenia, fever develops in virtually all patients with hematologic malignancies and in about half of those with solid tumours. More than two-thirds of the febrile episodes are likely to be caused by infection, which may occur with or without focal symptoms or signs. Because of the impaired host response, the classic signs of inflammation (i.e. pain, heat, redness, swelling, and purulent discharge) are often reduced or may even be absent. Therefore, fever is generally the first and frequently the only sign of infection.

**Common Pathogens**

- Enterobacteriaceae (e.g. *Escherichia coli*, *Klebsiella* sp)
- Nonfermenting gram-negative bacilli (e.g. *Pseudomonas aeruginosa*, *Acinetobacter* sp, *Stenotrophomonas maltophilia*)
- Gram-positive cocci (e.g. *Staphylococcus aureus*, coagulase-negative staphylococci, streptococci, enterococci)
- Gram-positive bacilli (e.g. *Bacillus* sp, *Corynebacterium* sp)

**Clinical features**

- **Fever:** Single oral temperature of ≥38.3°C (101°F) or a temperature of ≥38.0°C (100.4°F) for ≥1 hour **Neutropenia:** Neutrophil count of <500 cells/mm3 or a count of 1,000 cells/mm3 with a predicted decrease to <500 **c**ells/mm3

**Investigations**

- Review exposure history, recent anti-infective therapy, medications and conduct physical examination with particular attention to the pharynx, skin, intravenous access sites, lungs, sinuses, mouth, esophagus, and perianal area.
- Run laboratory tests, including complete blood cell count, liver function tests, and creatinine
- Obtain blood and urine cultures and other cultures on the basis of clinical circumstances
- Obtain chest radiographs
- Conduct site-specific imaging studies, as indicated

**Treatment**

**Objectives**

- Prevent morbidity related to the infection/s.

**Non pharmacologic**

None

**Pharmacologic**

**Initial Empiric Therapy for high risk neutropenic patients:** Over 90% of the first episodes of infection in neutropenic cancer patients are caused by Gram-positive and Gram-negative bacteria hence, direct treatment at aerobic and facultative gram positive cocci and gram negative bacilli:

**1. Monotherapy:**

**Cefepime,** 50mg/kg every 8 hours for 7-10 days or dependent on duration of neutropenia

| | |
|---|---|
| **ADRs:** | see those for other cephalosporins |
| **C/Is:** | hypersensitivity to Cefepime or any other cephalosporin group |
| **P/Cs:** | pregnancy and lactation, renal impairment, may cause antibiotic associated colitis |
| **D/Is:** | probenecid, aminoglycosides |
| **Dosage forms:** | Powder for injection, 500mg, 1gm/vial, 2gm/vial |

– *OR*

**Imipenem and Cilastatin,** 500mg every 6 hours *or* 1g every 8 hours; 1 year and older, 15mg/kg (max. 500mg) every 6 hours

**ADRs:** GI disturbances, eosinophilia, rash, dizziness, drowsiness, hallucinations, confusion, leucopenia, thrombocytopenia, thrombocytosis, hearing loss

**C/Is:** Hypersensitivity to the medicine or any component of the formulation; sensitivity to beta-lactam antibacterials; CNS disorders; severe renal impairment, Pregnancy.

**P/Cs:** Renal impairment, pregnancy, breastfeeding, prolonged use may result in superinfection, in patients with a history of seizures or hypersensitivity to beta-lactions, elderly patients, pediatric CNS infections, IV and IM preparations cannot be interchanged.

**D/Is:** Ganciclovir, Valproate, Typhoid Vaccine (oral),

**Dosage forms:** Powder for Infusion, 500mg (500mg+500mg),
250mg (250mg+250mg)

*OR*

**Piperacillin**, Adult: *IV:* usually 2-4g, 6-8 hourly, injected over 3-5 minutes, or infused over 20-40 minutes; maximum 24g/day. 2 months-12 years, 50-100mg/kg/dose 6-8 hourly (Maximum dose 2 – 4g). Give 12 hourly in the first week of life.

**ADRs:** Neutropenia, leucopenia and thrombocytopenia, thrombophlebitis at the injection site, holestatic jaundice, bloody diarrhoea, and reversible elevation of serum urea and creatinine levels.

**D/Is:** probenecid, aminoglycosides, oral contraceptives.

**P/Cs:** known hypersensitivity to any penicillin or cephalosporin.

**Dosage forms***:* Powder for injection (as sodium salt), 1g, 2g in vial

*OR*

**Ceftazidime**, 1gm IV every 8 hours for 7-10 days or dependent on duration of Neutropenia.

**2. Combination therapy:**

- Consider using an ***aminoglycoside-containing regimen (Gentamycin or Tobramycin)*** in critically ill patients, such as those with severe sepsis or septic shock, when a *P. aeruginosa* infection is suspected or when resistant Gram-negative bacteria prevail, including ESBL-producing strains aminoglycoside or ciprofloxacin plus ceftazidime, an antipseudomonal penicillin (eg, piperacillin), or carbapenem:

- Consider using a ***glycopeptide antibiotic (Vancomycin)*** in patients with catheter-related infections, when penicillin-resistant streptococcal or methicillin-resistant staphylococcal infections are suspected or in critically ill patients with severe sepsis or septic shock or prior fluoroquinolone prophylaxis.

3. **Include coverage for anaerobic bacteria (eg, metronidazole, meropenem, imipenem, piperacillin/) if:**

- Evidence of perianal infection
- Presence of necrotizing gingivitis
- Recovery of anaerobic bacteria in culture
- Potential intraabdominal infection
- Severe diarrhoea

4. **Include coverage with an antifungal and/or antiviral agent in patients with esophagitis**

**Lower-risk patients**

- Despite preliminary favorable clinical observations, it has not yet been unequivocally demonstrated that management of low-risk febrile patients on a fully outpatient basis is safe

- Oral ciprofloxacin plus amoxicillin–clavulanic acid (250mg P.Oevery 8 hours, doubled in severe infections) was found to be as efficacious and safe as standard parenteral treatment of low-risk patients in an inpatient setting. Do not use fluoroquinolones as an oral monotherapy.

**Amoxicillin–clavulanic acid**

**ADRs:** Diarrhoea, abdominal discomfort, anorexia and flatulence, rash and urticaria, pseudomembraneous colitis, headache, dizziness.

**C/Is:** Penicillin hypersensitivity, history of amoxicilline + clavulanic acid associated or penicillin associated jaundice or hepatic dysfunction.

**P/Cs:** During pregnancy, hepatic impairment and nursing women, history of allergy, renal impairment, erythematous rashes common in glandular fever, chronic lymphatic leukemia & HIV infection.

**D/Is:** Allopurinol, disulfiram, probenecid, anticoagulants, anti-inflammatory medicines, platelet aggregation inhibitor, contraceptives, heparin, thrombolytic agents, sulfinpyrazone.

**Dosage forms:** Tablet (Chewable), 125mg + 31.25mg, 250mg +62.5mg, (film coated), 250mg + 125mg, 500mg + 125mg; capsule, 500mg +125mg, 875mg +125mg; Oral Suspension, 125mg + 31.25mg in each 5ml, 250mg + 62.5mg in each 5ml, 228mg/5ml, 457mg/5ml; Injection, 500mg + 100mg, 1g + 200mg

**Pathogen-Directed Therapy**

- Base antibiotic selection on in vitro susceptibility data
- Consider combination therapy (eg, β-lactam plus aminoglycoside) for severe infection due to *P aeruginosa* or other resistant gram-negative organisms

**Persistent Fever Despite Empiric Antibiotic Therapy**

**Reassess response to treatment on day 3**

- If patient is stable, continue with same antibacterial program
- Discontinue vancomycin if cultures are negative for gram-positive organisms
- If patient is clinically worsening, change or augment antibacterial regimen

**Persistent fever and neutropenia by day 5**

- Add an antifungal agent (eg, Fluconazole, amphotericin B product,e or caspofungin) with or without a change in the antibiotic regimen; for patients who have been receiving antifungal prophylaxis with an azole, use either an amphotericin B product or caspofungin
- Repeat diagnostic clinical examination (with or without radiographs, as indicated)

**Duration of Antibiotic Therapy**

Stop antibiotic therapy when neutrophil count is ≥500 cells/mm3 for 2 consecutive days and patient is afebrile for ≥48 hours if

- No evidence of focal infection
- Cultures are negative

Continue antibiotic therapy for 4-5 days after neutrophil count is ≥500 cells/mm3 if fever persists.

If patient remains febrile and neutropenic with no other evidence of infection, continue anti-infective agents for 2 weeks, followed by clinical reassessment and consideration of discontinuation of antibiotic therapy

**Other Considerations**

- In patients with a history of a type 1 allergic reaction to penicillin, consider use of ciprofloxacin, or aminoglycoside for coverage of gram-negative organisms
- Guide choice of empiric anti-infectives by local or institutional antibiotic resistance profiles
- Consider removal of vascular catheter in patients with fungi or mycobacteria isolated in blood culture, or in patients with bacterial cultures that are persistently positive, or in haemodynamically unstable patients with positive cultures.

## 20. Onchocerciasis

Oncocerciasis is a disease caused by O*nchocerca volvulus*, transmitted by several species of simulium ("Black flies") and manifested by onchodermatitis. Mature worms and microfilariae are found in granulomatous dermal nodules mainly on the bony prominences, the trunks and extremities in Africans and the scalp in Central Americans. Inflammatory cells and sometimes giant cells accumulate around the worms and occasionally calcification may occur. Perivascular inflammatory response occurs in the dermis as a result of the presence of microfilariae. With chronicity, these reactions are replaced by fibrosis and atrophy of the dermis and epidermis. The presence of microfilariae in the eye causes keratitis, iritis and choroiditeis, which may eventually lead to blindness.

**Clinical features**

- Onchocercal dermaitis-Generalized intense prurituis, enlargement of inguinal and femoral lymph nodes, lymphatic obstruction and patchy hypopigmentation
- Oncocercoma-subcutaneous (or deeper) nodules that contain adult worms may be visible or palpable.
- Oncophthalmia-punctate keratitis, sclerosing keratitis and eventually blindness.

**Investigation**

- Demonstration of microfilariae by examination of skin snips
- Histological examination of the nodule (presence of adult worms and microfilariae)

**Treatment**

**Objective**

- Relieve itching
- Treat the infection

**Non pharmacologic**

- Surgical removal of accessible onchocercomas
- Minimize fly bites by avoiding fly-infested areas, wearing protective clothing and using insect repellents

**Pharmacologic**

**Ivermectin**, single oral dose of 150micrograms/kg. It should be continuously given once or twice a year until patients are asymptomatic or for people residing in endemic area. For those no more living in endemic area, single dose treatment is enough and a repeat dose should only be given in cases of relapse.

| | |
|---|---|
| **ADRs:** | Myalgia, dizziness, fever, headache, lymphadenopathy, skin rash or itching, postural hypotension |
| **C/Is:** | Pregnancy, hypersensitivity to ivermectin. |
| **P/C:** | Breast-feeding |
| **Dosage forms:** | Tablet, 3mg, 6mg (scored) |

*PLUS*

**Doxycycline**, 100mg P.O., BID for 8weeks prior to treatment with **Ivermectin**

*PLUS*

**Antihistamines** may be required in the first few days of treatment if there is severe exacerbation of the disease.

**Promethazine**, 25mg BID OR TID until the prurutis subsides.

**N.B.** Nodulectomy may have a place for eradication of the adult worm

**21. Rabies**

Rabies is a fatal viral disease that can affect almost all mammals. The causative agent is Rabies virus from class Rhabdoviridae, genus *Lyssavirus* and species Serotype 1. The virus is transmitted through inoculation of saliva, usually from the bite of an infected animal. The distribution is worldwide with as many as 10 million people annually receiving postexposure

treatment (PET) to prevent rabies but the human disease is more common in developing countries. An estimated 55000 people die from rabies per year in Africa and Asia.

More than 95% of the deaths are due to exposure to dogs, which are the major reservoir and transmitter of rabies, but transmission by wild animals such as bats, foxes, and wolves is also possible. The incubation period is relatively long (ranging from 3 weeks to 3 months) but can be as long as several years in rare cases. The closer the inoculation site is to the central nervous system, the shorter the incubation period.

**Clinical features**

**Prodrome** (2-10 days):

- Paresthesias (pins and needles sensation) around bite area are very suggestive of rabies.
- Fever, headache, malaise, muscle pain, nausea, vomiting, and cough.

**Acute neurologic phase** (2-7 days):

- Confusion, delirium, altered mentation, agitation, hallucinations.
- Excitation predominates in many cases with hypersensitivity or spasms in response to touch, noise, visual, or olfactory stimuli. Hydrophobia (fear of water) and aerophobia (fear of air) may occur, and when they occur they are very suggestive of rabies.
- In paralytic rabies, phobic spasms occur in only half of patients. In early paralytic rabies, piloerection and myoedema may occur at percussion site on the chest, deltoid muscle, and thigh.
- Autonomic system dysfunction: enlarged pupils, increased production of saliva, tears, perspiration.

**Coma, death** (0-14days):

- Occurs after several days to 1 week.
- Hypoventilation, loss of temperature control, heart dysfunction can lead to death.

**Ascending paralysis**:

Similar to Guillain-Barré syndrome, occurs in some cases and makes diagnosis more difficult. This can also occur during post-exposure rabies treatment.

**Investigations**

- Diagnosis rests on history of exposure and typical neurological findings.
- CSF: increased white cells (lymphocytes), mildly increased protein.
- Laboratory confirmation is usually postmortem (direct fluorescent antibody test (FAT); or by ELISA in clinical specimens, preferably brain tissue; or FAT after

inoculation of brain tissue, saliva, or CSF in cell culture; or after intracerebral inoculation in mice; or by PCR) although FAT or PCR on clinical specimens (e.g. skin from the nape of the neck) are possible antemortem.

**Treatment**

There is no effective treatment against rabies. It is almost always fatal. Supportive management is important; recovery is exceedingly rare and has only occurred in cases where intensive respiratory and cardiac support were available.

Apparently healthy dogs and cats at the origin of the exposure should be kept under observation for 10 days. Dogs and cats that are suspected of being rabid, as well as wild animals, should be humanely killed and their tissues examined in the appropriate laboratory.

**Objectives**

- Reduce the pain and suffering of patient.

**Non pharmacologic**

- Supportive treatment of a paralyzed patient mostly focused on nursing care and providing comfort to the patient.

**Pharmacologic**

**Palliative care**

The short clinical course of rabies entails much suffering, whether excitation or paralysis is predominant. Patients remain conscious, are often aware of the nature of their illness, and are often very agitated, especially when excitation is predominant. Patients with rabies should receive adequate sedation and comfort with emotional and physical support, preferably in a private room. Repeated IV morphine can relieve severe agitation and phobic spasms. Sedation with barbiturates can be added. Avoid intubation and other life support measures when the diagnosis is certain.

**Health worker safety**

It is theoretically possible for person-to-person rabies transmission to occur since secretions may contain the virus; this has not been described. As a precaution, medical and nursing staff must wear mask, gloves, and goggles.

**Rabies post-exposure vaccination after animal bites**

After an exposure to a possibly rabid animal, the following measures should be undertaken:

The cornerstone of rabies prevention is wound care, which potentially reduces the risk of rabies by 90%. Wound care for any scratches, abrasions, bites, or licks on broken skin.

- Immediately scrub with alkaline soap and water, and flush with water for 15 minutes
- Irrigate with Povidone-iodine

Decide on post-exposure vaccination and immunoglobulin use depending on the type of contact with the rabid animal**.**

**Types of contact are:**

- **Category I** – Touching or feeding animals, licks on the skin.
- **Category II** – Nibbling of uncovered skin, minor scratches or abrasions without bleeding.
- **Category III** – Single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva from licks; exposure to bat bites or scratches.

**Treat according to category of contact:**

- **Category I** – No treatment is required
- **Category II** – Immediate vaccination
- **Category III** – Immediate vaccination and administration of rabies immunoglobulin

Depending on vaccine type, the post-exposure schedule prescribes intramuscular doses of 1ml or 0.5ml given as 4 to 5 doses over 4 weeks.

**If no prior rabies vaccination:**

- In category III exposure, and if available, rabies immunoglobulin should be used in addition to human rabies vaccine.
- In category II exposure, only vaccination is necessary.

**Immunoglobulin:**

**Human rabies immune globulin** 20 IU/kg

*OR*

**Equine rabies immunoglobulin** 40 IU/kg

**N.B.**It is mostly injected at the site of the bite. If any is leftover, inject IM at a distant site. This can be given up to 7 days post-exposure if not available immediately.

**Vaccination:**

- Tissue-culture or purified duck-embryo vaccines with a potency of at least 2.5 IU per single intramuscular immunizing dose, should be applied according to the schedules below. Both regimens can be used in Category II and III exposures.
- **Intramuscular schedules**
    - One dose of the vaccine should be administered on days 0, 3, 7, 14, and 30.
    - In immune-competent people, a regimen consisting on 4 doses on days 0, 3, 7, and 14 plus immunoglobulin may also be used.
    - All intramuscular injections must be given into the deltoid region. The vaccine should never be administered in the gluteal region.
- **Abbreviated multisite schedule**
    - In the abbreviated multisite schedule, the 2–1–1 regimen, 1 dose is given in the right arm and 1 dose in the left arm at day 0, and 1 dose applied in the deltoid muscle on days 7 and 21.
- **Intradermal schedule**
    - In order to reduce the cost of post-exposure treatment, intradermal multisite regimens using a fraction of the intramuscular volume per intradermal inoculation site have been developed.
    - Only the cell-derived vaccines that meet the WHO requirements regarding safety, potency, and efficacy for this application may be considered for intradermal use.
    - This regimen can be used in Category II and III exposures.
    - WHO recommends the following intradermal regimen and vaccines for use by the intradermal route: 2-site intradermal method (2–2–2–0–1–1) for use with PVRV (Verorab TM, Imovax TM, Rabies vero TM, TRC Verorab TM) and PCECV (Rabipur TM).
    - 2-site intradermal method (2–2–2–0–1–1).The volume per intradermal site is: 0.1 ml for PVRV (Verorab TM, Imovax TM, Rabies vero TM, TRC Verorab TM) and PCECV (Rabipur TM).

**If prior pre-or post-exposure vaccination**

For rabies-exposed patients who have previously undergone complete preexposure vaccination or post-exposure treatment with cell-derived rabies vaccines, 2 intramuscular doses of a cell-derived vaccine separated by 3 days are sufficient. Rabies immunoglobulin treatment is not indicated in such cases.

**Pre-exposure vaccination**

Pre-exposure vaccination is recommended for those in rabies diagnostic and research laboratories and veterinarians, individuals at high risk of exposure such as stray dog handlers, park officials, or bat handlers. Pre-exposure vaccination is administered as 1 full dose vaccine given 3 times, IM or 0.1 ml intradermal, on days 0, 7, and 21 or 28.

## 22. Relapsing Fever

Relapsing fever is a louse-borne disease that is caused by the spirochaete, *Borrelia recurrentis*. The disease is common among the homeless and in those living in overcrowded living conditions. It is endemic in our country but outbreaks do also occur from time to time especially during the rainy season. It is characterised by recurrent acute episodes of spirochetemia with short febrile periods alternating with spirochetal clearance and pyrexia. Other febrile diseases like typhus, typhoid fever, malaria and meningitis should be considered in the differential diagnosis of relapsing fever.

**Clinical features**

- Fever, rigors/chills are the most common manifestations.
- Symptoms and signs of complications like bleeding tendency, confusion, gallop rhythm, etc may occur.

**Investigations**

- Microscopic examination of peripheral blood for presence of spirochets.
- In complicated cases: CBC,Liver function tests,ECG

**Treatment**

**Objectives**

- Treat the infection
- Prevent or minimize the Jarish Herxheimer reaction

**Non pharmacologic**

- Delousing

**Pharmacologic**

**First line**

**Procaine penicillin**, 400,000 unit I.M. single dose. For children: 25,000-50,000 units.

Check blood film after 12 hours of treatment. If negative, give tetracycline 250 mgTID for three consecutive days. If the blood film remains positive, repeat the same dose of procaine penicillin and continue with tetracycline later as described above.

**Alternative**

**Tetracycline hydrochloride**, 500mg P.O., single dose. The same dose could be repeated the following day

*OR*

**Erythromycin,** 500mg P.O., Single dose.

**N.B.**

1. **Jarish-Herxheimer reaction**: Some patients may develop Jarisch-Herxheimer reaction and is believed to be due to a rapid clearance of the spirochetes. The first dose of appropriate antibiotic causes transient worsening of clinical symptoms/signs. This mostly happens within the first two hours after antibiotic administration. This reaction is very common ocuring in 35-100% and is associated with increased mortality. In its classic form, it occurs in two distinct phases: Chills phase which consists of a rise in BP, pulse,and respiratory rate; and flush phase which is associated with dramatic fall of BP. The reaction should be actively anticipated and managed aggressively with fluid rescucitation and cardiovascular support.
2. In patients who remain febrile after treatment, consider other concomitant infections like typhus.

## 23. Schistsomiasis

Schistosomiasis is a disease caused by three major trematodes, which include *Schistsoma mansoni*, *Schistsoma japonicum and, Schistsoma haematobium*. The first two species inhabit venules of the intestines whereas the latter are found mostly in the venules of the urinary tract. Human infection occurs as a result of penetration of the unbroken skin by the free-swimming cercariae larva. This often occurs in individuals who have frequent contact with water bodies heavily infested with appropriate snail hosts.

**Clinical features**

- Acute symptoms are swimmer's itch and/or Katayama fever are seen in travellers from non-endemic areas
- Chronic complications related to schistosomiasis are more common in endemic areas where individuals are at increased risk of a high burden of infection. Almost all

chronic complications of the disease are related to the presence of eggs in tissues which induce inflammation. Some of the manifestations are colonic polyps, huge hepatosplenomegally, portal hypertentions and its complications, pulmonary hypertention with corpulmoale, calcified urinary bladder and in some cases bladder cancer (S.hematobium is classified as a carcinogen).

- Symptoms and signs of intestinal schistosomiasis may include diarreahea and hepatosplenomegaly while urinary schistosomiasis may manifest with gross hematuria.

**Investigations**

- Stool or urine examination to look for the parasites (stool for S. mansoni and japonicum or urine for S.hematobium)

**Treatment**

**Objectives**

- Eradicate the infection
- Prevent complications (hepatosplenic schistosomiasis or obstructive uropathy)

**Non pharmacologic**

None

**Pharmacologic**

**First line**

**Praziquantel,** 40 mg/kg in 2 divided doses 4-6 hours apart on one day OR 1200mg P.O., as a single dose OR 2 divided doses for both *S. haematobium* and *S.mansoni*

**Alternatives**

**Metrifonate**, 600 mg P.O., TID at 14 days interval for *S. haematobium.*

**Dosage forms:** Tablet, 100mg.

*OR*

**Oxamniquine**, 1250 mg (30 mg/kg) P.O. single dose for *S. mansoni.*

**Dosage forms**: capsule, 250 mg; suspension, 250-mg/5 ml

**24. Tetanus**

Tetanus is a neurological syndrome caused by a neurotoxin, tetanospasmin, elaborated by *Clostridium tetani* at the site of injury. It can largely be prevented by appropriate immunization.

Prognosis in all patients depends upon the severity of the disease, occurrence of complications and the setting.

**Clinical Features**

- The most common and important clinical features include trismus (lockjaw) localized or generalized muscular rigidity and spasm.
- The presence of arrhythmia, extreme oscillation in blood pressure, diaphoresis, laryngeal spasm and urinary retention may suggest autonomic dysfunction.

A short incubation period (time from injury to first symptom) of ≤4 days generally indicates severe disease. The period between the first symptom and the development of muscular spasms is termed the period of onset. Shorter periods of onset, particularly <48hrs, are again associated with more severe forms of tetanus.

**Investigations**

- Clinical, based on the history and examination findings.

**Severity Scoring:** There are several severity scores used but the Ablett classification has been used most commonly.

**Table 40-Ablett classification of severity of Tetanus**

| Grading | Clinical Features |
|---|---|
| **I- Mild** | Mild to modrate trismus;general spasticity; no respiratory embarassement; no spasm; little or no dysphagia |
| **II- Moderate** | Moderate trismus; well marked rigidity;mild to moderate but short spasms; moderate respiratory embarrasement with RR greater than 30;mild dysphagia |
| **III-Severe** | Severe trismus;generalized spasticity; reflex prolonged spasms; increased RR greater than 40; apnoeic spells; severe dysphagia; tachycardia greater than 120. |
| **IV-Very Severe** | Grade III and violent autonomic disturbances involving the cadiovascular system. Severe hypertention and tachycardia altenating with relative hypotention and bradycardia, either of which may be persistent. |

***Ablett JJL. Ellis M, ed. Symposium on Tetanus in Great Britain. 1967;1-10.**

**Treatment**

**Objectives**

- Reduce spasms
- Prevent serious complications like laryngeal spasm

**Non pharmacologic**

- Admit patients to a quite place, and in severe cases, to an intensive care unit if possible for continuous cardio-pulmonary monitoring.
- Wound care which includes thorough cleansing and debridement.
- Intubation or tracheostomy, and mechanical ventilation in severe cases.
- Adequate hydration and feeding should be given attention

**Pharmacologic**

Patients with severe tetanus should be managed in the intensive care setting where mechanical ventilator and appropriate medication are available. This may necessittate referal of most patients to specialized centers.

A. **Control of spasm**

**Diazepam**, 10 mg I.V. should be given every 4 hourly, the dose being titrated depending on the response. Large doses as much as 250mg QD could be used. NB: Heavy sedation with higher doses of diazepam has a potential to cause respiratory depression and should only be used while the patient is mechanically ventilated.

*PLUS*

**Chlorpromazine**, 25-50mg I.M. QID alternated with diazepam.

*PLUS*

**Magnesium sulphate**, loading dose of 40mg/kg IV over 30 min, followed by IV infusion of 2g/h for patients over 45kg and 1.5g/h for patients 45kg or under.

(It is used in patients with severe tetanus for whom tracheostomy has been done; it helps in controling spasms and reduces autonomic instability)

| | |
|---|---|
| **ADRs:** | flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and central nervous system depression proceeding to respiratory paralysis |
| **C/Is:** | Should not be given to mothers with toxemia of pregnancy during the two hours preceding delivery. Previous hypersensitivity to the medicine. |
| **P/Cs:** | Renal impairment, respiratory depression, |
| **D/I:** | Medicine induced renal losses of magnesium occus with the following medicines or medicine classes: aminoglycosides, amphothericin B,cyclosporine, diretics, digitalis, cisplatin and alcohol |

**Dosage forms:** Injection 500mg/ml in a 2ml ampoule (50% solution), 500mg/ml in a 10ml ampoule (20% solution)

B. **Antimicrobial treatment:**

**Metronidazole**, 500mg P.O., TID for 7-10 days

C. **Neuromuscular blockade**

**Suxamethonium,** 20-100mg I.V. depending on the effect with mechanical ventilation may be employed in patients with severe laryngeal spasm.

D. **Neutralization of circulating toxin**

**Tetanus, Human immunoglobulin**, 500 IU I.M. single dose

*OR*

**Tetanus Antitoxin (TAT)** 10,000 IU IM. after a skin test.

E. **Control of Autonomic dysfunction**

Hypertension and supra-ventricular tachycardia can be treated with combined alpha and Beta-blockers. Morphine can also be used to control the sympathetic hyperactivity. Beta blockers alone are not recommended.

**First line**

**Labetolol**, 0.25-1.0mg/min IV infusion

*OR*

**Morphine** 0.5-1.0mg/kg per hour

F. **Active immunization**

Provide active immunization with appropriate booster doses in those who were never immunized in the past.

**25. Toxoplasmosis (CNS)**

CNS Toxoplasmosis is an infection of the central nervous system by the protozoan *Toxoplasma gondii*. The disease develops in individuals with underlying immunodeficiency, usually occurring as a reactivation.

**Clinical features**

- Patients with cerebral toxoplasmosis typically present with headache confusion, fever. and/or signs of focal neurological deficit.

**Investigations**

- Neuro-imaging (CT scan or MRI of the brain).
- Serologic test for anti-toxo Ig-G antibody-if negative, it may help to exclude the diagnosis. On the other hand positive test or high titer for Ig-M would suggest a more recent infection.

**Treatment**

**Objectives**

- Prevent or minimize neurologic sequelae

**Non pharmacologic**

None

**Pharmacologic**

**First line**

**Sulfadiazine**, 1-2g P.O.,QID for six weeks

*PLUS*

**Pyrimethamine**, 25-100mg, P.O., QD for six weeks

*PLUS*

**Folinic acid**, 10-20mg P.O., QID for six weeks

**Followed by Maintenance treatment with Pyrimethamine**, 25mg/day P.O., QD

**Alternatives**

**Sulphamethoxazole-Trimethoprim** 320/1600mg P.O., BID for 4 weeks, then 160/800mg P.O. BID for 3 months

***Followed by*** Maintenance treatment with

**Sulphamethoxazole-Trimethoprim,** 160/800mg P.O., Q24 hrs

*OR*

**Sulfadoxin Pyrimethamine,** 1000mg/50mg, P.O., BID for two days, then one tablet/day for 6 weeks.

*PLUS*

**Folinic acid,** 10-20mg,P.O., QID for 6 weeks

*OR*

**Clindamycin**, initially 200-400mg I.V. QID followed by 300-900mg, P.O. TID

*PLUS*

**Pyrimethamine**, 25-100mg/day P.O.

*PLUS*

**Folinic acid**, 10-20mg/day P.O.

*PLUS*

**Azitromycin**, 900-1200mg P.O., QD

***Followed by*** Maintenance treatment with

**Pyrimethamine**, 25mg/day P.O.,QD

**N.B.** Administration of Dexamethasone is recommended in patients with altered sensorium and clinical evidence of marked increase in intra-cranial pressure.

**Primary prophylaxis**

**Sulphamethoxazole-Trimethoprim**, 160/800mg P.O., Q24 hrs

## 26. Tuberculosis

Tuberculosisis is a chronic bacterial infection caused by a group of bacteria, *Mycobacteria*ae, the most common of which is Mycobacterium tuberculosis. Less frequently, it can be caused by Mycobacterium bovis and Mycobacterium africanum. Tuberculosis usually affects the lungs in which case it is called pulmonary TB. Although the lung is the most commonly affected organ, almost all parts of the body can be infected with this bacterium and in this case it is called extra-pulmonary TB. Common extra-pulmonary sites affected include the lymph nodes, pleura, spine, urinary tract, the brain, joints, bone and abdomen. HIV infection has now become one of the most important risk factors for the development of active tuberculosis.

Causative organisms

- *M.tuberculosis*
- *M.bovis*
- *M.africanum*
- *M.canasi*

**Clinical features**

The clinical feature of tuberculosis is quite variable and depends on the specific organ affected by the disease. The symptoms of TB are grouped in to general, non-specific systemic symptoms and symptoms associated with the specific organ affected by TB.

The general symptoms of TB (pulmonary or extra-pulmonary):

- Weight loss
- fatigue, malaise
- low grade fever
- night sweats
- loss of appetite
- malnourished and chronically ill children with failure to thrive

Symptoms of Pulmonary tuberculosis; in addition to the general symptoms, patients with pulmonary TB present with the following symptoms and signs:

- Cough that lasts for more than 2 weeks with or without sputum production
- Chest pain
- haemoptysis
- difficulty breathing

Symptoms and signs of extra-pulmonary TB; in addition to the general symptoms of TB, patients with extrapulmonary TB present with signs and symptoms specific to the organ affected:

- Tuberculous lymphadenitis: Slowly developing painless lymph node enlargement, initially firm and discrete, later become matted and fluctuant. The overlying skin may breakdown with the formation of abscesses and chronic discharging sinuses, which heal with scarring.
- Tuberculous pleurisy: pain while breathing in, dull lower chest pain, intermittent cough, breathlessness on exertion.
- TB of bones and/or joints: localized pain and/or swelling of insidious onset discharge of pus, muscle weakness, paralysis, and stiffness of joints.
- Abdominal TB: loss of appetite, weight loss, chronic abdominal pain, diarrhoea or constipation, mass in the abdomen, fluid in the abdominal cavity (ascites).
- Tuberculous meningitis: Headache, fever, vomiting, neck stiffness, impaired consciousness and mental confusion of insidious onset. Tuberculous meningitis remains a potentially devastating disease that is associated with a high mortality and sequelae, despite prompt initiation of adequate chemotherapy. HIV-infected patients appear to be at increased risk of developing tuberculous meningitis.
- TB of the spine: collapse of vertebral bodies results in kyphosis (gibbus). A paravertebral cold abscess may also be formed

**N.B.** Suspect tuberculosis in any person who presents with a history of cough of at least two weeks duration.

**Investigations**

- Sputum Direct light Smear Microscopy with Ziehl Nielsen staining is the mainstay of diagnostic methods to test for the presence of acid fast bacilli (AFB). Three sputum specimens collected and examined in two consecutive days (spot-early morning-spot) and result must be available on the second day.
- Light emitting diode (LED) microscopy with flourscent staining is a newly introduced diagnostic tool to complement the conventional microscopy. It is recommended for centers with high case load as it saves time and improves sensitivity.
- Sputum culture and medicine susceptibility test is a highly sensitive diagnostic method which permits detection of a minimum of 10 to 100 viable bacilli (usually a tenth of an ml); hence; the method allows diagnosis of less infectious cases. Culture remains the gold standard in mycobacterial detection and phenotypic identification of medicine resistance.
- Line Probe Assay is a new test to identify the presence of specific mutations on the genes of TB bacilli which are responsible for Isoniazid and Rifampicin resistance. It is a rapid and accura te test to identify cases with MDR-TB.
- Gene Xpert MTB/RIF is a new, rapid and fully automated DNA/molecular diagnostic test to detect TB and Rifampicin medicine resistance simultaneously. It is indicated for the diagnosis of TB in high MDR-TB and TB/HIV settings.
- Fine needle aspiration from accessible mass like peripheral enlarged lymph nodes and histopathological examination.
- Tissue biopsy from any body tissues such as serous membranes, skin, endometrium, bronchial, pleural, gastric or liver tissue for histophatological examination
- Chest x-ray
- Other investigation: HIV test, ESR, CSF analysis,

A case of tuberculosis is a definite case of TB or a patient whom a health worker has diagnosed TB and has decided to treat the patient with a full course of TB treatment. A Definite/proven case of tuberculosis is a patient with two sputum smears (one sputum positive is enough for HIV positive patients) or culture positive for Mycobacterium tuberculosis. Definite case of tuberculosis is also defined as a patient with Mycobacterium tuberculosis complex identified from a clinical specimen, either by culture or by a newer method such as molecular line probe assay.

Patients with negative smears or when definite TB cannot be determined:

- Repeat sputum smear and request for a chest x ray
- If all investigations, including chest X-ray, do not suggest TB, prescribe two weeks of adequate antibiotic treatment

**Treatment**

**Objectives**

- Cure the TB patient and restore quality of life and productivity
- Prevent death from active TB or its late effects
- Prevent TB relapse
- Prevent the development and transmission of medicine resistance
- Decrease transmission.

**Non pharmacologic**

- Counselling
- Good nutrition
- Adequate rest
- Admission for severely ill patients

**Pharmacologic**

Treatment of TB is with a combination of 4 or more anti-TB medicines. The treatment is standardized by putting patients into different treatment groups based on smear status and previous history of treatment for TB. Standardized treatment means that all patients in a defined group receive the same treatment regimen. TB treatment strategy is referred to as DOT indicating that treatment is given under direct observation of a health worker or treatment supporter daily throughout the course of treatment.

**Treatment with 1st line anti-TB Medicines**

TB Patients with strains susceptible to first line anti-TB medicines are treated with standardized first line treatment regimen for 6 or 8 months, depending on the history of previous TB treatment

The first line anti-TB medicines available for TB treatment in Ethiopia are:

- Rifampicin(R);
- Ethambutol (E);
- Isoniazid (H);
- Pyrazinamide (Z) and
- Streptomycin (S)

The fixed dose combination (FDC) medicines available for adults and adolescents are:

- RHZE 150/75/400/275mg
- RHZ 150/75/400mg
- RH 150/75mg
- EH 400/150mg

TB medicines available as loose form are:

- Ethambutol 400mg;
- Isoniazid 300mg;
- Streptomycin sulphate vials 1gm

**Table 41-Recommended Doses of First-Line Anti-tuberculosis Medicines**

| Medicines | Recommended dose | |
|---|---|---|
| | **Dose and range (mg/kg)** | **Maximum** (mg) |
| Isoniazid (H) | 5 (4–6) | 300 |
| Rifampicin (R) | 10 (8–12) | 600 |
| Pyrazinamide (Z) | 25 (20–30) | 2,000 |
| Ethambutol (E) | 15 (15–20) | 1600 |
| Streptomycin (S) | 15 (12–18) | 1000 |

**1. TB treatment regimen with first line anti-TB medicines**

Treatment regimen for new patients: newly diagnosed smear positive, smear negative and extrapulmonary TB patients who have never had treatment for TB, or have taken anti-TB medicines for less than 1 month. This regimen consists of 8 weeks (2 months) treatment with Rifampicin, Isoniazid, Pyrazinamide and Ethambutol during the intensive phase, followed by four months with Rifampicin and Isoniazid in the continuation phase (2RHZE/4RH). Other Previously treated Smear Negative PTB and EPTB cases (Case definition 'Other') who were previously cured or treatment completed will be treated with New TB patient regimen

**Table 42-Anti TB Medicines Dosage of New TB cases for adults and adolescents**

| Patient's Weight in Kgs | Treatment Regimen and Dose | |
|---|---|---|
| | **Intensive Phase 2RHZE** | **Continuation Phase 4RH** |
| **20-29** | 1 ½ | 1 ½ |
| **30-39** | 2 | 2 |
| **40-54** | 3 | 3 |
| **≥55** | 4 | 4 |

***** *The recommended dose in the weight range of 20-30kg children is different from those in adults due to diferences in age. Children older than 15 years will be managed as adults*

**Table 43-FDC dosing regimens for new pediatric cases**

| Weight (kg) | Intensive phase (2 months) | | | Continuation phase (4 months) | | |
|---|---|---|---|---|---|---|
| | RHZ (60,30,150) | RHZE (150,75,400,275) | E (100) | RH (150,75) | RH (60,30) | RH (60,60) |
| 5 to 7 | 1 | | 1 | | 1 | 1 |
| 8 to 14 | 2 | | 2 | | 2 | 1 |
| 15 to 20 | 3 | | 3 | | 3 | 2 |
| 21 to 30* | | 2 | | 2 | | 2 |

**2. Treatment regimen for previously treated patients (Re-treatment Regimen)** Patients who have previously received 1 month or more of anti-TB medicines. Registration groups for previously treated patients are based on the outcome of their prior treatment course: failure, relapse and default. This regimen consists of an eight week (2 month) treatment with Streptomycin, Rifampicin, Isoniazid, Pyrazinamide and Ethambutol followed by a four week (1 month) treatment with Rifampicin, Isoniazid, Pyrazinamide and Ethambutol during the intensive phase, followed by five months on Rifampicin, Isoniazid and Ethambutol: 2SRHZE/1RHZE/5(RH)E. patients who had defaulted treatment and returned back with smear negative or extra-pulmonary TB case definition ‘others’ are treated with re-treatment regimen

**Table 44-Dose regimens of anti TB Medicines for Previously treated cases of adults and adolescents**

| Patient's Weight in Kgs | Dose regimens | | | |
|---|---|---|---|---|
| | Intensive Phase 2SRHZE/1RHZE | | Continuation Phase 5 (RH)E | |
| | **S** | **RHZE** | **RH** | **E** |
| **20-29** | 1/2(0.5g) | 1 ½ | 1 ½ | $1^{1/2}$ |
| **30-39** | 1/2(0.5g) | 2 | 2 | $1^{1/2}$ |
| **40-54** | 3/4(0.75g) | 3 | 3 | 2 |
| **≥ 55** | 1g | 4 | 4 | 3 |

S: streptomycin

**Table 45-FDC dose regimens for Retreatment Cases for children**

| Weight (kg) | Intensive phase (3Months) | | | Continuation phase (5Months) | | | | |
|---|---|---|---|---|---|---|---|---|
| | RHZ (60,30,150) | RHZE (150,75,400,275) | E (100) | RH (60,30) | RH (150,75) | RH (60,60) | E (100) | E (400) |
| 5 to 7 | 1 | | 1 | 1 | | 1 | 1 | |
| 8 to 14 | 2 | | 2 | 2 | | 1 | 2 | |
| 15 to 20 | 3 | | 3 | 3 | | 2 | 3 | |
| 21 to 30* | | 2 | | | 2 | 2 | | 1 |

* *Tthe recommended dose in the weight range of 20-30kg children is different from those in adults due to diferencexs in age. Children older than 15 years will be managed as adults.*

**Table 46-ADRs, precautions, contra-indications and medicine interactions of 1st line Anti-TB medicines**

| Medicine | ADRs | C/Is | D/Is | P/Cs |
|---|---|---|---|---|
| Isoniazid (H) | Skin rash, Sleepiness and lethargy, Peripheral neuropathy (paraesthesia, numbness and limb pain), Hepatitis. Rare: Convulsions, pellagra, arthralgia, anaemia, lupoid reactions | | $Al(OH)_3$ decreases its absorption, H Inhibits metabolism of phenytoin, diazepam carbamazepine and warfarin hence increases the serum concentrations | Medicine must be taken orally on daily basis, medicine should not be given in divided doses; slow and rapid inactivators (acetylators) of isoniazid; patients infected with HIV are at higher risk of ADR |
| Rifampicin (R) | Gastrointestinal reactions (abdominal pain, nausea, vomiting), Hepatitis, Generalized cutaneous reactions, Thrombocytopenic purpura. Rare: Osteomalacia, pseudomembranous colitis, pseudoadrenal crisis, acute renal failure, shock, haemolytic anaemia | Known MDR-TB cases | Increase metabolism of warfarin, corticosteroids, antifungal agents protease inhibitors, non-nucleoside reverse transcriptase inhibitors, oral hypoglycaemic agents, oral contraceptives hence reduces serum levels of these medicines | preferably be given at least 30 minutes before meal, restrict availability of rifampicin for programmatic use to prevent resistance |
| Ethambotol (E) | Retrobulbar/Optic neuritis, (impairment of vision, red–green blindness, blurring) Rare: Generalized cutaneous reactions, arthralgia, peripheral neuropathy, Very rarely: hepatitis | Patients with rrenal failure | | must be manufactured and stored appropriately to prevent absorption of moisture |
| Pyrazinamide (Z) | Arthralgia, Hepatitis Rare: Gastrointestinal reactions, cutaneous reactions, sideroblastic anaemia | patients with liver disorder | | |
| Streptomycin (S) | Minor: Pain, rash, induration at injection site, Numbness around the mouth and tingling soon after the injection Major: Cutaneous hypersensitivity, Vestibular and auditory nerve damage to the patient & fetus in pregnancy, Renal damage | Pregnancy Patients with renal failure | | For patients over 60 years of age, the maximum dose of streptomycin is 0.75 gm |

**Table 47-Symptom based approach to the management of Anti-TB medicines induced adverse effects**

| Adverse-effects | | Responsible Medicines | Management |
|---|---|---|---|
| **Minor (Continue Anti-TB medicine/s)** | Anorexia, nausea, abdominal pain | Rifampicin; Pyrazinamide | Give tablets with small meals or before bedtime |
| | Joint pains | Pyrazinamide | NSAIDs |
| | Burning sensation in feet | Isoniazid | Pyridoxine 100mg daily |
| | Orange/red urine | Rifampicin | Reassurance |
| **Major (Stop the responsible medicine/s)** | Itching, skin reaction | Streptomycin; Rifampicin or isoniazid | Stop and replace with ethambutol; Stop, then reintroduce with desensitization[1] |
| | Deafness | Streptomycin | Stop streptomycin and replace with Ethambutol |
| | Dizziness (vertigo, imbalance and nystagmus) | Streptomycin | Stop streptomycin and replace with Ethambutol |
| | Jaundice; hepatitis | Most anti-TB medicines | Stop all anti-TB medicines and refer |
| | Vomiting and confusion | Most anti-TB medicines | Stop all anti-TB medicines and refer |
| | Visual impairment | Ethambutol | Stop Ethambutol and refer |
| | Shock, purpura and acute renal failure | Rifampicin | Stop Rifampicin and refer |

**Precautions during treatment with 1st line anti-TB medicines**

**Treatment of patients with renal failure:**

Consult expert. If not possible to consult then avoid Streptomycin & Ethambutol; therefore the recommended regimen is 2RHZ/4RH.

**Treatment of patients with (previously known) liver disorder (e.g. hepatitis, cirrhosis):**

Most anti-TB medicines can cause liver damage. Do not give Pyrazinamide because this is the most hepatotoxic anti-TB medicine. Isoniazid & Rifampicin plus one or two non-hepatotoxic medicines, such as Streptomycin and Ethambutol, can be used for a total treatment duration of eight months. If the patient has severe liver damage, an alternative regimen is Streptomycin plus Isoniazid plus Ethambutol in the initial phase followed by Isoniazid & Ethambutol in the continuation phase with a total duration of 12 months. The dose of Rifampicin for these patients should not exceed 8mg per kg and Isoniazid dose should not exceed 4 mg per kg. Hence, for TB patients with liver disease, recommended regimens are: 2SERH/6RH or 9RHE. In the case of jaundice, the treatment regimen should be changed to 2 SEH /10 EH.

**Pericardial tuberculosis**

For patients with pericardial tuberculosis, the same regimen (as pulmonary) of anti-TB treatment is recommended (need expert opinion in diagnosis and treatment).

Corticosteroids are recommended as adjunctive therapy for 11 weeks during the first period of anti-tuberculosis therapy.

**Table 48-Prednisone dose for adult TB patients with TB pericarditis**

| Weeks of treatment | Prednisolone dosage |
|---|---|
| 1-4 | 60mg/day |
| 5-8 | 30mg/day |
| 9-10 | 15mg/day |
| $11^{th}$ week | 5mg/day<br>(then discontinue at the end of the $11^{th}$ week) |

**Pleural tuberculosis**

Tuberculous empyema, a chronic, active infection of the pleural space containing a large number of tubercle bacilli, usually occurs when a cavity ruptures into the pleural space. Treatment consists of drainage (often requiring a surgical procedure) and anti-TB medicines.

**Tuberculous meningitis**

Patients presenting with more severe brain impairment such as drowsiness, neurological signs, or coma have a greater risk of neurological sequelae and higher mortality.

Chemotherapy should be initiated with **RHZS** in an initial phase for 2 months and RH should be continued for 7 to 10 months in the continuation phase.

Adjunctive corticosteroid therapy is recommended for all patients. The recommended regimen is dexamethasone in an initial dose of 8 mg/day for children weighing less than 25 kg and 12 mg/day for children weighing 25 kg or more and for adults. The initial dose is given for 3 weeks and then decreased gradually during the subsequent 3 weeks.
Prednisolone at a dose of 2-4mg/kg/day for children; 60mg/day for adults, for 3 weeks, then tapered off gradually over the following three weeks, is used as an alternative.

**Treatment during pregnancy and breast-feeding**

- Avoid Streptomycin because of the risk of toxic effects on the fetus.
- Chemotherapy should not be discontinued during breast-feeding.
- When a breast-feeding mother has PTB, the infant should, regardless of prior vaccination with BCG, be given chemo-prophylaxis and then be vaccinated with BCG if not previously vaccinated.

**Treatment of patients also infected with HIV**

- HIV infection and Active TB disease should be started on HAART irrespective of CD4 cell count

Patients infected with HIV usually respond equally well to TB treatment as those without HIV infection, with a few exceptions:

- They should always be treated with short course chemotherapy.
- Initiation of ART in the course of treatment for tuberculosis should follow the WHO guidelines

**Table 49-Guideline for management of patients presenting with TB before initiation of ART**

| | **Recommendation** | **Preferred ARV regimen** |
|---|---|---|
| CD4 count <500cells/mm$^3$ | ▪ Start TB treatment.<br>▪ Start ART as soon as TB treatment is tolerated (usually between 2-8 weeks of TB treatment)[1] | EFV containing regimen is preferred.[2] However, if medicines are unavailable or there are problems with EFV (adverse effects with intolerance and risk of pregnancy) use triple Nucleoside regimen with caution (3). If patient develops ABC hypersensitivity continue NVP but monitor liver function every month[3]. |

| | Recommendation | Preferred ARV regimen |
|---|---|---|
| CD4 count <500cells/mm$^3$ | • Start TB treatment<br>• Defer ART | • Re-assess eligibility for ART[4] |
| CD4 not available | • Start TB treatment.<br>• Defer ART | • Start ART after determining CD4 count |

[1] It is recommended that ART be initiated as soon as TB therapy is tolerated. Ideally, this may be as early as 2 weeks and not later than 8 weeks.

[2]Patients who present with TB before initiation of ART the preferred regimen are EFV containing first line regimen. If patients develop TB while on ART for 3-6 months, continue ART throughout TB treatment and patients with NVP based treatment should be shifted to EFV.

The recommended regimens include EFV containing regimens: TDF/3TC/EFV or ZDV/3TC/EFV.

[3] NVP (200 mg daily for 2 weeks followed by 200 mg twice daily) may be used in place of EFV in absence of other options. NVP containing Regimens include: TDF/3TC/NVP or ZDV/3TC/NVP.

[4]Obtain CD4 cell count every six months for all patients including those with WHO stage 1 and 2 HIV infections

**Treatment monitoring**

- Health worker or a community TB treatment supporter must observe and ensure each patient swallows every single dose of the medicines; this is called directly observed treatment or DOT.
- During treatment follow-up, monitoring of patient's progress involves: clinical assessment of signs and symptoms, weight measurement and follow-up AFB sputum examination.
- Follow-up sputum examination is done for all new smear positive TB cases at the 2$^{nd}$, 5$^{th}$ and 6$^{th}$ month. If smear result is positive at 2$^{nd}$ month, a repeat sputum smear examination is done at the 3$^{rd}$ month and if it is still positive, the sample must be sent for DST. If smear result is positive at 5$^{th}$ month or later, it is declared that treatment has failed and patient will be started on re-treatment regimen and sputum is examined for DST. If smear is negative at 5$^{th}$ and 6$^{th}$ month of follow-up, patient is declared cured.
- Follow-up sputum examination is done for all previously treated smear positive TB cases at 3$^{rd}$, 5$^{th}$ and 8$^{th}$ month. If smear result is positive at the 3$^{rd}$ month, sample must be sent for DST. If smear result is positive at the 5$^{th}$ month or later, it is declared that treatment has failed and patient must be started on 2$^{nd}$ line treatment regimen pending

the DST result. If smear is negative at 5th and 8th month of follow-up, patient is declared cured.

**Medicine resistant TB**

TB is considered medicine-resistant (DR) when the TB causative agent (mycobacterium tuberculosis) is not killed by one or more of the available anti-TB medicines. Medicine-resistant TB can be primary or secondary (acquired). Primary resistance is medicine resistance among new cases; it is resistance to one or more anti-TB medicines in a person who has never been previously treated for TB. Secondary resistance is medicine resistance among previously treated cases; in people diagnosed with TB who start anti-TB treatment and subsequently acquire resistance to one or more of the medicines used during the treatment. Both medicine susceptible and resistant MTB spread in the same manner.

There are five different types of medicine resistance:

- **Mono-resistance**: Rresistance to one anti-tuberculosis medicine.
- **Poly-resistance**: Resistance to more than one anti-tuberculosis medicine, other than Isoniazid and Refampicin.
- **Multimedicine-resistance (MDR)-TB**: Resistance to at least isoniazid and rifampicin.
- **Extensive medicine-resistance (XDR-TB)**: Resistance to any of the fluoroquinolones, and at least one of the three injectable Second Line Medicines (capreomycin, kanamycin and Amikacin), in addition to resistance to INH andrefampicin
- **Total medicine-resistance (TDR-TB): resistance to all anti TB medicines.**

The clinical features of medicine susceptible and medicine resistant TB are the same.

**Investigations**

- direct smear microscopy
- Line Probe Assay (LPA) directly from the sputum specimen or cultured sample
- Culture and DST
- Gene Xpert MTB/RIF test
- CBC, HIV test, urinalysis, FBS, CXR,
- LFT, RFT, Serum electrolyte,
- TSH, HCG,
- Audiometric test

Definitive diagnosis of medicine-resistant TB depends on laboratory diagnosis through Medicine Susceptibility testing (DST); it requires that M. tuberculosis is isolated and medicine susceptibility test is completed.

**Treatment of MDR-TB**

**Objectives**

- Cure the TB patient and restore quality of life and productivity
- Prevent death from active TB or its late effects
- Prevent TB relapse
- Prevent the development and transmission of extensive medicine resistance
- Decrease transmission

**Non pharmacologic**

- Adherence counselling
- Psychosocial and emotional support
- Nutritional support
- Admission of severe cases

**Pharmacologic**

MDR-TB Patients with strains resistant to at least refampcin and Isoniazid are treated with standardized second line treatment regimen for at least 18-24 months. Medicine Resistance Survey (DRS) data from representative patient populations are used to design a standardized treatment regimen. The treatment approach that is widely used in Ethiopia is the standardized treatment regimen where all patients in a defined group or category receive the same regimen.

| **Standard MDR-TB Treatment Regimen in Ethiopia** |
|---|
| Patients with confirmed MDR-TB disease must receive the following medicine regimen: |
| **8E-Z-Km (Am)-Lfx-Eto-Cs/12 E-Z-Lfx–Eto–Cs** |

Threre are five groups of anti-TB medicines that can be used for the treatment of Medicine Resistance-TB as shown in the table beow:

**Table 50-Grouping of anti-tuberculosis medicines and dose for treatment of medicine resistance**

| Medicines (Abbrevation, common formulation) | <33kg | 33-50kg | 50-70kg | >70kg |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| **Group 1: FIRST-LINE ORAL ANTITUBERCULOSIS MEDICINES** | | | | |
| Isoniazid (H): 100mg, 300mg tabs | 4–6mg/kg daily or 8–12mg 3 x wk | 200–300mg daily or 450–600mg 3 x wk | 300mg daily or 600mg 3 | 300mg daily or 600mg 3 x wk |
| Rifampicin (R): 150mg, 300mg tabs | 10–20 mg/kg daily | 450–600mg | 600mg | 600mg |
| Ethambutol (E): 100mg, 400mg tabs | 25 mg/kg daily | 800–1200mg | 1200– | 1600– 2000mg |
| Pyrazinamide (Z): 500mg tabs | 30–40mg/kg daily | 1000–1750mg | 1750–2000mg | 2000– 2500mg |
| **GROUP 2: INJECTABLE ANTITUBERCULOSIS MEDICINES** | | | | |
| Streptomycin (S): 1g vial | 15–20mg/kg daily | 500–750mg | 1000mg | 1000mg |
| Kanamycin (Km): 1g vial | 15–20mg/kg daily | 500–750mg | 1000mg | 1000mg |
| Amikacin (Am): 1g vial | 15–20mg/kg daily | 500–750mg | 1000mg | 1000mg |
| Capreomycin (Cm): 1g vial | 15–20mg/kg daily | 500–750mg | 1000mg | 1000mg |
| **GROUP 3: FLUOROQUINOLONES** | | | | |
| Ofloxacin (Ofx): 200, 300, 400mg tabs | 15-20mg/kg daily | 800mg | 800mg | 800–1000mg |
| Levofloxacin (Lfx): 250, 500mg tabs | 7.5-10mg/kg daily | 750mg | 750mg | 750–1000mg |
| Moxifloxacin (Mfx): 400mg tabs | 7.5-10mg/kg daily | 400mg | 400mg | 400mg |
| **GROUP 4: ORAL BACTERIOSTATIC SECOND-LINE ANTITUBERCULOSIS MEDICINES** | | | | |
| Ethionamide (Eto): 250mg tabs | 15–20mg/kg daily | 500mg | 750mg | 750–1000mg |
| Protionamide (Pto): 250mg tabs | 15–20mg/kg daily | 500mg | 750mg | 750–1000mg |
| Cycloserine (Cs): 250mg tabs | 15–20mg/kg daily | 500mg | 750mg | 750–1000mg |
| Terizidone (Trd): 300mg | 15–20mg/kg daily | 600mg | 600mg | 900mg |
| P-aminosalicylic acid (PAS): 4 g tabs | 150mg/kg daily | 8g | 8g | 8-12g |
| Sodium PAS | Dosing can vary with manufacture and preparation: check dose recommended by the manufacturer | | | |
| **GROUP 5: AGENTS WITH UNCLEAR ROLE IN DR-TB TREATMENT (NOT RECOMMENDED BY WHO FOR ROUTINE USE IN MDR-TB PATIENTS). OPITMAL DOSES FOR DR-NOT YET ESTABLISHED** | | | | |
| Thioacetazone (Th) | Usual dose is 150mg for adults | | | |

| | |
|---|---|
| Clofazimine (Cfz) | Usual adult dose is 100mg to 300mg daily. Some clinicians begin at 300mg daily and decrease to 100mg after 4 to 6 weeks. |
| Linezolid (Lzd) | Usual adult dose is 600mg twice daily. Most reduce the dose to 600mg once a day after 4 to 6 weeks to decrease side effects |
| Amoxicillin/Clavulanate (Amx/Clv) | Dosages for DR-TB not well defined. Normal adult dose 875/125mg twice a day or 500/125mg three times a day. Dosages of 1000/250 have |
| Thioacetazone (Thz) | Usual adult dose is 150mg |
| Imipenem/Cilastatin (Ipm/Cln) | Usual adult dose is 500-1000mg IV every 6 hours |
| Clarithromycin (Clr) | Usual adult dose is 500mg twice daily |
| High-dose isoniazid (High-dose H) | 16-20 mg/kg daily |

**Table 51-Symptom based approach to the management of 2nd line Anti-TB medicines induced adverse-effects**

| ADR | Suspected agent | Management | Remarks |
|---|---|---|---|
| Nausea, vomiting | Eto/Pto, PAS, H, E, Z, Cfz | 1. Assess for dehydration; and rehydrate if indicated.<br>2. If mild symptoms and no signs of dehydration,<br>o Advise patient to take medicines with porridge.<br>o Initiate antiemetic therapy if needed (Metoclopromide)<br>o Encourage patient to continue treatment<br>o Encourage patients to increase fluid intake(water, juice, tea)<br>3. If there is dehydration or persistence of symptoms,<br>• Initiate rehydration accordingly<br>• Refer patient to treatment initiating centre | 1. Nausea and vomiting is very common in early weeks of therapy and usually abate with time and adjunctive therapy.<br>2. Electrolytes should be monitored and replaced if vomiting is severe.<br>3. Reversible upon discontinuation of suspected agent.<br>4. Clofazimine can cause severe abdominal pain and acute abdomen. This is rare, but if occurs, clofazimine should be suspended. |
| Gastritis | PAS, Eto/Pto | 1.Give antiTb medicines with small food, avoid caffeine, cigarettes and assess for signs of severity<br>2. If mild symptoms give H2-blockers, proton-pump inhibitors, or antacids.<br>3. If severe (severe persistent dyspepsia, hematemesis/coffee ground vomitus, black tarry stool, initiate rehydrationand refer. | 1. Severe gastritis, as manifested by haematemesis, melaena or haematechezia, is rare.<br>2. Dosing of antacids should be carefully timed so as to not interfere with the absorption of antituberculosis medicines (take 2 hours before or 3 hours after antituberculosis medications). |

| | | | |
|---|---|---|---|
| | | | 3. Reversible upon discontinuation of suspected agent(s). |
| Hearing loss | Km, Am, Cm | 1. Confirm that this is not due to ear wax or other conductive problems.<br>2. Check whether patient has history of hearing loss previously<br>3. Document hearing loss and compare with baseline audiometry if available.<br>4. Refer if it is new event or worsening of complaint. | 1. Patients with previous exposure to aminoglycosides may have baseline hearing loss. In such patients, audiometry may be helpful at the start of MDR-TB therapy.<br>2. Hearing loss is generally not reversible.<br>3. The risk of further hearing loss must be weighed against the risks of stopping the injectable in the treatment regimen.<br>4. While the benefit of hearing aids is minimal to moderate in auditory toxicity, consider a trial use to determine if a patient with hearing loss can benefit from their use |
| Electrolyte disturbance (Low K and Mg)<br>Manifesting as fatigue, muscle cramp, muscle spasm | Cm, Km, Am, | 1. Check potassium (if available).<br>2. If potassium is low also check magnesium (and calcium if hypocalcaemia is suspected).<br>3. Initiate potassium supplement if K+> 3.0meq/L) and monitor Potassium weekly<br>4. Correct if there are contributing causes of hypokalemia (Vomiting, diarrhoea)<br>5. Refer if K+<3.0meq/L | 1. If severe hypokalaemia is present, consider hospitalization.<br>2. Amiloride 5–10 mg QD or Spironolactone 25 mg QD may decrease potassium and magnesium wasting and is useful in refractory cases.<br>3. Oral potassium replacements can cause significant nausea and vomiting. Oral magnesium may cause diarrhoea. |
| Peripheral neuropathy | Cs, H, Km, Am, Cm, Eto/Pto | 1. Increase pyridoxine to maximum daily dose (200 mg per day).<br>2. Initiate therapy with tricyclic antidepressants such as amitriptyline. Non-steroidal anti-inflammatory medicines or acetaminophen may help alleviate symptoms.<br>3. If no improvement refer | 1. Patients with co-morbid disease (e.g. diabetes, HIV, alcohol dependence) may be more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the agents listed here.<br>2. Neuropathy may be irreversible; however, some patients may experience improvement when offending agents are suspended |
| Seizure | Cs, H, FQs | 1. Suspend suspected agent pending resolution of seizures.<br>2. Initiate anticonvulsant therapy (e.g. Phenytoin, Valproic Acid). | 1. Anticonvulsant is generally continued until MDR-TB treatment is completed or suspected agent discontinued. |

| | | | |
|---|---|---|---|
| | | 3. Increase pyridoxine to maximum daily dose (200 mg per day).<br>4. Refer after controlling seizure | 2. History of previous seizure disorder is not a contraindication to the use of agents listed here if a patient's seizures are well controlled and/or the patient is receiving anticonvulsant therapy.<br>3. Patients with history of previous seizures may be at increased risk for development of seizures during MDR-TB therapy |
| Psychosis | Cs, H, FQs, Eto/Pto | 1. Stop suspected agent (usually cycloserine) immediately<br>2. Initiate antipsychotic therapy.<br>3. Refer to TIC | 1. Some patients will need to continue antipsychotic treatment throughout MDR-TB therapy.<br>2. Previous history of psychiatric disease is not a contra-indication to the use of agents listed here but may increase the likelihood of psychotic symptoms developing during treatment.<br>3. Psychotic symptoms are generally reversible upon completion of MDR-TB treatment or cessation of the offending agent. |
| Jaundice/Hepatitis | Z, H, R, Eto/Pto, PAS, E, FQs | 1. Stop all therapy pending resolution of hepatitis.<br>2. Eliminate other potential causes of hepatitis.<br>3. Refer to the TIC | 1. History of previous hepatitis should be carefully analysed to determine most likely causative agent(s); these should be avoided in future regimens.<br>2. Generally reversible upon discontinuation of suspected agent |
| Nephrotoxicity (body swelling, decreasing urine, new onset or worsening hypertension) | Km, Am, Cm | 1. Discontinue Injectable.<br>2. Refer to the TIC | 1. History of diabetes or renal disease is not a contraindication to the use of the agents listed here, although patients with these co-morbidities may be at increased risk for developing renal failure.<br>2. Renal impairment may be permanent |
| Depression | Cs, FQs, H, Eto/Pto | 1. Improve socioeconomic conditions.<br>2. Group or individual counseling.<br>3. Initiate antidepressant therapy.<br>4. Refer if severe depression | 1. Socioeconomic conditions and chronic illness should not be underestimated as contributing factors to depression.<br>2. Depressive symptoms may fluctuate during therapy and may improve as illness is successfully treated.<br>3. History of previous depression is not |

| | | | |
|---|---|---|---|
| | | | a contraindication to the use of the agents listed but may increase the likelihood of depression developing during treatment. |
| Hypothyroidism (swelling, slowing, fatigue, day time sleepiness) | PAS, Eto/Pto | Check TFT if available to confirm,<br>Refer to TIC | 1.Completely reversible with discontinuation of the medicine<br>More frequent with combination medicine therapy |
| Blurring of vision | E, Eto | Refer | |
| Arthralgia | Z, FQ | 1. Initiate therapy with non-steroidal anti-inflammatory medicines (e.g Ibuprofen)<br>2. Refer if severe or no improvement. | |

**Medical Referrals and Indications for Hospitalization**

**Referral of TB patients**

A TB and/or leprosy patient is said to be **referred** when they are sent to another health facility temporarily for better diagnosis, consultation and management and/or other programmatic reasons.

Reasons for Patient referral:

- For diagnosis (X-ray, histo-pathology)
- For better management (serious side effect management, comorbid conditions, in-patient care, MDR-TB)
- Programmatic (to initiate treatment after diagnosis, patient preference)

**Indications for Admission of TB patients**

In the majority of cases, admission is not necessary for TB patients. However, admission may be indicated when there is:

- Severe clinical deterioration of the patient's condition
- Tuberculosis related complications like massive hemoptysis, pneumothorax, empyema
- Serious side-effects such as jaundice or severe allergic skin reaction
- Severe comorbid conditions diseases such as uncontrolled or complicated diabetes, kidney failure, chronic liver disease

**Prevention of Tuberculosis**

**INH prophylaxis (IPT)**

- Isoniazid is given to individuals with latent infection with *Mycobacterium tuberculosis* in order to prevent progression to active disease.
- Screening for exclusion of active TB in HIV infected persons, is the single most important step that should precede the decision to initiate IPT.

## 27. Typhoid Fever

Typhoid fever is an acute febrile illness caused mainly by *Salmonella typhi*. The mode of transmission is via contaminated food or water.

**Clinical features**

- Gradual increase in body temperature associated with headache, malaise and chills.

- Physical findings include fever, splenomegaly and hepatomegaly.
- Sometimes it may cause outbreaks.

**Investigations**

- Clinical
- Culture and sensitivity of blood, stool or urine is the mainstay of diagnosis
- Serological examination, such as the Widal test may be used as an adjunt to diagnosis in the proper clinical setup particularly in children less than 10 years old and travellers from non-endemic areas. The Widal test is, however, characterised by false positive results.

**Treatment**

**Objectives**

- Treat the infection
- Prevent chronic carriage

**Non pharmacologic**

None

**Pharmacologic**

**Symptomatic treatment**: Use of antipyretics, e.g. paracetamol to control fever.

**First line**

**Ciprofloxacin**, 500mg P.O., BID for 10-14 days

**Alternative**

**Amoxicillin**,1g, P.O.,QID., for children: 20 – 40mg/kg/day P.O., in 3 divided doses for 14 days

*OR*

**Chloramphenicol**, 500mg P.O., QID, for 14 days: For children: 25mg/kg.

*OR*

**Sulfamethoxazole+trimethoprim**, 800mg/160mg P.O., BID for 14 days. For children 6 weeks– 5 months, 100/20mg; 6 months – 5 yrs, 200/40mg; 6 – 12 yrs, 400/80mg BID

*OR*

For severe cases which are fluoroquinolone resistant:

**Ceftriaxone**, 1g QD as a single dose OR in 2 divided doses I.M. OR I.V. for 7-10 days.

*OR*

**Chloramphenicol**, 1g, IV bolus QID until 48 hrs after fever has settled, followed by 500mg P.O., QID for a total of 14 days. For children: 25mg/kg, IV bolus QID, until 48 hrs after fever has settled, followed by 525mg/kg P.O., QID for a total of 14 days.

Adjunct Corticosteroid treatment: This is recommended only for patients with evidences of CNS involvement (delirium, coma) or shock

**First line**

**Dexamethasone**, 3mg/kg IV initially, followed by 1mg/kg IV Q 6hrs for 48hrs total
(This is prefered in patients with severe disease)

*OR*

**Prednisolone**, 20-40mg P.O., (or equivalent) once daily for the first three days of antibiotic treatment.

## 28. Typhus

Typhus is a disease caused by *rickettisial organisms*. There are two types of epidemiologically distinct typhus. One caused by R.prowazekii is transmitted by a body louse and is known to casue epidemic typhus and the other caused by R.typhi is transmitted by tick and causes endemic typhus.

**Clinical features**

The clinical presentation of both types is similar and cause an acute febrile illness characterised by:

- an abrupt onset of fever, severe headache and prostration.
- Important differential diagnosis include relapsing fever, bacterial meningitis, and typhoid fever.
- It is a disease commonly seen among destitute individuals with poor personal hygiene.

**Investigation**

- The Weil Felix serology test with demonstration of a rising/high titer.

**Treatment**

**Objectives**

- Treat the infection and prevent complications

**Non pharmacologic**

- delousing

**Pharmacologic**

**First line**

**Doxycycline**, 200mg P.O., in a single or 2 divided doses for 7-10 days

*OR*

**Tetracycline**, 250mg, P.O.,QID for 7-10 days

**Alternatives**

**Chloramphenicol** 500mg P.O., QID for 7 days. For children: 25mg/Kg

## 29. Varicella (Chicken Pox)

The varicella virus causes two distinct syndromes in humans: a primary illness called chicken pox, which most often occurs in children and is relatively benign, and a second distinct syndrome called herpes zoster, which occurs in older adults or immunecompromized hosts and is due to reactivation of the dormant virus in the nerves. Herpes zoster causes significant morbidity due to the intense and sometimes long-standing pain that it causes. It has become more significant in recent years due to its propensity to affect patients with HIV infection. Herpes zoster in a young person is highly predictive of HIV infection and is a WHO clinical stage 2 condition.

**Clinical features**

- Prodrome of fever, malaise, nausea, “flu-like” illness. 2–5 days later a generalized, itchy rash appears.
- Crops of papules-vesicles, then crusted lesions appear all over, sparing the palms and soles.
- Lesions co-exist in different stages of progression, i.e. new papules appear when older lesions are already crusted. Intense itching occurs.

**Complications** are more often seen in patients who acquire the infection as adults, and particularly in pregnant women. Complications may include pneumonia,encephalitis, hepatitis or haemorrhagic syndromes.

**Varicella in pregnancy** carries a high risk of complications. If acquired before 28 weeks’ gestation, it will cause congenital abnormalities in the child (also called congenital varicella

syndrome). If acquired around the time of birth, it can cause neonatal varicella, which carries a high rate of pneumonia and other complications.

**Treatment**

**Objectives**

- Prevent complications

**Non pharmacologic**

None

**Pharmacologic**

In adults including pregnant women:

**Oral aciclovir**, 800mg 5 times daily for 7 days.

In immunocompromised adults or those with disseminated disease:

**IV aciclovir** 10mg/kg 3 times daily for 7 days; OR high-dose oral aciclovir, **if no IV available.**

Treatment should be started as early as possible, ideally less than 24 hours after the start of symptoms. For oral treatment, the value of starting after 24 hours is not well established

**N.B.** The rash can be pruritic and this can be treated with appropriate anti-histamines.

**Herpes zoster**

**Clinical features**

- Painful vesicular rash in a dermatomal distribution of a nerve supply that does not cross the midline.
- Pain sometimes comes before the appearance of the rash.
- Vesicles form in groups and progress to crusted lesions after a few days.
- Most common areas: trunk, particularly the flanks, and forehead.
- Can involve the eye and cause corneal scarring and blindness.
- HIV patients have more frequent multidermal involvement, involvement of the trigeminal nerve, presence of systemic symptoms, and have a higher risk of disseminated disease.
- Myelitis, meningitis, and encephalitis with headache, fever, neck stiffness, altered motor and sensory function.
- Guillain-Barre syndrome.

**Complications**

- Blindness due to corneal involvement.

– Post-herpetic neuralgia: chronic pain in the area where the lesions occurred that can last for months to years after the acute episode.

**Treatment**

**Objectives**

– Prevent post herpetic neuralgia

**Non pharmacologic**

– Local lesion care with daily bathing with soap and water.
– Isolation of the patient to avoid spreading the virus. Contact should be avoided until all lesions are crusted over.

**Pharmacologic**

– **Aciclovir** 800mg 5 times daily for 7 days can be considered for all adults, and is recommended for all HIV-positive adults. Start aciclovir within 72 hours from the onset of symptoms.
– **Paracetamol** for fever
– **Antihistamines or calamine lotion** may be used to reduce itching
– **Amitriptyline** 25–50mg before bed for neuropathic pain and post-herpetic neuralgia. Secondary bacterial infections may require antibiotics.

**N.B.** For ophthalmic involvement, topical acyclovir, 3% eye ointment applied into the eye every 4 hours should be given.

## CHAPTER VII: KIDNEY AND GENITOURINARY TRACT DISORDERS

### 1. Acute Kidney Injury

Acute kidney injury (AKI) has now replaced the term acute renal failure and a staging system has been proposed to allow earlier detection and management of AKI. The new terminology enables healthcare professionals to consider the disease as a spectrum of injury than only the end of the spectrum i.e. failure.

Acute kidney injury is diagnosed when one of the following criteria is met:

- Serum creatinine rises by ≥ 0.3mg/dl within 48 hours or
- Serum creatinine rises ≥ 1.5 fold from the baseline, which is known or presumed to have occurred within one week or
- urine output is < 0.5ml/kg/hr for >6 consecutive hours

**Table 52-Staging of AKI according to AKIN (Acute Kidney Injury Network) criteria**

| Stage | Increase in serum Creatinine | Urine output |
|---|---|---|
| **1** | ≥ 0.3mg/dl increase or 1.5-to 2-fold from baseline | < 0.5ml/kg/hour for > 6 hours |
| **2** | >2-to 3-fold increase from baseline | < 0.5ml/kg /hour for 12 hours |
| **3** | >3-fold from baseline or serum creatinine ≥ 4.0mg/dl with an acute increase of at least 0.5 mg/dl | < 0.3ml/kg/hour for 24 hours<br>or<br>Anuria for 12 hours |

The causes of AKI have traditionally been divided into three broad categories:

1. **Prerenal azotemia**-Hypovolemia, Heart Failure , liver failure, altered renal autoregulation (NSAIDS, ACE inhibitors)
2. **Intrinsic renal** – Ischemic acute tubular necrosis (ATN), nephrotoxic ATN (aminoglycoside, intravenous iodinated contrast, Rhabdomyolsis, Hemodialysis), acute glomerulonephritis, acute interstitial nephritis
3. **Post renal-**Bladder outlet obstruction, bilateral pelviureteral obstruction

Whenever a diagnosis of AKI is made the specific etiology/etiologies should be carefully searched.

**Clinical features**

The clinical features of AKI are dominated by those of the underlying cause unless the AKI is severe

- Oliguria/Anuria
- Fatigue
- Peripheral edema, pulmonary edema, pleural effusion or ascites
- Pericardial effusion
- Decreased appetite, nausea and vomiting
- Hiccups
- Mucocutaneous bleeding
- Change in mental status/flapping tremor/seizure

**Investigations**

- Urinalysis
- BUN and creatinine
- Serum electrolytes
- ECG – to look for evidence of hyperkalemia
- Abdominal ultrasound to exclude urinary tract obstruction and assess kidney size
- Renal biopsy-when glomerulonephritis is suspected, cause is not clear
- Other investigation should be done based on the suspected specific etiologies.

**Treatment**

**Objectives**

- Correct reversible causes of AKI
- Avoid worsening of kidney injury
- Maintain normal volume and electrolyte status
- Avoid overdoses of medications with renal clearance

**Non pharmacologic**

**Maintain Fluid & electrolyte balance**

- Strict fluid input and output chart
- Daily weighing

- Decrease salt intake in fluid overloaded patients
- Free water restriction in hyponatremia
- Decrease foods rich in potassium

**Surgical intervention:** For obstructive uropathy

**Prevent further injury**

- Avoid nephrotoxic medications and radiocontrast agents
- Adjust doses of medicines with renal clearance
- Treat Heart Failure

**Dialysis (Refer for)**

Indications for dialysis

- Pulmonary edema and anuria.
- Intractable metabolic acidosis
- severe hyperkalemia (> 7 mmol/l).
- Uremic complications-pericarditis, encephalopathy and bleeding
- Medicine overdose only if due to dialyzable toxin.

**Pharmacologic**

1. Correct fluid losses vigorously in pre renal azotemia:
2. **Furosemide –** indicated in state of fluid overload only.
   Furosemide 40mg, IV, starts dose 40mg-80mg, increase the dose every 1-2 hour till adequate response. Do not go beyond 200-240mg dose if no response. Doses above 100mg should be given very slowly (15-20 minutes)
3. **Treatment of hyperkalemia-see section on hyperkalemia**
4. **Treatment of hypertensive emergency-**see section on hypertension
5. **Treatment of specific cause** e.g. High dose steroid and cyclophosphamide in patients with severe lupus nephritis

There is no specific pharmacologic treatment for AKI caused by ischemic or nephrotoxic Acute Tubular Necrosis

## 2. Chronic Kidney Disease

Kidney damage for >3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR manifest by either:

- Markers of kidney damage, including abnormalities in blood urea, creatinine or urine abnormalities or abnormalities in imaging tests
- Pathological abnormalities
- GFR < 60ml/minute/1.73m for > 3 months

Common causes of chronic kidney disease are: hypertension, diabetes mellitus**,** glomerulonephritis, polycystic kidney disease and obstructive uropathy.

**End stage renal disease (ESRD)** – refers to a state of advanced CKD with estimated GFR being < 15ml/min where life long renal replacement therapy (dialysis or kidney transplantation) is necessary to suastain a reasonable quality of life and survival**.**

**Table 53-Stages of CKD according to Kidney Disease Outcomes Quality Initiative (K/DOQI) program**

| Stage of CKD | GFR or maker of kidney damage | GFR in ml/min |
|---|---|---|
| 1 | Kidney Damage with Normal or ↑ GFR | >90 |
| 2 | Kidney Damage with Mild ↓ GFR | 60-89 |
| 3 | Moderate ↓ GFR | 30-59 |
| 4 | Severe ↓ GFR | 15-29 |
| 5 | Kidney Failure | <15 or Dialysis |

**Clinical features**

- Generally asymptomatic in the early stages
- Common but non –specific symptoms:
    - Nocturia, Anorexia, nausea, vomiting, hiccup, loss of appetite, shortness of breath, palpitations, cramping, muscle pain, pruritus
    - Paresthesia, depression, anxiety, fatigue, sexual dysfunction

**Investigations**

- BUN, Creatinine and estimated GFR
- Electrolytes
- Urinalysis
- Abdominal ultrasound
- CBC, RBC indices
- Calcium, Phosphate, PTH levels
- Alkaline phosphatase
- Fasting blood glucose

| |
|---|
| In chronic kidney disease, kidney function should be followed with estimated GFR using GFR estimating formulae. Creatinine alone is not a good way of following kidney function in CKD patients |

- Fasting lipids

See Cockcroft Gault formula in the earlier section describing renal disease. Other formulae (MDRD or CKD-EPI) can be obtained from electronic GFR calculators, smartphone applications or as downloadable software.

**Treatment**

**Objectives**

- Detect chronic kidney disease early.
- Decrease the decline in kidney function
- Prevent, detect and manage complications

– Improve quality of life and survival

**Non pharmacologic**

– General health advice e.g. smoking cessation, weight reduction for obese individuals

– Restrict salt intake

– Avoid nephrotoxins e.g. NSAIDs

– Restrict dietary protein to (< 40g protein/day)

– Renal replacement therapy for ESRD – Renal transplantation, Chronic peritoneal dialysis, Chronic hemodialysis

In most patients with CKD protein restriction would worsen malnutrition and hence protein restriction should be avoided unless the patient is overtly uremic

**Pharmacologic**

1. **Treatment and control of hypertension –** target blood pressure < 130/80 mmHg

**First line**

**ACE inhibitors or angiotensin receptor blockers** (ARBs)-see section on hypertension

– Avoid ACE inhibitors/ARBs if patient is hyperkalemic
– Creatinine/BUN and electrolytes should be followed one to two weeks following initiation or dose increment
– Up to 20-30% increment in creatinine is expected and hence unless the rise is more than 30%.

**N.B**. Loop diuretics are good adjunct treatment in the treatment of hypertension in advanced CKD. Higher dose at more frequent intervals are usually needed e.g. Furosemide, 80-120mg, oral, 2-3 times daily

2. **Treatment and control of proteinuria**

**First line**

**ACE inhibitors or angiotensin receptor blockers** (ARBs). Higher dose is usually required to achieve target. See options below

**Enalapril**, 10-20mg P.O., BID

**Lisinopril**, 20-40mg P.O., daily
**Captopril** 12.5 – 25mg P.O., TID

- **Control of hyperglycemia in Diabetes**
  - In early CKD good blood sugar control is essential. Insulin based therapy is preferred in patients with CKD
  - In advanced CKD with Diabetes, hypoglycemia is a common and serious complication. Decrease or discontinue blood sugar lowering treatment.

**3. Treatment of anaemia of CKD**

- Correct iron and other micronutrients (folate and Vitamin B12) deficiency-see section on anaemia
- If haemoglobin is less than 9gm/dl despite iron supplement, Refer patient for specialist evaluation

**4. Treatment of hyperphosphatemia**

**First line**
**Calcium carbonate**, 500mg (elemental calcium content) P.O.,TID, with meals.
**Alternative**
**Aluminum hydroxide**, 300-600mg P.O., TID with meals.
**N.B-**Do not use aluminum hydroxide for long period of time to avoid aluminum toxicity

**5. Treatment of fluid overload (edematous state)**

**First line**
**Furosemide**, 40-120mg, PO/IV, two –three times per day.
**N.B.** Higher and more frequent doses are required in advanced CKD.

**6. Treatment of hyperkalemia-**see section on acute common electrolyte disorders

## 3. Electrolyte Disorders

**Hypokalemia**-Serum potassium level less than 3.5mmo/l. A serum K+ level <2.5 mmol/l is regarded as severe hypokalemia and a level of 2.5-3.0 mmol/l is considered moderate.

**Causes of hypokalemia**

**Potassium loss**

- Renal loss (e.g. diuretics, DKA , recovery phase of ATN, magnesium deficiency)
- GI loss (e.g. Diarrhoea)
- Integumentary loss(excessive sweating)

**Redistribution/shift into intracellular space**

- Medicines (e.g. Insulin, beta-2 agonists)
- Metabolic alkalosis
- State of increased beta adrenergic activity (e.g. acute MI)

**Clinical features**

- The severity of the manifestation is proportionate to the degree and duration of the hypokalemia. Serum $K^+$ of 3.0-3.5mmol/l does not usually cause symptoms.
- Muscle weakness (weakness of extremities, paralytic ileus and rarely rhabdomyolsis)
- Arrhythmias-risk is highest in the presence of old age, organic heart disease, digoxin or antiarrhythmic medicine
- Glucose intolerance

**Investigations**

- Serum electrolytes including magnesium
- ECG
- Investigations of the underlying cause

**Treatment**

**Objectives**

- Prevent and treat life-threatening complications (arrhythmias and paralysis)
- Correct potassium deficit
- Prevent ongoing potassium deficit
- Treat the underlying cause

**Non pharmacologic**

- Encourage foods rich in potassium e.g. Peanut butter, avocado, bananas, orange juice, papaya.

- Avoid exercise in patients with moderate to severe hypokalemia

**Pharmacologic**

**A. Severe hypokalemia**

**Potassium chloride,** IV infusion 40-60 meq of elemental potassium, in 1000ml Normal saline, 6-8 hours.

- Use non dextrose containing fluids
- Maximum concentration of potassium is 60meq in one liter of fluid
- Maximum rate of infusion (in the presence of perfuser machine) is 10meq/hour

*PLUS*

**Potassium chloride,** 600mg P.O., (8 meq of potassium) 2-3tabs, 3-4 times/day.

**B. Mild to moderate hypokalemia**

**Potassium chloride,** 600mg P.O., (8 meq of potassium) 2-3tabs, 3-4 times/day

For Hypokalemia due chronic loop diuretics**: Spironolactone-**see doses in each indication (Heart Failure , liver cirrhosis)

**Combination of potassium supplementation and spironolactone may result in severe hyperkalemia, hence monitoring of serum potassium level is strongly recommended**.

**4. Hyperkalemia**

Hyperkalemia is defined as a serum potassium level of > 5.5mmol/l. A decrease in renal $K^+$ excretion due to acute or chronic kidney disease is the most common underlying cause.

**Causes of hyperkalemia**

1. **"Pseudo" hyperkalemia** – tight tourniquet or fist during venous blood sample collection, thrombocytosis, erythrocytosis, leukocytosis, in vitro hemolysis.
2. **Intra-to extracellular shift –** Acidosis, adrenergic antagonists, digoxin, tumour lysis
3. **Inadequate renal excretion –** AKI/CKD, ACE inhibitors, ARBs, aldosterone antagonist, NSAIDs, adrenal insufficiency

**Clinical features**

- Mild hyperkalemia is generally asymptomatic
- Severe hyperkalemia results in muscle weakness or paralysis, cardiac conduction abnormalities and cardiac arrhythmias

**Investigations**

- Serum electrolyte
- Creatinine and BUN
- ECG

**Treatment**

**Objectives**

- Prevent cardiac arrhythmias
- Maximize potassium loss
- Enhance transcellular shift from the extracellular space to intracellular space

**Non pharmacologic**

- Decrease food rich in potassium-see section on hypokalemia
- Discontinue medicines which increase potassium-ACEi, ARBs, Spironolactone, NSAID
- Dialysis in severe AKI or end stage renal disease

**Pharmacologic (For severe hyperkalemia)**

**Calcium gluconate**, IV, 10mL of a 10% solution, over two to three minutes, with constant cardiac monitoring. The dose can be repeated after five minutes if the ECG changes of hyperkalemia persist or recur

*PLUS*

**Regular Insulin**, 10 units IV, followed immediately by 60-80ml ml of 40% dextrose (25g of glucose), every 4-6 hours

*PLUS*

**Salbutamol**, 10 to 20mg in 4 mL of saline by nebulization over 10 minutes or metered Dose Inhaler or MDI 100mcg/puff-8 to 10 puffs every 20-30 minutes.

*PLUS*

**Furosemide,** 40-120mg, IV,-dose should depend on previous response, degree of kidney function impairment. The dose can be repeated according to response.

## 5. Hyponatremia

Hyponatremia is defined as a plasma sodium concentration of <135mmol/L. Severe hyponatremia is defined as a plasma sodium concentration of <115mmol/L Acute hyponatremia is development of hyponatremia in < 48 hours. Hyponatremia can be due to a gain of water in excess of sodium, a loss of sodium in excess of water or both.

**Causes of hyponatremia**-classified based on the volume status of the patient

1. Hypovolemic hyponatremia-diarrhoea, vomiting, burn, polyuria
2. Euvolemic hyponatremia-syndrome of inappropriate ADH secretion (SIADH), hypothyroidism, low dietary solute intake
3. Hypervolemic hyponatremia-Heart Failure , Kidney failure, Liver failure, nephrotic syndrome.

**Clinical features**

**Acute hyponatremia** (<48 hr)

- Seizures
- Confusion and disorientation
- Coma
- Respiratory distress

**Chronic hyponatremia** (>48 hr)

- Frequently mild or no symptoms

**Investigations**

- Serum electrolytes
- Creatinine and BUN
- Urinalysis
- Chest X-ray
- Thyroid function test
- Investigation directed to the suspected underlying cause

**Treatment**

**Objectives**

- Restore plasma tonicity

- Prevent serious CNS complications
- Avoid rapid correction
- Detect and correct the underlying cause

**Non pharmacologic**

- Free water restriction – for Euvolemic and Hypervolemic causes
- Encourage table salt intake-if not Hypervolemic
- Discontinue thiazide diuretics
- Management of the underlying cause

**Pharmacologic**

**Hypovolemic hyponatremia**

**Normal saline,** IV infusion-volume depending on the estimated fluid deficit

**Hypervolemic hyponatremia**

**Furosemide,** dose depending on the underlying disease and previous response.

**N.B.** avoid thiazide diuretics

**Euvolemic hyponatremia**

**Severe acute hyponatremia**

- 3% NaCl (513mmol/L), 1-2 ml/kg IV per hour
- Should elevate the serum Na approximately 1-2mmol per hour
- Raising the serum Na 4-6mmol/L over 2-3 hours is enough to prevent serious neurologic complications
- Subsequently, the rate of correction should be less than 10mmol/L per 24 hour

## HYPERNATREMIA

Hypernatremia is defined as plasma sodium concentration of >145mmol/L. Severe hypernatremia is plasma sodium value of >160 mmol/L. Hypernatremia can be due to loss of water, gain of sodium, or both. Loss of water is the more common denominator.

Many patients with hypernatremia have an inability to access water, as hyperosmolality/hypernatremia is a very a strong stimulus for thirst. Hypernatremia leads to shrinkage of brain cell volume and secondary neurological symptoms

**Causes of hypernatremia**

1. **Hypovolemic**

Renal water loss

- Loop diuretics
- post obstructive dieresis
- osmotic diuresis

Extra renal water loss:

- burns
- diarrhoea

2. **Euvolemic-**Diabetes insipidus**,** hypodipsia
3. **Hypervolemic-**Iatrogenic (sodium bicarbonate, hypertonic saline), hyperaldosteronism

**Clinical features**

- Mild and chronic hypernatremia is usually asymptomatic
- If conscious most patients with hypernatremia will have excessive thirst
- Severe acute hypernatremia causes CNS symptoms-irritability, lethargy, seizure and coma

**Investigations**

- Urine specific gravity/osmolality
- Serum electrolytes
- Creatinine and BUN
- blood sugar
- If Diabetes insipidus is suspected refer for specialist work up and treatment.

**Treatment**

**Objectives**

- Correction of water deficit and restoration of serum tonicity
- Avoid rapid correction.
- Detection and treatment of the underlying cause

**Non pharmacologic**

- Encourage free water intake. This is the preferred route of correcting water deficit.

**Pharmacologic**

Depends on the severity of hypernatremia and the patient's volume state.

Hypovolemic Hypernatremia: Intravenous Isotonic saline (0.9% NaCl) until hypovolemia improves. Then calculate water deficit and use 0.45% NaCl or 5% Dextrose to replace the deficit and ongoing losses.

Euvolemic Hypernatremia: Correct water deficit and replace ongoing losses with Intravenous 0.45% NaCl or 5% Dextrose. Refer to specialist if Diabetes Insipidus is suspected.

Hypervolemic Hypernatremia: Furosemide IV or P.O., dose and route depending on severity

CALCULATION OF WATER DEFICIT

$$\text{Water deficit} = \text{CBW} \times \left(\frac{\text{serum [Na+]}}{140} - 1\right)$$

CBW refers to estimated current body water which is about 60 and 50 percent of lean body weight in younger men and women, respectively, and in the elderly it is about 50 and 45 percent in men and women, respectively.

RATE OF CORRECTION OF HYPERNATREMIA

In acute hyponatremia (developing within hours) immediate reduction of serum Na is recommended but at a rate not exceeding 0.5mmol/hour over 48-72 hours.

Correction should not exceed 10mmol/day.

## 6. Urinary Tract Infection

Urinary Tract Infection (UTI) refers to the presence of microorganisms in higher numbers to cause invasion of the urinary tract (UT) epithelium and inflammation that cannot be accounted for by contamination.

UTI is classified in different important ways that have implication to treatment and outcome

- According to anatomic site of involvement:

**Lower UTI**: cystitis, urethritis, prostatitis

**Upper UTI**: pyelonephritis, involving the kidneys

- According to the presence of structural urinary tract problems

- **Uncomplicated UTI**: UTI that occurs in individuals who lack structural or functional abnormalities in the UT that interfere with the normal flow of urine.Mostly in healthy females of childbearing age.

- **Complicated UTI**: UTI that occurs in individulas with structural or functional abnormalities in th UT that can interefere with normal flow of urine such as congenital distortion of the UT, a stone, a catheter, prostatic hypertrophy, obstruction, or neurological deficit. UTI in men are usually complicated.

- **Recurrent UTI**-referes to multiple symptomatic UTIs with asymptomatic periods in between. It is considered significant when there two or more symptomatic episodes per year or it interferes with patient's quality of life. It is usually a reinfection than a relapse

**Asymptomatic bacteriuria**: Bacteiruria > $10^5$ bacteria/ml of urine without symptoms. It is very common in elderly women and men.

**Symptomatic abacteriuria**: Symptoms of urinary frequency and dysuria in the absence of significant bacteriuria

The vast majority of acute symptomatic infections occur in young women. *Escherichia coli* cause approxmatley 80% of acute infections in patients without catheters, stone or other urologic abnormalities. On the other hand, organisms like *klebsiella*, *enterobacteria*, *proteus*, *serratia* and *psuedomonas* assume greater importance in complicated and nosocomial UTIS.

**Clinical features**

- The range of possible symptoms caused by UTI is extremely broad, from no symptoms to symptoms referable to the lower urinary tract (e.g. dysuria and frequency), to symptoms indicative of an upper UTI (e.g. loin pain, fever, chills andcosto-vertebral angle tenderness), to full-blown urosepsis.

**Investigations**

- Urine analysis and Gram stain showing pyuria and bacteriuria

- Urine culture – indicated in complicated UTIs, recurrent UTI, Pyelonephritis and urosepsis. Significant bacteriuria is defined as the presencr of $10^5$ bacteria /ml (CFU) of urine in clean catch specimen. In women with symptomatic UTI alower bacterial

count should be used as 1/3 of symptomatic women have CFU counts below$10^5$ bacteria /ml. (e.g. 100 CFU/ml will have higher positive predictive value)

- Ultrasound of the abdomen (kidneys and urinary tract)-in complicated UTIs, UTIs in men and recurrent UTIs

**Treatment**

**Objectives**

- Treat the infection.

**Non pharmacologic**

Postcoital voiding and liberal fluid intake for women with recurrent UTI

**Pharmacologic**

**A. Acute, Uncomplicated UTI in women**

**First line**

**Ciprofloxacin**, 500mg P.O., BID, for 3 days

*OR*

**Norfloxacin**, 400mg P.O.,BID, for 3 days.

**Alternatives**

**Nitrofurantoin** 50mg P.O., QID for 7 days

*OR*

**Cefpodoxime proxetil** 100mg P.O, BID for 3 days

*OR*

**Cotrimoxazole (Trimethoprim-sulphamethoxazole)** 160/800mg P.O, BID for 3 days

**B. Acute uncomplicated Pyelonephritis in non-pregnant women:**

**Mild and moderate acute uncomplicated pyelonephritis** (able to tolerate oral therapy with no vomiting, no dehydration, no evidence of sepsis):

**First line**

**Ciprofloxacin,** 500mg P.O., BID, oral for 7-10 days

**Alternatives**

**Cotrimoxazole(Trimethoprim-sulphamethoxazole)**, 160/800mg P.O, BID for 14 days

*OR*

**Cefpodoxime proxetil**, 200mg P.O., BID for 10 days

**Severe acute uncomplicated pyelonephritis** (high fever, high white blood cell count, vomiting, dehydration, or evidence of sepsis) or fails to improve during an initial outpatient treatment period – intreavenous therapy should be started and continued until the patient improves (usually at 48–72 hours). On discharge oral therapy is continued to complete 10-14 days course. Antibiotics should be started after urine culture sample is collected.

**First line**

**Ciprofloxacin**, 400mg, I.V**,** BID till patintient improves and continue oral Ciprofloxacin 500mg, PO, BID to complete 10-14 days course

**Alternatives**

**Ceftriaxone**, 2gm, I.V, daily or 1gm, I.V, BID till patintient improves and continue oral Ciprofloxacin 500mg, PO, BID to complete 10-14 days course.

If no response in 48-72 hrs ultrsasound is warranted therapy to evaluate for obstruction, abscess, or other complications of pyelonephritis. If no obstruction or complication is not found gram positive organisms such as enterococci and S. saprophyticus should be covered with Penicillins and aminoglycoside combination

**C. Complicated UTIs and UTI in men**

Factors which suggest complicated UTI**:** The presence of an indwelling catheter or the use of intermitten bladder catheterization, obstructive uropathy of any aetiology, stones, vesicoureteric reflux or other functional abnormalities, peri-and postoperative UTI, CKD and transplantation, diabetes mellitus and immunodeficiency states.

**First line and alternatives** – similar to uncomplicated UTIs but needs prolonged duration and response should be closely followed as gram postives could be the cause.

**D. Recurrent UTI in women**

Women with recurrent UTI who are sexually active should be advised to void after each sexual intercourse **(postcoital voiding**) and have liberal fluid intake.

Antibiotic prophylaxis is recommended for women who experience two or more symptomatic UTIs within six months or three or more over 12 months. The degree of discomfort experienced by the woman needs to be considered in the decision. Recurrent pyelonephritis deserves prophylaxis.

Any prophylaxis should be given after current active infection is treated.

**Antibiotic regimens:**

- **Continuous:** daily at night time
- **Postcoital:** Single dose after coitus

Duration of antibiotics-for **six** months followed by observation. If recurrent UTI comes again the prophylaxis can be prolonged for 1-2years.

**Antibiotic choices:**

**First line**
**Cotrimoxazole**, 240mg, P.O., daily OR 3x per week OR postcoital

**Alternatives**

**Cephalexin**, 125 – 250mg, P.O., once daily or postcoital

*OR*

**Norfloxacin**, 200mg, P.O., once daily or postcoital

*OR*

**Ciprofloxacin**, 125mg, P.O., once daily or postcoital

*OR*

**Nitrofurantoin**, 50 to 100mg, P.O, once daily or postcoita;

## CHAPTER VIII:MUSCULOSKELETAL DISORDERS

### 1. Osteoarthritis

This is a degenerative joint disease that damages the articular cartilage leading to reactive new bone formation. Osteoarthrites (OA) is described as progressive joint failure where all structures involved in joint function undergo pathologic changes. Weight bearing joints (hips, knees), cervical and lumbar spine and the metacarpo-phalangeal and distal interphalangeal joints of the hands are commonly affected. The wrist, elbow and ankle joints are chacterstically spared or very raely involved. It is more common in females than males. Risk factors include old age, trauma and obesity. Osteoarthritis has traditionally been subdivided by etiology into either **idiopathic or secondary forms**. Seconary OA rsults from other primary joint pathologies suchas trauma, crystal induced arthritis, rheumatoid arthritis, neuropathic arthropathy, acromegaly, DM, hypothyroidism etc.

OA can be categorized into localized or generalized forms. Generalized OA consists of involvement of three or more joint sites.

OA is generally a non inflammatory type of arthritis but some patients can have predominantly inflammatory arthritis charachterized history of swelling, night pain, morning stiffness greater than 30 minutes, warm and tender joints on physical examination.

**Clinical features**

- Pain at initiation of exercise (walking)
- Morning stiffness which improves with exercise
- Diminution of joint movement
- Crepitus on moving affected joint(s)
- Heberden's nodes and deformed joints in the hands
- Joint swelling, warmth and effusions (knee especially)
- Osteoarthritis of cervical and lumbar spine may lead to muscle weakness in hands and legs respectively (myelopathy)

**Investigations**

- CBC
- ESR
- X-ray of affected joints

**Treatment**

**Objectives**

- Relieve pain
- Prevent and manage deformities
- Educate patient

**Non pharmacologic**

- Encourage weight reduction if obese or overweight
- Increase physical activity, specific exercise, physiotherapy
- Weight supports (crutches, walking sticks or frames)
- Arthroscopic interventions (irrigations, debridement and synovectomy) in refractory cases

**Pharmacologic**

**1. Pain management**

**Inflammatory osteoarthritis**

**First line-NSAIDS, see options below**

**Ibuprofen**, 200-400mg P.O., TID

**Diclofenac**, 50-75mg P.O., BID or rectal suppository 100mg/daily

**Indomethacin**, 25-50mg, P.O., 2-3 times/day; maximum dose is 200mg/day or rectal suppository 100mg/daily. Avoid indomethacin in hip OA.

**Piroxicam**, 10-20mg, P.O., once per day. Maximum dose is 20mg/day

**Dosage forms:** Capsule, 10mg, 20mg ; Tablet, 10mg, 20mg

**Meloxicam**, 7.5-15mg/day. Maximum dose is 15 mg/day

**Dosage forms:** Tablet, 7.5mg, 15mg

*PLUS*

GI protection for high risk individuals: a history of peptic ulcer disease, on antiplatelet therapy, concomitant anticoagulant therapy, or have more than one of othr risk factors (Age ≥60 years, Corticosteroid use, Dyspepsia or GERD symptoms)

**First line** PPIs, see options below

**Omeprazole**, 20mg, P.O., once daily or BID.

**Esomeprazole**, 20-40mg, P.O., once daily

**Pantoprazole**, 40mg, P.O., once daily

**Alternative**-H2 blockers,see options below

**Cimetidine**, 400mg P.O., BID

**Ranitidine**, 150mg, P.O, BID

2. **Non inflammatory osteoarthritis**

**First line**

**Paracetamol**, 1g 4–6 hourly P.O., when required to a maximum of 4 doses per 24 hours

If ineffective: start NSAIDS as above

**Additional pain management –**for both inflammatory and non infla mmmatory OA.

Before additional therapy change the NSAIDS as there is response to the individual NSAIDS is quite variable.

**First line**

**Tramadol**, 50mg to 100mg, P.O., once to twice per day.

| | |
|---|---|
| **ADRs:** | Dizziness, headache, somnolence, insomnia, decrease seizure threshold dyspepsia, pruritis, flushing |
| **C/Is:** | Hypersensitivity to tramadol, opioids, opioid-dependent patients, acute intoxication with alcohol, hypnotics, or psychotropic medicines |
| **D/Is:** | Tramadol may enhance the adverse/toxic effect of other CNS Depressants, Selective Serotonin Reuptake Inhibitors and tricyclic antideprsaants enhance the neuroexcitatory and seizure-potentiating effect of tramadol |
| **Dosage forms:** | tablet/capsule, 50mg, 75mg, 100mg, 200mg |

**Alternative**

**Codeine phosphate** 30mg P.O., QID. **USE CODEINE FOR SHORT DURATION ONLY.**

**ADRs:** Drowsiness, confusion, dizziness, lightheadedness, paradoxical CNS stimulation, xerostomia, ureteral spasm, decreased urination.

**C/Is:** CNS depression, Hypotension, acute alcohol intoxication

**D/Is:** CNS depressants (enhance depressant effect), Selective SSRI (codeine enhances the serotonergic effect of SSRI)

**Dosage forms:** Tablet 30mg

**Intra-articular steroids**

- Consider in inflammatory osteoarthritis of the knee and shoulder when it is refractory to NSAIDS
- To be prescribed and administered by a specialist only
- Not more than 2–3 injections per year per joint are recommended.

**First line**

**Methylprednisolone acetate**, 20–80mg depending on joint size

**ADRs:** Postinjection flare, cushing's syndrome (if frequency greater than 1/month), charcot-like arthropathy, iatrogenic infection (very low incidence), tendon atrophy, fat necrosis, cataracts.

**CIs:** local infection, pyogenic arthritis

**D/Is:** None for intraarticular injections

**Dosage forms:** Injection, 40mg/ml in 1ml ampoule

*OR*

**Triamcinolone acetonide**: Initial: Smaller joints: 2.5-5mg, larger joints: 5-15mg, up to 40mg for large joints.

**ADRs, C/Is, D/Is:** see methylprednisolone above

**Dosage forms:** Injection, 10mg/ml, 40mg/ml in vial

**2. Pyogenic Osteomyelitis**

Pyogenic Osteomyelitis is an acute infection of the bone and its structures caused by bacteria. Osteomyelitis occurs as a result of hematogenous spread, contiguous spread from adjacent soft tissues or direct infection from trauma or surgery. Hematogenous osteomyelitis is usually

monomicrobial, while osteomyelitis due to contiguous spread or direct inoculation is usually polymicrobial. Staphylococcus aureus is the most common causative organism. Coagulase-negative staphylococci and aerobic gram-negative bacilli are also common causes. Streptococci, enterococci and anaerobes are also implicated.

**Clinical features**

Gradual onset varying from few days to weeks of local bone pain, swelling, low grade fever, malaise and weight loss.

**Investigations**

- Clinical, CBC, ESR, C-reactive protein, X-ray of the affected bone
- Culture of pus/sequester (if debridement is done)

**Treatment**

**Objectives**

- Control infection
- Prevent disability

**Non pharmacologic**

- Rest/immobilization
- Surgical debridement

**N.B.** Drainage by surgeon/orthopedic surgeon. Osteomyelitis frequently requires both surgical therapy for debridement of necrotic material together with antimicrobial therapy for eradication of infection. The debrided necrotic material should be sent for culture.

**Pharmacologic**

**Empiric antibiotic –** duration of antibiotics is for at least six weeks

**First line**

**Vancomycin**, 30mg/kg/day, IV, in two divided doses

*PLUS*

**Ciprofloxacin**, 750mg, P.O., BID

**Alternative**

**Cloxacillin**, 2gm, I.V. QID

*PLUS*

**Ciprofloxacin**, 750mg, P.O., BID

**N.B.**

- Further treatment is guided by culture sensitivity tests
- For pain and fever – Analgesic/antipyretic e.g. **Paracetamol,** 500-1,000mg P.O. as needed (4-6 times daily) can be given.

### 3. Rheumatoid Arthritis (RA)

RA is a chronic systemic autoimmune inflammatory disease characterised mainly by symmetrical inflammation of the synovial tissue of joints resulting in destruction of the joints and peri-articular tissues. It occurs more commonly in young and middle-aged women. The symptoms fluctuate widely with periods of remission and exacerbation. Other organs such as the lungs, kidneys, eyes and the hematopoietic system may occasionally be affected. Rheumatoid Arthritis should be treated as early as possible with disease modifying anti-rheumatic medicines (DMARDs) to control symptoms and delay disease progression.

**Clinical features**

See table below:

**Table 54-1987 American College of Rheumatology revised classification criteria for rheumatoid arthritis**

| Criterion | Description |
|---|---|
| Morning stiffness. | Morning stiffness in and around the joints, lasting at least one hour before maximal improvement. |
| Arthritis of 3 or more joint areas | At least 3 joint areas (out of 14 possible areas; right or left PIP, MCP, wrist, elbow, knee, ankle, MTP joints) simultaneously have soft-tissue swelling or fluid as observed by a physician |
| Arthritis of hand joints | At least one area swollen in a wrist, MCP, or PIP joint |
| Symmetric arthritis | Simultaneous involvement of the same joint areas on both sides of the body (bilateral involvement of PIPs, MCPs, or MTPs, without absolute symmetry is acceptable) |
| Rheumatoid nodules | Subcutaneous nodules over bony prominences or extensor surfaces, or in juxta-articular regions as observed by a physician |

| | |
|---|---|
| Serum rheumatoid factor | High serum rheumatoid factor by any method for which the result has been positive in <5 % of normal subjects |
| Radiographic changes | Radiographic changes typical of RA on PA hand or wrist radiographs, which must include erosions or unequivocal bony decalcification localised in, or most marked adjacent to, the involved joints. |

**Note:** RA diagnosed if at least four of these criteria are satisfied (the first four must have been present for at least six weeks). The major drawback of the criteria is insensitivity in identifying early disease which subsequently develop into typical RA.

**Other features**

- Fever, weight loss
- Pleural, pulmonary and pericardial involvement
- Anaemia-normocytic normochromic in character
- Vasculitis
- keratoconjunctivitis sicca (dry eyes) or xerostomia (dry mouth)
- Peripheral sensory neuropathy

**Investigations**

- ESR/CRP
- Rheumatoid factor
- ANA (antinuclear antibody)
- X-ray of involved joints

**Treatment**

**Objectives**

- Reduce pain, swelling and stiffness
- Prevent deformities
- Delay disease progression and onset of long term complications

**Non pharmacologic**

- Rest of affected joints during acute flares

- Physiotherapy

**Pharmacologic**

**Disease-modifying anti-rheumatic medicines** (DMARD): Initiate early in the course

**First line**

**Methotrexate**, 7.5mg P.O., **once per week**. Increase dose gradually to a maximum of 25mg per week.

**N.B.** Monitor: Liver function and CBC before and 12 weekly during treatment.

*PLUS*

**Folic acid,** 5mg P.O., per week with methotrexate at least 24 hours after the methotrexate dose.

*AND/OR*

**Chloroquine phosphate**, 150mg P.O., (as base) daily for 5 days of each week for 2–3 months.

Then reduce dose if possible and administer 5 days a week with an annual medicine holiday for 1 month.

Do ophthalmic examination annually to monitor for ocular damage.

*AND/OR*

**Sulfasalazine**, 500mg P.O., 12 hourly.

Gradually increase over one month from 500mg to 1 g 12 hourly. Liver function and CBCs monthly for first 3 months then every 3–6 months.

**1. Oral corticosteroids**

**Indications:**

- As bridging therapy while waiting for DMARDs to take effect.
- The elderly if threatened by functional dependence and intolerant to NSAIDs.
- Extra-articular manifestations, e.g. pleural effusion, scleritis.
- Acute flare

**Prednisolone**, 40mg P.O., daily for 2 weeks during acute flares. Thereafter gradually reduce the dose to $\leq$ 7.5 mg daily. Maintenance low dose prednisolone may be needed in many patients

**2. Joint pain management-NSAIDs**

Use for active inflammation with pain. NSAIDs are used for symptomatic control only, as they have no long-term disease modifying effects.

NSAID dose should be reduced and then stopped once the DMARDs have taken effect.

**Ibuprofen**, 800mg, P.O.,TID with meals. If not tolerated: 400mg 8 hourly.

An extra **night-time** dose of a NSAID may be added in some patients with severe nocturnal pain/morning stiffness

*OR*

**Diclofenac**, Immediate or delayed release tablet: 150-200mg/day P.O., in 2-4 divided doses.

Rectal suppository, insert 50mg or 100 mg rectally as single dose to substitute for final daily dose (maximum combined dose [rectal and oral]: 150 mg/day)

*OR*

**Indomethacin,** 25-50mg P.O., BID TO TID; maximum dose: 200mg/day**.**

Rectal suppository, insert 100mg, BID or once, at bed time.

**4. Septic Arthritis**

The term septic arthritis refers to bacterial infection of a joint. Septic arthritis is dangerous and destructive to the joint. It may occur secondary to haematogenous spread (80-90%), contiguous spread (10-15%), and direct penetration of microorganisms secondary to trauma, surgery or injection. Old age, Diabetes mellitus, skin infection, alcoholism, intra-articular injections are some of the common risk factors. S. aureus is the most common cause. Streptococci and other gram positive are also frequent causes. Gram-negative bacilli are found as causes in specific situations such as trauma, immunosuppression and very elderly.

**Clinical features**

- Septic arthritis presents acutely and mostly with a single swollen and painful joint.

**Investigations**

- CBC, ESR/CRP
- synovial fluid analysis including Gram stain and culture will help to reach the right diagnosis.
- X-ray of the affected joint should also be done.

**Treatment**

**Objectives**

- Treat infection promptly and prevent joint destruction

**Non pharmacologic**

- Aspiration/drainage when indicated
- Splintage, but early imobilization if joints are mobile.
- The joint must be splinted with a POP slab or skin traction to relieve pain and prevent contractures

**Pharmacologic**

**Empiric antibiotics** Duration of antibiotic treatment is 4-6 weeks. At least the first two weeks of antibiotics should be through intravenous route**.**

**If synovial fluid gram stain is unavailable or negative:**

**First line**

**Vancomycin**, 30mg/kg/day IV in two divided doses, not to exceed 2g per day

*PLUS*

**Ceftriaxone**, 2gm, I.V, daily

**Alternatives**

**Cloxacillin,** IV, 2g every 6 hr QID for 4-6 weeks

*OR*

**Ceftriaxone** 2gm,IV, daily

**If synovial fluid gram stain shows gram postive organism-**use vancomycin with the above dose as first line and Cloxacillin as alternative.

**If synovial fluid gram stain shows gram negative organism-**use ceftriaxone with the above dose as first line.

## CHAPTER VIX:NEUROLOGICAL DISORDERS

### 1. Meningitis

**Acute Bacterial Meningitis**

Acute Bacterial meningitis is an inflammation of the meninges in response to bacterial infection. It is mainly caused by *N. meningitides***,** *S. pneumoniae, and H. influenzae*. The disease is characterised by an intense headache, fever, vomiting, and photophobia with nuchal pain or rigidity and positive meningeal signs.

The only bacterial pathogen with a potential to cause epidemics is *N.meningitidis* and therefore is a reportable disease. Ethiopia is one of the countries in the so called "meningitis belt" of the Sub-Saharan Africa which spans from Gambia in the West to Ethiopia in the East of Africa. In the past century, several devastating epidemics have occurred cycling on an average of 8-12 years in this geographic area. One striking feature of the epidemic has been its seasonality by which it tends to occur during the dry and windy season between January and May.

**Clinical features**

- Headache (HA), Stiff neck, Fever, Photophbia
- Change in mental status (defined as GCS <14),
- Seizures
- 2 of 4 (fever, HA, stiff neck, change in MS) present in 95%
- Presentation may be *atypical* (eg,lethargy without fever) in the elderly and immunosuppressed
- Physical examination: Nuchal rigidity (Se 30%), Kernig's sign (Patient supine, hip flexed at 90, knee flexed at 90; + if passive extension of knee results in resistance), Brudzinski's sign (P supine and limbs supine;+ if passive neck flexion if followed by involuntary hip and/or knee flexion). Kernig's and Brudzinski's signs are + in only 5% of Pts, but will be very specific for meningeal irritation if present.

- Some patients may have focal neuro findings (about 30%; hemiparesis, aphasia, visual field cuts, CN palsies)
- Funduscopic findings: papilledema, absent venous pulsations
- Skin rash: maculopapular, petechial, or purpuric

**Investigations**

**Diagnostic studies**

- **Blood cultures *before antibiotics are administered***
- **WBC count**: >10,000 in 83% of bacterial meningitis
- *Consider* **head CT** to rule out mass effect before LP *if* presence of high-risk feature (age>60 y, immunosuppressed, history of CNS disease, new-onset seizure, change in mental state, focal neurologic findings, papilledema); absence of all these has negative predictive value (NPV) of 97%; however, in patients with mass effect, herniation may occur without LP and may not occur even with LP
- **Lumbar puncture:** CSF Gram stain has 60–90% Sensitivity; culture has 70–85% sensitivity if LP done prior to antibiotic administration. Repeat LP only if no clinical response after 48hrs of appropriate antibiotic, or CSF shunt present.
- **Rule of 2s**: CSF WBC >2,000, glucose<20, & Total protein>200 has >98% specificity for bacterial meningitis

**Table 55-CSF Findings in Meningitis**

| Typical CSF Findings in Meningitis | | | | | |
|---|---|---|---|---|---|
| **Condition** | **Appearance** | **Pressure (cm $H_2O$)** | **WBC/$mm^3$** *Predom type* | **Glc (mg/dL)** | **TP (mg/dL)** |
| **Normal** | Clear | 9–18 | 0–5 *lymphs* | 50–75 | 15–40 |
| **Bacterial** | Cloudy | 18–30 | 100–10,000 *polys* | <45 | 100–1000 |
| **TB** | Cloudy | 18–30 | <500 *lymphs* | <45 | 100–200 |
| **Fungal** | Cloudy | 18–30 | <300 *lymphs* | <45 | 40–300 |
| **Aseptic** | Clear | 9–18 | <300 *polys → lymphs* | 50–100 | 50–100 |

**N.B.** High index of clinical suspicion is very important for early diagnosis of Acute Bacterial Meningitis

Acute bacterial meningitis is a medical emergency. Institute empiric antimicrobial therapy promptly and adjust it after isolating the etiologic agent. The duration of pathogen-directed therapy depends on the causative organism.

**Objectives**

- Rapidly clear the organisms from the CSF
- Prevent acute complications and long term sequelae

**Non pharmacologic**

- Close supervision with regular monitoring of vital signs and neurological state.
- Institution of coma care for complicated cases.

**Pharmacologic**

**A. Community acquired, bacterial etiology unknown**

**First line**

**Ceftriaxone,** 4g/day, I.V., divided in 2 doses for 10-14 days

*PLUS*

**Where Penicillin resistance is common (particularly *S.pneumoniae*), Empiric treatment should include:**

**Vancomycin**, 1gm IV BID for 10-14days

**Alternative**

**Benzyl penicillin**, 20-24 million IU/day I.V. in 4-6 divided doses for 7 –10 days.

*PLUS*

**Chloramphenicol**, 500mg I.V. QID. In severe infections, up to 100mg/kg/day in 4 divided doses, may be used for 7 days

**If >50 y ok or alcoholic: for Listeria *monocytogens***

**Ampicillin**, 2g IV q4h

*OR* (if beta-lactam allergic)

**Trimetoprime/Sulphamethoxazole**, 20mg/kg per day divided Q6-12

**B. Empiric treatment, hospital acquired meningitis, particularly related to post-neurosurgery ventriculostomy/lumbar catheter, ventriculoperitoneal (atrial) shunt or penetrating trauma without basillar skul fructure**

**First line**

**Vancomycin**, 15mg/kg IV Q8h

*PLUS*

**Ceftazidime**, 2g IV q8h

**Alternative**

**Vancomycin**, 15mg/kg IV Q8h

*PLUS*

**Meropenem**, 2gm IV Q8hr (if indicated by microbiologic data)

| | |
|---|---|
| **ADRs:** | Swelling, redness, pain, or soreness at the injection site may occur. This medication may also infrequently cause upset stomach, headache, diarrhoea. |
| **C/Is:** | Hypersensitivity to IV components, beta-lactams, or other medicines in this class |
| **P/Cs:** | hyersensitivity, seizure, CDAD, |
| **D/I:** | valproic acid**,** bacterial vaccines (bcg vaccine live,typhoid vaccine live). Digoxin, estradiol, oestrogen conjugated synthetic |
| **Dosage forms:** | Powder for reconstitution 500mg/vial and 1000mg/vial |

**C. Immunosuppressed (HIV positive, uncontrolled diabetes, patients taking high dose**

**corticosteroids)**

**Ceftazidime**, 2g IV q8h

*PLUS*

**Vancomycin**, 15mg/kg IV Q8h

*PLUS*

**Ampicillin**, 2g IV q4h

*PLUS*

**Acyclovir 10mg/kg (infuse over 1h) Q8h for 14-21d**

(This is added in a situation where HSV-1 encephalitis is likey. Early diagnosis and treatment are imperative. Mortality is reduce from >70% to <20% with IV acyclovir treatment).

**Adjuvant Therapy:** Consider steroids in all bacterial meningitis prior to organism identification. Treatment must start before or withfirst dose of antibiotics to derive any benefit.

**Dexamethasone,** 10mg IV QID for 4 days

This treatment has been shown to reduce neurologic disability and mortality by about 50% particularly in patients with *S. pneumoniae* meningitis and & GCS 8–11. This benefit nas not been replicated in countries with high HIV prevalence although there was still some benefit)

## 2. Migraine

Migraine is a paroxysmal recurrent headache unilateral or bilateral lasting 4-72 hours, often preceded by aura and accompanied by nausea and/or vomiting. Migraine is thought to have a polygenetic and multifactorial etiology. Migraine is about three times more common in women than men.

**Clinical features**

- Headache
- Nausea and/or vomiting

**Investigations**

- Clinical

The International Headache Society (IHS) diagnostic criteria for migraine are as follows:

- Headache attacks last 4 to 72 hours
- Headache has at least two of the following characteristics: unilateral location; pulsating quality; moderate or severe intensity; aggravation by routine physical activity
- During headache at least one of the following occurs: nausea and/or vomiting; photophobia and phonophobia
- At least five attacks occur fulfilling the above criteria. History, physical examination, and neurologic examination do not suggest any underlying organic disease

**Danger signs of headache**-if these signs are present urgent evaluation is needed

- New headache in patients under the age of five or over the age of 50
- Sudden onset headache that reaches maximal intensity within seconds or minutes
- The "first" or "worst" headache
- Progressively worsening pattern of headache
- Focal neurologic symptoms other than typical visual or sensory aura
- Fever associated with headache
- Any change in mental status, personality, or fluctuation in the level of consciousness.
- New headache type in a patient with HIV
- Headache during pregnancy

**Treatment**

**Objectives**

- Relieve pain
- Prevent recurrences
- Improve quality of life

**Non pharmaclogic**

- Patients should be reassured that this is a benign condition.

- They should attempt to identify foods or drinks and other situations which precipitate the attack and try to diminish patterns of tension.

**Pharmacologic**

**1. Acute treatment, mild attacks:**

**First line-**Asiprin, Paracetamol, NSAIDS. Individual response is variable to each agent hence if one agent does not work another NSAID can be tried.

**Acetylsalicylic acid**, soluble, 600-900mg P.O., once, followed by 300 mg half hourly up to a maximum dose of 1800mg

*OR*

**Paracetamol**, 1000mg P.O., 4-6 hourly. > 4gm/day is associated with liver toxicity.

Initiate therapy during the attack or at the very onset of the headache.

*OR*

**Ibuprofen**, 600-1,200mg/day P.O., in 2-3 divided doses

*OR*

**Diclofenac**, 50-100mg P.O., or IM oer day

**2. Moderate to severe attacks**

**First line**

**Sumatriptan**, 50mg, P.O., once, taken with fluids. If asatisfactory response is not obtained at 2 hours, a second dose can be given.The total daily dose should not exceed 200mg.

| | |
|---|---|
| **ADRs:** | Chest pain, palpitation, syncope, dizziness, drowsiness, warm/cold sensation |
| **C/Is:** | Ischemic heart disease, stroke/TIA, eripheral arterial disease, uncontrolled hypertension, severe hepatic impairement |
| **D/Is**: | Avoid combination with ergot derivatives, MAO inhibitors and serotonin modulators |
| **Dosage forms:** | Tablet, 50mg, 100mg |

**Alternatives**

**Ergotamine tartrate and Caffeine**, 1mg +100mg P.O., 1-2 tablets immediately, followed by 1/2-1 tablet every 30 minutes to a maximum of 4 tables per attack or 10 tablets per week, or until vomiting occurs.

| | |
|---|---|
| **ADRs:** | cyanosis of extremity ischemia or gangerene, precordial pain, tachycardia, vertigo, nausea and vomiting. Prolonged use may result in pulmonary and visceral firbrosis. |
| **C/Is:** | Coronary artery disease, peripheral vascular disease, hepatic or renal disease; poorly controlled hypertension, sepsis |
| **D/Is:** | Avoid combination with Macrolid antibiotics, Azole antifungals, Protease inhibitors, Efavirenz, Nitroglycerin |
| **Dosage forms:** | Ergotamine Tartrate+Caffeineβ,tablet 1mg +100mg. Ergotamine Tartrate+Caffeine Hydrate+Cyclizine Hydrochloride tablet, 2mg +50mg +100mg |

*OR*

**NSAIDS –**see above in mild migrane

**3. Antiemetics —** IV metoclopramide is used as adjnvtive or monotherpy. Monotherpy requires high dose with prophylaxsis for dystonia

**Adjunctive –Metoclopramide**, 10mg, I.V, stat.

**4. Prevention of early recurrence-**add to abortive therapy to prevent early recurrence.

**Dexamethasone**, 12-24mg, IV, stat.

**5. Long term prophylaxis**

Prophylactic headache treatment is indicated if the frequency is more than four headaches per month, the headaches last long(>12 hours), significant total disability including patient's own opinion, hemiplegic or basilar migrane.

Start the medicine at a low dose and increase gradually until therapeutic benefit develops, the maximum dose of the medicine is reached or side effects become intolerable.

Give the chosen medication an adequate trial in terms of duration and dosage. Benefit is noticed first at around one month and can continue to increase for three months. If the headaches are well controlled, prophylactic medicine can be gradually tapered and discontinued.

**First line**

**Propranolol**, 80mg/day in divided doses; increase by 20-40mg/dose every 3-4 weeks to a maximum of 160-240mg/day)

*OR*

**Amitriptyline**, 10-25mg P.O., at bed time, titrate dose up to adequate response. It seldom requires more than 75-150mg as a single bedtime dose.

**Alternative**

**Carbamazepine,** P.O., start at 100mg/day, titrate to 200-600mg TID

*OR*

**Verapamil,** P.O., start at 120mg/day divided in 2 doses to 720mg/day

### 3. Seizure And Epilepsy

Epilepsy is a paroxysmal neurologic disorder characterised by a sudden onset of sensory perception or motor activity with or without loss of consciousness due to abnormal, excessive, hypersynchronous electrical discharges from the cortex. Its etiology is often unkown.

Secondary causes include congenital, perinatal injuries, intra cranial tumours, vascular and metabolic, among others.

**Clinical features**

- Focal involuntary non synchronized movement of the body
- Generalized tonic clonic convulsion
- Loss of conciousness

**Investigations**

- EEG
- CT scan (if there is suspicion of secondary causes)
- Random blood glucose, urea and electrolytes

**N.B.** Diagnosis is often clinical.

**Treatment**

**Objectives**

- Stop seizure
- Reduce frequency of attacks
- Treat underlying cause(if any)

**Non pharmacologic**

- Advice on a healthy lifestyle with good sleep habits and avoidance of excessive alcohol and caffeine.
- The patient should know the name and the dose of his/her medication and should be warned of the consequences of poor compliance

**N.B.**

- Epileptics are not allowed to drive a vehicle unless the patient has had a two-year attack-free period.
- They should not swim.
- Refer all adult onset epilepsy, complicated or atypical epilepsy, and if there is a progressive increase in uncontrollable attacks.
- Pregnancy is better avoided in patients with difficult-to-control epilepsy.

**Pharmacologic**

**Table 56-Antiepleptic medicines uses for different types of epilepsy their dosage regimens**

| Seizure type | First line | Dose | Alternative | Dose |
|---|---|---|---|---|
| **Primarly generalized tonic clonic** | Valproic acid | 750-2000mg/day or 20 – 60mg/Kg/day divided in 2 to 3 doses | Phenytoin | 300-400mg/day or 3-6mg/kg/day Once per day or divided in 2 doses |
| | | | Phenobarbitone | 60-200mg/day, once daily |
| | | | Carbamazepine | 600-1800mg/day divided in 2 to 4 doses |
| **Partial(simple, complex or secondarily generalized)** | Carbamazepine | 600-1800mg/day divided in 2 to 4 doses | Phenobarbitone | 60-200mg/day, once daily |
| | Phenytoin | 300-400mg/day or 3-6mg/kg/day | Valproic acid | 750-2000mg/day or 20 – 60mg/Kg/day divided in 2 to 3 doses |
| **Absence** | Valproic acid | 750-2000mg/day or 20 | Ethosuximide | 750-1250 mg/day. Once |

| | | | | |
|---|---|---|---|---|
| | | – 60mg/Kg/day divided in 2 to 3 doses | | per day or divided in 2 doses |
| **Atonic, Myoclonic or atypical absence** | Valproic acide | 750-2000mg/day or 20 – 60mg/Kg/day divided in 2 to 3 doses | Clonazepam | 1-12mg/day. Once per day or divided in 2-3 doses |

**Table 57-Dosage forms and common ADRs of commonly used antiepileptic medicines**

| Medicine | Available dosage forms | Common ADRs |
|---|---|---|
| **Carbamazepine** | Syrup-100mg/5ml<br>Tablet-100mg, 200mg | rash, hyponatremia, drowsiness, dizziness, blurred or double vision, lethargy, headache |
| **Clonazepam** | Tablet, 0.5mg, 1mg, 2mg | Amnesia, ataxia, behavioural problems, confusion, depression, dizziness, drowsiness |
| **Ethosuximde** | Capsule-250mg<br>Syrup-250mg/5ml | sleep disturbance, drowsiness, hyperactivity |
| **Phenobarbitone** | Tablet-15mg, 30mg, 60mg, 100mg<br>Elixir-20mg/5ml | rash,alteration of sleep cycles, sedation, lethargy, behavioural changes, hyperactivity, ataxia, tolerance, dependence |
| **Phenytoin** | Tablet/capsule-50mg, 100mg | Gingival hypertrophy, rash, confusion, slurred speech, double vision, ataxia |
| **Valproic acid** | Syrup-200mg/5ml<br>Tablet-200mg, 500mg | Weight gain, hair loss, easy bruising, tremor, dizziness |

**Principles of therapy**

- Therapy should not be initiated after only 1 attack. It should be initiated only if evidence of epilepsy has been established.
- The aim is to use monotherapy i.e. a single anticonvulsant, until the seizures are controlled or intolerable side effects occur
- If seizure is not well controlled with maximum tolerated dose of the first medicine or if the first one is not tolerated, a second medicine trial should be attempted.

- Except in case of a serious adverse event, the second medicine is started and dose increased without discontinuation of the first medicine to avoid seizure recurrence. After the second medicine is increased to optimal the first is gradually tapered and discontinued.

- Combination therapy: when possible try to maintain a patient on a singlemedicine. If trial of changing to a second agent is not successful a second medicine can be added but medicine–medicine interaction between the medicines is a serious concern

- Many of the antiepileptic medicines induce their own metabolism (auto induction) hence their dose needs to be increased gradually to achieve therapeutic serum levels.

- Many antiepileptic medicines induce the metabolism of other antiepileptic medicines. As result patients on combination of medicines needs to closely monitored.

- Anti-convulsants may make oral contraceptives ineffective.

**Antiepleptic medicines should not be discontinued (even if the seizure is well controlled) unless decided by specialist after complete control of seizures for years**

**When to discontinue therapy-this should be decided by a specialist only**

About 60% of adults whose seizures are completely controlled with antiepileptic medicines can eventually discontinue therapy. In most cases it is preferable to reduce the dose of the medicine gradually over 2 to 3 months. The following patient profile yields the greatest chance of remaining seizure-free after medicine withdrawal:.

- complete medical control of seizures for 1 to 5 years;

- single seizure type, either partial or generalized;

- normal neurologic examination, including intelligence; and

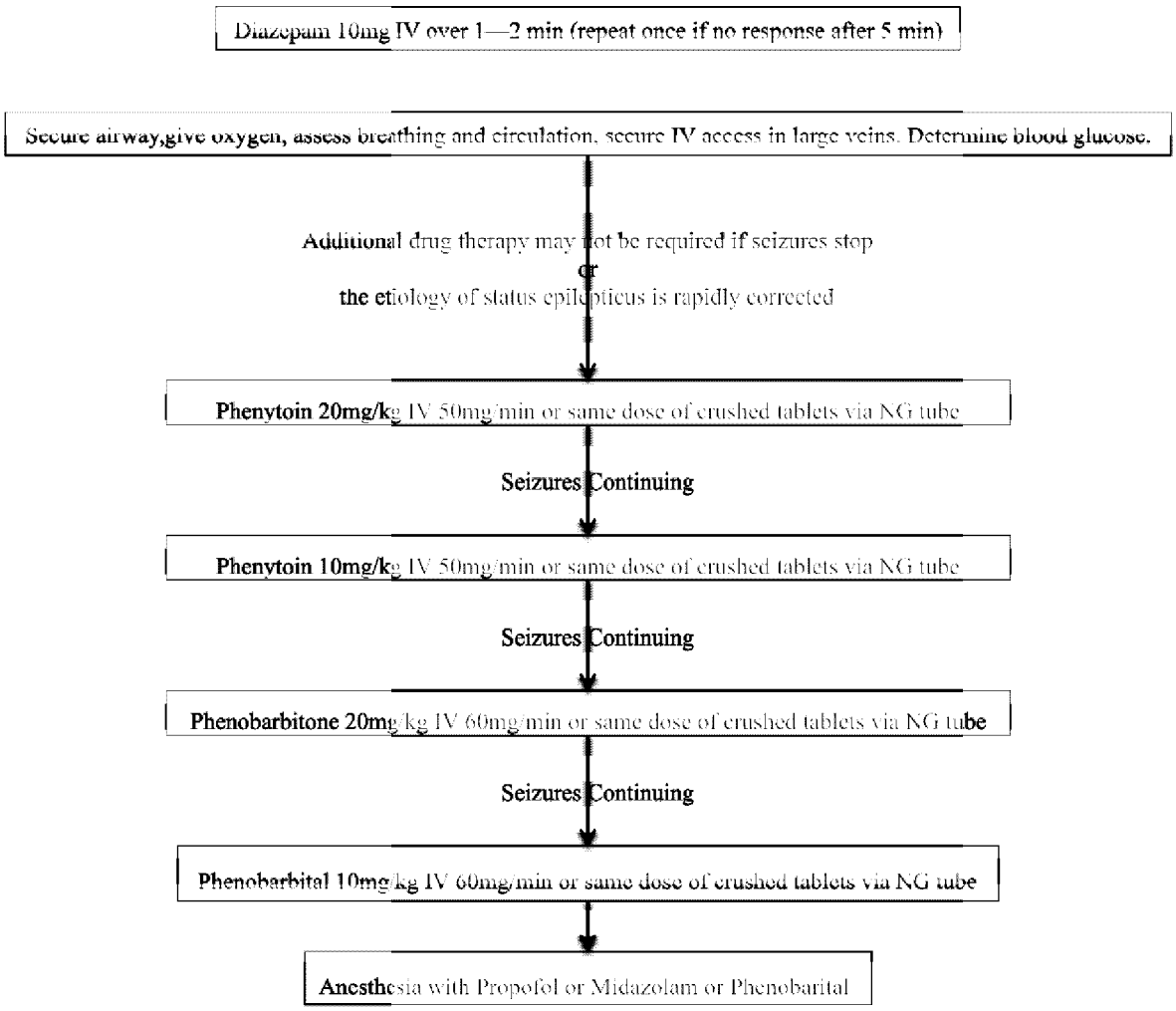
- normal EEG.

**Status epilepticus**-refers to continuous seizures or repetitive, discrete seizures with impaired consciousness in the interictal period. The duration of seizure activity sufficient to meet the definition of status epilepticus is about 15 minutes. Status epilepticus has two main subtypes-

generalized convulsive status epilepticus and nonconvulsive status epilepticus. See the diagram below for treatment of status epilepticus.

**Management of status epilepticus**

**Secure Airway, start oxygen, Secure IV line, Take blood sample & determine blood sugar**



## CHAPTER X: ONCOLOGY

### 1. Breast Cancer

Breast cancer is the leading cancer in females worldwide. In Ethiopia, based on Oncology Unit of Tikur Anbessa Hospital data it accounts for 20% of all referred cases to the unit. Based on the 2012, one year Addis Ababa Cancer Registry report, breast Cancer is the leading cancer in Addis Ababa City accounting for 25% of all cancer cases in both sexes. Early detection and treatment markedly improve mortality from breast cancer. Most Breast cancer patients in Ethiopia are relatively young.

**Clinical Features**

- Depends on the stage of the cancer

**Early Breast cancer**

- Lump in the breast
- Discharge or bleeding from nipple

**Locally Advanced Breast cancer**

- Axillary lymph node enlargement
- Nipple retraction
- Ulceration and Pain

**Metastatic Breast cancer**

Symptoms depend on the site of metastasis

- Bone – back pain is a danger sign
- Lung/Pleura – cough, shortness of breath, chest pain
- Liver – right upper quadrant pain, poor appetite, weigh loss
- Brain – headache, focal neurologic deficit

**Investigations**

The objective is to confirm the diagnosis and stage before starting treatment.

- CBC, renal and liver function tests
- Fine needle aspiration (FNA) and/or Preferably Biopsy of the breast lump or FNA from axillary lymph node

- Mammogram of Both Breasts
- CXR
- Ultrasound of Liver

**Treatment**

**Objectives**

Depends on the stage for management purpose, it is usually classified into 3 major groups:

- Early stage-cure the cancer
- Locally advanced Stage
    - Cure some and prolong survival in most patients
    - Convert inoperable tumour to operable by giving neo-adjuvant chemotherapy
- Metastatic disease- control symptom and prolong survival

**Non Pharmacologic**

Early stage breast cancer

- Surgery

Modified Radical Mastectomy (MRM) is the preferred treatment in Ethiopia. Breast conservative Surgery is not recommended as it always needs adjuvant Radiotherapy to reduce recurrence of cancer. The waiting time for Radiotherapy is currently very long.

- Radiotherapy

Radiotherapy is indicated to reduce loco regional (chest wall and axillary lymphnode) recurrence only if:

- It shows positive margin
- Four or more lymph nodes are positive on pathologic staging
- Axillary lymph nodes are not dissected.

**Pharmacologic**

Breast cancer is a systemic disease and micro metastasis occurs even at early stage. Chemotherapy/Hormonal therapy is used to eradicate microscopic residual tumour.

Indications for adjuvant Chemotherapy

- Tumour > 1cm in Diameter
- Positive lymph node

Elderly patients (>70 years), poor performance status, patient with co morbidity, patients with low WBC, low Platelet count can be treated with adjuvant hormonal treatment only to avoid side effects of chemotherapy.

Check always CBC, liver and renal function tests before each cycle of chemotherapy

- Haemoglobin > 10gm/dl
- WBC > 3000/$mm^3$ with ANC > 1500/$mm^3$
- Platelet >100,000/$mm^3$

Give premeditations to reduce nausea and vomiting 30 minutes before chemotherapy

**Metoclopramide**, 10-20mg IV

*PLUS*

**Dexamethasone**, 12mg IV

*PLUS*

**Ondansetron** 8 – 16 mg IV

**ADRs:** Constipation, dizziness, headache

**D/Is:** Not significant

**P/Cs:** Heart problems

**Dosage forms:** Tablet, 4mg, 8mg; Syrup, 4mg/5ml; Injection, 2mg/ml, 4mg/ml, 8mg/ml. Suppository, 16mg

**Cimetidine**, 400 mg IV

**N.B.** Use standared precautions and check leaflet before mixing and administering chemotherapy.

**Chemotherapy regimen**

**First line**

**AC regimen (**Doxorubucin+Cyclophosphamide**)**

**Doxorubucin**, 60mg/$m^2$ slow IV push or In 300ml of N/S over 1 hr

**ADRs:** Nausea, cardiac arrhythmias

**D/Is:** Not common

**C/Is:** Heart problems, high uric acid levels, bone marrow depression, precautions: infection

**Dosage forms:** Powder for injection, 10mg, 50mg in vial

**Cyclophosphamide**, 600mg/$m^2$ in 300ml of N/S over 1 hr

**ADRs:** hemorragic cystitis

**D/Is**: allopurinol, chloramphenicol, chloroquine, digoxin, nalidixic acid,, phenothiazines

**C/Is:** hypersensitivity, bone marrow depression, first trimester pregnancy

**P/Cs**: hepatic and renal impairment, leucopenia, thrombocytopenia

**Dosage forms:** Powder for injection, 200mg, 500mg, 1000mg in vial
Tablet, 50mg

*OR*

**FAC Regimen** (5-Florouracil + Doxorubucin +Cyclophosphamide)

(Usually for leftbBreast cancer to reduce cardiac toxicity, if they require radiotherapy in the future)

*PLUS*

**Doxorubucin**, 50mg/m2 slow IV push or In 300 ml of N/S over 1 hr

*PLUS*

**Cyclophosphamide**, 500 mg/m2 in 300 ml of N/S over 1 hr

**5-Florouracil**, 500 mg/m2 IV Push

**ADRS:** nausea, vomiting, loss of appetite, mild diarrhoea,

**D/Is:** metronidazole

**C/Is:** poor nutritional state, serious infections, recent serious surgery, hypersensitivity reactions,

**P/Cs:** liver and renal dysfunction

**Dosage forms:** Injection, 250mg/5ml, 500mg/10ml ampoule

**CMF regimen (**Cyclophosphamide +Methtrixate+5-Florouracil**)**

For elderly and cardiac patients

**Cyclophosphamide**, 500mg/m2 in 300ml of N/S over 1 hr

*PLUS*

**5-Florouracil**, 500mg/m2 IV

*PLUS*

**Methotrexate**, 40mg/m2 IV

**ADRs:** diarrhoea, liver damage, neurotoxicity, nephrotoxicity

**C/Is**: renal and hepatic impairment

**Dosage forms:** Tablet, 2.5mg, 5mg, 7.5mg, 10mg, 15mg Powder for Injection, 5mg, 50mg in vial

Each cycle to be repeated every 21 days CBC and organ (liver/renal) function tests permitting

**Hormonal Therapy**

**Tamoxifen,** 20mg PO/Day for 5 years after chemotherapy

| | |
|---|---|
| **ADRs:** | Hot flush, cataract, venous thrombosis, uterine carcinoma, |
| **D/I s:** | Erythromycin, Rifampcin, Nifedipine. |
| **C/Is:** | Hypersensitivity, Venous thrombosis |
| **P/Cs:** | use two forms of non hormonal birth control when using Tamoxifen) |
| **Dosage forms:** | Tablet, 10mg, 20mg |

**Locally Advanced cancer**

Breast tumour involving skin, chest wall (T4) and axillary lymph node fixed/matted (N2/3)

Chemotherapy regimen – same as early stage breast cancer

Patient with good response to chemotherapy should be assessed by surgeon for modified radical mastectomy

Radiotherapy-refer

**Metastatic Disease**

Patients with limited bone and skin metastasis have good prognosis and long survivals as compared to patients with visceral metastasis involving lung, liver, and brain etc and can be tried on hormonal treatment

a) **Palliative chemotherapy**

Regimen as early/locally advanced

Refer patients for second line chemotherapy when they fail to respond to first line

b) **Palliative radiotherapy**-For symptomatic bone lesion, spinal cord compression, brain metastasis

## 2. Chronic Lymphatic Leukemia (CLL)

Chronic lymphocytic leukemia (CLL) is one of the chronic lymphoproliferative disorders (lymphoid neoplasms) characterised by a progressive accumulation of functionally incompetent lymphocytes of monoclonal origin.

CLL is considered to be identical to small lymphocytic lymphoma (SLL), one of the indolent non-Hodgkin lymphomas.

The symptoms and signs of CLL relate to tissue infiltration (lymphadenopathy, organomegaly), peripheral blood cytopenias (anaemia, bleeding, infections), or immune suppression (infections and malignancies) and autoimmune phenomenon (hemolytic anaemia).

**Clinical features**

- Asymptomatic (1/4 of patients)
- "B" symptoms:
    - Unintentional weight loss ≥10% in six months
    - Fever >38ºC for ≥2 weeks without evidence of infection.
    - Drenching night sweats without evidence of infection.
    - Extreme fatigue
- Lymph node enlargement and symptoms related to mass effect
- Splenomegally
- Hepatomegally
- Recurrent infections (pneumonia, UTI) caused by usual bacterial pathogens

**Investigations**

- Complete blood count and differential
- Peripheral blood smear and bone marrow examination
- Chest x-ray and abdominal ultrasound studies
- RFT, LFT, LDH, Electrolyte and uric acid level

An absolute lymphocyte count of 10,000/μL in the peripheral blood and 30% lymphocytes in the bone marrow establish the diagnosis of CLL.

**Treatment**

**Objectives**

- Improve symptoms
- Manage complications

**Non pharmacologic**

Patients with early stage and asymptomatic disease should be observed without treatment.

- Patients with symptomatic anaemia should be transfused packed red blood cells.

**Pharmacologic**

The following are indications for the initiation of specific therapy:

- Persistent or progressive systemic symptoms
- Bulky lymphadenopathy that causes mechanical obstruction or bothersome cosmetic deformities
- Evidence of bone marrow failure (anaemia and/or thrombocytopenia), immune hemolysis or immune thrombocytopenia.

**First line**

**Chlorambucil,** 0.1 to 0.2mg/kg P.O., QD for 3 to 6 weeks. It is then discontinued after the desired effect is achieved. Alternatively, 15 to 30mg/$m^2$ P.O. may be given over 3 to 4 days every 14 to 21 days.

*PLUS*

**Prednisolone**, 0.5-1mg/kg may be added, particularly in the presence of hemolytic anaemia

**Alternative**

**Cyclophosphamide**, 2 to 4mg/kg P.O., daily until the desired effect is achieved (systemic symptoms improve and the size of enlarged lymph nodes and organomegaly are decreased).

PLUS

**Prednisolone**, 0.5-1mg/kg may be added, particularly in the presence of hemolytic anaemia

### 3. Chronic Myelogenous Leukemia (CML)

Chronic myeloid leukemia is classified as a myeloproliferative disorder, along with polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis.

This group of diseases are characterised by the dysregulated production of a particular lineage of mature myeloid cells with fairly normal differentiation. They exhibit a variable tendency to progress to acute leukemia.

CML is associated with the Philadelphia chromosome 9q[t(q;22)(q34;q11) resulting in a fusion gene called BCR-ABL. This genetic abnormality activates tyrosine kinase. This deregulated tyrosine kinase is implicated in the development of CML and has become a primary target for the treatment of this disorder. CML has got three phases: Chronic phase, Accelerated phase and Blast crisis.

**Clinical features**

- Fatigue, malaise, weight loss, abdominal fullness, early satiety, tenderness over the lower sternum
- Acute gouty arthritis may also present at this time, due to overproduction of uric acid

**Investigation**

- Complete blood count and differential
- Peripheral blood smear examination
- Bone marrow aspiration and/or biopsy
- Leukocyte alkaline phosphatase score
- RFT, LFT, LDH, Electrolyte and uric acid.

**Treatment**

**Objectives**

- Achieve clinical and cytologic remission

**Non-pharmacologic**

- Patients with symptomatic anaemia should be transfused packed red blood cells.
- Dehydration and electrolyte imbalance, if present, should be corrected.

**Pharmacologic**

**Palliative (Cytoreductive therapy) chemotherapy:**

**First Lline**

**Hydroxyurea**, oral, 2 to 4g/day, initially depending on the cell count.

The dose is then adjusted to the blood count. It should be stopped or withheld if the WBC count drops to < 10,000/μL. degree.

**ADRs:** edema, drowsiness, hallucinations, headache, dizziness, disorientation, seizure, fever, chills, erythema of hands and

| | |
|---|---|
| | face, rash, pruritus, hyperpigmentation, dry skin, skin cancer, hyperuricemia, GI disturbances, pancreatitis, dysuria, myelosuppression, hepatotoxicity, peripheral neuropathy, dyspnea, pulmonary fibrosis |
| **C/Is:** | severe anaemia, pregnancy. |
| **D/Is:** | zidovudine, zalcitabine, didanosine, fluorouracil, cytarabine, and stavudine. |
| **P/Cs:** | renal impairment, bone marrow suppression, erythrocytic abnormalities, and elderly |
| **Dosage forms***:* | Capsule, 500 mg |

*PLUS*

**Allopurinol**, 100 mg P.O., TID should be started before the initiation of specific treatment.

Molecular targeted therapy (tyrosine kinase inhibitors)-first line therapy for chronic phase CML

All patients suspected having CML should be referred to a hematologist so that they can access tyrosine kinase inhibitor treatment.

### 4. Colorectal Cancer

Cancer of the colon and rectum are by far the most frequent malignancies of the GI tract and account for the most deaths. The major histologic type of colorectal cancer is adenocarcinoma. Its development results from complex interaction between genetic (including familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer or Lynch syndrome) and environmental factors (including high fat and low fibre intake, consumption of red meat, alcohol and smoking). In most parts of the world colorectal cancer occurs after the age of 50. In Ethiopia, hospital based data indicate that 50% of the patients are below the age of 45 and most patients present with large bowel obstruction as emergency.

**Clinical Features**

The usual presentation is change in bowel habit, abdominal pain and tensmus. Because of delay in seeking medical advice and diagnosis the usual presentation in our case is as large bowel obstruction. Consider colo-rectal cancer as differential diagnosis and do colonoscopy

for patient presenting with the above symptoms in order to make the diagnosis early and improve outcome.

**Symptom depends on the anatomic site**

- Right colon – most patient present with unexplained iron deficiency anaemia, hence symptoms of anaemia due to occult blood loss.
- Left colon – abdominal cramp, constipation, blood in stool, obstruction or perforation
- Rectosigmoid colon-tenesmus, bleeding, narrowing of stool caliber
- Advanced stage – weight loss, loss of appetite, abdominal distention from ascites

**Depending on the stage**

- Pallor, jaundice,
- lymph node enlargement,
- Hepatomegally and ascites
- Palpable mass on rectal examination

**Investigations**

- Refer for specialist evaluation

**Treatment**

**Objectives**

Treatment and outcome depends on the stage of disease

- Early stage – cure with surgery alone or with adjuvant chemotherapy depending on the stage
- Advanced stage – improve survival and quality of life by controlling symptom

Staging – UICC/AJCC (**Simplified for treatment purpose**)

| **Stage** | **Definition** |
|---|---|
| I | Tumour extending to muscular layer with no lymph node involvement |
| II | Tumour invading through muscularis propria into subserosa (T3) or perforates visceral peritoneum (T4) |
| III | Any tumour with regional lymph node involvement |
| IV | Distant metastasis |

**Non pharmacologic**

Surgery

Rsection with clear resection proximal, distal and circumferential margin whenever possible for localized disease

Unresectable rectal cancer, refer for neoadjuvant (Convertive) chemoradiotherpy and evaluate patient for surgery 4 weeks after completion of radiotherapy

**Pharmacologic**

**Chemotherapy**

**Stage I** No Adjuvant chemotherapy, follow up every 4-6 months,

Adjuvant chemotherapy is indicated for

**Stage II** All T4 tumours

T3 with poorly differentiated histology, lymphovascular invasion require adjuvant Chemotherapy

**Stage III** Inadequate lymph node evaluation (When the number of lymph node examined is less than 10)

**Metastatic disease**

For patients with good performance status, normal CBC, RFT, LFT – palliative chemotherapy.

Patient with poor performance status, low CBC, abnormal organ function test, elderly>70 years of age do not benefit from chemotherapy. These groups of patients should be offered symptomatic treatment to control pain and other symptoms.

Chemotherapy Regimens

Adjuvant chemotherapy

**Premedication**

Give 30 minutes before chemotherapy

**Metoclopramide**, 10-20mg IV

*PLUS*

**Dexamethasone**, 12mg iv slowly

*PLUS*

**Cimetidine**, 200mg IV

*PLUS*

**Ondansetron**, 8-16mg IV

**First line chemotherapy**

**Regimen I**

**5-Florouracil,** 425mg/m2 IV push daily for 5 consecutive days

*PLUS*

**Leucoverin**, 20mg/m2, 30 minutes before 5-Florouracil daily for 5 consecutive days

Six Cycles, to be repeated every 4 weeks

**Regimen II**

**Capcitabin** 1500mg/m2 PO BID for 2 weeks every 3 weeks total 6 cycles

**ADRs:** Hand-foot syndrome, diarrhoea, stomatitis,

**C/Is:** severe renal failure

**D/I s:** Warfarin, phenytoin

**P/Cs:** Elderly

**Dosage forms:** Tablet, 150mg, 500mg; Injection, 26mg/ml

**Regimen III**

**Oxaloplatin**, 85mg/m2 in 500ml 5% DW over 2 hours

**ADRs:** Vomiting, sensory neuropathy,

**C/Is:** Renal failure, Precautions: Avoid cold exposure and cold drinks

**Dosage forms:** 50mg vials

*PLUS*

**Capcitabin**, 1000mg/m2 P.O., BID for 2 weeks.

Six cycles, to be repeated every 3 weeks

**N.B.** Regimen III increases survival and reduces relapse rate by 5% as compared to regimen I and II, but is very expensive

**Palliative chemotherapy for metastatic cancer**

The chemotherapy regimen depends on the patient general condition

- For elderly with co-morbidity use single agent chemotherapy
- For patient with good performance status use combination chemotherapy

1. Single agent chemotherapy-Use regimen I or II as above
2. Combination chemotherapy-Use regimen III as above

## 5. Head And Neck Cancer

Cancer arising from oral cavity, pharynx, larynx, nasopharynx, and the sinuses are classified under cancer of the head and neck region. They are considered together as most patients share

similar demographic and epidemiologic risk factors. The incidence of head and neck cancers increases with the use of alcohol and tobacco. About 90% of these cancers are squamous cell carcinoma.

Head and neck cancer occur in continuity, one with another, and is occasionally difficult to determine the exact site of origin in the close confines of the complicated interrelated structures comprising the oral cavity, pharynx, larynx, nasopharynx, and the sinuses. Furthermore the pattern of spread and their treatment is similar. With early diagnosis the cure rate with surgery or combined chemoradiotherapy is high.

**Clinical Features**

Symptoms depend on the exact site and stage

- Nasopharynx – Epistaxis, nasal blockage, headache, cervical lymph node enlargement
- Oropharynx -pain and difficulty of swallowing, cervical lymph node enlargement
- Hypopharynx/Larynx – hoarseness of voice, dysphagia, cervical lymph node enlargement

**Physical Examination**

- Visible mass or ulcer in any part the oral cavity, nostrils.
- Palpable cervical lymph nodes
- Cranial nerve deficit involving III, IV, VI and XII in advanced nasopharyngeal cancer

**Investigations**

- Refer patient to ENT specialist

**Treatment**

**Objectives**

- Cure patient without compromising structure and function in early cases
- In advanced stage the goal is to control symptom and prolong life

**Non pharmacologic**

- Refer patient to ENT specialist

**Pharmacologic**

For patients with recurrent or metastatic disease, palliative chemotherapy will control symptoms and improve survival.

Premedication

Give 30 minutes before chemotherapy

**Methoclopramide**, 10-20mg IV

*PLUS*

**Dexamethasone**, 12mg iv slowly

*PLUS*

**Cimetidine**, 200mg IV

*PLUS*

**Ondansetron**, 8-16mg IV

*PLUS*

**Promethazine**, 25mg IV/PO for patient taking Paclitaxel

**First line Regimen**

**Cisplatin**, 80mg/M2 in 500 – 800ml of N/S over 3 hr with proper pre and post chemotherapy hydration.

| | |
|---|---|
| **ADRs:** | nephrotoxicity,ototoxicity,peripheral neuropathy and hypomagnesemia |
| **P/Cs:** | renal impairment |
| **D/Is:** | aminoglycosides,diuretics |
| **Dosage forms:** | 1mg/ml, 10ml, 50ml or 100ml vials |

Cycle to be repeated every 3 weeks after checking CBC, RFT, Electrolytes. Cisplatin is highly emitogenic and nephrotoxic, hence needs close monitoring of RFT, Electrolyte and antiemetic administration before and after chemotherapy.

*OR*

**Cisplatin**, 60mg/m2 in 500 N/S over 3hr

*PLUS*

**5-Florouracil** 600mg/m2

Cycle to be repeated every 3 weeks after checking CBC, RFT, Electrolyte

**Second line Regimen (For recurrence or metastatic disease)**

**Cisplatin**, 60mg/m2 in 500 N/S over 3 hr

*PLUS*

**Paclitaxel**, 175mg/m2 in 300ml N/S

| | |
|---|---|
| **ADRs:** | Hypersensitivity, Hypotension, Bradycardia, Asthenia, |

| | |
|---|---|
| **C/Is:** | Hypersensitivity reaction, pregnancy, heart problem, |
| **P/Cs:** | Slow infusion |
| **Dosage forms:** | Concentrate for IV infusion 6mg/ml, 5ml vial |

## 6. Ovarian Cancer

Ovarian cancer can develop from three different cell types (epithelial cell, germ cell and stromal cell). Epithelial cancer is by far the most common of the three types. The incidence of epithelial ovarian cancer increases steadily, with peaks in the $7^{th}$ and $8^{th}$ decades of life. Germ cell ovarian cancer occurs at a younger age and is associated with excellent treatment outcome.

These three histologic types have different natural course and presentation:

1. Germ cell ovarian cancer

These malignancies typically occur in young women and are curable. They often present as asymptomatic pelvic mass.

2. Stromal cell Ovarian cancer

Rare neoplasm occurring at any age and are characterised by production of sex hormones. In childhood granulosa cell tumour typically present with precocious puberty.

3. Epithelial Ovarian cancer

Accounts for about 75% of ovarian cancer and generally occurs after menopause. Most patients present with advanced disease at the time of diagnosis and are rarely curable.

**Clinical Features**

**Early stage ovarian cancer**

- Incidentally discovered on routine ultrasound examination
- Non specific abdominal discomfort, irregular menses (in premenopausal women)
- Urinary frequency and constipation caused by enlarged pelvic mass.

**Advanced stage ovarian cancer**

- Abdominal swelling, early satiety, vomiting and constipation
- Poor appetite and weight loss

- Early stage – Adnexal mass on pelvic examination
- Advanced stage – Mass, and or ascites, and
- Metastatic Disease – emaciated, jaundice, palpable liver, sign of plural effusion

**N.B**. Adenexal mass in premenopausal and post menopausal women is most likely pathological and needs further investigation and follow up.

**Investigations**

- CBC, RFT, LFT
- CA-125 for suspected epithelial ovarian cancer
- AFP, B-HCG for suspected germ cell tumour
- Ultrasound of pelvis and abdomen
- CXR

Ovarian cancer is diagnosed and staged surgically. Depending on the stage maximal cytoreductive surgery and staging is important for both decision on adjuvant treatment and survival. In young premenopausal womenl conservation of the ovary should be considered in early stage disease.

**Staging**

AJCC/FIGO C Staging (**in simplified form with out sub-stage**)

| **Stage** | **Definition** |
|---|---|
| I | Tumour confined to ovaries |
| II | Ovarian tumour with pelvic extension |
| III | Ovarian tumour with peritoneal metastasis and retroperitoneal or inguinal lymph node involvement |
| IV | Distant metastasis |

**Treatment**

**Objectives**

Depends on stage and histologic type of ovarian cancer

- Early stage – cure and preservation of ovary.
- Advanced stage – control symptoms and prolong survival.

**N.B.** Low malignant potential tumours of ovary do not require adjuvant chemotherapy

**Non pharmacologic**

- Early stage – appropriate surgery with staging
- Locally advanced-maximal debulking surgery followed by chemotherapy
- Metastatic cancer – palliative chemotherapy and/or surgery

**Pharmacologic**

**For Epithelial Ovarian cancer**

**I. Early stage (stage I –IIA)**

Adjuvant chemotherapy 4-6 cycles is indicated for stage IC and II. For stage Ia/b adjuvant chemotherapy is indicated only for poorly differentiated or clear cell histology.

**II. Advanced stage (IIB-III C)**

Six cycles adjuvant chemotherapy after maximal debulking surgery

**III. Metastatic cancer (IV)**

Palliative chemotherapy after debulking surgery improves survival

Chemotherapy regimen for all stages is similar.

Before each cycle of chemotherapy make sure that the patient CBC, RFT, LFT are all in normal limit. Proper premedication to prevent adverse effects is important both for adherence for chemotherapy and also to prevent life threatening side effects.

Premedication

Give 30 minutes before chemotherapy

**Methoclopramide**, 10-20mg IV

*PLUS*

**Dexamethasone**, 12mg iv slowly

*PLUS*

**Cimetidine**, 200mg IV

*PLUS*

**Ondansetron**, 8-16mg IV

*PLUS*

**Promethazine**, 25mg IV/PO for patient taking Paclitaxel

**N.B.** Paclitaxel is associated with anaphylactic reaction and patient should be monitored during treatment. Adrenalin, Hydrocortisone and resuscitative equipments should be available.

**First line Regimen I**

**Cisplatin**, 50mg/m2 in 500ml l N/S over 3 hrs

*PLUS*

**Paclitaxel**, 175mgm/m2 in 300ml N/S over 3hr, every 3 week Total 6 cycles

**Alternative** (First line Regimen II)

**Carboplatin** (AUC 4-6)

*PLUS*

**Paclitaxel**, 175mg/m2 in 300ml N/S over 3hr, every 3 week Total 6 cycles

*OR*

Regimen III – is inferior regimen as compared to regimen I & II, (use for patients can't afford paclitaxel)

**Cisplatin**, 60mg/m2 in 500 ml N/S over 3 hrs

*PLUS*

**Cyclophosphamide** 700mg/m2 in 500 ml N/S over 1 hr, every 3 week total 6 cycles

## CHAPTER XI: PSYCHIATRIC DISORDERS

### 1. Anxiety Disorders

There are different types of anxiety disorders:

**Specific Phobia** – At least 6 months of irrational and persistent fear and marked avoidance of a specific thing, place or circumstance, to the extent that it interferes with normal functioning.

**Social Phobia** – At least 6 months of noticeable and persistent fear of being negatively evaluated for at least one social or performance situation.

**Obsessive-Compulsive Disorder (OCD)** – recurrent, intrusive, inappropriate and unwanted thoughts, or images, causingsignificant anxiety that interfere with usual functioning.

**Panic Disorder**– At least one panic attack (acute episode of unprovoked, intense fear/distress accompanied by somatic or cognitive symptoms) resulting in worry about having another panic attack.

**Post-Traumatic Stress Disorder (PTSD)** – Following an exposure to significant trauma avoidance or re-experiencing of the trauma for at least one month as illustrated by: intense fear, disturbing dreams, flashbacks, helplessness, physiological agitation upon seeing reminders of the event, or disorganized/agitated behaviour.

**Generalized Anxiety Disorder (GAD)** – At least 6 months of excessive and uncontrollable daily worry about multiple themes (e.g. school, family safety, world issues, natural calamities, friends, personal performance) that results in physical symptoms and functional impairment.

**Clinical features**

- See specific anxieties

**Investigations**

- Clinical

**Treatment of Generalized anxiety disorder**

**Non pharmacologic**

- Cognitive behavioural therapy (education, behavioural exposure, behavioural control and somatic control)

**Pharmacologic**

- Either pharmacotherapy or cognitive behavioural therapy can be used as first-line treatment for generalized anxiety disorder (GAD).

**First line**

**Fluoxetine**, 20-40 mg /day

| | |
|---|---|
| **ADRs:** | headache and gastrointestinal disturbances, decreased libido and sexual dysfunction, weight loss, asthenia, hypoglycemia, hyponatraemia, and elevated transaminase levels. Altered platelet function and abnormal bleeding. |
| **D/Is:** | flecainide, metoprolol, nifedipine, diclofenac, omeprazole, clozapine, fluphenazine, haloperidol, risperidone, antidepressants, terfenadine, carbamazepine and phenytoin; |
| **P/Cs:** | hepatic or renal impairment, epilepsy and diabetes. |
| **Dosage forms:** | Capsule, 20mg |

**Alternatives**

**Diazepam**, starting at 2.5 to 5.0mg, P.O., once or twice daily and titrated up to 10mg/day two or three times daily based on response.

*OR*

**Imipramine**, P.O., 25-50mg/day. Increase by 25mg based on response up to 150mg. The patient's tolerance will determine the rate of increase and the maximum dose

## 2. Mood Disorders

Mood disorders are characterised by a disturbance in the regulation of mood, behaviour, and affect. Mood disorders are subdivided into:

**I.** Depressive disorders

**II.** Bipolar disorders

**III.** Depression in association with medical illness or alcohol and substance abuse

### I. Depressive disorders

**Major depression** — A major depressive syndrome or episode manifests **five or more** of the following symptoms, present most of the day, nearly every day, for a minimum of **two**

**consecutive weeks**. At least one symptom is either depressed mood or loss of interest or pleasure. The symptoms should cause clinically significant distress impairment in social, occupational, or other important areas of functioning and should not due to the direct physiologic effects of a substance.

The nine symptoms of major depression

- Depressed mood
- Loss of interest or pleasure in most or all activities
- Insomnia or hypersomnia
- Change in appetite or weight
- Psychomotor retardation or agitation
- Low energy
- Poor concentration
- Thoughts of worthlessness or guilt
- Recurrent thoughts about death or suicide

**Dysthymic disorder**-is marked by chronically depressed mood for at least two years. Depression is present for most of the day and for more days than not. The depressed mood is accompanied by two or more of the following symptoms:

- Decreased or increased appetite
- Insomnia or hypersomnia
- Low energy
- Poor self-esteem
- Poor concentration
- Hopelessness

These symptoms are less severe than symptoms of major depression.

**Minor depression** — Patients with minor depression have several of the nine symptoms of major depression (see above).

- It is also called 'subsyndromal,' and 'sub-threshold' depression.
- Diagnosis of minor depression requires between two and four of the nine symptoms of major depression present most of the day, nearly every day, for at least two weeks, at least one being depressed mood or loss of interests/pleasure.
- When minor or subsyndromal depression persists for more than two years, the criteria for dysthymic disorder may also be met.

**Clinical features-**see descriptions above

**Investigations**

- Primary depressive disorders are diagnosed by syndrome criteria so diagnosis depends on clinical history and mental examination**.**
- Assessment should include evaluation for suicide risk, a comprehensive medical history, exploration of comorbid psychiatric disorders including substance use, and family history.
- When depression secondary to medical disorders is suspected the following investigation could be helpful:
    - CBC
    - Creatinine and BUN
    - Liver function tests,
    - TSH
    - VDRL/RPR
    - B12 and folate levels

**Treatment**

**Objectives**

- Prevent suicide
- Full symptom remission
- Improve functionality at home, work or school

**Non pharmacologic**

- Psychotherapy-cognitive or behavioural or interpersonal therapy.
- Family and couples' therapy, psychodynamic psychotherapy, and problem-solving therapy.

**Pharmacologic**

**First line**

**Fluoxetine**, starting dose, 20 mg /day P.O., usual total dose per day 20-60mg/day.

**Alternative**

**Amitriptyline**, starting dose 25-50mg/day P.O.,Usual total dose per day 100-300mg/day. Increase by 25mg every 3-5 days up to 150mg orally at night by end of second week. The patient's tolerance will determine the rate of increase and the maximum dose

**ADRs:** sedation, blurred vision, difficulty with micturation; arrhythmias, postural hypotension, tachycardia, gynaecomastia, galactorrhoea;

**C/Is:** recent myocardial infarction, heart block, manic phase, severe liver disease.

**D/Is:** alcohol, other CNS depressants, antithyroid agents, phenothiazine, cimetidine, clonidine, guanadrel, guanethidine

**P/Cs:** cardiac disease, history of epilepsy, pregnancy and breastfeeding, elderly, hepatic impairment; anaesthesia

**Dosage forms:** Tablet, 10mg, 25mg, 50mg

*OR*

**Imipramine**,oral, 25-50mg/day. Usual total dose per day 100-300mg/day. Increase by 25mg every 3-5 days up to 150mg orally at night by end of second week. The patient's tolerance will determine the rate of increase and the maximum dose.

- Admit patients with suicidal tendencies and keep under close observation
- Give maximum tolerable dose for at least 6 weeks before deciding a particular antidepressant is not effective.
- For a first episode continue antidepressants for 6-9 months.
- When antidepressants are discontinued, they should be tapered over two to four weeks.
- If night sedation is required, Diazepam 5-10mg or Bromazepam 3-6mg/day, oral, can be used for not more than 2 weeks.
- Stop antidepressants immediately if manic swing occurs.
- Evaluate at a minimum of every one-two weeks for six to eight weeks.

**ADRs:** blurred vision, and difficulty with micturition. Extrapyramidal symptoms, allergic skin reactions

**C/Is:** early post myocardial infarction period and heart block.

**D/Is:** antihistamines, antipsychotics and anti-cholinergic type antiparkinsonian agents, cimetidine, fluoxetine, paroxetine and steroids, hepatic enzyme-inducing agents, MAO inhibitors.

**P/Cs:** hyperthyroidism, arrhythmias, epilepsy, prostatic enlargement, closed-angle glaucoma, impaired liver function.

**Dosage forms:** Tablet, 10mg, 25mg

**Precautions to be observed in antideppresant medications** (Adapted from WHO mental health GAP interventions guide, 2010)

- **To avoid overdoses** in people at risk of self harm/suicide, make sure that they have access to a limited supply of antidepressants only (e.g. dispense for one week at a time).

- **Adolescents 12 years and older-**avoid TCAS and use fluoxetine. Monitor adolescents on fluoxetine frequently (ideally once aweek) for emergence of suicidal ideas during the first month of treatment.

- **Older people-**TCAs should be avoided, if possible. SSRIs are first choice. Consider the increased risk of medicine interactions in the presence of comorbid conditions and give greater time for response (a minimum of 6 – 12 weeks)

- **People with cardiovascular disease-**SSRIs are first choice. Do not prescribe TCAs to people at risk of serious cardiacarrhythmias or with recent myocardial infarction.

**Monitoring people on antidepressant medication** (Adapted from WHO mental health GAP interventions guide, 2010)

- If **symptoms of mania** emerge during treatment: immediately stop antidepressants and assess for and manage the mania andbipolar disorder.

- If people on SSRIs show **marked/prolonged akathisia** (inner restlessness or inability to sit still), review use of the medication. Either change to TCAs or consider concomitant use ofdiazepam (5-10mg /day) for a brief period (1 week).

- If **poor adherence**, identify and try to address reasons for poor adherence (e.g. side-effects, costs, person's beliefs about the disorder and treatment).

- If **inadequate response** (symptoms worsen or do not improve after 4 – 6 weeks): review diagnosis (including co-morbid diagnoses) and check whether medication has been taken regularly and prescribed at maximum dose.

- Switch from one antidepressant to another with care, that is: stop the first medicine; leave a gap of a few days if clinically possible; start the second medicine. If switching is from fluoxetine to TCA the gap should be longer, for example one week.

**Terminating antidepressant medication** (Adapted from WHO mental health GAP interventions guide, 2010)

- **Consider stopping** antidepressant medication when the person (a) has no or minimal depressive symptoms for 9–12 months and has been able to carry out routine activities for that time period.

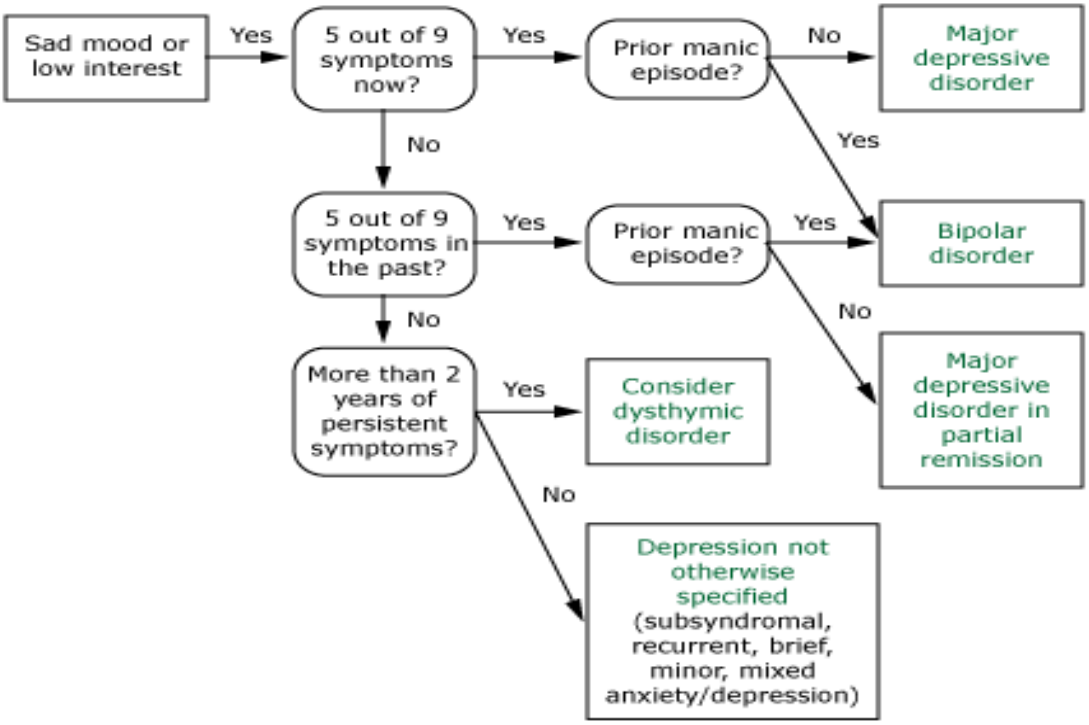
- **Terminate contact** as follows: in advance, discuss with person the ending of the treatment.

    i. For TCAs and most SSRIs (but faster for fluoxetine): Reduce doses gradually over at least a 4-week period; some people may require longer period.
    ii. Remind the person about the possibility of discontinuation/withdrawal symptoms on stopping or reducing the dose, and that these symptoms are usually mild and self-limiting but can occasionally be severe, particularly if the medicationis stopped abruptly.
    iii. Advise about early symptoms of relapse (e.g. alteration in sleep or appetite for more than 3 days) and when to come for routine follow-up.

**II. Bipolar disorders**

- Bipolar I disorder-has episodes of sustained mania, and often experience depressive episodes.
- Bipolar II disorder-has one or more major depressive episodes, with at least one hypomanic episode.
- Recognition of bipolar disorder is important; untreated it is associated with substantial morbidity and mortality, and treatment differs from that of unipolar depression.

**Figure 2-Algorithim for depression**




**Clinical features**

Bipolar disorder is characterised by unpredictable swings in mood from mania (or hypomania) to depression. In bipolar II disorder the full criteria for mania are lacking, the recurrent depressions are separated by periods of mild activation and increased energy (hypomania)**.**

**Diagnostic criteria for manic episode**

A. Distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary).

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1) Inflated self-esteem or grandiosity
2) Decreased need for sleep (e.g. feels rested after only 3 hours of sleep)
3) More talkative than usual or pressure to keep talking
4) Flight of ideas or subjective experience that thoughts are racing
5) Distractibility (i.e. attention too easily drawn to unimportant or irrelevant external stimuli)
6) Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7) Excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, engaging in unrestrained buying, sexual indiscretions, or foolish business investments)

C. The symptoms do not meet criteria for a mixed episode.

D. The mood disturbance 1) is sufficiently severe to cause marked impairment in occupational functioning, usual social activities, or relationships with others, 2) necessitates hospitalization to prevent harm to self or others, or 3) has psychotic features.

E. The symptoms are not due to the direct physiological effects of a substance (eg, a medicine of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism).

**Treatment**

**Objectives**

The objectives of treatment varies based upon the patient's current stage of illness:

- The acute phase
  - Protect patient’s safety, preventing suicide and controlling symptoms.
- The continuation phase (weeks to months)
  - Prevent relapse of the mood episode.
- The maintenance phase (months to years)
  - Prevent recurrence of a new mood episode**.**

**Non pharmacologic**

Psychotherapy-usually cognitive/behavioural

- Supportive psychotherapy
- Group and family therapy

**Pharmacologic**

**Acute mania, hypomania or mixed state**

**First line**

**Haloperidol**, P.O., initial dose 5 to 15mg/day e or in two divided doses OR 5-10mg IM, QD, depending upon the severity of symptoms

**ADRs:** extrapyramidal symptoms, particularly dystonic reactions and akathisia especially in thyrotoxic patients; epilepsy, acute infections, pregnancy, breastfeeding, renal and hepatic impairment

**C/Is:** impaired consciousness due to CNS depression; bone-marrow depression; phaeochromocytoma; porphyria, basal ganglia disease.

**D/Is:** amitriptyline, carbamazepine, clomipramine, ether (anaesthetic), ethosuximide, halothane, ketamine

**P/Cs:** cardiovascular and cerebrovascular disorders, respiratory disease, parkinsonism

**Dosage forms:** Tablet, 1mg, 2mg, 5mg; Oral liquid, 2ml/ml; Injection, 5mg/ml in 1ml ampoule

**Alternative**

**Lithium**, P.O., starting dose 300mg BID to TID; Dose should be increased by 300 to 600mg every 1-5 days based upon response and tolerability. The goal is to reach to a dose of 900-1800mg/day

**ADRs:** gastrointestinal disturbances, syncope, oliguria, circulatory failure

**C/Is**: cardiac disease, renal impairment or urinary retention, CNS disorders, e.g. epilepsy.

**D/Is:** ACE inhibitors, antithyroid agents of iodides, neuroleptics, non-steroidal anti-inflammatory agents, thiazide and loop diuretics, xanthines.

**P/Cs:** diarrhoea, vomiting and intercurrent infection, pregnancy, breastfeeding, elderly, diuretic treatment

**Dosage forms:** Tablet, 300mg, 400mg

*OR*

**Carbamazepine**, starting dose of 100-200mg P.O., one or two times per day; Dose should be increased by 200mg /day every 1 to 5 days. The goal is a dose of 800 to 1000mg/day.

*OR*

**Sodium valproate**, initial dose.250mg P.O., BID to TID; Dose should be increased by 250-500mg every 1-5 days as tolerated. The goal is a dose of 1500-2500mg/d

**N.B.** For severely sick patients start a **combination** of an antipsychotic (e.g. Haloperidol) with Sodium Valproate or Lithium

CAUTION!

Lithium treatment requires close monitoring of serum level, since the medication has a narrow therapeutic range. In addition, thyroid function must be checked every 6 – 12 months. If laboratory examinations are not available or feasible, lithium should be avoided. Erratic compliance or stopping lithium treatment suddenly may increase the risk of relapse. Do not prescribe lithium where the lithium supply may be frequently interrupted.

**Maintenance therapy-**Most patients require maintenance treatment for years, and many for their entire lives.

**First line**

**Lithium**, P.O., 900-2400mg/day in 3-4 divided doses or 900-1800mg/day in two divided doses of extended release

For inadequate but partial response:

*ADD*

**Sodium valproate,** 750mg/day P.O.,in two-three dived doses; dose should be increased based on response and tolerability; maximum dose: 60mg/kg/day. For extended release use the same dose once daily.

*OR*

**Carbamazepine**, P.O., 400mg/day in 2 divided doses, adjust dose according to response and tolerability by 200 mg/day increments; maximum dose: 1600mg/day

### 3. Schizophrenia

Schizophrenia is a severe psychiatric disorder disorder with chronic or recurrent psychosis and marked functional impairment. It is one of the most disabling and economically catastrophic disorders.

Psychosis is a break with reality with delusions, hallucinations, disorganized or illogical thinking, and chaotic behaviour. Although psychosis is a hallmark of schizophrenia, it is not pathognomonic for the disorder.

**Clinical features**

**'Positive' symptoms**

- Hallucinations
- Delusions
- Incoherent speech or illogicality
- Odd or disorganized behaviour
- Disorders of thought possession

**'Negative' symptoms**

- Poverty of speech or of content of speech
- Apathy
- Reduced social contact or withdrawal
- Flattened effect (showing little facial expressive responses)

Delusions may be persecutory (undue suspicion) or bizarre

Hallucinations – of any sense auditory ones are most common

Disorders of thought possession include feeling of the patient's thoughts being accessible to others.

**Diagnostic subtypes**

**Paranoid** — "Paranoid" in this context does not refer specifically to persecutory delusions or pervasive suspiciousness, but rather to any type of delusion or hallucination.

**Disorganized** — Patients with the disorganized subtype, characterised by prominent disorganization of thought and bizarre or inappropriate affect, are most impacted functionally.

**Catatonic** — Catatonia is a syndrome characterised by lack of interaction with the environment and with specific motor symptoms, including bizarre posturing, maintenance of awkward postures.

**Residual** — Patients may enter extended periods free of prominent positive symptoms, yet continue to experience mild manifestations of illness, including slight illogical thinking, blunted or inappropriate affect.

**Undifferentiated** — The largest group of patients do not fit neatly into one of the other categories or have symptoms that overlap more than one subtype.

**Schizophreniform disorder** — Patients who have all the symptoms of schizophrenia, but for less than six months, are diagnosed with schizophreniform disorder.

**Investigation**

- Clinical

**Treatment**

**Objectives**

- Abolish symptoms and restore functioning to the maximum level possible
- Reduce the chances of recurrence

**Non pharmacologic**

- Supportive psychotherapy
- Rehabilitation

**Pharmacologic**

Antipsychotic medicines are the mainstay of treatment.

**A. Emergency phase**

**First line**

**Haloperidol**, 5-10mg I.M./I.V. over 30-60 minutes. Daily dose may go as high as 40mg.

**Alternative**

**Chlorpromazine** hydrochloride, 25mg, I.M. and raise to 200mg QD for acute attacks

**ADRs:** akathisia, parkinsonian extrapyramidal effects ammenorrhea and gallactorrhea (female), gynecomastia and impotence (in male), hypothermia, weight gain, cholestatic jaundice, corneal opacity.

**C/Is:** severe cardiovascular disease, severe CNS depression, and comatose states.

**D/Is:** alcohol, CNS depressants, tricyclic antidepressants such as amitriptyline, antithyroid agents,

**P/Cs:** respiratory disease, parkinsonism, epilepsy, acute infection, pregnancy, breast-feeding, renal and hepatic impairment, history of jaundice, leucopenia, hypothyroidism,

**Dosage forms:** Tablet, 25mg, 50mg, 100mg; Oral Drop, 25mg/ml in 10ml bottle, 40mg/ml in 10ml and 30ml bottles; Syrup, 25mg/5ml; Injection, 25mg/ml in 1 and 2ml ampoules, 50mg/ml in 2ml ampoule

**B. Stabilization phase**

**First line**

**Haloperidol**, 1-15mg/day P.O.

**Alternative**

**Chlorpromazine**, 75-300mg/P.O., in divided doses.

**C. Maintenance (chronic therapy)**

**First line**

**Haloperidol,** 1-15mg/day P.O.

**Alternatives**

**Chlorpromazine**, 75-300mg/day P.O. QD. in divided doses.

*OR*

**Fluphenazinedecanoate**, 12.5-100mg IM every 3-4 weeks

**N.B.** After 6 months in remission the medicine can be withdrawn for a trial period to see if relapse occurs, at which point therapy is instituted.

**D**. **Adjunct treatment**

Antiparkinsonian medicines should only be used if reactions occur or when antipsychotics are administered at higher doses likely to cause reactions.

**Trihexyphenidyl**, oral, initial 1 mg/day; increase as necessary to usual range: 5-15mg/day in 3-4 divided doses

**ADRs:** Agitation, confusion, dizziness, drowsiness, hallucinations, headache, paranoia, tacicardia, constipation, urinary retention

**C/Is:** None

**Dosage forms:** Tablet, 2mg, 5mg

## 4. Suicide/Self-Harm

Suicide is the act of deliberately killing oneself. It is a psychiatric emergency which requires urgent evaluation and management.

Self-harm is a broader term referring to intentional self-inflicted poisoning or injury, which may or may not have a fatal intent or outcome.

Any person over 10 years of age experiencing any of the following conditions should be asked about thoughts or plans of self-harm in the last month and about acts of self-harm in the last year:

- Depression, bipolar disorder, psychosis, alcohol and medicine use disorders
- Chronic pain
- Acute emotional distress

***Asking about self-harm DOES NOT provoke acts of self-harm. It often reduces anxiety associated with thoughts or acts of self harm and helps the person feel understood. However, try to establish a relationship with the person before asking questions about self-harm. Ask the person to explain their reasons for harming themselves***

**Evaluation and treatment**

- **Observe evidence of self-injury and emergency conditions**
- Look for evidences of poisoning or intoxication, bleeding from self-inflicted wound, loss of consciousness, extreme lethargy-if present provide emergency treatment
- **Assess for an imminent risk of self-harm/suicide-**the presence of one or more of the followings indicate the risk
- Current thoughts or plan to commit suicide or self-harm
- History of thoughts or plan of self-harm in the past month or act of self-harm in the past year
- Severe emotional distress, hopelessness, extreme agitation,violence, uncommunicative behaviour, social isolation

If there is a risk of imment self-harm/suicide, take the following measures:

- Remove means of self-harm.
- Create secure and supportive environment; if possible, offer separate, quiet room while waiting.
- Do not leave the person alone.
- Supervise and assign a named staff member or a family member to ensure safety.
- Attend to mental state and emotional distress.
- Offer and activate psychosocial support
- Maintain regular contact and follow
- **Assess for the presence of mental illness, chronic medical illness, neurologic illness, chronic pain or medicine use disorders**
- Depression, bipolar disorder, alcohol or medicine use disorders, psychosis, behavioural disorders, epilepsy, chronic medical illness.

If any of these predisposing disorders are present, manage them accordingly.

- **Assess for the presence of severe emotional that warrant clinical management**
- Difficulty carrying out usual work, school, domestic or social activities
- Marked distress or repeated help-seeking
- Repeated self-medication for emotional distress or unexplained somatic symptoms

In case of bereavement: support culturally appropriate mourning/adjustment and reactivate social networks.

In case of acute distress after recent traumatic events: offer basic psychological support i.e., listen without pressing the person to talk; assess needs and concerns; ensure basic physical needs are met; provide or mobilize social support and protect from further harm.

**AVOID** psychological debriefing (i.e., **DO NOT** push the person to recount perceptions, thoughts, and emotional reactions experienced during a recent, stressful event)

## CHAPTER XII: RESPIRATORY DISORDERS

### 1. Bronchitis (Acute)

Acute Bronchitis is an infection of the trachea and the bronchi which is often caused by viruses. Therefore, treatment is often symptomatic. Anti-microbial treatment is indicated when patients develop high-grade fever and purulent sputum or when they have an underlying illness like diabetes mellitus,chronic bronchitis and HIV/AIDS.

**Clinical features**

- Productive cough, symptoms of upper respiratory infection, like rinorrhea.
- There may be crepitations and rhonchi on chest auscultation

**Investigations**

- Full blood count
- Chest X-ray
- Sputum gram stain and culture

**Treatment**

**Objectives**

- Relieve symptoms
- Eradicate suspected bacterial infection

**Non pharmacologic**

- Avoid confounding factors like smoking

**For Dry Cough**

**First line**

**Dextromethorphan hydrobromide**,

children 2-6 years; 7.5mg TID or QID

children 6-12 years; 7.5-15mg

adults; 15 – 30mg P.O., TID to QID

**ADRs:** mild dizziness, mild drowsiness, stomach pain

**C/Is:** respiratory failure, acute asthma, in children up to two years of age

**P/Cs:** asthma; chronic, persistent, or productive cough, renal impairment

**Dosage forms:** Tablet, 15mg; Syrups, 5mg/5ml, 7.5mg/5ml, 15mg/5ml
Drops, 15mg/ml

**Alternative**

**Codeine phosphate**,

children; 0.5mg/kg P.O., QID

adults;10-20mg P.O., TID or QID

**ADRs**: dizziness, difficulty with micturation; ureteric or biliary spasm; dependence, sedation, respiratory depression,

**C/Is:** children under 1 year old, productive cough, elderly, respiratory depression, head injury, acute alcoholism, acute asthma

**P/Cs:** asthma, hepatic and renal impairment, history of medicine abuse

**D/Is:** alcohol, CNS depressants, buprenorpine, monoamine oxidase inhibitors, naltrexone, antidiarrhoeal agents

**Dosage forms:** Tablet, 30 mg; Linctus, 15 mg/5ml

**For productive cough**

**Guaifenesin**,

children 2-6 yrs; 50-100mg P.O., QID

children 6-12 yrs; 100-200mg

adults; 200-400mg P.O., QID

**ADRs:** diarrhoea, drowsiness, stomach pain

**C/Is:** hypersensitivity

**P/Cs:** persistent or chronic cough

**D/Is:** heparin

**Dosage forms:** Tablet, 100mg, 200mg; Capsules, 200mg; Syrup, 100mg/5ml

**For infection**

**Antibiotic treatment** is indicated when bronchitis is complicated by bacterial infections. In general, the choice of antibiotics should be based on gram stain result of the sputum.

**First line**

**Amoxicillin**

children; 20 - 40mg/kg/day P.O., in 3 divided doses

adults; 250 - 500mg P.O.,TID

**ADRs:** allergic reaction, GI disturbances

**C/Is:** known hypersensitivity (allergy) to any penicillines.

**P/Cs:** renal impairment, erythematous rashes, chronic lymphatic leukaemia

**D/Is:** probenecid, allopurinol, oral contraceptives, methotrexate, warfarin

**Dosage forms:** Tablet, 500mg; Capsule, 250mg, 500mg;

Injection, 250mg, 500mg in vial; Syrup, 125mg/5ml, 250mg/5ml

**Alternatives**

**Ampicillin**, 500 mg P.O., QD, in 4-divided dose for 5-7 days.

**Dosage forms:** Capsule, 250mg, 500mg; Oral suspension; 125mg/5ml, 250mg/5ml ; Drop, 100mg/ml Injection, (sodium), 250mg, 500mg, 1g in vial.

*OR*

**Sulfamethoxazole+trimethoprim**,

children 6 weeks – 5 months; 100/20mg

children 6 months – 5 yrs; 200/40mg

children 6 – 12 yrs; 400/80mg BID

adults; 800mg/160mg. P.O.BID for 7 days

*OR*

**Erythromycin**,

children; 30-50mg/kg/day P.O. in 4 divided doses; 15-20mg/kg/day IV over 5 minutes in 3-4 divided doses.

adults; 250-500mg P.O. QID for 7 days

**ADRs:** GI disturbances, reversible loss of hearing, recurrent fainting, hypersensitivity, cholestatic, inflammation or phlebitis at injection site

**P/Cs:** pregnancy and breast-feeding, renal and hepatic function impairment, cardiac arrhythmias, porphyria, in neonates less than two weeks risk of hypertrophic pyloric stenosis.

**D/Is:** carbamazepine, chloramphenicol, itraconazole, terfenadin, warfarin, methyl xanthines.

**Dosage forms:** Tablet (stearate), 250mg, 500mg; Capsule, 250mg; Oral suspension, 125mg/5ml, 200mg/5ml, 250mg/5ml; Injection, 50mg/ml in 2ml ampoule

*OR*

**Tetracycline**, 250-500mg P.O., QID, for 5-7 days

**ADRs:** GI disturbances, photosensitivity, skin discoloration, blood dyscrasias.

**D/Is:** aluminium and/or magnesium containing antacids, laxatives, calcium (e.g. milk or other dairy products, eggs) and/or iron supplements, penicillines, or streptomycin.

**P/Cs:** renal function impairment

**C/Is:** pregnant or nursing women, infants and children under 8 years of age

**Dosage forms***:* Tablet, 250mg, 500mg (coated) Capsules, 250mg, 500mg
Injection, 100mg, 250mg, 500mg in vial

*OR*

**Azithromycin,** 500mg P.O., on day 1 followed by 250mg/day on days 2–5

**ADRs:** diarrhoea, abdominal pain, cramping, acute renal failure, allergic reaction, aggressive behaviour, anaphylaxis, angioedema, arrhythmia, cholestatic jaundice, headache, hearing loss, hepatic necrosis

**C/Is:** hypersensitivity to azithromycin

**P/Cs:** hepatic and renal dysfunction, prolonged cardiac repolarization.

**D/Is:** pimozide, phenytoin, ergot alkaloids, alfentanil bromocriptine, carbamazepine, cyclosporine, digoxin, disopyramide, triazolam; nelfinavir, aluminium and magnesium containing antacids.

**Dosage forms:** Capsule, 250mg; Powder for oral suspension, 200mg/5ml

## 2. Bronchial Asthma

Asthma is a clinical syndrome that is characterised by recurrent or persistent symptoms of shortness of breath, wheezing, cough and chest tightness which are usually reversible with bronchodilator treatment or spontaneously. It is associated with variable airflow limitation and airway hyperresponsiveness to endogenous and exogenous stimuli.

**Clinical features**

- Wheezing—high-pitched whistling sounds during expiration. Wheezes are usually recurrent. Lack of wheezes does not exclude asthma.
- Cough-worse particularly at night
- Shortness of breath (breathlessness)
- Chest tightness
- Tenacious mucus-difficult to expectorate
- Symptoms occur or worsen at night
- Tachypnea (fast breathing)
- Wheeze/Rhonchi
- Use of accessory muscles of respiration

**Danger signs during acute attacks:**

- Paradoxical breathing
- Profound diaphoresis
- Cyanosis
- Exhaustion Arrhythmia
- Silent chest on auscultation
- Drowsiness or confusion
- Agitation
- $SPO_2 < 90$ %

**Investigations**

- Spirometry or Peak expiratory flow meter-to confirm the diagnosis and assess severity.
- Chest X-ray-is not routinely needed. It is indicated when superimposed pneumonia is strongly suspected or when there is evidence of complications (Pneumothorax)
- The diagnosis of bronchial asthma is mainly clinical.
- Confirmation of diagnosis is done by demonstrating airflow obstruction and its reversibility with bronchodilators with spirometer or peak expiratory flow meter.

**Treatment of acute asthma attack**

**Objectives**

- Prevent respiratory failure
- Relieve symptoms promptly
- Shorten hospital stay

**Non-pharmacologic**

1. **Hospital admission-**Admit patients with any feature of a severe attack persisting after initial treatment in the emergency room to wards. Admit patients with life threatening attacks directly to ICU.
2. **Oxygen-**give supplementary oxygen via face mask or nasal cannula to all hypoxic patients with acute asthma to maintain a SpO2 level of >90%. Lack of pulse oximetry should not prevent the use of oxygen.
3. **Positioning-**sitting upright and/or leaning.
4. **Hydration**-most patients need IV hydration.

CAUTION!
Do not give any form of sedatives during acute attacks

**Pharmacologic**

**First line**

**Salbutamol**, 4 to 6 puffs every 20 minutes in the first 1-4 hours. Then the same dose every 1-4 hours depending on the patient need.

*OR*

**Salbutamol**, 2 –5mg every 20 minutes for 3 doses, then 2.5–10mg every 1–4 hours as needed, or 10–15mg/hour continuously

**ADRs:** headache, nervousness, dizziness, palpitation, tachycardia, fine tremor, muscle cramp, paradoxical broncho-spasm.

**C/Is:** cardiac arrythmias

**Dosage forms:** Oral inhalation (aerosol) preparation, 100mcg per dose; tablet, 2mg, 4mg; syrup, 2mg/5ml; nebulizer solution, 5mg/5ml, 20ml ampoule.

*PLUS*

**Ipratropium bromide**, 4–8 puffs every 20 minutes as needed up to 3 hours, 0.25–0.5mg every 20 minutes for 3 doses, then as needed.

**ADRs:** urinary retention, constipation, tachycardia, palpitations and arrhythmias, hypersensitivity reactions, including uriticaria, angioedema, anaphylaxis.

**D/Is:** anticholinergics.

**P/Cs:** prostatic hypertrophy; pregnancy; acute angle closure glaucoma.

**Dosage forms:** Aerosol Solution, 20mcg/metered; Inhalation; 400mcg/metered inhalation

**N.B.** It should be additional therapy to SABA. Can be mixed with SABA during nebulization.

*OR*

**Aminophylline**, IV 250mg IV bolus slowly over 20 minutes

Maintenance: 0.5mg/kg/hour (maximum: 900mg/day). For patients cardiac decompensation, cor pulmonale, hepatic dysfunction, Multiorgan dysfunction decrease dose by 50%.

Old patients (>60 years): 0.38 mg/kg/hour (maximum: 400mg/day).

**ADRs:** Arrhythmia, GI disturbances, headache, irritability, nervousness, insomnia, and tremor.

**C/Is:** Ischemic heart disease, epilepsy, hyperthyroidism, Heart Failure

**Dosage form:** 250mg/10ml in 10 and 20ml ampoule

**N.B.** Should not be first line therapy in the presence of inhaled SABA. Adding it on top of inhaled SABA does not have significant benefit.

Caution !
When giving Aminophylline to adults who have been on Theophylline tablets, avoid bolus injection as there is a high risk of cardiac arrhythmias, seizures.

**When there are no other options:**

**Adrenaline**, 1:1000, 0.5ml sc. Repeat after 1/2 if patient doesn't respond.

| | |
|---|---|
| A**DRs:** | Arrythmias, headache, nervousness, dizziness, cardiac |
| **C/Is:** | cardiac arrythmias |
| **Dosage forms:** | injection, 0.1% in 1ml ampoule |

*PLUS*

**Systemic steroids**

**Hydrocortisone**, 200mg IV as a single dose. Further IV doses are needed only if oral dosing is not possible (100mg, IV, 3-4 X per day).

| | |
|---|---|
| **ADRs:** | GI disturbances, hyperglycemia, headache, and psychiatric reactions |
| **P/C:** | hypertension, infection, diabètes, osteoporosis |
| **Dosage forms:** | Tablet (acetate), 5mg, 10mg,; powder for injection; 25mg/ampoule, 500mg vial; injection (sodium succinate), 50mg/ml in 2ml ampoule, 125mg/ml |

*Followed by*

**Prednisolone**, 40-60mg P.O., should be started immediately, for 5-7 days. Discontinuation does not need tapering.

| | |
|---|---|
| **ADRs:** | GI disturbances, osteoporosis, proximal myopathy; adrenal suppression, Cushing's syndrome;,immunosuppression, psychiatric complications, glaucoma. |
| **C/Is:** | systemic infection; use of live vaccines |
| **P/C:** | Use the lowest effective dose for the shortest period possible; withdraw gradually after systemic use. |
| **Dosage forms:** | Tablet, 1mg, 3.5mg, 5mg, 10mg; |

**Maintenance therapy for chronic asthma in adults**

**Objectives**

- Prevent chronic and troublesome symptoms
- Minimize use of inhaled SABA for quick relief of symptoms

- Maintain (near) normal pulmonary function
- Maintain normal activity levels.
- Prevent recurrent exacerbations
- Minimize adverse effects of therapy

**Non pharmacologic**

- Avoid identified allergens and smoking

**Pharmacologic**

- Depends on the severity of asthma
- Assess the severity of asthma and scale up or down treatment based on the severity.

**Intermittent asthma**

**First line**

**Salbutamol**, inhaler 200microgram/puff, 2 puffs to be taken as needed but not more than 3-4 times a day, or tablet, 2-4mg 3-4 times a day

**Alternative**

**Ephedrine + Theophylline,** 11mg + 120mg P.O., BID OR TID

| | |
|---|---|
| **ADRs:** | GI disturbances, headache, irritability, nervousness, insomnia, tremor |
| **C/Is:** | hypertension, ischemic heart disease, epilepsy, hyperthyroidism, congestive cardiac failure |
| **Dosage forms:** | Tablet, 120 mg theophylline+11 mg ephedrine; Elixir, 6mg+30mg in each 5ml; Syrup, 2.24% + 0.30% |

**Persistent mild asthma**

**Salbutamol**, inhaler, 200micro gram/puff 1-2 puffs to be taken, as needed but not more than 3-4 times/day, or tablet, 2-4mg 3-4 times a day

*PLUS* (Inhaled corticosteroid)

**Beclomethasone**, oral inhalation 200µg, BID. Decrease the dose to 100µg, BID if symptoms are controlled after three months.

| | |
|---|---|
| **ADR:** | GI disturbances, hyperglycemia, headache, and psychiatric reactions |
| **C/Is:** | hypertension, infection, diabetes, and osteoporesis |

**Dosage forms:** oral inhalation (aerosol), 50 mcg/dose, and 100 mcg/dose

**Persistent moderate asthma**

**Salbutamol**, inhalation 200/puff 1-2pμg/puffs as needed PRN not more than 3-4 times a day.

*PLUS* (Inhaled corticosteroid)

**Beclomethasone**, oral inhalation 200μg, BID. Decrease the dose to 100μg, BID if symptoms are controlled after three months.

*OR* (Preferred if symptoms are mor severe or if response is not optimal to Beclomethasone )

**Fluticasone/Salmeterol**, 250/50μg oral inahalation, BID

**Dosage forms:** 250/50 μg per dose, 500/50 μg per dose

*PLUS* (if required)

**Ephedrine + Theophylline**, 11mg + 120mg P.O., BID OR TID

**Severe persistent asthma**

**Salbutamol,** inhalation 200/puff 1-2pμg/puffs as needed PRN not more than 3-4 times a day.

PLUS (Inhaled corticosteroid)

**Beclomethasone**, oral inhalation 200μg, BID. Decrease the dose to 100μg, BID if symptoms are controlled after three months.

*OR* (Preferred if symptoms are mor severe or if response is not optimal to Beclomethasone)

**Fluticasone/Salmeterol**, 250/50μg oral inahalation, BID

**Dosage forms:** 250/50μg per dose, 500/50μg per dose

*PLUS*

**Ephedrine + Theophylline**, 11mg + 120mg P.O., BID OR TID

*PLUS* (if required)

**Prednisolone**, 5-10mg P.O., QOD. Doses of 20-40mg daily for seven days may be needed for short-term exacerbations in patients not responding to the above treatment.

### 3. Chronic Obstructive Pulmonary Disease (COPD)

Chronic obstructive pulmonary disease (COPD) is characterised by chronic air flow limitation that is not fully reversible and a range of pathological changes in the lung. The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease and parenchymal destruction, the relative contributions of which vary from person to

person. COPD is generally a progressive disease. Cigarette smoking is the most common risk factor. Indoor air pollution, especially from burning biomass fuels in confined spaces, is associated with increased risk for COPD in developing countries, especially among women. Occupational dusts and chemicals (vapors, irritants, and fumes) are known to be risk factors for COPD.

COPD is staged based on the severity of airflow limitation and clinical feature

**Clinical features**

- Dyspnea: progressive, worse with exercise, persistent (present every day)
- Chronic Cough-intermittent and may be nonproductive.
- Chronic sputum production: production may indicate COPD
- Wheezes and chest tightness
- Cyanosis
- Expiratory wheezes and decreased breath sounds on auscultation
- Raised JVP, enlarged liver and edema when right side Heart Failure develops

**Investigations**

- CBC
- Chest X-ray
- Spirometry
- Echocardiography (in severe or very severe disease)
- Chest CT-scan (when other the diagnosis is doubted)

**Table 58-Spirometric Classification of COPD Severity Based on Post-Bronchodilator**

**(Adapted from global strategy for the diagnosis,management, and prevention of chronic obstructive pulmonary disease,2006)**

| Stage | Spirometric finding | Clinical features |
|---|---|---|
| **Stage I: Mild** | FEV1/FVC < 0.70 | Chronic cough and sputum production may be present, but not always |
| **Stage II: Moderate** | FEV1/FVC < 0.70 | Shortness of breath on exertion |
| **Stage III: Severe** | FEV1/FVC < 0.70 | Worsening shortness of breath reduced exercise capacity, fatigue, exacerbations that almost always have an impact on patients' quality of life |
| **Stage IV: Very Severe** | FEV1/FVC < 0.70<br>FEV1 < 30% predicted or FEV1 <50% predicted plus chronic | Respiratory failure SPo2 < 90%<br>Signs of core pulmonale |

**Treatment**

**Objectives**

- Relieve symptoms and improve exercise tolerance
- Prevent disease progression
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality

**Non pharmacologic**

- Stop smoking
- Decrease indoor and outdoor air exposure to airway irritants and polluted air
- Pulmonary rehabilitation

**Pharmacologic**

**Management of acute exacerbations**

**Chronic therapy**

**Step up the treatment based on the severity of COPD**

I. **Mild COPD**

- Rapid-acting bronchodilator when needed

II. **Moderate COPD**

- Add regular treatment with one or more long-acting bronchodilators
- Add pulmonary rehabilitation (including exercise training)

III. **Severe COPD**

- Add medium- to high-dose inhaled steroids

IV. **Very severe COPD-**

- Long-term oxygen if chronic respiratory failure
- Consider surgical referral

**Inhaled ß2 agonist**

**Salbutamol**, MDI, 200mcg 6 hourly as needed using a spacer.

*PLUS*

**Inhaled corticosteroids and long acting inhaled beta-2 agonist**

**Beclomethasone**, oral inhalation 200µg, BID. Decrease the dose to 100µg, BID if symptoms are controlled after three months.

*OR* (Preferred if symptoms are mor severe or if response is not optimal to Beclomethasone)

**Fluticasone/Salmeterol,** 250/50µg oral inahalation, BID

**Dosage forms:** 250/50µg per dose, 500/50µg per dose

*PLUS*

**Theophedrine (Ephedrine + Theophylline),** P.O., 131mg 12 hourly.

**Doasage forms:** Tablet, 11mg + 120mg

*PLUS*

**Long term home $O_2$** (>15 hrs per day) For patients with resting hypoxemia with signs of pulmonary hypertension or right Heart Failure , the use of $O_2$ has been demonstrated to have a significant impact on mortality rate.

**Management of Acute exacerbation**

1. **Oxygen** via nasal cannula or facemask for hypoxic patients to keep $O_2$ saturation above 90%

*PLUS*

2. Short-acting beta2 agonists
   **Salbutamol**, MDI, 200 mcg 6 hourly as needed using a spacer

*PLUS*

3. **Corticosteroids**
   **Prednisolone,** 30- 40mg/day or its equivalent for 7-14

*PLUS*

4. **Antibiotic therapy** in patients with a moderate to severe COPD exacerbation (increased dyspnea, increased sputum volume, or increased sputum purulence or requiring hospitalization)

**First line for moderate exacerbation managed as out patient**

**Doxycycline**, 100mg, P.O., BID for 7 days

*OR*

**Azithromycin**, 500mg, P.O., daily for 3days

*OR*

**Clarithromycin**, 500mg, P.O., BID for 7 days

If there is high risk for Pseudomonas (frequent use of antibiotics, recent admission and frequent use of antibiotics)

*PLUS*

**Ciprofloxacin**, 500mg, P.O., BID for 7 days

**Alternative**

**Cefuroxime**, 500mg, P.O., BID for 7 days

*OR*

**Amoxicillin /Clavulanate**, 500/165mg, P.O.,TID for 7 days

**For severe exacerbations requiring hospitalization**

**Ceftriaxone**, 1gm, IV, BID for 7-10 days or until discharge whichever is shorter. On discharge change to oral antibiotic mentioned above.

*PLUS*

**Doxycycline**, 100mg, oral, BID

*OR*

**Clarithromycin**, 500mg, oral, BID

### 4. Pneumocystis Carinni (P. Jiroveci) Pneumonia

PCP frequently causes pneumonia among immuno-compromised individuals. It is caused by the fungus *Pneumocystis jiroveci*. The onset is typically suba-cute over 2 to 4 weeks, with prominent symptoms of fever, non-productive cough, progressive dyspnoea, and fatigue. Patients will have an increasing tachypenia, tachycardia and cyanosis as the disease progresses.

**Clinical features**

- The clinical presentation of PCP is non-specific. Therefore, it should always be considered in those patients with evidence of moderate to severe immuno-suppresion who come up with cough, progressive dyspnea or fatigue.

**Investigations**

- Demonstration of the organism in secretions or tissue by using appropriate stain (sputum)
- Chest X-ray

**Treatment**

**Objectives**

- Suppress multiplication of the organism
- Relieve symptoms.

**Non pharmacologic**

- Oxygen should be given in moderate and severe cases.

**Pharmacologic**

**First line**

**Trimethoprim+Sulphamethoxazole**, 15-20mg/kg/day based on the trimethoprim component and administered in divided in three or four divided doses for 21 days.

Usual dosage-4 single strength (480mg) tabs, P.O., TID OR 2 double strength (960mg), P.O., TID

Give the same medicine IV if the patient is not able to swallow the medicine.

**N.B.** Pay due attention to side effects which at times could be life threatening. Steven Johnson syndrome may occur if the patient is allowed to take the medicine after the development of rash.

**Alternative**

**Clindamycin,** 300-450mg P.O., TID for 3 weeks

*PLUS*

**Primaquine,** 30mg base P.O., QD for 3 weeks.

**N.B.** Typically a mild rash with fever develops 7 to 10 days after initiation of therapy. Bone marrow suppression may occur, and CBC monitoring is useful. Possible hepato-toxicity and nephro-toxicity may also be evaluated at the third week of therapy.

*OR*

**Pentamidine Isethionate,** 4mg/kg I.V. QD for three weeks. It should be given to those who fail to tolerate the above regimen.

*OR*

**Dapsone,** 100mg P.O., QD for 3 weeks

*PLUS*

**Trimethoprim**, 20mg/kg administered P.O., in divided doses QID for 3 weeks.

**Adjuvant treatment**

Corticosteroids – Indicated if SPO2< 90%, while breathing room air as measured by pulse oximetry before or in the course of treatment. In the absence of pulse oximetry, clinical judgement should be used to select moderatly to severely sick patients who benefit from corticosteroids.

Regimen

- **Prednisolone** 40mg BID for 5 days,
- Then 20mg BID for 5 days,
- Then 20mg QD until therapy is complete (for 11 days).
- No tapering from the 20 mg dose is necessary.

If the patient can not tolerate oral corticosteroid, an equivalent dose of intravenous hydrocortisone or dexamethasone can be given until the patient can can take oral medication.

**Prophylaxis**

Primary prophylaxis against PCP should be commenced in patients with HIV infection with the following conditions:

- When the CD4 cell count drops below 350cells/ml or
- When there are clinical signs of advanced immune deficiency

**The following regimen is recommended:**

**First line**

**Trimethoprim+Sulphamethoxazole** One double strength tablet P.O., QD OR 3 times weekly.

**Alternatives**

**Dapsone**, 100mg P.O., QD

*OR*

**Aerosol pentamidine** 300mg via nebulizer every 4 weeks.

**N.B.** Secondary prophylaxis should be continued for all patients who have completed a full course treatment for PCP.

## 5. Pneumonia

Pneumonia refers to acute inflammation of the distal lung-terminal airways, alveolar spaces, and interstisium. The clinical presentation and the etiology vary greatly depending on the age of the patient, the infecting organism, the site/s the infection has involved, the immune status of the patient and the place of acquisition of infection.

**Microbiology of Pneumonia**

**Community acquired-*S. pneumoniae*** *Mycoplasma*, *Chlamydia,* viral (espec. in young & healthy), *H. influenzae*, *M. catarrhalis* (espec. in COPD'ers), *Legionella* (espec. in elderly, smokers, T immunity), *Klebsiella* & other GNR (espec. in alcoholics & aspirators), *S. aureus* (espec. post-viral infection), Influenza A & B et al. (see "Viral Respiratory Infections"), (no organism identified in 40–60% cases)

**Hospital acquired-**GNR including *Pseudomonas*, *Klebsiella*, *E. coli, Enterobacter*,*Serratia*, *Acinetobacter*, & *S. aureus* (including MRSA), Acid suppression may increase risk of acquiring PNA

**Immunosuppressed** *Above* + PCP, fungi, *Nocardia*, atypical mycobacteria, CMV, HSV

**Aspiration** *Chemical pneumonitis* due to aspiration of gastric contents, *Bacterial pneumonia* 24–72h later, due to aspiration of oropharyngeal microbes. Outpatients: typical oral flora (*Strep*, *S. aureus,* anaerobes); Inpatients or chronically ill: GNR and *S. aureus*

**Clinical features**

**"Typical":** acute onset of fever, cough with purulent sputum, dyspnea, consolidation on CXR

**"Atypical":** (originally described as culture negative): tends to present with insidious onset of dry cough, extrapulm symptoms (N/V, diarrhoea, headache, myalgias, sore throat), patchy interstitial pattern on CXR, and elevated transaminases & low serum Na with *Legionella.*

Signs, symptoms & imaging do *not* reliably distinguish between "typical" (*S. pneumo*, *H. flu*) and "atypical"(*Mycoplasma*, *Chlamydia, Legionella,* viral)

**Investigations**

**Sputum Gram stain**: Utility debated and is not routinely recommended. Is it a good sample (ie, sputum or spit)? Should be <10 squamous cells/low power field. Is it a purulent sample? Should be >25 PMNs/lowpower field.

**Sputum bacterial culture**: In selected situations particularly in the inpatient setup. Should be transported to lab with in 1–2h of collection. In select situations, consider respiratory viral testing (DFA or PCR), rarely viral culture.

**Blood cultures (*before antibiotics!*):** Positive only in about 10% of inpatients, depending on pathogen

**CXR (PA & lateral):** This is the most important investigation for the diagnosis of pneumonia.

**Pleural fluid analysis**: If >5 cm or severe pneumonia.

**Other labs**: SaO2 or PaO2, CBC with diff, electrolytes, BUN/Cr, serum glucose, LFTs; etc.

**Other microbiologic studies** (paired serologies available for most atypicals):

*Mycoplasma*: PCR of throat or sputum/BAL *before* first dose antibiotic.

*Legionella*: urine Ag (detects *L. pneumophila* L1 serotype, 60–70% of clinical disease)

*S. pneumoniae* urinary Ag (Se 50–80%, Sp _90%)

**MTB:** expectorated/induced sputum for AFB stain and mycobacterial culture (*empiric respiratory isolation while pending*); avoid quinolones if considering TB;

**Induced sputum for PCP if HIV+** or known T cell-mediated immunity; HIV test

**Bronchoscopy**: available only in specialized hospitals. useful in patients with difficulty of producing sputum samples and when other alternative diagnosis is considered.

**Treatment**

**Objectives**

- Treat the infection.
- Prevent complications.

Identify those that are at high risk and may require hospitalization. Ther CURB-65 scoring systems suggested to evaluate the prognosis and determine subsequent management:

**CURB-65**

**C-**Confusion=1point

**U-**Uremia: BUN >19mg/dL=1point

**R-**RR >30/min= 1point

**BP** <90/60=1point

**Age**≥65=1point

If score is 1point, it is ok to give outpatient treatment. If the score is greater than 1 point, the patient needs hospitalization. The higher the score, the higher the mortality.

**Non pharmacologic**

- Bed rest
- Adequate hydration

**Pharmacologic**

**Community acquired ambulatory patients (Mild Pneumonia):**

**First line**

**No recent antibiotic use:**

**Clarithromycin**, 500mg P.O., BID for 5-7 days

*OR*

**Azitromycin,** 500mg P.O., first day then 250mg P.O., for 4d.

*OR*

**Doxycycline,** 100mg P.O., BID for 7-10 days.

**If recent antibiotic use within 3months:**

**Clarithromycin,** 500mg P.O. BID for 5-7 days

*OR*

**Azitromycin,** 500mg P.O first day then 250mg P.O., for 4d.

*PLUS*

**Amoxicillin,** 1000mg P.O., TID for 5 to 7 days.

*OR*

**Amoxicillin-clavulanate,** 625mg P.O., TID for 5-7days

**Community acquired hospitalized patients (Severe Pneumonia)**

**Non-pharmacologic**

- Bed rest
- Frequent monitoring of temperature, blood pressure and pulse rate in order to detect complications early and to monitor response to therapy.
- Give attention to fluid and nutritional replacements.
- Administer Oxygen via nasal prongs or face mask

**Pharmacologic**

The Antibiotic choice should be aimed at the most likely causative agent.

**Empiric treatment for pneumonia due to common organisms:**

**First line**

**Ceftriaxone,** 1g I.V. OR I.M every 12-24 hours for 7 days.

*OR*

**Benzyl penicillin**, 2-3 million IU I.V. QID for 7-10 days.

*PLUS*

**Azithromycin,** 500mg on day 1 followed by 250mg/day on days 2 – 5

*OR*

**Clarithromycin,** 500mg P.O., BID for 7-10 days

**N.B.** In a situation of beta lactam allergy, respiratory fluoroquinolones (moxifloxacin or levofloxacin) can be used. As these medicines are second line medicines for Tuberculosis, they should only be used when it is absolutely important.

**Hospital acquired pneumonias (Nosocomial Pneumonias):**

The antibiotic choice should depend on the epidemiology and susceptibility of local pathogens. Empiric treatment should include antimicrobials effective against resistant gram-positive and gram-negative organisms particularly *S.aureus* and *P.aeruginosa*. The following are possible combinations:

**Empiric treatment for commonly suspected etiologies of HAP**

**First line**

**Ceftazidime,** 1gm I.V. TID for 10-14days

*PLUS*

**Vancomycin** 1g I.V. BID for 10-14 days

*OR* (particularly in the ICU setup and in ventiltor associated pneumonia)

**Imipenem-cilastatin**, 500mg IV (infused slowly over 1hour) Q6h

*OR*

**Meropenem**, 1gm IV (infused slowly over 30min) Q8h

**Alternatives**

**Ceftriaxone,** 1-2g I.V. OR I.M. BID for 7 days.

*PLUS*

**Gentamicin**, 3-5mg/kg I.V. QDdaily in divided doses for 7 days**.**

*OR*

**Ciprofloxacin**, 500mg P.O./I.V. BID every 12 hours for 7 days**.**

**If methicillin-resistant (MRSA) suspected**

**Vancomycin**, 1 g I.V. BID should be added to the existing empric regimen

**N.B.** All empiric regimens are subject to modification on the arrival of microbiologic results and other evidences. De-escalation to narrow spectrum antibiotics and oral regimens are always encouraged in the appropriate circumstances.

## 6. Empyema And Complicated Parapneumonic Effusions

Empyema refers to invasion of the pleural space by significant number of bacteria resulting in pus and/or positive gram stain or culture from pleural fluid. Pleural fluid culture can sometimes be negative even in grossly pussy pleural fluid.

Complicated paraneumonic effusion occurs when there is envasion of the pleural space by bacteria but pleural fluid culture and gram satina are negative due to rapid clearance of the

bacteria. The prescence of one of the following characterstics would indicate the presence of complicated paraneumonic effusion:

- Large pleural effusion->1/2 of the hemithorax
- Loculated pleural effusion
- Pleural effusion with thickened pleura
- Pleural fluid glucose <60mg/dl.

Uncomplicated pleural effusion referes to a sterile exudative pleural effusion which results from the movement of pulmonary interstitial fluid to the pleural space. The interstial fluid result from the pneumonic inflammatory process in the lung paranchyma.

**Investigations (**in addition to the investigations mentioned for pneumonia**)**

- Pleural fluid cell conunt with differential, LDH, Protein, glucose, gram stain, culture and AFB
- Chest ultrasound-useful for suspected loculated pleural effusion
- Chest CT scan-if chest X-ray and ultrasound are not conclusive

- Empyemas and complicated parapneumonic effusions require chest tube drainage in addition to proper antiobiotic treatment. Multi loculated pleural effusions require thoracoscopic or open surgical drainage and debridement.
- Uncomplicate parapneumonic parapneumonic effusion requires proper antibiotic treatment as mentioned for Pneumonia and obseravation alone.

## 7. Aspiration Pneumonia And Lung Abscess

Aspiration pneumonia is a pulmonary reaction resulting from the abnormal entry of fluid, particulate exogenous substances, or endogenous secretions into the lower airways. Most cases arise following gross "aspiration" of microorganisms from the oral cavity or nasopharynx. If untreated, pneumonia may complicate to lung abscess, necrotizing pneumonia, or empyema secondary to a bronchopleural fistula.

Lung abscess refers to a localized area of destruction of lung parenchyma, which results in tissue necrosis and suppuration. Anaerobic bacteria such as *Peptosterptococci, Fusobacterium nucleatum, and Prevotella melaninogenica* are found in about 90% of lung abscesses and are the only organisms present in about half of cases. Pathogens that commonly produce pneumonia, such as *Streptococcus pneumoniae, Haemophilus influenzae, gram-negative bacilli, and Staphylococcus aureus* may cause lung abscess.

**Clinical features**

- Fever
- Cough with expectoration of copious malodorous sputum

**Investgations**

- Chest X-ray confirms the diagnosis in the majority of patients.
- Gram stain and culture help to identify the specific causative agent.
- AFB and KOH examination of sputum should be done if TB or fungal causes are considered.

**Treatment**

**Objectives**

- Treat abscess collection
- Treat underlying disease

**Non pharmacologic**

- Chest physiotherapy and postural drainage
- Surgery in selected cases

**Pharmacologic**

**Aspiration pneumonia:**

**First line**

**Benzyl penicillin**, 1-2 million IU I.V. OR I.M. every 4-6 hours for about 10-14d.

*OR*

**Ceftriaxone**, 1-2g I.V. BID for 10-14d

*PLUS*

**Metronidazole**, 500mg I.V. every 8-12 hours for 10-14 days**.**

*OR*

**Clindamycin**, 600mg I.V. TID for 14 days.

**Alternatives**

**Amoxicillin + clavulanic acid,** 500mg + 125mg, I.V. TID for 10-14 days

**Lung abscess:**

**First line**

**Benzyl penicillin**, 1-2 million IU I.V. OR I.M. every 4-6 hours for about 4 weeks or until the abscess radiologically resolves

*OR*

**Ceftriaxone**, 1-2g I.V. BID for 4-6weeks or until the abscess radiologically resolves

PLUS

**Metronidazole**, 500mg I.V. every 8-12 hours for 4-6weeks or until the abscess radiologically resolves

*OR*

**Clindamycin**, 600mg I.V. TID for 4-6weeks or until the abscess radiologically resolves

**Alternatives**

**Amoxicillin + clavulanic acid**, 500mg + 125mg, I.V. TID for 4-6 weeks or until the abscess radiologically resolves

**N.B.** There is no generally agreed-on duration for the treatment of lung abscess. Patients often are treated for 6 to 8 weeks or longer. Do weekly or biweekly chest radiographs in patients showing clinical improvement, with discontinuation of therapy when the radiograph is clear or there is a small, stable, residual lesion.

**Parenteral-to-Oral Switch of antibiotics**: After treatment with intravenous antibiotics for the first 2-3weeks or until significant resolution of symptoms, patients can be treated with oral antibiotics until the end of treatment. The following medicines are preferred:

**First line**

**Clindamycin**, 600mg P.O., TID

**Alternative**

**Amoxicillin + clavulanic acid**, 500mg + 125mg, P.O., TID

## CHAPTER XIII: EMMERGENCY CONDITIONS

### 1. Anaphylaxis

An acute allergic reaction or anaphylaxis is a life-threatening but rapidly reversible condition if treated promptly. Anaphylaxis can develop within minutes of injection or ingestion of medicines or contact with trigger factors. Common causes are, medicines, intravenous contrast media, vaccines and antisera (e.g. TAT), insect bites, foods (e.g. sea foods, nuts).

**Clinical features**

- Severe itching
- Urticarial rash
- Difficulty in breathing
- Collapse
- Facial edema
- Angio-edema causing difficulty in breathing due to laryngeal edema and obstruction
- Bronchospasm with wheeze
- Shock with severe hypotension
- Tachycardia
- Cyanosis

**Investigation**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Remove the offending cause if possible
- Maintain airways, breathing and circulation

**Non pharmacologic**

- **Airway:** Immediate intubation if evidence of impending airway obstruction from angioedema; delay may lead to complete obstruction; cricothyrotomy may be necessary
- **Oxygen:** Give 6 to 8 liters per minute via face mask
- **Circulation:** All patients with anaphylaxis should receive intravenous fluids. Some patients may require large amount of intravenous fluids due shift of intravascular fluid to the interstitial space.
- Adults-1 to 2 liters NS fast, then depending on the patient response to adrenaline and the initial bolus of NS.
- **Position-**recumbent position, if tolerated, and elevate lower extremities
- **Remove-**the offending agent, if possible

**Pharmacologic**

**Adrenaline**, IM, 0.5ml (500microgram) of 1:1000 at mid-anterolateral thigh; can repeat every 3 to 5 minutes as needed. If symptoms are not responding to epinephrine injections, prepare IV adrenaline (2 to 10 micrograms per minute by infusion)

*PLUS*

**Hydrocortisone**, IV, 200mg, IV, stat; then 100mg 6-8 hourly for 3 – 4 days and discontinue without tapering.

*PLUS*

**Promethazine hydrochloride**, IM, 25mg 8-12 hourly. Then cetirizine 10mg. P.O., once/day OR Loratadine 10mg, P.O., once /day OR Chlorpheniramine 4mg, P.O., QID

*PLUS*

If wheeze develops **Salbutamol**, aerosol, 100μg/dose, 2-4 puffs every 4-6 hr.

## Bites and Stings

### 2. Mammalian And Human Bites

Dog bites-cause a range of injuries from minor wounds (scratches, abrasions) to major complicated wounds (deep open lacerations, deep puncture wounds, tissue avulsions).

Cat bites-scratches typically occur on the upper extremities or face. Deep puncture wounds are of particular concern because cats have long, slender, sharp teeth. When the hand is the target of such a puncture wound, bacteria can be inoculated below the periosteum or into a joint and result in osteomyelitis or septic arthritis.

Human bites – human bites cause a semicircular or oval area of erythema or bruising that is usually visible; the skin itself may or may not be intact.

The predominant organisms in animal bite wounds are the oral flora of the biting animal (notable pathogens include Pasteurella, Capnocytophaga, and anaerobes) as well as human skin flora (such as staphylococci and streptococci).

**Clinical features**

- Pain
- Bleeding
- Swelling
- Teeth impression on bitten site
- Foreign body
- Fever
- Tenderness

**Investigations**

– CBC
– X-ray of the affected area if bone involvement
– Ultrasound of the abdomen if visceral involvement suspected
– Culture from the wound discharge

**Treatment**

**Objectives**

- Treat associated infections
- Prevent tissue loss

**Non pharmacologic**

**Wound care**

- The surface should be cleaned with 1% povidone iodine
- Irrigate the depths with copious amounts of saline using pressure irrigation.
- Debridement of devitalized tissue
- Explored to identify injury to underlying structures and presence of a foreign body

**Primary closure**

- Nearly all cat, human and most dog bites are left open (to heal by secondary intention).
- When primary closure is strongly considered because of cosmetic reasons the wound should be:

    - Clinically uninfected,
    - Less than 12 hours old
    - NOT located on the hand or foot

**Pharmacologic**

**Antibiotic prophylaxis**

Indications

- Deep puncture wounds
- Associated crush injury
- Wounds on the hand(s) or in close proximity to a bone or joint
- Wounds requiring closure

Bite wounds in compromised hosts (eg, immunocompromised and adults with diabetes mellitus**)**

**First line**

**Amoxycillin-clavulanate**, 500/125mg, P.O., TID for 3-5 days

**Alterantive**

**Doxycycline**, 100mg, P.O., BID for 3-5 days

*OR*

**Cotrimoxazole** 960mg, P.O., BID for 3-5 days

*OR*

**Cefuroxime** 500mg, P.O., BID for 3-5 days

*PLUS*

**Metronidazole** 500mg, P.O., TID for 3-5 days

**Cloxacillin and cephalexin should be avoided in human, dog or cat bites**

**1. Infection treatment**

For infected wound use the above antibiotics mentioned for prevention but for prolonged duration 10-14 days

**2. Tetanus and Rabies prevention**

**Tetanus toxoid (TT)**, I.M.0.5ml once, for primary or booster immunization

**TAT** (Tetanus Antitoxin), 3000 units, sc,stat, for all adults with animal or human bites except for those with clean and minor wounds after skin test

**Rabies prophylaxis** both passive administration of rabies immune globulin (with as much of the dose as possible infiltrated into and around the wound) and active immunization – for the details see section on Rabies.

**3. Snake Bites**

The majority of snakebites are non–poisonous; only few species are venomous (poisonous). Most common venomous snakes are the pit vipers (vasculotoxic) and the elapidae and hydrphidae (primarily neurotoxic).

Children, because of their smaller body size, are far more likely to have severe envenomination.

**Clinical features**

- Cranial nerve paralysis-ptosis, opthalmoplegia, slurred speech
- Bulbar respiratory paralysis-drooling, and inability to breath properly
- Impaired consciousness, seizures
- Meningism
- Tender and stiff muscles
- Rapid progression of swelling to more than half of bitten limb
- Blistering, necrosis and bruising
- Fascial compartmentalization on bitten digits.

**Investigations**

- CBC
- BUN and Creatinine, electrolytes
- 20 minutes whole blood clotting test (leave 2-5ml of blood in dried test tube. Failure to clot after 20 minutes implies incoagulable blood)
- Liver function test

**N.B.** Avoid venopuncture in state of generalised bleeding

**Treatment**

**Objectives**

- Relieve pain and anxiety
- Rupport the respiration or circulation if indicated
- Counteract the spread and effect of the snake venom
- Prevent secondary infection

**Non pharmacologic**

**First Aid**

- Immobilization/splinting of the affected limb.
- Do not move the limb
    - Carry the person on a stretcher and tie the limb to a straight piece of wood.
    - If ice is available, wrap pieces in cloth and place it around the bite.
    - Clean the wound and reassure the patient.

**At the hospital**

- Bed rest, reassure, keep warm
- Assess patient's airway, breathing and circulation (ABC of resuscitation)
- For probable venomous bites:
    - Clean site of bite with antiseptic lotion or soap and water
    - Do not attempt to suck or make any incisions at the site of the bite
    - Leave wound open; punctured wounds are especially likely to be infected.

- If the snake is identified as non-poisonous or there is absence of swelling or systemic signs after 6 hours reassure the patient
- Surgical debridement when required

**Pharmacologic**

**Secondary infection**:

**First line**

**Amoxicillin/clavulanic acid,** oral, 500/125mg, TID for 5-7 days.

**Immunization, primary or booster**:

**Tetanus toxoid vaccine**, IM, 0.5mL immediately.

**Analgesia**

***For mild pain:***

**Paracetamol**, 1 g 4–6 P.O., hourly when required to a maximum of 4 doses per 24 hours.

***For severe pain:***

*ADD*

**Tramadol**, 50-100mg, 2-3X per day

**N.B.** The use of an NSAID is not recommended due to the potential danger of Acute Kidney Injury in a hypotensive patient.

**Polyvalent antivenom**

Indications for polyvalent antivenom:

- Any sign of systemic toxicity or extensive swelling.
- All patients with confirmed mamba bites before symptom onset
- Patients with confirmed puff adder or Gaboon adder bites should receive antivenom at the onset of any symptoms

**N.B.**

- In most cases patients do not need and should not be given antivenom.
- The dose of antivenom is the same for adults and children.
- Serum sickness is a relatively common adverse event.
- Even after the administration of antivenom, patients with neurotoxic snakebites may need ventilation.

Polyvalent snake antivenom, slow IV infusion. Dilute 100 mL in 300ml of NS.

- Have resuscitation tray ready (adrenaline 1: 1000)
- Test dose-0.2 ml, subcutaneous, to test for anaphylaxis
- Administer slowly for the first 15 minutes, as most allergic reactions will occur within this period.
- Increase the flow rate gradually to complete the infusion within one hour.
- Repeat if there is no clinical improvement after the infusion.
- Mild hypersensitivity reactions should not be a reason not to give polyvalent.

**4. Burn**

Burn is a traumatic injury to the skin or other tissues caused by thermal, chemical, electrical, radiation or cold exposures. Burns are an acute wound and pass through series of healing steps. The most common type of burn in children is from a scald injury; in adults, the most common burn occurs from a flame.

**Table 59-Classification of burns based on the depth of injury** ***(Adapted from, Med Clin North Am 1997 and Am Fam Physician 1992)***

| Depth | Appearance | Sensation | Healing time |
|---|---|---|---|
| **First degree (Superficial)** | Dry (no blister)<br>Erythematous<br>Blanches with pressure | painful | 3-6 days |
| **Second degree (partial-thickness)-superficial** | Blisters<br>Moist, red, weeping<br>Blanches with pressure | Painful (even to air) | 7 to 21 days |
| **Second degree (partial-thickness)-deep** | Blisters (easily unroofed)<br>Wet or waxy dry<br>Variable color (cheesy white to red)<br>Does not blanch with pressure | Senses pressure only | Perceptive >21 days-requires surgical treatment |
| **Third degree(full thickness)** | Waxy white to gray or black<br>Dry and inelastic<br>No blanching with pressure | Deep pressure only | Rare, unless surgically treated |
| **Fourth degree(extending beyond the skin)** | Extends into fascia and/or muscle | Deep pressure only | Never, unless surgically treated |

A thorough and accurate estimation of burnt surface area is essential to guide therapy.

**Table 60-Burn injury severity grading (modified from the American Burn Association burn injury severity grading system. J Burn Care Rehabil 1990)**

| Burn type | Criteria | Disposition |
|---|---|---|
| **Minor** | <10% TBSA burn in adults<br><5%TBSA burn in young or old<br><2% full-thickness burn | Outpatient |
| **Moderate** | 10-20%TBSA burn in adults<br>5-10% TBSA burn in young or old<br>2-5% full-thickness burn<br>High voltage injury<br>Suspected inhalation injury<br>Circumferential burn<br>Medical problem predisposing to infection (eg, diabetes mellitus) | Admit |
| **Major** | >20% TBSA burn in adults<br>>10% TBSA burn in young or old<br>>5 %full-thickness burn<br>High voltage burn<br>Known inhalation injury<br>Any significant burn to face, eyes, ears, genitalia, or joints<br>Significant associated injuries (fracture or other major trauma) | Refer after emergency management (Make sure the referral center provides burn services) |

TBSA: total body surface area; Young or old: <10 or >50 years old; Adults: >10 or <50 years old

**Treatment**

**Objectives**

- Prevent ongoing burn
- Secure airway and maitain ventilation
- Correction of fluid and electrolyte deficits
- Prevetion and managemnt of infection

- Avoid or minimize permanent disablity

**Non pharmacologic**

**Emergency measures**

- Remove clothing and jewelry.
- Maitain adequate airway and give oxygen via face mask
- Establish an IV line. Insert NG tube and avoid oral fluids in children with burns greater than 15% BSA.
- Insert Foley catheter
- Wrap all wounds with sterile towels unti further decision is made.

**Pharmatorogic management**

**Fluid resuscitation**

- Ringer's lactate or NS 4mL/kg/% BSA burned: 1/2 the fluid is given over the first 8 hrs calculated from the time of onset of the injury and the remaining 1/2 is given at an even rate over the next 16 hrs
- The rate of the infusion is adjusted according to the patient's response to therapy.
- Adequacy of the resuscitation is reflected by vital signs, skin turgor, adequate urine out put (1mL/kg/hr in children and 0.5 mL/kg in adults). Clinical signs of adequate perfusion are monitored every hour for the first twenty-four hours
- During the 2nd 24 hr patients begin to reabsorb edema fluid and to diurese. ½ of the first day fluid requirement is needed as Ringer's lactate in 5% dextrose.
- Oral supplementation may be started after 48hr post burn

**Estimate body surface area of the burnt body-**see annex 15

**Pharmacologic management**

**Wound management**

**Minor burns**

- Treated in an outpatient setting
- Debride all loose skin. Blisters are better not excised

- Cleanse with mild soap and irrigate with isotonic saline.
- The wound is then covered with **Silver sulfadiazine** and properly dressed.
- The first dressing change and dressing evaluations are performed 24-48 hrs after injury

**Silver sulfadiazinecream 1%,** apply daily with sterile applicator

*OR*

**Fusidic acid**, thin films of 2% cream applied to skin 3-4 times daily

**Moderate and Severe burns**

- Do all recommended for minor burns
- Apply local antibiotic or Vaseline coated dressing
- Antibiotic prophylaxis is not recommende unless there is obvious infection.

**Prevention of stress ulcer –** for severe burns only

**First line** for patients who are able to take oral medications

**Omeprazole**, 40mg, oral, daily

**First line** for patients who are unable to take oral medicatoons

**Cimetidine**, 200mg-400mg IV, every 12 hours

**Tetanus prophylaxis**

**Tetanus** immunization should be updated for any burns deeper than superficial-thickness.

**Pain Management:**

**First Line** use depending on pain severity and response in step wise fashion

**Paracetamol**, 500-1000mg P.O., 4-6 times a day

*OR*

**Tramadol** 50-100mg, Slow IV or P.O, 3-4 times daily(maximum 400mg/day)

*OR*

**Morphine hydrochloride injection** (for severe pain only), 10-20 mg IM OR SC, repeat every 4 hours PRN.

*OR*

**Pethidine** 50mg IM every 4 hrs (depending on the need) or 5-10 mg IV 5 minutes

**Systemic antibiotics**

- Not indicated for prophylaxis
- When there is evidence of infection (e.g. persitent fever, leukocytosis) take specimens for culture and start emperic antibiotics based on suspected site of infection. If wound infection is the suspected source of infection emperic antibiotics should cover *Pseudomonas aeruginosa*, other gram negative bacterias and *Staphylococcus aureus*

**Prevention, management and follow up of complications**

- Electrolytes-Hypokalemia, hyponatremia/hypernatremia
- Acute Kidney injury-Correction fluid deficit, avoidance of nephrotoxic medication
- Malnutrition-burn patients require high calorie and high protein diet
- Deep vein thrombosis-Prophylaxis with heparin if patient is immoblized
- Joint Contractures-proper wound care and phsiotherapy
- Psychiatric attention

## 5. Hypoglycemia

Hypoglycemia is a clinical syndrome in which low serum (or plasma) glucose concentrations leads to symptoms of sympathoadrenal activation and neuroglycopenia. Hypoglycemia can cause significant morbidity and may be lethal if not promptly recognized and managed.

**Clinical features**

**Adrenergic symptoms:**

- Sweating, sensation of warmth, anxiety, tremor or tremulousness, nausea, palpitations and tachycardia, and perhaps hunger.

**Neuroglycopenic symptoms:**

- Fatigue, dizziness, headache, visual disturbances, drowsiness, difficulty speaking, inability to concentrate, abnormal behaviour, loss of memory, confusion, and ultimately loss of consciousness or seizures.

The presence of **Whipple's triad**

1. Symptoms consistent with hypoglycemia (see above)
2. A low blood glucose glucose (<55mg/dl) level measured with a precise method (not a glucometer)
3. Relief of those symptoms after treatmentthe plasma glucose level is raised.

**Hypoglycemia unawareness**-absent symptoms (usually related to autonomic diabetic neuropathy)

Major causes of hypoglycemia:

1. In patients with Diabetes Mellitus-Insulin and sulfonylureas excess dose or previous doses with unaccustomed exercise or omission of meals. Development of CKD.
2. In non-diabetic patients with critical illnesses – Hepatic or renal failure, adrenal insufficiency, sepsis, malaria.
3. Seemingly normal patients-endogenous hyperinsulinemia, accidental or surreptitioususe sulfonylureas or insulin.

Hypoglycemia caused by sulfonylureas can be prolonged for several days hence these patients should not be discharged with emergency room correction of hypoglycemia alone

**Treatment**

**Objectives**

- Quickly bring the level of blood glucose within the normal range to prevent serious brain damage.
- Maintain the level of blood glucose within the normal range until the patients begin eating normally.

**Non pharmacologic**

- 2-3 teaspoons of granulated sugar or 3 cubes of sugar or 1/2 a bottle of soft drink to individuals who are conscious.
- The above measures should be followed immediately by a meal or snack.

**Pharmacologic**

**Dextrose**, 40%, IV, 40-60ml over 1 to 3 minutes through a large vein, followed by 10% **Glucose** IV, 500ml, 4 hourly until the patient is able to eat normally.

## 6. Near Drowning

Drowning is death from suffocation (asphyxia) following submersion in a liquid medium. Near-drowning is survival, at least temporarily, after suffocation with/without loss of consciousness.

**Risk factors of near-drowning:**

- Inability to swim or overestimation of swimming capabilities.
- Risk-taking behaviour.
- Use of alcohol and/or illicit medicines.
- Inadequate adult supervision.
- Hypothermia, which can lead to rapid exhaustion or cardiac arrhythmias.
- Concomitant trauma, cerebrovascular accident, or myocardial infarction.
- Undetected primary cardiac arrhythmia,
- Hyperventilation prior to a shallow dive which can lead to cerebral hypoxia, seizures, and loss of consciousness, which again can result in drowning.

Suffocation by submersion leads to hypoxemia by means of either aspiration or reflex laryngospasm. Hypoxemia in turn affects every organ system, with the major being cerebral hypoxia.

**Clinical features**

- Shortness of breath, difficulty breathing, apnea
- Persistent cough, wheezing
- In stream, lake, or salt water immersion, possible aspiration of foreign material
- Level of consciousness at presentation, history of loss of consciousness, anxiety
- Vomiting, diarrhoea
- Bradycardia or tachycardia, dysrhythmia

Clinical deterioration mostly develops within 7 hours of immersion.

**Treatment**

**Objectives**

- Prevent fluid and electrolyte problems related to burn
- Prevent/treat infections
- Prevent complications like contractures

Has three phases: prehospital care, emergency unit care, and inpatient care.

**Prehospital care**

- Cardiopulmonary resuscitation (CPR) should be done as soon as possible without compromising the safety of the rescuer or delaying the removal of the victim from the water.
- High flow supplemental oxygen should be administered to the spontaneously breathing patient by facemask, while the apneic patient should be intubated.
- Rewarming all hypothermic patients with a core temperature <33ºC should be initiated, either by passive or active means as available.

**N.B.** The Heimlich maneuver or other postural drainage techniques to remove water from the lungs have no proven value.

**Emergency unit management**

**Rule out** injuries to the axial skeleton and internal injuries to the abdomen and chest. In the symptomatic patient, indications for elective intubation include signs of neurologic deterioration and an inability to maintain a SPO2 >90mmHg on high fractions of supplemental oxygen.

**Inpatient management**

Symptomatic patients require hospitalization for supportive care and treatment of organ specific complications.

**Useful modalities of treatment**:

- Mild hyperventilation to reduce intracranial pressure.
- Elevate head of the bed, if potential cervical spine injuries are excluded.
- Diuretics to avoid hypervolemia
- Seizure activity should be controlled. Phenytoin is the preferred agent as it does not depress consciousness.
- Manage both hypoglycemia and hyperglycemia

**Respiratory failure**

- Bronchospasm is treated similarly to acute asthma; most cases rapidly improve with inhaled beta-adrenergic agonists.
- Antibiotics should be used only in cases of clinical pulmonary infection or if the victim was submerged in grossly contaminated water.

**Hypotension-**Persons with hypothermia can have significant hypovolemia and hypotension due to a "cold diuresis." Optimal fluid replacement and inotropic support.

## 7. Poisioning And Overdose

Poisoning represents the harmful effects of accidental or intentional exposure to toxic amounts of any substance. The exposure can be by ingestion, inhalation, injection, or through skin. The effects may occur immediately or several hours or even days after the exposure. The damage could be local or systemic.

Poisoning can be from household substances (e.g. bleach), industrial (e.g. methanol), pesticides e.g. organophosphates), therapeutic medicine overdose (e.g. phenobarbitone, Amitriptyline), toxic plants (e.g. poisonous mushrooms, toxic herbal medications), bites and stings of venomous animals (e.g. snakes, bees).

**Clinical features**

- Clinical presentation is variable depending on the type of poison/medicine, route and dose.
- Many of the manifestation are nonspecific.
- Toxidromes are sets of clinical findings which could help in guiding the possible class of the poison/medicine
- It is very helpful to have a sample of the substance or the container in which it was stored as only few poisons can be identified instantly

**Table 61 – Toxidromes (adapted from Hand book for the Mangement of poisioning and overodose, Singapore MOH, 2000)**

| Toxidrome | Mental status | Pupil | Vital signs | Other | Examples of toxic agents |
|---|---|---|---|---|---|
| **Cholinergic** | ConfusionComa | Miosis | BradycardiahHypertension or Hypotension | Salivation, urinary & fecal incontinence, diarrhoea, vomiting, lacrimation, bronchoconstriction, fasciculations,weakness, seizures | Organophosphate and carbamate insecticides, nerve agents, |
| **Anticholinergic** | Agitation, hallucinations, delirium with mumbling speech, coma | Mydriasis | Hyperthermia, tachycardia, hypertension, tachypnea | Dry skin & mucous membranes, decreased bowel sounds, urinary retention, myoclonus, choreoathetosis | Antihistamines, tricyclic antidepressants,antiparkinson agents, antispasmodics, phenothiazines, atropine |
| **Tricyclic antidepressant** | Confusion, agitation, coma | Mydriasis | Hyperthermia, tachycardia, hypertension then hypotension | Seizures, myoclonus, choreoathetosis, cardiac arrhythmias | Amitriptyline, nortriptyline, imipramine, |
| **Sedative-hypnotic** | CNS depression, stupor, coma | Miosis | Hypothermia, bradycardia, hypotension, hypopventilati-on | Hyporeflexia | Benzodiazepines, barbiturates, alcohols, |
| **Opioid** | CNS depression, coma | Miosis | Hypothermia, bradycardia, hypotension, hypopneventi-lation | Hyporeflexia pulmonary edema, needle marks | Opiates (eg, heroin, morphine, methadone, oxycodone) |

| | | | | | |
|---|---|---|---|---|---|
| **Sympathomimetic** | Hyperalert, agitation, hallucinations, paranoia | Mydriasis | Hyperthermia, tachycardia, hypertension, widened pulse pressure, tachypnea, | Diaphoresis, tremors, hyperreflexia, seizures | Cocaine, amphetamines, ephedrine, pseudoephedrine, phenylpropanolamine, theophylline, caffeine |

**Investigations**

- Random blood sugar
- CBC
- BUN and creatinine,
- Electrolytes
- Liver function tests
- Chest X-ray for possible aspiration pneumonia
- Toxicological analysis of identified substance (e.g.gastric aspirate) or from serum

**Treatment**

**Objectives**

- Maintain airway, breathing and circulation
- Reduce absorption and enhance elimination
- Antagonize or neutralize the effects
- Relieve symptoms
- Prevent organ damage or impairment

**Non pharmacologic-**see table below

**Table 62-Fundamentals of poisoning management (adapted from Harrison's principles of Internal Medicine, 18th edition,Mc Graw Hill)**

| | |
|---|---|
| **Supportive Care** | |
| Airway protection | Treatment of seizures |
| Treatment of hypoxia | Correction of temperature abnormalities |
| correct hypotension/arrhythmia | Correction of metabolic derangements |
| **Prevention of Further Poison Absorption** | |
| Gastric lavage | Decontamination of eye, skin decontamination |

| | |
|---|---|
| Activated charcoal | |
| **Enhancement of elimination** | |
| Multiple-dose activated charcoal | Hemodialysis |
| Urinary pH alkalization | Hyperbaric oxygenation |
| **Administration of Anti-dotes** | |
| Neutralization by antibodies | Metabolic antagonism or Physiologic antagonism |
| **Prevention of Re-exposure** | |
| Child-proofing | Psychiatric referral |

**N.B-Induction of vomiting is contraindicated in patients who ingested caustic or corrosive substances and hydrocarbons, comatous patients and those with seizures.**

**Pharmacologic**

**Initial Management**

1. **Hypoglycemia**

**40% Dextrose**, IV, 40-60ml over 1-3 minutes

*PLUS*

2. **Hypotension**

**Normal saline**, IV, 1000ml fast then according to response

3. **Seizure management and medicine-associated agitated behaviour**

**Diazepam 10mg**, IV, stat repeat doses as needed. CAUTION-respiratory depression

**Activated charcoal**, 50gram, P.O., or via NG tube, diluted in 400–800ml water

Activated charcoal may reduce systemic absorption of a variety of substances.

The greatest benefit is achieved if activated charcoal is given within one hour after ingestion.

When mixing, add a small amount of water to charcoal in a container. Cap and shake container to make a slurry and then dilute further.

| | | |
|---|---|---|
| [redacted] | [redacted] | acids or bases, ethanol. |

**Catharsis**

Should be given only with the first dose of multiple dose charcoal in order to prevent electrolyte abnormalities and osmotic diuresis.

**Magnesium sulphate**, 250mg/kg

*OR*

**Sodium sulfate**, 250mg/kg

**Doasge form**: Crystals

**Alkalization of urine**

- This is a high risk procedure and should only be performed in consultation with a specialist.
- May be of benefit in salicylate, lithium, barbiturate and, tricyclic antidepressant poisoning.

**Sodium bicarbonate**, IV, 50–100mEq in 1 L sodium chloride 0.45%. Administer 250–500mL over 1–2 hours. Attempt to achieve urine pH of 7.5.

**Table 63-Common antidotes(adapted from Hand book for the Mangement of poisioning and overodose, Singapore MOH, 2000)**

| Poison | Antidote(s) | Dose for adults |
|---|---|---|
| **Carbon monoxide** | Oxygen | high-flow oxygen by tight-fitting facemask or ventilator |
| **Benzodiazepines** | Flumazenil | Initial dose: 0.1-0.2mg IV over 30-60 sec, repeat 0.1-0.2mg IV every minute up to 1mg |
| **Acetaminophen** | N-acetylcysteine | Initial oral dose: 140mg/kg, then 70mg/kg q 4h x 17 doses |
| **Heparin** | Protamine sulfate | 1 mg neutralizes 90-115 U heparin; Initial dose: 1 mg/min to total dose 200mg in 2 h |

| | | |
|---|---|---|
| **Isoniazid** | Pyridoxine (Vitamin B6) | Initial dose: 1 gm pyridoxine for every gm INH ingested or empiric 5gm IV over 10 min if amount ingested unknown |
| **Opiates** | Naloxone | Initial dose: 0.1-2.0mg IV push (opioid dependent patients should receive 0.1 mg IV every 30-60 sec until clinical response) |
| **Ticyclic antidepressants** | Sodium bicarbonate | Initial dose: 1-2 ampules (50-100mEq) IV push, then IV infusion to maintain blood pH 7.45-7.55 (Preparation: 3 amps 50mEq of NaHCO3 in 1liter D5W infused at 200-250 mL/h) |
| **Organophosphates Carbamates Nerve agents** | Atropine | Initial dose: 0.5-2.0mg IV; repeat q 3-5 min until sweat and secretions clear |
| | Pralidoxime | Initial dose: 1 gm IV over 15 min, then IV infusion of 3-4mg/kg/h for 24-72 hrs |

## 8. Specific Poisons

### Carbamates And Organophosphates

Poisoning due to parathion, malathion and other organophosphates. Absorption occurs through the skin or the agent is taken orally. Patients present with muscarinic and nicotinic manifestations of intoxication.

**Clinical features**

- Muscarinic overstimulation causes salivation, lacrimation, vomiting, diarrhoea and increased bronchial secretions.
- Nicotinic overstimulation causes muscle fasciculations and paresis or paralysis.
- Patients may present with either bradycardia or tachycardia.

**Investigations**

- Clinical
- Toxicological analysis

**Treatment**

**Objectives**

- Support physiological function
- Treat symptoms
- Remove the poison from the body

**Non pharmacologic**

- Supportive treatment

**Pharmacologic**

**Atropine**, IV, 1-3 mg, every 3-5 minutes, until pulmonary secretions are dry

- Do not stop atropine therapy abruptly. Wean the rate of administration slowly.
- During weaning monitor the patient for possible worsening.

**Carbon Monoxide**

**Clinical features**

- Poisoning with carbon monoxide is common where there is incomplete combustion of charcoal.
- Acute poisoning results in headache, nausea and vomiting, mental confusion and agitation.
- Severe toxicity causes confusion, impaired thinking, and may progress to coma, convulsions, and death.

**Investigations**

- Clinical
- Toxicological analysis

**Treatment**

**Objectives**

- Support physiological function
- Treat symptoms

- Remove the poison fro the body

**Non pharmacologic**

- Supportive treatment
- Take the patient out to open air.

**Pharmacologic**

**Oxygen**, 100% via face mask

**Barbiturates (Commonly Phenobarbitone)**

**Clinical Features**

- Overdose is associated with depression of the CNS, coma, hypotension, loss of reflexes, hypothermia, respiratory arrest, and death.
- A characteristic of a barbiturate overdose is the persistence of the pupillary light reflex even with stage IV coma.
- Bullous skin lesions often occur over the hands, buttocks and knees.

**Investigations**

- Clinical
- Toxicological analysis (determination of barbiturate levels)

**Treatment**

**Objectives**

- Support physiological function
- Treat symptoms
- Remove the poison from the body

**Non pharmacologic**

- Mechanical ventilation required in severe cases
- Hemodialysis

**Pharmacologic**

**Activated charcoal –** see doses above

Multiple-dose activated charcoal every 4 to 6 hours is specifically indicated

*PLUS*

**Alkaline diuresis**-see above

**9. Shock**

**Pharmacologic**

**Cardiogenic shock (pump failure)**

**First line**

**Dopamine**, 5-50mcg/kg/min IV diluted with dextrose 5% in Water, or in sodium chloride solution 0.9%;

**Alternatives**

**Norepinephrine (noradrenaline)**, Initial: 0.5-1 mcg/minute and titrate to desired response; 8-30 mcg/minute is usual range

**ADRs:** tachycardia, tachyarrythmia, tremor, raised blood pressure

**Dosage form:** Injection, 8mg/ml in 1ml ampoule, Injection, 1:1000

*OR*

**Dobutamine**, 2.5-40 micrograms/kg/min IV diluted in dextrose 5%.

**ADRs:** tachycardia, raised blood pressure;

**P/C:** severe hypotension complicating cardiogenic shock

**Dosage form:** powder for injection, 250 mg per vial

*OR*

**Adrenaline,** I.V. infusion: Initial: 0.1-0.5 mcg/kg/minute (7-35 mcg/minute in a 70 kg patient); titrate to desired response

**Hypovolemic shock**

**Infusion of fluid (Normal saline or Ringer lactate)** 1-2 liters fast; reassess the patient for adequacy of treatment; if needed repeat the bolus with maximum tolerated dose being 60 – 80 ml/kg with in the first 1 – 2 hr.

If due to haemorrhage, apply transfusion of packed Red Blood Cells (RBC) or whole blood 20ml/kg over 4 hrs, repeat as needed until hgb level reaches 10gm/dl and the vital signs are corrected.

**Septic shock**.

Adequate organ system perfusion with IV fluids (large volume of IV fluids are required in septic shock patients)

**First line**

**Dopamine**, 5-50 mcg/kg/min IV diluted with dextrose 5% in Water, or in sodium chloride solution 0.9%;

**Alternatives**

**Norepinephrine (noradrenaline),** Initial: 0.5-1mcg/minute and titrate to desired response; 8-30 mcg/minute is usual range

**ADRs:** tachycardia, tachyarrythmia, tremor, raised blood pressure

**Dosage form:** Injection, 8mg/ml in 1ml ampoule, Injection, 1:1000

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**ADRs:** tachycardia, raised blood pressure;

**P/C:** severe hypotension complicating cardiogenic shock

**Dosage form:** powder for injection, 250 mg per vial

*OR*

**Adrenaline, I.V. infusion:** Initial: 0.1-0.5 mcg/kg/minute (7-35 mcg/minute in a70 kg patient); titrate to desired response

*PLUS*

**Hydrocortisone**, 50 mg IV every 6 hrs (when vasopressor dependent)

**Adrenal crisis**

1. Normal saline Large volumes (1 to 3 liters) or 5 % dextrose in 0.9% percent saline should be infused intravenously /infusion like hypovolemic shock.
2. **Hydrocortisone**, 200mg, IV, stat then 100mg, IV, QID

**Stroke (Cerebrovascular Accident)**

Cerebrovascular accident (stroke) is an acute event in/of the blood vessels of the brain resulting in ischemia or infarction and sudden loss of focal brain function. It is the major neurological disease of our times. The symptoms of brain ischemia may be transient; lasting seconds to minutes, or may persist for longer periods of time.

The causes may be intrinsic to the vessel, as in atherosclerosis, lipohyalinosis, inflammation, amyloid deposition, arterial dissection, developmental malformation, aneurysmal dilation, or

venous thrombosis OR may originate remotely, as occurs when an embolus from the heart or extracranial circulation lodges in an intracranial vessel OR result from inadequate cerebral blood flow due to decreased perfusion pressure or increased blood viscosity OR result from rupture of a vessel in the subarachnoid space or intracerebral tissue.

Stroke can lead to transient brain ischemia (transient brain ischemic attack or TIA) or permanent brain infarction (ischemic stroke)-which accounts for 80% of strokes or may be due to subarachnoid haemorrhage or an intracerebral haemorrhage (primary haemorrhagic stroke) which constitute 20 % of all strokes.

**Investigations**

- CBC
- PT and PTT
- Blood glucose
- Serum lipid profile
- Blood urea, electrolytes and creatinine
- ECG
- Echocardiography
- CT scan/MRI of the head
- Chest X-ray

**Treatment**

**Objectives**

- Limit the area of brain damage
    - Protect patients from the dangers of unconsciousness and immobility
    - Treat the underlying cause if possible
    - Institute measures to improve functional recovery
    - Support and rehabilitate patients who survive with residual disability
    - Prevent recurrence of cerebrovascular lesions

**Non pharmacologic**·

Admit and monitor patient`s vital signs and neurological signs frequently

- Establish adequate airway in unconscious patients.
- Nurse in the lateral position with suctioning where necessary
- Prevent pressure sores by regular turning (every 2 hours) in bed.
- Maintain adequate hydration
- Insert nasogastric tube as early as possible for feeding and medicationsin unconscious patients or those with swallowing difficulties
- Insert urethral/condom catheter to keep patient clean and dry.
- Early physiotherapy as soon as practicable

**Pharmacologic-Provide emergency support (satblize vital signs and refer)**

**Sudden cardiac arrest**

Sudden cardiac arrest (SCA) refers to the sudden cessation of cardiac activity with haemodynamic collapse, typically due to sustained ventricular tachycardia/ventricular fibrillation when the event is reversed with intervention or spontaneously; if it is not reversed it will be labeled as sudden cardiac death.

It usually occurs in individuals with structural heart disease but in the absence of detectable clinical findings. Acute myocardial ischemia, electrolyte abnormalities, antiarrhythmic medicines and worsening Heart Failure can precipitate sudden cardiac arrest.

**Clinical features**

- Instantaneous or abrupt onset collapse with or without prodrome
- Absent pulse
- Absent or gasping type of breathing
- Unresponsive

**Investigations**

- During the episode no work up is needed except having continuous ECG monitoring together with emergency management.
- Post SCA work up is needed-Troponin, Echocardiography, Electrolytes, RFT

**Treatment**

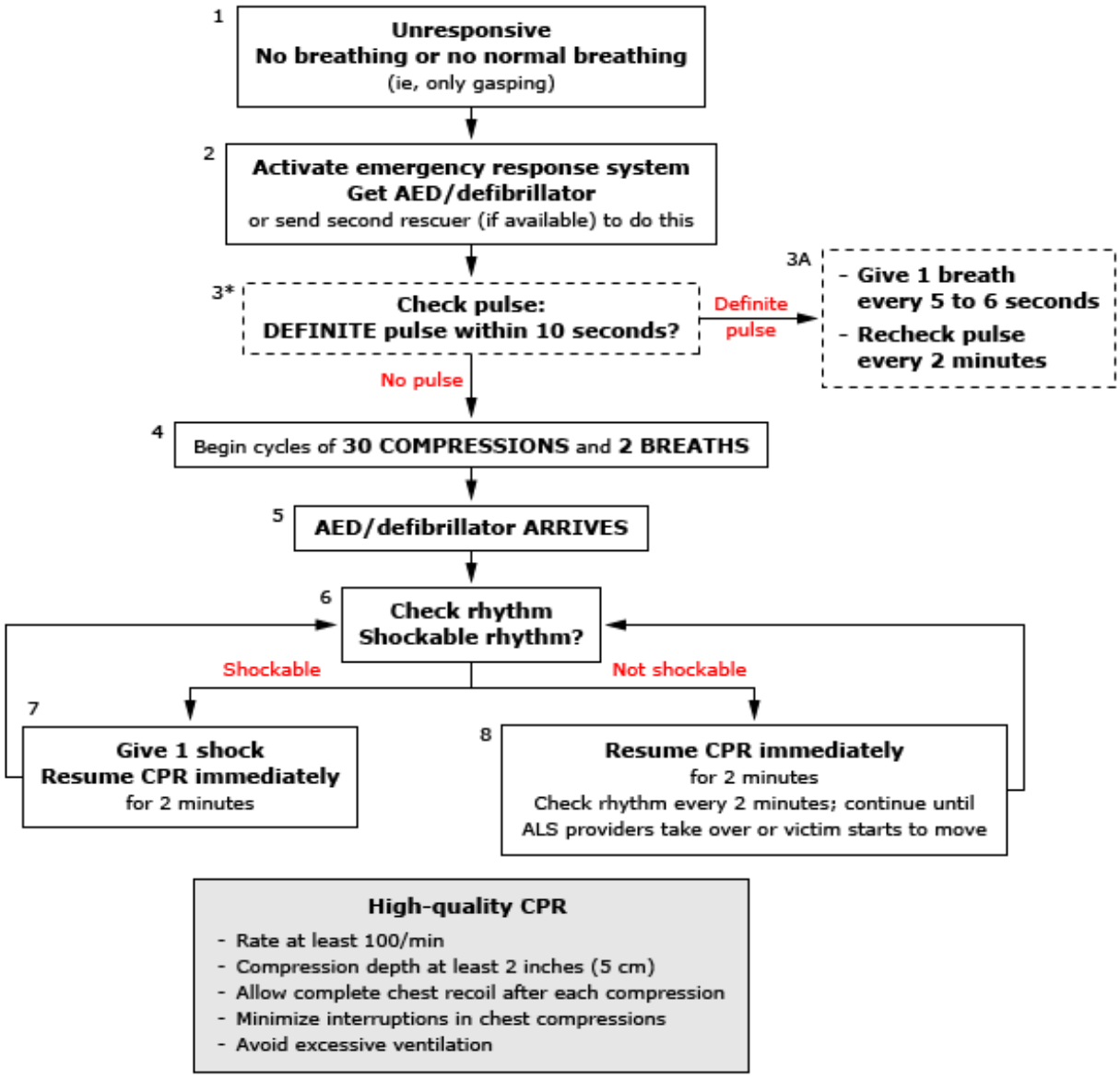
**Objectives**

- Achieve adequate ventilation
- Control cardiac arrhythmias
- Stabilize blood pressure and cardiac output
- Restore organ perfusion

**Non pharmacologic**

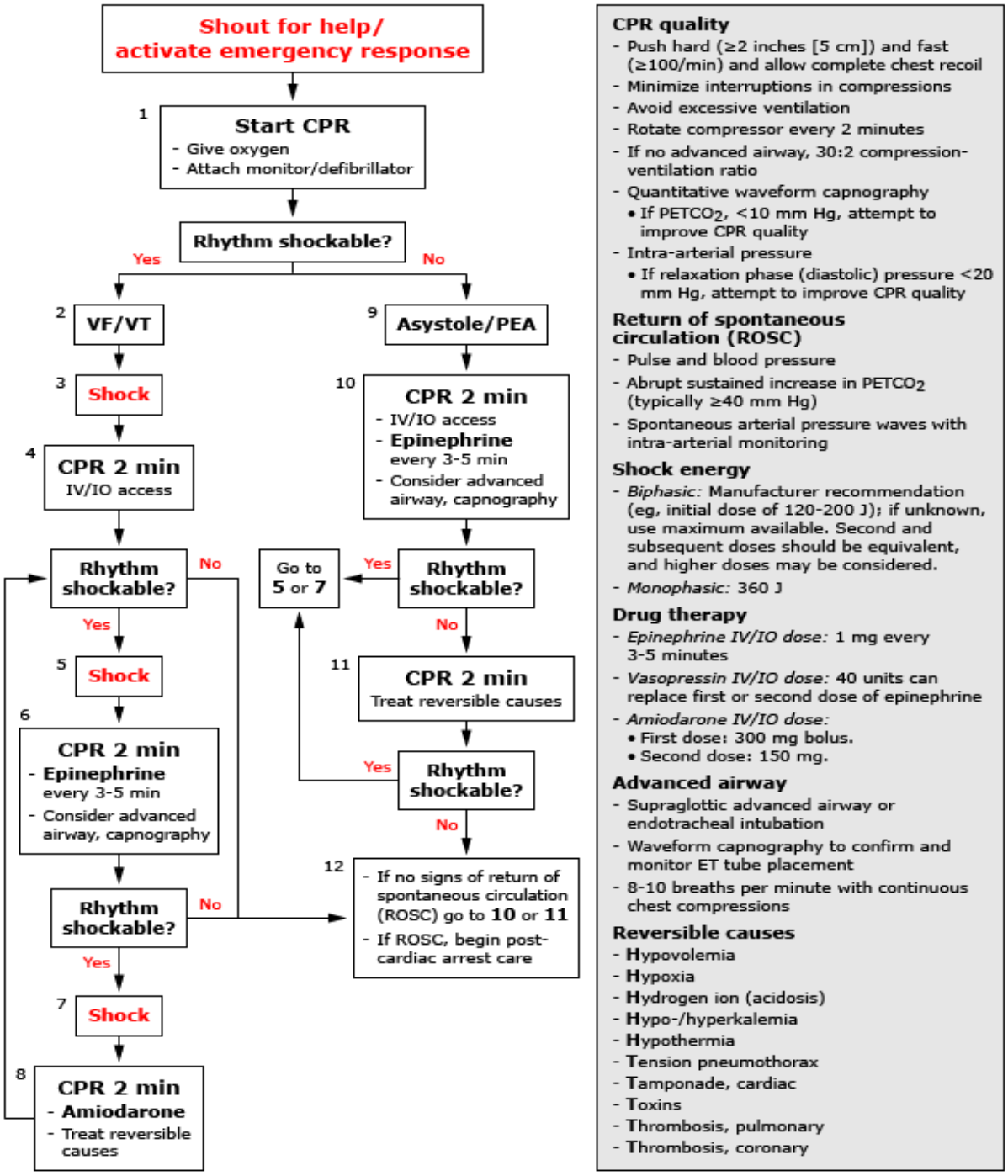
Provide Basic life support (BLS) and refer with escort

**Figure 3-Basic life support guideline**




(*adapted from the 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care)*

**Figure 4-Adavnced Cardiac Life Support for adults**




**1.** (*adapted from the 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care)*

**Upper gastrointestinal bleeding (acute)**

Upper gastrointestinal (GI) bleeding is bleeding from the GI tract proximal to the ligament of Treitz. It commonly presents with hematemesis (vomiting of blood or coffee-ground like material) and/or melena (black, tarry stools). Hematochezia (frank blood per rectum) can also result from massive upper GI bleeding.

Causes: Bleeding PUD, esophageal varices, erosive gastritis, mucosal tears of the esophagus or fundus (Mallory-Weiss tear), Bleeding stress ulcer, erosive esophagitis, gastric varices, gastric cancer, and other rare vascular malformations.

**Clinical features**

- Hematemesis
- Dark/tarry stool
- Frank hematochezia in massive bleeding
- Abdominal pain
- Postural dizziness and fatigue
- History of liver disease, longstanding dyspeptic symptoms, NSAID use, preceding vomiting
- Tachycardia
- Hypotension
- Pallor
- Upper abdominal tenderness
- Features of portal hypertension (splenomegaly, ascites, dilated abdominal wall vessels)

**Investigations**

- CBC
- PT and PTT
- AST, ALT, Alkaline phosphatase, Bilirubin

- BUN, Creatinine

**Treatment**

**Objectives**

- Correct hypovolemia/shock
- Arrest bleeding
- Prevent recurrence of bleeding

**Non pharmacologic**

Airway protection (in patients with massive hematemesis and impaired consciousness)

- Oxygen via nasal cannula or face mask
- Transfusion of whole blood and preparation of additional cross matched blood
- Position patients with impaired consciousness laterally
- Elevate leg if hypotensive
- Discontinue NSAIDS
- Balloon tamponade with Sigesten-Blakmoore tube
- Surgery in massive and refractory bleeding

**Endoscopic management is the main stay of treatment in acute upper GI bleeding following stabilization. After stabilization, call for a center with emergency endoscopic intervention and consider refe**

**Pharmacologic**

**First line** High dose proton pump inhibitors (PPI), see options below

**Esomeprazole**, 40mg, IV, daily or P.O., BID

**Omeprazole**, 40mg, P.O., BID

**Pantoprazole**, 40g, P.O., BID

**Alternatives-**High dose H2-blockers

**Cimetidine**, 400mg, IV, BID

**N.B.** $H_2$ blockers are not preferred in this setting unless there are no PPI

**Antibiotics prophylaxis for variceal bleeding**

**First line**

**Ceftriaxone** 1gm, IV, daily for 5-7 days

**Alternatives**

**Norfloxacin** 400mg, P.O., BID for 5-7 days

*OR*

**Ciprofloxacin** 500mg, P.O., BID for 5-7 days

**H. Pylori eradication-**for H. pylori positive non-variceal bleeding

**N.B.** H. pylori eradication treatment is should be started after patient is stabilized.

## CHAPTER XIV: PEDIATRIC DISORDERS

### 1. Acute Post Streptococcal Glomerulonephritis

Acute post streptococcal glomerulonephritis is one of the non-suppurative complications of streptococcal throat or skin infection. It follows streptococcal throat infection by a latent period of 1-2 weeks and skin infection by 4–6 weeks. The condition is characterised by a sudden onset of hematuria, oliguria, edema and hypertension.

**Clinical features**

- Hematuria (usually described as smoky or cola colored)
- Edema (usually periorbital and pretibial, but may be generalized)
- Hypertension (may complicate to hypertensive encephalopathy or Heart Failure )
- Decreased urine output

**Investigations**

- Urinalysis: Macroscopic or microscopic hematuria, RBC casts, WBC, cellular casts
- Proteinuria: Rarely exceeding 3+
- Blood chemistry: BUN, Creatinine, sodium, potassium levels
- EKG for evidence of hyperkalemia
- ESR or C-reactive protein
- Complete Blood Count
- ASO titer
- Renal ultrasound (not essential to diagnosis)

**Treatment**

**Objectives**

- Avoid complications of hypertension and hyperkalemia

- Relieve edema
- Treat renal failure

**Non pharmacologic**

- Input and output monitoring chart and daily weight measurements
- Salt restriction
- Determine 24-hour fluid requirement (400ml/$m^2$/24hours + urine output+ any other losses)
- Giving maintenance fluid orally unless there is indication to give intravenously

**Pharmacologic**

**First-line**

**Amoxicillin 30-50mg/kg/24hours divided into 2-3 doses orally for 7-10 days**

Control blood pressure with **furosemide** (4-6mg/kg in two divided doses, intravenously)

If furosemide is not enough to control the blood pressure, add **nifedipine** 0.25-0.5mg/kg/dose Q6hours (maximum dose 10mg/dose or 3mg/kg/24hours)., If hyperkalemia (serum potassium > 5.5mmol/litre), give **calcium gluconate** 10%, 0.5ml/kg IV over 10 minutes,

*OR*

Glucose 0.5-1.0gm/kg and insulin 0.1-0.2units/kg as a bolus

**Alternative**

**Refer**: for peritoneal dialysis if the above measures fail

## 2. Acute Rheumatic Fever

Acute rheumatic fever is a condition, generally classified as connective tissue disease or collagen vascular disease. It follows group A beta-hemolytic streptococcal throat infection by a latency period of about 3 weeks. It is the most common cause of acquired heart disease in children in developing countries. Acute rheumatic fever primarily affects the heart, the joints and the central nervous system. However, carditis is the only known long-term complication while all the others are self-limiting. It is rare before 5 years of age; the peak age for its occurrence is 5– 15 years. Both sexes are equally affected. Proper treatment of streptococcal pharyngitis virtually eliminates the risk of rheumatic fever.

**Clinical features**

Clinical features are generally grouped in to major and minor as follows (Modified Jones criteria):

**Major**

- Carditis (occurs in about 50-60% of patients. It affects all the layers of the heart (endocardium, myocardium and pericardium).
- Migratory polyarthritis
- Sydenham's chorea
- Erythema marginatum
- Subcutaneous nodules

**Minor**

- Arthralgia
- Fever
- Elevated acute phase reactants (ESR, CRP)
- Prolonged PR-interval on ECG

**Investigations**

- ASO titer
- Culture from throat swab
- C-reactive protein (CRP), ESR
- ECG
- Echocardiography
- Chest X-ray

Diagnosis of acute rheumatic fever is established with:

2 major criteria or 1 major and 2 minor criteria and supporting evidence for antecedent streptococcal pharyngitis (mandatory).

Strict adherence to Jones criteria is not needed under the following situations:

- Sydenham's chorea
- Indolent carditis
- Rheumatic fever recurrence

**Treatment**

**Objectives**

- Alleviate symptoms

**Non pharmacologic**

- Place on bed rest and monitor for evidence of carditis
- Withhold anti-inflammatory treatment till full clinical pictures appear
- Emotional support, especially crucial when Sydenham's chorea is present
- Counseling of the child and family on the nature of the disease, long-term management, prognosis and prevention of recurrence

**Pharmacologic**

**First line**

Single dose of **Benzathine penicillin** (1.2M IU for weight > 27kg and 600,000IU IM for weight ≤27kg).

Same dose of **Benzathine penicillin** every month up to the age of 21 years for prophylaxis.

For penicillin allergic patients, refer to a pediatrician or pediatric cardiologist.

**Alternative** (considered when patient is hypersensitive to penicillin)

**Erythromycin** 40mg/kg/24 orally divided into 2-4 doses for 4 days

*OR*

**Azithromycin** 500mg orally on the first day, then 250mg daily for 4 days.

**Anti-rheumatic treatment**

Migratory polyarthritis and carditis without cardiomegaly: **Aspirin** 100mg/kg/24 hours divided into 4 doses, orally for 3-5 days, then 75mg/kg/24hours for 4 weeks.

Carditis with cardiomegaly or congestive Heart Failure : **prednisolone** 2mg/kg/24hours divided into 4 doses orally for 2-3 weeks, and while tapering prednisolone, start Aspirin 75mg/kg/24 hours in 4 divided doses for 6 weeks.

### 3. Bronchial Asthma

Bronchial asthma is a disease characterised by recurrent, reversible airway obstruction, airway inflammation and increased airway responsiveness to a variety of stimuli (hyper-reactive airway). Diagnosis of childhood asthma is entirely clinical symptoms such as intermittent dry coughing and expiratory wheezes, which are severe at night. Shortness of breath or chest tightness may be reported by older children. These symptoms are usually triggered or aggravated by viral infection of the respiratory tract or inhaled allergens.

**Clinical features**

- Intermittent dry cough
- Wheezing which is severe at night
- Shortness of breath or chest tightness, reported by older children
- Tachypnea

**Danger signs during acute attacks:**

- Paradoxical breathing
- Profound diaphoresis
- Cyanosis
- Silent chest on auscultation
- Drowsiness or confusion
- Agitation
- Exhaustion
- Arrhythmia

**Investigations**

Diagnosis of childhood asthma is generally made on clinical grounds and investigations are no needed unless complication or concurrent chest infection is suspected.

Chest X-ray: if complications like pneumothorax, atelectasis or concurrent pneumonia is suspected.

**Treatment**

**Acute asthmatic attack in children**

**Objectives**

- Prevent respiratory failure
- Relieve symptoms

**Non pharmacologic**

- Oxygen: administer oxygen via mask or nasal cannula.
- Positioning: upright or leaning position in older children.
- Treatment of comorbid conditions: Treat rhinitis, sinusitis or pneumonia as appropriate.
- Nutrition: Increase feeding and fluid intake as appropriate.

**Pharmacologic**

**First-line**

**Salbutamol**, 0.1-0.2mg/kg (1-2 puffs) 3-4 times a day or 0.075-0.1mg/kg P.O 3 times a day.

**Dosage form:** Metered Dose Inhaler or MDI 100mcg/puff.

*OR*

**Salbutamol Nebulizer**, for 30 minutes (can be repeated every 20 minutes till relief of symptoms.

*PLUS*

**Prednisolone,** 1-2mg/kg/24hrs for 4 days in addition to the inhaled beta agonist.

**Alternatives**

**Beclomethasone**, 336-672µg (8 – 16puffs of 42µg/puff or >8puffs of 84µg/puff) daily in two divided doses.

*OR*

If a child does not improve after 3 doses of rapid acting bronchodilator given at short intervals plus oral prednisolone, give:

**Aminophylline** – initial dose of 5 – 6mg/kg (up to maximum of 300mg), followed by a maintenance dose of 5mg/kg every 6 hours. Weigh the child carefully and give the intravenous dose over at least 20 minutes and preferably over 1 hour**.**

## 4. Croup (Acute Laryngo-Tracheo-Bronchitis)

Infectious croup is a syndrome caused by upper airway obstruction due to infection of the larynx and trachea. The spectrum of the syndrome ranges from laryngotracheobronchitis or epiglottitis to diphtheria and other bacterial tracheitis. Infants and young children develop more severe disease because of their narrow upper airway.

**Clinical features**

- Inspiratory stridor, hoarseness of voice, brassy cough, apnea
- Symptoms and signs of upper respiratory tract infection

**Danger signs**

- Severe stridor on inspiration and expiration
- None or markedly reduced air entry
- Change in sensorium (lethargic or unconscious)
- Duskiness or cyanosis

**Table 64-Modified Westley Clinical Scoring System for Croup**

| | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| **Inspiratory Stridor** | Not present | When agitated/active | At rest | | | |
| **Intercostal recession** | | Mild | Moderate | severe | | |
| **air entry** | Normal | Mild decreased | Severely decreased | | | |
| **Cyanosis** | None | | | | With agitation/activity | At rest |
| **level of consciousness** | Normal | | | | | Altered |

Total possible Score = 0 – 17.

<4= Mild Croup; 4 – 6= Moderate Croup; >6= Severe Croup

**Investigations**

- The diagnosis of croup is generally clinical and investigations are seldom required.
- Neck X-ray: Sub-glottic narrowing of the trachea ("pencil end") appearance.
- Chest X-ray: If complications or comorbid chest infections are suspected.

**Treatment**

**Objectives**

- Prevent respiratory failure
- Relieve symptoms

**Non pharmacologic**

- Humidified air given by vaporizer or inhalation of steam at home or by croup tent in the hospital is the mainstay of therapy.
- Some patients may need needle cricothyroidotomy or intubation or tracheostomy.

**Pharmacologic**

**First line**

**Dexamethasone**, 0.6mg/kg IM, single dose (for severe cases).

**Dosage forms:** Tablet 0.5mg, 1mg, 2mg; Injection 4mg/ml, 25mg/ml, 50mg/ml

**Alternative**

**Epinephrine (nebulized),** 0.5ml/kg of 1:1000 (1mg/ml) in 3ml NS (maximum dose is 2.5ml for age ≤4years old, 5ml for age >4years old). Hospitalize the child if more than one nebulization is required

## 5. Diarrhoeal Disease (Acute)

Acute diarrhoeal disease is a common problem in infants and children and its complications-dehydration and malnutrition-are major causes of morbidity and mortality in developing countries. Clinically it is useful to distinguish two syndromes produced by gastrointestinal infection: watery diarrhoea and bloody diarrhoea. The leading cause of diarrhoea in infants is the rotavirus followed by enteric adenoviruses. Shigella is most frequently a pathogen in

children between 1 to 5 years with bloody diarrhoea. Other bacterial pathogens include campylobacter, salmonella and Escherichia Coli.

**Clinical features**

1. **Severe dehydration: If two or more of the following signs are present,**
   - Lethargic or unconscious
   - Sunken eyes
   - Not able to drink or drinking poorly
   - Skin pinch goes back very slowly

2. **Some dehydration: if two or more of the following signs are present,**
   - Restless, irritable,
   - Sunken eyes,
   - Drinks eagerly, thirsty
   - Skin pinch goes back slowly

3. **No dehydration: if there are no enough signs to classify as "some" or "severe" dehydration. N.B:-Diarrhoea can also be classified as:**
   a. **Severe persistent diarrhoea:** If diarrhoea lasts for 14 days or more and dehydration is present.

   b. **Persistent diarrhoea:** Diarrhoea lasting for 14 days or more and there is no dehydration.

**Dysentery:** If there is blood in the stool**.** Dysentery can be an acute or persistent diarrhoea and it can also be associated with dehydration.

**Investigations**

- Diagnosis is generally based on clinical profile.

- Stool examination or stool culture may be indicated in children with dysentery or persistent diarrhoea but is not commonly needed for acute watery diarrhoea.

**Treatment**

**Objectives**

- Prevent dehydration, if there are no signs of dehydration;
- Treat dehydration, when it is present;
- Prevent nutritional damage, by feeding during and after diarrhoea; and

- Reduce the duration and severity of diarrhoea, and the occurrence of future episodes, by giving supplemental zinc.

**Non pharmacologic**

**Plan A**

**If no dehydration, treat diarrhoea at home.**

- Counsel the mother on the three components of home treatment.
- Give extra fluid, continue feeding and advise the mother when to return.
- Tell the mother to breastfeed frequently and for longer period at each feed.
- If the child is exclusively breastfed give ORS or clean water in addition to breast milk.
- If the child is not exclusively breastfed, give one or more of the following: ORS solution, food based fluids (such as soup, rice water, and yoghurt drinks or clean water).
- It is especially important to give ORS at home when the child has been treated with plan B or plan C during this visit.
- If the child cannot return to clinic, if diarrhoea gets worse, teach the mother how to mix and give ORS and give the mother two packets of ORS to use at home.
- Show the mother how much fluid to give in addition to the usual fluid intake:
    - Up to two years-50 to 100 ml after each loose stool
    - Two years or more:100 to 200 ml after each loose stool
- Tell the mother to give frequent small sips from a cup
- If the child vomits, wait 10 minutes, then continue but more slowly. Continue giving extra fluid until the diarrhoea stops

**Dangerous fluids not to be given**

- Drinks sweetened with sugar #Commercial carbonated beverages
- Commercial fruit juices #Sweetened tea
- Fluids with stimulant, diuretic or purgatives effects (e.g., coffee)
- Some medicinal teas or infusions

**Plan B**

**Treat some dehydration with ORS in Clinic**

- Give the recommended amount of ORS over 4-hour period
- Use the child's age only when you do not know the weight. The approximate amount of ORS required (in ml) can be calculated by multiplying the child's weight (in kg) times 75.
- If the child wants more ORS than shown, give more.
- For infants less than 6 months who are not breastfed, also give 100-200 ml clean water during the 4-hour period.
- Show the mother how to give ORS solution
- Give frequent small sips from a cup.
- If the child vomits, wait 10 minutes. Then continue, but more slowly.
- Continue breastfeeding whenever the child wants.

**Table 65-Amount of ORS to be given during the first 4 hours depending on the age of the child**

| Age | Up to 4 Months | 4 Months up to 12 months | 12 months up to 2 years | 2 years up to 5 years |
|---|---|---|---|---|
| Weight | 6 kg | 6-10 kg | 10-12 kg | 12-19 kg |
| ORS in ml | 200-400 | 400-700 | 700-900 | 900-1400 |

**After 4 hours:**

- Reassess the child and classify the child for dehydration.
- Select the appropriate plan to continue treatment.
- Begin feeding the child in clinic.

**If the mother must leave before completing treatment**

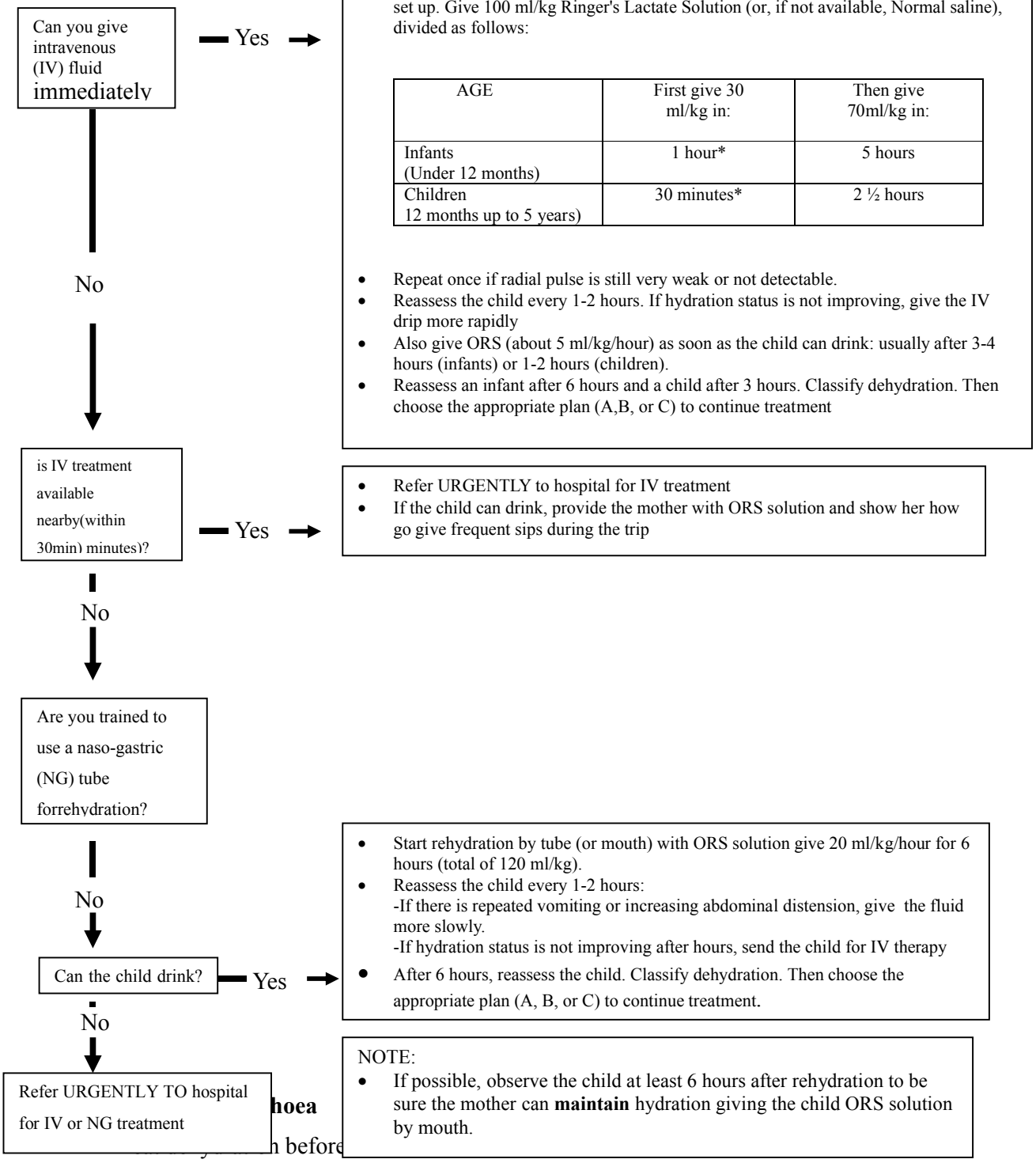
- Show her how to prepare ORS solution at home.
- Show her how much ORS to give to finish 4-hour treatment at home
- Give her enough ORS packets to complete rehydration. Also give her 2 packets as recommended in Plan A.

- Explain the 3 components of home treatment

**Treatment plan C: treat severe dehydration quickly**

Follow the arrows. If Answer is "Yes", go across. If "No", Go Down

START HERE




**hoea**

n before

**Pharmacologic**

**Vitamin A,** 50,000 IU for children less than 6 months of age, 100,000 IU for 6 – 12 months and 200,000 IU for those older than 12 months**.**

| | |
|---|---|
| **ADRs:** | diarrhoea, vomiting, irritability, drowsiness |
| **C/Is:** | renal impairment |
| **D/Is:** | cholestyramine or colestipol reduces its absorption |
| **Dosage forms:** | capsule, 25,000 IU, 50,000 IU, 100,000 IU; oral suspension, 150,000 IU/ml (concentrate), 50,000 IU/ml: tablet, 50,000 IU, 100,000 IU, 200,00 IU; injection, under 200,000 IU/ml |

## 6. Foreign Body Aspiration

Foreign body aspiration is a common problem in children aged 6 months to 4 years. Commonly aspirated materials include: nuts, seeds, or other small objects. The foreign body commonly lodges in the bronchus, usually the right one. The obstruction can lead to collapse or consolidation of portion of the lung distal to the site of obstruction.

**Clinical features**

- Choking at the time of aspiration followed by symptom free interval
- Chronic cough
- Persistent wheeze, usually unilateral
- Localized area of decreased air entry which is either dull or hyper resonant
- Deviation of trachea and/or apex beat to one side of the chest
- Symptoms/signs of pneumonia, which fail to respond to antibiotic treatment
- If a large foreign body is aspirated, it may lodge in the trachea and may lead to asphyxia and sudden death.

**Danger signs**

- Severe stridor on inspiration and expiration
- None or markedly reduced air entry
- Change in sensorium (lethargic or unconscious)
- Duskiness or cyanosis

**Investigations**

- Diagnosis of foreign body aspiration is generally clinical based on a classic history of choking episode or high index of suspicion.
- Chest X-ray may show aspirated material if it is radio-opaque or may show unilateral or localized collapse or hyper-inflation of the lung or mediastinal shift
- Bronchoscopy will help for accurate diagnosis as well as removal of the foreign body.

**Treatment**

**Non pharmacologic**

- Attempt to dislodge and expel the foreign body as an emergency first aid for the choking child.

**For infants:**

- Lay the infant on one arm or on the thigh in a head down position.
- Strike the infant's back five times with the heel of the hand.
- If the obstruction persists, turn the infant over and give five chest thrusts with two fingers, one finger's breadth below the nipple level in the midline.
- If the obstruction persists, check the infant's mouth for any obstruction which can be removed.
- If necessary, repeat this sequence with back slaps again.

**For older children:**

- While the child is sitting, kneeling or lying, strike the child's back five times with the heel of the hand.

- If the obstruction persists, go behind the child and pass your arms around the child's body; form a fist with one hand immediately below the sternum; place the other hand over the fist and thrust sharply upwards in to the abdomen (Heimlich's maneuver). Repeat this up to five times.
- If the obstruction persists, check the child's mouth for any obstruction which can be removed.
- If necessary, repeat the sequence with backslaps again.

Once this has been done, it is important to check the patency of the airway by:

- Looking for chest movements.
- Listening for air entry, and
- Feeling for breath.

If the above measures are unsuccessful,

- Refer the child to a center that can make correct diagnosis and remove the foreign body through bronchoscopy.

**Pharmacologic**

- If there is evidence for pneumonia start antibiotics (see section on treatment of pneumonia)

## 7. Heart Failure In Children

Heart Failure in infants and young children is usually manifested by respiratory distress making it usually difficult to differentiate it from pneumonia. However, presence of marked Hepatomegaly and absence of fever may help in making the diagnosis. Older children with Heart Failure usually present with clinical features that are more or less similar to the adult with Heart Failure .

Underlying causes of Heart Failure in children include: congenital heart diseases (usually in the first year of life), acute rheumatic fever with carditis, infective endocarditis, myocarditis, cardiomyopathies, pericarditis, glomerulonephritis, severe anaemia etc

**Clinical features**

The most common signs of Heart Failure , on examination, are:

- Feeding difficulty (exhaustion during breast feeding with interruption of feeding, diaphoresis and sleep)
- Failure to gain weight
- Recurrent lower respiratory infections
- Exercise intolerance in older children
- Tachycardia (heart rate>160/min in a child under 12 months of age; >120/min in a child aged 12 months to 5 years).
- Gallop rhythm
- Basal rales
- Enlarged, tender liver.
- Edema of the feet, hands or face, or distended neck veins – in older children.
- Severe palmar, buccal mucosa or conjuctival pallor, if severe anaemia is the cause of Heart Failure

**Investigations**

- Chest x-ray: May show cardiomegaly, pulmonary congestion or frank pulmonary edema.
- ECG may suggest arrhythmias or structural heart diseases as a cause of Heart Failure .
- Echocardiography will establish the cause of Heart Failure and gives structural as well as functional details of the heart.

**Treatment**

**Objectives**

- Relieve congestion by removing excess retained fluid
- Augment contractility
- Reduce after load

- Improve tissue perfusion
- Remove precipitating cause
- Improve functional status of the patient

**Non pharmacologic**

- Give oxygen if the infant or child is showing signs of respiratory distress.
- Avoid the use of intravenous fluids whenever possible.
- Support the child in a semi – sitting position with hand and shoulders elevated and lower limbs dependent.
- Relieve fever with paracetamol to reduce the cardiac work load.
- Avoid added salt diets.

**Pharmacologic**

**Diuretics**

**First line**

**Furosemide,** 1mg/kg, intravenously and wait for marked diuresis within 2 hours. If not effective, give 2mg/kg and repeat in 12 hours, if necessary. Then a single dose of 1 – 2mg/kg P.O. is usually sufficient. If furosemide is given for more than 5 days, or if it is given with digoxin, potassium supplementation is necessary.

**Alternative**

**Spironolactone**, 2 – 3mg/kg/24 hours in two to three divided doses.

*PLUS*

**Hydrochlorothiazide** 2mg/kg/24hr, (maximum dose 100mg/24hr) in two divided doses**.**

**Positive inotropic medicines**

These are used when the cause of Heart Failure is due to decreased contractility

**Digoxin**, 15 micrograms/kg P.O. loading dose followed by 5 micrograms/kg after 12 hours starting the loading dose and the same dose after 24 hours

Give maintenance dose of digoxin 5micrograms/kg/day.

## 8. HIV/AIDS in children

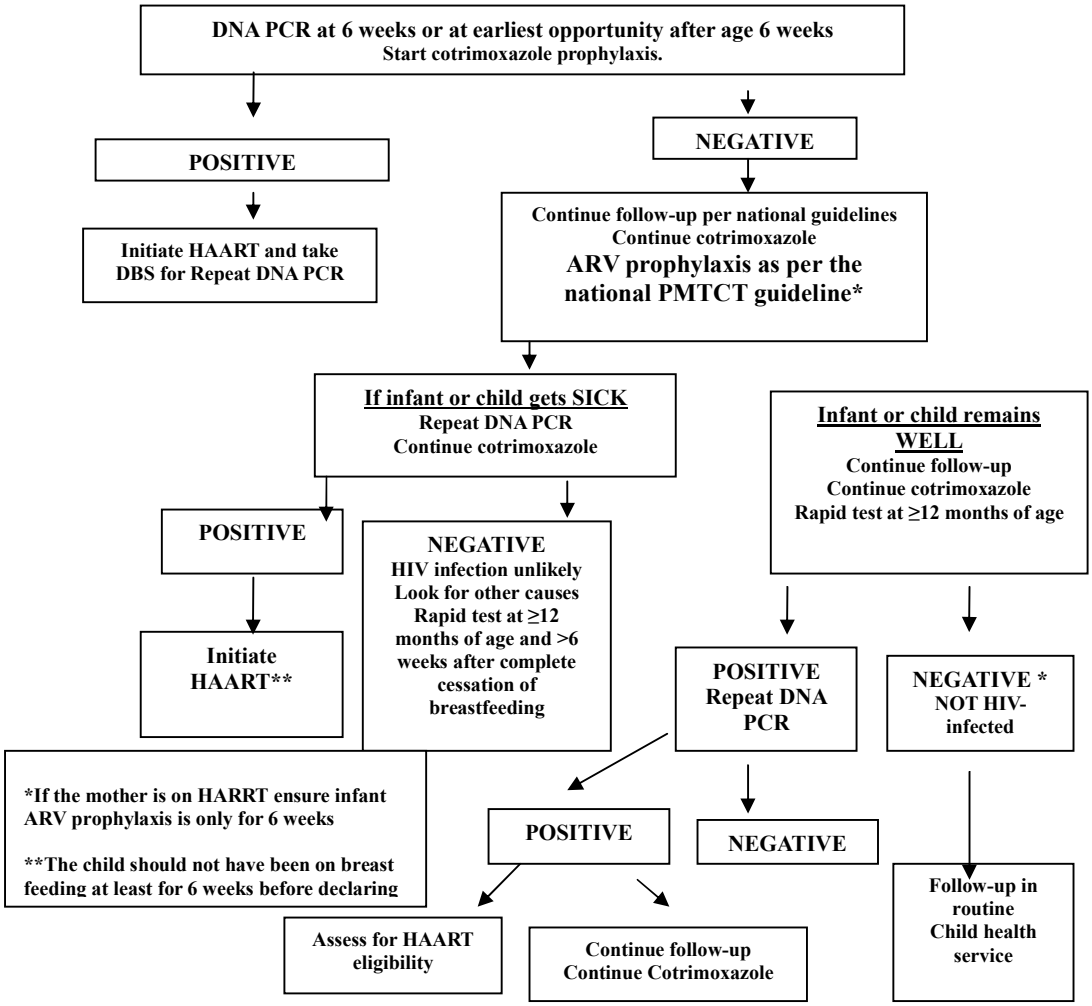
HIV/AIDS has created an enormous challenge to mankind since its recognition; close to 65 million people are infected and about 33 million people are living with HIV, out of which about 2.1 million are children under 15 years of age. Of these children, 90% live in sub-Saharan Africa and about 182,813 live in Ethiopia.

Mother-to-child transmission is the primary mode of HIV acquisition in children accounting for about 90% of cases; therefore, the most efficient and cost-effective way to tackle pediatric HIV

globally is to reduce mother-to-child transmission (MTCT). Despite ongoing efforts to prevent transmissions, there are nearly 1200 new infections each day, indicating a critical need to provide antiretroviral treatment for HIV-infected children.

ART has radically changed the natural course of HIV infection in countries where it has been successfully implemented and HIV-infected infants and children now survive to adolescence and adulthood.

**Figure 5-Antiretroviral therapy in children HIV Testing in HIV-exposed Infants <12 months where Virologic Testing is Available**



**Care of the HIV-Exposed Infant**

- HIV-exposed infants need regular follow-up since it is difficult to exclude HIV infection at early age and as they are at higher risk of morbidity and mortality regardless of infection status.
- Goals of care for the HIV-exposed infants are to:
    - Recognize HIV infection early using age-appropriate testing
    - Enrol early HIV-infected children into ART care
    - Minimize risk of vertical transmission of HIV

**Comprehensive Care for the HIV-Exposed Infant (HEI)**

- Infants should be seen monthly for the first six months and then every three months.
- Infants with poor growth, failure to thrive, or recurrent illnesses should have more frequent close follow-up.
- Care for HIV exposed infants should start at birth.
- Mothers should be given appointment for the first postnatal visit at delivery.
- Mothers who do not deliver at a health facility should be given appointment at first contact with the healthcare system.
- Mothers should be counseled on infant prophylaxis
- Immunizations should be given according to the National Expanded Program on Immunization
- Counseling on infant feeding, maternal nutrition and support
- Follow-up visit at 6 weeks of age
- Components of HEI care at this visit include:
    - History: Including use of PMTCT, parental concerns, inter-current illnesses.
    - Nutrition and growth assessment-plot weight, height and headcircumference on the growth chart
    - Developmental assessment using developmental check list provided
    - TB risk assessment:Screen for TB disease by using TB screening tool
    - Physical examination:Giving special emphasis for symptoms and signs suggestive of HIV infection.
    - Determination of HIV status**:** All HIV exposed infants should have the initial DNA PCR test done at six weeks of age

- Care givers should be counseled on the rationale for infant diagnosis; explain the possible test results, and need for additional testing to determine infection status definitely.
- Cotrimoxazole preventive therapy should be provided to all HIV- exposed infants starting at six weeks of age, and continued until HIV infection has been excluded and infant is no longer at risk from breastfeeding
- Infant for ARV prophylaxis**: e**nsure that ARV provision to the infant is per the nationalguideline for PMTCT

- Follow-up visit for HIV-exposed infants at two months:
  - Infants should be assessed to ensure they are tolerating Cotrimoxazole.
  - Results of the initial DNA PCR test should be made available to care giver.
  - In every visit the above assessments should be done including inter-current illness evaluation.

**N.B.** For Management of Pediatric HIV/AIDS, please refer to the latest national guideline.

## 9. Jaundice In Neonates

About 60% of full-term and 80% of preterm infants may normally develop jaundice in the first week of life. The color usually results from the accumulation of unconjugated Bilirubin in the skin. Unconjugated bilirubin is neurotoxic, while the conjugated is not. The most important pathologic causes of unconjugated hyperbilirubinemia include: Rh incompatibility, ABO incompatibility, concealed haemorrhage etc. The most important danger of pathological jaundice in the newborn is Kernicterus (neurotoxicity resulting from unconjugated bilirubin). "*Physiologic*" jaundice is a diagnosis made by exclusion when the following criteria are strictly met:

1. Jaundice first appears between the $2^{nd}$ and $3^{rd}$ day, peaking between the $2^{nd}$ and $4^{th}$ day and generally decreasing within the $1^{st}$ week of life;
2. Peak Bilirubin level ≤ 12mg/dl in full term infants and ≤15mg/dl in preterm infants;
3. Rate of rise of Bilirubin < 5mg/dl/24 hours;
4. Jaundice not persisting beyond the first two weeks of life;
5. Direct reacting bilirubin <1mg/dl at any time;

*PLUS*

Absence of known causes of jaundice on the basis of history, physical examination and laboratory examination.

**Clinical features**

- Yellowish discoloration of the eyes and skin
- Neurologic symptoms, if progressed to kernicterus

**Investigations**

- Serum bilirubin (total and direct fraction);
- Blood group and Rh type;
- Evidence of hemolysis including Coomb's test, reticulocyte count, hematocrit, peripheral morphology;
- VDRL;
- Septic work up whenever infection is suspected.

**Treatment**

**Objective**

- Prevent development of kernicterus (bilirubin encephalopathy)

**Non pharmacologic**

- Phototherapy using either day light (white light) or blue light.
- Exchange transfusions with double volume of cross-matched blood.

**Table 66-Size of exchange transfusion and replacement of infant's blood**

**Donor volume as fraction of blood volume**

| Infants blood volume exchange | Removed and replaced by |
|---|---|
| 0.5 | 40% |
| 1 | 63% |
| 2 | 87% |
| 3 | 95% |

**Pharmacologic**

- No pharmacologic treatment is needed for neonatal jaundice.
- Treat sepsis or syphilis if these are suspected causes of jaundice (see section on neonatal sepsis for treatment).

**10. Malnutrition (Severe)**

**Table 67-Definition for Severe acute Malnutrition**

| Age | Criteria |
|---|---|
| 6 months to 18 years | ▪ Weight for height or length <70% OR<br>▪ Mid upper arm circumference (MUAC)>110mm with a length >65cm OR<br>▪ Presence of bilateral pitting edema of the feet |
| *Infants < 6 months or <3kg | ▪ The infant is too weak or feeble to suckle effectively (irrespective of his/her weight-for-length, weight-for-age or other anthropometry) **or**<br>▪ The infant is not gaining weight at home (by serial measurement of weight during growth monitoring, i.e. change in weight-for-age) **or**<br>▪ W/L (Weight-for-Length) less than <-3 Z-score, **or**<br>▪ Presence of bilateral pitting oedema. |

***T**he aim of treatment of these patients is to return them to full exclusive breast feeding. Thus, the admission criterion is failure of effective breast feeding and the discharge criterion is gaining weight on breast milk alone (anthropometry is not used as primary admission criterion). For details in the management of severe malnutrition in this group of infants, the reader is advised to refer to the Integrated Management of Newborn and Childhood illnesses, WHO, 2011.

**Treatment**

**Objective**

- Treat life-threatening complications
- Rehabilitate with nutrition
- Achieve catch-up growth

**Phase I (Inpatient facility)**

- Poor appetite and/or major medical complications.
- Formula used during this phase is F75.
- Weight gain at this stage is dangerous.

**Transition phase**

- Avoid a sudden change to large amount of diet before physiological function is restored.
- Patients start to gain weight as F100 is introduced.
- The quantity of F100 given is equal to the quantity of F75 given in phase I.

**Phase II**

- Good appetite
- No major medical complications
- Can occur at inpatient or outpatient setting
- F100 (inpatient only) or ready to use therapeutic feeding (RUTF).

**Table 68-Criteria for admission to in-patient or outpatient care**

| Factor | Inpatient care | Outpatient care |
|---|---|---|
| **Anthropometry** | 6 months to 18 yrs:<br>➢ W/H or W/L <70% OR<br>➢ MUAC <110mm with length >65cm<br>Adults:<br>➢ MUAC <180mm with recent weight loss or underlying chronic illness OR MUAC<170mm OR<br>➢ BMI <16 | |
| **Bilateral pitting edema** | Bilateral pitting edema grade 3(+++)<br>Marasmic – kwashiorkor | Bilateral pitting edema<br>Grade 1 to 2 (+ and++) |
| **Appetite** | Poor appetite | Good appetite |
| **Choice of caregiver** | ➢ Chooses to start, continue or transfer<br>to inpatient treatment<br>➢ No suitable or willing caregiver | ➢ Chooses to start, continue transfer to outpatient treatment<br>➢ reasonable home circumstance and a willing caregiver |
| **Skin** | Open skin lesions | No open skin lesions |
| **Medical complications** | ▪ severe/intractable vomiting<br>▪ hypothermia: axillary T° <35°C OR rectal <35.5°C<br>▪ fever>39°C<br>▪ fast breathing based on age<br>▪ extensive skin lesions<br>▪ very weak, lethargic, unconscious<br>▪ fitting/convulsions<br>▪ severe dehydration based on history & physical examination<br>▪ Any condition that requires an infusion or NG – tube feeding.<br>▪ Very pale (severe anaemia), jaundice, bleeding tendencies | Alert with no medical complications |

**Non pharmacologic**

**PHASE I**

**Treatment of complications**

**Dehydration**

- "Therapeutic window" is narrow in a patient with severe acute malnutrition
- Quickly go from having depleted circulation to over – hydration with fluid overload and cardiac failure
- IV infusions should be avoided whenever possible.
- The standard protocol for the well-nourished dehydrated child should not be used.
- A supply of modified ORS or ReSoMal should never be freely available for the caretakers to give to the child whenever there is a loose stool.
- Ongoing loss replacement should not be given when there is no dehydration.

**a. Marasmic patient**

- The usual signs of dehydration are not reliable.
- History is more important than physical examination.
    - A definite history of significant recent fluid loss – usually diarrhoea which is clearly like water (not just soft or mucus) and frequent with sudden onset within the past few hours or days.
    - History of a recent change in the child's appearance.
    - If the eyes are sunken then the mother must say that the eyes have changed to become sunken since the diarrhoea has started.
    - The child must not have any edema.
    - Shock may be diagnosed when there is definite dehydration plus a weak or absent radial or femoral pulse, and cold hands and feet, and decrease in level of consciousness.

**Treatment**

- Rehydration should be oral whenever possible.
- IV infusions should be avoided except when there is shock or loss of consciousness from confirmed dehydration.

- Weight is the best measurement of fluid balance.
- Before starting any rehydration treatment, weigh the child; mark the edge of the liver and the skin with indelible pen and record respiratory rate.
- Start with 5ml/kg of Rehydration salt for malnourished (ReSoMal), (not in the National Medicine List) every 30 minutes for the first 2 hours orally or by NG – tube and then adjust according to the weight change observed. If continued weight loss, increase the rate of administration of ReSoMal by 10ml/kg/hr.
- Weigh the child every hour and assess liver size, respiration rate, and pulse rate and pulse volume.

**Table 69-Composition of ReSoMal, Standard WHO_ORS and reduced Osmolarity ORS**

| **Composition** | **ReSoMal (mmol/L)** | **Standard ORS (mmol/L)** | **Reduced osmolarity ORS** |
|---|---|---|---|
| **Glucose** | 125 | 111 | 75 |
| **Sodium** | 45 | 90 | 75 |
| **Potassium** | 40 | 20 | 20 |
| **Chloride** | 70 | 80 | 65 |
| **Citrate** | 7 | 10 | 10 |
| **Magnesium** | 3 | .. | .. |
| **Zinc** | 0.3 | .. | .. |
| **Copper** | 0.045 | .. | .. |
| **Osmolarity (mOsm/L)** | 300 | 311 | 245 |

To make ReSoMal (45 mmol Na/L) from the new 75 mmol Na/L WHO-ORS, add 1.7 L of cooled boiled water to each 1-litre sachet of WHO-ORS, add 33ml electrolyte mineral solution and 40g sugar.

**Figure 6-Rehydration monitoring**

**Non pharmacologic treatment of dehydration in the Marasmic patient**

Only rehydrate until the weight deficit (measured or Estimated) is corrected and then stop – do not give extra fluid to prevent dehydration.

Conscious

ReSoMal

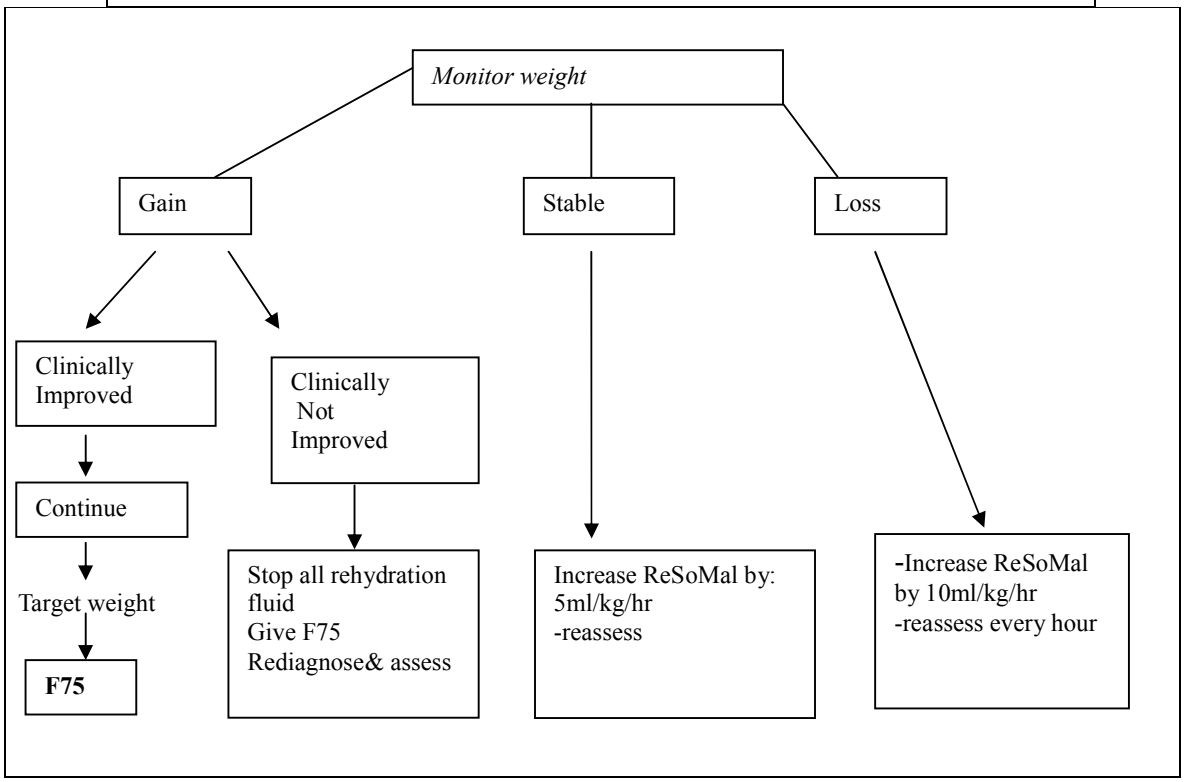
5ml/kg/30min first hour
5 to 10ml/kg/hour for 10hrs

Unconscious

IV fluid

Darrow's solution OR
½ N/S in 5% glucose, OR
R/L in 5% dextrose
At 15ml/kg for the first hour and reassess

-if improving, 15ml/kg 2nd hr
-if conscious NGT: ReSoMal
-if not improving septic shock



**b. Kwash patient**

- All children with edemahave an increased total body water and sodium – they are over – hydrated.
- Edematous patients cannot be dehydrated although they are frequently Hypovolemic.
- If a child with kwashiorkor has definite watery diarrhoea and the child is deteriorating clinically (excessive weight loss, more than 2% of the body weight per day), then the fluid lost can be replaced on the basis of 30ml of ReSoMal per day.

**Septic shock**

- A fast weak pulse with cold extremities
- Disturbed consciousness
- Give broad – spectrum antibiotics
- Keep warm to prevent or treat hypothermia
- Give sugar – water by mouth or nasogastric tube as soon as the diagnosis is made.
- Full blown septic shock – treat as in the Marasmic patient.
- Treat hypothermia, severe anaemia, severe pneumonia and any major medical complications

**Diet**

- F-75 (130ml=100kcal) should be used at this phase (see table for amounts).
- Use NG – tube for feeding if the child is taking <75% of prescribed diet per 24hrs or has pneumonia with a rapid respiratory rate or consciousness is disturbed.

**Table 70-Amounts of F75 to give during Phase 1**

| Class of Weight (Kg) | 8 feeds per day ml for each feed | 6 feeds per day Ml for each feed | 5 feeds per day Ml for each feed |
|---|---|---|---|
| 2.0 to 2.1 Kg | 40 ml per feed | 50 ml per feed | 65 ml per feed |
| 2.2 – 2.4 | 45 | 60 | 70 |
| 2.5 – 2.7 | 50 | 65 | 75 |

| | | | |
|---|---|---|---|
| 2.8 – 2.9 | 55 | 70 | 80 |
| 3.0 – 3.4 | 60 | 75 | 85 |
| 3.5 – 3.9 | 65 | 80 | 95 |
| 4.0 – 4.4 | 70 | 85 | 110 |
| 4.5 – 4.9 | 80 | 95 | 120 |
| 5.0 – 5.4 | 90 | 110 | 130 |
| 5.5 – 5.9 | 100 | 120 | 150 |
| 6 – 6.9 | 110 | 140 | 175 |
| 7 – 7.9 | 125 | 160 | 200 |
| 8 – 8.9 | 140 | 180 | 225 |
| 9 – 9.9 | 155 | 190 | 250 |
| 10 – 10.9 | 170 | 200 | 275 |
| 11 – 11.9 | 190 | 230 | 275 |
| 12 – 12.9 | 205 | 250 | 300 |
| 13 – 13.9 | 230 | 275 | 350 |
| 14 – 14.9 | 250 | 290 | 375 |
| 15 – 19.9 | 260 | 300 | 400 |
| 20 – 24.9 | 290 | 320 | 450 |
| 25 – 29.9 | 300 | 350 | 450 |
| 30 – 39.9 | 320 | 370 | 500 |
| 40- 60 | 350 | 400 | 500 |

**Pharmacologic**

**Table 71-Routine medications**

| | **Direct admission to in-patient (phase I)** | **Direct admission to out patient (phase II)** |
|---|---|---|
| **Vitamin A*** | One dose at admission<br>One dose on discharge | One dose on the 4th week |
| **Folic acid** | One dose at admission if signs of anaemia | One dose at admission if signs of anaemia |
| **Amoxicillin** | Every day in phase I + 4 more days | One dose at admission + give |

| | | |
|---|---|---|
| | in<br>Transition | Treatment for 7 days at home |
| **Malaria** | According to the national protocol | According to national protocol |
| **Measles (in Those above 9 months Old** | One vaccine at admission if no card<br>One vaccine at discharge | One vaccine on the 4th week |
| **Iron** | Add to F100 in phase 2 | No. iron is already in all RUTF |
| **Deworming** | One dose at the start of phase 2 | One dose on the 2nd week |

*Do not give Vitamin A to edematous children (wait till edema disappears).

**Transition phase**

Progress to from phase I to transitions phase when

- Appetite has improved
- Begins to loose edema and weight
- No IV line or NGT.
- The only change made to the treatment in phase I, is a change in the diet that is given from F75 to F100 or RUTF.
- The number of feeds, their timing and the volume of the diet given remains exactly the same as in phase I.

**Table 72-Transition Phase: Amounts of RUTF to give**

| Class of Weight | Beza | Plumpy Nut | BP 100 | Total |
|---|---|---|---|---|
| | Gram/day | Sachets/day | Bars/day | Kcal |
| **3 – 3.4** | 90 | 1.00 | 1.5 | 500 |
| **3.5 – 3.9** | 100 | 1.00 | 1.5 | 550 |
| **4 – 4.9** | 110 | 1.25 | 2.0 | 600 |
| **5 – 5.9** | 130 | 1.50 | 2.5 | 700 |
| **6 – 6.9** | 150 | 1.75 | 3.0 | 800 |
| **7 – 7.9** | 180 | 2.00 | 3.5 | 1000 |
| **8 – 8.9** | 200 | 2.00 | 3.5 | 1100 |

| | | | | |
|---|---|---|---|---|
| **9 – 9.9** | 220 | 2.50 | 4.0 | 1200 |
| **10 – 11.9** | 250 | 3.00 | 4.5 | 1350 |
| **12 – 14.9** | 300 | 3.50 | 6.0 | 1600 |
| **15 – 19.9** | 370 | 4.00 | 7.0 | 2000 |
| 20-24.9 missing | | | | |
| **25 – 39** | 450 | 5.00 | 8.0 | 2500 |
| **40 – 60** | 500 | 6.00 | 10.0 | 2700 |

The amounts given in the table are for the full 24 hour period. The amounts represent an average increase in energy intake of about one third over the amount given during Phase I. However, this varies between an increment of 10% and 50% depending upon the actual weight and the product used.

Each of the RUTF products is nutritionally equivalent to F 100, with the exception that they have an appropriate amount of iron added during manufacture for children in Phase 2 (i.e. children who pass the appetite test).

If both F100 and RUTF are being given they can be substituted on the basis that about 100 ml of F100 = 20g of RUTF.

**Table 73-Transition Phase: amounts of F100 to give**

| Class of Weight (Kg) | 8 feeds per day | 6 feeds per day | 5 feeds per day |
|---|---|---|---|
| **Less than 3Kg** | F100 full strength should not be given – Only F100 diluted should be given | | |
| **3.0 to 3.4 Kg** | 60 ml per feed | 75 ml per feed | 85 ml per feed |
| **3.5 – 3.9** | 65 | 80 | 95 |
| **4.0 – 4.4** | 70 | 85 | 110 |
| **4.5 – 4.9** | 80 | 95 | 120 |
| **5.0 – 5.4** | 90 | 110 | 130 |
| **5.5 – 5.9** | 100 | 120 | 150 |
| **6 – 6.9** | 110 | 140 | 175 |
| **7 – 7.9** | 125 | 160 | 200 |
| **8 – 8.9** | 140 | 180 | 225 |
| **9 – 9.9** | 155 | 190 | 250 |
| **10 – 10.9** | 170 | 200 | 275 |

| | | | |
|---|---|---|---|
| **11 – 11.9** | 190 | 230 | 275 |
| **12 – 12.9** | 205 | 250 | 300 |
| **13 – 13.9** | 230 | 275 | 350 |
| **14 – 14.9** | 250 | 290 | 375 |
| **15 – 19.9** | 260 | 300 | 400 |
| **20 – 24.9** | 290 | 320 | 450 |
| **25 – 29.9** | 300 | 350 | 450 |
| **30 – 39.9** | 320 | 370 | 500 |
| **40 – 60** | 350 | 400 | 500 |

The table gives the amount of F100 (full strength) that should be offered to patients in Transition Phase. They should normally be taking 6 feeds during the day and none at night. The table below gives the amount of RUTF to give per feed if some of the feeds are being given as F100 and others as RUTF.

A common variation is to give 5 or 6 feeds of F100 during the day and then 3 or 2 feeds of RUTF during the night – this gives 8 feeds in total during the day. The volume of F100 is then read off from the previous table and the grams of RUTF from the next table, both using the 8 meals per day column and the appropriate class of weight.

Criteria to move back from transition phase to phase I

- Increasing edema.
- If a child who did not have edema develops edema.
- Rapid increase in the size of the liver.
- Any other sign of fluid overload.
- Tense abdominal distension.
- Significant refeeding diarrhoea with weight loss.
- Develops medical complications.
- If NG tube is needed.
- If patient takes <75% of the feeds in transition phase even after interchange between RUTF and F100.

**Phase II**

Progress to Phase II from transition phase when:

– Good appetite is restored (at least 90% of the RUTF or F100 prescribed in transition phase)
– No or minimal edema (+).

**Table 74 - Phase 2 amounts of F100 and RUTF to give at each feed for 5 or 6 feeds per day**

| Class of weight (Kg) | 6 feeds/day | | 5 feeds/day | |
|---|---|---|---|---|
| | F100 | RUTF | F100 | RUTF |
| | ml/feed | g/feed | ml/feed | g/feed |
| < 3kg | Full strength F100 and RUTF are not given below 3 kg | | | |
| 3.0 to 3.4 | 110 | 20 | 130 | 25 |
| 3.5 – 3.9 | 120 | 22 | 150 | 30 |
| 4.0 – 4.9 | 150 | 28 | 180 | 35 |
| 5.0 – 5.9 | 180 | 35 | 200 | 35 |
| 6.0 – 6.9 | 210 | 40 | 250 | 45 |
| 7.0 – 7.9 | 240 | 45 | 300 | 55 |
| 8.0 – 8.9 | 270 | 50 | 330 | 60 |
| 9.0 – 9.9 | 300 | 55 | 360 | 65 |
| 10.0 – 11.9 | 350 | 65 | 420 | 75 |
| 12.0 – 14.9 | 450 | 80 | 520 | 95 |
| 15.0 – 19.9 | 550 | 100 | 650 | 120 |
| 20.0 – 24.9 | 650 | 120 | 780 | 140 |
| 25.0 – 29.9 | 650 | 140 | 900 | 160 |
| 30.0 – 39.9 | 850 | 160 | 1000 | 180 |
| 40.0 – 60.0 | 1000 | 180 | 1200 | 220 |

**Table 75 - Phase 2 (out-patients): amounts of RUTF to give**

| **Class of weight (Kg)** | **RUTF Paste** | | **PLUMPY'NUT ®** | | **BP100 ®** | |
|---|---|---|---|---|---|---|
| | **Grams per Day** | **Grams per Week** | **Sachet per Day** | **Sachet per week** | **Bars per Day** | **bar per week** |
| 3.0 – 3.4 | 105 | 750 | $1\ ^{1/4}$ | 8 | 2 | 14 |
| 3.5 – 4.9 | 130 | 900 | $1\ ^{1/2}$ | 10 | $2^{1/2}$ | $17^{1/2}$ |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5.0 – 6.9 | 200 | 1400 | 2 | 15 | 4 | 28 |
| 7.0 – 9.9 | 260 | 1800 | 3 | 20 | 5 | 35 |
| 10.0 – 14.9 | 400 | 2800 | 4 | 30 | 7 | 49 |
| 15.0 – 19.9 | 450 | 3200 | 5 | 35 | 9 | 63 |
| 20.0 – 29.9 | 500 | 3500 | 6 | 40 | 10 | 70 |
| 30.0 – 39.9 | 650 | 4500 | 7 | 50 | 12 | 84 |
| 40.0 – 60.0 | 700 | 5000 | 8 | 55 | 14 | 98 |

**11. Meningitis**

## Neonatal

Meningitis in the neonatal period may be caused by bacteria, viruses, fungi or protozoa. Meningitis may be associated with sepsis or present itself as a focal infection. The most common bacterial causes of neonatal meningitis are group B streptococcus, *E. coli* and Listeria.

**Clinical features**

- Initially, non-specific, including fever or hypothermia, failure to feed, vomiting
- Lethargy
- Seizure
- Full fontanel
- Nuchal rigidity, generally rare.

**Investigations**

- Lumbar puncture and Cerebrospinal fluid (CSF) analysis and culture
- Blood culture
- White Blood Cell count and differential count

**Treatment**

**Objectives**

- Decrease the risk of grave complications and mortality
- Avoid residual sequelae
- Shorten hospital stay

**Non pharmacologic**

- Restrict fluid intake to 70% of calculated maintenance.

- Monitor urine output

**Pharmacologic**

**First Line**

**Ampicillin**, 200mg/kg/day, IV every 12 hours for 14-21 days

*PLUS*

**Gentamicin**, 5mg/kg /day, IM every 24 hours for 14-21 days

**Alternative**

If there is no response to the first line antibiotics within 48-72 of initiation of antibiotics, or if the infant has hospital acquired infection, or if the mother had culture proven gram-negative infection;

**Ceftriaxone**, 100mg/kg/24hr, IV in two divided doses (max. 4g/24hours)

*PLUS*

**Gentamicin**, 5mg/kg/day, IM every 8 hours for 14-21 days

## 2. Pyogenic meningitis beyond neonatal period or generally after 2-3 months

This is an acute and one of the most potentially serious infections in infants and children that affects the central nervous system. The usual etiologic agents in causing meningitis in children are: *H. influenzae, N meningitidis*and *S. pneumoniae.*The signs and symptoms of meningitis are variable and depend on the age of the patient.

**Clinical features**

In infants whose cranial sutures are still open,

- fever
- vomiting
- irritability
- lethargy
- convulsion
- bulging of the anterior fontanel

In older children focal neurologic signs, such as:

- A sixth nerve palsy, may be more prominent

- Signs of meningeal irritation, such as nuchal rigidity, kerning's sign or Brudziniskisign are usually present.

**Investigations**

- Examination of cerebrospinal fluid is mandatory if there is clinical suspicion of meningitis. Increased number of white cell count, low level of CSF glucose and elevated protein level are the usual findings. gram, stain and culture will reveal the microorganism which is responsible.

**Treatment**

**Non pharmacologic**

- Restrict fluid intake to 70% of calculated maintenance.
- Monitor urine output and daily weight
- Support feeding
- Monitor vital signs

**Pharmacologic**

**First line**

**Ceftriaxone**, 100mg/kg, IV once daily for 10 days for all cases

**Alternative**

**Cefotaxime**, 100mg/kg, IV divided in to 2-3 doses for 10 days.

**N.B.** Antibiotic treatment may be modified when culture and sensitivity results are collected.

**Adjunct to treatment with antibiotics**

**Dexamethasone**, 0.6mg/kg/day divided QID for four days in cases of suspected H. influenza meningitis

**12. Nephrotic Syndrome**

Nephrotic syndrome is characterised by heavy proteinuria (40mg/$m^2$/hour on timed urine collection or spot urine protein to urine Creatinine ratio > 2, or dipstick on early morning urine sample of 3+ or 4+), hypoalbuminemia (<2.5gm/dl) hypercholesterolemia (> 200mg/dl) and edema. About 90% of children beyond one year of age and less than 12 years of age, with

nephrotic syndrome have minimal change disease with steroid responsiveness. The commonest age at presentation is 2 – 6 years. After an apparent response to steroid treatment a patient may have relapse, which is defined as proteinuria of 2+ or more on dipstick for 3 consecutive days with or without edema.

**Clinical features**

- Periorbital and pedal edema
- Generalized edema, including ascites and pleural effusion in some patients
- Hypertension: Generally rare but can occur in some patients

**Investigations**

- Urine dipstick (protein, blood)
- Early morning spot urine protein to Creatinine ratio or urine albumin to urine Creatinine ratio
- Serum albumin, cholesterol, BUN, Creatinine
- Complete blood count

**Treatment**

**Objectives**

- Relieve symptoms
- Alleviate proteinuria
- Spare the kidney from damage by proteinuria

**Non pharmacologic**

- While the child is edematous, restrict salt and reduce maintenance fluid to 70% of normality.
- Critical assessment of temperature, blood pressure, pulse, capillary refill time and weight changes
- Educate the child and family about the disease, its management and its prognosis.

**Pharmacologic**

**Prednisolone**, 60mg/$m^2$ or 2mg/kg (maximum dose of 80mg) once daily for 6 weeks, followed by 40mg/$m^2$ (1.5mg/kg) given as a single dose on alternate days for a further 6 weeks after a meal to prevent gastrointestinal upsets**.**

If a patient fails to respond to 4 weeks of steroid treatment, then steroid resistance is diagnosed and the patient should be referred for renal biopsy and further treatment.
If the child is edematous, give empirical **amoxicillin** 50mg/kg in two divided doses till the edema disappears.
If slightest suspicion of infection, treat with **penicillin and aminoglycoside** for 7 – 10days

**Treatment of relapsing disease**

If infrequent relapse (< 2 relapses in 6 months or < 3 relapses in one year), **prednisolone** 60mg/$m^2$ (maximum 80mg) daily until urinary protein turns negative or trace for 3 consecutive days followed by alternate day therapy with 40mg/$m^2$ (maximum 60mg) for 28 days or 14 doses.
If frequent relapse (2 or more relapses in the initial 6 months or more than 3 relapses in any 12 months), **prednisolone** 60mg/m2 (maximum 80mg) daily until urinary protein turns negative or trace for 3 consecutive days followed by alternate day therapy with 0.1-0.5mg/kg for 6 months and then taper.
If the child relapses while on alternate day **prednisolone,** add levamisole 2.5mg/kg on alternate days for 6-12 months, then taper prednisolone and continue levamisole for 2-3 years.
If the child develops steroid toxicity, refer to a tertiary center.

## 13. Oral Thrush

This is a condition caused by candida species and is a punctate or diffuse erythema and white pseudomembranous plaque affecting the oral mucosa. The lesions may become confluent plagues involving extensive regions of the mucosa. Plagues can be removed with difficulty to reveal a granular base that bleeds easily. After the neonatal period, the presence of oral thrush-without antibiotic treatment, or lasting over 30 days despite treatment or recurring is highly suggestive HIV infection.

**Clinical features**

- Pain and difficulty of feeding
- Fever, occasional
- Vomiting if extends to the esophagus
- Whitish curd-like plaques on the tongue and oral mucosa
- Bleeding upon removal of the plaque

- Evidence for immunosuppression usually present, especially beyond the neonatal period

**Investigations**

- Diagnosis of oral thrush is entirely clinical and investigations are not needed

**Treatment**

**Objectives**

- Alleviate symptoms and improve feeding
- Decrease the risk of complications
- Identify the underlying cause, if any

**Non pharmacologic**

- Support feeding (if admitted, use naso-gastric tube feeding, especially in severe cases)

**Pharmacologic**

**First line**

**Nystatin** (100 000 units/ml) suspension: Give 1-2ml into the mouth 4 times a day for 7 days.

**Alternatives**

**Miconazole**, apply thin films of 2% cream BID for four days or until lesion disappears

*OR*

**Ketoconazole**, apply thin films of 2% cream BID until lesion disappears.

*OR*

**Gentian violet,** paint the mouth with half strength twice daily

### 14. Osteomyelitis

Treatment of infections to bones and joints in children are important because of their potential to cause permanent disability. Skeletal infections are more common in infants and toddlers than in older children. The risk of permanent disability is increased if the growth plate of bone or the synovium is damaged. Bacteria are the most common pathogens in acute skeletal infections with *S. aureus* being the most common cause in all age groups including newborns.

**Clinical features**

- Earliest signs and symptoms may be subtle.

- Neonates may exhibit pseudoparalysis or pain with movement of the affected extremity
- Older infants and children may have fever, pain and localizing signs such as edema, erythema and warmth.

**Investigations**

- Diagnosis of osteomyelitis is generally clinical
- Definitive diagnosis is by aspirations of the infected site for gram stain and culture
- X-ray changes may not be seen for the first 7 – 14 days but then periosteal elevation and lytic changes may suggest the diagnosis.
- Radionuclide scans are definitive and establish the diagnosis very early in the course.

**Treatment**

**Objectives**

- Alleviate symptoms
- Decrease the risk of complications
- Facilitate appropriate growth

**Non pharmacologic**

- Immobilize and elevate the affected limb

**Pharmacologic**

Control pain with oral **paracetamol** 10mg/kg every 4 – 6 hours. If pain is not controlled with paracetamol, follow the analgesic ladder of pain management.

**Cloxacillin**, 50-100mg/kg/day divided every six hours for 3-6 weeks

### 15. Pertusis (Whooping Cough)

Pertusis or whooping cough is a highly contagious clinical syndrome caused by a variety of agents including *Bordetella pertussis*, other Bordetella species and adenovirus. History of similar illness in the vicinity is an important evidence for diagnosis. A course of Pertussis can be divided in to catarrhal, paroxysmal and convalescent stages. Appropriate and timely immunization is protective.

**Clinical features**

- The catarrhal stage is marked by nonspecific upper respiratory tract symptoms including runny nose and low grade fever.
- The characteristic paroxysmal stage follows during which repetitive coughs are followed by an inspiratory whoop
- The child is well and playful between paroxysms of cough
- Post tussive vomiting
- Cyanosis, occasionally after a paroxysm of cough
- The convalescent stage begins after 4-6 weeks.

**Investigations**

- Diagnosis of pertussis is entirely based on clinical grounds and presence of similar illness in the vicinity.
- Chest X-ray may show paracardiac infiltrates and may be helpful in suggesting comorbid conditions
- White blood cell count may be elevated

**Treatment**

**Objectives**

- Relieve symptoms
- Avoid complications

**Non pharmacologic**

- Nutritional support

**Pharmacologic**

**First line**

**Erythromycin**, 12.5mg/kg P.O., QID for ten days

**Alternatives**

**Clarithromycin**, 15 – 20mg/kg/24hours, P.O., divided in to two doses for 7 days

*OR*

**Azithromycin**, 10mg/kg/24hours, P.O. for 5 days

## 16. Pneumocystis Carini Pneumonia (PCP)

A presumptive diagnosis of pneumocystis pneumonia can be made in a child who has severe or very severe pneumonia and bilateral interstitial infiltrate on chest x-ray. Consider the possibility of pneumocystis carinii pneumonia in children, known or suspected to have HIV, whose ordinary pneumonia does not respond to treatment. Pneumocystis pneumonia occurs most frequently in infants (especially those <6 months of age) and is often associated with hypoxia. Fast breathing is the most common presenting sign.

**Clinical features**

- Fever
- Fast breathing
- Flaring
- Cyanosis
- Dyspnea
- Intercostal and subcostal retractions
- Crackles and rhonchi on chest examination

**Investigations**

- Diagnosis is based on high index of suspicion from clinical features and presence of an underlying immunosuppression
- Chest X-ray may be normal in early disease, but may show diffuse bilateral infiltrates extending from the perihilar region are visible in most patient
- Computed Tomography may help when chest X-ray findings are equivocal
- Pulse oximetry
- Blood gas determination, in patients with $O_2$ saturation is <90% on room air
- Serum LDH levels, usually elevated and decrease with successful treatment

**Treatment**

**Objectives**

- Prevent respiratory failure
- Decrease the risk of complications
- Shorten hospital stay

**Non pharmacologic**

- Oxygen via face mask or nasal cannula
- Appropriate fluid management

**Pharmacologic**

**First line**

**Cotrimoxazole, trimethoprim** P.O., 5mg/kg/day, sulfamethoxazole 25mg/kg/day, 4 times a day for 3 weeks.

**Alternative**

**Pentamidine** (4mg/kg once per day) by IV infusion for 3 weeks

| | |
|---|---|
| **ADRs:** | Renal impairment, pancreatitis, leucopenia, hypoglycemia |
| **C/Is:** | Diabetes, renal damage |
| **Dosage forms**: | Nebulizer solution, 300mg/vial; powder for injection, 200mg/vial. Children who react adversely to trimethoprim-sulfamethoxazole are usually aged less than 1 year and often become hypoxic, and require oxygen therapy for several days. Their response to treatment is poor and the case-fatality rate is high. Recovery from hypoxia can be prolonged. |

**Prophylaxis**

**Trimethoprim,** 5mg/kg/24 hours and Sulfamethoxazole 25mg/kg/24 hours orally divided Q12 hours OR Q24 hours 3 days /week on consecutive days. OR Q12 hours 7 days a week OR Q12 hours on alternative days 3days /week

**N.B.** Children who have had PCP should receive lifelong prophylaxis

## 17. Pneumonia In Children

Pneumonia defined as inflammation of lung parenchyma, is caused virtually by every class of microorganisms and a specific etiologic diagnosis is often difficult in children. Viruses and mycoplasma pneumoniae are the primary agents causing pneumonia followed by bacteria. WHO recommends diagnosis of pneumonia when children under five have acute on-set cough with tachypnea. A child presenting with cough or difficult breathing may be classified as follows:

**Clinical features**

According to the IMNCI classification, a child presenting with cough or difficult breathing is classified as having severe pneumonia, pneumonia or no pneumonia: cough or cold.

**Severe pneumonia:**

- Cough or difficult breathing
- Lower chest indrawing,
- Nasal flaring,
- Grunting in young infants.
- Fast breathing or abnormal breath sounds may also be present.

**Pneumonia:**

- Cough
- Fast breathing
- But no signs for severe pneumonia

**No pneumonia**

- Cough or cold, if no sign for pneumonia or severe pneumonia.

**Investigations**

- Chest X ray
- The decision to treat a child who has pneumonia is usually made clinically
- Antibiotic therapy is directed at the most likely pathogens as suggested by the child's age, clinical presentation (including severity of illness), and not on investigations.

**Treatment**

**Objectives**

- Alleviate symptoms
- Prevent respiratory failure
- Prevent complications

**Non pharmacologic**

- Soothe the throat; relieve the cough with a safe remedy
- Safe remedies to recommend include;
    - breast milk for exclusively breast-fed infant
    - home fluids such as tea with honey, fruit juices
- Give oxygen for those in respiratory distress via nasal cannula

**Pharmacologic**

**Antipyretic**

**First line**

**Paracetamol,** 10-15mg /kg P.O., up to 4 times a day for the relief of high fever equal to or above 39 ºC

**Alternatives**

**Ibuprofen**, 5 – 10mg/kg/dose every 6 – 8hr P.O. (max. 40mg/kg/24hours).

**Antibiotic**

**First-line**

**Amoxicillin**, 30-50mg/kg/24hourss P.O. TID for 7 days

**Alternatives**

**Azithromycin**, 10mg/kg/24 P.O., once daily for 3 days

**1. Severe Pneumonia**

**Indication for admission (inpatient treatment)**

- Respiratory distress (Apnea, grunting, nasal flaring,chest indrawing)
- Hypoxemia (<90% Oxygen Saturation) or cyanosis
- All infants under age 4 months
- Toxic appearance
- Dehydration with Vomiting or poor oral intake
- Immune-compromised patient
- Pneumonia refractory to oral antibiotics
- Unreliable home environment

**Benzyl penicillin,** 50,000units/kg/24hours IM OR IV QID for at least 3 days

**N.B.** When the child improves switch to oral Amoxicillin: 30-50mg/kg/24 hours 3 times a day. The total course of treatment is 10 days.

If the child doesn't improve within 48 hours, switch to ceftriaxone 50mg/Kg/24 hours IM/IV for 5 days

**2. Presumed Atypical pneumonia**

**Azithromycin,** 10mg/kg P.O., on day 1, 5mg/kg on day 2-5

## 18. Rickets

Rickets is a disease caused by deficiency of vitamin D. It is a condition in which there is failure to mineralize growing bone or osteoid tissue. The early changes of rickets are seen radiographically at the ends of long bones, but evidence of demineralization in the shafts is also present. If rickets is not treated at this stage, clinical manifestations appear. Rickets can result from either inadequate intake of vitamin D caused by inadequate direct exposure to sunlight, the rays of which do not pass through ordinary window glass or inadequate vitamin D intake, or both. Rickets usually appears toward the end of the first and during the second year of life.

**Clinical features**

- Craniotabes: one of the earliest clinical sign of rickets caused by thinning of the outer table of the skull (ping-pong ball sensation when pressing firmly over the occiput or posterior parietal bones).
- Box like appearance of the head (caput quadratum)
- Delayed teeth eruption
- Palpable enlargement of the costochondral junctions (rachitic rosaries)
- Thickening of the wrists (wrist widening)
- Thickening of the ankles (double malleoli)
- Pigeon breast deformity (projecting forward of the sternum)
- A horizontal depression along the lower boarder of the chest (Harrison's groove)
- Bowing of the legs (genu varum deformity) or knock-knees (genu valgum deformity), are relatively late signs occurring after the child starts to bear weight.
- Deformed pelvis and retardation of linear growth
- Greenstick fractures (late signs)

**Investigations**

- X-ray of the wrist: Decreased bone density, cupping and fraying at the ends of the long bones (best appreciated at the distal end of the radius and ulna) and widened joint space (best appreciated at the wrist joint)
- Normal or low serum calcium, low serum phosphate and high serum alkaline phosphatase, and high serum parathormone levels

**Prevention**

- Regular exposure to direct sun light of infants and young children
- Oral administration of vitamin D especially to those breast fed infants whose mothers are not exposed to adequate sun light (supplemental dose of 400 IU Vitamin D daily, orally).

**Treatment**

**Objectives**

- Ensure proper physical growth of the child
- Avoid long term complications of bone deformity
- Avoid acute complications, including recurrent pneumonia, hypocalcaemia etc.
- Avoid pathological fractures

**Non pharmacologic**

- Regular exposure to direct sun light without clothing, without applications of any ointments and no glass windows

**Pharmacologic**

- Mega dose of Vitamin D (600,000 IU intramuscularly as a single dose)

## 19. Seizures (Neonatal)

Seizures can be the most dramatic indication of neurologic abnormality in the newborn, yet most neonatal seizures are subtle or even silent. There are five types of neonatal seizures:

Subtle seizures (presenting with apnea, starring, lip smacking, chewing or eye blinking); Focal clonic; Multifocal clonic; tonic, and Myoclonic seizures. The causes of neonatal seizures include metabolic, toxic, structural and infectious diseases.

**Clinical Features**

- Neurologic signs like abnormal focal movements
- Subtle manifestations like sucking movements

**Investigations**

- Laboratory –blood glucose level, electrolytes (calcium,magnesium)
- CSF analysis and CSF culture if meningitis is suspected
- Neuroimaging –MRI, CT scan of the brain (if underlying brain lesions are suspected)

**Treatment**

**Objectives**

- Terminate seizure
- Prevent brain damage
- Ensure appropriate brain development
- Prevent disability

**Non pharmacologic**

- Ensure patency of the airway
- Check breathing and circulation

**Pharmacologic**

**First line**

**Phenobarbital**, I.M/I.V/P.O.15-20mg kg/day loading dose, followed by 5mg/kg in two divided doses given after 24 hours after loading dose

**Alternative**

**Phenytoin**, **I.M**/I.V/P.O.15-20kg/day loading dose, followed by 5mg/kg in two divided doses

**If seizures are associated with;**

1. **Hypocalcaemia (Hypocalcaemic-tetany)**

**Calcium gluconate** solution, 10% 1-2ml/kg/; repeat PRN after 6 hours

**ADRs:** bradycardia, cardiac arrest, extra vascular leakage may cause local necrosis.

**Dosage forms:** *S*yrup 4gm/15ml; injection, 10% solution, 10 ml.

**2. Hypoglycemia**

Glucose 10%

**3. Vitamin B6 deficiency**

Vitamin B6 (pyridoxine), 50mg IM as single dose.

**Dosage forms:** Injection, 50mg/ml in 2ml.

**20. Sepsis (Neonatal)**

Neonatal sepsis is defined as bacteremia with systemic manifestation in the absence of other primary systemic problems during the first 28 days of life' Neonatal sepsis can be divided into two subtypes:

**Early onset sepsis**: Occurs within the first 72 hours of life. It is caused by organisms prevalent in the genital tract of the mother or in the labour room, which includes mainly group B streptococci, *E coli*, Coagulase-negative Staphylococcus and L. monocytogenes. Majority of the neonates with early onset sepsis clinically manifest with respiratory distress due to intrauterine pneumonia. Early onset sepsis has usually fulminant course and high mortality.

**Late onset sepsis**: The onset is delayed for a minimum of four days in most cases symptoms appear by the end of first week of life. About 2/3 cases of late onset septicemia are caused by gram negative bacilli while the rest are contributed by gram positive organisms. Meningitis is more frequent.

**Recognition of systemic sepsis** signs are usually non-specific since other conditions cause similar clinical states (e.g., cardiac or respiratory failure, metabolic disorders)

**Clinical features**

- Pallor, lethargy, jaundice, fever, hypothermia
- temperature instability (note 1/3 of confirmed sepsis cases are normothermic)
- hypoglycemia, increased respiratory rate, apnea, grunting, cyanosis
- tachycardia, bradycardia episodes, poor perfusion, hypotension
- petechiae, bleeding from puncture sites

- poor feeding, vomiting, abdominal distension, feed intolerance
- bilious aspirates/vomitus and loose stools
- lethargy, irritability,seizures

Any baby who is unwell must be considered at risk of sepsis and appropriate antibiotics commenced as soon as possible after taking cultures. Inability to obtain cultures should not delay administration of antibiotics.

**Investigations**

- Laboratory:-complete blood count, blood culture, CSF analysis and culture, urinalysis and culture, stool culture
- Chest X-ray
- Ultrasonography of the brain and CT-scan of the brain (in complicated meningitis).

**Treatment**

**Objectives**

- Alleviate symptoms
- Avoid life-threatening complications
- Prevent multi-organ failure

**Non pharmacologic**

- Maintenance of body temperature (Kangaroo mother care, radiant warmer, incubator)
- Adequate calorie and fluid maintenance
- Correction of associated metabolic abnormalities

**Pharmacologic**

Till the culture report is collected start with broad-spectrum antibiotics, which includes penicillin and Aminoglycoside.

**First line**

**Ampicillin**, 100mg /kg/day every 12 hours IV.for 10 days.

*PLUS*

**Gentamicin**, 5mg/kg /day IV Daily for 10 days

**Alternative**

**Penicillin G Sodium Crystalline**, 50,000IU/kg QID for ten days

*PLUS*

**Gentamicin**, 5mg/kg /day IM Daily for 10 days

## 21. Tuberculosis In Children

Tuberculosis is (TB) a chronic infectious disease caused in most cases by Mycobacterium tuberculosis. Occasionally it can be caused by Mycobacterium bovis or Mycobacterium africanum Diagnosis of TB in children is difficult because of the presence of a wide range of non-specific symptoms. It is important to make a clear distinction between infection and disease. In infection, only the Mantoux test may be positive (10mm), but the child is healthy and does not have any signs and does not, therefore, need anti TB treatment. If there is TB-disease there are clear signs and symptoms.

**Clinical features**

- Symptoms and signs may be confusing in children co-infected with HIV
- Fever
- Cough lasting for more than 2 weeks (sputum production uncommon in infants and young children)
- Dyspnea
- Recent weight loss or failure to gain weight
- Night sweats are uncommon in infants and young children
- Rales, wheezing and decreased air entry, more common in infants
- Extra-pulmonary involvement, more common in infants and young children

**Investigations**

- Chest X-ray: Hilar or mediastinal adenopathy, segmental/lobar infiltrates, military disease, consolidations, pleural effusion, or normal in about 15% of patients
- Tuberculin skin test (PPD)
- Sputum or gastric aspirate for acid-fast stain
- Erythrocyte Sedimentation rate (ESR)
- WBC and differential count

**Table 76-Criteria for the diagnosis of tuberculosis in children**

| **Suspected tuberculosis** |
| --- |
| An ill child with a history of contact with a confirmed case of pulmonary tuberculosis |

Any child:

- Not regaining normal health after measles or whooping cough
- With loss of weight, cough and wheeze not responding to antibiotic therapy for respiratory disease
- With painless swelling of superficial lymph nodes

**Probable tuberculosis**

A suspect case and any of the following:

- Positive (10 mm in diameter) induration on tuberculin testing
- Suggestive appearance on chest radiograph (e.g. unilateral hilar/mediastinal lymphnode enlargement with or without lobar or segmental opacity, miliary patter, pleural effusion, infiltrates and cavitation)
- Suggestive histological appearance of biopsy material

**Confirmed tuberculosis**

- Detection by microscopy or culture of tubercle bacilli from secretions or tissues
- Identification of tubercle bacilli as Mycobacterium, tuberculosis by culture

**Treatment**

**Objectives**

- Avoid complications and mortality
- Cure the infection
- Ensure adequate growth and development

**Non pharmacologic**

- Nutritional support
- Emotional support for the child and family

**Pharmacologic**

Short course chemotherapy as Category III

The treatment regimen for this category is 2 (RHZ)/6EH. This regimen consists of 8 weeks' treatment with **Rifampicin, Isoniazid** and **Pyrazinamide** during the intensive phase followed by six months of **Ethambutol** and **Isoniazid.**

## CHAPTER XV: DERMATOLOGICAL DISORDERS

### 1. Acne Vulgaris

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous follicles, characterised by comedones, papules, pustules, nodules, and often scars. Acne typically begins at puberty. The disease is characterised by a great variety of clinical manifestations, non inflammatory or inflammatory.

**Clinical features**

- Comedones (black or white heads).
- Papules, pustules, nodules, cysts or scars.
- Lesions are mostly confined to the face, upper arm, chest and back.

**Investigations**

- Diagnosis is clinical.

**Treatment**

**Objectives**

- Improve cosmetic appearance
- Prevent complications particularly scarring.

**Non pharmacologic**

- Cleansing the face with oil-free cleansers twice daily
- Avoiding oil containing moisturizers and vaseline.
- Use oil free moisturizers and alcohol containing toners instead.
- Avoiding squeezing
- Counselling of patient.

**Pharmacologic**

**1. Mild Acne:**

**First line**

**Retinoic acid (Tretinoin)** – start with 0.025% cream or 0.01% gel and gradually increase the concentration to 0.05% cream or 0.025% gel, then to 0.1% cream, then to 0.05% lotion. Start

with every other day regimen and make twice daily based on tolerance of the skin for irritating effect of retinoids. Improvement is seen after 2–5 months.

**ADRs:** Transient burning, excessive redness, dryness, oedema or blistering, heightened susceptibility to sunlight

**C/Is:** hypersensitivity to retinoic acid

**D/Is:** sulphur, benzoyl peroxide, salicyclic acid, resorcinol, thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides).

**P/Cs**: eczema.

**Dosage forms**: Cream, 0.025%; Gel, 0.01%, 0.025%; Lotion, 0.025%, 0.05%; Ointment, 0.05%

**Alternatives**

**Clindamycin**, 1% gel or lotion;

*OR*

**Erythromycin** 2-4% gel, lotion or cream,

*OR*

**Azelaic Acid** 20% applied twice daily.

**ADRs:** Skin irritation

**Dosage form:** Cream,20%

**2. Moderate Acne**

**First line**

The above topical medications

*PLUS*

**Doxycycline**, 100mg P.O., QD for a minimum of 6 months depending on clinical response

*OR*

**Tetracycline**, 250-500mg two to four times daily for a minimum of six months.

*OR*

**Azithromycin**, 250-500mg three times weekly 12 weeks

**3. Severe Acne**

**First line**

**Isotretinoin**,0.5-2mg per kilogram of body weight in two divided doses with food for 15 to 20 weeks.

**N.B.** Contraception should be secured in females for treatment time and for 4 months after treatment and serum lipid monitoring in all patients is mandatory.

**Dosage form:** Capsule, 10mg, 20mg

**Alternatives**

**Dapsone**, 50-100 mg P.O, daily

*OR*

**Spironolactone**, 50–100 mg daily for up to six months

*OR*

**Combined oral contraceptive pill** for women for up to six months.

*OR*

**Intralesional Triamcinolone acetonide** 40mg per ml diluted with equal amount of Normal saline or local anesthesia repeated every four weeks is effective for few nodules or hypertrophied acne scars.

## 2. Bacterial Folliculitis

Bacterial folliculitis (follicular pustules) is an infection usually caused by *Staphylococcus aureus*. Predisposing factors may be local or systemic impairment of the immune system, increased or changed bacterial flora of the follicles, systemic diseases e.g. diabetes mellitus, prolonged contact or treatment with fatty oils. It can progress to furuncles.

**Clinical features**

- Small, 1-4 mm pustules or crusted
- Papules on an erythematous base that heal without scarring.
- Frequently involved areas are the face, chest, back, axillae or buttocks.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Prevent complications like furuncles.

**Non pharmacologic**

- Frequent washing with detergents e.g. soap and water to reduce the bacterial flora.
- Evacuate the pustules with sterile needle and apply a disinfecting solution.

**Pharmacologic**

**For Localized**: Topical antibiotics like **Mupirocin**, 2% ointment, or **Fusidic acid** cream applied twice daily to the affected area for 7-10 days.

**For Generalized:**

**First line**

**Cloxacillin**,

children; 50 – 100mg/kg /day P.O., for 7 to 10 days divided into four doses

adults; 500mg P.O., QID for 7 to 10 days

| | |
|---|---|
| **ADRs:** | Hypersensitivity reactions, nausea, loose stools, increased transaminases |
| **CIs:** | Hypersensitivity to penicillin |
| **Dosage forms:** | Capsule, 250mg. Syrup 250 mg/5ml and 125mg/5ml. Injection 500ml vial |

**Alternatives**

**Erythromycin**:

children; 30–50mg/kg/day for 7 to 10 days in 4 divided doses

adults; 500mg P.O., QID for 7 to 10 days

| | |
|---|---|
| **ADRs:** | Hypersensitivity reactions, GI symptoms, Cholestatic jaundice |
| **CIs:** | Liver disease, hypersensitivity to the medicine |
| **Dosage forms:** | Capsule 250mg. 500mg. Syrup 125 mg. & 250 mg/5 ml |

*OR*

**Cephalexin**,

children; 25 to 100mg/kg in 4 divided doses for 7 to 10 days.

adults; 250 to 500mg QID for 7 to 10 days

**For Recurrent (Chronic S**. ***aureus*** **carriage)**

**Mupirocin**, 2% ointment applied twice daily to the nares, axillae/groin and/or sub mammary area for 5 days.

### 3. Candidiasis (Candidiasis, Moniliasis, Thrush)

Candidiasis is an infection caused by the yeast like fungus *Candida albicans*. Infection by this fungus may cause different types of lesions on the skin, nail, mucous membrane and viscera. The areas where warmth, and maceration of the skin permit the organism to thrive, are frequently affected. These are the perianal and inguinal folds, the interdigital areas and the axillae. It may be a normal inhabitant at various sites until there is some change in the state of the area, and then it becomes a pathogen. Abnormal moisture also promotes its growth, as in moist lip corner.

**Clinical features** and **investigations** depend on each specific site.

**1. Balanoposthitis** refers to candida infection of the penis.

**Clinical features**

- Small papules or fragile papulopustules on the glans or in the coronal sulcus

**Investigations**

- Microscopic examination after KOH preparation

**Treatment**

**Objectives**

- Eradicate infection

**Non pharmacologic**

- Manage predisposing factors like maceration and underlying diseases like diabetes and immunosupprssion.

**Pharmacologic**

**First line**

**Clotrimazole**, thin film of 1% cream applied to the lesion BID for about 2-3 weeks

**Alternative**

**Miconazole**, thin film of 2% cream applied to the lesion bid for about 2-3 weeks.

### 2. Candidal Intertrigo

Usually involves the great folds of the body (groin, inframammary, axillae, perianal areas). It also affects the area between the fingers and toes.

**Clinical features**

- Red, oozing band with a whitish macerated centre and a scaly border at the affected fold.

- Isolated, flaccid, satellite, vesiculo-pustules which, when they break, show collar of scale at the periphery.

**Investigations**

- Microscopic examination after KOH preparation

**Treatment**

**Objectives**

- Eradicate infection

**Non pharmacologic**

- Avoidance of chronic exposure to moisture.

**Pharmacologic**

Topical application of, **Clotrimazole, Miconazole**

| |
|---|
| In those suffering form diabetes mellitus, treatment consists of bringing the diabetes under control. |

**3. Candidal paronychia**

Chronic inflammationof the nail fold. This type of infection is usually caused by *C.albicans* but frequently is of bacterial causation. It is often seen individuals whose hands are constantly wet as a result of their occupation and in elderly diabetics.

**Clinical features**

- Chronic paronychia causes redness, swelling, and pain of the tissue around the nail.
- Pressure on the affected region may elicit a malodorous pus.
- In chronic paronychia, the cuticle separates from the nail plate, leaving the region between the proximal nail fold and the nail plate vulnerable to infection.
- It can be the result of dish washing, finger sucking, aggressively trimming the cuticles, or frequent contact with chemicals.

**Investigations**

- Microscopic examination after KOH preparation

**Treatment**

**Objectives**

- Eradicate infection

**Non pharmacologic**

- Avoidance of chronic exposure to moisture is an important prophylactic measure.

**Pharmacologic**

Topical application of, **Clotrimazole, Miconazole**

*OR*

**Systemic treatment with**

**First line**

**Fluconazole**, 150mg P.O., QD for 4-6 weeks

**Alternatives**

**Itraconazole**, pulse dosing with 200mg BID for 1 wk of each of 3 consecutive months.

*OR*

**Terbinafine** (250mg qd for 3 mo) is recommended.

**4. Genital Candidiasis (Vulvovaginitis)**

Refer gyne section

**5. Oral candidiasis (thrush)**

**4. Carbuncle**

Carbuncle is a deep bacterial infection of the skin, usually a confluence of two or more furuncles with separate heads.

**Clinical features**

- Painful smooth dome shaped lesion that increases in size to 3-10cm or occasionally more followed by suppuration in 5-7days and pus discharge begins through multiple orifices.
- Affects nape of the neck, back, shoulder, hip, thigh.

**Investigations**

- Gram stain and culture of pus

**Treatment**

**Objectives**

- Eradicate infection
- Minimize scarring

**Non pharmacologic**

- Incision and drainage is usually necessary

**Pharmacologic-**See treatment of furuncules

**5. Cellulitis**

Cellulitis is a diffuse inflammation of the subcutaneous tissue and the skin due to bacterial infections. It usually occurs through a breach in the skin surface especially if tissue edema is present, but may abruptly affect normal skin. Cellulitis is usually caused by *Streptococcus pyogenes* but other bacteria such as *Haemophilus influenzae* and gram–negative organisms can cause cellulitis especially in children.

**Clinical features**

- Fever and malaise
- Warmth, redness,tenderness of the affected site
- Enlarged and tender regional lymph nodes.

**Investigations**

- CBC
- Fasting blood glucose.
- Wound swab for culture and sensitivity, if there is pus
- Blood culture (in the seriously ill).

**Treatment**

**Objectives**

- Relieve pain.
- Control the infection
- Treat predisposing infection/s.

**Non pharmacologic**

- Bed rest
- Application of warm compresses
- Elevation of an affected limb.

**Pharmacologic**

**First line**

**Procaine penicillin**,

children; 50,000u/kg/24 hrs. in a single dose for 10 days.

adults; 1.2 million IU intramuscularly daily for 7 to 10 days.

If no improvement occurs within a day, penicillinase resistant staphylococcus should be suspected and semi-synthetic penicillins (e.g. **Cloxacillin** 0.5 – 1gm every 4 hrs.) should be administered intravenously until the fever subsides, (usually 2 – 3 days). Then **Cloxacillin** 500 mg. P.O QID should be continued for 7 days.

Hospitalized patients should be treated with **Crystalline Penicillin** 1.2-2.4 million units IV 4 hourly.

**Alternative**

**Erythromycin**

**N.B**. In all children with facial or periorbital cellulitis, coverage for *Haemophilus* should be provided with **Chloramphenicol** 30 to 50mg/kg/d divided in two four doses

*OR*

**Cephalexin**, 500 mg P.O., QID

**Dosage form:** Capsule 250 mg, 500mg; syrup,125 ml

**6. Dermatophytoses**

Superficial fungal infections (**Dermatophytoses**) usually affect all parts of the skin from head to toes. These include:

- Infection of the scalp-tinea capitis
- Infection of the skin of the trunk and extremities-tinea corporis
- Infection of the axillae or groin-tinea cruris
- Infection of the nails-tinea unguium (onychomycosis)
- Infection of the palms and soles-tinea palmo-plantaris
- Infection of the cleft of the fingers and toes-tinea interdigitalis

**Clinical features**

- Lesions with ring shaped scaly erythema with active margins.
- Deformed nails and onycholysis in case of nail infections.
- Hair loss and whitish scale in tinea capitis.

**Investigations**

- KOH mount

**Treatment**

**Objectives**

- Eradication of the infection

**Non pharmacologic**

- Good basic hygiene
- Use of loose clothing

**Pharmacologic**

The application of topical antifungals is usually enough for tinea corporis and cruris whereas patients with tinea capitis, tinea unguium will require systemic treatment.

**Topical:**

**First line**

**Clotrimazole**, thin film of 1% cream applied BID for 2-3 weeks.

**ADRs:** skin irritation,

**Dosage forms:** Cream, 10%; solution, 1%

*OR*

**Ketoconazole**, thin film of 2% cream applied BID until the infection clears (usually for 2-3 weeks)

**ADRs:** Occasionally, skin irritation or sensitivity

**Dosage form:** Cream, 2%; lotion, 2%; shampoo, 2%

*OR*

**Miconazole** thin film of 2% cream applied BID until the infection clears (usually for 2-3 weeks).

**Dosage forms:** Cream, 2%; lotion, 2%; tincture, 2%.

**Table 77-Common Systemic Anti-fungal Medicines and Their Dosage schedules**

| **First line** | | | **Alternatives** | |
|---|---|---|---|---|
| Fungal infection | Griseofulvin | Ketoconazole | Fluconazole | Itraconazole |
| Tinea corporis & cruris (only to those resistant to topical RX) | Adult 500-1000 mg P.O. daily<br>Children: 15-25mg/kg/day<br>Duration 2-6 weeks | Adult-200-400mg/day P.O.<br>Children-3mg./kg/day<br><br>Duration: 3 weeks | Adult 200-400 mg once a week P.O.<br>Children 8 mg/week<br>Duration 3-4 weeks | 200 mg. daily P.O.<br>Duration:<br>1-2 weeks |
| Tinea capitis | Same dose as above | Adult same dose as above | Adult 150 mg. P.O. | 200 mg. P.O.daily |

| | | | | |
|---|---|---|---|---|
| | Duration 6-8 weeks<br>occasionally<br>up to 12 weeks | duration 4 weeks<br>Children same dose<br>duration 4 weeks | daily Duration:<br>4-6weeks<br>Children 4-6mg/kg<br>per day for 4-6 weeks | Duration:<br>4-6 weeks |
| Tinea unguium | Not<br>recommended because<br>long duration of treatment<br>increases toxicity | Not<br>recommended because<br>long duration of treatment<br>increases toxicity | 400 mg. P.O.<br>once a week<br>Duration:<br>Finger nails<br>6-9 months<br>Toe nails<br>12-18 months<br>Children<br>8-10 mg po/kg/week | **Pulse therapy**<br>200mg BID one<br>week per month<br>Finger nails<br>2 pulse<br>Toe nails<br>3 pulse |
| Tinea pedis | Adult 500-1000mgP.O.<br>Daily<br><br>Children:15-25 mg/kg/day<br>Duration: 4-8 weeks | Adult: 200-400mg/day<br>P.O.<br>Children:3mg./kg/day<br>duration: 3 weeks | 200-400 mg P.O.<br>once a week or<br>150mg P.O. daily<br>Duration: 3-4 weeks<br>Children 4-6mg/kg<br>per day for 3 weeks | 200-400mg P.O.<br>QD<br>Duration<br>4 weeks |

**Table 78-ADRs, contraindications and dosage forms of common systemic antifungal medicines**

| Medicine | ADRs | C/Is | Dosage forms |
|---|---|---|---|
| Griseofulvin | hypersensitivity reactions, neutropenia, headache, nausea, vomiting, rashes and photosensitivity | liver failure, prophyria, pregnancy and hypersensitivity | Tablet, 125mg, 250mg, 500mg; suspension, 125mg/5ml |
| Fluconazole | Nausea, vomting, headache, rash, abdominal discomfort, diarrhoea | Hepatic damage | Capsule/tablet, 50mg, 100mg, 200mg; oral suspension, 50mg/5ml, 200mg/5ml |
| Ketoconazole | Nausea, vomiting, urticaria, abdominal pain, pruritis, articaria, rashes, headache | Hepatic impairment, pupurea | Tablet, 200mg; suspension, 100mg/5 ml |
| Itraconazole | Same but milder | Hepatic damage | Capsule, 100mg, 200mg; oral solution, 10mg/ml |

| | | | |
|---|---|---|---|
| Miconazole | nausea, vomiting abdominal pain, headache, rashes, urticaria, pruritus | hepatic impairment, porphyria | Tablet, 200 mg., suspension, 100ml./5ml. |

**7. Eczema**

## 1. Atopic Dermatitis (AD)

AD is a Chronic, highly pruritic inflammatory skin disease, associated with remitting and flaring course, that starts during infancy and early childhood and persists into puberty and sometimes adulthood. AD may be exacerbated by social, environmental, and biologic factors and has association to the other atopic diseases (allergic rhinitis, bronchial asthma and allergic sinusitis).

**Clinical features**

**Infant** usually begins as erythema and scaling of the cheeks. The eruption may extend to the scalp,neck, forehead, wrists, and extensor extremities. Lesion may be papular or exudative.

**Children:** lesions are apt to be **less exudative**.

The classic locations are the antecubital and popliteal fossae;

- Flexor wrists, eyelids, face,and around the neck.
- Lesions are often lichenified, indurated plaques.

**Adolescents & Adults:**

Localized erythematous, scaly, papular, exudative, or lichenified plaques.

**In adolescents**, the eruption often involves the classic-antecubital and popliteal fossae;

- Front and sides of the neck,
- forehead, and area around the eyes.

**In older adults,** the distribution is generally less characteristic, and chronic hand eczema may predominate. **S**imilar lesion with flexural distribution.

**Diagnostic features of atopic dermatitis as defined by Hanifin and Rajka**

**Major features (3 of 4 present**)

1. pruritus
2. typical morphology and distribution of skin lesions

3. chronic or chronically relapsing dermatitis
4. personal or family history of atopy

**Minor features (3 of 23 present**)

1. xerosis
2. ichthyosis/palmar hyperlinearity/keratosis pilaris
3. immediate (type I) skin test reactivity
4. elevated serum IgE
5. early age of onset
6. tendency towards cutaneous infections/impaired cell-mediated immunity
7. tendency towards non-specific hand or foot dermatitis
8. nipple eczema
9. cheilitis
10. recurrent conjunctivitis
11. Dennie-Morgan infraorbital fold
12. keratoconus
13. anterior subcapsular cataracts
14. orbital darkening
15. facial pallor/erythema
16. pityriasis alba amoebiasisanterior neck folds
17. itch when sweating
18. intolerance to wool and lipid solvents
19. perifollicular accentuation
20. food intolerance

21. course influenced by environmental/emotional factors
22. white dermographism/delayed blanch

**Treatment**

**Objectives**

- Alleviate the pruritus, and prevent scratching.
- Decrease triggering factors
- Suppress inflammation
- Lubricate the skin
- Manage complications

**Non pharmacologic**

- Atopic patients should bathe with cold or luke warm water once daily using mild soaps.
- Patient should dry quickly and immediately (with in 3 minutes) and lubricate the skin.

**Emollients:**

**Vaseline cream** OR **Liquid paraffin** applied liberally all over the body

**Pharmacologic**

**First line**

**Topical corticosteroids** are the standard of care compared with other treatments:

Eczematous lesions should be treated by mid-high strength topical steroids for up to 2 weeks except on the face, neck, breast, axillary, groin and perianal areas.

For the face, neck, axillae and other soft areas of the body low-to-mild strength medications are preferred. Patients should apply the ointment after bathing.

The use of long-term intermittent application of corticosteroids appears helpful and safe.

**N.B.** Systemic steroids are preferably avoided.

*PLUS*

**Cloxacillin** if a superimposed bacterial infection is suspected.

**Antihistamins**

**Diphenhydramine**, 25-50mg P.O., QD

**ADR:** sedation

**C/Is:** driving, involvement in heavy physical activity

**Dosage Forms:** Capsule,25mg, 50 mg; elixir,12.5mg/5ml;injection, 50 ml in 1 ml ampoule.

**Alternative**

**Chlorpheniramine,** 4-6mg P.O., QD

**ADRs:** sedation, dizziness

**C/Is:** active work such as driving

**Dosage forms:** Tablet, 2mg, 10mg; syrup, 2mg/5ml

for severe, recalcitrant and generalized cases, refer to dermatologist

## 2. Contact dermatitis

### Allergic contact dermatitis (ACD)

Allergic Contact Dermatitis is an inflammatory response of the skin to an antigen that can cause discomfort or embarrassment.

Allergic contact Dermatitis can be classified as acute, subacute and chronic

**Clinical features**

- Acute contact dermatitis manifests by fluid filled vesicles or bullae on an edematous skin
- Subacute contact dermatits is characterised by less edema and formation of papules, excorations and scaling
- Chronic eczema is characterised by scaling, skin fissuring and lichenfication.

**Irritant Contact Dermatitis (ICD)**

ICD is inflammation of the skin which manifests with edema and scaling and is non specific response to the skin by irritants and dirsct chemical damage (e.g. corrosive agents which cause chemical burn). The hands are the most important sites of ICD.

**Clinical features**

- Macular erythema, hyperkeratosis or fissuring
- Glazed, parched or scalded appearance of the epidermis
- Healing process on withdrawal

**Table 79 - ICD and ACD**

| | **ICD** | **ACD** |
|---|---|---|
| Symptom | Stinging, smarting→ itching | Itching →pain |
| Lesions<br>acute<br>Chronic | Erythema→vesicle→ erosion→ crust →scaling<br>Papules, plaques, fissures, scaling, crusts | Erythema→**papules** vesicle→ erosion→ crust →scaling<br>Papules, plaques, fissures, scaling,, crusts |
| Marigination,site & evolution | Sharp,strictly confined to site of exposure | spreading in the periphery;<br>usually tiny papules; may become generalized |
| Causative agent | Dependent on concentration of agent and state of skin barrier | Relatively independent of amount agents and state of skin barrier |
| Incidence | May occur in practically everyone | Occurs only in the sensitized |

**Irritant versus Allergic contact dermatitis**

**Investigations**

- KOH mount and culture to rule out fungal infection.
- Patch testing can be done to rule out ACD.
- Skin biopsy can help exclude other disorders such as fungal infection, psoriasis, cutaneous T-cell lymphoma

**Treatment**

**Objectives**

- Improve the quality of life by reducing symptoms.

**Non pharmacologic**

- Removal of the offending agent
- Lukewarm water baths (antipruritic)

**Emollients:**

**Vaseline cream** OR **Liquid paraffin** applied liberally to affected area

**For acute lesions**

- Topical soaks with cool tap water plus saline (TSP/Pint)
- Oat meal bath

**Pharmacologic**

**Topical steroids:**

**First line**

**Triamcinolone acetonide**, thin films applied BID initially, reduce to once daily as lesions remit.

**Alternative**

**Hydrocortisone**, thin films applied on face, axillae, breasts, groins and perianal area twice daily initially, reduce as the lesions remits.

**Dosage forms:** Cream, ointment, 1%

*OR*

**Mometasone**, thin films applied QD

**Dosage forms:** Cream, lotion, ointment, 0.1%

**Systemic steroids** (for severe, recalcitrant and generalized cases)

**Prednisone**, 0.5mg/kg P.O. QD for 1-2 weeks.

**Antihistamines:** (adjuncts)

**First line**

**Diphenylhydramine**, 25-50mg cap P.O., QD

**Alternative**

**Chlorpheniramine,** 4-6mg P.O., QD

**ADRs:** sedation, dizziness

**C/Is:** active work such as driving

**Dosage forms:** Tablet, 2mg, 10mg; syrup, 2mg/5ml

**N.B.** for severe, recalcitrant and generalized cases, refer to dermatologist

## 8. Erysipelas

Erysipelas is a bacterial infection of the skin and subcutaneous tissues. Predisposing factors include mechanical trauma, endogenous infection, venous and lymphatic system disorders (as in erysipelas recurrences). General susceptibility is increased by malnutrition, alcoholism and dysgammaglobulinemia. It is usually caused by Group A streptococci, and is contagious.

**Clinical features**

- Red, tender and erythematous skin without vesicles.
- Systemic symptoms like fever,chills and malaise are common.

**Invstigations**

- CBC

**Treatment**

**Objectives**

- Treat the infection.

**Non pharmacologic**

- Bed rest.
- Limb elevation and immobilization.
- Warm compresses

**Pharmacologic**

**First line**

**Procaine Penicillin**,

children: 50,000 IU/kg/d in single dose for 7 – 10 days.

adults: 1.2 million IU intramuscularly daily for 7 to 10 days.

Severe cases require intravenous therapy with crystalline penicillin in hospital until the fever subsides, at which time treatment is continued with procaine penicillin.

Relapsing erysipelas requires a small maintenance dose of penicillin or erythromycin for months or years.

**ADRs:** hypersensitivity reactions: urticaria, fever, joint pains, angioedema, anaphylactic shock.

**C/Is:** known hypersensitivity to penicillin and cephalosporins

**Dosage forms:** Injection (Buffered), Vial of 4 million unitsIU

**Alternative**

**Erythromycin**, if the patient is penicillin allergic

**Cephalexin**, 500mg P.O., QID

**Dosage form:** Capsule 250mg, 500mg; syrup,125ml

*OR*

**Cloxacillin**, 500mg P.O., QID

**Dosage form:** Capsule 250mg, 500mg; syrup,125ml

### 9. Erythema Multiforme (EM)

An acute, self-limiting and commonly recurrent inflammatory skin eruption with variable involvement of the mucous membranes and without systemic symptoms.

This condition is usually due to an infection, commonly herpes simplex or mycoplasma.

**Clinical features**

- Symmetrically distributed crops of targetoid lesions often involving palms and soles.

**Investigations**

- Diagnosis is clinical

### 10. Stevens Johnson Syndrome (SJS) & Toxic Epidermal Necrolysis (TEN)

An acute, systemic condition with vesico-bullous lesions involving the skin and mucous membranes. This condition is usually due to medication, e.g. sulphonamides, antiretrovirals (nevirapine), anti-epileptics (phenytoin, phenobarbitone,carbamazepine), herbal medications.

**Clinical features**

- start as a red morbilliform rash
- purple skin necrosis and blisters
- large areas of denuded skin
- Mucous membrane erosions are common and internal organ involvement may be present
- SJS when body surface area involvement is less than 10%.
- SJS –TEN overlap 10-30 % body surface area involvement
- TEN when more than 30 % of body surface area affected.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Management is supportive, good nursing and the prevention of dehydration and sepsis.
- Stop all medicines.
- Patients usually require care in ICU

**Non pharmacologic**

Should be managed as burn patients, if possible should be admitted to burn unit.

**Dressings**

- Skin hygiene; daily cleansing and bland, non-adherent dressings as needed.
- Do not use silver sulfadiazine if condition is thought to be due to cotrimoxazole or other sulphonamide.

**Mucous membranes**

Regular supervised oral, genital and eye care to prevent adhesions and scarring.

**Fluids**

- Oral rehydration is preferred but intravenous fluid therapy may be required in significant dehydration.
- Encourage oral fluids to prevent pharyngeal adhesions
- Provide soft, lukewarm food or nasogastric feeds if unable to eat.

**Pharmacologic**

**Corticosteroids**

The practice of using systemic corticosteroids is not supported by evidence and is therefore not recommended.

**Antibiotic therapy**

Systemic antibiotics may be indicated, depending on results of appropriate cultures.

**11. Furuncle**

Furuncle is a deep seated infectious folliculitis and perifolliculitis with a purulent core caused by *Staphylococcus aureus*. It affects mainly young men who are otherwise healthy but patients must be evaluated for predisposing factors: alcoholism, medicine abuse, diabetes mellitus, leukemias and other malignancies, AIDS and chronic liver disease.

**Clinical features**

- Fever, Pain, swelling and erythema of the involved area.
- Occur mostly in areas subjected to maceration or friction, poor personal hygiene, acne or dermatitis; e.g.face, neck, axillae

**Treatment**

**Objectives**

- Eradication of the infection.

**Non pharmacologic**

- Bed rest for patients with systemic symptoms, impaired immunity and with involvement of the face.

**Pharmacologic**

Systemic therapy is required for furunclosis of the face or when generalized symptoms or impairment of the immune system are present. Penicillenase resistant antibiotics like cloxacillin or dicloxacillin are preferable.

**First line**

**Cloxacillin**,

Children; 50 – 100mg/kg /day P.O., for 7 to 10 days divided into four doses

Adults; 500mg P.O., QID for 7 to 10 days.

**ADRs:** Hypersensitivity reactions, nausea, loose stools, increased transaminases

**C/Is:** Hypersensitivity to penicillin

**Dosage forms:** Capsule, 250mg., Syrup 250mg/5ml and 125mg/5ml. Injection 500ml vial

**Alternatives**

**Erythromycin**,

Children; 30–50mg/kg/day for 7 to 10 days in 4 divided doses

Adults; 500mg P.O., QID for 7 to 10 days.

**ADRs:** Hypersensitivity reactions, GI symptoms, Cholestatic jaundice

**C/Is:** Liver disease, hypersensitivity to the medicine

**Dosage forms:** Capsule 250mg. 500mg. Syrup 125 mg. & 250mg/5 ml

*OR*

**Cephalexin**,

Children; 25 to 100mg/kg in 4 divided doses for 7 to 10 days.

Adults; 250 to 500mg QID for 7 to 10 days.

## 12. Herpes Simplex (HS)

Herpes simplex skin lesion is characterised by painful grouped microvesicles which soon rupture to form yellow crust. The site of predilection is the adjacent areas of mucous membranes and skin. It has a tendency to recur. Infection with H.S. virus is so common in man as to be regarded as almost universal and antibodies can be demonstrated in the plasma of virtually in over 85% of the adult population. A fetus may be infected in utero. It is caused by Herpes virus hominis.

The mode of transmission is probably by droplet infection. Infection takes place in two stages, during the first few years of life and after puberty.

**Clinical features**

- Painful grouped vesicles or blisters.
- Fever, malaise and headache.

**Investigations**

- Diagnosis is clinical.

**Treatment**

**Objectives**

- Relieve pain and discomfort
- Limit extent of disease spread in the immunocompromised and atopic eczema patients
- Prevent secondary infection

**Non pharmacologic**

- No specific measure.

**Pharmacologic**

**Acyclovir**, 200mg P.O., 5 times daily OR 400mg P.O., three time daily for 7 days.

Children <2 years; half adult dose.

Children >2 years; adult dose.

(For ADRs, C/I and dosage forms: see below). Other antiviral therapy – STI section

**N.B.** Secondary bacterial infection can be treated by systemic antibiotics (see pyoderma).

*PLUS*

**Paracetamol** for pain

## 13. Impetigo

Impetigois a contagious superficial infection of the skin. It is caused by S*treptococci* or *Staphylococci* or by both organisms. Infection is acquired either from external sources by

direct contact or through objects or from internal infection, e.g. nasopharyngeal sources.

Impetigo contagiosa is highly infectious and is common in children. There are two forms; superficial or common impetigo and bullous impetigo.

**Clinical features**

- Superficial or common impetigo-lesions are thick, adherent and recurrent dirty yellow crusts with an erythematous margin.
- Bullous impetigo characterised by superficially thin walled bullous lesions that rupture and develop thin, transparent, varnish like crust.

**Investigations**

- Microscopy and culture of the exudate from the blisters (not routinely required except in recurrent cases)

**Treatment**

**Objectives**

- Treat infection.
- Break the cycle of transmission.

**Non pharmacologic**

Careful removal of crusts by bathing with Normal saline or Hydrogen peroxide ensures more rapid healing.

**Pharmacologic**

**Topical:** for localized

**First line**

**Mupirocin**, applied thin film of 2% cream/ointment 2-3 times a day for 10 days.

**ADRs:** irritaion

**Dosage forms:** Ointment, 2%

**Alternatives**

**Fucidic acid**, applied thin film of 2% cream 2-3 times in a day for 10 days.

**ADRs:** irritation

**Dosage form:** Cream, 2%

**N.B.** Anti-bacterial ointments are usually applied after the wet lesion has dried.

**Systemic: for extensive**

**First line**

**Cloxacillin**,

**Alternative**

**Cephalexin**, 250mg to 500mg P.O., QID for 7 to 10 days for adults; 25 to 100mg/kg P.O. in 4 divided doses for 7 to 10 days for children

**Dosage forms:** Capsule, 250mg, 500mg; Syrup, 125mg/5m

*OR*

**Erythromycin**

**14. Molluscum Contagiosum**

Molluscum Contagiosumis a common childhood disease caused by Pox virus. Its second peak in incidence occurs in young adults because of sexual transmission.

**Clinical features**

- The typical lesion is a pearly, skin colored papule with central umblication.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Prevent autoinoculation and transmission to close contacts and sexual partners.

**Non pharmacologic**

Surgical: Curettage – with or without electrodessication under local anesthesia

Cryotherapy

**Pharmacologic**

**First line**

**KOH 5-10% solution**, first apply vaseline to perilesional area (to avoid normal skin irritation) then applied over the lesion with cotton tip applicator daily

Duration depending on clinical response

**ADRs:** Irritation erythema

*OR*

**Iodine**, applied 2-3 times per week by unroofing the top of the lesion and the procedure is continued until the lesions disappear (1-2 weeks).

**ADRs:** rare, complication of ulcer, skin hypersensitivity

**Dosage forms:** Solution, 2%

**Alternative**

**Retinoic acid (Tretinoin)**, thin films applied to the lesions daily.

**ADRs:** Irritation erythema, peeling, changes in pigmentation, photosensitivity.

**C/Is:** Pregnancy, eczema, broken or sunburned skin, personal or family history of epithelioma.

**Dosage forms:** Cream, 0.25% ; gel, 0.01%, 0.025%; lotion, 0.025%, 0.05%; ointment, 0.05%.

*OR*

**Silver Nitrate + Potassium Nitrate,** thin film ointment applied 2 to 3.

**ADRs:** Rare

**Dosage forms:** Ointment, 95%+5%

**N.B**. Therapy based on physical removal of the lesions is considered best. Sexual partners should also be examined and treated. Treatment is aimed at removal of the lesions or at least the central core of each lesion. This is thought to initiate the lost immune response via injury to the epidermis and release of viral antigens.

**15. Pediculosis Corporis And Capitis**

This disorder is due to lice infestations. It is caused by Human Ectoparasite**:** *Pediculus humanus corporis*-the body louse-and *Pediculosis humanus capitis*-the head louse.
Sites of predilections are shoulders, trunks and buttocks. Bacterial infection is a typical complication in neglected cases. Untreated cases may persist indefinitely. Crowded population with inadequate sanitation, lack of opportunity to change clothes frequently, poor persons living in cold climate with heavier clothing contribute to this disease.

**Clinical features**

The primary bite lesion is a small red macule, or occasionally a papule with a characteristic central haemorrhagic punctum

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Eradicate the parasite from clothing.

**Non pharmacologic**

- Boil clothes with hot water or iron the clothes after washing with cold water
- Nits should be removed using fine comb

**Pharmacologic**

**First Line**

**Malathion 1**, applied to the scalp and left for 2 hours before rinsing.

**ADRs:** Rare

**P/C:** when used for pregnant women, lactating women and infants

**Dosage forms:** Shampoo, 1%

*OR*

**Permethrin**, applied on the scalp for 10 minutes and washed off

**ADRs:** Pruritis, stinging, transient burning

**Dosage forms:** Cream, 5%; lotion, 1%, 5%

**16. Pityriasis Versicolor (PV)**

PV is a chronic asymptomatic scaling dermatosis associated with the overgrowth of the hyphal form of Pityrosporum ovale, Malassezia furfur. It is a common disorder seen in older children and adolescents around puberty. The lesions sometimes may involve other areas such as the abdomen, upper arms, thighs and face. The disorder is insidious in onset and persistent. After successful treatment recurrences are common.

**Clinical features**

- Well demarcated scaling patches with variable pigmentation.most commonly seen on the trunk.

**Investigations**

- KOH preparation and culture

**Treatment**

**Objectives**

- Eradicate infection
- Prevent transmission

**Non pharmacologic**

- Good personal hygiene
- Avoid sharing bath towels, sponges and clothing

**Pharmacologic**

**Topical imidazoles** such as **Clotrimazole, Miconazole** and K**etoconazole** cream can be applied once or twice daily for four to six weeks. **Ketoconazole** shampoo can also be used to wash and left for 10 minutes to the affected areas daily for a period of 7 days. Similarly 2.5% selenium sulfide shampoo can be used.

**Systemic therapy**: in cases with extensive and long standing eruptions one of the following regimens can be used.

**First line**

**Ketoconazole**, 400mg single dose, repeated after a week.

OR 200mg daily or 3-4 mg/kg/day for 7-14 days

**Alternative**

**Fluconazole**, 400mg single dose, repeated after a week.

*OR*

**Itraconazole**, 400mg P.O., single dose OR 200mg P.O., BID on first day, then 200mg P.O., daily for 5 days.

**Secondary prophylaxis**

- **Selenium sulfide** or **ketoconazole** shampoo once or twice a week
- **Salicylic acid/sulfur bar, zinc pyrithione** (bar or shampoo) can be used weekly.

## 17. Psoriasis

Psoriasis is a common, chronic, and recurrent inflammatory disease of the skin characterised by circumscribed, erythematous, dry scaling plaques of varying sizes often with predilection to certain parts of the body. Psoriasis is universal in occurrence. It is usually a life long disease. But most patients develop the initial lesion in the third decades of life.

**Clinical features**

- Skin lesion characterised by circumscribed plaques with erythematous base and, silivery-white dry scaling of varying sizes often with predilection to certain parts of the body

- The most common sites of involvement are the scalp, elbows and knees, followed by the nails, hands, feet and trunk (including the interglutealfold).

**Investigations**

- Clinical
- Histopathologic Examination

**Treatment**

**Objectives**

- Relieve symptoms

**Non pharmacologic**

- Explain regarding precipitating factors and chronicity.
- Counselling the patient never to rub or scratch lesions (to minimize Koebner's phenomenon).
- Advise frequent exposure to sunlight

**Pharmacologic**

**For Local plaques**

**General Measures**

- Liberal use of moisturizers like urea, 10 – 20% or liquid paraffin between treatments
- Removal of excessive scale by soaking in water or by using salicylic acid, 5–10% in vaseline base applied twice daily

**Topical**

**First line**

**Betamethasone dipropionate**, thin film applied twice daily for short period of time are effective. For lesions of the face, neck, flexural areas and genitalia mild potency steroids are preferred.

**Dosage forms:** Cream, 0.025%, 0.05%

**Alternative**

**Dithranol**, started using low concentrations (0.05 to 0.1%) incorporated in petrolatum or zinc paste and given once daily. To prevent autooxidation, salicylic acid (1 to 2%) can be added. Short contact therapy (minute therapy for 10-30 minutes). The concentration is increased

weekly starting from 1% up to about 5% until the lesions resolve, then it can be tapered and discontinued gradually.

**Dosage forms:** Paste, 1%; Scalp application, 0.25%, 0.5%

**Calcipotriene**, thin films applied twice daily at the area of plaques. Not more than 100gms per week should be used. Exposure to sunlight facilitates remission. Salicylic acid should not be used in combination with calcipotriol due to the possible inactivation of this compound by the former.

**Dosage forms:** Cream, 0.005%; ointment, 0.005%; scalp application, 0.005%

**18. Scabies**

Scabies is a persistent and intensely itchy skin eruption due to the mite *Sarcoptes scabiei.* The disease is commonly seen in people with low socio-economic status and poor personal hygiene.

**Clinical features**

- Red papules and burrows in the axillae, groin and digital web spaces associated with complaints of nocturnal pruritus.
- In infants, the face, palms and soles are often involved and blisters may develop.

**Treatment**

**Objectives**

- Eradicate the mite
- Prevent transmission to family members and close contacts

**Non pharmacologic**

- Washing clothes in hot water or ironing clothes after normal washing.

**Pharmacologic**

**Topical:**

**First line**

**Permethrin 5%**, Thin films of cream applied to all areas of body from the neck down for 8-14 hrs. then washed off. Repeat the same dose after a week

**Alternative**

**Benzyl benzoate,** applied to the entire body, neck to toe for 3 to 5 consecutive evenings. Bath should be taken before the first and after the last application.

**ADRs:** skin irritation, burning sensation especially on the genitalia, excoriations, occasionally rashes.

**Dosage form:** Lotion, 25%

*OR*

**Sulphur ointment**, Children 5%, Adult 10%: thinly applied to the entire body for 3 consecutive nights. The patient should wash thoroughly before each new application and 24 hours after the last treatment.

**ADRs:** skin irritation.

**C/Is:** pregnancy or lactation, children younger than 2 years.

**P/C:** avoid contact with eyes, mouth and mucous memberanes.

**Dosage forms:** Ointment, 5%, 10%.

**Systemic:**

**Ivermectin**, 200µg/kg as a single dose, for Norwegian (crusted scabies) and resistant forms of scabies.and it is ideal for institutional outbreaks.

| |
|---|
| **N.B.** Any person who has had close contact with the infected patient should be treated. |

**19. Urticaria**

Urticaria or hives, is a common disorder affecting up to 25% of the population. Urticaria may be the presenting feature of other systemic diseases such as systemic lupus erythematous, cryoglobulinemia, autoimmune thyroid diseases, and urticarial vasculitis. Urticaria may present in the acute or chronic form.

**Acute urticaria:** Acute urticaria is defined as outbreaks of urticarial lesions that do not extend in duration beyond six weeks. The lesions of acute urticaria are characterised by a rapid onset and resolution within several hours and they can be recurrent. A presumptive trigger such as medicine, food ingestion, insect bite, or infection can occasionally be identified.

**Chronic urticaria:** Chronic urticaria is defined by the presence of hives, usually on most days of the week, for a duration of longer than six weeks. The chronic form accounts for approximately 30% of cases of urticaria. A careful history should be performed to identify

external triggers. However, in 80 to 90% of adults and children with chronic urticaria, no external cause can be identified.

**Clinical features**

- The usual urticarial lesion is an intensely pruritic, circumscribed, raised, erythematous plaque, often with central pallor.
- Individual lesion enlarges and coalesces with other lesions, and then typically will disappear over a few hours (< 24 hrs).

**Investigations**

- CBC
- Stool exam
- Skin prick testing

**Treatment**

**Objectives**

- Provide immediate relief
- Prevent complications such as shock or asphyxiation

**Non pharmacologic**

- Identification and removal of the offending trigger.

**Pharmacologic**

**First line**

**Cetrizine**,

6-12 months; 2.5mg P.O., QD

12 months-2 years; 2.5mg P.O., once daily; may increase to 2.5mg every 12hrs if needed

2-5 years: Initial; 2.5mg P.O., once daily; may be increased to 2.5mg every 12 hours or 5 mg QD

greater than 6 years and adults;10mg P.O. QD initial dose (max 40mg/d)

**Dosage forms:** Tablet, 5mg, 10mg; oral solution, 1mg/ml

*OR*

**Loratadine**,

< 2 years: 2.5mg P.O., QD,

2-5 years: 5mg daily P.O.,

above 5 years and adults: 10mg P.O., QD (or BID)

**Alternatives**

**Diphenhydramine**,

from 2 to 6 years; 6.25mg every 4-6 hours; maximum: 37.5mg/day

from 6 to 12 year; 12.5-25mg every 4-6 hours; maximum: 150mg/day

above 12 years and adults; 25-50mg every 4-6 hors; maximum: 300mg/day

*OR*

**Ranitidine**,

children 1 month to 16 years; 2-4 mg/kg/day P.O. QD; maximum treatment dose: 150mg/day

adults; 150mg P.O. QD to BID

*OR*

**Cimetidine**,

children; 20-40mg/day P.O., BID,

adults; 300 to 800mg P.O., BID.

**N.B.** $H_2$ blockers should be used in combination with with $H_1$ blocker and also use the combination therapy when the first line not respond with maximum dose.

*OR*

**Prednisone**, 20-25mg P.O., alternate day or 10-15mg P.O. /d.in a single early morning dose. After one week of treatment time taper by 5mg every two to three days until the minimal dose that controls the urticaria is found.

**20. Verruca Vulgaris (Common Warts)**

Verruca Vulgaris is a benign epidermal overgrowths caused by human papilloma virus (HPV). It is transmitted by contact, often at small skin breaks, abrasions, or other trauma. The onset from exposure is variable with a range of 1-6 months. Duration is variable, spontaneous resolution with time is typical. In children, approximately two-thirds of warts spontaneously regress within 2 years. Warts in immunocompromised persons can be widespread and chronic. Common sites are the hands, periungual skin, elbows, knees and planter surfaces.

**Clinical features**

- Flesh-colored papules that evolve into dome-shaped, gray-brown surface black dots and are usually few.

**Treatment**

**Objectives**

- Improve appearance

**Non pharmacologic**

- Duct tape*:* cut wart size and applied. Leave for 6 days, then remove, wash skin, gently debride.
- Reapply as required, up to one month.

**Pharmacologic**

**Salicylic acid**, thin films of ointment applied once a day. Occlusion with tape increases penetration. Treatment duration may be 8-12 weeks.

**Dosage forms:** Ointment, 5%, 10%,20%

**N.B.** Multiple visits are often necessary when treating with ablative therapy.

# CHAPTER XVI: SEXUALLY TRANSMITTED INFECTIONS (STI)

## SYNDROMIC MANAGEMENT OF STI

STIs are serious and common problems worldwide. There are more than 20 types. Many of these are curable with effective treatment, but continue to be a major health problem for an individual and the community at large. Currently, with the emergence of HIV/AIDS the management of STIs makes more serious issue and calls for effective and urgent management. Patients presenting with STIs should be counseled to undergo HIV testing.

There are two basic approaches in the management of STIs namely etiologic diagnosis using laboratory tests to identify the causative agent and syndromic approach. The former approach is often regarded as the ideal way of diagnosing disease and the second one is the choice of resort when there are no laboratory facilities. However both classic approaches present with a number of problems. The syndromic case management which has the following key features:

It enables all trained first line health care providers to diagnose STI syndromes and treat patients on the spot, without waiting for laboratory results. This will help to offer treatment on the initial visit which is an important step to stop the spread of the disease.

- It is problem oriented (it responds to the patient's symptoms).
- It is highly sensitive and does not miss mixed infections.
- Uses flow charts that guide the health worker through logical steps.
- Provides opportunity and time for education and counseling.

A number of different organisms that cause STIs give rise to only a limited number of syndromes.

**A syndrome** is simply a group of symptoms a patient complains about and the clinical signs one can observe during examination of the patient. The aim of syndromic STI management is to identify one of the seven syndromes and manage accordingly. These are vaginal and urethral discharges, genital ulcer, lower abdominal pain, scrotal swelling, inguinal bubo and neonatal conjunctivitis.

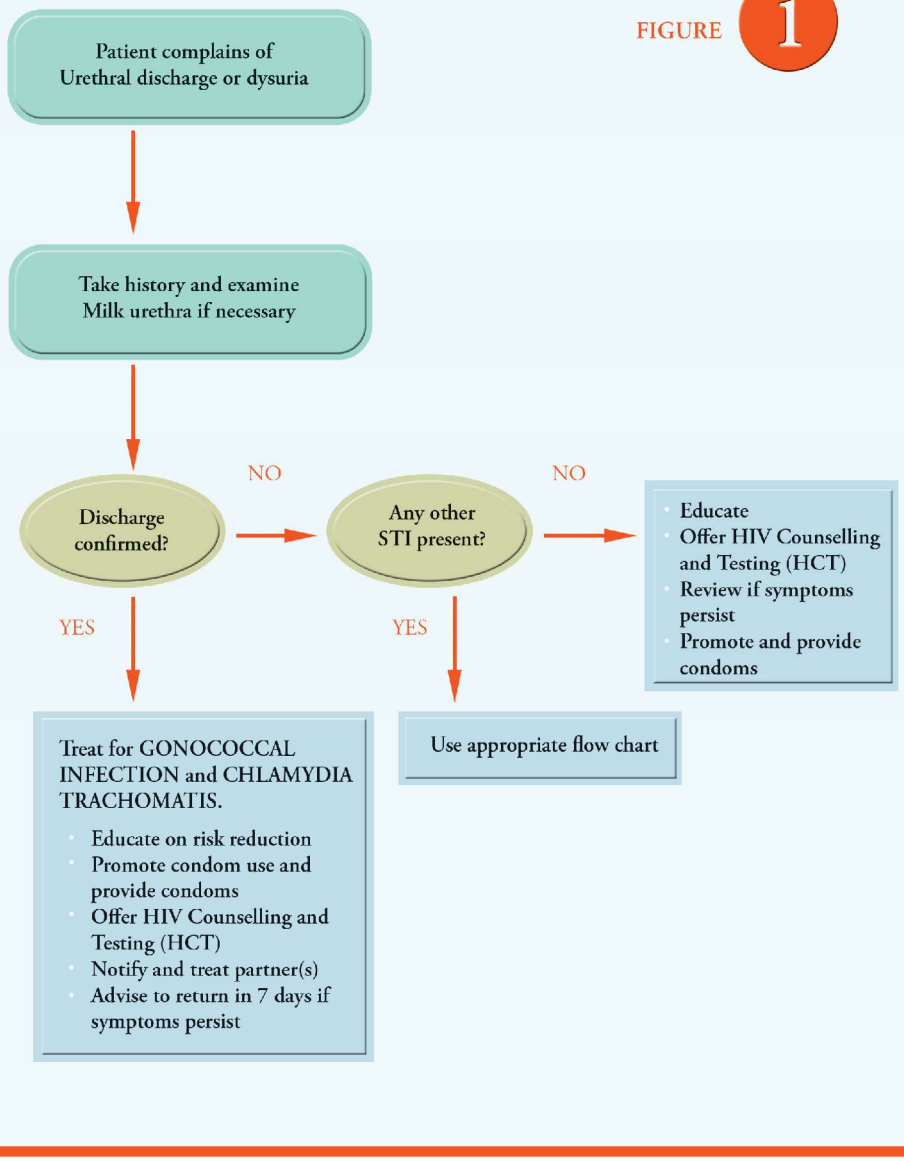
The syndromes are relatively easy to identify and it is possible to devise a flowchart for each one. **A flow chart** is a diagram or type of map representing steps to be taken through a process of decision making. A major benefit of the flow chart is that, once trained, service providers find them easy to use- so non-STI specialists at any health facility are able to manage STI cases.

**Each flowchart is made up of a series of steps:**

1. The clinical problem- the patient's presenting symptoms at the top; this is the starting point
2. A decision to make, usually by answering "yes" or "no" to a question
3. An action to take: what you need to do

## URETHRAL DISCHARGE SYNDROME

FIGURE 1



## 1. Urethral Discharge

**Treatment:**

**Objectives**

- Prevent long term complications including urethral stricture, infertility
- Prevent recurrence

**Non pharmacologic**

- None

**Pharmacologic**

Treatment should target gonorrhea and chlamydial infections.

**First line**

**Ciprofloxacin**, 500mg PO stat (For ADRs, C/Is and dosage forms see page **Error! Bookmark not defined.**)

OR

**Spectinomycin**, 1gm IM as single dose

**Dosage form**: injection, 2g vial

PLUS

**Doxycycline**, 100 mg PO bid for 7 days

OR

**Tetracycline**, 500mg PO QID for 7days

OR

**Erythromycine,** 500 mg po qid for 7 days if the patient has contraindications; for **Tetracyclines** (pregnancy, children)

**NB**: Patients should be advised to return if symptoms persist for 7days after the initiation of treatment. Single dose treatment is encouraged as much as possible

## 2. Persistent/Recurent Urethral Discharge

Patient complains of Persistent/recurrent urethral discharge or dysuria.If there is persistent and recurrent urethral discharge despite treatment the possibilities could be drug resistance, poor compliance or re-infection. In some cases the etiologic agent could be *T.vaginalis*, hence the index patient should be treated for this.

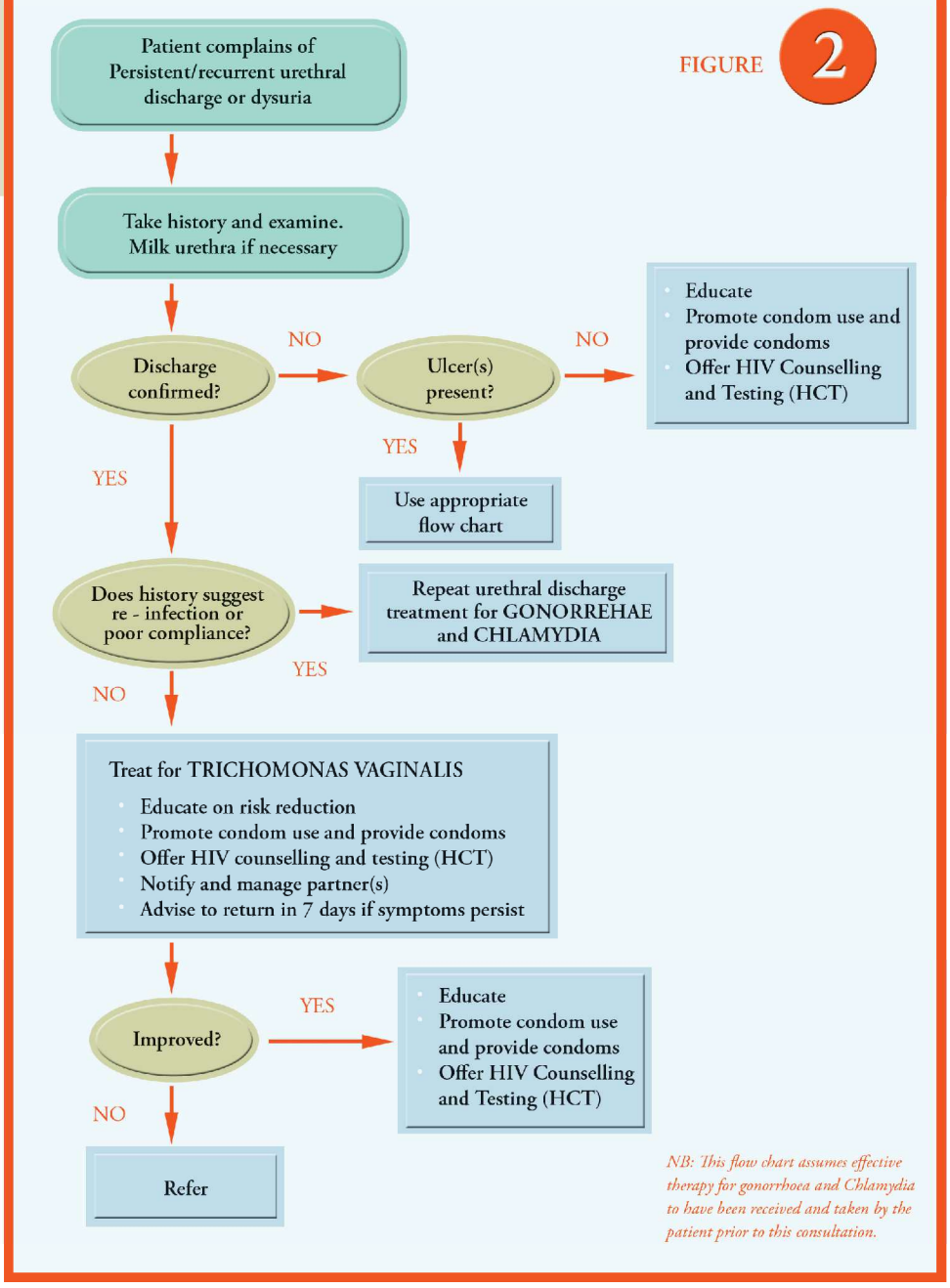
**Treatment**

**Metronidazole**, 2gm PO as a single dose

Patient should avoid use of alcohol while taking metronidazole.

**Referral**: Despite all these treatments, if symptoms still persist the patient should be referred for further work-up.

## PERSISTENT/RECURRENT URETHRAL DISCHARGE IN MEN



### 3. Genital Ulcer Diseases (GUD)

The relative prevalence of causative organisms for GUD varies from place to place; hence clinical differential diagnosis of genital ulcers is inaccurate in places where there are several etiologies.

Clinical manifestation and patterns of GUD may vary with presence of HIV infection.

The causes of genital ulcer are Trreponema Pallidum (syphilis), HSV2 infection, Haemophilus ducreyi (chancroid), C.thrachomatis serovar L1, L2 & L3 (LGV), Claymmatobacterium granulomatis (Donovanosis)

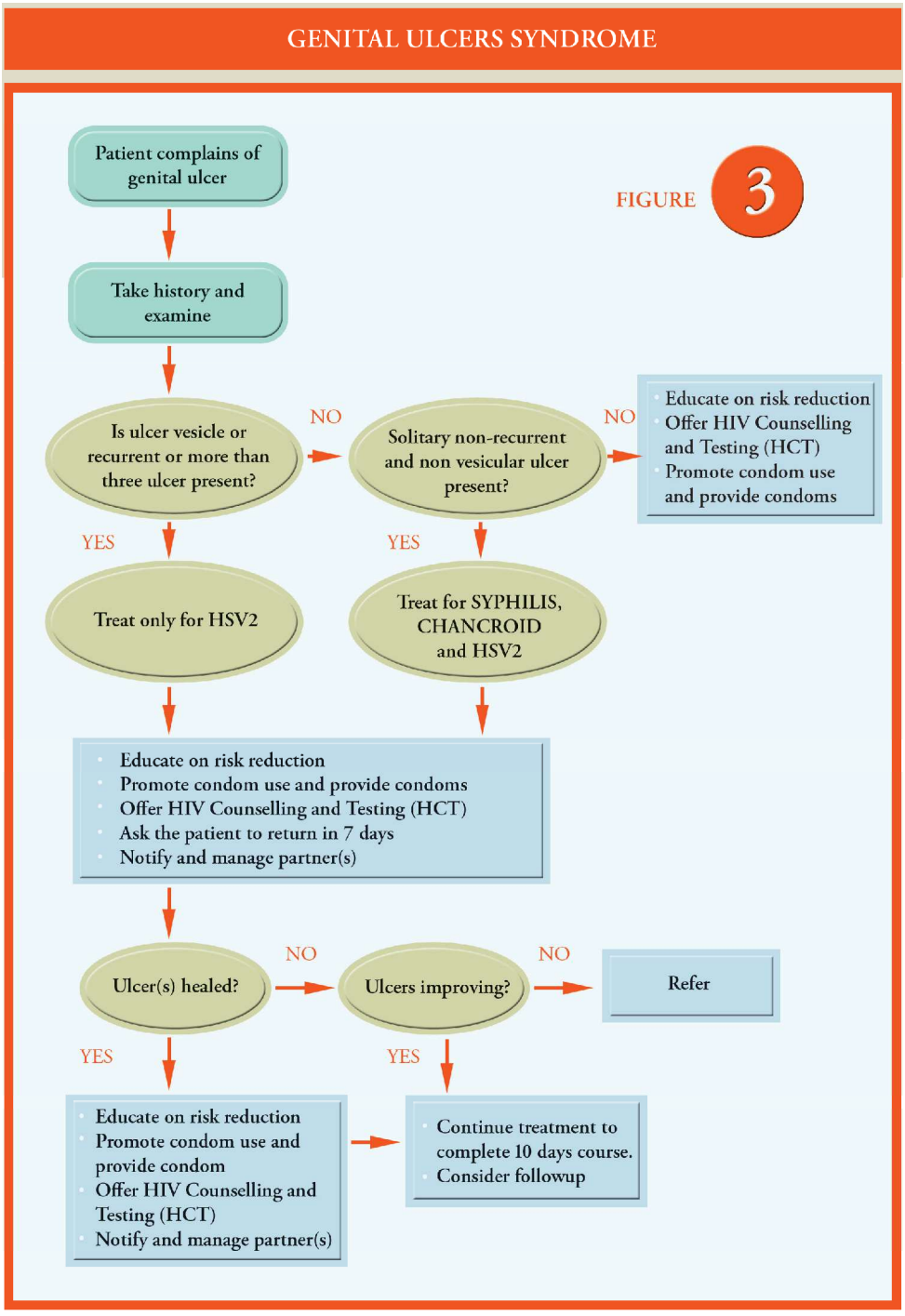
**Syphilis** Clinically has three stages (primary, secondary, teritiary). The ulcer starts during the primary stage of the disease as papuples & rapidly ulcerat.The uler is typicaly painless,clean base and raised boarder.

**Genital Herpes** herpes simplex virus is the most common causes of genital ulcer worledwide.it produces life long infection after the primary infection (latency). The lisions are painful, erythemathous macules which progressively form vesicles, pustules, ulcer and crusts.

**Chancroid** It is also the common cause of genital uler in developing countries.The lision started as painful papules and pustules which ulcerate with derty base and soft edge.Inguenal fluctuant adenopathy (buboes) may occur following ulcer.

**Lymphogranulomaveneurum (LGV)** The disease starts as painless papules that developes an ulcer.After afew dayes painful regional lymphadenopathy develop and associated systemic symptoms may occur.

**Granuloma inguinale (Donovanosis)** is chronically progresive ulcerative disease without systemic symptomes,presents with non supperative painless genital ulcer and beefy-red appearance


GENITAL ULCERS SYNDROME
FIGURE 3
Patient complains of genital ulcer
Take history and examine
Is ulcer vesicle or recurrent or more than three ulcer present?
NO
Solitary non-recurrent and non vesicular ulcer present?
NO
Educate on risk reduction
Offer HIV Counselling and Testing (HCT)
Promote condom use and provide condoms
YES
YES
Treat only for HSV2
Treat for SYPHILIS, CHANCROID and HSV2
Educate on risk reduction
Promote condom use and provide condoms
Offer HIV Counselling and Testing (HCT)
Ask the patient to return in 7 days
Notify and manage partner(s)
Ulcer(s) healed?
NO
Ulcers improving?
NO
Refer
YES
YES
Educate on risk reduction
Promote condom use and provide condom
Offer HIV Counselling and Testing (HCT)
Notify and manage partner(s)
Continue treatment to complete 10 days course.
Consider followup

**Treatment**

**Objective**

- Screen patient for HIV and other ulcerative STIs
- Prevent long term complications
- Halt the transmission of the infection

**Non pharmacologic:** Prevent secondary infection by local cleaning

**Pharmacologic**

**I. Treatment for non vesicular genital ulcer**

**Benzathine penicillin G**, 2-4 million units IM single dose

OR

**Doxycycline**, 100 mg P.O. BID for 14 days

PLUS

**Ciprofloxacin** 500 mg po bid for 3 days

(For ADRs, C/Is and dosage forms, see page **Error! Bookmark not defined.**)

OR

**Erythromycin** 500 mg po qid for 7 days

**II. Treatment for vesicular, multiple or recurrent genital ulcer**

**Acyclovir**, 200 mg P.O 5 times daily for 10 days OR 400 mg P.O. TID for 10 days

(For ADRs, C/Is and dosage forms, see pages **Error! Bookmark not defined.**)

**N.B**. There is no medically proven role for topical acylovir, its use is discouraged.

**Episodic treatment of recurrent episodes**

Treatment should be initiated during prodrome or immediately after onset of symptoms.

**Non pharmacologic:** Local care: Keep affected area clean and dry

**Pharmacologic**

**Acyclovir** 400 mg P.O. TID for 5 days,

**Suppressive treatment**: recommended for patients with 6 recurrences or more per year

**Acyclovir**, 400mg P.O. BID for 1 year

**Dosage forms**: Tablet, 125mg, 250mg, 500mg

(For ADRs and C/Is, see under acyclovir page **Error! Bookmark not defined.**)

**N.B.** The need for continued suppressive therapy should be reassessed.

## 4. Vaginal Discharge

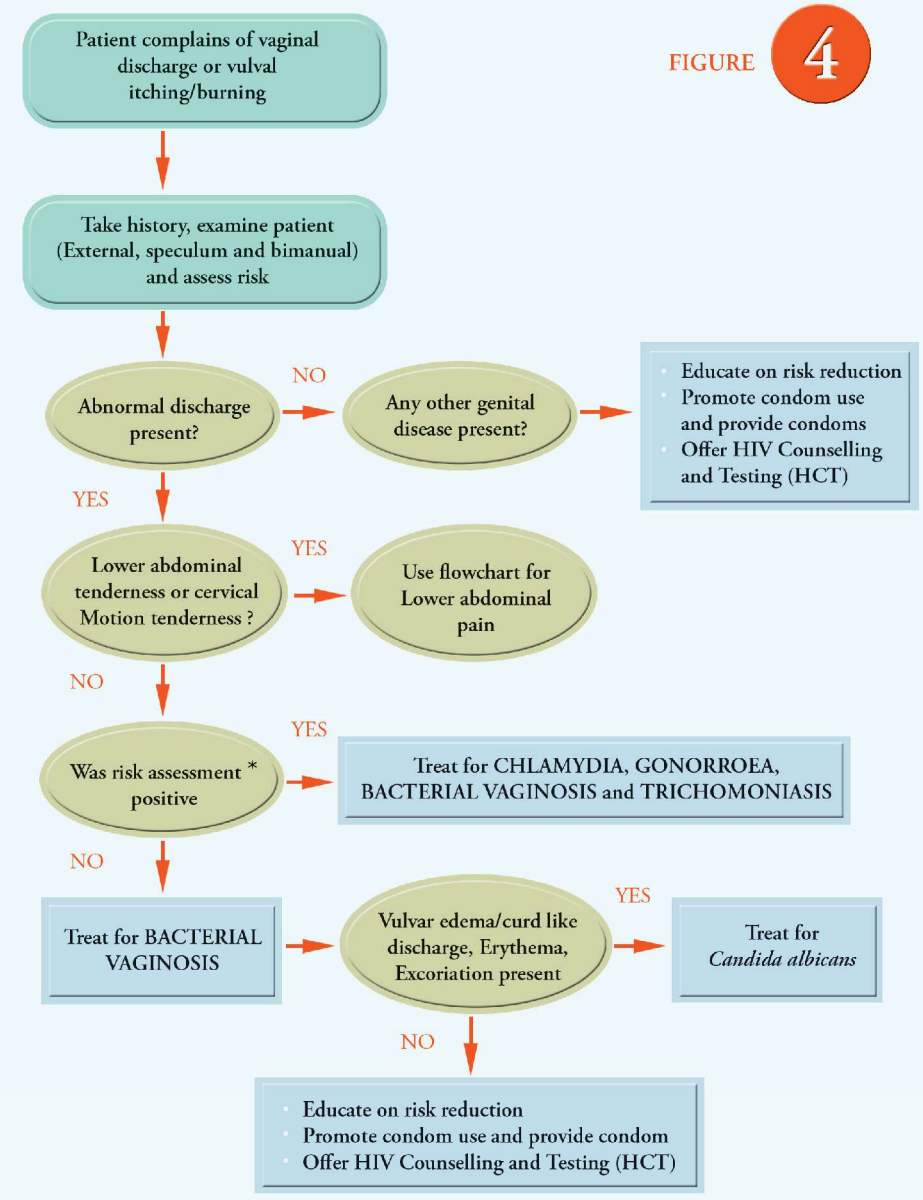
Abnormal Vaginal discharge in terms of quantity, colour or odor could be most commonly as a
result of vaginal infections. But it is a poor indicator of cervicitis, especially in young girls because a large proportion of them are asymptomatic. The most common causes of vaginal discharge are Neisseria gonorrhoeae, Chlamydia trachomati, *T.vaginalis,Gardnerella vaginalis , C.albicans. The firs*t three are sexually acquired & the last two are endogenous infections etiologic agents.

**N.B.** One or more of the following are risk factors for STI related cevicitis in Ethiopia

- Multiple sexual partners in the last 3months.
- New sexual partner in the last 3 months
- Ever traded sex
- Age below 25 years

## VAGINAL DISCHARGE (SPECULUM AND BIMANUAL)

FIGURE 4




* *Risk factors include age< 25 years, trading sex, multiple or new partner in the last 3 months.*

**Treatment**

**Pharmacologic**

**For risk assessment positive**

**Ciprofloxacin** 500mg po stat

OR

**Spectinomycin** 2 gm IM stat

PLUS

**Doxycycline** 100 mg po bid for 7 days

PLUS

**Metronidazole** 500 mg po bid for 7 days

**For risk assessment negative**

**Metronidazole** 500 mg po bid for 7 days

**PLUS**

**Clotrimazole** vaginal tabs 200 mg at bed time for three days

**Sex Partners**

Examination and treatment usually not necessary. However treatment with an imidazole cream (e.g, miconazole, clotrimazole) may be indicated in some cases of recurrent infection, or if the partner has penile candidiasis (Balanitis).

## 5. Lower Abdominal Pain

All sexually active women presenting with lower abdominal pain should be carefully evaluated for the presence of upper genital tract infections (tube, uterus, ovaries, and pelvic cavity). In addition, all women with presumptive STI should undergo thorough bimanual and abdominal examination because some of the women with PID may not complain of lower abdominal pain. Other suggestive symptoms include pain during intercourse, vaginal discharge, abnormal vaginal bleeding (inter-menstrual), painful urination, pain during menstruation, fever and sometimes nausea and vomiting.

PID is difficult to diagnose because the clinical manifestations widely vary. PID becomes highly probable when one or more of the above symptoms are seen in a woman with adenexal tenderness, vaginal discharge and cervical motion tenderness.

**Indications for Patients referral with acute PID**

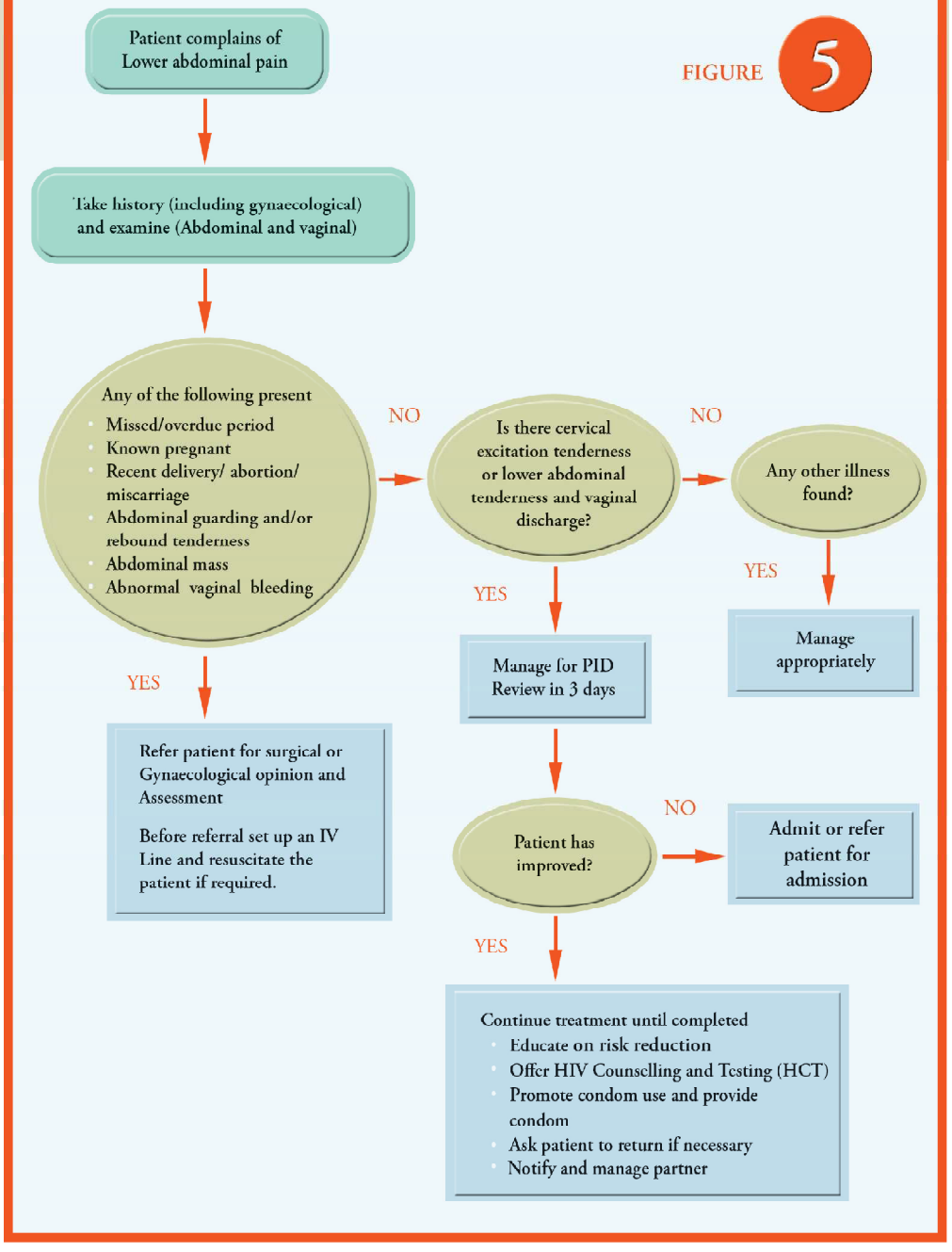
- The diagnosis is uncertain
- Surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded
- A pelvic mass is suspected
- Severe illness precludes management on an outpatient basis
- The patient is pregnant
- The patient is unable to follow or tolerate an outpatient regimen; or
- The patient has failed to respond to outpatient treatment.

**N.B.** Many experts recommend that all patients with PID should be admitted to hospital for Treatment

The most common causative agents responsible for this syndrome include *N.gonorrhae*, *C.trachomatis,* and *anaerobic bacteria*. Facultative Gram negative rods and *Mycoplasma hominis* are also implicated sometimes. As it is difficult to differentiate between these clinically, and a precise microbiological diagnosis is nearly impossible in most clinical set ups, hence the treatment regimen must be effective against the incriminated microorganisms.

## LOWER ABDOMINAL PAIN

FIGURE 5



**Treatment**

**Pharmacologic**

**Outpatients**

**Ciprofloxacin**, 500mg po single dose (For ADRs, C/Is and dosage forms see page **Error! Bookmark not defined.**)

OR

**Spectinomycin** 2gm IM stat

PLUS

**Doxycycline**, 100mg P.O., BID for 14day

PLUS

**Metronidazole**, 500mg P.O, BID for 14days

**N**.**B**. If patient does not show improvement within 72hours of initiation of treatment, futher investigation is required.

**In patient**: Recommended syndromic management for PID

**First line**

**Ceftriaxone**, 250 mg IV/IM once daily

(For ADRs, C/Is and dosage forms see page **Error! Bookmark not defined.**)

PLUS

**Doxycycline**, 100mg Po, BID for 14 days )

PLUS

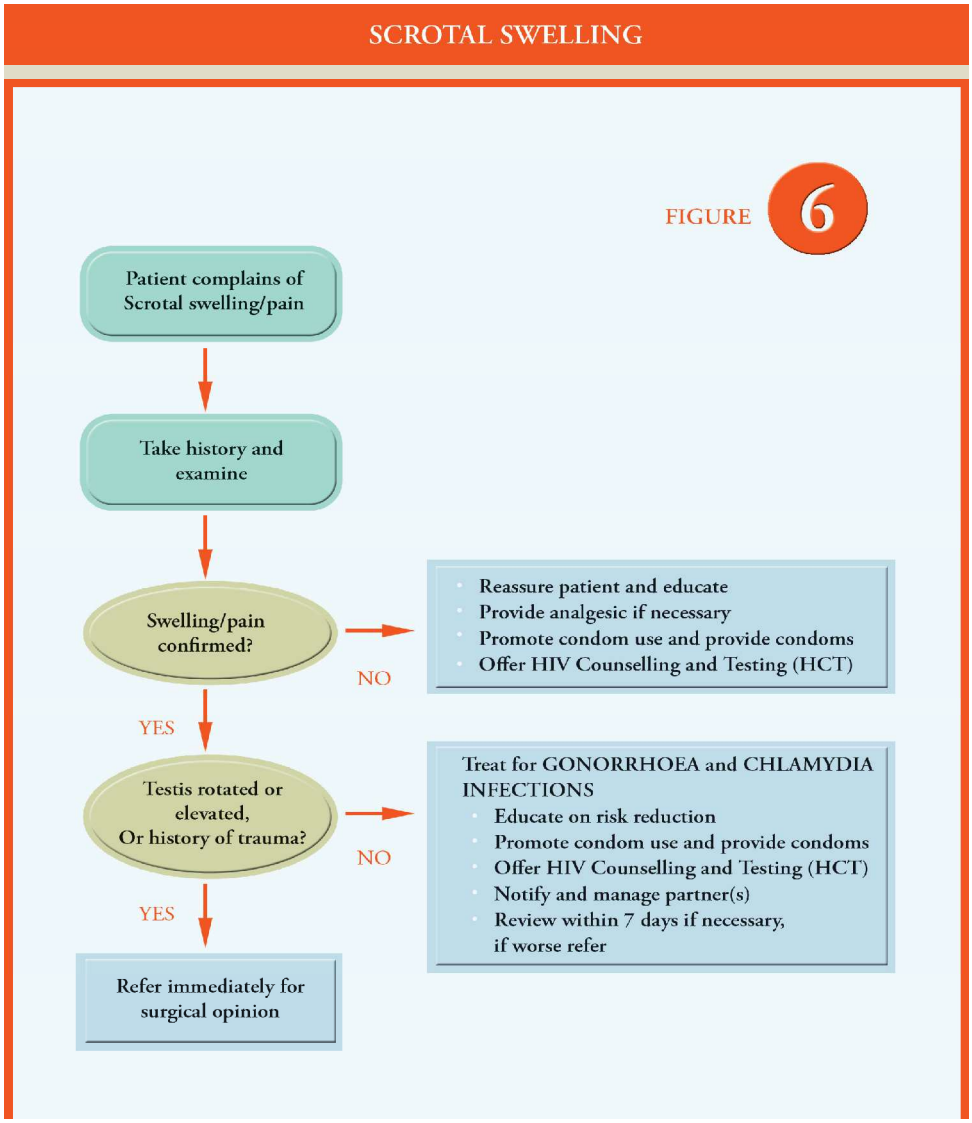
**Metronidazole**, 500mg P.O, BID

OR

**Chloramphenicol**, 500mg P.O or IV QID

**6. Scrotal Swelling**

Inflammation of the epididymis usually manifests with acute onset of unilateral testicular swelling, often with tenderness of the epididymis and vas deferens, and occasionally with erythema and edema of the overlying skin. When it occurs in young male accompanied with urethral discharge it is usually due to *gonococcal* or *chlamydial* infections. In older people the etiologic agent may be non-STIs such as *E.coli, Klebsiella spp. or Psydomonas.* TB orchitis is generally accompanied by an epididymitis




**Treatment**

**Non Pharmacologic:** Scrotal support

**Pharmacologic**

**Ciprofloxacin** 500 mg po stat OR **Spectinomycin** 1 gm IM stat

PLUS

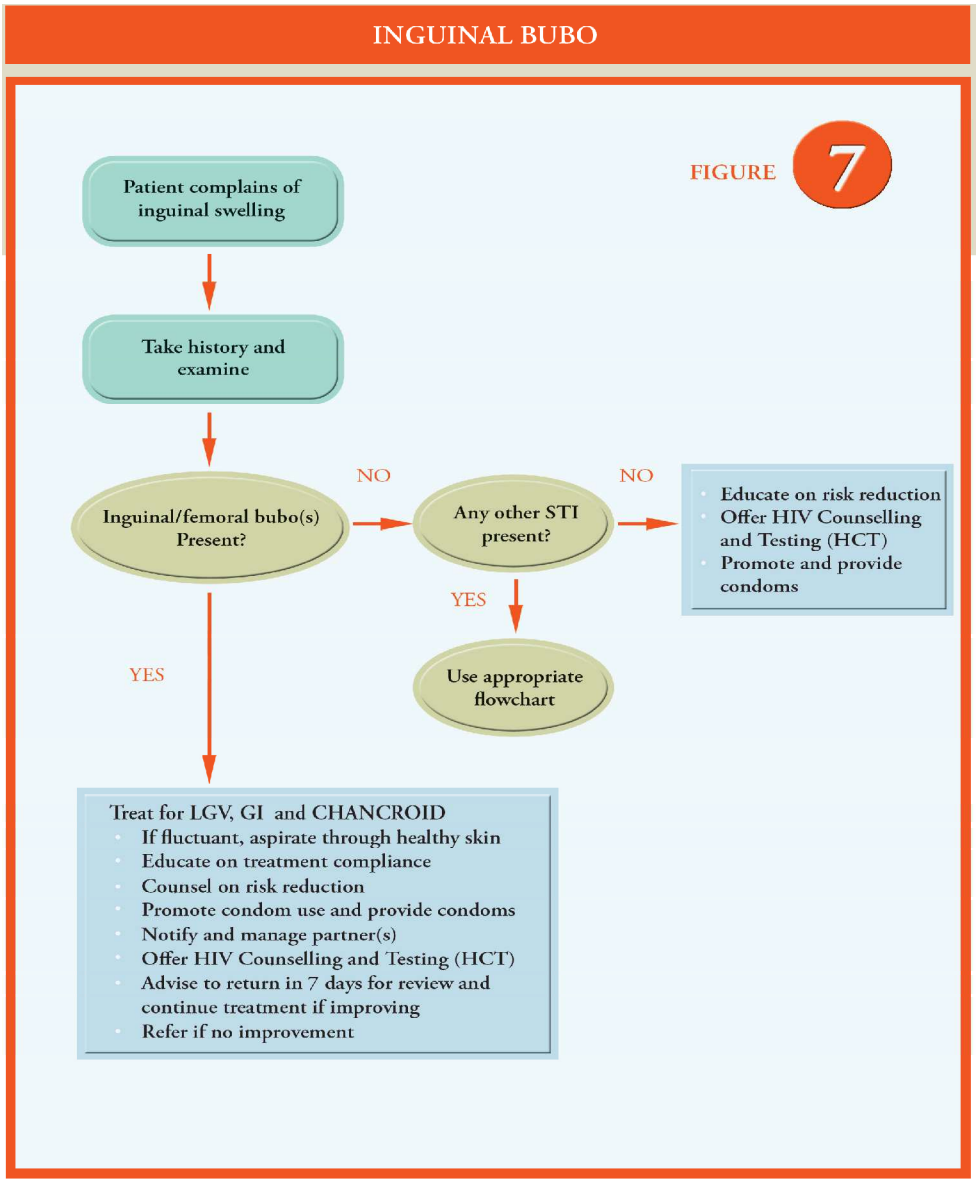
**Doxycycline** 100 mg po bid for 7 days

OR

**Tetracycline** 500 mg po qid for 7 days

## 7. Inguinal Bubo

This is a painful, fluctuant, swelling of the lymph nodes in the inguinal region (groin). Buboes are usually caused by either chancroid or LGV. In many cases of chancroid, but not all, an associated ulcer is visible. Infection of the lower limb and other non-STIs like TB can also cause swelling of the inguinal lymph nodes.



**Treatment Objectives**

- Prevent complication, which includes fistula formation, lymphatic obstruction
- Screen for other STIs

**Non pharmacologic:** Keep the lesion clean and dry

**Pharmacologic**

**First line**

**Ciprofloxacin**, 500mg P.O, BID for 3days

(For ADRs, C/Is and dosage forms see page **Error! Bookmark not defined.** )

PLUS

**Doxycycline**, 100mg P.O, BID for 14days

OR

**Erythromycin**, 500mg, P.O, QID for 14days

**N.B.** Fluctuant lymph nodes should be aspirated through healthy skin but incision and drainage or excision of nodes may delay healing and should not be attempted.

Referral is indicated where there is doubt with diagnosis and/or treatment failure.

NB:The term 'refer' stand for;

At General hospital where culture and sensitivity test is available,it to do the test and treat accordingly. But if culture and sensitivity test is not available, the term 'refer' indicates to refer the patient to regional or centeral lab where culture and sensitivity test and DNA PCR(polymerase chain reaction) are available and then treat the patient according to the lab result.

## CHAPTER XVII: OPHTHALMOLOGICAL DISORDERS

### 1. Acute Dacryocystitis

Acute dacryocystitis is an inflammation or infection in the lachrymal sac. It may have various etiologies. It is, however, commonly caused by complete nasolacrimal duct obstruction preventing normal drainage from the lacrimal sac into the nose. Chronic tear stasis and retention lead to secondary infection with bacteria leading to erythematous, tender swelling on the nasal aspect of the lower eyelid, mocoid or purulent discharge which can be expressed as pressure to the lacrimal sac.

**Clinical features**

- Pain, tenderness, redness, swelling on the innermost aspect of the lower eyelid (over the lacrimal sac), tearing, discharge.
- Fistula formation, lacrimal sac cyst or mucocele can occur in chronic cases.

**Investigations**

- Gram's stain
- Pus culture

**Treatment**

**Objectives**

- Relieve pain
- Cure the infection
- Open the drainage and reduce tearing

**Non Pharmacologic**

- Warm compresses and gentle massage to the inner canthal region QID
- Incision and drainage of a pointing abscess
- Surgical correction (Dacryocystorhinostomy=DCR), once the acute episode has resolved, particularly with chronic dacryocystitis

**Pharmacologic**

**A. Mild Cases**

**First line**

**Cloxacillin**,

children; 50-100mg/kg/day in 4 divided doses for 10-14 days

adults; 500mg P.O., QID for 10-14 days

*PLUS*

**Chloramphenicol,** 1 drop QID for 10-15 days

**Alternatives**

**Cefaclor**,

children; 20-40mg/kg/day P.O., TID for 10-14 days for children.

adults; 250-500mg P.O., TID for 10-14 days

*PLUS*

**Gentamicin**, 1 drop QID for 10-15 days

*OR*

**Amoxicillin/clavulanate**,

children; 20-40mg/kg/day P.O. TID for 10-14 days for children.

adults; 625mg P.O. BID for 10-14 days

*PLUS*

**Gentamicin,** 1 drop QID for 10-15 days

**B. Moderate-Severe Cases:** hospitalize and treat with IV medications

**First line**

**Cephazoline Sodium**,

children; 25-100mg/kg/day P.O.TID for 10-14 days

adults; 1gm IV TID for 10-14 days

**Alternatives**

**Cefuroxime**,

children; 50-100mg/kg/day IV TID for 10-14 days

adults; 750mg IV TID for 10-14 days

*OR*

**Clindamycin**,

adults; 300mg IV QID for 10-14 days

children; 1mg/kg/day IV in 6hours for 10-14 days

*PLUS*

**Gentamicin**, 2.0mg/kg IV loading dose, and then 1 mg/kg IV TID for 10-14 days.

**N.B.** IV antibiotics can be changed to comparable oral antibiotics after significant improvement is observed.

**Refer:** in severe and complicated cases refer to an ophthalmologist

## 2. Acute Infectious Dacryoadenitis

It is an infection of the lachrymal gland. It is usually caused by bacteria (Staphylococcus aureus, Neisseria gonorrhea, streptococci) or virus (mumps, infectious mononucleosis, influenza, herpes zoster). Acute dacryoadenitis typically occurs in children and young adults.

**Clinical Features**

- Unilateral pain, redness, erythema, warmth, tenderness, and swelling over the outer one third of the upper eyelid, often with tearing or discharge.
- It may be associated with hyperemia of the palpable lobe of the lacrimal gland.

**Investigations**

- Complete blood cell count
- Gram's stain
- Blood culture
- Pus culture from any discharge

**Treatment**

**Objective**

- Alleviate the pain and cure the infection

**Non Pharmacologic**

- Incision and drainage if there is an abscess.

**Pharmacologic**

**A. Bacterial or infectious (but unidentified) etiology**

**1. Mild-to-Moderate**

**First line**

**Cloxacillin**,

children; 50-100mg/kg/day in 4 divided doses for 7-14 days

adults; 500mg P.O., QID for 7-14 days

**Alternatives**

**Amoxicillin/clavulanate**,

children; 20-40mg/kg/day P.O., TID for 10-14 days

adults; 625mg P.O., BID for 10-14 days

*OR*

**Cefaclor**,

children; 20-40mg/kg/day P.O. TID for 10-14 days

adults; 250-500mg P.O., TID for 10-14 days

*OR*

**Cephalexin**,

adults; 250-500mg P.O., QID for 7-14 days

children; 25-50mg/kg, P.O., in 4 divided doses for 7-14 days

2. **Moderate-to-severe:** Hospitalize and treat them with IV medications (see under acute dacryocystitis)

**N.B.** The antibiotic regimen should be adjusted according to the clinical response and the result of culture and sensitivity. IV medications can be changed to oral depending on the rate of improvement of the patient.

**B. Viral (mumps, infectious mononucleosis)**

**Treatment**

**Objectives**

- Alleviate the pain
- Shorten the course of the disease

**Non Pharmacologic**

- Cold compresses to the area of swelling and tenderness

**Pharmacologic treatment**

**First line**

**for adults:**

**Acetaminophen**, 650mg P.O., every 4-6 hours for adults

**Alternative**

**for children:**

**Acetylsalicylic acid**, 30-60mg/kg/day P.O. in 4-6 divided doses for children

**Refer:** In severe and complicated cases refer to an ENT specialist

### 3. Allergic Conjunctivitis

#### a) ATOPIC KERATOCONJUNCTIVITIS

Atopic Keratoconjunctivitis may occur in patients who have or had Atopic Dermatitis. About one third of patients with atopic dermatitis develop one or more manifestations of atopic keratoconjunctivitis. As a consequence of depressed cell mediated immunity, patients are susceptible to herpes simplex virus keratitis, and to colonization of the eyelids with staphylococcus aureus.

**Clinical features**

- Itching, blepharospasm, photophobia, blurred vision
- Copious mucous discharge.

**Investigations**

- Clinical

**Treatment**

**Objective**

- Relieve the symptoms

**Non Pharmacologic**

- Avoidance of responsible allergens
- Cold compresses

**Pharmacologic**

Treatment should be based on the severity of patient symptoms, and consists of one or more of the following:

- Topical vasoconstrictors
- Topical antihistamines
- Topical nonsteroidal anti-inflammatory medic ations
- Judicious and selective use of topical corticosteroids

- Artificial tears

**Topical vasoconstrictors**

**First line**

**Tetrahyrdazoline**, 1 drop 3-4 times per day for not more than one week.

**ADRs:** Conjunctival hyperemia, photosensitivity, hypersensitivity reactions

**Dosage form:** Eye drop, 0.05%

**Alternative**

**Oxymetazoline**, 1 drop 3-4 times per day for not more than one week.

**ADRs:** Conjunctival hyperemia, photosensitivity, hypersensitivity reactions

**Dosage forms:** Eye drop, 0.025%, 0.05%

**N.B.** Topical vasoconstrictors, alone or in combination with antihistamines, may provide symptomatic relief. But, their use for more than 5-7 consecutive days may predispose to rebound conjunctival hyperemia, tachyphlaxis, and compensatory chronic vascular dilatation.

## Topical vasoconstrictor-Antihistamine Combinations

**First line**

**Naphazoline + Antazoline**, 1 drop 3-4 times per day

**Dosage forms:** Solution, 0.025%+0.5%.

**Alternative**

**Naphazoline + Phenylephrine**, 1 drop 3-4 times per day

**Dosage form:** Solution, 0.25% + 0.3%

## Topical antihistamines

**First line**

**Levocabastine**, 1 drop 3-4 times per day

**Dosage forms:** Solution, 0.5%

**Alternative**

**Olopatadine**, 1 drop 3-4 times per day

**Dosage form:** Solution 0.1%

**N.B.** Oral antihistamines may provide symptomatic relief in some patients

## Topical mast-cell stabilizers

**First line**

**Cromolyn Sodium**, 1 drop 3-4 times per day

**Dosage forms:** Solution 4%

**Alternatives**

**Lodoxamide**, 1 drop 3-4 times per day

**Dosage form:** Solution 0.1%

**N.B.** Topical mast-cell stabilizers may be useful for treatment of seasonal allergic conjunctivitis. They are, however, ineffective at the acute phase due to their slow onset of effect.

## Topical non-steroidal anti-inflammatory agents

**First line**

**Diclofenac**, 1 drop 3-4 times per day

**Dosage form:** Solution, 0.1%

**Alternatives**

**Flurbiprofen**, 1 drop 3-4 times per day

**Dosage form:** Eye drop, 0.03%

*OR*

**Ketorolac**, 1 drop 3-4 times per day

**Dosage form:** Solution, 0.5%

*OR*

**Suprofen**, 1 drop 3-4 times per day

**Dosage form:** Solution, 0.5%

## Topical corticosteroids

**First line**

**Dexamethasone**, 1 drop every 2-4 hours per day depending on the severity of the disease and tapered every 5-7 days down to 1 drop every other day.

**Dosage form:** Eye drop, 0.1%

**Alternatives**

**Prednisolone**, 1 drop every 2-4 hours per day depending on the severity of the disease and tapered every 5-7 days down to 1 drop every other day.

**Dosage forms:** Suspension (Eye drop), 0.25%, and 1%

*OR*

**Dexamethasone Sodium Phosphate**, single strip of ointment applied 2-3 times daily.

**Dosage form:** Ointment 0.05%

*OR*

**Fluoromethalone**, 1 drop every 2-4 hours per day depending on the severity of the disease and tapered every 5-7 days down to 1 drop every other day OR single strip of ointment applied 4-6 times daily.

**Dosage forms:** Suspension, 0.1%, 0.25%; Ointment 0.1%

**Combined Topical Corticosteroids-Antibiotic Ophthalmic Preparations**

**First line**

**Dexamethasone + Chloramphenicol**, 1 drop every 2-4 hours per day depending on the severity of the disease and tapered every 5-7 days down to 1 drop every other day.

**Dosage form:** Eye drop, 0.1% + 0.5%

**Alternative**

**Dexamethasone + Tobramicin**, single strip of ointment applied 4-6 times daily

**Dosage forms:** Ointment 0.1% + 0.3%

**N.B.** Patients should be carefully evaluated for secondary infection and get treated accordingly.

**Refer:** In severe and complicated cases refer to an ophthalmologist

**b) HAY FEVER AND PERENNIAL ALLERGIC CONJUNCTIVITIS**

Hay fever (seasonal) and Perennial Allergic Conjunctivitis are type I IgE-mediated immediate hypersensitivity reactions. Patients with this condition often suffer from other atopic conditions, such as allergic rhinitis and asthma.

**Clinical features**

- Itching, eyelid swelling, conjunctival hyperemia and chemosis, and mucoid discharge.

- Intense itching is a hallmark symptom, and attacks are usually short-lived and episodic.

**Investigations**

- Conjunctival scraping to look characteristics of eosinophils or their granules

**Treatment**

**Objective**

- Avoid exposure to allergen
- Alleviate the symptoms

**Non Pharmacologic**

- Cleaning of carpets, linens, and bedding to remove accumulated allergens such as animal dander and dust house mites.
- Cold compresses

**Pharmacologic**

1. **Mild disease:** Topical antihistamines ± non-steroidal anti-inflammatory medications (see under Atopic Keratoconjunctivitis)
2. **Moderate to Severe disease:** Topical mast-cell stabilizers ± non-steroidal anti-inflammatory medications (See under Atopic Keratoconjunctivitis)
3. **Severe disease:** Steroids ± topical antihistamines ± non-steroidal anti-inflammatory medications ± mast-cell stabilizers (See under Atopic Keratoconjunctivitis)

## c) VERNAL KERATOCONJUNCTIVITIS

Vernal keratoconjunctivitis is usually a seasonal recurring, bilateral inflammation of conjunctiva, predominantly occurring in male children who frequently but not invariably have personal or family history of atopy.

**Clinical features**

- Itching, blepharospasm, photophobia, blurred vision, and copious mucous discharge.

**Investigations**

- Clinical

**Treatment**

- Therapy should be based on the severity of the patient's symptoms and of the ocular surface disease.

**Objective**

- Relieve symptomatic surface disease.

**Non Pharmacologic**

- Climatotherapy such as the use of air-conditioning or relocation to cooler environment.

- Ice packs and frequent face washing with cold water gives temporary relief.

**Pharmacologic**

1. **Mild disease:** Topical antihistamines ± non-steroidal anti-inflammatory medications (see under Atopic Keratoconjunctivitis)
2. **Moderate to Severe disease:** Topical mast-cell stabilizers ± nonsteroidal Anti-inflammatory medications (see under Atopic Keratoconjunctivitis)
3. **Severe disease:** Steroids ± topical antihistamines ± non-steroidal anti-inflammatory edications ± mast-cell stabilizers (see under Atopic Keratoconjunctivitis)

**N.B.**

1. Corticosteroids should be reserved for exacerbations with moderate to severe discomfort and/or decreased visual acuity.
2. Corticosteroids should be discontinued between attacks.
3. The patient and family must be thoroughly informed about the potential risk of chronic steroid therapy.

**Refer:** In severe and complicated cases refer to an ophthalmologist

**4. Bacterial Conjunctivitis**

## 1. CONJUNCTIVITIS IN CHILDREN AND ADULTS

Acute purulent conjunctivitis is a bacterial infection of the conjunctivae.

**Clinical features**

- Generalized conjunctival hyperemia, edema, muco-purulent eye discharge, gumming of eye lashes and a varying degree of ocular discomfort.

- Visual acuity is not usually affected.

**Investigations**

- Gram stain
- Culture and sensitivity

**Treatment**

**Objective**

- Treat the infection
- Prevent complications

**Non Pharmacologic**

- Frequent cleaning of the eyelids and warm compression

**Pharmacologic**

**First line**

**Chloramphenicol**, 1 drop every 4-6 hours OR single strip of ointment applied 2-4 times per day for 10-15 days.

**Dosage forms:** Eye drops, 0.5%; Ointment, 1%

**Alternatives**

**Tetracycline**, single strip of ointment applied 2-4 times per day for 10-15 days.

**Dosage forms:** Eye drops, 0.5%; Ointment, 1%

*OR*

**Gentamicin**, 1 drop every 4-6 hours per day for 10-15 days.

*OR*

**Tobramicin**, 1 drop every 4-6 hours per day for 10-15 days.

**Dosage form:** Eye drop, 0.3%

**N.B.** Frequent topical instillation of antibiotic eye drops or ointments is useful. **Ciprofloxacin** should be reserved for cases refractory (resistant) to initial therapy.

**Refer:** In severe and complicated cases refer to an ophthalmologist

## 2. NEONATAL CONJUNCTIVITIS

Conjunctivitis in the newborn is commonly to the result of infection with Neisseria gonorrhoeae or *Chlamydia trachomatis*. The etiologic agent can sometimes be distinguished by the timing of infection: infection with gonococcus typically occurs on day 3 to 5, while infection with Chlamydia occurs between 5 to 14 days. Conjunctivitis in the newborn might have occurred from prophylactically administered Silver Nitrate drops; in this case the inflammation occurs within the first days of life. Gonococcal conjunctivitis (*Ophthalmic neonatorum*) is a serious infection in neonates and, if untreated, it progresses to corneal ulceration, corneal perforation and endophthalmitis (deeper infection of the globe), leading to blindness.

**Clinical feature**

- Rapid progressive copious purulent conjunctival discharge,
- Marked conjunctival hyperemia and chemosis,
- Eyelid edema

**Investigations**

- Gram stain
- Culture from eye discharge.

**Treatment**

**Objective**

- Treat the infection
- Prevent corneal perforation and blindness

**Non Pharmacologic**

- Saline irrigation of the conjunctiva

**Pharmacologic**

**I. Systemic antibiotics**

**First line**

**Penicillin G Sodium Crystalline**, 50,000 IU/kg QID for 10 days.

**N.B.** Most gonococcal strains are now resistant to penicillin.

**Alternatives**

**Ceftriaxone**, 50 mg/kg to a maximum of 125 mg as a single IM injection

*OR*

**Cefotaxime**, 25mg/kg IV OR IM every 8-12 hours for 7 days.

**II. Topical antibiotics**

**First line**

**Tetracycline**, single strip of ointment applied 2-3 times daily for 2 weeks

*OR*

**Erythromycin**, single strip of ointment applied 2-3 times daily for 2 weeks

Alternatives

**Chloramphenicol**, 1-2 drops 3-4 times daily OR single strip of ointment applied 2-3 times daily.

**Dosage forms:** Eye drops, 0.5%; eye ointment, 1%

*OR*

**Gentamicin**, 1-2 drops 4-6 times daily for 10-15 days

**Dosage form:** Solution (Eye Drop), 0.3%

**Prophylaxis of gonococcal conjunctivitis**

- Clean the newborn's eye with 0.9% saline or clean water using sterile gauze
- Apply single strip of ointment into each eye any of the above antibiotic eye ointments

**Refer:** In severe and complicated cases refer to an ophthalmologist

**5. Blepharitis**

Blepharitis is a general term for inflammation of the eyelids. It is one of the most common causes of external ocular irritation. There are two main types of blepharitis: Seborrhoeic blepharitis and Staphylococcal Blepharitis. If it is associated with conjunctivitis, it is termed Blepharoconjunctivitis.

## 1. SEBORRHOEIC BLEPHARITIS

The inflammation is located predominantly at the anterior eyelid margin. One third of patients with seborrhoeic blepharitis have aqueous tear deficiency. Seborrhoeic blepharitis may occur alone or in combination with Staphylococcal Blepharitis. It is the milder form of blepharitis.

**Clinical features**

- Chronic eyelid redness, burning, foreign body sensation, itching,
- A variable amount of oily or greasy crusting, eye discharge,
- Easily plicable eyelashes.

**Investigations**

- Clinical

**Treatment**

**Objectives**

- Alleviate the symptoms

**Non Pharmacologic**

- Use of warm compresses
- Expression of meibomian gland secretions
- Cleanliness of the eyelid margins to remove keratinized cells and debris with baby shampoo, tea water, salt water or commercially available eyelid scrub.

**Pharmacologic**

**First line**

**Oxytetracycline+Polymixin B+Hydrocortisone,** 1 drop 2-3 times a day for 2-4 weeks.

**Dosage form:** Suspension, 0.977g + 1million I.U + 0.5g

**Alternatives**

**Neomycin sulphate + Polymixin B + Dexamethasone,** 1 drop 2-3 times a day for 2-4 weeks.

*OR*

**Tetracycline,** single strip of ointment applied 2-3 times daily for 2-4 weeks

**Dosage form:** Eye ointment, 1%

*OR*

**Erythromycin**, single strip of ointment applied 2-3 times daily for 2-4 weeks

**Dosage form:** Eye ointment**,** 0.5%

## 2. STAPHYLOCOCCAL BLEPHARITIS (ulcerative blepharitis)

The most common causes of blephritis are staphylococcal infections usually caused by staphylococcus aureus. It is more common in younger individuals.

**Clinical features**

- Irritation and burning to peak in the morning and improve as the day progresses.
- Foreign body sensation, itching, and crusting, particularly upon awakening.
- Hard, brittle fibrinous scales and hard, matted crusts surrounding individual cilia (eyelash) on the anterior eyelid margin
- Ulceration of anterior eyelid margin
- Injection and telangiectasis of anterior and posterior eyelid margin
- White lashes (Poliosis)
- Loss of eyelashes (madarosis)
- Trichiasis can be seen in varying degrees depending on the severity and duration of blepharitis

**Investigations**

- Clinical

**Treatment**

**Objectives**

- To alleviate the symptoms
- Prevent losses of eye lashes
- Correct trichiasis
- Prevent blindness

**Non Pharmacologic**

- See under seborrhoeic blepharitis
- Surgical correction for trichiasis

**Pharmacologic treatment**

**I. Topical**

**First line**

**Dexamethasone**, 1 drop 4-6 times a day for 3-6 weeks and tapered every 5-7 days

**Alternatives**

**Oxytetracycline+Polymixin B+Hydrocortisone**, 1 drop 2-3 times a day for 2-4 weeks.

**Dosage form:** Suspension, 0.977g + 1million I.U + 0.5g

*OR*

**Neomycin sulphate + Polymixin B + Dexamethasone**, 1 drop 2-3 times a day for 2-4 weeks.

**P/Cs:** pregnancy, breast feeding

**Dosage forms:** Suspension (eye drop), 3.5mg (base) + 10mg +10,000 units (base) in each ml

*OR*

**Tetracycline**, single strip of ointment applied 2-3 times daily for 2-4 weeks

*OR*

**Erythromycin**, single strip of ointment applied 2-3 times daily for 2-4 weeks

**II. Systemic (for recurrent cases)**

**First line**

**Tetracycline**, 250mg P.O., QID for 6 weeks, then tapered slowly

**Alternative**

**Doxycycline**, 100mg P.O., BID for 6 weeks, then tapered slowly

**N.B.** Topical and systemic medications should be given simultaneously.

**Refer:** In severe and complicated cases refer to an ophthalmologist

## 6. Cataract

Cataract is opacity of the crystalline lens of the eye. It is the leading causes of blindness in Ethiopia and worldwide. The commonest cause of cataract is old age. It can be caused by trauma to the eye, inflammation within the eye, metabolic conditions especially diabetes mellitus and congenitally.

**Clinical features**

- Disturbance of vision

- Reduced visual acuity
- Lens opacity

**Investigations**

- Fasting blood sugar

**Treatment**

**Objective**

- Restore vision

**Non pharmacologic**

- Surgical removal of the cataract

**Pharmacologic**

Nil

**Refer**: Refer all cases to ophthalmologist or cataract surgeon for surgical management

### 7. Chemical Burns

Chemical Burns can include **Alkaline chemicals** (e.g. lye, cements, plasters), **Acids, Solvents, Detergents, and Irritants.** Alkaline chemicals are more harmful than acids. The degree of chemical burn can be classified as mild, moderate or severe, and the symptoms and signs depend on the degree of the injury.

**Clinical features**

- Focal area of conjunctival chemosis, hyperemia, and/or haemorrhage; mild eyelid edema;
- First, second or third degree burn of the periorbital skin

**Danger Signs**

- Corneal epithelial defects
- Pronounced chemosis and perilimbal blanching
- Corneal edema and opacification, sometimes with little-to-no view of the anterior chamber, iris, or lens

**Investigations**

- Examination under slit lamp biomicroscopy
- Corneal staining with fluorescein or rose Bengal

**Treatment**

- Treatment must be instituted IMMEDIATELY, even before making vision test!!

**Objectives**

- Prevent corneal dryness, ulceration and infection
- Avoid corneal opacity and blindness

**Non Pharmacologic (Emergent)**

- Copious irrigation of the eyes, preferably with saline or Ringer's lactated solution, for at least 30 minutes.
- However, if non-sterile water is the only available liquid, it should be used.
- Pull down the lower eyelid and evert the upper eyelid, if possible, to irrigate the fornices.
- Manual use of IV tubing connected to an irrigation solution facilitates the irrigation.
- Five minutes after ceasing the 30 minutes irrigation to allow for equilibrium, litmus paper is touch the inferior conjunctival fornix (cul-de-sac) to measure the pH. If the pH is not neutral the irrigation should be continued until neutral pH is reached.

**Pharmacologic**

- Give any available pain medications
- Apply any available antibiotic eye ointments and put pressure patch for 24 hours

**N. B.** Refer to an ophthalmologist immediately if the injury is severe. In mild cases, evaluate after 24 hours and refer the patient if the vision is still compromised.

## 8. Glaucoma

Glaucoma is characterised by progressive optic nerve head damage and visual field loss, for which raised intra-ocular pressure (IOP) is a primary risk factor. Glaucoma may occur as a primary condition or secondary to other ocular conditions or systemic diseases. Glaucoma can be further classified as acute or chronic and open-versus closed-angle. Glaucoma is usually a bilateral disease, but may be unilateral or asymmetrical (especially with underlying causes).

**Clinical features**

**Chronic glaucoma**

- Mostly asymptomatic.
- History of gradual loss of vision in the affected eye or loss of visual field.
- Often suspected after identifying cupping of optic disc on routine fundoscopy or finding elevated intra-ocular pressure on screening.
- RAPD (useful to detect an eye with advanced glaucoma)

**Acute closed-angle glaucoma**

- Sudden onset of severe eye pain and redness, associated with nausea, vomiting and hemi-cranial headache.
- Loss of vision in the affected eye.
- Coloured haloes or bright rings around lights.
- Hazy or edematous cornea.
- Fixed, semi-dilated pupil.
- Severely elevated intra-ocular pressure.
- The affected eye feels harder compared to the other eye when measured with finger palpation/ballotment.

**Investigations**

- Measurement of intra-ocular pressure

- Visual field test
- Fundus picture

**Treatment**

**Objectives**

- Control intra-ocular pressure
- Preserve vision
- Halt progressive optic nerve head damage and visual field loss

**Non Pharmacologic**

- Filtration Surgery – Trabeculectomy, Tube-shunt implant surgery
- Laser treatment

**Pharmacologic**

**Open angle glaucoma (chronic)**

**First line**

**ß-blocker**

**Timolol**, 0.25%, 0.5% ophthalmic drops, instil 1 drop 12 hourly.

| | |
|---|---|
| **ADRs:** | burning**,** allergic, transient conjunctivitis, keratitis, decreased corneal sensitivity |
| **P/Cs:** | older people; angle-closure glaucoma. |
| **C/Is:** | uncontrolled Heart Failure , bradycardia, heart block; asthma, obstructive airways disease. |
| **D/Is:** | acetazolamide, alcohol, epinephrine, lidocaine, nifedipine, prazosin, procainamide, quinidine, verapamil, thiopental, reserpine, metformin, hydralazinee forms: |
| **Dosage forms:** | Solution (eye drop), 0.25%, 0.5 % |

*OR*

**Betaxolol**, 0.25–0.5%, ophthalmic drops, instill 1 drop 12 hourly.

| | |
|---|---|
| **ADRs:** | bradycardia, breast abscess, cataracts, cystitis, diabetes melitus |
| **P/Cs:** | older people; angle-closure glaucoma. |
| **C/Is:** | hypersensitivity to the medicine, sinus bradycardia, overt cardiac failure, pregnancy ($2^{nd}$ and $3^{rd}$ trimester). |

**D/Is:** amiodarone, ciprofloxacin, ketoconazole, norfloxacin, chlorpromazine, fluoxetin, quinine, ritonavir, phenobarbital.

**Dosage forms:** Solution (eye drop), 0.5 %

**N.B.** If there is no response despite adequate adherence to the above medicines

*ADD*

**Prostaglandin analogues, e.g.**

**Latanoprost**, 0.005%, ophthalmic drops, instil 1 drop daily

**ADRs:** brown pigmentation, blepharitis, ocular irritation and pain, conjunctival hyperaemia, transient punctuate epithelial erosion

**P/Cs:** Hepatic impairment, renal impairment

**C/Is:** Hypersensitivity to bimatoprost or any component of the formulation.

**Dosage forms:** Eye drops, 0.005%

**N.B.**

- Use as first line if patient has contra-indication to ß-blocker.
- Use in place of ß-blocker if patient has intolerable side effects with ß-blocker or if there is no significant reduction in IOP with other medicines.
- Use in combination with ß-blocker

**Alpha Agonist**

**Brimonidine** 0.15–0.2%, ophthalmic drops, instill 1 drop 12 hourly.

**ADRs:** conjunctival hyperaemia, stinging, pruritus, allergy, and conjunctival folliculosis, visual disturbances, blepharitis, epiphora, corneal erosion, superficial punctuate keratitis,

**P/Cs:** severe cardiovascular disease; cerebral or coronary insufficiency, hepatic or renal impairment; pregnancy, breast-feeding; Driving

**Dosage forms:** Eye drop, 0.2%

**N.B.** Use as second line if patient has allergic reaction to prostaglandin analogue.

Use in place of prostaglandin analogue if there is no significant further reduction in IOP when adding prostaglandin analogue to ß-blocker.

Use in combination with ß-blocker and prostaglandin analogue if there is significant reduction in IOP with ß-blocker and prostaglandin analogue, but patient still has progression of disease or target IOP is not reached.

**Failure to respond:** Alternatives in consultation with a specialist:

**Parasympathomimetic agent:**

**Pilocarpine**, 2-6%, ophthalmic drops, instil 1 drop 6 hourly

| | |
|---|---|
| **ADRs:** | eye pain, blurred vision, ciliary spasm, lacrimation, myopia, conjunctival vascular congestion |
| **P/Cs:** | retinal disease, conjunctival or corneal damage |
| **C/Is:** | acute iritis, acute uveitis, anterior uveitis, some forms of secondary glaucoma |
| **D/Is:** | beta-blockers, anticholinergic medicines |
| **Dosage forms:** | Eye drop, 2-6% |

**N.B.** In severe cases, use as a temporary measure before ocular surgery in consultation with a ophthalmologist

**Carbonic anhydrase inhibitors**

**Acetazolamide**, oral, 250mg 6 hourly

**Refer:** Refere all cases of glaucoma to an ophthalmologist

**Angle closure glaucoma (acute)**

Institute initial therapy and then refer to an ophthalmology unit.

Try to achieve immediate reduction in IOP.

**Acetazolamide**, oral, 500mg immediately as a single dose, Followed by 250mg 6 hourly.

*PLUS*

**Timolol**, 0.25–0.5%, ophthalmic drops, instill 1 drop 12 hourly.

**N.B.** Where those measures fail, for short-term use only:

**Mannitol**, IV, 1.5–2 g/kg as a 20% solution over 30–60 minutes.

*OR*

**Glycerol**, oral, 1 g/kg of 50% solution as a single dose immediately.

| | |
|---|---|
| **ADRs:** | headache, nausea, vomiting, diarrhoea, thirst |
| **P/C:** | Corneal application |
| **Dosage forms:** | Oral solution, 50%, 70% |

**Refer:** Refer all to an ophthalmology unit.

**9. Hordeolum (External) Or Stye**

It is an acute small staphylococcal infection of an eyelash follicle and associated with glands of Zeis or Moll. Tender inflamed swelling in the lid margin may point anteriorly through the skin. More than one lesion may be present and occasionally minute abscesses may involve the entire lid margin.

**Clinical features**

- Visible or palpable, well-defined nodule in the eyelid margin or painful and tender swelling of eyelid margin of short duration.
- In severe cases a mild preseptal cellulitis may be present.

**Investigations**

- Clinical

**Treatment**

**Objectives**

- Reduce the pain and swelling
- Treat the infection

**Non Pharmacologic**

- Warm compresses; applied for 10 minutes twice daily for 2-4 weeks
- Epilation of the involved eyelashes
- Incision and curettage if it does not disappear with other treatments

**Pharmacologic**

No treatment in most cases, styes frequently resolve spontaneously or discharge anteriorly.

**If it is not resolved spontaneously:**

**First line**

**Oxytetracycline + Polymixin B + Hydrocortisone**, 1 drop 2-3 times a day for 2-4 weeks.

**Alternatives**

**Neomycin sulphate + Polymixin B + Dexamethasone**, 1 drop 2-3 times a day for 2-4 weeks.

*OR*

**Tetracycline**, single strip of ointment applied 2-3 times daily for 2-4 weeks

*OR*

**Erythromycin**, single strip of ointment applied 2-3 times daily for 2-4 weeks

PLUS (if associated with cellulitis)

**First line**

**Ampicillin**, 50mg/kg P.O., in four divided doses for 7 days

**Alternative**

**Cloxacillin**, 50mg/kg P.O., in four divided doses for 7 days

**10. Internal Hordeolum**

Hordeolum is an inflammatory or infectious nodule that develops in the eyelid within the tarsal plate. Most frequently, it results from inspissations and secondary infection of sebaceous glands caused by staphylococcus.

**Clinical features**

- Eyelid lump, swelling, pain, tenderness, erythema
- Visible or palpable, well-defined subcutaneous nodule within the eyelid (tarsus)

**Investigations**

- Clinical

**Treatment**

**Objectives**

- Reduce the pain and swelling
- Cure the infection

**Non Pharmacologic**

- Warm compresses; applied for 10 minutes twice daily for 2-4 weeks
- Incision and curettage if it does not disappear with other treatments

**Pharmacologic treatment:** See under "**External hordeolum**"

**11. Meibomian Cyst (Chalazion)**

It is a chronic lipogranulomatous inflammatory lesion caused by blockage of meibomian gland orifices and stagnation of sebaceous secretion. Patient with acne rosacea or seborhoeic

dermatitis are at increased risk of chalazion formation which may be multiple or recurrent. If it is recurrent, one should think of sebaceous gland carcinoma.

**Clinical features**

- Painless visible or palpable, well-defined nodule in the eyelid (eyelid lump) within the tarsal plate.
- Eversion of the lid may show an associated polyploidy granuloma

**Investigations**

- Clinical

**Treatment**

**Objective**

- Remove the lump/nodule from the eyelid

**Non Pharmacologic and Pharmacologic treatment:** See under "Internal hordeolum".

**N.B.** If the chalazion is recurrent, refer the patient to an ophthalmologist for further management to rule out malignant lesion like **Sebaceous Gland Carcinoma.**

**12. Molluscum Contagiosum**

Molluscum contagiosum is uncommon skin infection caused by poxvirus. It is a self-limited disease, but spontaneous resolution may take months to years. Extensive facial and eyelid molluscum lesions have been reported in immunocompromized patient. Complete resolution in these cases is often difficult.

**Clinical features**

- Painless and raised skin lesions which are dome-shaped,
- Usually multiple, umblicated, shiny nodule on the eyelid or eyelid margin.
- Follicular conjunctival reaction from toxic viral products and corneal pannus are serious signs.

**Investigations**

- Clinical

**Treatment**

**Objective**

- Remove the lump/nodule from the eyelid

**Non Pharmacologic**

- Shave excision, Expression, Cauterization, Cryotherapy or Laser

**Pharmacologic**

**For follicular conjunctivitis**

**First line**

**Oxytetracycline + Polymixin B+Hydrocortisone**, 1 drop 2-3 times a day for 2-4 weeks.

**Alternatives**

**Neomycin sulphate + Polymixin B + Dexamethasone**, 1 drop 2-3 times a day for 2-4 weeks.

**Refer:** In severe and complicated cases refer to an ophthalmologist

**13. Ophthalmic Zoster (Herpes Zoster Ophthalmicus, HZO)**

It is caused by Varicella-zoster virus from established latency in sensory neural ganglia after primary infection. Age is the most common predisposing factor; most patients are in their 60-90 years of age. It is generally common in immunocompromised patient. The ophthalmic division ($V_1$) of CN V is affected more often than the maxillary and mandibular division. It is usually unilateral. Ocular involvement is common with HZO, occurring in more than 70% of patients. It is most likely to appear with infection of the nasociliary branch of $CNV_1$.

**Clinical features**

- Pain and dysesthesia
- Maculopapular rash in the forehead
- Development of vesicles, pustules and crusting ulceration
- In severe cases, periorbital edema due to secondary bacterial cellulitis.

**Investigations**

- Clinical
- Serology for HIV

**Treatment**

- Antiviral should be given within 48-72 hrs after rash, because the medicine needs active viral replication

**Objectives**

- Reduce pain
- Prevent scar formation
- Prevent ocular involvement
- Treat the infection

**Non Pharmacologic**

- Wound care

**Pharmacologic**

**First line**

**Acyclovir**, 800mg 5x/day for 7-10days for adults.

*PLUS*

**Aspirin**, 600mg every 4hours P.O., PRN

*OR*

**Paracetamol**, 1gm every 4hours P.O., PRN

**For the wound:** Clean the wound with Gentian Violet

**N.B.** If the tip and side of the nose is infected, the eye is likely to be involved even if it looks normal. So treatment is indicated with the following medications.

**Atropine**, 1 drop BID OR single strip of ointment applied BID

**Dosage forms:** Eye drop, 1%; Eye ointment, 1%

**If eye is red and painful, it could be Corneal Ulcer**

**Chloramphenicol**, 1-2 drops QID

**If there is no corneal ulcer**;

**First line**

**Dexamethasone Sodium Phosphate**, 1 drop 4-6 times a day (taper it every 5-7 days)

**Alternative**

**Oxytetracycline+Polymixin B+Hydrocortisone,** 1 drop 3-4 times a day for 2-4 weeks and tapered every 5-7 days.

*OR*

**Neomycin sulphate + Polymixin B + Dexamethasone**, 1 drop 2-3 times a day for 2-4 weeks.

**Post herpetic Neuralgia**

**Aspirin,** 600mg Q4hr P.O., PRN

*OR*

**Paracetamol,** 1gm Q4hr PRN

*OR*

**Carbamazepine**, 100gm P.O., per day, increase the full dose 300 to 400gm BID

**Refer:** In severe and complicated cases refer to an ophthalmologist

## 14. Orbital Cellulitis

Orbital cellilitis implies active infection of the orbital soft tissue posterior to the orbital septum. In more than 90% of cases orbital cellilitis occurs as a secondary extension of acute or chronic bacterial sinusitis. Therefore evaluation of the paranasal sinuses is essential in any patient with orbital cellilitis. Delay in treatment may result in progression of the infection an orbital apex syndrome or cavernous sinus thrombosis. Blindness, cranial nerve palsies, brain abscess, and even death can result and best avoided by aggressive management. Decreased vision and pupillary abnormalities suggest involvement of the orbital apex and demand immediate investigation and aggressive management.

**Clinical features**

- Red eye, pain, blurred and double vision, fever and headache.
- Eyelid edema, erythema, warmth, tenderness, proptosis, conjunctival chemosis
- Restriction of ocular motility
- Pain upon movement of the globe
- Decreased vision and pupillary abnormality.

**Investigations**

- Complete blood cell count and differential
- Blood culture
- X-ray of the paranasal sinuses
- CT scan/MRI

**Treatment**

**Objectives**

- Reduce pain and suffering
- Treat the infection
- Prevent complications and loss of life

**Non Pharmacologic**

- Hospital admission
- Abscess drainage through orbitotomy if there is evidence of unresolving abscess collection in the orbit

**Pharmacologic**

**First line**

**Ceftriaxone**,

children: 40mg/kg/day IV in 2 divided doses for 14 days

adults: 1-2g IV BID for 14 days

*PLUS*

**Gentamicin**, 2.0mg/kg IV loading dose, then1mg/kg IV TID for 10-14 days

**Alternative**

**Clindamycin**,

children: 1mg/kg/day IV QID in 4 divided doses for 10-14 days

adults: 300mg IV QID for 10-14 days

*PLUS*

**Gentamicin,** 2.0mg/kg IV loading dose, then1mg/kg IV TID for 10-14 days

**N.B.** Consider adding **Metronidazole** 15mg/kg IV load, then 7.5mg/kg IV QID for adults with chronic orbital cellulitis or when anaerobic infection is suspected to all the above medicines other than clindamycin.

**Additional treatments**

**Nasal decongestants** (See ENT section)

**Tetracycline or Chloramphenicol or Erythromycin**, single strip ointments applied QID for corneal exposure if there is severe proptosis.

**N.B.** When orbital cellulitis is consistently improving, the regiment can be changed to oral antibiotics to complete the 14 day course. Often used antibiotics include:

**First line**

**Amoxicillin clavulanate,**

children; 20-40mg/kg/day P.O., TID

adults; 250-500mg P.O., TID

**Alternative**

**Cefaclor**,

children; 20-40mg/kg/day P.O., TID

adults; 250-500mg P.O., TID

**Refer:** In severe and complicated cases, refer to an ophthalmologist

**15. Preseptal Cellulitis**

It is an inflammation and infection confined to the eyelids and periorbital structures anterior to the orbital septum. It usually results from inoculation following trauma or skin infection. The globe is not usually involved; papillary reaction, visual acuity, and ocular motility are not disturbed; pain upon eye movement and chemosis are absent. S. aureus and streptococci are the most common organisms, H. influenzae should, however, be considered in children. Preseptal cellulitis in infants and children under age 5 may be associated with bacteremia, septicemia, and meningitis. In such cases; hospitalization and intravenous antibiotics are indicated. Suspect anaerobes if a foul smelling discharge or necrosis is present or there is a history of animal or human bite. Consider viral if there is skin rash (herpes simplex or herpes zoster).

**Clinical features**

- Pain, tenderness, erythema, swelling/edema, warmth, and redness of eyelid, mild fever, and irritability

**Investigations**

- Complete blood cell count and differential
- Gram's stain
- Pus culture.
- Blood culture

**Treatment**

**Objectives**

- Reduce pain and suffering
- Treat the infection
- Prevent complications

**Non Pharmacologic**

- Incision and drainage if there is an abscess
- Warm compresses to the affected area TID PRN

**Pharmacologic**

**A. Mild preseptal cellulitis**

**First line**

**Amoxicillin/clavulanate**,

children; 20-40mg/kg/day P.O., TID for 10 days

adults; 250-500mg P.O., TID for 10 days

**Alternatives**

**Trimethoprim/Sulfamethoxazole**,

children; 8mg/40mg/kg/day P.O., in 2 divided doses for 10 days

adults; 160mg/800mg BID for 10 days

*OR*

**Erythromycin**,

children; 30-50mg/kg/day P.O., 3-4 divided doses for 10 days

adults; 250-500mg P.O., QID for 10 days

*OR*

**Cefaclor**,

children; 20-40mg/kg/day P.O. TID for 10 days

adults; 250-500mg P.O. TID for 10 days

**B. Moderate-to-severe preseptal cellulitis:** Admit to the hospital for IV antibiotics

**First line**

**Ceftriaxone**,

children; 40mg/kg/day IV in 2 divided doses for 10-14 days

adults; 1-2g IV BID for 10-14 days

*PLUS*

**Gentamicin**, 2.0mg/kg IV loading dose, then1mg/kg IV TID for 10-14 days

**Alternative**

**Clindamycin**,

children; 1mg/kg/day IV QID for 10-14 days

adults; 300mg IV QID for 10-14 days

*PLUS*

**Gentamicin**, 2.0mg/kg IV loading dose, then1mg/kg IV TID for 10-14 days

**N.B.** IV antibiotics can be changed to comparable oral antibiotics after significant improvement is observed.

**Refer:** In severe and complicated cases, refer to an ophthalmologist

## 16. Trachoma

Trachoma is a chronic keratoconjunctivitis caused by the organism *Chlamydia trachomatis* that primarily affects the superior and inferior tarsal conjunctiva and cornea. Trachoma is related to poor hygiene, and is a disease of poverty. It is the most important preventable disease and a major cause of avoidable blindness in the world.

**Clinical features**

- Non specific symptom like, foreign body sensation, redness, tearing and mucopurulent discharge.
- Progressive conjunctival follicular hyperplasia
- Conjunctival scarring
- Entropion of the eyelid and trichiasis
- Corneal neovascularization and opacity.

**Investigations**

Trachoma diagnosis is often made on the symptoms and typical physical signs. The World Health Organization (WHO) has introduced a simple severity grading system for trachoma based on the presence or absence of **five key signs:**

1. **Trachomatous Inflammation–Follicular (TF):** The presence of five or more follicles in the upper tarsal conjunctiva.
2. **Trachomatous Inflammation–Intense (TI):** Pronounced inflammatory thickening of the tarsal conjunctiva that obscures more than half of the deep tarsal vessels.
3. **Trachomatous Scarring (TS):** The presence of scarring in the tarsal conjunctiva.
4. **Trachomatous Trichiasis (TT):** At least one eye lash rubs on the eye ball.
5. **Corneal opacity (CO):** Easily visible corneal opacity over the pupil.

**Prevention and Treatment**

The World Health Organization (WHO) advocates **SAFE** strategy.

**S =** Surgery for complications (TT & CO)

**A =** Antibiotics for active (inflammatory) trachoma (TT & TI)

**F =** Face washing, particularly in children

**E =** Environmental improvement including provision of clean water

**Treatment**

**Objectives**

- Identify infection early
- Prevent complications

**Non Pharmacologic**

- Regular face washing
- Good water and sanitation
- Surgical correction of entropion/trichiasis

**Pharmacologic**

**1. Trachomatous Inflammation–Follicular (TF)**

**First line**

**Tetracycline**, single strip of ointment applied BID for 6 weeks, OR asintermittent treatment BID for five consecutive days per month, OR QD for 10 consecutive days, each month for at least for six consecutive months.

**Alternative**

**Erythromycin**, single strip of ointment applied BID for 6 weeks

**2. Trachomatous Inflammation – Intense (TI)**

Topical First line & Alternative (See under TF)

*PLUS*

**Tetracycline**, 250mg P.O., QID for 3 weeks (only for children over 7 years of age and adults).

*OR*

**Doxycycline**, 100mg P.O., QD for 3 weeks (only for children over 7 years of age and adults).

*OR*

**Erythromycin**, 250mg P.O., QID for 3 weeks. For children of less than 25kg, 30mg/kg daily in 4 divided doses.

**N.B. Azithromycin** is given as a single dose of 20mg/kg. It represents long acting macrolides which has shown very promising effects in the treatment of trachoma in clinical research. It is still a very expensive medicine.

## 17. Vitamin A Deficiency (Xerophthalmia)

Vitamin A is required for growth, health and proper functioning of surface tissues, including the epithelium of skin, mucus membranes, ocular tissues, particularly the cornea, conjunctiva and retina. Vitamin A is found naturally in dark-green leafy and yellow vegetables, tubers, and fruits; and occurs (preformed) in eggs, milk, liver, and fish.

**Xerophthalmia** is a term used to describe milder form of ocular changes resulting from Vitamin A deficiency. **Xerosis** means drying of the conjunctiva and corneal epithelium. **Keratomalacia** (softening and melting of the cornea) is the most severe form of VITAMIN A DEFICIENCY. Children with corneal xerosis are likely to suffer from systemic illnesses, including diarrhoea, pneumonia, and measles. The presence of keratomalacia indicates a poor

prognosis for health and life; more than 50% of children with keratomalacia die because of associated poor nutritional status and susceptibility to disease.

**Clinical features**

- Night blindness or nyctalopia
- Thinning and lightening of hair,
- Weight loss,
- Dry and scaling of skin.

**Classification of Xerophthalmia**

**$X_N$**-Night blindness

**$X_{1A}$**-Conjunctival xcrosis

**$X_{1B}$**-Bitot's spots

**$X_2$**-Corneal xerosis

**$X_{3A}$**-Corneal ulceration/keratomalasia involving less than one third of the corneal surface

**$X_{3B}$**-Corneal ulceration/keratomalasia involving one third or more of the corneal surface

**$X_S$**-Corneal scars presumed secondary to xerophthalmia

**$X_F$**-Xerophthalmic fundus

**Investigations**

- Nutritional history and clinical findings

**Treatment**

**Objectives**

- Correct Vitamin A Deficiency
- Prevent blindness in patients with measles and malnutrition

**Non Pharmacologic**

**Both for treatment and prevention**

- Dietary, economic and social factors
- Breast feeding up to the age of 2 years
- Adequate fat, protein in the diet
- Nutritional: dark-green leafy vegetables, yellow vegetables, fruits, milk, eggs

**Pharmacologic:** Vitamin A in different doses based on the objective of treatment

**Table 80-Xerophthalmia Treatment Schedule for Children over one Year and under 6 Years Old**

| | |
|---|---|
| Immediately on diagnosis | 200,000 IU vitamin A P.O. |
| Following day | 200,000 IU vitamin A P.O. |
| Four weeks later | 200,000 IU vitamin A P.O. |

**N.B.** If there is persistent vomiting or profuse diarrhoea, 100,000 IU (water soluble) vitamin

**Table 81-Disease-Targeted Prevention Schedule for Preschool Children at High Risk***

| | |
|---|---|
| Children over 1 year and under 6 years old | 200,000 IU vitamin A P.O. at first contact with a health care worker for each episode of illness |
| Infants under 1 year old and children of any age who weigh less than 8 kg | 100,000 IU vitamin A P.O. at first contact with a health care worker for each episode of illness |

*Those presenting with measles, severe PEM, acute or prolonged diarrhoea, acute lower respiratory infections.

**Table 82-Universal Distribution Prevention Schedule for Preschool Children and Lactating Mothers**

| | |
|---|---|
| Children over 1 year and under 6 years months old who weigh 8 kg or more | 200,000 IU vitamin A P.O. every 3-4 |
| Children over 1 year and under 6 years months old who weigh less than 8 kg | 200,000 IU vitamin A P.O. every 3-4 |
| Infants | 100,000 IU vitamin A P.O. at 6 months* |
| Lactating mothers | 200,000 IU vitamin A P.O. at delivery or during the next 2 months; this will raise the concentration of vitamin A in the breast milk and help to protect the breast-fed infant |

* **Best treatment protocol:** 25,000IU orally at each of the three DPT visits, the polio immunization, and then at 9 months (measles immunization).

**ADRs:** irritability

**Dosage forms:** Capsule, 25,000IU, 50000IU, 100,000IU; tablet, 50,000IU, 100,000IU, 200,000IU oral solution, 150,000IU/ml (concentrate) 50,000IU/ml; injection, 200,000IU/ml

**Refer:** In severe and complicated cases refer to an ophthalmologis

## CHAPTER XVIII: EAR, NOSE AND THROAT

### 1. Acute Otitis Media

Acute otitis media is an inflammation which usually affects not only the mucosa of the middle ear, but also that of the entire pneumatic system. The infection is 90% monomicrobial. The infecting organisms are: streptococci (in adults), pneumococcal (in children), hemophilus influenzae, staphylococci and coli forms. A viral infection may prepare the way for secondary bacterial infection.

The younger the child, the more severe the generalized symptoms are and the more discrete the local signs are. On occasion the gastrointestinal symptoms are the most pressing. Every attack of acute otitis media is accompanied by mastoiditis.

**Clinical features**

- In the first phase of exudeative inflammation which lasts 1 – 2 days temperature increases to 39–40°C often no fever in older patients)
- In severe cases, rigors and occasionally meningismus in children.
- Pulsating pain worse by night than by day.
- Muffled noise, deafness and sensitivity of the mastoid process to pressure.
- In the second phase (lasts 3-8 days) middle ear exudate usually discharges spontaneously.
- Otoscopy shows hyperemia, moist infiltration and opacity of the surface of tympanic membrane, a pinhole size fistula forms usually in the poterosuperior quadrant of the tympaic membrane.

**Investigations**

- CBC
- Ear swab for culture and sensitivity
- Schuller's view x-ray may show clouding of the pneumatic air cell system of the mastoid without osteolysis.

**Treatment**

**Objectives**

- Relieve symptoms

- Return hearing to normal
- Prevent chronicity and complications (like perforation,meningitis,brain abscess, etc).

**Non Pharmacologic**

- Drink lots of fluid
- Paracentesis when indicated

**Pharmacologic**

**First line**

**Amoxicillin**

children under 6 years; 125mg/5ml, 250mg/5ml 1 tsp. P.O., TID for ten days

children above 6 years; 250 mg P.O., TID for ten days

adults; 500mg PO TID times for ten days for 10 days.

**ADRs:** diarrhoea, pseudomembranous colitis, acute interstitial nephritis, anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia.

**C/Is:** in patients with known hypersensitivity to any other penicillin or cephalosporins.

**Dosage forms:** Capsules: 250mg, 500mg; Suspension: 125mg/5ml, 250mg/5ml, 50mg/5ml; Tablets (chewable): 125mg, 250mg)

**Alternatives**

**Ampicillin**, 250 – 500mg P.O, QID for 10 days for adult. 50 – 100mg/kg 1 tsp. PO QID or 100-200mg/kg IV into divided doses QID for children for 10 days.

**ADRs:** diarrhoea, glossitis, stomatitis, acute interstitial nephritis, anaemia, thrombocytopenia, Thrombocytopenic purpura, leukopenia and eosinophilia

**C/Is:** in patients with known hypersensitivity to any other penicillin or to cephalosporins. Ampicillin should not be used in patients with infectious mononucleosis

**Dosage forms:** capsules: 250mg, 500mg; Suspension: 100mg/ml, 125mg/5ml; 250mg/5ml, 500mg/5ml; Parenteral: 125mg, 250mg, 500mg, 1g, 2g; Infusion: 500mg, 1g, 2g

*OR*

**Amoxicillin/Clavulanate**, 375mg P.O. TID for 10 days OR 625mg P.O. BID for 10 days for adults 312mg/5ml suspension P.O. TID for 10 days OR 156mg/5ml suspension P.O. TID for 10 days for children

**ADRs:** skin rashes, Stevens-johnson syndrome, vasculitis, headache

**C/I:** In patients with a known history of hypersensitivity reaction to penicillin, hepatic dysfunction and jaundice patints.

**Dosage forms:** Tablets: 375 mg, 625 mg; Suspension: 156mg/5ml, 312mg/5ml

*OR*

**Ciprofloxacin**, 500mg P.O., BID FOR 7-10 days.

**ADR:** rash and pruritus fever, joint pain, urticaria, neurlogical reactions, epistaxis, laryngeal edema, hypertension, angina pectoris, myocardial infarction.

**C/Is:** in patients allergic to the medicine quinolone antibiotics, pregnancy, lactation.

**Dosage forms:** Tablets: 250mg, 500mg, 750mg.

*PLUS*

**Ciprofloxacin ear drop eye ear solution**, 0.3%, 5ml. 2 – 3 drops twice daily.

**ADRs:** pain or itching in the ear, headache.

**C/I:** hypersensitivityto quinolone groupof antibiotics.

**Dosage forms:** Ciprofloxacin USP: 0.3% w/v; Benzalkonium chloride NF: 0.01%

*OR*

**Chloramphenicol,** Solution ear drop, 1%, 2%, 5%. Apply 2–3 drops 2–3times daily.

**ADRs:** Peripheral neuropathy, itching, burning sesation, decreased visual acuity.

**C/I:** Hypersensitivity to the medicine, perforated ear drum, breast feeding mothers.

**Dosage forms:** Otic Solution: 0.5%

*PLUS*

**Paracetamol**, 30-40mg/kg/24hrs.

**ADRs:** Increased transaminase, thrombocytopenia, leucopenia, neutopenia skin rashes, vomiting, gastro intestinal haemorrage.

**C/Is:** Hepatic impairment, impaired kidney.

**Dosage forms:** Tablet: 500mg of paracetamol (N-Acetyl – P aminophenol)
Suspension: 120mg/5ml paracetamol (N-Acetyl – P aminophenol).

**N.B.** Paracentisis should be carried out early if the tympanic membrane does not perforate spontaneously. Antrotomy should be carried out early if it is indicated on clinical grounds.

## 2. Acute Tubal Occulsion With Seromucinous Otitis Media

This occurs due to obsttructive process of the nasopharynx, disorder of or icompetence of the muscles opening the eustachain tube. Virus infections are the most common underlying mechanism.

**Clinical Features**

- A feeling of pressure in the ear accompanied by stabbing pain
- Deafness and a crackling noise on swallowing which occurs during rhinopharyngitis.
- Pain is absent.
- Otoscopy shows a retracted tympanic membrane and injection of the handle of the malleus and the vessels of the tympanic membrane.

**Investigations**

- Audiogram shows a conductive deafness frequency range 40 to 50Db.
- Schuller x–ray view shows opacity of the cell system (pneumatic air cells).

**Treatment**

**Objectives**

- Remove underlying diseases such as rhinopharyngitis.
- Stop the danger of progression to otitis media.
- Reduce hypermia and edema in the eustachain tube.
- Treat infection of the sinus.

**Non pharmacologic**

- Adeniodectomy in children for elimination of infection of the sinus.
- Paracentesis and drainage of the middle ear (insertion of grommet) under general anesthesia in childeren and under local anaesthesia in adults.

**Pharmacologic**

**First line**

**Amoxicillin**

adults; 500mg. P.O., TID for ten days

chideren above 6 years; 250mg. P.O., TID for ten days

childeren under 6 years; 125mg /5ml, 250mg/5ml P.O., TID for ten days

**Alternatives**

**Amoxicillin /Clavulante**,

children;156mg/5ml suspension P.O., TID for ten days or 312mg/5ml suspension P.O., TID for ten days or 228mg/5ml PO BID for ten days or 457mg/5ml suspension P.O., BID for ten days

adults; 375mg. P.O., TID for ten days or 625mg P.O., BID for ten days or 1gm P.O., BID for seven days

**ADRs**: diarrhoea, pseudomembranous colitis, acute interstitial nephritis, anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia.

**C/Is:** in patients with known hypersensitivity to any other penicillin or cephalosporins.

**Dosage forms:** Capsules: 250mg, 500mg. Suspension: 125mg/5ml, 250mg/5ml 250mg/5ml. Tablets (chewable): 125mg, 250mg.

*PLUS*

**Xylometazoline hydrochloride**,

infants and small children up to 6 years; 1-2 drops of 0.5% solution in each nostril

children over 6 years and adults; 2-3 drops of 1% solution 3-4 times a day

**ADRs:** Hypertension, rebound effect after discontinuation.

**C/Is:** Patients with narrow angle glaucoma, in patients receiving tricyclic

antidepressant, should be used with caution in patients with hyperthyrodism cardiac disease, hypertension, diabetes mellitus.

**P/Cs**: Never use for longer than 5 days.

**Dosage forms:** Solution (nasal drop): 0.05%, 0.1%; Nasal spray: 0.1%

*PLUS*

**Chlorpheniramine**,

children age 2-5; 1mg 3-4 times a day (maximum dosage 4mg/day)

children age 6-12; 2mg 3-4 times a day (maximum dosage 12mg/day)

children above 12years and adults; 4mg 3-4 times a day (maximum 24mg/day)

**ADRs:** fatigue, dizziness

**Dosage forms:** Tablet: 5mg, 10mg; syrup, 2, mg/5ml

*OR*

**Cetrizine**,

children below 12 years; 5-10mg daily

children above 12 years and adults; 10mg daily

**ADRs:** Drowsiness, headache, dry mouth, fatigue, dizziness and gastro – intestinal discomfort.

**C/Is:** Patients with a history of hypersensitivity to it.

**Dosage forms:** Oral solution: 1mg/ml; Tablets: 5mg, 10mg

### 3. Acute Vestibular Paralysis (Vestibular Neuronitis)

This condition is largely unexplained. The disease may be caused by disturbance of the microcirculation due to infection, an autoimmune disease or metabolic disorder.

**Clinical Features**

- Rotatory dizziness
- Ataxia
- Nausea & Vomiting.
- Dizziness persisting for days or week.
- Spontaneous Nystagmus

- Positive Romberg test

**Investigations**

- Audiometry, if possible vestibulometry

**Treatment**

**Objectives**

- Ameliorate symptoms

**Non pharmacologic**

- Immediate active physiotherapy

**Pharmacologic**

**In acute phase:**

**Diazepam**, 5-20mg IV rapidly to make the patient stable. IV diazepam may be continued briefly in an IV drip but shift to maintenance oral diazepam preferred (5-10mg/day) as soon as possible.

**ADRs:** fatigue, hypertension, and respiratory depression.

**C/Is:** Shock, coma, acute alcohol intoxications, known hypersensitivity to the medicine and patients with acute-narrow angle glaucoma

**Dosage forms:** Tablets: 2mg, 5mg, 10mg; Oral solution: 5mg/ml; 5mg/5ml Oral suspension: 5mg/5ml; Injection: 5mg/5ml in 2-ml ampules or 10-ml vials.

*PLUS*

**Meclizine hydrochloride**, 12.5 – 25mg or 50mg P.O., daily in divided doses for the control of nausea and vomiting. Dosage varies with patient response.

**ADRs:** blurred vision, dry nose and throat, constipation, diarrhoea

**C/Is:** patients with known hypersesitivity to this medicine or other antiemetic antihitamines with a similar chemical stracture, patients with narrow-angle glaucoma, asthma, prostatic hypertrophy.

**Dosage forms:** Tablets: 12. 5mg, 25mg, 50 mg; Tablets (chewable): 25mg.)

*OR*

**Promethazine**,

children: 12.5 to 25mg P.O., IM or rectally BID.

adults: 25mg P.O., BID for the control of Nausea and vomiting

**ADRs:** confusion, restlesness, tremors, drowsiness, diziness, hypotension, hyprtension, nasal congestion, myopia, durinary retention, leukopenia, thrombocytopenia.

**C/Is:** patients with known hypersensitivty to promethazine, during asthmatic attack, dehydrated children, patients with bone marrow depression, in epilipsy patient, with narrowangle glaucoma, peptic ulcer.

**Dosage Forms:** Tablets: 12.5mg, 25mg, 50mg; Syrup: 6. 25mg/5ml, 10mg/5ml, 25mg/5ml Suppositories: 12.5mg, 25mg, 50mg; Injection: 25mg/5ml, 50g/5ml

*OR*

**Dimenhydrinate**,

children 2-6 years: 12.5 - 25mg 6 - 8 hours as needed

children 6-12 years; 25 – 50mg every 6 – 8 hours as needed

teenagers and adults; 50-100mg P.O., every four hours as needed

**ADR:** Sore throat and fever; unusual bleeding or bruising; unusual tiredness or weakness.

**C/Is:** History of allergic reaction to antihistamines, enlarged prostate, Urinary tract blockage, glaucoma and history of heart rhythm problems, pregnancy and breast feeding mother.

**Dosage forms:** Tablet, 50 mg; Liquid: 12.5mg/4ml; Injection: 50mg/5ml Rectal: 50mg, 100mg)

*PLUS*

**Thiamine+Pyridoxine+Cyanocobalamine** 1 tab P.O., BID daily

**ADRs:** aggravation of existing acne, diarrhoea and itching sensation.

**C/Is:** Psoriasis, liver disease.

**Dosage forms:** Tablet, Thamine; 97.00mg; Tablet, Pyridoxine HCL:50.00mg; Tablet, Cyanocoblamin: 100.00mcg

**N.B.** Not recommended for children.

**If there is objective evidence of bacterial infection:**

**First line**

**Amoxicillin**, 500mg P.O., TID for 10 days

**ADRs**: diarrhoea, pseudomembranous colitis, acute interstitial nephritis, anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia.

**C/Is:** in patients with known hypersensitivity to any other penicillin or cephalosporins.

**Dosage forms:** Capsules: 250mg, 500mg. Suspension: 125mg/5ml, 250mg/5ml, 50mg/5ml. Tablets (chewable): 125mg, 250mg

**Alternatives**

**Amoxicillin/Clavulanate**, 375mg P.O., TID or 625mg P.O., BID for 10 days

**ADRs:** colitis, acute interstitial nephritis, anaemia, thrombocytopenia, thrombocytopenic pupura Leucopenia

**C/Is:** Infectious mono-nucleosis, Hypersensitivity to any other penicillin or to cephalosporins.

*OR*

**Cefixime**, 200mg P.O., BID for 6 days

**4. Bacterial and viral diffuse otitis externa**

There is complete obstruction of the external auditory meatus with an accompanying retroauricular lymphoadenitis especially in infants and young children. A characterstic eryspelas occurs in streptococcal infection. In swimmer's otitis due to maceration of the skin by halogen-containing swimming poolwater.

**Clinical Features**

- Fever with generalized illness
- Regional lympadenitis
- Pain onpullingon the auricule or pressure on the tragus
- A phlegmonous formcan extendto the surrounding tissues and organs (paratoid, mastoid skull base).
- Complete obstruction of the external auditoy meatus with retroauricular

lymphadenitis.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Reduce the swelling of the skinof the external auditory meatus.
- Stop further complications.

**Non pharmacologic**

- Ear pack with 70-90% pure alcohol

**Pharmacologic**

**First line**

**Oxytetracycline hydrochloride + Polymyxin B sulphate + Hydrocortisone acetate**, 2 drops 2-3 times daily

| | |
|---|---|
| **ADRs:** | local sensitivity reactions |
| **C/I:** | perforated tympanic membrane P/Cs: avoid prolonged use |
| **Dosage forms:** | Ear drop, 5mg +15mg + 10,000 units in each ml |

**Alternatives**

**Cloxacillin**, 500mg P.O., QID for 7 – 10 day. 50-100mg/Kg/24hrs P.O., divided into 4 doses for 7 – 10 days for children

| | |
|---|---|
| **ADRs:** | epigastric distress, diarrhoea, intrahepatic cholestasis, acute interstitial nephritis, eosinophilia, leucopenia, granulocytopenia, thrombocytopenia, rash, chills, fever, sneezing and anaphylaxis. |
| **C/Is:** | on patients with known hypersensitivity to any other penicillin or to cephalosporins |
| **Dosage forms**: | Capsule: 250mg, 500mg; Syrup: 125mg/5ml, 250mg/5ml; injection, 250mg, 500mg in vial |

*OR*

**Amoxicillin** 250-500mg P.O., TID for 7-10 days for adults. 50-100mg/kg P.O., TID for 7 – 10 days for children

**ADRs:** diarrhoea, pseudomembranous colitis, acute interstitial nephritis, anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia.

**C/Is:** in patients with known hypersensitivity to any other penicillin or cephalosporins.

**Dosage forms:** Capsules: 250mg, 500mg. Suspension: 125mg/5ml, 250mg/5ml 50mg/5ml. Tablets (chewable): 125mg, 250mg

*OR*

**Erythromycin**,

children; 30 to 50mg /kg PO daily divided 6 hrs, OR 15 to 20mg/kg IV daily divided doses Q 4 to 6hrs.

adults; 250mg to 500mg P.O., Q 6 hrs

**ADRs:** Allergic reactions, gastro intestinal symptoms, overgrowth of micro organisms, cholestatic jaundice, hearing loss (with high IV doses in renal failure)

**C/Is:** Decreased liver function, hypersensitivity to this medicine.

**Dosage forms**: Tablets (enteric coated) 250mg, 500mg; Suspension: 200mg/5ml, 125mg/5m, 400mg/5ml; Tablets (chewable): 125mg, 250mg; Injection: 250-mg, 500-mg 1-g vials; Drops: 100mg/ml

## 5. Barotrauma

Barotrauma is due to the development of a negative pressure in the middle ear cleft, relative to the environment. It may occur during descent from altitudes, as in flying, during under water descent as in diving.

**Clinical features**

- Cause bleeding into the middle ear mucosa and into the tympanic membrane
- Rupture of the tympanic and round window membrane.
- Deafness and discomfort
- Tinnitus

**Investgations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Restore hearing capacity especially with severe sensory neural hearing loss
- Treat tinnitus

**Non pharmacologic**

None

**Pharmacologic**

**First line**

**Xylometazoline hydrochloride**, 2 drops 2 – 3 times ddaily 5 – 7 days.

**ADRs:** Short-lived irritation (burning or dry sesation of the nasal mucosa), headache, insomnia, palpation.

**C/Is:** Hypertension, cardiovasculardiseases, hyperthyrodism, diabetus mellius, pregnancy and breast feeding mothers.

**Dosage forms:** Nasal forms: 0.5% and 1%; Nasal gel: 1%; Nasal spray: 0.5% and 1% aqueous solution)

*PLUS*

**Paracetamol**, 30-40mg/kg/24hrs.

**ADRs:** Increased transaminase, thrombocytopenia, leucopenia, neutopenia, skin rashes, vomiting, gastro intestinal haemorrage.

**C/Is:** Hepatic impairment, impaired kidney.

**Dosage forms:** Tablet: 500mg of paracetamol (N-Acetyl – P aminophenol); Suspension: 120mg/5ml paracetamol (N-Acetyl–P aminophenol).

**6. Chronic Otitis Media**

Chronic otitis media is defined as long-standing inflammation of the middle ear cleft in which signs of acute inflammation are charcteristically missing.

**Clinical Features**

- Constant or intermittent discharge (usually odurless) from the ear

- Conductive hearing impairment of slight to moderate
- Absence of pain
- Occasionally granulations or polyps may form with in the middle ear and a large aural polyp may occlude the external auditoy meatus.
- Usually there is a large centeral or anerior defect of the tympanic membrane (perforation).

**Investigations**

- Basic audiological test including Tuning-fork test (Rinne, Weber and Absolute Bone conduction).
- Culture of of the ear discharge.
- Radiology of the petrous pyramids (Schuller's lateral view and Stenver's view) and paranasal sinuses.

**Treatment**

**Objectives**

- Keep the ear dry
- Eliminate the foci of infection in the temporal bone and the middle ear
- Constuct the sound–conducting apparatus.

**Non pharmacologic**

- Patient should be treated as early as possible by ENT Surgeon.

**Pharmacologic**

**N.B.** In acute exacerbations only. Antibiotic treatment, whenever possible, must be directed by the results of culture and sensitivity of the ear discharge.

**First line**

**Amoxicillin**, 500mg P.O., TID for 10-15 days for adults 125mg/5ml or 250mg/5ml 1 tsp. PO TID for 10 days.

**Alternatives**

**Amoxicillin-Clavulanate**,

children; 156mg/5ml or 312mg/5ml 1 tsp. P.O., TID or 248mg/5ml or 457mg/5ml 1 tsp. P.O., BID.

adults; 625mg or 1gm P.O., BID for 10 days

*OR*

**Ceframed**,

chidren; 75 to 100mg/kg/day in divided doses every 6 to 12 hours 7 – 10 days

adults; 250mg P.O., QID or 500mg P.O., QID for 7 – 10 days

**ADRs:** Skin rashes, diarrhoea

**C/I:** In patients with known hypersensitivity to the cephalosporin group of antibiotic.

**Dosage form:** Capsules: 250mg, 500mg Suspension: 125mg/5ml, 250mg/5ml)

*PLUS*

**Hydrogen peroxide**, solution 3% apply 5 to 10 drops twice daily for ear cleaning; patient should be treated as early as possible by ENT specialist.

**Dosage forms:** Solution, 1.5%, 3%

## 7. Otogenic Infective Complications

### Labyrinthitis

The usual cause is erosion of the latera semicircular canal. This occurs more commonly in chronic suppurative otitis media espicallywit cholesteatoma. Lbyrinthitis may also occur as a complicationof acute otitis mediaor may be due to viral infection.

**Clinical Features**

- Spontaneous nytagmus to the affected side
- Dizziness with nausea and vomiting
- Whistling noises in the ears
- Deafness
- Patient has no fever and no pain at early presentation
- Patient lies curled up in bed with the affected ear down.Any movement aggravates the vertigo
- On standing the patient falls to the unaffected side.

**Investigations**

- Audiometry

**Treatment**

**Objective**

- Stop further severe complications.

**Non pharmacologic**

- Drain the middle ear
- Mastoidectomy

**Pharmacologic**

**First line**

**Crystaline penicillin**,

children; 250,000 U/kg/24 hr, divided 8 doses IV for 7 – 10 days

adults; 3 to 4 million IU I. V. in 8 divided doses For 10 days for adults

**ADRs:** hypersensitivity reactions including uriticaria, fever, joint pains, rashes, angio-Edema anaphylaxis, parasthesia, Diarrhoea and colitis

**C/Is:** Penicillin hypersensitivity

**Dosage forms:** Injection, 1 million IU, 10 million IU, and 20 million IU in vial. 1 million units Equivalent to 600mg

**Alternatives**

**Gentamicin sulfate**, 80mg I.V.TID for 7-10 days. 5mg/kg/day divided into 3 doses for 7 to 10 days

**ADRs:** headache, lethargy, respiratory depression, ototoxicity, diarrhoea, nephrotoxicity.

**C/Is:** in patients with known hypersensitivity to other aminoglycoside.

**Dosage forms:** Injection: 40mg/ml (adult), 10mg/ml (pediatric)

*OR*

**Ampicillin**,

children; 200 mg/kg/day IV every 6 hours for 7-10 days

adults; 500-1 gm IV QID 7-10 days

*OR*

**Ceftriaxone**, 100mg/kg in divided doses every 12 hours IV, IM for 7 to 10 days.

| | |
|---|---|
| **ADRs:** | headache, dizziness, seizures, maculopapular rashes, diarrhoea, abdominal cramps, leukopenia, anaemia, neutropenia,eosinpilia, hemauria. |
| **C/Is:** | in patients with known hypersensitivity to any cephalosporin |
| **Dosage forms:** | injection: 250mg, 500mg, 1g, 2g; Infusion: 1g, 2g |

### 8. Otogenic Menengitis

Micro–organisms which are feebly pathogenic, if they gain acess to the brain, may cause intracranial infection with fatal consequences. Local sources of infection cause a significent number of cases mostly from the middle ear, mastoid, paranasal air sinus. Pneumococci and Streptococci are organisms usually found in these instances.

**Clinical Features**

- Headache
- Stiffness of the neck
- Increasing loss of conciousness
- Restlessness
- Tonic-clonic convulsions
- Facial paralysis
- Otorrhea, otalgia

**Investigation**

- Cerebro spinal fluid (CSF)
- Otoscope findings
- Radiographs of the temporal bone (in Shuller and stenvers view), CT scan or MRI of the brain.

**Treatment**

**Objectives**

- Treat the underlying cause
- Early and vigorous specific treatment

**Non-pharmacologic**

Immediate drainage of the middle ear cavity by mastoidectomy or radical mastoidectomy is required with wide exposure of the durs by ENT Surgeon.

**Pharmacologic**

**First line**

**Crystaline penicillin**,

children; 250,000 U/kg/24 hr, divided 8 doses IV for 7 – 10 days

adults; 3 to 4 million IU I. V. in 8 divided doses for 10 days

**ADRs:** hypersensitivity reactions including uriticaria, Fever, joint pains, rashes angio-Edema anaphylaxis, parasthesia, diarrhoea and colitis

**C/Is:** Penicillin hypersensitivity

**Dosage forms:** Injection, 1 million IU, 10 million IU, and 20 million IU in vial. 1 million units equivalent to 600 mg

**Alternatives**

**Gentamicin sulfate**,

children; 5mg/kg/day divided into 3 doses for 7 to 10 days

adults; 80mg I.V.TID for 7-10 days

**ADRs:** headache, lethargy, respiratory depression, ototoxicity, diarrhoea, nephrotoxicity.

**C/I:** in patients with known hypersensitivity to other aminoglycoside.

**Dosage form:** Injection 40mg/ml (adult), 10mg/ml (pediatric)

*OR*

**Ampicillin**,

children; 200 mg/kg/day IV every 6 hours for 7-10 days

adults; 500mg-1gm IV QID 7-10 days

*OR*

**Ceftriaxone**, 100mg/kg in divided doses every 12 hours IV, IM for 7 to 10 days.

**ADRs:** headache, dizziness, seizures, maculopapular rashes, nausea, vomiting, diarrhoea, abdominal cramps, leukopenia, anaemia, neutropenia,eosinpilia, hemauria.

**C/I:** in patients with known hypersensitivity to any cephalosporin

**Dosage forms:** injection: 250mg, 500mg, 1 g, 2 g; Infusion: 1g, 2g

**Pharmacologic**

**First line**

**Crystaline penicillin**,

children; 250,000 U/kg/24 hr, divided 8 doses IV for 7 – 10 days

adults; 3 to 4 million IU I. V. in 8 divided doses For 10 days

**ADRs:** hypersensitivity reactions including uriticaria, fever, joint pains, rashes angio-Edema anaphylaxis, parasthesia, with prolonged us Diarrhoea and antibiotic associated colitis

**C/Is:** Penicillin hypersensitivity

**Dosage forms:** Injection, 1 million IU, 10 million IU, and 20 million IU in vial. 1 million units equivalent to 600 mg

**Alternatives**

**Gentamicin sulfate**,

children; 5mg/kg/day divided into 3 doses for 7 to 10 days

adults; 80mg I.V.TID for 7-10 days.

**ADRs:** headache, lethargy, respiratory depression, ototoxicity, diarrhoea, nephrotoxicity.

**C/I:** in patients with known hypersensitivity to other aminoglycoside.

**Dosage form:** Injection: 40mg/ml (adult), 10mg/ml (pediatric)

*OR*

**Ampicillin**,

children; 200mg/kg/day IV every 6 hours for 7-10 days

adults; 500-1gm IV QID 7-10 days

*OR*

**Ceftriaxone**, 100mg/kg in divided doses every 12 hours IV, IM for 7 to 10 days.

| | |
|---|---|
| **ADRs:** | headache, dizziness, seizures, maculopapular rashes, nausea, vomiting, diarrhoea, abdominal cramps, leukopenia, anaemia, neutropenia,eosinpilia, hemauria. |
| **C/I:** | in patients with known hypersensitivity to any cephalosporin |
| **Dosage forms:** | injection: 250mg, 500mg, 1g, 2g; Infusion: 1g, 2g |

## 9. Foreign Bodies In The Ear

The majority of patients with foreign bodies in the ear are children.

The organic or inorganic objects may give rise to otitis externa (especially organic) by local irritation of the epithelium of the meatal walls.

**Clinical Features**

- Itching sensation
- Pain, purulent discharge and debris
- Deafness
- Foreign body detected on otoscopic examination.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Open the ear canal which is completely or partially closed by removing the foreign body.
- Eliminate secondary infections

**Non pharmacologic**

- Irrigation of the suspected ear with water by ENT specialist if there is no perforation of the tympanic membrane.
- Manual removal is another approach.

**Pharmacologic**

Patient should be kept on antibiotic if there is sign of infection on the ear canal or purulent discharge.

**First line**

**Amoxicillin**

children under 6 years; 125mg/5ml or 250mg/5ml P.O., TID 10 days

children above 6 years; 250mg P.O., TID 10 days

adults; 500mg P.O., TID 10 days

**Alternatives**

**Amoxicillin/clavulanate**,

children; 156mg/5ml P.O., TID or 312mg/5ml P.O., TID 10 days

adults; 375mg P.O., TID for 10 days or 625mg P.O., BID 10 days

*OR*

**Cloxacillin**,

children; 50mg-100mg/kg/day P.O. divided into 4 doses 7-10 days

adults; 500mg P.O., QID 10 days

*OR*

**Oxytetracycline hydrochloride + Polymyxin B sulphate + Hydrocortisone acetate;** 2 drops 2-3 times daily.

| |
|---|
| **N.B.** Foreign bodies that cannot be removed by irrigation should be removed manually, using general anesthesia in small children.<br>Ears with vegetable foreign bodies should not be irrigated, since this may cause the vegetable matter to swell. Crushing insect foreign bodies is to be avoided. |

**10. Idiopathic Facial Paralysis (Bell's)**

A viral infection may also be responsible. Exposure to cold, emotional stress and pain over mastoid may precede the onset of the lesion. Recovery occurs in approximately 80% of patients within a few weeks or months of onset.

There is sudden onset and occurs at any age, particularly healthy adults between 20-35 years and children of 6-12 years of age.

**Clinical features**

- Inability to close the eye on the affected side
- Deviation of the corner of the mouth to the opposite side.
- Paralysis of the facial nerve (peripheral type) is detectable on clinical examination

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objective**

- Regain the function of the facial nerve as early as possible.

**Non pharmacologic**

- Use of paper tape to depress the eye lid during sleep to prevent corneal dryness.
- Massage of the weakened muscles.
- Surgical decompression may rarely be indicated.

**Pharmacoglogic**

Patients should receive both prednisone and acyclovir.

**Prednisolone**, 60-80mg/day P.O., for five days to be tapered over the next five days.

**ADRs:** insomnia, headache, psychotic behaviour, nervousness, restlessnes, hypertension, catract glaucoma, peptic ulcer and immunosuppression.

**C/Is:** GI ulceration, renal disease, hypertension, osteoporosis, diabetes mellitus, tuberculosis, liver cirrhosis, glaucoma, hyperthyrodism.

**Dosage forms:** Tablets: 5mg; Syrup: 15mg/5ml; Injection: 25mg/ml, 50mg/ml, 100mg/ml suspension

*PLUS*

**Acyclovir**, 800mg 5 times daily for 7 days or 5mg/kg body weight IV TID for 7 days.

**ADRs:** headache, encephalopathic signs, hypotension, diarrhoea, hematuria

**C/Is:** Patients with known hypersensitivity, dehydreted patients, renal dysfunction

**Dosage forms:** Capsules: 200mg, Injection: 500mg/vial; Ointment: 5%

**N.B.** Immediate decompression of the nerve should be undertaken for progressive denervation after careful assessment of the indication.

## 11. Mastoiditis

The most frequent complication of middle ear inflammation is mastoiditis, an extension of the infection from the middle ear cavity to the pneumatic system of the temporal bone.

**Clinical Features**

- Aural discharge
- Tenderness to pressure over the mastoid
- Retro auricular swelling with a protruding ear.

**Investigations**

- Mastoid radiographs in Shuller's view.

**Treatment**

**Objective**

- Eliminate the foci of infection in the temporal bone and the middle ear cavity.

**Non pharmacologic**

- Surgery if the inflammation is no longer confined to the mucosa but has extended to the bone

**Pharmacologic**

**Amoxicillin clavulanate**,

children; 156mg/5ml 1 tsp. P.O., TID or 312mg/5ml 1 tsp. P.O., TID 10 days

adults; 375mg P.O., TID for 10 days OR 625mg P.O., BID 10 days

*OR*

**Cefixime**,

children; 8mg/kg suspension as a single dose or 4mg/kg BID P.O.

children weight more than 50kg or above 12 years and adults; 200mg P.O. BID for 6 days,

| | |
|---|---|
| **ADRs:** | diarrhoea, abdominal pain, nausea, vomiting, skin rashes, urticaria transient elvation in liver enzymes |
| **C/Is:** | patients with known allergy to cephalosporin |
| **Dosage forms:** | Capsule, 200mg Cefixime (as trihydrate); Suspension: 100mg/5ml cefixime (as trihydrate). |

## 12. Meniere's Disease

The disease caused by a disturbance of the quantitative relation between the volume of the peri-and endolymph. Characteristically there is no predisposing factor apart from psychological stress.

**Clinical Features**

- Tinnitus
- Deafness
- Vertigo
- Nausea and vomiting

**Investigations**

- General examination of the patientis mandatory, particular attention being paid to the cardiovascular system and the central nervous system.
- Audiological investigation like Tuning forktests, Pure-tone audiometry
- Vestibular test (Electronystagmography).
- Radiological examination (Views of the petrous bones)
- If possible electrocochleography.

**Treatment**

**Objectives**

- Relieve symptoms by blocking cholinergic inputs to the vestibuli

**Non pharmacologic**

- Avoid stress

**Pharmacologic**

**First line**

**Meclizine**, 25-100mg/day in divided doses. Doses vary with patient's response

**ADRs:** anorexia, blurred vision, dry nose and throat, diarrhoea.

**C/Is:** in patients with known hypersensitivity to the medicine.

**Dosage forms:** Tablet, 12.5mg, 25mg

**Alternatives**

**Dimenhydrinate**,

children age 6-12; 25-50mg P.O., Q 6-8 hrs

children age 12 and older and adults; 50-100mg. 24hrs P.O., or IM or IV

**for acute attack:** 50 mg, IM

**for maintenance dose:**25-50mg, TID

**ADRs:** dizziness, convulsion, palpation, hypotension, tinnitus, blurred vision, diarrhoea, anorexia,dysuria.

**C/Is:** in patients with known hypersesitivity to this medicine or to other antiemetic and antihistamines

**Dosage Forms:** Tablet: 50mg; Liquid: 12.5mg/4ml; Injection: 50mg/ml; Suppository: 50mg, 100mg

*OR*

**Cyclizine hydrochloride**,

chidren age 6 to 12; 3mg/kg IM divided TID or 25mg P.O., PRN

children above 12-years and adults; 50mg P.O., or IM q 4-6 hrs P.R.N.

**ADRs:** vertigo, dizziness, hallucination, reslesness, hypotension, palpation tachycardia, tiinitus, dry nose and throat, blurred vision, diarrhoea, dysuria.

**Dosage Forms:** Tablets: 50mg; Injection: 50mg/ml

**13. Nonspecific Inflammation Of The External Ear**

This is an inflammation of the external auditory meatus caused by gram negative bacteria and anaerobes. The inflammation is localized to the auricle, external auditory meatus and the regional lymph nodes. The tympanic membrane is intact but may be difficult to assess because of the accumlation of debris.

**Clinical features**

- The cartilaginous part of the meatus is painful
- Retroauricular region is tender to pressure
- Pain on pressure on the tragus strongly suggests otitis externa

**Investigations**

- Otoscopy
- Examination of pus for bactriology
- Tuning fork test

- Audiogram
- Radiology using Shuller's view to exclude mastoiditis

**Treatment**

**Objectives**

- Relieve the classic triad symptoms
- Shorten hospital stay
- Regain hearing capacity

**Non pharmacologic**

Clean the external auditory canal meatus manually under visualization with water or saline or 3% H202 at 37 °C repeatedly

**Pharmacologic**

**First line**

**Oxytetracycline hydrochloride + polymyxin B sulphate + Hydrocortizone acetate**, 2 drops 2 to 3 times daily.

**ADRs:** Not significant.

**C/Is:** Acute herpes simplex, Varicella, acute purulent infections**.**

**Dosage forms:** Ear drop, 0.977g+1million IU+ 0.5g

**Alternatives**

**Chloramphenicol**, 2–3 drops 2 to 4 times daily.

**Dosage forms:** Solution (Ear Drop), 1%, 2% and 5%

*OR*

**Gentamicin**, 1 – 2 drops 3 to 4 times daily

**In severe cases:**

**First line**

**Amoxicillin**

children; 50 - 100mg/kg P.O., BID for ten days

aduts; 500 mg P.O., TID for 7-10 days

**Alternatives**

**Amoxicillin/Clavulanate**,

children; 156mg/5ml PO TID 7 – 10 days or 312mg/5ml P.O., TID 7 to 10 days

adults; 375mg P.O., TID or 625mg P.O., BID for ten days

*OR*

**Ciprofloxacin,** 500mg PO BID for 10 days

| | |
|---|---|
| **ADRs:** | Diarrhoea, abdominal pain, headache restlessness and skin rash |
| **C/Is:** | Hyposensitivity to fluoroquinolones or the quinolone group of antibacterial agents. |
| **Dosage Forms:** | Tablets: 250mg, 500mg, 750mg |

### 14. Herpes Zoster Oticus

Herpes zoster, or Ramsay Hunt syndrome, is the third most frequent cause of facial paralysis. The disease occurs particularly in adults between 20 and 30, and 50 and 70 years of age. The disease is characterised by multiple herpetic vesicles arranged in groups on the auricle, the external auditory meatus and occasionally the tympanic membrane. In severe cases disorders of hearing and balance and facial paralysis may occur.

**Clinical Features**

- Herpetic vesicles are found mostly around the auricle, in the external meatus and in the concha
- Usually starts with acute and severe pain
- Sensory neural hearing loss
- Tinnitus
- Vertigo
- Herpatic palsy is usually complete

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Relieve pain and symptoms
- Prevent complications

**Non Pharmacologic**

None

**Pharmacologic**

**Acyclovir**, 800mg. P.O., 5 times a day for 7 – 10 days or 5mg/kg body weight IV every 8 hours for 7 days.

**ADRs:** Rashes, gastro intestinal disturbances, rises in bilirubin and liver related enzymes,increase in blood urea and creatinen, decrease in heamatological indices, headache and fatigue.

**C/Is:** Current administration of steroids.

**Dosage forms:** Tablet, 200mg, 400mg; Powder for injection, 250mg, and 500mg

**N.B.** Broad spectrum antibiotics (Amoxicillin Cefixime, Amoxicillin/Clavulnate, Julmentin, etc) might be needed to avoid secondary infections.

## 15. Temporal Bone Fracture

Caused by the effect of external violence. The course of the fracture may run either along the pyramidal axis (a longitudinal fracture) extending into the middle ear, or across the pyramidal axis (transversal fracture) extending into the body labyrinth and internal auditory meatus.

**Clinical Features**

Depends on the type of fracture.

Longitudinal fracture:

The tympanic membrane are frequently torn with bleeding.

- Conductive deafness.
- Facial nerve injuries are uncommon and when they occur are usually delayed in onset.

Transverse fractures:

Haemotympanum but no bleeding from the ear.

- Severe or complete sensorineural deafness on the affected side
- Very severe rotatory vertigo with nausea and vomiting.
- Nystagmus is usally present.
- Facial nerve injuries occurs in about 50% and the onset is usually immediate.

**Investigations**

- Plain Radiograph
- CT
- MRI

**Treatment**

**Objectives**

- Avoid the introduction of infection into the middle ear
- Avoid the danger of cerebrospinal fluid leak

**Non pharmacologic**

- Regular monitoring of vital signs and neurological state

**Pharmacologic**

**First line**

**Ampicillin**,

children; 200 mg/kg/day IV every 6 hours for 7-10 day

adults; 500-1 gm IV QID 7-10 days

**Alternatives**

**Benzyl Penicillin**, 3-4 mls. IV Q 3hrs for 10 – 15 days.

**ADRs:** Hyperseneitivity reactions including urticaria, fever joint pains, rashes, angio-edema, anaphylaxis, parasthesia with prolonged use, diarrhoea and antibiotic associated colitis.

**C/Is:** Hypersensitivity to penicillin and cephalosporins, serious or fatal anaphylactic

*PLUS*

**Gentamicin**,

neonates under age 1 week; 2.5mg/kg I.V. every 12hrs

infanats; 2.5mg/kg I.M. or I.V. infusion every hour

children; 2.5mg/kg I.M.or I.V.q 8hrs for children.

adults; 3-4mg/kg I.M.or I.V. daily in divided doses every 8hrs

**ADRs:** renal damage, ear damage, neural damage

**C/Is:** **i**n patients with known hypersensitivity or any other aminoglycoside. Gentamicin should be used cautiously in patients with decreased renal function.

**P/Cs:** potantiate neuromuscular blockade produced by general anesthetics.

**Dosage forms:** Injection: 40mg/ml, 40mg/2ml

*OR*

**Ceftriaxone**, 100mg/kg IV, in divided doses every 12 hours.

**N.B.** Danger of Otogenic Meningitis prophylactic antibiotics in high doses should be given.

**16. Nose And Nasal Sinuses**

**17. Acute Rhinitis**

The symptoms are not uniform. The general symptoms including chills and feeling of cold alternating with a feeling of heat, headache, fatigue, loss of appetite, possibly sub-febrile or high temperature.

**Clinical features**

- Low to high temperature in chidren
- Itching, burning and feeling of dryness in the nose and throat.
- The nasal mucosa is usually pale and dry later with watery secretions and obstruction.
- Temporary loss of smell
- On rhinoscopy the nasal mucosa is deep red in color, swollen and secretes profusely.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Relieve symptoms
- Prevent secondary bacterial infections

**Non pharmacologic**

- Bed rest
- Steam inhalation

**Pharmacologic**

**First line**

**Chlorpheniramine**,

children; 2mg P.O., 2-3 times daily

adults; 4mg P.O., TID

**Alternative**

**Cetrizine hydrochloride**,

children below 12years; 5-10mg P.O., daily

children above 12 years and adults; 10mg P.O., daily

*PLUS*

**Xylometazoline**,

infants and small children up to 6 years; 1-2 drops of 0.5% solution a day in each nostril

children over 6 years and adults; 2-3 drops of 1% solution 3-4 times a day

**18. Acute Rhino Sinusitis**

This usually arises as a complication of viral rhinitis but it is possible that the disease begins as a viral sinusitis. The most frequently occuring micro-organisms are Haemopilus inffunezae, the pneumococcus and the stretococcus. Dental origin can be caused by extension of a periapical inflammation or acsess.

**Clinical Features**

- Pains in the face and the head.
- Feeling of pressure in the skull or a lancinating, boring, pulsating pain especially in the anterior part of the skull.
- Sensitivity to pressure or tapping over the affected sinus is common

**Investigations**

- Anterior and posterior rhinoscopy

- Nasoendoscopy
- Radiography, possibly including acontrastmedium
- CT scan
- Puncture and irrigation
- Sinoscopy by Beck's trephination
- Bactriologic examinationof the secretion

**Treatment**

**Objectives**

- Relieve symptoms
- Clear the infection

**Non pharmacologic**

- Bed rest
- Hot bath
- Apply heat or microwave (infrared light) locally
- Apply cold if heat is not tolerated

**Pharmacologic**

**First line**

**Amoxicillin**

children; 50 - 100mg/kg P.O., BID for ten days

adults; 500 mg P.O., TID for 7-10 days

**Alternatives**

**Amoxicillin – Clavulanate**,

children; 156mg /5ml or 312mg/5ml P.O., TID every 8 hrs.

adults; 375mg P.O., TID for 10 days, or 625mg P.O., BID for ten days or 1gm P.O., BID for 7 days (depending on the severity).

*OR*

**Azithromycin**,

children; 200mg/5ml P.O., daily for 3 days

adults; 500mg P.O., daily for 3 days

*PLUS*

**Xylometazoline hydrochloride** 0. 05% or 0. 1%, 2 drops BID daily

*PLUS*

**Loratadine**,

children 2-6 years; 1 teaspoonful once daily

children over 6 years; 2 teaspoonfuls P.O., daily

adults; 10mg P.O., daily for 7 to 10 days

### 19. Allergic Rhinitis

The most common form is hay fever but other allergens may be responsible. The shock organ is usually the nasal mucosa but it may also be the conjunctiva or other mucous membranes. The disease is often hereditary.

**Clinical features**

- Itching in the nose, nasal obstruction, sneezing attacks, A clear watery nasal discharge
- Feeling of fullness and irritation of the entire head
- Conjunctivitis
- Temporary fever
- Loss of appetite

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Give temporal relief

**Non pharmacologic**

- Avoid exposure to which the patient is hypersensitive

**Pharmacologic**

**First line**

**Xylometazoline**,

adults; 1% 2 to 3 drops 2-3 times into each nostril daily

infants and small children; 0.5% 1 to 2 drops 1 – 2 times a day into each nostril

*PLUS*

**Cetrizine**,

children below 12 years; 5 - 10 mg P.O., daily

children above 12 years and adults; 10mg tab P.O., daily

*OR*

**Loratadine**, one tablet (10mg) once daily Syrup: two teaspoonful (10mg) once daily.

body weight <30kg; 5ml [5mg], (one teaspoonful), once daily.

body weight >30kg; 10ml [ 10mg ], (two teaspoonfuls), once daily.

*OR*

**Dexchlorpheniramine maleate,** 6mg PO BID Syrup for adults and children12 years or older: one-half teaspoonful 3-4 times a day. For children 6-12 years of age: one-quarter teaspoonful 3 or 4 times a day for children 2-6 years of age

**ADRs**: fatigue

**Dosage forms**: tablet, 2mg, 4mg, 6mg; Syrup, 2mg/5ml

**Alternative**

**Beclomethasone**,

children age 6-12 years; One to 2 Inhalation TID or QID maximum of 10 inhalation

adults; 2 - 4 inhalation TID or QID for adults

**ADRs:** Flushing, skin rash, hoarseness, irritation of the tongue or throat, impaired sense of taste and bloody mucus

**C/Is:** Patients with acute status asthmatics and in patients who are hypersensitive to any component of the preparation.

**Dosage forms**: Oral inhalation (Aerosol), 50mcg/dose, and 100mcg/dose

**20. Atrophic Rhinitis And Ozena**

Atrophic rhinitis (Ozena) mostly accompanied by a foul smell from the nose. The disease occurs in both sexes but more so in young girls. The term ozena is used when the nasal

atrophyis is accompanied by a marked formation of crysts and foetor. The aetiology of ozeana is not known.

**Clinical features**

- Nasal cavity usually is filled completely by greenish-yellow or brownish-black crusts.
- The nasal cavity is very wide.
- The mucosa is atrophic and dry.
- Patient has ansomia
- Dryness and dry, thick crust involving the entire pharynx, larynx and trachea.
- The nose contains gluey, dry greenish-yellow secretions and crust. The nasal cavity is wide and the crusts give off a smell in ozena.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objective**

- Keep the nose free of crusts and foetor

**Non pharmacologic**

- Clean the nasal cavity by douching several times a day with diluted salt water**.**
- Apply oily nasal drops emulsions, or ointment and possibly vitamin A supplements.
- Apply steam inhalation with saline solution.

**Pharmacologic**

None

### 21. Chronic Rhinosinusitis

Three or more episodes in 6 Months or 4 or more episodes in one year

**Clinical features**

- Pressure symptoms or dull pain over the face in the infra or supra orbital area

- Nasal obstruction and purulent nasal discharge

**Investigations**

- X-ray of the paranasal sinuses

**Treatment**

**Non pharmacologic**

- Repeated lavage of the sinus with Normal saline
- Surgery if no resolution after repeated lavage

**Pharmacologic**

**First line**

**Amoxicillin** 500mg P.O., TID for 10 days

**ADRs:** diarrhoea, pseudomembranous colitis, acute interstitial nephritis, anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia.

**C/Is:** in patients with known hypersensitivity to any other penicillin or cephalosporins.

**Dosage forms:** Capsules: 250mg, 500mg. Suspension: 125mg/5ml, 250mg/5ml 50mg/5ml. Tablets (chewable): 125mg, 250mg

**Alternatives**

**Amoxicillin – Clavulanate**,

children; 156mg /5ml or 312mg/5ml P.O., TID Q 8 hrs.

adults; 375mg P.O., TID for 10 days, or 625mg P.O., BID for ten days or 1gm P.O., BID for 7 days (depending on the severity)

*OR*

**Cefixime**,

children; 8mg/kg suspension as a single dose or 4mg/kg BID P.O.

children weight more than 50kg or above 12 years, and adults; 200mg PO BID for 6 days

**ADRs:** diarrhoea, abdominal pain, skin rashes, urticaria transient elevation in liver enzymes

**C/I:** patients with known allergy to cephalosporin

**Dosage form:** 200mg Cefixime (as trihydrate). Suspension 100mg/5ml cefixime (as trihydrate)

*OR*

**Azithromycin**,

children; 200mg/5ml P.O., daily for 3 days

adults; 500mg P.O., daily for 3 days

**N.B.** Operation is advised if the disease is not resolved after repeated lavages.

## 22. Epistaxis

Epistaxis occurs in 60% of persons worldwide and approximately 6% of those seek medical treatment. Epistaxis may be a life-threatening disease which is extremely difficult to treat, whose causes may not be remediable, and which may lead to death. More than 90% of episodes of epistaxis occur along the anterior nasal septum at a site called Kiesselbach's area. Its vascular supply moves from the external and internal caratoid artery.

**Clinical features**

- Bleeding from one or both nostrils.
- The heammorrhage may occasionally be severe and may lead to anaemia and shock.

**Investigations**

- CBC
- Localize the source of bleeding.
- Coagulation profile when systemic cause is suspected.

**Treatment**

**Objectives**

- Stop epistaxis
- Replace blood if bleeding is severe
- Prevent recurrence of epistaxis

**Non pharmacologic**

Most anterior nose-bleeds are self-limited and do not require medical treatment.

- Pinching the anterior aspect of the nose for 15 minutes.
- Relax the head; position can be either forward or backward

- Avoid swallowing or aspirating any blood that may drain into the pharynx
- Posterior packing for the posterior nasal bleeding;
- Apply inflatable balloons or foley catheter or cotton gauze introduced through the mouth and then retracted up into the nasopharynx (but care must be taken to avoid trauma to the ala).

**Pharmacologic**

**First line**

**Topical vasoconstrictor; Oxymetazoline**, spray 0.05% adults and children greater than 6 years of age; 2-3 drops every 12 hours usually in the morning or evening.

*OR*

Chemical cautery;

**Silver Nitrate + Potassium Nitrate**, apply to mucous membranes and other moist skin surfaces only on area to be treated 2-3 times/week for 2-3 weeks

**ADRs:** burning and skin irritation, staining of the skin, hyponatremia, methaemoglobinemia.

**C/Is:** broken skin, cuts, or wounds, eyes

**P/Cs:** prolonged use may result in skin discoloration.

**Dosage forms:** Toughened, 95% + 5%

**Alternatives**

Anterior nasal packing; gauze coated with petroleum jelly or absorbable materials like Gelfoam and oxidized cellulose.

*PLUS*

Topical antibiotics; **Tetracycline** 3% ointment. Apply on the affected site QD or BID

*OR*

**Chloramphenicol** 1%. Solution, apply 2 – 3 drops into the ear 2 – 3 times daily

**ADRs:** high incidence of sensitivity reactions to vehicle, optic and peripheral neuritis

**D/Is:** alfentanil, chlorpropamide, phenytoin, tolbutamide, rifampicin, warfarin, vitamin $B_{12,}$ folic acid

**C/Is:** hypersensitive to the medicine or any ingredients in the formulations; perforated tympanic membrane, breast feeding

**P/Cs:** over growth with non-susceptible organisms, Avoid prolonged use

**Dosage forms:** 1%, 2%, 5% ear drop

**If additional infection is suspected Oral antimicrobials are added**

**First line**

**Amoxicillin**

children; 125mg/5ml – 250mg/5ml P.O., TID 7 – 10 days

adults; 250 – 500mg. caps P.O., TID 7 – 10 days

**Alternatives**

**Ciprofloxacillin**, 500mg P.O., BID for 7 – 10 days.

**Amoxicillin/Clavulanate**,

children;156mg/5ml P.O., TID or 312mg/5ml P.O. TID 7-10 days

adults; 375mg P.O., TID for 7-10 days or 625mg P.O., BID for 7-10 days

**N.B.** When conservative measures fail to stop the bleeding, embolization or surgical ligation of the offending vessels is needed.

**23. Nasal Furuncle**

Caused by broken skin in the nasal vesibule from nose picking or blowing, allowing entry of Staphylococcal bacteria. The disease is always limited to the skin and never affects the mucsa. The frununcle coalesces to abcess which may be drained. Manuplation and incision should be avoided until the furuncle points because it is in the danger triangle of the face.

**Clinical features**

- Pain
- Pus and central necrotic cove
- Fever

Sensitivity to pressure followed by reddening and swelling of the tip of the nasal cavity

**Investigations**

- CBC
- Pus culture and sensitivity

**Treatment**

**Objectives**

- Relieve pain
- Treat infection

**Non pharmacologic**

- Drain the pus
- Apply ice bag

**Pharmaclogic**

Applied to the nasal vestibule:

**Tetracycline hydrochloride**, 2.2mg/ml solution, 3% Ointment

*OR*

**Hydrocortisone**, Cream or ointment 0.25%, 0.5%, 1%, 2.5%,

*PLUS*

**Cloxacillin sodium**,

adults; 500mg P.O., QID for ten days

children; 50-100mg /kg P.O., QID for ten days

*OR*

**Amoxicillin-Clavulanate**,

children; 228mg/5ml mg or 457mg/5ml (suspension) P.O., BID

adults; 625mg -1gm P.O., BID for ten days

**24. Foreign Bodies In The Nose**

These are usually found in children in the 2 – 3 year age group. Usually the insertion is done while playing by themselves, when left alone.

**Clinical features**

- These include unilateral nasal obstruction
- Worsening chronic purulent rhinitis or sinusitis
- Unilateral fetid secretion and formation of rhinolith due to deposition of calcium around the foreign body.

**Investigations**

- Anterior rhinoscopy
- Radiology

**Treatment**

**Objectives**

- Prevent danger of spreading the infection and of complications.
- Relieve pain

**Non pharmacologic**

Remove the foreign body with instrument under a short general anesthetic, since long-standing foreign bodies are often firmly fixed and provoke brisk bleeding when they are removed.

**Pharmacologic**

**If there is sign of infection**

**Amoxicillin-Clavulanate** 625mg-1gm PO BID for ten days for adults. 312mg/5ml PO TID for 7 to 10 days 228mg/5ml mg or 457mg/5ml (suspension). PO BID for 7 to 10 days for chidren.

**25. Mouth And Pharynx**

**26. Abcess Of The Floor Of The Mouth**

The infection may arise primarily in the subliguealor submandibular glands on the floor of the mouth. The infection advances in the loose musculature of the tongue and in the numerous connective tissue spaces. Penetration of small foreign bodies such as fishbones, bone splinters, kernels of corn, etc. are also possible causes.

**Clinical features**

- Swelling and limitation of tongue movement
- Severe diffculty in swallowing
- Difficulty in articulation progressing to complete loss of speech.
- Complete inability to eat.
- Protrusion and induration of the floor of the mouth with marked sesitivity of

pressure.

- Fever.
- Limitation of movement of the tempromandibular joint with trismus.

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Relieve pain
- Prevent disease progression

**Non pharmacologic**

- Apply ice bag
- Surgical drainage of abscess

**Pharmacologic**

Treatment depends on the condition of the patient.

**First line**

**Amoxicillin**

adults:500-1gm P.O., TID for at least 10 days

children: 125mg/5ml-250mg/5ml susp. P.O., TID for 7-10 days

**Alternative**

**Amoxicillin-Clavulanate**, 625mg-1gm P.O., BID for at least 10 days. 156mg/5ml or 312mg/5ml PO TID or 228mg/5ml or 457mg/5ml susp. P.O., BID for 7-10 days for children.

**Parentral**

**First line**

**Ampicillin**,

children; 200 mg/kg/day IV every 6 hours for 7-10 days

adults; 500mg-1 gm IV QID 7-10 days

**Alternatives**

**Crystaline penicillin**,

children; 250,000U/kg/24 hr, divided 8 doses IV for 7 – 10 days

adults; 3 to 4 million IU I. V. in 8 divided doses For 10 days

*OR*

**Gentamicin**,

children; 3-5mg /kg/24 hr IV TID for 10 to 15 days

adults; 80mg IV TID for 10 days

*OR*

**Ceftriaxone**, 1-2gm IV once daily or in equally divided doses BID. 50 to 75mg /kg IV in divided doses every 12 hrs.

**N.B.** The abcess should be aspirated and then opened widely. A tracheotomy is indicated for those with respiratory obstruction (in severe cases).

**27. Acute Tonsillitis**

Acute infection of the lymphoepithelial tissue of the faucial isthmus, the palatine tonsil is known as tonsillitis. The main cause are Beta-Streptococci, Staphylococci, Stretococcous Pneumoniae (Diplococcus pneumoniae) and Heamophilus.

**Clinical features**

- High temperature and possibly chills, espeically in chideren.
- Burning sensation of the throat
- Persistant pain in the oropharynx
- Pain on swallowing thatradiates to the ear.
- Opening the mouth is often difficult and painful.
- Headache and marked feeling of malaise.
- Swelling and tenderness of the regional lymph nodes.
- Both tonsils and the surrounding area are deep-red and swollen

**Investigations**

- CBC and ESR
- Culture from throat swab.

**Treatment**

**Objectives**

- Treat infection
- Relieve pain

**Non pharmacologic**

- Gargling with warm Normal saline solution

**Pharmacologic**

**First line**

**Amoxicillin** 250-500mg P.O., TID for 7 – 10 days. 125mg/5ml, 250mg/5ml P.O., TID for 7 – 10 days.

**Alternatives**

**Ampicillin,** 250mg to 500mg P.O., in divided doses QID. 50-100mg/kg P.O., TID for 7 – 10 days QID. 100 - 200mg/kg IV in divided doses TID

*OR*

**Amxoicillin – Clavulanate:** 375mg P.O., TID for ten days or 625mg P.O., BID for ten days 156mg/5ml P.O., TID for ten days or 312mg/5ml P.O., TID for ten days or 228mg/5ml P.O., BID or 457mg/5ml P.O., BID for ten days.

*PLUS*

**Paracetamol**, 500mg P.O., PRN.

**28. Peritonsillar Abscess**

This is a complication during and after tonsillitis where the inflammation spreads from the tonsillar parenchyma to the surrounding tissue and forms an abscess. Usually occurs in those with chronic tonsillitis who have been inadequately treated.

**Clinical features**

- Severe pain such that the patient often refuses to eat
- The head is held over to the diseased side, and rapid head movements are avoided.
- The patient has sialorrhea and oral fetor
- Swelling of the regional lymph nodes,

- Fever with high temperatures of 39°C to 40°C and the general condition deteriorates rapidly.
- Redness, and protrusion of the tonsil, the faucial arch, the palate and the uvula
- Marked tenderness of the tonsillar area

**Investigations**

- Diagnosis is clinical
- Culture of pus

**Treatment**

**Objectives**

- Relieve pain
- Prevent complications

**Non pharmacologic**

- Needle aspiration of pus
- Drainage of the abscess followed by tonsillectomy.

**N.B.** An incision should not be made until the abscess is ripe, i.e., that fluctuation can be shown or is proven.

**Pharmacologic**

**First line**

**Amoxicillin**,

children; 125mg/5ml, 250mg/5ml PO TID for 7 – 10 days

adults; 250-500mg PO TID for 7 – 10 days

**Alternatives**

**Ampicillin,** 250mg to 500mg PO in divided doses QID for adults. 100 – 200mg/kg IV in divided doses TID

*OR*

**Amxoicillin – Clavulanate**, 375mg P.O., TID for ten days or 625mg. P.O., BID for ten days. 156mg/5ml P.O., TID for ten days or 312mg/5ml P.O., TID for ten days.

*OR*

**Cefixime**, 200 mg P.O., BID for 6 days

**29. Larynx And Hypopharynx**

**30. Acute Epiglottits**

Epiglottitis, more appropriately termed supraglottitis, is an acute infectious process that is usually caused by Haemophilus influenzae type B. The disease is rarer than croup. It occurs especially in infants aged 2 to 4 years. There a slight male predominance. Onset is acute.

**Clinical features**

- Severe pain on swallowing
- Inspiratory stridor usually forces the patient to sit upright in bed.
- Speech is thick.
- Fever

**Investigations**

- CBC
- Blood culture.
- Laryngoscopy
- Lateral radiograph of the neck

**Treatment**

**Objectives**

- Relieve airway obstruction as soon as possible.
- Treat bacteremia

**Non pharmacologic**

- Admit all children suspected to have epiglottitis.
- Prepare to do tracheostomy as soon as it is indicated

**Pharmacologic**

**First line**

**Amoxicillin**

children; 125mg/kg P.O., TID or 250mg/kg P.O., TID

adults; 250 – 500mg P.O., TID for ten days

**Alternatives**

**Amoxicillin-Clavulanate potassium**,

children; 156mg/5ml or 312mg/5ml P.O., TID days

adults; 375mg P.O., TID or 625mg or 1gm P.O., BID for 10 days

*OR*

**Ceftriaxone**, 100mg/kg IV, in divided doses every 12 hours.

*OR*

**Ampicillin**,

children; 100mg/kg-200mg/kg IV QID for 7-10 days

adults; 500mg-1gm IV QID for 7-10 days

*PLUS*

**Hydrocortisone**,

children; 0.16 to 1mg/kg IM or IV daily BID

adults; 100 to 500mg IM or IV, then 50 to 100mg as indicated.

*OR*

**Prednisolone**,: 2 to 30mg IM or IV Q 12 hours.

**N.B.** In patients with respiratory obstruction, particlarly children, diagnostic procedures may lead to complete obstruction. Preparations for intubationor tracheotomy must therefore be made before investigation. The patient should be referred to a hospital if epiglottitis is suspected.

## 31. Acute Laryngitis

This is an inflammation strictly localized to the vocal cords, usually of viral origin. Acute laryngitis is usually due to ascending or descending infection from the other parts of the airway. In children there is a danger of airway obstruction.

**Clinical features**

- Hoarseness of the voice
- Aphonia
- Pain in the larynx and coughing attacks
- In chidren there is a danger of airway obstruction

**Investigations**

- Laryngoscopy shows red and swollen vocal cords lose their normal colour

**Treatment**

**Objective**

- Relieve airway obstruction

**Non pharmacologic:**

- Voice rest

**Pharmacologic**

**First line**

**Amoxicillin**

children; 125mg/5ml or 250mg/5ml 1 tsp. P.O., TID for ten days

adults; 250mg – 500mg PO TID for ten days

**Alternatives**

children; 50 - 100mg/kg PO QID or 100 - 200mg/kg IV into divided doses TID

adults; Ampicillin, 250 - 500mg P.O., in divided doses QID for ten days

*OR*

**Amxoicillin – Clavulanate**, 375mg P.O., TID for ten days or 625mg P.O., BID for ten days or 1gm P.O., BID for 7 days 156mg/5ml or 312mg/5ml 1 tsp. P.O., TID for ten days or 228mg/5ml or 458mg 1 tsp P.O., BID for ten days

*OR*

**Cefixime**, 200 mg P.O., BID for 6 days

*PLUS*

**Prednisolone**, 40-60mg P.O., daily based on severity, the dose is reduced by 5mg every 5 days

**32. Salivary Glands**

**33. Mumps (Epidemic Parotitis)**

Mumps is a contagious disease caused by a filterable virus. The parotid glands are the salivary glands most commonly involved with mumps, but the sublingual and submandibular glands may also be affected. In 75-80% of cases both glands are involved.

**Clinical features**

- Swelling of the involved gland.
- Redness and slight swelling of the duct opening.
- Displacement of the auricle.
- The secretions are not purulent.
- There is no fever

**Investigations**

- Diagnosis is clinical

**Treatment**

**Objectives**

- Relieve symptoms

**Non pharmacologic:**

- Massage the gland

**Pharmacologic**

**First line**

**Paracetamol**,

children; 30-40mg/kg/24 hr. divided into 4 – 6 doses

adults; 1000mg P.O., every 6 hrs PRN

**Alternatives**

**Tramadol**, 100 mg P.O., every 6 hrsPRN for adults.

**ADRs:** dependence, abdominal pain, anorexia, central nervous stimulation, vertigo, skin rashes, sweating and vomiting.

**C/Is:** Respiratory depression, in the presence of acute alcholism, head injury, during pregnancy and lactation

**Dosage forms:** Tablet: 100 mg.

**N.B.** Not recommended for chidren below 12 years of age

## 34. Acute And Non Chronic Nonobstructive Suppurative Sialadenitis

Acute bacterial infection of the salivary glands usually involves the paratoid glands. This condition is usually seen in deblitated patients. The usual causative organism is Staphylcoccus aureus.

**Clinical features**

- Pain and swelling of the involved gland
- Purulent secretions can be expressed from the orifice of the duct
- Fever

**Investigations**

- Sialography shows a tree in leaf appearance
- Tissue should be taken for histology in doubtful cases

**Treatment**

**Objective**

- Control pain
- Prevent recurring episodes

**Non pharmacologic**

- Bed rest
- Restricted jaw movement

**Pharmacologic**

**First line**

**Clindamycin**, 150 to 450mg P.O., QID or 300mg IM or IV QID or TID. In severe infections 20mg/kg/24hr. IM or IV into 4 doses.

**Alternatives**

**Cloxacillin**, 500mg P.O., QID for 7 – 10 days. 50 – 100mg /kg/24hrs. P.O., divided into 4 doses for 7 - 10 days.

*OR*

**Cephalexin**,

children; 6 to 12 mg/kg PO Q 6 hours. Maximum 25mg/kg Q 6 hours

adults; 50mg to 1gm QID P.O., 6 hours

*OR*

**Methicillin**, 4 to 12 g IM or IV daily divided into dosesq 4 to 6 hours for adults. 100 to 200mg/kg IM or IV daily divided into doses every 4 to 6 hours

**ADRs:** neuropathy, seizures, glossitis, stomatitis, diarrhoea, hemolytic anaemia, thrombocytopenia, neutopenia, veinirritation, thrombophlebitis

**C/Is:** in patients with known hypersensitivity to any other penicillin o cephalosporins

**Dosage forms:** Injection: 1g, 4g, 6g.

## CHAPTER XIX: GYNAECOLOGY AND OBSTETRICS

### 1. Hypertensive Disorders In Pregnancy

Hypertension is a common medical problem that complicates pregnancy. It is also one of the three major causes of maternal death. It may be manifested as chronic hypertension, chronic hypertension with superimposed pre-eclampsia, pregnancy induced hypertension, pre-eclampsia or eclampsia. The cause of this disease entity is not well defined.

**Clinical features**

- Increased BP≥ 140mmHg (systolic) and 90mmHg (diastolic) during pregnancy.
- The presence of other clinical signs and symptoms of hypertension in pregnancy depends on the severity of the disease.

**Investigations**

- The presence of significant proteinuria greater than 300mg/24hour urine specimen or, less accurately, more than 1+ protein (equivalent to approximately 100mg/dl) on dipstick sampling of random urine specimen.
- Proteinuria is usually late manifestation of pre-eclampsia that follows the hypertension and correlates with glomerular lesions in the kidneys. Proteinuria is usually variable and should be carefully interpreted because it can be influenced by factors like contamination of the urine specimen with vaginal secretions, blood, or bacteria; urine specific gravity, pH, exercise; and posture.

**Classes**

**I. Pregnancy induced hypertension (PIH)**

Pregnancy induced hypertension is defined as a rise in BP≥ 140/90 mmHg after the $20^{th}$ week of gestation measured twice at least six hours apart or a single measurement of diastolic BP>110mmHg, except in Gestational Trophblastic diseases (GTD) and multiple pregnancy when this can be diagnosed before the $20^{th}$ week of pregnancy. There are different types of PIH.

**A. Gestational hypertension:**

This is diagnosed when the systolic BP is raised to 140mmHg and the diastolic BP to 90mmHg or more after the 20$^{th}$ week of gestation without significant proteinuria. Mostly, this is used until a more specific diagnosis can be assigned. Gestational hypertension may represent pre-eclampsia prior to proteinuria or chronic hypertension previously unrecognized.

**B. Pre-eclampsia**

Pre-eclampsia is part of PIH which is defined as a BP$\geq$ 140/90mmHg in the presence of significant proteinuria of $\geq$ 300 mg/24 hours urine specimen or, less accurately, more than 1+ protein (equivalent to approximately 100mg/dl) on dipstick in at least two randomly collected urine specimen at least 6 hours apart after the 20$^{th}$ week of gestation. Pre-eclampsia may be categorized as mild or severe, primarily on the basis of degree of hypertension or proteinuria and involvement of other organ systems.

**1. Mild pre-eclampsia**

The mild form of pre-eclampsia is diagnosed when the Systolic and diastolic blood pressure is between 140-160 and 90-110mmHg respectively without signs of severity.

**2. Severe pre-eclampsia**

In the presence of any one of the following clinical manifestations, severe pre-eclampsia can be diagnosed:

- Diastolic BP $\geq$ 110 mmHg and the systolic $\geq$160mmHg measured twice at least six hours apart or a single measurement of $\geq$120mmHg
- Proteinuria $\geq$ 5gm/24 hours or $\geq$3+ in randomly collected urine
- Hyperbilirubinemia, Hemolytic anaemia, Thrombocytopenia (<100,000/µl), Elevated Liver Enzymes (HELLP syndrome)
- Disseminated intravascular coagulation (DIC)
- Headache, visual disturbance and right upper abdominal pain
- Oliguria (<400ml in 24hours or 30ml/hour)
- Intrauterine growth restriction (IUGR)
- Cardiac decompensation, Pulmonary edema, cyanosis

- Exaggerated Deep Tendon Reflexes (DTR)

### C. Eclampsia

Eclampsia is the occurrence of convulsions in woman who meets the diagnostic criteria for pre-eclampsia. There could also be atypical eclampsia. Any convulsion occurring during pregnancy is eclampsia unless proven otherwise.

## II. Chronic hypertension

This is a hypertension existing before pregnancy or diagnosed before the $20^{th}$ week of gestation, except in GTD and multiple pregnancy, or persists indefinitely after delivery. Women with mild hypertension may have normal BP during the mid-trimester and many of these women show greater decrease in their BP during pregnancy than normotensive women. However, in some pregnant women the BP may become severe and develop superimposed pre-eclampsia, which is defined as an exacerbation of the BP, i.e, an increment of the systolic BP by 30 mmHg and diastolic BP by 15mmHg over the baseline with development significant proteinuria.

**Prevention:**

Women with the following risk factors for pre-eclampsia can benefit from taking low dose aspirin, 75mg, oral, daily starting from 16 weeks of gestation onwards:

- Pre-eclampsia in the previous pregnancy
- Family history of pre-eclampsia (in mother or sister)
- Multiple pregnancy
- Chronic hypertension
- Renal disease
- Diabetes mellitus
- Anti-phospholipids syndromes or Systemic lupus erythematosis (SLE)
- Raised BMI

**Treatment**

**Mild pre-eclampsia**

Most patients are asymptomatic and can be managed conservatively. Such patients are not candidates for urgent delivery.

**Objectives**

- Control BP by administering potent anti-hypertensive medicines, to keep the diastolic BP below 100mmHg.
- Prolong pregnancy as much as possible
- Prevent convulsion
- Monitor maternal and foetal condition frequently for worsening of disease condition and plan treatment accordingly.
- Assure delivery of the fetus and placenta at the appropriate time, which is the definitive treatment for PIH.

**Non pharmacologic**

- Bed rest at home in the lateral decubitus position. Individuals rarely require admission unless they develop any sign and symptom of severe pre-eclampsia.
- Frequent evaluation of foetal well being by foetal movement recording, biophysical profile
- Maternal well being (BP measurement four times per day, assessment LFT, RFT, Hematocrit, proteinuria, visual disturbances, epigastric pain etc)
- Advise patient to immediately report whenever they develop symptoms of severity such as headache, epigastric pain, blurring of vision etc
- Plan termination of pregnancy at term. Most authorities recommend pregnancy to be terminated between 37-38 weeks of gestation.
- If the disease progresses to severe range, manage as severe case.

**Pharmacologic**

Anti-convulsant such as Magnesium sulphate, as well as anti-hypertensive medications, are rarely required for patients on conservative management. However, if the Systolic BP is >150mmHg or the diastolic BP is above 100mmHg, give,

**Methyldopa**, 250-500mg P.O., 8 to 12 hourly

**ADRs:** water and salt retention, and drowsiness, medicine fever, hepatitis.

**C/I:** active hepatic disease

**Dosage forms:** tablet, 250mg, and 500mg

**Alternative**

**Nifedipine**, 10-40mg P.O., 12hourly

*OR*

**Nifedipine,** slow release 30-60mg P.O., daily

**N.B.** Advise patient to immediately report whenever they develop severe symptoms such as headache, epigastric pain, blurring of vision etc

**Severe pre-eclampsia**

Delivery is the appropriate treatment for mothers with severe pre-eclampsia; otherwise it may pose significant risks to the mother and fetus.

**Objectives**

- The primary objective is**,** to forestall convulsions, prevent intracranial bleeding and other vital organ damage and deliver a healthy fetus.
- Lower the BP but should not be under 140/90mmHg
- Stabilize the mother and plan delivery
- Lower the BP to a mildly hypertensive level (diastolic BP between 90-100mmHg)

**Non pharmacologic**

- Meticulous measurement of input and output is important part of the management.
- All non-pharmacologic measures for mild pre-eclampsia mentioned above should be applied here.
- Delivery: The vaginal route of delivery is preferable as long as there are no contraindications.

**Pharmacologic**

- Pre-hydration without overloading the patient: N/S or Ringer lactate
- Control of hypertension: The ideal medicine for this clinical scenario is the one that reduces the BP in a controlled manner, avoiding precipitous reduction in BP that may compromise placental perfusion.

**First line**

**Hydralazine,** 5-10mg intravenous every 20 minutes whenever the diastolic BP≥ 110mmHg. As hydralazine has a duration of action of several hours, adequate control of severe hypertension is often achieved after one or two intravenous treatments.

**ADRs:** headache, weakness, palpitation, flushing, aggravation of angina, anxiety, restlessness, hyperreflexia.

**C/Is:** Porphyria, aortic stenosis, lupus erythematosis renal failure

**Dosage forms:** injection, 20m/ml in 1ml ampoule

**Alternative**

**Labetolol,** 20-50mg intravenously is a useful second line medicine for women whose hypertension is refractory to hydralazine.

**ADRs:** foetal and neonatal bradycardia

**P/C:** may cause sudden death

**Dosage forms:** Tablet, 50mg, 100mg, 200mg, 400mg, injection, 5mg/ml

*OR*

**Nifedipine**,10 mg sublingual whenever the diastolic BP ≥ 110mmHg.

## Prevention of convulsion

**First line**

**Magnesium sulphate**, A loading dose of 4gm as 20% solution IV over 10-15 minutes followed by 10gm as 50% IM injection divided on two sides of the buttock, followed by maintenance dose of 5gm every 4 hours as 50% concentration over 2minutes, 2gm IV as 50% solution over 2minutes if convulsion recurs. Reduce the maintenance dose by half if there are signs of renal derangement during labour and for the first 24 hours postpartum.

**ADRs:** Colic, abdominal pain

**C/Is:** Insignificant

**Dosage forms:** Injection, 10%, 20%, 50% in 20ml

**Toxic S/S:** Decreased respiratory rate, heart rate, oliguria, depressed deep tendon reflexes (DTR)

**Management of Magnesium toxicity:** If DTRs are depressed discontinue $MgS0_4$ and monitor the patient closely.

**Treatment:**

**Calcium gluconate** (if respiratory rate below 12/min), 1 gm as 10% in 10 ml ampoule IV over 2minutes.

**ADRs:** Bradycardia, cardiac arrest, extra-vascular leakage may cause local necrosis.

**Dosage forms:** syrup, 4mg/15ml, injection, 10% solution, and 10ml

**Alternative**

**Diazepam,** 30 IU/1000ml of D/W or D/S 20 drops /minutes and increase the drops as needed depending on the patients sedation status.

**ADRs:** Drowsiness, fatigue, hypotension, paradoxical excitement

**C/I**: Acute pulmonary insufficiency

**Dosage forms:** Injection, 10mg/ml in 2ml ampoule, Syrup, 2mg/5ml, Tablet, 2mg, 5mg, 10mg

**N.B.** Continuous infusion is unnecessary because the half life of the medicine is 18 hours. When the maternal dose exceeds 30mg neonatal side-effects become prominent. These include low Apgar score, respiratory depression, poor feeding and hypothermia.

**Treatment of eclampsia**

**Objectives**

- Prevent maternal injury
- Control convulsion: Control the acute fit and prevent further recurrence
- Control extreme hypertension
- Expedite delivery
- Prevent patient from falling

**Non pharmacologic**

- Turn patient on her side to minimize aspiration
- Apply mouth gag to prevent tongue injury
- Establish airway and administer adequate oxygen
- Catheterization

**Pharmacologic**

The same as for severe pre-eclampsia (see above). In addition broad spectrum antibiotics should be given to prevent aspiration pneumonitis.

**N.B.** Do not give furosamide as part of the treatment for hypertension unless there is pulmonary edema.
Do not give ACE-inhibitors anti-hypertensives, such as captopril, as they may damage the developing fetus.

**Post-partum management:** The first 48 hour postpartum period is critical as one in three fits can occur during this period. No management should be altered during this period.

- Check BP and urine protein frequently
- Discontinue anti-convulsants within 48 hours
- Follow the mother for 6 weeks

## 2. Hyperemesis Gravidarum

Nausea and vomiting are common complaints in the first trimester of pregnancy affecting about 50% of pregnant mothers, and is considered by many as diagnosis of pregnancy. The symptoms are severe in multiple gestations and gestational trophoblastic neoplasm. Protracted vomiting associated with dehydration, starvation, weight loss, electrolyte disturbances, acidosis and ketonuria is known as **hyperemesis gravidarum.** The cause is not exactly known. If not treated appropriately, protracted vomiting may cause Mallory-Weiss oesophageal tear, neulogical dysfunction specifically Wernicke's encephalopathy due to vitamin $B_1$ deficiency, Korsakoff's psychosis and central pontine myelinolysis, retinal haemorrhage and Mendelson's syndrome.

**Clinical features**

- Excessive vomiting, loss of appetite, sign of dehydration, low BP, increase pulse rate, weight loss
- In severe cases acidotic pattern of breathing (deep and shallow) may ensue.
- In addition the clinician should look for other medical and surgical causes like hyperthyroidism, food poisoning, diabetes, appendicitis, etc.

**Investigations**

- Ketonuria, Elevated AST and SGOT
- Screen the patient for UTI and other medical causes
- Ultrasound examination to look for GTD, Multiple gestation

**Treatment**

**Objectives**

- Adequate fluid, electrolyte and calorie replacement
- Arrest the vomiting with potent anti-emetics
- Manage hypovolemic shock if present
- Identify obstetric conditions that are associated with hyperemesis garvidarum
- Rule out other medical or surgical causes, e.g., UTI, malaria, appendicitis etc

## Non pharmacologic

- For uncomplicated nausea and vomiting of pregnancy, give reassurance.
- Advice on small, dry, high calorie frequent feeding
- Avoid fatty and spicy foods
- Emotional support
- Remove stressful home environments
- Withdraw oral nutrition and fluid for 24-48 hours

**Pharmacologic**

Majority of Hyperemesis gravidarum cases requires admission for inpatient care**.** Few mild cases can be treated as outpatient.

- Re-hydrate with N/S, Ringers lactate, D/W, D/S eight hourly
- Calorie replacement: Add 40% Glucose 2 vials (40 ml) in each bag.
- Add Vit. B complex 2 ampoules in each bag

**Control of vomiting:**

**First line**

**Chlorpromazine**, 12.5-25 mg I.M. BID until vomiting is controlled and then P.O.

**ADRs:** Bone marrow suppression, drowsiness, apathy, alteration in liver function, cutaneous reactions, occasionally tardive dyskinesia.

**C/Is:** Bone marrow depression, coma caused by CNS depressants.

**Dosage forms:** Tablet, 25mg, 50mg, 100mg; drop, 25mg/ml in 10ml bottle, 40mg/ml in 10ml and 30ml bottles; syrup, 25mg/5ml; injection, 25mg/ml in 1ml and 2ml ampoules, 50mg/ml in 2ml ampoule.

**Alternatives**

**Promethazine**, 25-50 mg IM/IV BID, followed by 25 mg P.O., BID. Maximum daily dose, 100mg

**ADRs:** Drowsiness, headache, blurring of vision, GI disturbance

**P/C:** Close monitoring of the patient is required during the first few days of therapy.

**Dosage forms:** Elixir, 5mg/5ml; injection, 25mg/ml 1ml and 2ml ampoules; Suppository, 25mg, 50mg; tablet, 10mg, 25mg, Tablet, 10mg, 25mg,

*OR*

**Metoclopromide,** 5-10 mg IV/IM BID or TID.

**ADRs:** Drowsiness, fatigue, dizziness, weakness

**C/Is:** Epilepsy, pheochromocytoma, and mechanical bowel obstruction, concomitant administration of atropine like medicines.

**S/P:** Concomitant administration of phenothiazines.

**Dosage forms:** Tablet, 10mg; syrup, 5mg/5ml; injection, 5mg/ml in 2ml ampoule; drop, 0.2mg/drop**.**

*OR*

**Pyridoxine hydrochloride**, oral, 25mg/day, 8 hourly

**ADRs:** Rare

**Dosage forms:** Injection, 50mg/ml in 2ml ampoule. 150mg/ml; Tablet, 5mg, 10mg, 100mg, 300mg

In severe and refractory cases:

**Dexamethasone**, IM/IV, 4-8mg daily

*PLUS*

**Ondansetron**, IV 4-8mg over 5minutes daily

**N.B.** If these fail to control the vomiting, pregnancy may be terminated.

### 3. Pain During Labour And Delivery

When giving analgesics and anesthetics to pregnant mothers, the safety of the mother and fetus should be of constant concern to the health care provider. Virtually all analgesics and anesthetics administered during pregnancy cross the placental barrier, though to different extent; thus, a balance must be sought between pain relief for the mother and safety of the fetus.

**Treatment**

**Objectives**

- Alleviate pain without affecting maternal and foetal condition

**Non pharmacologic**

- Hypnosis, attention focusing and distraction
- Maternal movement and change of position: when the mother moves she alters the relationships between gravity, uterine contractions, the fetus and her pelvis.
- Counter pressure: Steady and strong force applied to a spot on the lower back during contraction or pressure on the side of each hip.
- Hot compresses applied to the lower abdomen
- Immersion in warm water during labour but not birth

**Pharmacologic**

**Analgesics**

**I. Opioids**

**First line**

**Pethidine**, 50-100mg IV or IM QID to TID.

**ADRs:** Maternal: orthostatic hypotension, nausea, vomiting, dizziness, and delayed stomach emptying, respiratory depression.
Foetal: respiratory depression, low apgar score. Its half life in the newborn is approximately 13 hours.

**Dosage forms:** Tablet, 50mg; injection, 50mg/ml in 1 and 2 ml ampoule

**Alternatives**

**Morphine**, 10-15mg IM, TID

**ADRs:** Respiratory depression, withdrawal syndrome

**Dosage forms:** Capsule (m/r), 20mg, 50mg, 100mg, 200mg; Tablet, 5mg, 10mg, 15mg, 20mg, 30mg; injection, 10mg/ml, 20mg/ml in 1ml ampoule

*OR*

**Pentazocine**, 30mg IM/IV

**ADRs:** tachycardia, rise in blood pressure

**Dosage forms:** Tablet, 50mg; injection. 30mg/ml in 1 ml ampoule

**II. Local Anaesthetics**

The complete relief of pain in obstetrics can be accomplished by blocking the sympathetic pathways of eleventh and twelfth thoracic nerves and the parasympathetic and sensory fibres of the sacral nerves.

**Epidural block:** is a more effective form of pain relief than alternative forms of analgesia.

**First line**

**Bupivacaine**, 3-5mg of 0.75% in 8.25% dextrose.

**ADRs:** cardiotoxicity in case of inadvertent IV administration.

**Dosage forms:** Injection, 0.25%, 0.5% in 10ml as ampoule

**Alternative**

**Lidocaine (Xylocaine)**, 1-2% concentration IM, 5-10ml

**ADRs:** foetal bradycardia, inadvertent IV administration of the local anaesthetics lead to cardiac arrest, hypotension, high spinal block with respiratory paralysis, headache, foetal bradycardia.

**Dosage forms:** Injection, 0.5%, 1%, 2%, 5%

### 4. Post-Partum Haemorrhage (Pph): Prevention And Management

Post-partum haemorrhage refers to bleeding of more than 500ml from the genital tract within the first 24 hours of normal delivery or any amount of blood loss that compromises the haemodynamic of the patient which is referred as primary. It usually occurs during or immediately after the third stage of labour. Secondary post-partum haemorrhage is defined as excessive vaginal bleeding occurring from twenty-four hours to six weeks after delivery. Postpartum haemorrhage becomes life threatening if the mother is already anaemic.

**Causes**

- Retained product of conceptus in the uterine cavity
- Uterine atony
- Prolonged labour
- Infection within the uterine cavity (endo-myometritis)
- Genital tract trauma
- Clotting disorders

**Risk factors for PPH**

- Suspected or proven abruptio placentae
- Known placenta previa
- Multiple pregnancy
- Pre-eclampsia/Gestational hypertension
- Previous history of PPH
- Anaemia
- Big baby

**Clinical features**

- Excessive or prolonged vaginal bleeding
- Lower abdominal pain, supra-pubic tenderness
- Bleeding from the genital tract
- Conjunctival pallor
- Rapid pulse rate
- BP may be low or normal

**Investigations**

- CBC

- Coagulation profile (PT, PTT, INR)
- Liver function test
- Renal function test
- Blood grouping and cross-matching
- Ultrasound scan

**Prevention:**

Every woman is considered a potential risk for PPH, hence active management of the third stage of labour must be applied, i.e., from the time of delivery of the fetus until the delivery of the placenta. Active management of third stage of labour, is a series of procedures applied during the third stage to speed up the delivery of the placenta, increase uterine contractions to prevent PPH by averting uterine atony. It has the following components:

1. To give oxytocin within one minute after the birth of the baby without waiting for sign of placental separation. OR Ergometrine, IM, 0.2mg, provided the woman is not hypertensive
2. Clamping and cutting the cord as soon as the baby is delivered
3. Apply Controlled Cord Traction (CCT) when the uterus becomes globular and firm and the cord lengthens
4. Continuous uterine massage, repeated every 15 minutes for 2 hours

Despite these measures, if bleeding continues, management of PPH should be started immediately.

## 5. Obstetric Care And Obstetric Disorders

**Treatment**

**1. Primary PPH**

**Objectives**

- Identify the causes
- Arrest bleeding as quickly as possible

- Resuscitate patient

**Non-pharmacologic**

The following management options should be applied step by step:

- Continuous rubbing of the uterus
- Ensure the urinary bladder is empty
- Call for help
- If the placenta cannot be expelled in this fashion within 30 minutes, do manual removal, preferably under anaesthesia.
- If bleeding continues or is heavy which lead to derangement of the vital sign; start blood transfusion, a minimum of 2 units.
- If the placenta has been delivered and is incomplete, explore the uterus under general anesthesia
- If the placenta is complete and the uterus is well contracted: examine the patient with adequate analgesia and/or anaesthesia, any lacerations in the cervix or vagina, must be sutured using through-and-through sutures. If the tear extends into the uterine body, it would be difficult to suture it from below and laparotomy may be required for effective suturing.
- For ruptured uterus, repair or hysterectomy should be done
- Avoid dextrans; they interfere with blood grouping and cross matching as well as with coagulation of blood
- If bleeding continues despite uterine rubbing, employ interventions such as manual compression of the uterus and compression of the abdominal aorta, use condom tamponade or uterine packing
- If bleeding continues despite the above mentioned measures: Bilateral internal artery ligation or B-Lnych procedures can be applied.

**N.B.** If all the above measures fail, resort to hysterectomy SOONER rather than LATER, especially in cases of placenta accreta or uterine rupture.

**Pharmacologic**

**First line**

**Oxytocin**, IM, 10 units stat.

**Alternative**

**Misoprostol**, oral/sublingual, or rectal 600-800micrograms,

Subsequently, maintain uterine contractions by massaging the fundus and infusing **Oxytocin**, IV, 10units in 500 ml 5% Glucose in sodium chloride 0.9%.

Anaesthesia for manual removal of placenta **Pethidine** IV, 100mg and **Diazepam** IV, 10 mg OR **Ketamine**, IM/IV bolus or infusion, 6-10 mg/kg

Set up IV infusion of Sodium Chloride 0.9% to run in fast: First 1000 ml rapidly in 15-20 minutes. Give at least 2000 ml in first hour. Aim to replace 2-3x the volume of estimated blood loss.

If condition stabilizes then adjust rate to 1000 ml /6 hourly

*OR*

**Oxytocin**, infusion, 20 mg in 1L of Normal saline

*OR*

**Ergometrine**, 0.25mg 8 P.O., 8hourly for 3 days

**2. Secondary PPH**

**Objectives**

- Identify the cause and treat appropriately
- Prevent overwhelming infection

**Non parmacologic**

- Resuscitate the patient
- Explore the uterus for retained product of conceptus

**Pharmacologic**

Use of the uterotonic agents is similar as to primary PPH

**Antibiotics**

**Amoxicillin-Clavulonic acid**, IV, 1gm, 12hourly

*PLUS*

**Gentamicin**, IV/IM, 80mg, 8hourly

*PLUS*

**Metronidazole**, IV, 500mg, 8hourly

*OR*

**Clindamycin**, IV, 450mg, 8-12hourly

When the clinical condition of the patient improves the IV antibiotics can be changed to PO.

## 6. Premature Rupture Of Membranes (PROM)

Premature rupture of membranes is rupture of the foetal membranes after the 28$^{th}$ week of gestation and before onset of labor. It includes preterm PROM (before the gestational age of 37 weeks) and term PROM (after the 37$^{th}$ week of gestation). The exact cause of PROM is not known. The incidence of PROM in preterm and term pregnancies is approximately 8% and 2%, respectively.

The amniotic fluid surrounding the fetus is important for the development of foetal lung and limb, heat exchange, and protection of the umbilical cord and infant from compression. In addition, the amniotic fluid has bacteriostatic chemicals. Whenever the membranes rupture, there will be leakage of fluid; hence these protective mechanisms may be compromised. In addition, if a dent is created a portal of entry will be established for bacteria to access the amniotic fluid from the vagina. Rupture of membranes often leads to onset of labor. Thirty-five percent of preterm neonates result from preterm PROM.

**Causes**

- preterm labour, trauma

**Clinical features**

- Gush of fluid per vaginum.
- Sterile speculum examination reveals leakage of clear or greenish fluid through the cervical opening.
- If immediate delivery is not planned, vaginal digital examination is not advisable.

**Investigations**

- Microscopic examination of the fluid reveals; Foetal products (squamous cells), fat, lanugo hair, fibronectin, AFP, prolactin) Ferning test (arborization)

- Nitrazine paper test which changes from yellow to dark blue. But care should be taken as blood, semen, alkaline urine and vaginal infections can give false positive results.
- Ultrasound examination: for assessing amniotic fluid, gestational age, foetal weight etc
- Vaginal swab culture and sensitivity for group B streptococcus

**Classes**

- **Pre-term PROM:** Rupture of membrane before 37$^{th}$ week of gestation
- **Term PROM:** Rupture of membrane after 37$^{th}$ week of gestation
- **Prolonged PROM:** Rupture of membranes for more than 12 hours

**Treatment**

Treatment depends on the gestational age, presence of infection, condition of the fetus and spontaneous healing of the membrane.

**Objectives**

- Prevent or early detect for sign of chorioamnionitis by clinical means (uterine tenderness, malodorous amniotic fluid, fever, maternal and foetal tachycardia) and laboratory (increase WBC, c-reactive protein)
- Prolong pregnancy until foetal maturity is assured, i.e., until 34 weeks and above.

**Pre-term PROM**

**1. Preterm PROM without chorioamnionitis**:

**Non Pharmacologic**

- Admit
- Bed rest and IV hydration
- Avoid vaginal examination,
- Avoid coitus
- Closely follow indications of intra-amniotic infection.

**Pharmacologic**

**First line**

**Ampicillin**, 2gm IV QID for 48 hours followed by 500mg P.O., QID or 7-10 days.

**ADRs:** Hypersensitivity reactions

**C/Is:** Known hypersensitivity reactions to penicillins or cephalosporins

**Dosage forms:** Drop, 100mg/ml; capsule, 250mg, 500 mg; injection, 250mg, 500mg, 1mg in vial; oral suspension, 125mg/ml, 250mg/ml.

**Alternative**

**Erythromycin**, 500mg IV QID for 48 hours followed by Erythromycin 500mg P.O., QID for 7-10 days.

**ADRs:** abdominal discomfort, diarrhoea (antibiotic–associated colitis), rash and other allergic reactions, cholestatic jaundice)

**C/Is:** Liver disease.

**Dosage forms:** Capsule, 250mg; tablet (stearate), 250mg, 500mg; oral suspension, 125mg/5 ml, 200mg /ml, 250mg /5ml; Injection, 50mg/ml in 2ml ampoule.

**2. Pre-term/Term PROM with chorioamnionitis**

- Admit to the labor ward and facilitate delivery as feasible
- Use ampicillin, chloramphenicol or gentamicin and terminate pregnancy.

**First line**

**Ampicillin**, 2gm IV QID for 48 hours followed by 500mg P.O., QID or 7-10 days.

**ADRs:** Hypersensitivity reactions

**C/Is:** Known hypersensitivity reactions to penicillins or cephalosporins

**Dosage forms*:*** Drops, 100mg/ml; capsule, 250mg, 500mg; injection, 250mg, 500mg, 1mg in vial; oral suspension, 125mg/ml, 250mg/ml.

**Alternatives**

**Chloramphenicol**, 500-1000mg intravenously QID

**ADRs:** Bone marrow depression, grey baby syndrome.

**C/Is:** Impaired hepatic function, bone marrow depression.

**D/Is:** Inhibits hepatic metabolism of several medicines like phenytoin and warfarin.

**Dosage forms:** Capsule, 250mg; injection 1g in vial; oral suspension, 125mg/5ml.

*OR*

**Gentamicin**, 80mg intravenously TID

**ADRs:** Ototoxicity, nephrotoxicity

**C/Is:** myastenia gravis

**Dosage forms:** Injection, 40mg/ml, 80mg/2ml

**3. Term PROM with no evidence of chorioamnionitis:**

- Admit to the labor ward and follow for evidence of infection
- If labour does not start spontaneously after the latency period, induce labour with oxytocin.

**4. Prolonged PROM:**

**Ampicillin**, 2gm I.V. QID during labor until she delivers, then 500 mg QID for 7 days.

**ADRs:** Hypersensitivity reactions

**C/Is:** If there is known history of hypersensitivity reactions to penicillins or cephalosporins

**Dosage forms:** drops, 100mg/ml; capsule, 250mg, 500mg; injection, 250mg, 500mg, 1mg in vial; oral suspension, 125mg/ml, 250mg/ml.

**7. Preterm Labour**

Preterm labor can be defined as regular uterine contractions that cause progressive dilatation of the cervix after 28$^{th}$ weeks of gestation and before 37 completed weeks. Approximately 8-10% of all pre-pregnancies end in preterm labour. Prematurity is one of the major causes of perinatal mortality and morbidity.

**Causes**

The etiology of preterm labor is multi-factorial, including;

- Multiple gestation

- Infection like UTI, febrile illness, abdominal surgery
- Uterine anomalies, APH (placenta previa and abruptio placentae)
- PROM
- Low socioeconomic status

**Clinical features**

- Pushing down sensation in the mother and if the clinician detects regular rhythmic uterine contraction of four in 20 minutes or eight in 60 minutes that leads to progressive cervical dilatation and effacement.
- Cervical dilatation greater than 1cm
- Cervical effacement of 80 percent or greater

**Investigations**

- CBC
- FBS
- Transvaginal ultrasound can show cervical dilatation and effacement
- Fibronectin in vaginal secrection

**Treatment**

When the diagnosis of preterm labour is made, the medical team should attempt to determine the cause and whether further continuation of the pregnancy will be beneficial or harmful to the mother and fetus. The choice of treatment depends on the answer to these questions and maturity of the fetus. Once foetal maturity is assured there is no benefit to conservative management and pregnancy should be terminated through the safest route. But if the fetus is premature, conservative management should be attempted.

**Objectives**

- Prevent or detect early intrauterine infection
- Prolonged pregnancy until foetal maturity is achieved
- Promote foetal lung maturity by administering corticosteroids
- Treat any underlying causes e.g. UTI, malaria, pyelonephritis etc

**Non pharmacologic**

- Bed rest
- Oral hydration, especially with nutritive calories, such as fruits juices, milk etc.
- Circlage

**Pharmacologic**

Use of a tocolytic medicines is not associated with a clear reduction in perinatal or neonatal mortality or neonatal morbidity. The main effect of tocolytic medicines when used for women in preterm labour is to reduce the numbers who deliver within 48 hours or within 7 days after the medicine administration. Data on long-term outcome are sparse. It remains plausible that, for selected women, such as those who require transfer for neonatal care or time to complete a course of corticosteroids, there may be benefits associated with tocolysis. However, the benefits have not been formally evaluated in randomised trials.

**N.B.** There is no benefit from maintenance tocolytic therapy.

**Nifedipine**, initial 20mg orally, followed by 10-20mg three to four times daily, adjusted according to uterine activity for up to 48 hours; a total dose of 60mg appears to associated with 3-4 fold in adverse events such as headache and hypotension.

**ADRs**: Flushing, oedema of ankle, headache, gingival hypertrophy

**C/Is:** Unstable angina, hypotension

**D/Is:** Cimetidine may enhance its anti-hypertensive effect

**Dosage forms:** Tablet, 10mg, 20mg; capsule, 5mg, 10mg, 20mg

*PLUS*

**Steroid therapy** for stimulation of surfactant production to be given 28-34weeks of gestation

**First line**

**Bethamethasone**, two doses of 12mg IV 24 hours apart. After 48 hours from the first dose, the full effect on maturing the surfactant has been obtained. If patient does not deliver within one week, the treatment should be repeated if the fetus is less than 34 weeks of gestation.

**ADRs:** Hyperglycemia, psychiatric reactions, gastrointestinal disturbance, infections, osteoporosis, central obesity, hirstusim

**C/Is:** Herpes simplex infection of the eye, epilepsy, peptic ulcer, psychic instability, thromboembolic disorders,

**P/C:** In hypertension, diabetis mellitus, liver cirrhosis, epilepsy, osteoporosis

**Dosage forms:** Tablet, 0.5mg

**Alternative**

**Dexamethasone,** 6mg P.O./IM for two doses six hours apart for two doses.

**Dosage forms:** Injection, 4mg/ml, 25mg/ml, 50mg/ml; Tablet, 0.5mg, 0.75mg, 1mg, 2mg

**N.B.** Use of corticosteroids in the presence of infection is contraindicated

**Sympathomimetics:** Ritodrine and salbutamol are associated with significant; potentially life threatening maternal side effects (particularly if given in combination with corticosteroids) which include fluid overload, pulmonary edema, myocardial ischemia, hyper of hypoglycemia, hence, these combinations should be abandoned totally in the management of preterm labour.

**8. Prolonged Pregnancy**

The terms "Prolonged, post-date and Post-term pregnancy" which are synonymously used, to define pregnancy that exceeds 42 weeks (294 days), from the day since the last menstrual period. The incidence of post-term pregnancy averages 4-5%. Post-term pregnancy may be complicated by foetal postmaturity, macrosomia, oligohydramnios, meconuim aspiration syndrome and placental insufficiency due to placenta ageing. Management of post pregnancy can take two forms; either expectant management with foetal surveillance, or elective induction of labour. **Induction of labour** is any attempt to initiate uterine contractions before the spontaneous onset of labour to facilitate the expulsion of conceptus product.

**Clinical features**

- Prolonged pregnancy is diagnosed from the last menstrual period or ultrasonography done in early pregnancy.
- Prolonged pregnancy may manifest with foetal macrosomia or IUGR, decrease foetal movement, decrease amniotic fluid.

**Investigations**

- Ultrasonography
- Cardiotography
- Biophysical profile

- Foetal movement
- Non-stress test (NST) and Stress Test

**Treatment**

**Objectives**

- Prevent maternal birth trauma and operative deliveries
- Prevent perinatal morbidity and mortality
- Assess risk factors before any intervention
- Asses the inducebility of the cervix

**Induction of labour:** This is one option of treatment of prolonged pregnancy, but before induction is attempted the cervix must be favourable, the bladder must be empty and the following risk factors should not be present in the pregnant woman:

- Previous scar on the uterus (C/S, myomectomy etc)
- Cephalopelvic disproportion (CPD)
- Malpresentation or malposition
- Non re-assuring FHB pattern
- Placenta previa

**Non pharmacologic induction of labour**

- Breast stimulation:
- Amniotomy (artificial rupture of membrane)
- Stripping of membrane (digital separation of the membranes from the lower uterine segment)
- Mechanical methods: iinsertion of Laminaria or Foley catheter into the cervical canal.

**Pharmacologic induction of labour**

**A. Oxytocin**

It is administered intravenously in different ways ranging from simple manually adjusted, gravity-fed systems, through mechanically or electronically controlled infusion pump, to fully automated closed-loop feedback systems.

**Dosage schedule**

**Low dose regimen**

**For primigravida**, 5 units in 1000ml N/S to run at 20drops/min (2mU/min), double the drop every 20 minutes until adequate contraction is achieved to maximum of 80 drops/minute, if adequate contraction could not be achieved with the maximum dose add 5 units to the same bag and start the drop from 40/minute, if there is no adequate contraction with this dose add 5 units more to the same bag to a maximum dosage of 64mU/min.

**For Mulitgravida:** Use half of the dose for primigravida women.

**High dose regimen**

Start with 6mU/min and increase the dosage by 6mU/min every 15 minutes until adequate contraction is achieved to maximum of 64mU/min for primigravida and 32mU/min for multigravida.

**ADRs:** Maternal: Uterine hyperstimulation, i.e, more than six contractions in 10 minutes lasting longer than 90 seconds without a period of relaxation and resting pressure of above 20mmHg. The hyperstimulation can cause uterine rupture and foetal distress. It has an ADH like effect that may lead to water intoxication and electrolyte imbalance. Oxytocin causes relaxation of the vascular smooth muscles resulting in hypotension and tachycardia, pulmonary edema. With prolonged use it may increase the blood pressure.

Foetal: Foetal distress, low apgar score, hyperbilirubinemia, hyponatremia

**Dosage forms:** Injection, 1unit/ml, 5unit/ml, 10unit/ml

**B. Prostaglandins**

Vaginal or cervical applications of PGs (E2, F2α and E1) are widely used for cervical ripening. They are administered intra-vaginally and intra-cervically.

**Dosage:** $PGE_2$ 3mg into the posterior fornix six hours apart for 2 doses followed by administration of oxytocin 12 hours later

**Advantages of administration of $PGE_2$ for cervical ripening**

- Enhances cervical inducebility

- Decreased need for oxytocin for induction
- Decrease oxytocin induction time and dosage
- Decreased C/S rate related to failed induction

**ADRs:** Uterine hyperstimulation leading to hypertonic uterine contraction and uterine rupture.
Foetal heart beat abnormalities, low apgar score
Fever, nausea, vomiting, diarrhoea

**Dosage forms:** Suppository (vaginal), 20mg; tablet (vaginal), 3mg

### 9. Prolonged Labour

Prolonged labour has been variously defined from one exceeding 24 hours to one exceeding 12 hours of established labour, when labour is actively managed. The causes of prolonged labour could be cephalopelvic disproportion (CPD) or insufficient uterine contraction in terms of frequency, duration and strength. The treatment of prolonged labour depends on the cause. If prolonged labour is due to inefficient uterine action the treatment is augmentation of labour using oxytocics. **Augumentation** is any attempt to stimulate uterine contractions during the course of labour to facilitate the expulsion of the fetus. But cephalopelvic disproportion should be excluded before augumentation.

**Clinical features**

- The frequency of uterine contraction is less than three in 10 minutes, duration is less than 30 seconds and strength is weak.
- This can be assessed clinically by palpating the uterus or using an intrauterine that measures the intrauterine pressure.

**Investigations**

- Ultrasound
- CTG
- Doppler

**Treatment**

**Objectives**

- Prevent uterine rupture
- Prevent foetal distress and IUFD
- Carefully assess for side effects of oxytocin

**Non Pharmacologic**

None

**Pharmacologic**

- The only pharmacologic agent available thus far is oxytocin.

**Common Medical Disorders In Pregnancy**

**10. Anaemia In Pregnancy**

Anaemia secondary to iron deficiency is the commonest medical disorder in pregnant women, particularly in the developing countries. The other varieties of anaemia are rare in this part of the world. Anaemia is one of the major indirect causes of maternal death.

Anaemia in pregnancy is defined as when the Haemoglobin (Hgb) level is below 11gm/dl in the first and third trimesters and below 10.5gm/dl in the second trimester of gestation. The causes of anaemia are the same as in non-pregnant period. Iron demand is increased by a factor of 4-5times during pregnancy.

**Classes**

- Mild anaemia: when the haemoglobin level is 8-11gm/dl
- Severe anaemia: when the haemoglobin level is < 7gm%

**Clinical features**

- Nonspecific symptoms like weakness, dizziness, palpitation, shortness of breath.
- Physical examination may reveal significant pallor of the conjunctiva and other parts of the body.

**Investigations**

- CBC, Hgb/Hematocrit

- Peripheral RBC morphology
- Bone marrow aspiration
- Stool examination for hookworm infestation
- Blood film for malaria
- RFT, LFT

**Treatment**

Treatment depends on the severity of anaemia and the underlying medical and obstetric condition of the mother.

**Objectives**

- Correct the anaemia as urgently as possible before the patient goes to labour.
- Identify the cause of anaemia like hookworm infestation, malaria etc.

**A. Mild to moderate anaemia**

**Non pharmacologic**

- Iron-rich diet
- Avoid frequent childbirth
- Minimize haemorrhage during pregnancy and childbirth

**Pharmacologic**

**First line**

**Ferrous sulphate**, 300mg P.O., TID with food.

*PLUS*

**Folic acid**

**Severe anaemia:** Requires admission and blood transfusion in the presence of complications.

**Refer:** if the anaemia is severe (Hgb <7gm/dl) refer patient for further investigation and fast correction of the anaemia.

## 11. Jaundice In Pregnancy

Jaundice occurring in pregnancy may be a sign or symptom of a severe disease and should be considered seriously.

**Causes**

**Obstetric**

- Severe pre-eclampsia/eclampsia/HELLP Syndrome (Haemolysis, Elevated Liver enzymes, Low Platelets syndrome)
- Severe hyperemesis gravidarum
- Intrahepatic cholestatic of pregnancy
- Acute fatty liver of pregnancy

**Non-obstetric**

- Viral hepatitis (E, B and C)
- Haemolytic jaundice due to malaria,septicaemia, medicines and herbal medications
- Surgical causes of jaundice; acute cholecystitis, cholelithiasis, obstructive jaundice

**Clinical features**

- Severe pruritis, malaise, anorexia, vomiting, jaundice, RUQ abdominal pain, fever, headache

**Investigations**

- CBC, Blood film for malaria parasites and peripheral morphology
- Group and cross matching
- Renal function test, liver function tests, serum electrolytes
- Bile acid level, lipid profile, Hepatitis B surface antigen
- Abdominal ultrasound scan, CT scan and MRI

**Treatment**

Treatment essentially depends on the underlying cause of jaundice.

**1. Severe pre-eclampsia (HELLP) syndrome**

**2. Hyperemesis gravidarum**

**3. Acute fatty liver of pregnancy (AFLP):**

It is common in obese multiparous women to experience multiple gestation in their third trimester of pregnancy. This is due to defect in the mitochondrial fatty acid beta oxidation; fatty acids and later trigycerides accumulate in the liver and impair its function.

**Clinical features**

AFLP should be considered in any pregnant woman presenting with one or more of the following:

- epigastric pain, symptoms suggestive of reflux esophagitis,nausea, vomiting, jaundice
- bleeding diathesis even in the absence of hepatic encephalopathy.
- 50% patients will show signs of pre-eclampsia.

**Investigations**

- liver biopsy, CBC, uric acid, bilirubin, liver function test, bile acid
- Hepatitis B, C and E, bile acid determination

**Treatment**

**Objectives**

- Prevent grave complications
- Terminate pregnancy at the appropriate time

**Non pharmacologic**

- Bed rest
- Strict measurement of BP, blood sugar level and coagulation status and electrolytes
- If there is DIC: Transfuse fresh frozen plasma, fresh blood, platelate
- Termination of pregnancy

**4. Intra-hepatic cholestasis pregnancy (IHCP):**

IHCP occurs from late second trimester to third trimester of pregnancy. Common in women of advanced age, multiparous, previous personal or family history of IHCP. It is diagnosed when otherwise unexplained pruritus occurs in pregnancy and abnormal liver function tests (LFTs) and/or raised bile acids occur in the pregnancy. Pruritus that involves the palms and soles of the feet is particularly suggestive. Other causes of itching and liver dysfunction should be excluded before labeling the woman as suffering from IHCP. Women with persistent pruritus and normal biochemistry should have LFTs repeated every 1–2 weeks. Typically, jaundice develops 2-4 weeks after the debut of pruritus. Postnatal resolution of the pruritus and the abnormal LFTs should be confirmed. It is associated with preterm labour, foetal distress and meconium staining liquor, and still birth.

**Clinical features**

- Generalized purirtus which mainly affects the palm an sole and severe a night, jaundice, pale stool and dark urine.

**Investigations**

- AFLP

**Treatment**

**Objectives**

- Alleviate symptoms
- Differentiate the disease from other cholestasis causes: intra-hepatic (viral infections) and extra-hepatic (e.g cholelithiasis)

**Non pharmacologic**

- Termination of pregnancy alleviates the symptoms

**Pharmacologic**

There is no evidence that any specific medicine treatment improves foetal or neonatal outcome. However, the following medicines can be tried to alleviate the pruritus;

- Topical emollients: Calamine lotion
- Systemic medicines
- Chlestyramine, P.O., 20mg/day
- Anti-histamines, e.g, chlorpheniramine
- Vit K

## 12. Cardiac Diseases In Pregnancy

The commonest causes of cardiac disease in pregnancy are secondary to rheumatic heart disease followed by the congenital ones, in the ratio of 10:1 respectively. Due to the increase in cardiac output during pregnancy, patients with underlying cardiac disease can be decompensated easily, particularly near 28 weeks of gestation, during labour and immediate post partum period, hence women with severe heart disease will benefit immensely from preconception counseling. On the other hand, due to these haemodynamic changes, normal pregnant patients may report signs and symptoms that may mimic cardiac disease; hence, differentiation of normal from abnormal is difficult.

The severity of heart disease is assessed according to the classification of the New York Heart Association (NYHA), which by and large depends on the response of the heart to physical activities, not the extent of cardiac lesion.

- Class I: Asymptomatic at all degrees of activity: uncompromised
- Class II: Symptomatic with ordinary activities: slightly compromised
- Class III: Symptomatic minimal exertion: markedly compromised
- Class IV: Symptomatic at rest; incapacitated.

**Causes**

- Rheumatic heart disease
- Hypertension
- Cardiomyopathy
- Anaemia
- Congenital heart diseases
- Hyperthyroidism

**Clinical features**

- Progressive dyspnea or orthopnea, nocturnal cough, hemoptysis, syncope, chest pain, cyanosis, clubbing of fingers, persistent neck distension, systolic murmur grade 3/6 or greater, diastolic murmur, cardiomegaly, persistent arrhythmia etc

**Investigations**

- ECG, Echocardiography, CXR, CBC, Blood urea and electrolytes
- Thyroid function test, when indicated
- Other ante-natal investigations

**Treatment**

A cardiologist, obstetrician and pediatrician should work as a team in the treatment of these patients.

**Objectives**

- Avoid aggravating factors
- Treat exacerbating factors: thyrotoxicosis, anaemia, infection etc
- Prevent or detect cardiac decompensation early

**Non pharmacologic**

- Early booking and assessment for severity of the disease
- Bed rest and limitation of activities
- Reduce cardiac work load: restrict fluid intake, reduce tachycardia, correct anaemia
- Avoid supine position in late pregnancy
- Apply elastic stocking to the lower leg to prevent pooling of blood
- Assist vaginal delivery by instruments to shorten the second stage of labour
- Put patient in propped up (semi-fowler's) position.

**Pharmacologic**

**Anterpartum**

**First line**

**Furosemide**, 40mg P.O., QD of BID.

| | |
|---|---|
| **ADRs:** | hyponatraemia, hypokalemia, hypomagnesaemia alkalosis |
| **C/Is:** | precomatose states associated with liver cirrhosis, renal failure with anuria |
| **Dosage forms:** | tablet, 40mg, 80mg; injection, 10mg/ml in 2ml ampoule |

**Alternative**

**Propranolol**, 40mg P.O., TID

**Digoxin**, same dose as that of non-pregnant women

- To control the heart rate in atrial fibrillation
- To suppress some other supra-ventricular tachycardias
- To increase the force of contraction

**Anti-coagulants, for**

- Valvular heart disease with fibrillation
- Prosthetic heart valves

**First trimester**

**Unfractionated heparin**, IV, 5000 units as bolus, followed by 1000-1200 units/hour as infusion.

**Unfractionated heparin**, SC, 10,000-15000 units 12hourly. The dose must be adjusted to achieve mid-target a PTT at 2-3x of the control

**Second trimester**

**Warfarin**, 5mg P.O., daily. Control with INR to keep within the therapeutic range of 2.5–3.5.

**After 36 weeks until delivery**

**Unfractionated heparin**, IV, 5000 units as bolus, followed by 1000-1200 units/hour as infusion.

*OR*

**Unfractionated heparin**, SC, 10-15,000 units 12hourly. Adjust dosage to keep the aPTT 2-3 times of the control.

**A. During labour**

- Vaginal delivery is the preferred route.
- Reduce labour pain by giving epidural anesthesia or pethidine 50-100mg, IM/IV with promethazine 25-50mg, IM
- Oxygen, 5-6L/min, through nasal catheter
- Broad spectrum antibiotics to prevent SBE: **Gentamicin,** 80mg IM/IV TID and Ampicillin 1g, IV/IM TID at the onset or induction labour.

- Stop heparin on the morning of elective caesarean section or when there is an established labour, restart heparin 6hours after vaginal delivery or 12 hours after caesarean section.

**B. Post partum**

The first one hour is critical because of the remobilization of the fluid into the vascular bed. Ergometrine should be avoided especially if the lesion is tight mitral stenosis or an Atrio-Ventricular (AV) shunt, because it may precipitate pulmonary edema. Post partum haemorrhage, anaemia, infection and thromboembolism can precipitate Heart Failure and should be managed accordingly.

**13. Deep Vein Thrombosis/Thromboembolism (Dvt/Te) In Pregnancy**

The adaptation of the maternal haemostatic system to pregnancy predisposes women to an increased risk of venous thromboembolism. Pregnancy produces the components of Virchow's triad, including an increase in vascular stasis, changes in the coagulation system, and vascular injury. That is why pregnancy is said to be thrombogenic. It is not surprising that venous TE is a potential risk of complication of pregnancy and puerperium, because the incidence of TE is five times higher than non-pregnant patients. Venous thrombo-embolism (VTE) can manifest in three forms: Superficial thrombophlebitis which can be treated with analgesics, elastic support and rest, deep vein thrombosis (DVT) and pulmonary thrombo-embolism (PTE). These forms represent spectrum of diseases, as one form may progress to the next.

**Clinical features**

- **Superficial thrombophlebitis:** hot, red and tender area in relation to a superficial vein.
- **DVT**: Clinical presentation vary, from severe pain and edematous white leg (phlegmasia alba dolens) to being asymptomatic, manifesting with pulmonary thrombo-embolism only.
- **Pulmonary thrombo-embolism (PTE):** Acute chest pain, breathlessness, cyanosis, and hemoptysis may be accompanied by hypotension and collapse.

**Investigations**

- Ascending phlebography
- Isotope venography
- Doppler ultrasound
- Radioactive iodine test is contraindicated in pregnancy
- Impedance plethysmography

**Treatment**

**Objectives**

- Liquefaction of the already formed thrombus
- Prevent further propagation of thrombus
- Prevent PTE
- Prevent recurrence of thrombosis
- Prevent long term complications, including venous insufficiency, pulmonary hypertension, right sided Heart Failure , post-thrombotic syndrome

**Non pharmacologic**

- Elevation of legs
- Apply a graduated elastic compression stocking to reduce leg edema
- Encourage ambulation while graduated compression stocking applied

**Pharmacologic**

**Heparin,** IV, in the order of 5,000-10,000IU, followed by 1000-1200IU/hour, and should be administered in saline through an infusion pump.

| | |
|---|---|
| **ADRs:** | Bleeding, allergy, reversible allopecia, osteoporosis, thrombocytopenea, paradoxical thrombo-embolism. |
| **C/Is:** | Hypersensitivity to the medicine, active bleeding, hemophilia, thrombocytopenia, purpura, severe hypertension, intracranial haemorrhage, infective endocarditis, & during or after neuro-surgical procedures. |

**Dosage forms:** Injection, 1000 IU/ml, 5000 U/ml in 5 ml ampoules; 5000 IU/ml, 12,500 IU/ml, in 1ml ampoules; 24000 USP IU/5 ml

***Followed by***

**Warfarin**, 2.5-5mg/day, excluding the first trimester upto the 36weeks of pregnancy.

**ADRs:** Readily crosses the placenta and lowers the Vit K-dependent clotting factors. There is a risk of embropathy if used in the first trimester. The commonly reported abnormality is *chondrodysplasia punctata.* Due to repeated small bleeding there could be ***microcephaly***. Breast feeding is not contraindicated.

**C/Is:** Bleeding, pregnancy (first trimester and during perpartum period)

**Dosage forms:** tablet, 2mg, 5mg, 10mg.

**Postpartum:**

- Therapuetic anticoagulants should continue for at least 6 weeks
- Warfarin should be avoided until the third day or longer in women at increased risk of PPH.

**14. Diabetes Mellitus Complicating Pregnancy**

Diabetes is one of the most common medical problems that complicate pregnancy. Diabetes in pregnancy can be gestational or pre-gestational. Women with pre-gestational diabetes need to have preconception counseling to achieve good glycemic control at the time of conception and organogenesis to avoid congenital abnormality. Women with gestational diabetes mellitus become normoglycemic immediately, but a significant number of them can become diabetic if followed for long period of time.

Diabetes in pregnancy, if not well controlled, may cause many obstetric and non-obstetric complications that include; macrosomia, polyhydramnios, congenital anomalies, maternal hyper or hypoglacemia depending on the gestational age, UTI, hypertension, exacerbation of retinopathy etc.

Types of diabetes in pregnancy:

- Gestational Diabetes Mellitus
- Pre-existing type I and II Diabetes mellitus

**Gestational Diabetes Mellitus (GDM)** is a carbohydrate intolerance of variable severity with onset or first recognized during pregnancy.

**Clinical features**

- Usually it is asymptomatic and identifications of the risk factors is important.
- There could be symptoms of polyuria, polydepsia and polyphagia etc

**Investigations**

**Screening;** by administering 50gm glucose load and determine the blood glucose level one hour later. If the value is more than 140mg/dl, the woman needs Oral Glucose Tolerance Test (OGTT) using 100gm anhydrous glucose which is a confirmatory test. According to the American Association of Diabetes women with the following risk factors should be screened for GDM between the gestational age of 24-28 weeks**.**

- Family history of DM in the first sibling (mother, father, sister or brother)
- Obese (BMI >27)
- Mothers above the age of 25 years
- Race (being black)

Previously, in addition to the above mentioned risk factors, the following were included as a screening criteria; previous delivery of macrosomic fetus (>4kg), previous pregnancy complicated by GDM, unexplained foetal losses, persistent glucosuria, but if the screening is based on these criteria, 50% of pregnant women prone to being diabetic can be missed.

**Table 83 - Upper limit for normal glucose level (mg/dl)in OGTT**

| Sample | Fasting | 1st hour | 2nd hour | 3rd hour |
|---|---|---|---|---|
| Whole blood | 90 | 165 | 145 | 125 |
| Plasma | 105 | 190 | 165 | 145 |

**Additional investigations**

- Ultrasound: between 16-22 weeks for congenital anomalies, at 32 weeks for foetal size
- CBC
- Urinalysis, urine culture and sensitivity
- Vaginal swab for candidiasis
- Renal function tests and electrolytes
- Liver function tests
- FBS and 2 hours post-prandial every 2-4 weeks
- HgbA1c every 2-3months

**Treatment**

**Objectives**

- Maintain good glycemic control, i.e, the fasting plasma glucose level to be < 105mg/dl and the two hours post-prandial <120mg/dl
- Prevent maternal and foetal complications.
- Prevent neonatal morbidity
- Minimize long term complication of diabetes

**Non pharmacologic**

**Diet**: most women with GDM can be managed with diet alone.

- Three meals and 3-4 snacks/day
- Diet with 40-50% carbohydrate, 20% protein and 30-40% fat content.
- 10% of calorie at breakfast, 30% at lunch and dinner and 30% with snack.
- Heavy meals must be avoided

**Exercise**

- Walking or exercise using the upper part of the body is recommended
- Mild to moderate exercise, preferably non-weight bearing, at least 3 times/week is recommended

- Avoid exercise in the supine position after the first trimester
- Exercise is contraindicated in the presence of the following conditions:
    - Pregnancy induced hypertension
    - Rupture of membrane
    - Preterm labour
    - Cervical incompetence
    - Vaginal bleeding
    - Intrauterine growth restriction (IUGR)

**Pharmacologic**

**Insulin**, 0.5 units/kg in the first half of pregnancy and increase the dosage to 0.7units/kg in the second half. This is the average dosage otherwise the dose requirement may vary from individual to individual. By splitting injection to 2/3 in the morning (as 2/3 long-acting and 1/3 short-acting) and 1/3 in the evening (as 1/2 long-acting and 1/2 short-acting) good blood glucose control should be achieved. Combination of 1/3 short and 2/3 intermediate acting insulin is used to maintain the FBS to 60-90mg/dl 1-hour post-prandial values at<120mg/dl.

**ADRs:** Hypoglycemia, lipohypertrophy

**C/Is:** Hypoglycemia

**Dosage forms:** Injection, insulin zinc suspension /insulin lente (HPB), 40 unit/ml, 100 unit/ml in 10ml vial.

**N.B.** Oral hypoglycemic agents are contraindicated during pregnancy, they cross the placenta and can cause prolonged neonatal hypoglycemia. In addition, there is an increased rate of congenital anomalies associated with these medicines.

**Follow up:**

- Fasting blood glucose and 1 hour postprandial every 2-3 weeks
- $HgbA_{1c}$ every 2-3months

There is no place for urine glucose determination in the management of diabetes in pregnancy except for screening.

**Delivery:**

- Unless there are other obstetric contraindications, induction of labour and vaginal delivery is the preferred route of delivery.
- If the blood glucose control is satisfactory with diet and exercise, follow the pregnancy until term with close foetal surveillance until spontaneous onset of labor. But if the blood glucose control is unsatisfactory, plan delivery after ascertaining the lung maturity using shake test, laminar bodies count etc.

**Intra-partum/Intra-operative Glycemic management**:

1. Withhold the AM insulin injection for planned delivery
2. Start IV infusion with 5% D/W at 100ml/hour
3. Start Insulin infusion with regular insulin at 0.5units/hour
4. Monitor maternal glucose levels hourly and adjust insulin infusion accordingly
5. Closely follow the foetal heartbeat

**Post-partum management**:

- The need for insulin declines is in post-partum period, therefore adjust the dose based on sliding scale. Insulin may not be required the first 24-48 hours for gestational and type II diabetes patients. For type I diabetes check the blood glucose every 2 hours and follow the scalding scale.
- If the blood glucose level becomes normal, OGTT should be done at the $6^{th}$ post-partum week.
- The newborn should be assessed for the following risks:
    - **Hypoglycaemia:** This can be prevented by initiating immediate breast feeding, or, by giving **Dextrose** 10%, IV, 4ml/kg body weight as bolus, followed by maintenance of 60ml/kg body weight in 24 hours.
    - Respiratory distress syndrome
    - Hyperbilirubinaemia
    - Congenital abnormalities.
- Breast feeding should be encouraged.

- Encourage contraception with progestins or surgical sterilization.

**A. Type I and II Diabetes Mellitus**

Many serious problems can ensue in women with type I and II diabetes during pregnancy. These complications are dependent on the presence of vascular problems which in turn are dependent on the duration of the diabetes. Based on this concept the White's classification (classes A-F) is used to predict outcome, though, the predictive value of this classification is less precise in modern management. All women with type II on oral hypoglycemic agents in the pre-pregnancy period must be shifted to insulin. If hypertension combines with diabetes it is an ominous sign. Therefore, the BP should be closely monitored.

**Clinical features**

- The same as those for GDM

**Treatment**

**Objectives**

- Same as those of GDM

**Non pharmacologic**

- Same as that of GDM

## Pharmacologic

The pharmacologic treatment is the same as that of gestational diabetes mellitus. However, insulin requirement should be adjusted according to gestational age. Maternal hypoglycemia may occur in the first half of the pregnancy. Hence, the insulin should be slightly decreased from the pre-pregnancy dosage. Whereas on the second half of pregnancy the insulin resistance increases, typically between the gestational age of 20-30weeks, hence, the dosage of insulin should be adjusted accordingly. Sometimes, a decrease need to insulin may arise towards late pregnancy which implies that the placenta is failing to function which implies the insulin resistance is disappearing. This is an ominous sign for the fetus.

**15. Thyroid Diseases In Pregnancy**

The thyroid gland produces $T_4$ and $T_3$ hormones in the ratio of 5:1. $T_3$ is produced by peripheral conversion of $T_4$ in a larger proportion. To produce this hormone the thyroid gland

requires enough iodine. More than 95% of these hormones are found attached to thyroid binding globulin (TBG) in the circulation. The production of these hormones is controlled by TSH which is secreted by the anterior pituitary and this in turn is controlled by the negative feedback and TRH from the hypothalamus. The main function of the thyroid hormones ($T_3$ and $T_4$) are: energy production, stimulation of protein synthesis and facilitate growth in children.

During pregnancy there is moderate enlargement of the thyroid gland due to its hyper-function. The TBG is markedly increases, almost doubles by the $12^{th}$ week, proportionally, the $T_4$ and $T_3$ level also increases and the concentration of free hormone in the circulation is changed. There are different types of thyroid disorders in pregnancy:

**A. Hypothyroidism**

**Clinical features**

Fatigue, hair loss, dry skin, excessive weight gain despite poor appetite, cold intolerance, muscle ache, stiffness, pain or tingling in the median nerve distribution due to carpal tunnel syndromes, low pulse rate, etc.

**Investigations**

- $T_4$, $T_3$ and TSH determination, ultrasound

**Treatment**

**Non pharmacologic**

None

**Pharmacologic**

**Thyroxin ($T_4$)** 0.1mg every morning for one week and adjust the replacement dose to 2μg/Kg. Breast feeding is not contraindicated. Dosage should be reduced in the postpartum period.

**ADRs:** Tachycardia, irritation, hyperglycemia,

**C/Is:** Cardiac disease

**Dosage form:** Tablet, 0.05mg, 0.1mg

**B. Hyperthyroidism**

Hyperthyroidism also causes anovulation and amenorrhea. In 95% of the cases thyrotoxicosis is due to Grave's disease but few could be due to solitary toxic adenoma or multinodular goiter or associated with obstetric conditions such gestational trophoblastic neoplasia. Foetal

hyperthyroidism is one of the complications which may lead to neonatal hyperthyroidism, IUGR, intrauterine death etc.

**Clinical features**

Family history of autoimmune thyroid disease, failure to gain weight despite good appetite, presence of exophthalmos or lid lag, persistent tachycardia, heat intolerance etc.

**Investigations**

- $T_4$, $T_3$, TSH and FTI. It is preferable to determine free $T_4$ and $T_3$,
- Fine needle aspiration
- Ultrasound
- Doppler ultrasound

**Treatment**

**Objectives**

- Identify the cause of hyperthyroidism
- Assess the severity of hyperthyroidism
- Prevent complications
- Manage appropriately to bring down to euthyroid level

**Non pharmacologic**

None

**Pharmacologic**

**First line**

**Propylthiouracil,** 150mg TID for 4-5weeks. The dose is then progressively lowered to maintenance dose of 150mg per day.

**ADRs:** Agranulocytosis, allergy, arthralgia, hepatitis, medicine fever

**C/I:** Liver damage

**Dosage form:** Tablet 25 mg, 100mg

**N.B.** Radioactive iodine should not be given to pregnant women

**Alternative**

**Carbimazole**, 15mg TID for 4-5 weeks. The dose is then progressively lowered to maintenance dose of 15mg per day.

**ADRs and C/Is:** Same as for those of Propylthiouracil

**Dosage form:** Tablet 5mg

**C. Thyroid crisis (storm)**

Thyroid crisis is a rapid worsening of thyrotoxicosis brought about by stress such as infection, labour and surgery. This scenario is common in women whose thyrotoxicosis is not well controlled, but it can occur also in well treated women.

**Clinical features**

- Fever, tachycardia, extreme nervousness, restlessness and psychosis, eventually may lapse into coma.

**Investigations**

- Free $T_3$, $T_4$,
- ultrasound

**Treatment**

**Non pharmacologic**

- Reduce fever by tepid sponging or covering in wet sheet or turning on electric fan.
- Prevent aspiration

**Pharmacologic**

**First line**

**Propylthiouracil**, 1000mg orally initially, followed by 200mg QID.

**N.B.**

- Administration of either of the antityroid medicines is followed by administration of sodium or potassium iodide, 500mg TID by infusion or orally QID to inhibit the release of thyroid hormone and Dexamethasone 2mg every QID for the first day to decrease the peripheral conversion of T4 to T3.
- If the patient develops Heart Failure ; **Propranolol**, 0.5mg IV initial dose followed as necessary by 0.5mg/min up to a maximum of 5mg, orally in a dose of 80mg three times per day.

**Chlorpromazine**, 25-50mg orally or intravenously 6-8hourly is administered to reduce fever.

**N.B. Aspirin** should not be used to reduce fever as it displaces thyroid hormones from TBG and thus increases the free hormones in the circulation, hence the condition could be worsened.

### D. Postpartum thyroiditis

It is a well recognized that 10-20% of women develop some form of thyroid dysfunction in the postpartum period due to autoimmune diseases. Three quarters develop hyperthyroidism and the rest hypothyroidism in the 1-3 month postpartum period. Most of those who develop hyperthyroidism go into remission within 2-3 months but 30% will enter hypothyroid phase.

**Clinical features**

- Fatigue and palpitation, 50% will have goiter.

**Investigations**

- Fine needle aspiration-lymphocytic thyroiditis is the common finding.

**Treatment**

- **Hyperthyroid phase:** Anti-thyroid medicines are not indicated.
- **Hypothyroid phase:** Most of the time, it is self limiting, but if symptoms are severe and prolonged, treatment with $T_4$ is warranted.

## 16. HIV/AIDS IN PREGNANCY

In the last 20-25 years HIV/AIDS has become a major indirect cause of maternal mortality. The majority of HIV positive women (77%) lives in Sub-Saharan Africa, and constitutes 57% of the global adult HIV positive population. According to the EDHS 2011, the national adult HIV prevalence was 1.5% with women disproportionately infected (1.9% compared to 1.0% in men). Prevalence was also markedly higher in urban areas (4.2 %) compared to rural (0.6 %). The urban/rural prevalence for women was 5.2% and 0.8% respectively. The National estimate for HIV positive pregnant women was 38,404 for the year 2012 (HIV estimates, EHNRI/FMOH, 2012). The HIV prevalence in pregnant women is 7.7% and about 7,792 children are born with HIV every year. This is as a result of mother to child transmission (MTCT) during pregnancy (5-10%) and labour and delivery (10-15%). Quite a significant number could be infected through breast feeding (5-20%).

Pregnancy by itself does not affect the course of the disease, but HIV may increase the risk of premature deliveries, small for date uterus and the rate of still birth. Factors that influence MTCT include: maternal viral load, nutritional status of the mother, presence of concomitant parasitic infection like malaria, severe immunodeficiency, advanced HIV/AIDS stage, presence of PROM and injury to the fetus and birth canal during labour and delivery. To reduce the rate of MTCT of HIV/AIDS, the Ethiopian government has adopted the four pronged approaches in its PMTCT strategies, namely: primary prevention, prevention of unintended pregnancy, prevention of HIV transmission from infected women to their infants, and treatment, care & support of HIV infected women, their infants and their families.

**Clinical features**

- Symptoms suggestive of opportunistic infections/malignancies or direct effects of HIV. History of sero-postivity, history of HAART and other HIV/AIDS related illnesses, duration of illness, status of partner, WHO staging, any medication given for HIV-related illnesses since the beginning of pregnancy.

**Investigations**

- Serologic test for HIV after counseling. If she is HIV positive, carry out CD4 count, viral load, baseline tests such as CBC, RFT, LFT.
- Test for syphilis (VDRL), Hgb
- Test for opportunistic infections like TB

**Prevention**

- **HIV positive women who intend to get pregnant:** The following general health measures should be taken:
    - Adequate nutrition that includes: high calorie and food staff rich in iron, micronutrient supplementation such as iron, zinc and folic acid at least for three months prior to getting pregnant.
    - Prevention of malaria infection.
    - Prevention and treatment of STIs.
    - Prophylaxis and treatment of opportunistic infections.

- Avoid pregnancy for at least six months following recovery from TB and other opportunistic infections.
- Administer ART, if not already on treatment

- **During antenatal care (ANC):** Advocate the benefits of VCT and persuade every pregnant woman to be tested. If the pregnant woman turns out to be positive apply the primary preventive measures that include; early and appropriate treatment of STI, education about safer sex practice during pregnancy and lactation.
- **Intrapartum care: Labour and delivery:** These include avoiding invasive procedures, application of infection prevention and performing elective C/S on selected patients.
- **Post partum care:** Avoiding breast feeding or exclusive breast feeding.

**PMTCT clinical scenarios and ARV regimens**

In August 2012, the Government of Ethiopia (GoE) endorsed the strategic shift to PMTCT Option B + which addresses the four prongs for PMTCT and consists of provision of a single triple medicine ART regimen to HIV positive pregnant women without regard to CD4 count and maintains continuity of care and treatment for the mother and infant within the MNCH platform from antenatal detection to post-breast feeding testing of the infant. Option B+ is a strategy that is expected to not only reduce transmission of HIV from mother to child but also improve the health of pregnant women and reduce sexual transmission in sero-discordant couples and partners.

**Key features of Option B+ include:**

- ANC health care provider initiates antiretroviral therapy (ART) for HIV + pregnant women at ANC at the time of diagnosis regardless of CD4 level. Labour and delivery health care provider starts ART for new HIV positive pregnant women and refers her to ANC clinic for follow-up;
- A HIV positive pregnant woman is started on ART, treatment is intended to be continued for life;

- A single triple medicine regimen is used for all newly diagnosed HIV + pregnant women and lactating mothers;
- The ANC health care provider continues to provide primary care to mother and infant, including prescribing and monitoring of ART, until risk of MTCT has passed. Exception to this practice is if infant is diagnosed as HIV positive, in which case immediate referral should be made with transfer of care to the nearest ART site; or if mother or infant becomes ill, which necessitate either referral to or transfer of care to nearest ART site
- Dry Blood Spot (DBS) testing is done by ANC health care provider or designated trained personnel in the MNCH unit;
- Maintaining continuity of care from antenatal period to post-weaning should improve infant testing at 6 weeks and at cessation of breast feeding as well as improve post-partum uptake of Family Planning (FP) services;
- Provision of ART at ANC clinic and the fact that ART is provided in the form of just one or two pills (depending on TDF/3TC/EFV formulation availability) taken once daily is expected to improve adherence and retention.

**Rationale for using TDF/3TC in HIV positive pregnant women**

- NVP containing regimen will cause severe toxicity in patients with high CD4 count.
- TDF is more suitable for HIV+ pregnant women than AZT because it does not cause anaemia which is a particular risk in pregnancy
- TDF is more suitable over d4T for HIV+ women because long term side effects are less likely
- TDF/3TC can as well treat Hepatitis B virus co-infection

**Use of Efavirenz in HIV positive pregnant women**

- Efavirenz has been suspected to cause birth defects; however recent findings indicate the safety of Efavirenz.
- Efavirenz can be used at any time during pregnancy
- There is no need to stop or switch Efavirenz containing regimen for woman who gets pregnant while on such treatments

**Scenario 1. Women who become pregnant while on ARV treatment:**

HIV positive women already on ART, if they get pregnant, should stay on the same regimen. The treating health provider at the HIV Chronic Care unit can decide on continuing the treatment at the MCH clinic.

**Scenario 2: Women presenting during pregnancy**

- TDF+ 3TC + EFV is prefeerd regimen to all HIV positive pregnant mothers irrespective of CD4; (Triple ARV started as soon as diagnosed and continued for life). AZT/ZDV + 3TC +EFV is alternative prefeerd regimen
- Infants born to HIV positive mothers will be on daily **Nevirapine** for six weeks starting at birth
- HIV positive status is the only requirement for starting ART for a pregnant or lactating woman
- No need to wait for CD4 count to initiate treatment
- CD4 count is important to monitor response to treatment and to detect emergence of treatment failure (not expected for several years if patient is adherent to treatment)
- Once started, it is hoped that the woman will be taking ART for her entire life. Thus, make sure that client understands the importance of adherence.
- HIV infected pregnant and lactating women need to be supported for adherence.
- HIV infected pregnant/lactating women may have multiple problems that may need other supplementary medicines in addition to ARVs.
- Understanding medicine-medicine interactions between medicines that may be prescribed to the HIV-infected pregnant woman are necessary to ensure the clients' safety and to obtain the maximum benefit from the medicines administered.
- Infants born from HIV positive women who started treatment with Option B+ will be monitored and continue their follow up at MNCH clinic until the infant is free from risk of HIV; that is six week after breast feeding stopped; approximately until the age of 18-24 months.

**Regimens**

**I. Maternal**

1. During pregnancy
    a. TDF/3TC/EFV if for the first time

b. Continue HAART if already initiated

2. During labor and delivery
   a. If on HAART continue it
   b. For women presenting for the first time start TDF/3TC/EFV
   c. All Women who are on combined (option A) will be transitioned to TDF/3TC/EFV
3. Lactating or post-partum.
   a. Continue ART if started
   b. Initiate ART if on no treatment
   c. Those who took combined ARV prophylaxis (option A) during ANC or labor should also be transitioned to option B+

**II. Infant**

- NVP for six weeks post-partum

**Continuing ARVs and follow up schedule for PMTCT client**

**ANC**

- Once the woman is identified HIV positive at ANC clinic, she needs more than the four focused visits of ANC.
- The first appointment is scheduled after 2 weeks of the initiation of TDF/3TC/EFV to detect medicine side effects, assess adherence and find out if the mother has any other problems
- The subsequent follow up would be continued on monthly basis for the first six months (plus a six day and 6 week post-partum visit), then every two months until the mother is transferred to ART clinic/referred to the nearest ART facility.
- HIV positive pregnant women already on ART regimen other than TDF/3TC/EFV will have her ANC follow up service at the ANC/PMTCT clinic and attend her HIV treatment follow-up at her usual place. (However, the health provider at the ART Clinic can decide on the treatment option for the best interest of the client)

**L&D**

- Appointment should be arranged for the mother and the baby in the same facility
- The mother and the baby are provided health care in the ANC/PMTCT clinic and followed-up until the HIV status of the infant is confirmed;

- The first appointment is scheduled within one week matching with the 2nd post-natal care follow-up to assess for adherence, detect medicine side effects and find out if the mother and baby have any other problems. Routine second appointment can be scheduled at 6 weeks matching with the third postnatal care for both the infant and the mother. Through this period MSG should be in contact with the mother.
- The subsequent follow up will be scheduled on monthly basis

**17. Malaria In Pregnancy**

Malaria is a public health problem worldwide. More than 23 million pregnant women live in malaria endemic area and few of them have access to medical care, particularly in Sub-Saharan Africa. As a result malaria is becoming one of the major indirect causes of maternal death along with HIV/AIDS. Pregnant women, particularly in the second and third trimesters are more likely to develop severe malaria than other adults, often complicated by pulmonary edema and hypoglycemia. Maternal mortality is 50% higher than in the non-pregnant period. The commonest complications are; maternal anaemia, spontaneous abortion, still birth, premature labours, and low birth weight.

**Causative agents**

*P. falciparum, P. vivax, P. ovale and P. malariae*

**Clinical features**

Fever, chillness, rigor, anaemia, headache, joint pain etc

**Uncomplicated malaria:**

- Fewer than 2% parasitized RBC in woman with no sign of severity and no complicated features.

**Severe/complicated malaria:** If the following conditions are present severe malaria can be diagnosed:

- **Clinical:** prostration, impaired consciousness, respiratory distress, pulmonary edema, circulatory collapse, DIC, jaundice, haemoglobinuria
- **Laboratory:** Severe anaemia (Hgb <8), thrombocytopenia, hypoglycemia, acidosis, renal impairment, hyperlactataemia (correlates with mortality),

hyperparasitemia (more than 2% parasitized RBC), algid malaria-gram negative septicemia

**Investigations**

- Blood film (thin and thick), Rapid Diagnostic tests (not reliable in pregnancy)
- CBC
- RBS/FBS
- RFT, LFT, bluribin level
- Blood culture
- Electrolytes
- Lumbar puncture to exclude meningitis

**Treatment**

**Objectives**

- Correct the fluid and electrolyte imbalance, hypoglycemia, fever
- Identify the causative species and treat appropriately
- Treat the malaria aggressively to prevent obstetric complications
- Treat secondary bacterial infections
- Provide supportive care

**Non pharmacologic**

- Keep NPO
- Lower the temperature by administering tepid sponging, fanning
- Correct anaemia: Transfuse packed RBC
- DIC: Fresh frozen plasma

**Pharmacologic**

A. **Severe or complicated:**

***P. falciparum* and *P. vivax*:**

**First line**

**Artesunate**, IV, 2.4mg/kg at 0, 12 and 24 hours, then daily thereafter. When the patient is well enough to take oral medication she can be switched to oral artesunate 2mg/kg (or IM artesunate 2.4mg/kg) once daily, plus clindamycin. If oral artesunate is not available, use quinine 600mg TID and clindamycin at 450mg TID for 7 days.

**Alternative**

**Quinine**, IV 20mg/kg loading dose (no loading dose if patient already taking quinine or mefloquine) in 5% dextrose over 4 hours and then 10mg/kg IV over 4 hours TID plus clindamycin IV 450mg TID (max. dose quinine 1.4g). When the patient is well enough to take oral medication, she can be switched to oral quinine 600mg TID to complete 5–7 days and oral clindamycin 450mg TID for 7 days.

**N.B.** quinine dosing should be reduced to 12-hourly dosing if IV therapy extends more than 48 hours or if the patient has renal or hepatic dysfunction. Quinine is associated with severe and recurrent hypoglycaemia in late pregnancy.

*OR*

**Arthemether**, IM, Day1, 3.2mg/kg, day2, 1.6mg/kg, day3, 1.6mg/kg

**N.B.** Arthmether IM, should only be used in the first trimester of pregnancy when IV/IM artesunate (preferred) or quinine IV/IM is not available.

**Uncomplicated malaria**

**1. *P. falciparum:* Oral quinine** 600 mg TID and oral clindamycin 450 mgTID for 7 days (can be given together)

Vomiting but no signs of severe or complicated malaria:

**Quinine**, 10 mg/kg dose IV in 5% dextrose over 4 hours TID

**Alternative**

**Artemether (120mg)-Lumefantrine (20mg)**, P.O., 4tablets BID for three days

**2. *P. vivax***

**Chloroquine (base)**, 600mg P.O., followed by 300mg TID later. Then 300mg on day 2 and again on day 3.

**N.B.** Primaquine should not be used in pregnancy

## 18. Urinary Tract Infection In Pregnancy

Urinary tract infections (UTIs) are one of the most common medical complications of pregnancy. It is estimated that one in three women of childbearing age will have a UTI. Because of the normal physiologic changes induced by pregnancy, pregnant women are especially susceptible to UTIs, including asymptomatic bacteriuria, cystitis and pyelonephritis. Urinary tract infection is common in women with diabetes. Half of the women with asymptomatic bacteriuria, would develop pyelonephritis later in pregnancy, if left untreated. For this reason, pregnant women with asymptomatic bacteruria should be treated and 70% of pyelonephritis can be prevented.

**Causative organisms**

*E.coli* (most common, 75-90%), klebsiella, proteus, coagulase negative staphylococci, and pseudomonas

**Classes**

- Asymptomatic bacteruria
- Symptomatic UTI:
    - Lower UTI: Cytitis, urethritis
    - Upper UTI: Pyelonephritis

**Clinical features**

**Lower UTI** (cystitis and uretheritis) will have supra-pubic tenderness, abdominal discomfort, hematuria, urgency, frequency, dysuria

**Upper UTI:** Flank pain (unilateral or bilateral) and abdominal pain, anorexia, nausea, vomiting, fever, chillness headache, dehydration, tachypnea

**Investigations**

- Urine analysis
- Urine culture: Growth of bacteria $10^5$ organisms/ml of urine
- Blood culture when needed
- CBC

- BUN, creatnine
- Ultrasound

**Treatment**

**1. Asymptomatic bacteruria**

**Objectives**

- Prevent pyelonephritis
- Identify the predisposing factors, if there is any
- Eradicate the infection and prevent recurrence

**Non pharmacologic**

- Take a lot of fluid and ecourage frequent voiding.

**Pharmacologic**

The treatment would be more rational if the choice of antibiotics is based on culture and sensitivity results.

**First line**

**Amoxicillin** 500mg P.O., TID for three days

**Alternatives**

**Cephalexin**, PO, 500mg, BID for 7days

OR

**Amoxicillin**, PO, 500mg, TID, for 7days

(For **ADRs, C/Is** and **Dosage forms,** see page **Error! Bookmark not defined.**)

OR

**Trimetoprim/Sulphamethoxazole** 480mg BID for three days.

(For **ADRs, C/Is** and **Dosage forms**, see under Sulphamethoxazole Trimetoprim)

**N.B.** Avoid Trimethoprim sulphamethoxazole in the first and third trimester of pregnancy because it has potential risk to cause open neural tube defect and neonatal jaundice.

**2. Symptomatic UTIs:**

About 11-15% of women develop symptoms of UTI in pregnancy. However, 3.2% of them could be symptomatic with sterile urine.

**2.1 Lower UTI (cystitis and urethritis)**

The symptoms are often difficult to distinguish from those due to the pregnancy itself. Features that may indicate true infection include hematuria, dysuria, urethral discharge and supra-pubic discomfort.

**Treatment**

Treatment is the same as asymptomatic bacteruria but the duration of treatment should lasts for 7 days instead of 3 days.

**2.2 Upper UTI (pyelonephritis)**

Acute pyelonephritis is a serious medical problem in pregnancy which requires admission and aggressive management. Acute pyelonephritis could lead to complications like miscarriage, IUGR, preterm labour, intrauterine foetal death and sepsis. The incidence increases with gestational age; 90% of the cases occur in the second and third trimesters of pregnancy and 20-40% follows asymptomatic bacteruria.

**Treatment**

Women with pyelonephritis require admission for parenteral medication.

**Objectives**

- Prevent foetal complications which include preterm labour, low birth weight, IUGR, PROM
- Prevent maternal complication from, overwhelming sepsis, perinephric abscess, pre-eclampsia, acute renal failure
- Identify the predisposing factors, including renal stone, congenital anomalies, diabetes mellitus
- Prevent recurrence of UTI

**Non pharmacologic**

- Adequate nutrition and hydration
- Tepid sponging to lower fever

**Pharmacologic**

The choice of antinbiotics would be more rational if it is based on culture and sensitivity

**First line**

**Ampicillin,** 2gm IV QID until 48 hours after the fever subsided and then 500mg P.O., for 10-14 days.

*PLUS*

**Gentamicin**, 80mg IV TID until 48 hours after the fever subsided and then IM for 10-14 days.

**Alternatives**

**Cephotaxime**, 500mg-1gm IV BID until 48 hours after the fever subsided and then continue IM BID for 7days

| | |
|---|---|
| **ADRs:** | Granulocytopenia, GI disturbance, and Positive coomb's test |
| **C/Is:** | Hypersensitivity reaction |
| **Dosage forms:** | 0.5g, 1g in vial |

*OR*

**Ceftriaxone**, IV, 1gm, BID, until 48hours after the fever subsided and then continue IM for 7days.

*OR*

**Cefuroxime**, IV, 750-1500mg, TID, until 48hours after the fever subsided and then continue P.O., BID for 7days.

## 19. Syphilis In Pregnancy

Syphilis is a common sexually transmitted disease, which can cause significant intrauterine infection leading to abortion, pre-term birth, perinatal death and congenital anomalies. It is caused by *Treponema pallidum.* Routine screening is done at booking and at the third trimester of pregnancy, because it can infect the fetus at any point during gestation. Previously, it was believed that congenital infection is not possible before 16 weeks of gestation because of the protective effect of the Langerhans cell layer of the placenta. However, it is now known that the spirochete can transgress the placenta during the first trimester. The risk of foetal infection is proportional to the degree of spirochetemia in the mother. Hence nearly, all fetuses are at risk of infection during maternal primary and secondary syphilis.

**Clinical features**

- Most mothers are asymptomatic.

**Investigations**

**Microscopy:** by dark field examination or direct immuno-fluorescent Microscopy.

**Serology**

21. specific treponemal tests such as TPHA or FTA-Ab
22. nonspecific treponemal tests
    a. the Venereal Disease Research Laboratory (VRDL) test
    b. the Rapid Plasma Reagin (RPR) test

**Treatment**

**Objectives**

- Prevent long term and short term complications
- Prevent mother to child transmission

**Non pharmacologic**

None

**Pharmacologic:**

**First line**

Pregnant women with syphilis must be treated with penicillin, since no other medication effectively crosses the placenta to treat the fetus, even if allergic to penicillin must be desensitized and treated.

**Benzathine penicillin**, 2.4 Mil IU IM (1.2 Mil in each buttock) weekly for three consecutive weeks. Treat the partner similarly

**Dosage forms:** Injection, 0.6, 1.2, 2.4 million IU in vial

**Alternatives**

**Erythromycin,** 500 mg P.O., QID for 14 days, but may not prevent congenital infection.

**N.B.** Patients treated for syphilis in the second half of pregnancy can develop Jarisch-Herxheimer reaction, which can precipitate premature labor and foetal distress.

**20. Pelvic Inflammatory Diseases (Pid)**

Pelvic inflammatory disease (PID) is usually the result of infection ascending from the endocervix causing endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abscess

and/or pelvic peritonitis. Sexually transmitted infections (STIs) are the main causative agents but anaerobes and other organisms from the lower genital and gastrointestinal tracts may also be implicated. PID could be post-sexually transmitted infection, post-partal and post-operative. It is caused by polymicrobial organisms such as *gonoccocus, chlamydia trachomatis, mycoplasma hominis and genitalium,* other intestinal and vaginal normal flora.

**Clinical features**

The following clinical features are suggestive of a diagnosis of PID:

**Major criteria**

- Bilateral lower abdominal tenderness (sometimes radiating to the legs)
- Cervical motion tenderness on bimanual vaginal examination
- Adnexal tenderness on bimanual vaginal examination (with or without a palpable mass).

**Minor criteria**

- Fever (greater than 38°C)
- Abnormal vaginal bleeding (intermenstrual, post-coital or 'breakthrough')
- Deep dyspareunia
- Abnormal cervical or vaginal mucopurulent discharge
- Presence of abundant numbers of white blood cells (WBCs) on saline microscopy of vaginal secretions
- Elevated erythrocyte sedimentation rate
- Elevated C-reactive protein

**Investigations**

- WBC with differential count, ESR
- Culture and sensitivity of blood, pus, or vaginal discharge
- Nucleic acid amplification test (NAAT)
- Vaginal Swab: excess WBC in wet mount smear may indicate PID
- RFT, LFT, electrolytes

- Ultrasonography
- Laparascopy for visualization of hyperemic tubes, purulent discharge

**Treatment**

**Objectives**

- Determine whether the patient can be treated as outpatient or requires hospitalization
- Treat the acute infection: to eradicate the offending organism and prevent further dissemination of the infection
- Prevent the damage of the fallopian tube which may lead to recurrent infection, infertility, chance of ectopic pregnancy, chronic pelvic pain

**Non pharmacologic**

- Patient should refrain from sexual activities or douching
- Consider removal of IUD if the woman is not improving with medication
- Surgical management includes, laparatomy and drainage of abscess, salpingo-oopherectomy, colpotomy, hysterectomy with or without salpingo-oopherectomy

**Pharmacologic**

**Out patient treatment**

**First line**

**Ceftriaxone**, 250mg IM single dose

*PLUS*

**Doxycycline**, 100mg P.O., BID.

*PLUS*

**Metronidazole,** 500mg P.O., BID for two weeks.

**Inpatient treatment**

Inpatient antibiotic treatment should be based on intravenous therapy which should be continued until 48 hours after clinical improvement and followed by oral therapy. Admission to hospital would be appropriate in the following circumstances:

- If the diagnosis is uncertain

- Clinically severe disease
- Tubo-ovarian abscess
- PID with pregnancy
- PID in HIV positive women
- Lack of response to oral therapy
- Intolerance to oral therapy
- Poor compliance

**First line**

**Ampicillin**, 500 – 1000mg IV, QID**,** followed by 500mg P.O., QID

*PLUS*

**Gentamicin**, 80mg, IV, TID followed by IM injection of similar dose

*PLUS*

**Clindamycin**, IV, 900mg, TID

*OR*

**Metronidazole**, 500mg IV TID followed by 500mg P.O.,TID

**Alternative**

**Ceftriaxone**, IV, 2gm/day, BID

*PLUS*

**Gentamicin**, IV, 80mg, TID

*PLUS*

**Metronidazole**, IV, 500mg TID

Followed by either

**Clindamycin** 300mg P.O., QID

*OR*

**Doxycycline**, 100mg P.O., BID

*PLUS*

**Metronidazole**, 500mg P.O., TID for 14 days

**N.B.**

- In the outpatient setting, review of patient condition at 72hours after initiation of medication is recommended, particularly for those with a moderate or severe clinical presentation

- In patients who have been on IV medication should continue oral treatment for 14 days after clinically being improved.
- In pregnancy, the physician should refrain from using deoxycycline
- Patients with PID wearing IUD: Consideration should be given to removing the IUD, especially if symptoms have not resolved within 72 hours.
- Women on hormonal contraception presenting with breakthrough bleeding should be screened for genital tract infection, especially for *C. trachomatis*
- When a sexually transmitted infection is either proven or likely to be the cause of PID, the current sexual partner(s) should be traced and offered health advice and screening for gonorrhoea and chlamydia.

## 21. Puerperal Mastitis

Puerperal mastitis is breast inflammation that develops during the first month after delivery. Puerperal mastitis is a commonly encountered infection, hence early diagnosis and prompt management minimizes the impact on the mother and infant. Despite appropriate management, abscess formation occurs in 4-10% of cases. It is commonly caused by *Staph. aureus* and in some cases *Staph. epidemidis*.

**Clinical features**

- Fever, chills, flu like symptoms, breast pain with warm, erythromatous, indurated, engorged and tender breast (one or both breasts) and axillary lymphadenopathy. Fluctuating breast mass.

**Investigations**

- CBC
- Gram stain from the pus
- culture and medicine sensitivity from the breast abscess if any

**Treatment**

**Non Pharmacologic**

- Suctioning of the breast

- Breast-feeding with only the healthy breast
- Drainage of breast abscess

**Pharmacologic**

**Cloxacillin**, 500mg P.O., TID for 7-10 days

If there is evidence of sepsis, the patient requires hospitalization

**Cloxacillin**, 500mg IV QID until the fever and clinical symptoms subside, and continue with oral Cloxacillin for 7-10 days.

**N.B.** Do not wait until fluctuation; if there is induration, tap and confirm the diagnosis.

**22. Vaginal Discharge Syndromes**

## BACTERIAL VAGINOSIS (BV)

Bacterial vaginosis (BV) is a clinical syndrome characterised by the presence of malodorous vaginal discharge, with or without vaginal pruritus. Usually there is no external genital irritation or dysuria. The discharge is generally a homogeneous, non-viscous, milky white fluid which smoothly coats the vaginal mucosa and cervix. Imbalance of the normal vaginal flora is thought to play a role in the aetiology of BV, resulting in overgrowth of gardnerella, anaerobes, or genital Mycoplasmas. The absence of Hydrogen peroxide-producing Lactobacillus in the vagina appears to correlate with development of this disease. BV may cause adverse pregnancy outcomes like PROM, chorioamnionitis, preterm labour, premature birth, post-partum endometritis, post-caesarean wound infection.

**Clinical features**

Vaginal secretions characterised by at least three of the following:

1. Amine ("fishy") odor before or after addition of 10% KOH solution.
2. PH $\geq$ 4.5 (unreliable if blood present)
3. Homogeneous, smooth, non-inflammatory discharge
4. Presence of clue cells (epithelial cells coated with bacteria) on microscopic examination.

**Treatment**

**Objectives**

- Alleviate ymptoms

- Prevent adverse pregnancy outcomes following infection
- Avoid precipitating factors

**Non pharmacologic:**

- Avoid frequent douching

**Pharmacologic**

**First line**

**Metronidazole**, 500mg P.O., BID for 7 days or 2g P.O., single dose

**Alternative**

**Metronidazole**, 0.75% gel 5gm intra-vaginally QD for 5 days

*OR*

**Clindamycin** 2% cream 5gm intra-vaginally,OR 300mg P.O., BID for 7 days OR 100mg intra-vaginally QHS for 3 days

In **Pregnancy**

**Metronidazole**, 250mg P.O., TID for 7 days;

*OR*

**Clindamycin**, 300mg P.O., BID for 7 days.

**P/C:** Avoid alcohol during treatment with oral metronidazole and for 24 hours thereafter, due to possible disulfiram-type reaction. Clindamycin cream is oil based, and may weaken latex condoms.

**Sex Partners**

Routine treatment of male partners(s) with **metronidazole** does not prevent recurrence of Bacterial Vaginosis. For recurrent BV without evidence of other STD, use of condoms and avoiding douching is encouraged.

### 23. Mucopurulent Cervicitis

Mucopurulent cervicitis (MPC) has been called the female counter part of urethritis in males. It can be caused by infection with *N. gonorrhoeae* or *C. trachomatis*, although in most cases test are negative for both gonorrhea and chlamydia. The syndrome is characterised by muco-purulent cervical discharge and a cervical inflammatory response (friability, edema, ectopy, increased numbers of polymorphonuclear leukocytes (PMNs). However, presence of IUCD,

ectopy, oral contraceptives and menses may be associated with PMNs in endocervical smears without MPC. Patients with MPC may note vaginal discharge, dyspareunia, post-coital or inter-menstrual bleeding, or other non-specific symptoms.

**Causes**

- Gonorrhea or Chlamydial infections
- Herpes cervicitis
- Trichomoniasis (ectocervicitis)

**Clinical features**

1. MPC is diagnosed by the presence of criterion (a) below and at least one other criterion (b, c or d).

a. Endocervical gram-stained smear with a monolayer of ≥ 15 PMNs/1000 X (oil immersion) field, (in a specimen obtained from the endocervix with a swab to wipe the cervix free of vaginal epithelial cells or menstrual blood, and in the absence of primary herpes, trichomoniasis, or candidiasis)
b. Purulent endocervical discharge; or positive "swab test" (yellow or green color on endocervical swab).
c. Hypertrophic or edematous cervical ectopy.
d. Endocervical bleeding induced by gentle swabbing.

**Investigations**

- CBC
- Wet smear
- KOH mount
- Gram stain from vaginal swab for gonorrhea
- Culture and medicine sensitivity of gonorrhea and chlamydia
- Ultrasound

**Treatment**

**Objective**

- Alleviate symptoms

- Treat aggressively to prevent short and long complications
- Identify the partner and halt further transmission of infection

**Non pharmacologic**

None

**Pharmacologic**

**First line**

**Doxycycline**,100mg P.O., BID for 7 days

**Alternatives**

**Erythromycin base**, 500mg P.O., QID for 7 days

*OR*

**Azithromycin,** 1.0gm P.O., single dose

**N.B.** If gonococcal infection is likely on clinical or epidemiological grounds, proceed treatment with a single dose gonorrhea regimen.

**Sex Partners**

1. All current sex partners should receive full STD evaluation. It is probably most important to evaluate those partners within the past 30 days of diagnosis or onset of symptoms.
2. If Non-Gonococcal Urethritis (NGU) or gonorrhea present; treat accordingly.
3. If no urethritis is documented in the partners, it is generally safe to defer treatment pending results of tests for gonorrhea and Chlamydia. However, empiric therapy at the time of initial examination may be indicated if follow-up cannot be assured.

**24. Trichomonal Vaginitis**

Trichomoniasis is a parasitic infection caused by Trichomonas vaginalis. Trichocomonal vaginitis is characterised by the development of profuse, purulent malodorous vaginal discharge (occasionally foamy). Cervical petechiae are commonly seen ("strawberry cervix"). External dysuria and genital irritation are sometimes present. As in BV, the vaginal PH in trichomoniasis is generally above 4.5. Trichomonas vaginalis may be linked to adverse pregnancy outcomes such as PROM, premature birth, and low birth weight.

**Clinical features**

- Frothy, greenish and profuse vaginal discharge associated with itching.

**Investigations**

- Demonstration of motile trichomonads on saline wet mount of vaginal exudates

**Treatment**

**Objectives**

- Alleviate symptoms
- Prevent pregnancy adverse pregnancy outcomes including PROM, premature labour, low birth weight
- Halt further transmission of the infection by identifying and treating the partner/s

**Non pharmacologic**

None

**Pharmacologic**

**First line**

**Metronidazole**, 500mg P.O., BID for 7 days OR 2gm P.O., single dose

**Alternative**

**Tinidazole**, 2gm P.O., stat

**In Pregnancy**

**Metronidazole**, 2gm P.O., single dose regimen.

**N.B.**

- Advise sexual abstention until symptoms improve and partner(s) treated
- Avoid alcohol during treatment with oral metronidazole and for 24 hours thereafter, due to possible disulfiram-type reaction.
- Treatment failure (persistence or recurrence despite sexual abstention, or after intercourse only with a treated partner), metronidazole 500mg P.O bid for 7 days.
- Repeated treatment failure: metronidazole 2.0gm P.O. QD for 3 to 5 days.
- Metronidazole gel is not effective for the treatment of T-vaginalis.
- Consider metronidazole resistance if patient is persistently infested after multiple treatment courses.
- Tinidazole appears to be effective against metronidazole resistant T. Vaginalis: dose is 2 gm once P.O

**Sex Partners**

1. Routine examination for sexually transmitted disease is required.
2. Metronidazole 2.0 gm P.O, single dose for all partners.
3. Abstain from sexual contact until 7 days after therapy is initiated.

## 25. Vulvo-Vaginal Candidiasis

Vulvo vaginal candidiasis is a common cause of pruritic vaginal discharge which is commonly caused by *Candida albicans.*

**Clinical features**

- The main manifestations include pruritis vulvae, whitish curd like vaginal discharge, vulval irritation, dyspareunia, and splash (external) dysuria.

**Investigations**

- KOH test, Culture

**Treatment**

**Objective**

- Alleviate symptoms
- Indetify the underlying cause and manage accordingly including diabetes mellitus, eccessive use of board spectrum antibiotics, other causes that can jeopardize the immune status of the patient

**Non pharmacologic**

- Avoid frequent douching using detergents

**Pharmacologic**

**First line**

**Nystatin**, 100,000 IU per vaginum, QD for 14 days

**Alternative**

**Clotrimazole**, 100mg BID to be inserted in the vagina for three days OR 200mg/day for 03 days. OR 100mg/day for 6 days OR 1% cream 5gm 10-14 days.

*OR*

**Miconazole,** 200mg/day to be inserted in the vagina for three days OR 100mg/day for 7 days OR 2% cream 5gm intra-vaginal for 7 days.

**Chronic Vulvo-vaginal Candidiasis**

**First line**

**Ketoconazole**, 400mg /day OR 200mg BID for 5-10 days. Then 100mg /day for 6 months as prophylaxis.

**Alternative**

**Fluconazole**, 150mg P.O., single dose, then 100mg ketoconazole /day for 6 months prophylaxis.

**Sex Partners**

Examination and treatment of the partner usually is not necessary. However, if the partner has penile candidiasis or there is recurrent infection, treatment with an imidazole cream (e.g, miconazole, clotrimazole) may be indicated.

## 26. Abortion

Abortion is defined as the initiation or expulsion of the fetus and other products of conception before the 28th week of pregnancy. It may be spontaneous (threatened, inevitable, incomplete, complete or missed) or induced.

**Causes**

- Infections e.g. malaria, HIV, UTI, bacterial vaginosis etc.
- Foetal abnormalities
- Incompetent cervix and other congenital anomalies of the uterus
- Chronic illness e.g. diabetes, thyroid disorders, HIV etc.
- Intentional interference with the pregnancy with medications or instrumentation
- Trauma

**Threatened Abortion**

This is bleeding from the uterus before 28 weeks of gestation without cervical dilatation.

**Clinical features**

- This variety of abortion usually manifests with scanty to moderate painless vaginal bleeding without cervical dilatation and effacement. There may be mild discomfort. Usually the uterine size corresponds with the stated gestational age.

**Investigations**

- CBC
- Blood film for malaria and other hemoparasites
- VDRL
- FBS
- HIV test
- Ultrasound scan (confirms viable fetus in utero with closed cervix)

**Treatment**

**Objectives**

- Maintain a viable pregnancy to term if possible

**Non pharmacologic**

- Explain the condition to the patient
- Strict bed rest at home or hospital
- Abstain from sexual intercourse
- Report if bleeding or pain increases

**Pharmacologic**

None

**Inevitable Abortion**

Inevitable abortion is bleeding from the uterus before 28 weeks of gestation leading to cervical dilatation with the membranes bulging or leakage of fluid.

**Clinical features**

- There is lower abdominal pain associated with heavy bleeding, cervical dilatation and effacement. There may also be painless loss of amniotic fluid.

- If the bleeding continues for more than one week, it can be considered as inevitable abortion, even if the cervix is closed.

- The uterine size is compatible with the gestational age.
- Depending on the amount of blood loss, there may be signs of shock (pallor, collapsed peripheral vessels, rising pulse with reducing volume, falling BP and cold clammy skin).

**Investigations**

- CBC
- Blood grouping and cross matching
- Ultrasound scan to see the viability of the fetus, for assessment the cervix and amniotic fluid

**Treatment**

**Objectives**

- Resuscitate patient
- Relieve pain
- Facilitate conditions that the process of abortion to be accomplished in aseptic condition within short period of time
- Evacuate the retained products of conception from the uterus.
- Identify cause of abortion if possible
- Prevent infection with antibiotic prophylaxis

**Non pharmacologic**

- Keep the patient NPO
- Evacuation of the uterus by Manual Vacuum Aspiration (MVA) or by the conventional evacuation and curettage under local or general anaesthesia especially when uterine size is smaller than 12-14 weeks size.
- Blood transfusion, if required

**Pharmacologic**

**If the uterine size larger than 14 weeks**

**IV fluids** as necessary.

**Pethidine**, IM, 75-100mg stat. Followed by 50-100mg 8 hourly promethazine hydrochloride, IM, 25mg stat

**Oxytocin**, IV, 10-20 units/litre of Normal saline

*OR*

**Misoprostol**, per vaginum or rectum, 600-800micrograms, two doses 4 hours apart

**Incomplete abortion**

In this clinical scenario part of the conceptus material is expelled and some is remaining in the uterine cavity or cervical canal.

**Clinical features**

- The patient may complain of the passage of large clots and/or the fetus and some products of conceptus material per vaginum.
- Depending on the extent of bleeding patient may manifest with shock (collapsed peripheral vessels, fast pulse, falling BP and cold clammy skin).
- Usually the uterine size is smaller than the stated gestational age.
- Cervix is dilated and part of the conception material may be in the cervical canal.

**Investigations**

- CBC
- Blood grouping and cross matching
- Ultrasound scan
- RFT, LFT
- Erect plain film of the abdomen, if perforation is suspected

**Treatment**

**Objectives**

- Resuscitate patient
- Evacuate the retained products of conception from the uterus
- Prevent infection with antibiotic prophylaxis
- Identify the cause of abortion, if possible
- Prevent risk of Rh isoimmunization

**Non pharmacologic**

- Digital curettage during the time of vaginal examination to decrease blood loss
- Arrange for surgical evacuation of the retained products of conception by manual vacuum aspiration (MVA) or metallic evacuation and curettage (E&C)
- Abstain from sexual intercourse for at least 2 weeks
- Counseling and psychological support of the patient
- Blood transfusion when needed

**Pharmacologic**

**IV fluids** as necessary.

**Ergometrine**, IM/IV,0.2-0.4mg stat

**Oxytocin**, IV, 20 units into 1 Lt of N/S and infuse at 30-60 drops per minute

*OR*

**Misoprostol**, rectal, 600-800micrograms two doses 4hours apart

If the woman is RH negative and husband is RH positive: Anti D Rh Immune Globulin 250-300 Units (150mg), IM, stat within 72 hours.

**Amoxicillin**, 1gm P.O., 6 hourly for 7days

**Complete Abortion**

Cessation or reduction of vaginal bleeding following heavy bleeding with passage of clots and/or the fetus and placenta.

**Clinical features**

- Usually the patient has no pain.
- The uterus is smaller than the gestational age.
- The cervix is closed and firm.

**Investigations**

- CBC
- Blood grouping and cross matching
- Ultrasound scan: to confirm empty uterine cavity

**Treatment**

**Objectives**

- Assess for and manage anaemia if present
- Investigate for the cause of abortion if possible

**Non pharmacologic**

- Counseling and psychological support of the mother

**Pharmacologic**

- Resuscitate patient if necessary
- Treat anaemia if present

- Follow up

**Septic Abortion**

This is a life threatening complication of abortion. Most often the patient gives history of interference with pregnancy under septic technique or incomplete abortion which stayed for some time without being evacuated. If not managed appropriately, this may lead to further complications such as septic shock, uterine damage, peritonitis, haemorrhage, disseminated intravascular coagulation (DIC), acute renal failure, adult respiratory distress syndrome, tetanus or gas gangrene.

**Clinical features**

- Severe lower abdominal pain**,** fever**,** vomiting**,** headache**,** offensive and bloody vaginal discharge**,** tachycardia**,** sign of peritonitis.
- If conditions worsen, patient may manifest with septic shock.

**Investigations**

- CBC
- Coagulation profile
- Blood grouping and cross matching
- Blood culture and sensitivity
- Urine culture and sensitivity
- Endo-cervical swab for culture and sensitivity
- Blood urea and electrolytes
- Chest and abdominal X-ray (to exclude foreign body, gas under the diaphragm suggesting uterine perforation)
- Abdomino-pelvic ultrasonography (for intra-abdominal and pelvic abscesses, peritonitis and gas in the pelvis)

**Treatment**

**Objectives**

- Resuscitate patient
- Treat infection
- Evacuate uterus and prevent further infection or organ damage
- Provide counseling

**Non pharmacologic**

- Evacuate the retained products of conception. Careful evacuation of the uterus must be done as risk of uterine perforation is high.
- Do gentle digital curettage followed by the instrumental curettage under general anaesthesia within 6 hours of initiation of antibiotic therapy. Extreme care is needed in order not to perforate the uterus (if it has not been perforated already).
- If there is sign of peritonitis or uterine perforation, laparotomy may be required
- Psychological support and family planning counseling.
- Blood transfusion when required

**Pharmacologic**

IV fluids as necessary.

If the gestational age is above 14weeks and the fetus is not aborted yet, **Oxytocin**, IV, 20units in 1Lt of N/S to run 50-60drops/min

**Ampicillin**, IV,1-2 g 6 hourly for 24-72 hours

*PLUS*

**Gentamicin**, IV, 80 mg 8 hourly for 24-72 hours

*PLUS*

**Metronidazole**, IV,500 mg 8 hourly for 24-72 hours

Switch over from IV to oral therapy when appropriate. Continue with gentamicin, IM or IV, 80 mg for at least 7 days. (The culture and sensitivity test results will direct the antibiotic therapy)

**Pethidine**, IM, 100 mg 4-6 hourly with Promethazine, IM, 25 mg 8-12 hourly

Tetanus prophylaxis, if there is interference with pregnancy under septic condition.

**Missed Abortion**

This refers to foetal death in-utero before 28 weeks gestation which does not show any sign of expulsion.

**Clinical features**

- There is reversal of the symptoms of pregnancy with recurrent bloody vaginal discharge**.**

- The mother fails to perceive the foetal movements (if quickening has already occurred).
- The uterus is smaller than the stated gestational age. The foetal heart beat is absent.

**Investigations**

- CBC
- Blood grouping and cross matching,
- Blood film for malaria parasites if the clinical features suggest acute febrile illness
- Blood clotting profile
- Pregnancy test
- Ultrasound scan
- Fasting Blood Sugar
- VDRL

**Treatment**

**Objectives**

- Prepare the patient for uterine evacuation
- Ensure safe uterine evacuation
- Ensure there is no DIC before attempting to evacuate the uterus
- Establish cause of foetal death if possible

**Non pharmacologic**

- First trimester (<12 weeks): Evacuation of the uterus can be accomplished by suction curettage (manual or with machine) or using the metallic curettes (E&C).
- Hysterotomy may be indicated where induction fails or is contraindicated.
- Blood transfusion when the need arises

**Pharmacologic**

**IV fluids** as necessary

**Misoprostol**, oral or vaginal, 400micrograms stat, at least 3 hours prior to suction curettage. This will facilitate curettage and prevent damage to the cervix by metallic dilatation. Misoprostol can also be used to both ripen the cervix and facilitate evacuation of the uterus.

**12-24 week gestation:**

**Misoprostol**, 200micrograms, vaginal, 12 hourly until expulsion or 400micrograms, oral, 4 hourly until expulsion

**4-12 week gestation:**

**Misoprostol**, 800micrograms, vaginal or sublingual, every 24 hours for two days

## 27. Gynaecological Disorders

**Intrauterine foetal death (>24 weeks) with previous caesarean section**

**13-17 weeks**: 200microgram 6hourly

**18-26 weeks**: 100microgram 6hourly

**27-42 weeks**: 25-50microgram 4hourly

**Induction of labour (live fetus >24 weeks)**

25-50microgram vaginally 4 hourly

## 28. Induced Abortion

This refers to the deliberate termination of pregnancy. Termination of pregnancy is requested for and done for reasons permissible by law either through a surgical procedure or by pharmacological means. The Ethiopian law permits to terminate pregnancy under the following conditions:

- In case of rape, defilement or incest
- Threat to physical and mental health of the mother
- Presence of foetal abnormality
- Mental retardation of the mother
- Minors aged under 18
- Any medical condition that endangers the life of the mother if pregnancy continues

**Treatment**

**Objectives**

- Ensure that legal requirements for termination are met
- Ensure the termination is performed safely
- Provide family planning counseling after the procedure

**Non pharmacologic**

- Pre-abortion Counseling

- Advise on the other possible options before deciding on termination.
- Explore the reasons for the abortion request to ensure that it meets the legal and medical requirements.
- Provide information of other care options and on the available methods of abortion.

**Surgical**

- 4-12 week gestation:
  - Manual Vacuum Aspiration
  - Dilatation and curettage
- 12 weeks gestation
  - Cervical ripening with misoprostol or prostaglanding E2, followed by dilatation and evacuation

**Pharmacologic**

**4-12 weeks of gestation**:

**Mifepristone**, 200mg P.O., stat followed by after 24 hours misoprostol 800 microgram, then the same dose 4 hours

**12-24 weeks gestation:**

**Misoprostol**, 400micrograms P.O., 4 hourly until expulsion

*OR*

**Mifepristone,** 200mg P.O., stat, followed by **Misoprostol** 200microgram P.O., after 24 hours

**29. Abnormal Uterine Bleeding (Aub)**

Menstruation is considered normal if the cycle comes every 21 to 35 days, the duration of bleeding is 1 to 7 days; the amount is less than 80ml and is not associated with any pain. Anything other than this is considered abnormal. Abnormal uterine bleeding includes dysfunctional uterine bleeding (DUB), i.e, uterine bleeding with no organic cause and bleeding from structural causes. Dysfunctional bleeding can be anovulatory or anovulatory. The Anovulatory variety is the commonest type (greater than 80%), usually occurring in post-menarchal and premenopausal periods. It is characteristically acyclic, unpredictable as to the onset of bleeding, and variable in the duration and amount of bleeding which sometimes the terms metrorrhagia or menometrorrhagia have been used to describe this syndrome.

Ovulatory DUB is usually associated with premenstrual symptoms such as breast tenderness, dysmenorrhea, and weight gain and regular periodicity but heavy in amount (e.g menorrhagia). Usually, it is caused by organic lesions, although a dysfunction of the corpus luteum or atrophic endometrium may be the causes. Structural causes include fibroids, polyps, endometrial carcinoma, and pregnancy complications.

**1. Dysfunctional Uterine Bleeding (DUB)**

**Causes**

- Hypothalamic dysfunction (physiologic)
- Premature ovarian failure
- Polycystic Ovarian Syndrome
- Hypo or Hyper-thyriodism
- Coagulation disorders

**Clinical features**

- The diagnosis is made by excluding all other obvious causes of abnormal uterine bleedings.

**Investigations**

- CBC, coagulation profile, pregnancy test, ultrasound, Saline Infusion Sonography, hysterosalpingiography, endometrial sample
- TSH, $T_3$, $T_4$
- Differentiate between ovulatory and anovulatory: serum progesterone, endometrial biopisy, Basal Body Temperature (BBT)
- If anovulatory: Prolactin, FSH, LH, free testeosterone, 17-hydroxprogesterone
- For advanced chronic diseases: LFT and RFT

**2. 1 Anovulatory DUB**

**Treatment**

The treatment depends on the age of the patient, her desire for contraception or fertility, and the severity and chronicity of the bleeding.

**Objectives**

- Control active bleeding
- Prevent recurrences, restoration of normal cycle
- Induce ovulation in patients desiring to conceive.

**Non pharmacologic**

- None, unless there is a strong clinical suspicion of endometrial pathology.
- If the haemoglobin level is low (less than 7gm/dl), transfuse 2 units of blood.

**Pharmacologic**

**a. Control of active bleeding:**

**First line**

**Norethisterone**, 5mg QID P.O. for 2-3 days followed by 5mg P.O. QD for ten days with or without **Medoxyprogesterone,** 10-25mg QID, P.O. until bleeding stops

**Dosage forms**: Tablet, 5mg

**Alternative**

**High dose of Combined oral contraceptive pill** (COP) 1tablet QID, for 4 days, followed 1tablet, TID for 3days, then followed 1tab BID for 2 days until the bleeding is controlled and then the standard dose of the COP one tablet/day for 21 days. If there is vomiting while taking the high dose COP, promethazine 25mg, PO or IM should be given.

**N.B.** If bleeding failed to stop despite high dose of Combined oral contraceptive pill, D&C may be required.

**b. Restoration of the cycle:**

- Combined oral contraceptive pills 1 tablet/day for 21 days for 3-4 consecutive months.
- Norethisterone 5mg/day from day 14-24 each month for three months.

**c. If fertility is desired**, ovulation induction using clomiphene citrate is one modality of treatment.

**2.2. Ovulatory DUB**

This is commonly diagnosed by the presence of clinical evidence of ovulation and is confirmed by hormone analysis and/or endometrial biopsy, Basal Body Temperature (BBT) and stretching of cervical mucus. It is usually due to follicular or luteal phase defect.

**Treatment**

**Objectives**

- Identify the underlying cause
- Prevent recurrence

**Non pharmacologic**

If there is any clinical suspicion of endometrial pathology, either of the following measures is appropriate:

- Manual (electrical) Vacuum Aspiration
- Dilatation & curettage
- Endometrial ablation
- Hysterectomy

**Pharmacologic:** Before embarking on treatment, organic causes should be ruled out beyond shadow of doubt.

**First line**

**Prostaglandin inhibitors or NSAID:** Medicines are given few days before the bleeding starts and the first three days of the bleeding.

**Ibuprofen,** 400mg 3 times /day or **Indomethacin**, 25-50mg P.O., TID

**Alternative:**

**Danazol**, 200-400mg P.O., daily for 12 weeks

| | |
|---|---|
| **ADRs:** | Nausea, dizziness, menstrual disturbance, and emotional instability |
| **C/Is:** | Pregnancy, lactation, genital tumour, cardiac, renal, or hepatic dysfunction |
| **Dosage forms:** | Capsule 100, 200mg tabs |

**Structural causes:** The treatment depends on the underlying cause.

**N.B.**

- Minor variations of normal bleeding pattern may not require evaluation, particularly in the first 2 years of menarche

- Post-menstrual spotting associated with uterine tenderness could be due to endometritis, can be treated with deoxcycline 100mg, BID for 10 days
- If there is breakthrough bleeding in women taking low dose OCP and persists for 3months, high dose COP can be tried and if the client has uterine tenderness, treat for endometritis targeting Gonorrhea and Chlamydia.
- Women on Depoprovera, if they have breakthrough bleeding, can be treated with oestrogen.
- In clients with IUCD with abnormal bleeding pattern and uterine tenderness, treatment for endometritis should be instituted or COP for one cycle can be tried. Despite these if no improvement, the IUCD should be removed.

**30. Dysmenorrhoea**

Dysmenorrhoea is excessive pain during menses. It occurs in about 50% of menstruating women. It may be primary or secondary**.** Primary Dysmenorrhoea is believed to be due to increased endometrial prostaglandin production, whereas secondary dysmenorhoea is due to outflow obstruction, pelvic tumours, infections, endometriosis etc. Dysmenorrhea in the first few years following menarche is usually primary but the secondary characteristically occurs many years after menarche.

**Clinical features**

- The pain of primary dysmenorrheal usually begins a few hours prior to or just after the onset of menstrual flow and may last as long as 48-72 hours. Thorough pelvic assessment is important to rule out organic causes.

**Investigations**

- CBC, vaginal smear, ultrasound etc

**Treatment**

**Objectives**

- Alleviate pain
- Treat underlying cause

**Primary dysmenorrhoea**

**Non pharmacologic**

- Reassurance

**Pharmacologic**

**First line**

**Prostaglandin inhibitors (NSAID)**: **Ibuprofen**, 400 mg, P.O., TID

*OR*

**Mefenamic acid**, 500mg, P.O, TID.

| | |
|---|---|
| **ADRs:** | Gastro-intestinal disturbances, hypersensitivity hearing disturbances, photosensitivity, and haematuria, Blood disorders, Stevens-Johnson syndrome |
| **C/Is:** | Allergic disorders, coagulation defects, severe Heart Failure , active gastro-intestinal ulceration or bleeding or perforation, Pregnancy, Breast-feeding, severe liver disease, renal disease |
| **Dosage forms:** | Tablet, 500mg; Dispersible tablet, 100mg |

*OR*

**Acetylsalicylic acid**, 600mg, P.O., TID for 2-days

**N.B.** The medicines have to be administered prior to the onset of menses or at the onset of pain every 6 to 8 hours for the first few days of menses. This modality of treatment should continue for 4-6 months before declaring treatment failure.

**Alternative**

**Monophasic Combined oral contraceptive pills**; if contraception is also needed

**Secondary dysmenorrhoea**

It is cyclic pain in association with underlying pelvic pathology. The pain is often begins 1-2 weeks prior to the onset of menses and persists until a few days after cessation of bleeding.

**Treatment**

Unlike primary dysmenorrhea, Non-steroidal anti-inflammatory medicines (NSAID) and oral contraceptive have limited roles. The underlying cause should be treated. The most common cause is endometriosis.

## 31. Infertility (Male And Female)

Infertility is defined as one year of unprotected intercourse without pregnancy. It could be primary or secondary. The major causes of infertility in female could be fallopian tube occlusion or anovulation. In males, it could be pre-testicular, testicular or post-testicular affecting the semen quality in terms of volume, sperm count, morphology, concentration, and motility. In sub-Saharan Africa it is estimated that 11-20% couples have difficulty conceiving. The effect may be amplified for those living in the infertility belt of Africa which stretches from Tanzania in the east to Gabon in the west.

**Causes**

- Infection:
    - STI (chamydial, gonorrhea, syphilis etc)
    - Infectious and parasitic diseases: mumps, TB, schistosomiasis
    - Post partum/abortal
- Exposure to toxic substances: arsenic, aflatoxins, pesticides, caffeine, tobacco, alcohol, heat
- Anovulation: the main cause being PCOS (75%)
- Surgery, trauma

**Clinical features**

- History of STD, features of endocrinopathies,
- History of contraception usage,
- surgical history (ovarian cyst, appendectomy, pelvic abscess, ochidopexy, repair of inguinal hernia),
- medicine intake, diet (smoking, excessive alcohol and caffeine consumption),
- galactorrhea,
- menstrual pattern (menorrhagia, intermenstrual bleeding),dysmenorrea,
- current illness,
- occupation (male)

**Investigations**

- CBC

- FBS
- Vaginal smear
- Hormone profile:
    - To evaluate ovarian reserve (serum FSH and LH in 1-3$^{rd}$ day of the menstrual cycle)
    - For ovulation evaluation: Serum progesterone, 7 days before the expected menses
    - If menstruation is irregular: TSH, $T_3$, $T_4$, Testosterone, DHEA, DHEAS, prolactin
- Post-coital tests
- Hysterosalpingography (HSG)
- Ultrasound: ovarian volume, counting ovarian follicles
- Laparoscopy: to look for endometriosis and tubal patency

**Male**: Sperm analysis, vasography, testicular biopsy, trans-rectal ultrasound, hormone assay (FSH, LH, prolactin, thyroid function tests, testosterone), post-ejaculatory urine examination for male with an ejaculatory volume < 1ml

**Treatment**

**Objectives**

- Identify the exact cause of infertility and manage it accordingly
- Give couples a realistic prognosis of treatment
- Provide information, support and counseling to the couples to cope with the stress of treatment and possible failure

**Non pharmacologic**

- Overweight or underweight should be normalized
- Stress should be alleviated
- Avoid smoking, excessive alcohol and caffeine consumption

**Pharmacologic**

**A. Female**

**Clomiphene citrate,** starting dose 50mg/day PO for five days starting from the 5th day of the menstrual cycle, and if no ovulation increase the dosage by 50mg/day up to 200mg/day over three to four treatment cycles. If possible check mid-luteal phase progesterone in each cycle for ovulation

**ADRs:** ovarian enlargement, abdominal bloating or pain, vasomotor flushes, nausea, vomiting, irritability, fatigue, headache, mastagia, allergic dermatitis, diarrhoea, weight gain, urinary frequency, constipation, reversible hair loss, multiple pregnancy, blurred vision

**C/Is:** pregnancy, liver disease, undiagnosed genital tract and breast diseases, history of hypersensitivity, ovarian failure

**Dosage forms:** Tablet, 50mg

**N.B** HCG, 5000-10,000IU IM 5days after the last clomiphene tablets may enhance ovulation

*OR*

**Metformin:** Recently metformin has been used to induce ovulation, if the cause of anovulation is PCOS Starting dose: 500mg/day for one week, if tolerated, double the dose for another one week, then 1500mg daily, gradually increase the dose to reach maximum, 2500mg/day. The treatment can continue for six months.

**N.B.** There is no need of increasing the dose if the menstrual cycle becomes regular.

**ADRs:** diarrhoea, abdominal bloating.

*OR*

**Clomiphene and metformin combined:** Women with PCOS, 90% will ovulate

*OR*

**Tamoxifen**, P.O., 20-40mg/day, from day 3 of the menstrual cycle for 5 days

**ADRs:** hot flushes; endometrial changes tumour flare; liver enzyme changes; thromboembolic events; decreased platelet count; oedema; alopecia; rash; headache; visual disturbances

**C/Is:** Pregnancy; breast-feeding.

**D/Is:** Warfarin, allopurinol, cyclosporine, delavirdine, fluconazole, gemfibrozil, ketoconazole, NSAIDs, sulfonamides,

**P/Cs:** Leukopenia, thrombocytopenia, or hyperlipidemias, chlorpromazine, miconazole, fluoxetine, quinidine, quinine,

ritonavir, erythromycin, ciprofloxacin, diclofenac, doxycycline, isoniazid, verapamil, carbamazepine, phenobarbital, phenytoin, Rifampicin, nevirapine.

**Dosage forms:** Tablet, 10mg, 20mg

*OR*

**Gonadotrophins:** Human menopausal gonadotrophins (HMG), (for women resistant to above mentioned medicines), IM, 75IUday for 14days in step-up manner.

**B. Male:**

**Non pharmacologic**

- Avoid smoking, excessive alcohol and caffeine consumption
- Avoid exposure to environmental toxic substances (arsenics, aflatoxins) and heat
- Surgical: Varicocele repair, vassal reconstructions, Intracytoplasmic sperm injection (ICSI)

**Pharmacologic**

None except in retrograde ejaculation, sympathomimetics such as imipramine and pseudoephedrine, can be tried.

## 32. Menopause And Perimenopausal Hormone Syndrome

Menopause refers to the point in time when permanent cessation of menstruation occurs usually due to loss of ovarian function. A woman is considered to be menopausal if there is no menstruation for a period of at least 12 months in the absence of pregnancy or lactation.

Menopause is associated with physical, emotional and psychological upheaval of varying intensity in the affected individual. Sixty percent of menopausal women may be asymptomatic. To alleviate symptoms and prevent osteoporosis and other cardiovascular problems, Hormone Replacement Therapy (HRT) used to be recommended for every post menopausal woman. However, following the release of Women Health Initiative (WHI) study result in 2002, many societies and health organizations consider HRT as dangerous and the routine use of HRT was disrupted. Recently, several high ranking Obs/Gyn specialists and the International Menopausal Society (IMS) re-affirmed and re-legitimized the use of HRT for at least 5years in healthy post-menopausal women less than 60 years of age.

**Causes**

- Natural onset due to the age of the individual
- Due to surgical removal of the ovaries (bilateral oophorectomy)
- Pelvic irradiation
- Premature ovarian failure due infection and other causes
- Pituitary damage from primary post-partum haemorrhage (PPH) (Sheehan's syndrome)
- Cytotoxic (anticancer) therapy

**Clinical features**

- Hot flushes (heat or burning in the face, neck and chest with resultant sweating).
- The flushes may be associated with palpitations, faintness, dizziness, fatigue, weakness, emotional and psychological problems which include: mood changes, depression, anxiety, nervousness, irritability, loss of libido.
- Atrophic changes in the genital tract may give rise to the following: increased frequency of micturition and dysuria, vaginal dryness and dyspareunia.

**Investigations**

- Hormone tests if available (serum LH, FSH, estradiol)
- Routine investigations e.g. CBC, blood glucose, lipid profile
- X-ray to evaluate bone density
- Investigation to exclude pregnancy

**Treatment**

**Objectives**

- Control symptoms e.g. severe hot flushes, atrophic vaginitis and recurrent cystitis
- Prevent osteoporosis especially in individuals with premature menopause
- Prevent cardiovascular morbidity and mortality

**Non Pharmacologic**

- Counseling and reassurance.

- Encourage active lifestyles, exercise and regular physical checkups for common medical problems.
- Avoid hot weather conditions
- Light clothing, cold shower
- Balanced diet

**33. Cological Disorders**

**Pharmacologic**

**A. In women with intact uterus:**

HRT can be given as sequentially opposed or continuous combined preparations. The continuous preparations have the advantage of less breakthrough bleeding, but should only be commenced once the woman has been stable on sequentially opposed therapy for a year. Treatment should last 5 years but should be reviewed annually.

**1. Sequentially opposed HRT**

**Conjugated equine oestrogen**, 0.3-0.625mg P.O., daily for 21 days

*PLUS*

**Medroxyprogesterone acetate**, MPA 5-10mg P.O., daily

*OR*

**Norethisterone acetate**, oral, 1mg daily from day 11-21 followed by no therapy from day 22-28

*OR*

**Estradiol valerate**, oral, 1-2mg daily for 11days

*PLUS*

**MPA**, 10mg P.O., daily from day 11-21 followed by no therapy from day 22-28

**2. Continuous combined therapy**

**First line**

**Conjugated equine oestrogen**, 0.3-0.625mg P.O.,

*PLUS*

**MPA**, 2.5-5mg P.O., daily

**Alternative**

**Estradiol valerate**, 0.5-1mg P.O.,

*PLUS*

**Norethisterone acetate**, 0.5-1mg P.O., daily

**C/Is:** Breast cancer, Endometrial cancer, Thrombo-embolism phenomena, Coronary heart disease, Active liver disease

**B. In women with previous hysterectomy:**

Conjugated oestrogens 0.625 microgram daily**.** Women with intact uteruses should never be given oestrogen alone.

**N.B.**

- Start at the lowest dose of HRT to alleviate symptoms. The need to continue HRT should be reviewed annually. If HRT is continued, it should be gradually tapered because abrupt discontinuation of oestrogen may cause recurrence menopausal symptoms.
- A mammogram should be done once every two years.
- Abnormal vaginal bleeding requires evaluation by a specialist to exclude endometrial cancers.

**Refer**

- Refer cases with osteoporosis or severe unremitting symptoms.
- Women with premature ovarian failure
- Women with post-menopausal vaginal bleeding

## 34. Carcinoma Of The Cervix

Carcinoma of the cervix is the commonest form of female genital cancer in the developing countries. Though common, it is preventable and curable if detected early. In developed countries, the incidence of this disease has fallen considerably owing to regular screening procedures using the Pap smear. In the absence of an effective screening system in Ethiopia, most cases seek clinical care very late and thus the only modality of treatment left for these patients is radiation.

**Causes**

- Human papilloma virus, the high oncogenic types are implicated in the causation of the disease. There are more than 18 high oncogenic types. The other associated factors include:
    - Associated risk factors
    - Sexual promiscuity
    - First coitus at early age, multiple child births
    - Infections with Herpes Simplex Hominis type II, HIV
    - Smoking
    - Low socio-economic status
    - Family history
    - Immunosuppression

**Clinical features**

- Some are asymptomatic in the early stage of the disease (diagnosed on routine screening or assessment during antenatal care, family planning etc.)
- Commonly patients present with abnormal vaginal bleeding after sexual intercourse, post menopausal bleeding, and increased vaginal discharge.
- In early cases there will be erosion of cervix or changes of chronic cervicitis but in advanced cases ulcerative or fungating cervical lesion is observed on speculum examination.

**Investigations**

- Cervical biopsy
- CBC
- Renal function test
- Serum uric acid
- Chest radiograph

- Intravenous urography
- CT Scan and or Magnetic Resonance Imaging (to detect aortic nodes and metastases to the lungs and liver)
- Examination Under Anaesthesia for clinical staging

**Prevention**

**Vaccine:** Recently, a quadrivalent vaccine against 16,18,6 and 11(Gardasil) from MSD and bivalent vaccine against 16 and 18 (Cervarix) from GSK has been developed and made available to the market. These vaccines are 70-80% effective in preventive cervical cancer.

**Screening:** Pap smear, VIA, VILI and colposcopy

**Treatment**

**Objectives**

- Treat central tumour
- Treat areas of tumour spread with the aim of eradicating the disease
- Alleviate symptoms in advanced cases

**Non pharmacologic**

The treatment modalities for carcinoma of the cervix are:

- Surgery, the main stay treatment
- Radiotherapy: as treatment or palliation to arrest vaginal bleeding or alleviate pain
- A combination of surgery and radiotherapy
- Adequate nutrition
- Correction of anaemia
- For advanced terminal cases: provide emotional and psychological support

**1. Early disease**

- **Stage IAI** (depth of stromal invasive less than 3mm with horizontal expansion of 7mm) simple conization of the cervix may be enough if the patient desires fertility and provided surgical margins are free of cancer or extrafascial hysterectomy if childbearing has been completed. If there is lympho-vascular invasion more aggressive treatment is appropriate.

- **Stage IA2** (depth of invasion 3-5mm with 7mm horizontal spread) requires extensive surgery (modified radical hysterectomy with pelvic lymphadenoctomy)

**2. Overt disease (Stage IB and IIA)**

Radical hysterectomy with pelvic and para-aortic lymphadenoctomy.

**3. Advanced disease (Stage IIB to IV)**

The modality of treatment is radiotherapy, with or without chemotherapy. Currently, in USA the standard treatment is to give weekly cisplatin 1mg/kg during radiation therapy.

**Pharmacologic**

**Neoadjuvant chemotherapy**

**Cisplatin**, 1mg/kg, IV, diluted in 1Lt N/S over 24hours weekly for 3 weeks

If given before surgery or radiation, patient will have better survival rate.

**Palliative treatment**

Patients with end-stage cervical cancer may present with different clinical presentations such as pain from bony metastasis, respiratory distress from lung metastasis and renal failure secondary to tumour growth.

**Palliative chemotherapy:** A combination of cisplatin and paclitaxel has a better response rate

**Pain management:** Follow the WHO ladder approach: Start with **Non-steriodal anti-inflammatory medicines (NSAIDs)** or **the newer cyclo-oxygenase-2 (COX-2) inhibitors.** If the patient fails to respond to these agents, proceed to second line of medicines which are opioids such morphine.

Respiratory distress: **Oxygen support** and withhold toxic medicines

Renal failure: **Percutaneous nephrostomies**

**Refer:** All patients must be referred to a specialist for evaluation and decide on mode of treatment. The treatment of carcinoma of the cervix is best done by a specialist who has experience in cancer management.

## 35. Gestational Trophoblastic Diseases (Gtd)

GTD comprises a spectrum of neoplastic conditions in women derived from the placenta. The term GTD includes hydatidform mole (complete mole &partial mole) invasive mole, gestational choriocarcinoma, and placental trophoblastic tumour (PTT), while Gestational

Trophoblastic Neoplasia (GTN) refers specifically to forms with the potential for tissue invasion and metastasis which includes invasive mole, choriocarcinoma, PTT and post molar trophoblastic diseases. GTN is recognized today as the most curable gynecologic malignancies.

The precise incidence of molar pregnancy is not known, but studies indicate the incidence is high in the Far East (as much as 1 in 500 pregnancies). The incidence is related to age and it very common in both extremes of life in younger than 15 and older than 40. Patients with prior history of molar pregnancy have an increased risk of trophoblastic disease.

**Classes**

- Hydatidform mole (Complete mole and Partial mole)
- Invasive mole
- Choriocarcinoma.
- Placental Trophoblastic Tumour (PTT)

**Clinical features**

- The classic presentation includes irregular vaginal bleeding, hyperemesis, execessive uterine enlargement, expulsion of vesicles and failed early pregnancy.
- Rarer presentations include hyperthyroidism, early onset pre-eclampsia or abdominal distension due to theca lutein cysts.
- Very rarely, women can present with acute respiratory failure or neurological symptoms such as seizures; these are likely to be due to metastatic disease.

**Investigations**

- Ultrasound: snow-storm appearance is observed complete mole and in partial mole there will be cystic spaces in the placenta and transverse to antro-posterior diameter of gestational sac is greater than 1.5
- Serum or urine hCG
- Histological examination of the tissue removed
- Thyroid function tests (TSH,$T_3$,$T_4$)
- Coagulation profile (PT,PTT, INR)
- CBC
- Renal function test (urea, creatinine)
- Liver function test
- Blood group and cross-match

**Treatment**

**Objective**

- Resuscitate and stabilize the patient
- Early detection of persistent mole and manage appropriately
- Institute chemotherapy using the FIGO 2000 risk scoring system

**Non pharmacologic**

- If there is heavy bleeding resuscitate the patient
- Surgical evacuation of the uterus (suction curettage is the preferred method)
- Hysterectomy, if the woman has completed her family. This may eliminate local invasion but not distant metastasis.
- If there is sign of pulmonary insufficiency: Oxygen and cardiopulmonary support

**Pharmacologic**

- Medical evacuation using uterotonic is not recommended, because it increases blood loss, increases risk for malignant transformation, potential risk for embolization and dissemination of trophoblastic tissue through the venous system. Even if the woman is experiencing significant bleeding prior to evacuation, surgical evacuation should be expedited and the need for oxytocin infusion weighed up against the risk of tumour embolization.
- Using of mifepristone and misoprostol for evacuation should be avoided because these agents increase the sensitivity of the uterus for prostaglandins.
- If there is sign of hyperthyroidism, it is important to administer a beta-adrenergic antagonist before the induction of anesthesia for surgical evacuation because of the risk of precipitated thyroid storm.

**Proporanolol**, IV, 40mg BID

**Post-molar surveillance**

- After evacuation of the molar tissue or hysterectomy with mole in situ, weekly determinations of βhCG until the results are within normal limit for 3 consecutive weeks, then at monthly intervals for 6 months.
- FIGO criteria for the diagnosis of post-molar GTD
    - Four values or more of hCG documenting plateau (10%of hCG value) over at least 3 weeks: days 1, 7, 14, 21

- A rise of hCG of 10% or greater for 3 values or longer over at least 2 weeks: days 1, 7, 14
- The presence of histologic choriocarcinoma
- Persistence of hCG 6 months after molar evacuation

**Risk for post-molar gestational trophoblastic neoplasia**

- Increase serum hCG level
- Uterine size larger than the expected by date
- Theca-lutein cysts
- Increasing maternal age

**Chemotherapy**

The need for chemotherapy following complete mole is 15% and 0.5% for partial mole. Women are assessed before chemotherapy is initiated using the FIGO 2000 risk scoring system.

- Women with score ≤6 are at low risk category and treated with a single agent:

**Metotrixate**, 1mg.kg IM/P.O. days 1, 3, 5, 7 alternating with Folinic acid 0.1mg/kg days 2, 4, 6, 8 (repeated every 14days)

**N.B.** Women with score ≥7 are at high risk category and treated with multiple agent chemotherapeutic agents that include:

**Table 84 - EMA-CO regimen for high risk malignant GTD**

| Day | Agent | Dose and route |
|---|---|---|
| **1** | Etoposide | 100mg/$m^2$ IV infusion over 30minutes |
| | Methotrexate, | 100mg/$m^2$ IV bolus |
| | D actinomycin | 350mg/$m^2$ IV bolus |
| **2** | Etoposide | 100mg/$m^2$ IV infusion over 30minutes |
| | D actinomycin | 350mg/$m^2$ IV bolus |
| | Folinic acid | – 15mg, Po/IM Q 12hourly 4doses, |

| | | |
|---|---|---|
| | | 24hours after methoterixate bolus |
| **8** | Cyclophosphamide | 600mg/$m^{2,}$ IV infusion over 30minutes |
| | Vincristine, | 1mg/$m^2$, IV bolus |
| **15** | Begin next cycle | |

**Toxicities:** Neutropenia and thrombocytopenia are the most common toxicities

- Treatment should continue, in all cases, until the hCG level has returned to normal and then for a further six consecutive weeks
- The cure rate for low risk is 100% and for high risk is 95%.
- PTT is less sensitive to chemotherapy and requires surgery

**Table 85 - FIGO scoring system**

| **FIGO scoring** | **0** | **1** | **2** | **3** |
|---|---|---|---|---|
| Age | <40 | >40 | | |
| Antecedent pregnancy | Mole | Abortion | Term | |
| Interval from end index pregnancy to treatment(months) | <4 | 4-<7 | 7->13 | ≥13 |
| Pre-treatment serum hCG | $<10^3$ | $0^3$-$<10^4$ | $10^4$-$<10^5$ | $\geq 10^5$ |
| Largest tumour size, including uterus(cm) | <3 | 3-<5 | ≥5 | |
| Site of metastasis | Lung | Spleen, Kidneys | Gastrointestinal | Liver, Brain |
| Number of metastasis | - | 1-4 | 5-8 | ≥8 |
| Previous failed chemotherapy | - | - | Single | 2 or more |

**N.B.**

- Histological examination of all failed product of conception is recommended to exclude GTN
- A urinary pregnancy test should be performed in all cases of persistent or irregular vaginal bleeding after pregnancy events
- Women who undergo chemotherapy are advised not to conceive for one year after completion of treatment
- Women with GTD should be advised to use barrier methods of contraception until hCG level normalizes. Once hCG is normalized, Combined oral contraceptive pill can be used.
- IUCD should not be used until hCG levels are normal to reduce the risk of uterine perforation
- Anti-D prophylaxis: Because of the poor vascularization of the chorionic villi and absence of the anti-D antigen in complete mole, anti-D gammaglobulin is not required after evacuation of complete mole but should be given following partial mole.
- Women who receive chemotherapy for GTN are likely to have an earlier menopause.

## 36. Hormonal Contraceptives

Contraceptives include different kinds of methods used to prevent the occurrence of pregnancy. The variety of contraceptive methods includes, natural methods, barrier methods, intrauterine contraceptive devices, hormonal and permanent surgical methods. Hormonal contraceptives are one of the most effective methods that are prescribed to a client based on informed choice.

### 1. Combined Oral Contraceptives (COC)

A group of contraceptive medications composed of synthetic oestrogens and progesterone in different doses; 20mcg, 30mcg or 50mcg of oestrogen and 0.15-1mg of progesterone in each tablet. They act primarily by inhibiting ovulation, and also by making the cervical mucus less favourable to sperm penetration and rendering the endometrium more atrophic.

**First line**

**Levonorgesterol+ethnylestradiol** and iron, in starting from the first day of menses

**ADRs:** Gastrointestinal disturbance, loss of libido, weight gain etc.

**C/Is:** Pregnancy, cardiac illness, thrombo-embolic conditions, genital tract malignancies, Hepatic dysfunction, Migraine headaches.

**D/Is:** Care should be taken while prescribing anticonvulsants, hypnotics, antibiotics and antacids to women using COC, since these medicines may reduce the effectiveness of COC. Combined Oral Contraceptives (COC) may also reduce the effectiveness of medicines like anti-convulsants, anti-coagulants, anti-depressants, steroids, sedatives and hypoglycemic agents.

**Dosage forms:** levonorgesterol+ethnylestradiol and iron: Tablet, 0.15mg + 0.03mg; 0.25mg + 0.05mg; 0.5mg + 0.05mg; 0.3mg + 0.03mg

**Alternative**

**Norethindrone + Ethnylestradiol**, 0.5mg + 0.035mg /day starting from the first day of menses

**Dosage forms:** Norethindrone + ethnylestradiol: Tablet, 0.5mg + 0.035mg

*OR*

**Norethindrone + Mestranol**, 1mg + 0.05mg /day starting from the first day of menses

**Dosage forms:** Norethindrone + mestranol: Tablet, 1mg + 0.05mg

**2. Progesterone Only Contraceptives (POP)**

This is indicated whenever there is contraindication for oestrogen as in lactating mothers, Diabetics and Hypertensive patients. However, it is less effective compared with COC.

**Orals**

**Lynestrenol**, 0.5 mg/day

**ADRs:** Irregular vaginal bleeding, headache, mood changes, weight changes, acne, functional ovarian cysts

**C/Is:** Pregnancy, genital malignancies, cardiovascular diseases, hepatic disease

**Dosage form:** Tablet, 0.5mg,

**Injectables**

**Medroxyprogesterone acetate**, 150 mg deep IM injection within the first 5 days of the cycle to be repeated every three months.

**ADRs:** As indicated for the POPs. There is also a delay in return of fertility

**Dosage forms:** injection (aqueous suspension), 150 mg/ml in 1 ml vial

**Implants**

**Levonorgesterel** in six silastic capsules implanted in the left upper arm under local anesthesia, effective up to five years.

**ADRs:** As indicated for the POPs.

**Dosage forms:** Levonorgesterel 36mg/implant capsule of 6 implants Jadelle A two-rod subdermal Levonorgesterol implant (Jadelle®) five years of use. Each rod is 0.25cm in diameter, 4.3cm long,

**Dosage:** Levonorgesterel 75mg/implant of two implants. **Implanon** is a single-rod progestin implant used for contraception. The 40 mm by 2mm semi-rigid rod is made of plastic (ethylene vinyl acetate) in which crystals of the progestin are suspended.

**Dosage forms:** Contraception is provided by slow release of 68 mg of the progestin etonogestrel

### 3. Emergency contraception (EC)

Contraception aimed at preventing pregnancy after unplanned sexual exposure in a woman who is not on regular contraception. EC cannot be used as a regular method of contraception.

**First line**

**Levonorgesterol**, two 0.75mg tablets to be taken 12 hours apart within 72 hours unplanned sexual exposure.

*OR*

**Combined oral contraceptive pill (COC) with 50microgram of oestrogen**, 2 tabs BID within 72hours of unplanned sexual exposure for 2doses.

*OR*

**Combined oral contraceptive pill (COC) with 35microgram of oestrogen**, 4 tabs BID within 72 hours unplanned sexual exposure for two doses

**ADRs:** menstrual disturbance

**C/Is:** As in COC, POP

**Alternative**

**IUD:** This would be effective if inserted within five days of unplanned exposure, after ruling out the existence of infection.

## 37. Sexual Assault

Sexual assault is defined as any sexual act performed on another person without consent. Physician evaluating the victim of sexual assault should aim at providing adequate medical care and collect evidence. Rape is the most common reported sexual assault.

**Clinical features**

- History and physical examination

**Investigations**

- Identification of spermatozoa from specimen over the genitalia or high vaginal swab.
- Tests for chlamydia and gonorrhea
- Wet mount for trichomonas.
- The wet mount can also be examined for evidence of bacterial vaginosis and candidiasis.
- Serum testing for HIV infection, hepatitis, and syphilis
- Pregnancy testing should be done for women of childbearing age

**Treatment**

**Objectives**

- Medical or surgical treatment of acute injury.
- Screen for STI, HIV, Hepatitis virus B infection and pregnancy at initial visit, repeat screening for HIV, HbsAg at three and six months.
- Prevention of STI.
- Prevention of pregnancy
- Rehabilitation
- Medical recording should be meticulous and management approach should be multidisciplinary

**Non pharmacologic**

- Rehabilitation: counseling and psychological support.
- Surgical repair of physically injured parts of the body

**Pharmacologic**

**1. Treatment of infection** such as gonococcal, trichomonas and chlamydial **Ceftriaxone**, 250 mg IM in single dose

*PLUS*

**Metronidazole**, 2gm orally in single dose,

*PLUS*

**Doxycycline**, 100mg P.O., BID for 7 days

**In Child Abuse**

**Ceftriaxone**, 125-250mg IM

*OR*

**Erythromycin**, 250mg P.O., TID seven days

**2. Prevention of Pregnancy:** provide emergency contraception, within 72 hours after exposure

**Levonorgesterol** two 0.75mg tablets to be taken 12 hours apart.

**Combined oral contraceptive pills with 50-mcg oestrogen,** two tabs 12 hours apart for two doses.

**Combined oral contraceptive pills with 30-mcg oestrogen,** four tabs 12 hours apart for two doses.

**IUD** insertion up to 5 days following exposure

**N.B.** Screen for infection and pregnancy before inserting IUD

**3. Post Exposure Prophylaxis (PEP) for prevetion of HIV infection**

# ANNEXES

## ANNEX 1: NEONATAL RESUSCITATION

Most episodes of birth asphyxia can be anticipated based on high risk antepartum and intapartum factors. For effective resuscitation, it is important to anticipate the need for resuscitation and prepare equipment and personnel. Around 5-10% of normal births require some support to initiate breathing. Antepartum factors that call attention to prepare for resuscitation include:

- Maternal diabetes
- Pregnancy induced hypertension
- Maternal chronic illness
- Previous Rh-sensitization124
- Polyhydramnios or oligohydramnios
- Maternal infection
- Poor obstetric history including difficult or operative delivery, abortion, still births, low birth weight babies, developmental defects etc.
- Multiple gestation and post-term gestation
- Maternal medicine treatment like reserpine, lithium carbonate, diazepam etc.
- Maternal under-nutrition (height < 145cm, weight < 40kg)
- Maternal anaemia, Hgb < 8gm%
- Maternal age (<20 years or > 35 years).

The intrapartum factors include:

- Elective or emergency cesarian section
- Abnormal presentation
- Premature labor and precipitous labor
- Rupture of membrane more than 24 hours prior to delivery
- Foul smelling amniotic fluid
- Prolonged labor greater than 24 hours or prolonged 2$^{nd}$ stage of labour greater than 2 hours
- Foetal distress of whatever cause
- Use of general anesthesia
- Narcotics administered to the mother within 4 hours of delivery

- Meconium stained amniotic fluid
- Prolapsed cord
- Antepartum haemorrhage

**Preparation for resuscitation**

For normal term deliveries, a trained person, such as a midwife or nurse, should be capable of at least providing Bag and Mask ventilation. A radiant warmer or simple room heater, preheated mattress, dry clothes should be ready for use. All resuscitation equipment should also be immediately available and in working order. When asphyxia is anticipated, trained health workers capable of intubating the baby (e.g. pediatrician) should attend the delivery. If pediatrician is not available, an obstetrician or a general practitioner who is trained to intubate the newborn baby should attend the delivery. All equipment should be ready for use. Equipment and medicines that need to be ready include:

- Radiant warmer, sterile sheets
- Suction catheters
- Suction machine
- Infant resuscitation bag
- Appropriate size face-masks
- Laryngoscope with blade
- Endotracheal tube (2.5, 3.0, 3.5, and 4.0)
- Scissors, adhesive tape, gloves and stethoscope
- Syringes of different sizes
- Needles
- Alcohol and iodine
- Umbilical catheters of 5F to 8F
- Feeding tubes
- IV canula (24G) and 3-way connectors, if available

Other equipment/medicines may be needed based on the specific condition and situation of the newborn.

**Initial steps of neonatal resuscitation**

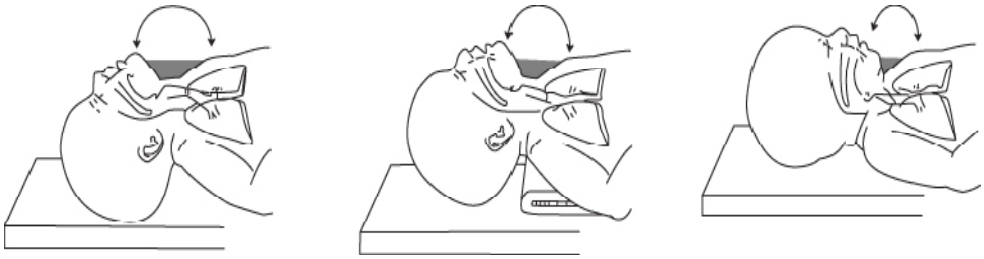
For most normal deliveries, all that is required is Essential Newborn Care (ENC); drying, warming, cord care, eye care and initiation of breast milk within the 1$^{st}$ one hour of life.

In every case of neonatal resuscitation, remember that a delay or ineffective resuscitation can lead to an increased chance of brain damage and make resuscitation more difficult.

**Procedures of Initial steps of resuscitation:**

**Open airway:**

- Place on back in horizontal position with neck slightly extended (may use shoulder roll). Both hyperextension and under-extension of the neck can compromise air entry.



**hyperextended** **slightly extended** **flexed**

- Suction mouth, then nose
- Start bag and mask ventilation

**Bag and Mask ventilation**

**Indications**

1. No spontaneous breathing at all
2. Gasping respiration
3. Recurrent apnea or irregular breathing

**Contraindication to bag and mask ventilation**

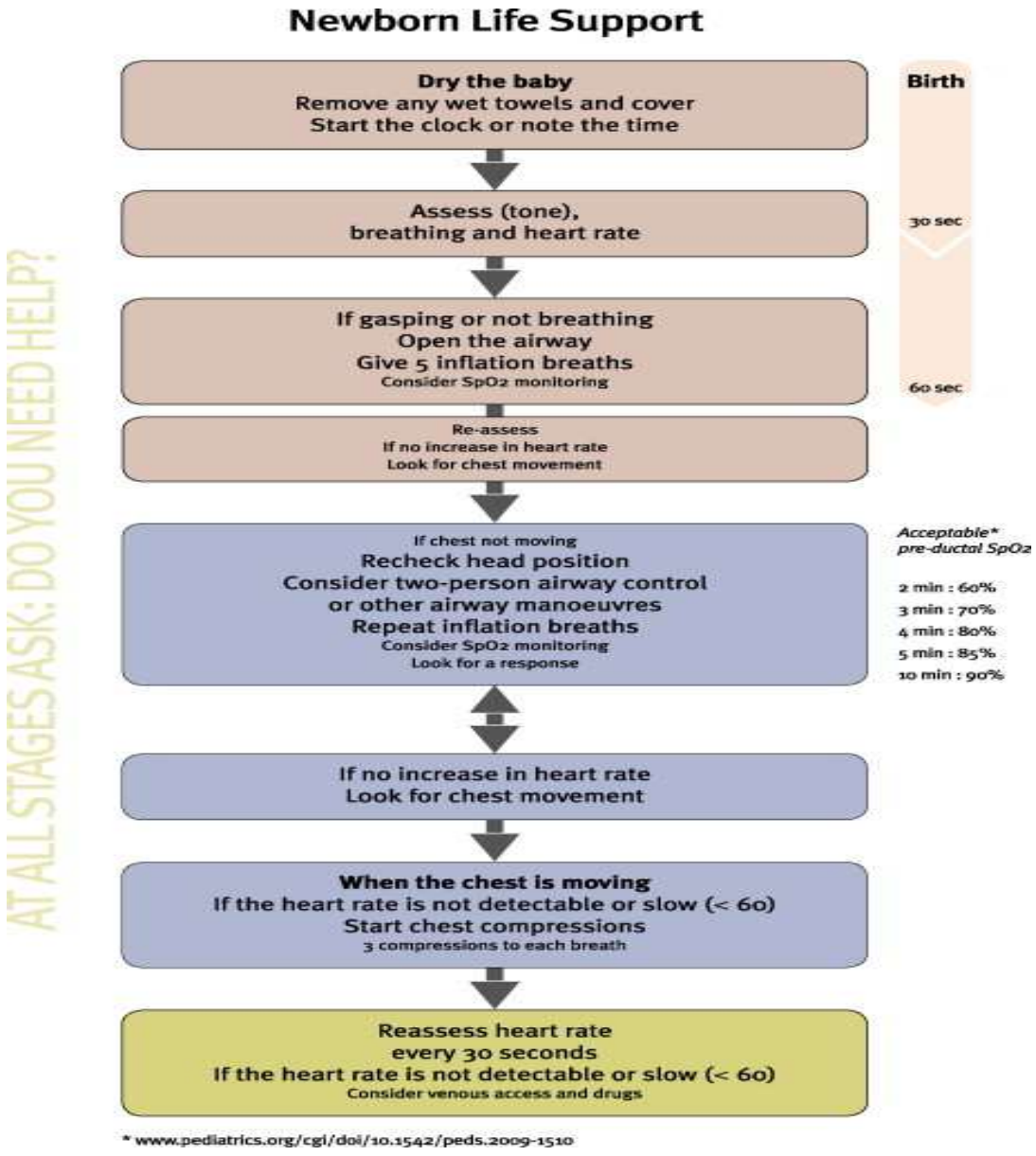
1. Diaphragmatic hernia
2. Baby born with thick meconium stained liquor

**Cautions:**

- Select the proper size mask, which should cover from the tip of the chin to the nose in an air tight manner
- Ensure neck is slightly extended and there are no secretions
- If bag and mask ventilation is given for > 2 minutes, insert and oro-gastric tube

- If HR>100bpm and respiratory efforts are good, stop ventilation and provide free flow oxygen. Continue monitoring HR, respiration and color.
- If HR is 60-100bpm and increasing, continue ventilation
- If HR is 60-100 and not increasing, continue ventilation and start chest compression.
- If HR < 60bpm, continue ventilation and start chest compression

**Figure 7 - Algorithm for neonatal resuscitation**



**Adrenaline**

**Indication:**

- Heart rate < 80bpm after 30 seconds of chest compression along with positive pressure ventilation with 100% oxygen
- If heart rate is zero

Dose: 0.1 – 0.3ml/kg of 1:10,000 solutions

Route: Intravenous or intra-tracheal. Give as rapid as possible. After 30 seconds of giving adrenaline, check the heart rate. If the heart rate is still <100bpm, consider repeating adrenaline.

## ANNEX 2: RECOMMENDED IMMUNIZATION SCHEDULE

**Table 86- Recommended schedule for immunization according to EPI program**

| Age | Vaccination |
|---|---|
| Birth | BCG<br>OPV-0 |
| 6 weeks | OPV-1<br>DPT1-HBV1-Hib1 (Pentavalent) |
| 10 weeks | OPV-2<br>DPT2-HBV2-Hib2 (Pentavalent) |
| 14 weeks | OPV-3<br>DPT3-HBV3-Hib3 (Pentavalent) |
| 9 months | Measles |

**Table 87 - Recommended schedule of immunization for children attending clinic at later age but before 5 years**

| Age | Vaccination |
|---|---|
| First visit | BCG if Mantoux test is negative<br>OPV-1<br>DPT1-HBV1-Hib1 (Pentavalent) |
| Second visit (after one month) | OPV2<br>DPT2-HBV2-Hib2 (Pentavalent) |
| Third visit (after one month) | OPV-3<br>DPT3-HBV3-Hib3 (Pentavalent)<br>Measles |

**Table 88 - Hepatitis B vaccine doses**

| Vaccine | Type of vaccine | Route of administration | Adverse reaction |
|---|---|---|---|
| **BCG** | Life attenuated | Intradermal | BCGioma |
| **DPT-HBV-Hib (Pentavalent)** | Toxoid (DT)<br>Inactivated bacteria (P)<br>Protein conjugated polysaccharide (Hib)<br>Recombinant product (HBV) | IM | Fever, anaphylaxis, crying, & shock |
| **OPV** | Life attenuated virus | Oral | Paralysis |
| **Measles** | Life attenuated virus | Subcutaneous | Fever |

Engrix B 10 microgram is also available and three doses are recommended (at birth, at one month and at six months of age). Booster dose is given after 10 years.

## ANNEX 3: FEEDING PROBLEMS

**Feeding of normal baby:**

The mother should be instructed to start feeding the baby within one to two hours after delivery. The first feed should be the breast milk and there is no need for any test feed with water or dextrose. The first few feeds should be supervised and records of feeds should be documented.

**Feeding of a preterm, small for date (SGA) and infants of diabetic mothers (IDM):** Infants less than 1500 grams should receive all the fluids and calories intravenously for the first 24 hours. SGA and IDM babies should be started feeding by one hour of age, First few feeds may be given by NG tube and they should be fed at least two hourly if sucking is poor. Once sucking is well established and blood sugar is normal these babies should be given to the mother for supervised breast feeding.

**Feeding of term asphyxiated infants**:

Mildly asphyxiated infants should feed like any healthy baby but must be closely supervised for the first 12 hours. Babies with severe asphyxia should be started with 2/3 maintenance IV fluids and strict intake records should be maintained routinely.

**Evidence for adequate nutrition**

Weight gain should be 20–30g/kg/day for premature infants and 10g/kg/day for full term infants

**Adequate growth requires**:

100-120kcal/kg/day in term infants

115-130kcal/kg/day for preterm infants

150kcal/kg/day for very low birth weight infants

## ANNEX 4: FLUID AND ELECTROLYTE

Normal maintenance requirements (volume of fluid/kg/day)

| | |
|---|---|
| Day 1 | 60 m1/kg/day |
| Day 2 | 80 m1/kg/day |
| Day 3 | 100 m1/kg/day |
| Day 4 | 120 m1/kg/day |
| Day 5 | 140 m1/kg/day |
| Day 6 & above | 150 m1/kg/day |

Additional allowance:

Increase insensible water loss:

a. Radiant warmer 20 m1 /kg /day

b. Photo therapy 20 m1 /kg /day

c. Increase body temperature 10-20 m1 /kg/day

Increase loss of water from other routes:

Example: neonatal entrocolitis, GI aspirates, diarrhoea. The loss in the above conditions are variable, they should be replaced volume for volume.

Stomach contents should be replaced with half saline with KCL loss. Small intestinal contents should be replaced with Normal saline and KCL.

## ANNEX 5: KANGAROO MOTHER CARE

Kangaroo Mother Care (KMC) is defined as early, prolonged and continuous skin to skin contact between a mother and her low birth weight infants (LBWI), both in hospital and after early discharge until at least the $40^{th}$ week of postnatal gestational age. KMC does not need sophisticated equipment, and for its simplicity it can be applied almost everywhere including peripheral hospitals. Kangaroo Mother Care also contributes to the humanization of neonatal care and the containment of cost, for which reason it may also be attractive for neonatal units in high-income countries.

Kangaroo care a program of skin-to-skin contact between mother (or any family member) and a LBWI is part of the revolution in the care of premature infants. Since its first description in 1983 in Bogota, Colombia, KMC has drawn the attention of international agencies and the scientific community leading to a publication of more than 200 papers and abstracts.

The multi center study including the neonatal unit of Addis Ababa, Ethiopia showed that LBWI in KMC had better growth, early discharge from hospital, lower cost, was acceptable by both hospital staff and mothers when compared to the conventional method of care. KMC is not only feasible but also easily grasped by the hospital staff and accepted by the community. The feasibility of the KMC is also testified by the growing number of reported experiences and by its inclusion in national guidelines for perinatal care. The neonatal unit of Tikur Anbessa hospital also uses KMC as a routine care for all babies weighing less than 2000 grams since 1997.

The benefits of Kangaroo Mother Care: Many studies showed that Kangaroo Mother Care offers the preterm infants many physical and emotional benefits, which includes:

- A stable heart rate
- More regular breathing
- Improve dispersion of oxygen throughout the body

- Prevention of cold stress and also warming babies who are already in cold stress, Kangaroo transportation where transport incubators are not there to keep the warm chain
- Longer period of sleep (during which the brain matures)
- More rapid weight gain and earlier discharge from hospital
- Reduction of purposeless activity which simply burns calories at the expense of infants growth and health
- Decreased crying
- Opportunities to breast feed and enjoy all the healthful benefits of breast milk
- Earlier bonding

The KMC works so beautifully because of three factors affecting the infant:

1. It creates conditions similar to those with which the infant had become familiar in utero, such as the proximity of the mother's heart beat sounds and her voice coupled with the gentle rhythmic rocking of her breathing
2. It provides containment and allows for flexion and prevent heat loss and provides heat from skin to skin contact
3. Protects the infant and offers a reprieve from the stressful elements of NICU

**When to Discharge from Kangaroo position:**

The decision of discharging from Kangaroo position is made by the baby itself (at about the $40^{th}$ week (gestational age + postnatal age) and weight of about 2000 grams. When the baby is restless and the mother can no longer maintain the Kangaroo position, it is time to take the baby out of the kangaroo "pouch".

## ANNEX 6: WHO CLINICAL STAGING OF HIV/AIDS FOR CHILDREN [Revised 2006]

(For the purpose of WHO staging system, children are defined as individuals aged < 15 years)

**Clinical stage 1**

- Asymptomatic
- Persistent generalized lymphadenopathy

**Clinical stage 2**

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infections
- Extensive molluscum contagiosum
- Fungal nail infections
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections (Otitis media, otorrhoea, sinusitis or tonsillitis)

**Clinical stage 3**

- Unexplained[a] moderate malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhoea (14 days or more)
- Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than one month)
- Persistent oral candidiasis (after the first 6 – 8 weeks of life)
- Oral hairy leukoplakia
- Acute ulcerating gingivitis or periodontitis
- Lymph node tuberculosis
- Pulmonary tuberculosis
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis (LIP)
- Chronic HIV – associated lung disease including Bronchoectasis
- Unexplained anaemia (<8g/dl), neutropenia (<0.5 X $10^9$ per liter) and/or chronic thrombocytopenia (<50 X $10^9$ per liter)

**Clinical stage 4**[b]

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis carinii pneumonia
- Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection or meningitis but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month duration or visceral at any site)
- Extra pulmonary tuberculosis
- Kaposi sarcoma
- Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Central nervous system toxoplasmosis (after one month of life)

- HIV encephalopathy
- Cytomegalovirus infection: retinitis or cytomegalovirus infection affecting another organ, with onset at age older than one month.
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated non – tuberculous mycobacterial infection
- Cerebral or B cell non – Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- Symptomatic HIV – associated nephropathy or HIV – associated cardiomyopathy

a unexplained refers to where the condition is not explained by other causes.

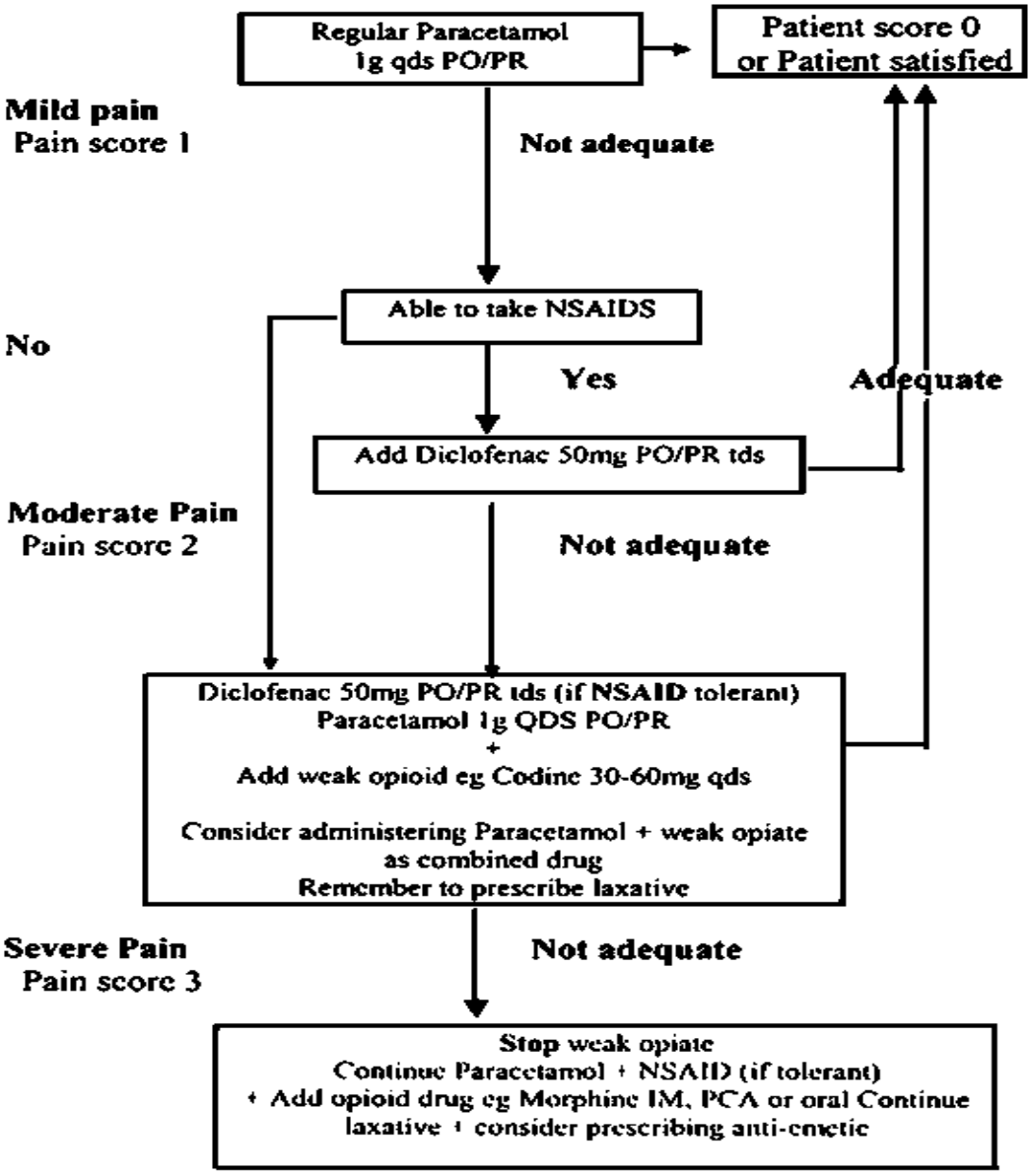
b Some additional specific conditions can also be included in regional classifications (reactivation of American trypanosomiasis [Meningoencephalitis and/or Myocarditis] in the WHO region of the Americas, penicilliosis in Asia and HIV – associated rectovaginal fistula in Africa).

## ANNEX 7: PERCENTAGE OF ADULT DOSE REQUIRED AT VARIOUS AGES AND BODY WEIGHTS

| Age | Mean weight For age (Kg) | Percentage of adult dose |
|---|---|---|
| Newborn (full term) | 3.5 | 12.5 |
| 2 months | 4.5 | 15 |
| 4 months | 6.5 | 20 |
| 1 year | 10 | 25 |
| 3 years | 15 | 33.3 |
| 7 years | 23 | 50 |
| 10 years | 30 | 60 |
| 12 years | 39 | 75 |
| 14 years | 50 | 80 |
| 16 years | 58 | 90 |
| Adult | 68 | 100 |

**N.B.** The percentage method is derived from the surface area formula for children. This table is to be used only for medicines with a high therapeutic index. The clinical response of the child, age-or disease-related changes in medicine clearance and any adverse effects that might present should be given due consideration when calculating doses.

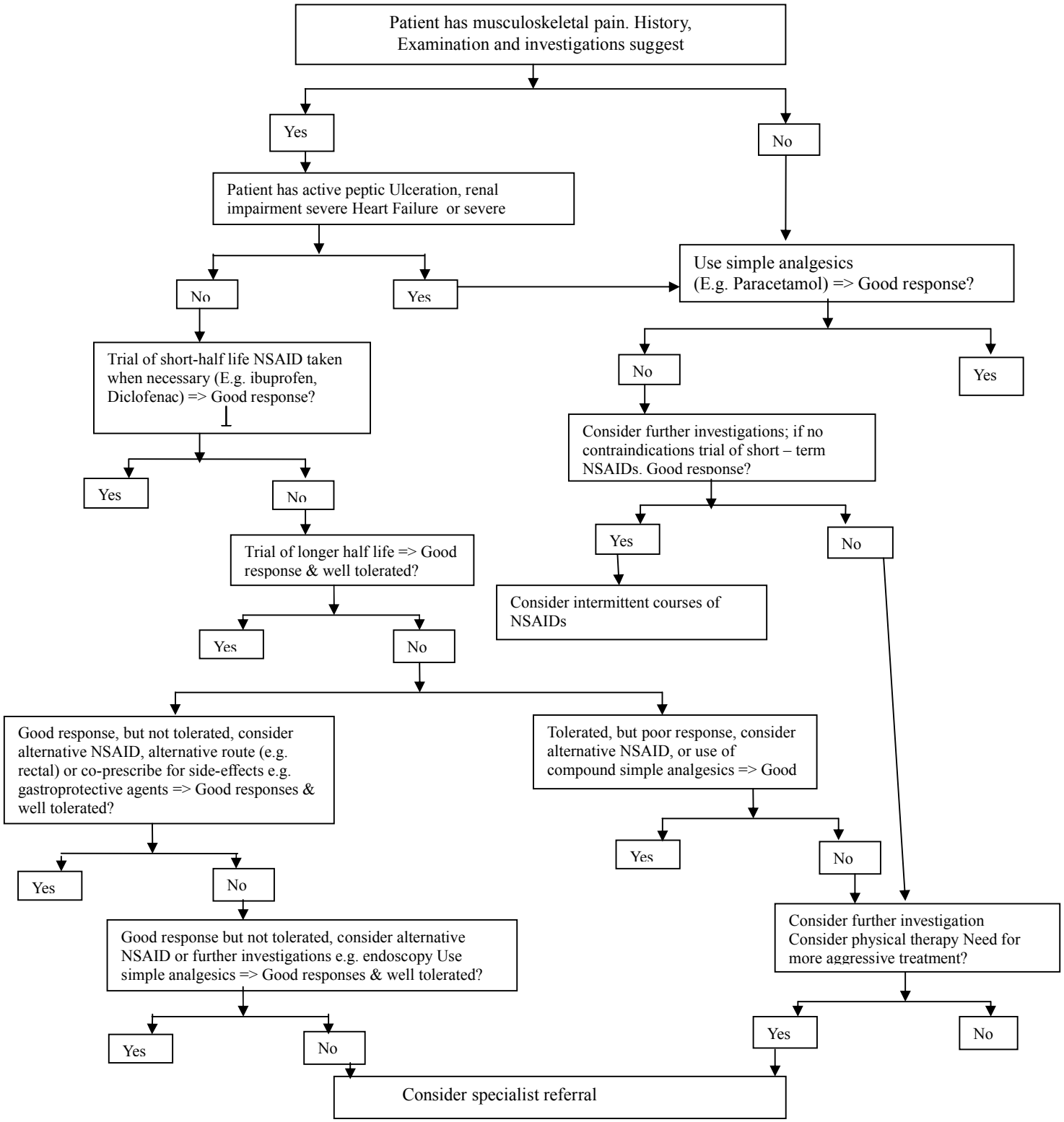
**ANNEX 8: GUIDELINE FOR THE MANAGEMENT OF PAIN (including post-operative pain)**




Pain score should be assessed after asking the patient to take a deep breath, cough and move.

| | | |
|---|---|---|
| 0 | No pain | |
| 1 | Mild pain | able to continue with whatever patient is doing |
| 2 | Moderate pain | beginning to interfere with activities, less able to concentrate |
| 3 | Severe pain | unable to think of anything else but pain |

## ANNEX 9: GUIDELINES FOR USING NON-STEROIDAL ANTI INFLAMMATORY MEDICINES (NSAIDS)



## ANNEX 10: WHO RECOMMENDATION ON MULTIPLE MEDICINE THERAPY FOR LEPROSY

The basic WHO recommendations on multiple medicine therapy for leprosy, using adult doses (Technical report series 675, 1982) are:

**Table 89 - Multibacillary leprosy (adult dosage)**

| | |
|---|---|
| Duration | A minimum of 2 years (or 24 monthly doses within a 36-month period) in all cases, but wherever possible until slit-skin smears are negative |
| Number of medicines used | three: Rifampcin, Dapsone and clofazimine. |
| Dosage:<br>Rifampicin<br>Dapsone<br>Clofazimine | 600mg once-monthly, supervised<br>100mg daily, self-administered<br>300mg once-monthly, supervised and<br>50mg daily, self-administered. |
| Surveillance | minimum of 5 years after stopping treatment, with clinical, and bacteriological examination at least every 12 months |

**N.B**. Ethionamide/prothionamide, in a daily self-administered dose of 250-375mg, may be used if the skin pigmentation or other side effects of clofazimine render this medicine totally unacceptable.

**Table 90 - Paucibacillary leprosy (adult dosage)**

| | |
|---|---|
| Duration | 6 months (or 6 monthly doses within a 9 month period). |
| Number of medicines used | Two: Rifampicin and Dapsone |
| Dosage: Rifampicin<br>Dapsone | 600mg once-monthly, upervised 100mg daily, self-adminstered. |
| Surveillance | Minimum of 2 years after stopping treatment with clinical examination at least every 12 months |

**Table 91 - Multibacillary leprosy (3 medicines-Dapsone, Rifampicin Clofizimine)**

| Age groups | Dapsone daily dose, Unsupervised | Rifampicine Monthly dose, Supervised | Clofazimine Unsupervised dose | Clofazimine Monthly dose Supervised |
|---|---|---|---|---|
| Upto 5 years | 25mg | 150-300mg | 100mg once weekly | 100mg |
| 6-14 years | 50-100mg | 300-450mg | 150mg once weekly | 150-200mg |
| 15 years and above (i.e use adult dose) | 100mg | 600mg | 50mg daily | 300mg |

**Table 92 - Paucibacillary Leprosy (2 medicines-Dapsone and Rifampicin)**

| Age groups | Dapsone: daily dose, unsupervised | Rifampicin, monthly doses supervised |
|---|---|---|
| Upto 5 years | 25mg | 150-300mg |
| 6-14 years | 50-100mg | 300-450mg |
| 15 years and above i.e. use adult dose | 100mg | 600mg |

## ANNEX 11: THE GLASGOW COMA SCALE (GCS)

This gives a reliable objective way of recording the conscious state of a person. It can be used by medical and nursing staff for initial and continuous assessment. It has value in predicting ultimate outcomes. 3 types of response are assessed and graded as follows.

| | |
|---|---|
| **Eye Opening:** | |
| Spontaneously | 4 |
| To speech | 3 |
| To pain | 2 |
| Never | 1 |
| **Best Verbal Response:** | |
| Oriented | 5 |
| Confused | 4 |
| Inappropriate words | 3 |
| Incomprehensible words | 2 |
| None | 1 |
| **Best Motor Response:** | |
| Obeys command | 6 |
| Localizes pain | 5 |
| Withdrawal | 4 |
| Flexor response to pain | 3 |
| Extensor response to pain | 2 |
| None | 1 |

**An overall score is made by summing the score in the 3 areas assessed.**
**Severe injury GCS< 8; Moderate injury GCS 9-12; minor injury GCS 13-15**

## ANNEX 12: RED EYE

**Table 93 - Signs of Red Eye**

| Signs | Referral Advisable If Present | Acute Glau-coma | Acute Irido-cyclitis | Keratitis | Bacterial Conjun-ctivitis | Viral Conjun-ctivitis | Allergic Conjun-ctivitis |
|---|---|---|---|---|---|---|---|
| Ciliary flush | Yes | 1 | 2 | 3 | 0 | 0 | 0 |
| Conjunctival Hyperemia | No | 2 | 2 | 2 | 3 | 2 | 1 |
| Corneal opacification | Yes | 3 | 0 | 1 to 3 | 0 | 0 or 1 | 0 |
| Corneal epithelial disruption | Yes | 0 | 0 | 1 to 3 | 0 | 0 or 1 | 0 |
| Pupillary Abnormality | Yes | Mid-dilated, nonreactive | Small, may be irregular | Normal or small | 0 | 0 | 0 |
| Shallow anterior chamber angle | Yes | 3 | 0 | 0 | 0 | 0 | 0 |
| Elevated intraocular pressure | Yes | 3 | -2 to +1 | 0 | 0 | 0 | 0 |
| Proptosis | Yes | 3 | 0 | 0 | 0 | 0 | 0 |
| Discharge | No | 0 | 0 | Sometimes | 2 or 3 | 2 | 1 |
| Preauricular lymph-node enlargement | No | 0 | 0 | 0 | 0 | 1 | 0 |

N.B. The range of severity of the sign is indicated by-2 (subnormal) to 0 (absent) to 3 (severe).

**Table 94 - Symptoms of Red Eye**

| | Referral Advisable | Acute Glau- | Acute Irido- | Keratitis | Bacterial Conjun- | Viral Conjun- | Allergic Conjun- |
|---|---|---|---|---|---|---|---|

| Symptoms | If Present | coma | cyclitis | | ctivitis | ctivitis | ctivitis |
|---|---|---|---|---|---|---|---|
| Blurred vision | Yes | 3 | 1 to 2 | 3 | 0 | 0 | 0 |
| Pain | Yes | 2 to 3 | 2 | 2 | 0 | 0 | 0 |
| Photophobia | Yes | 1 | 3 | 3 | 0 | 0 | 0 |
| Colored halos | Yes | 2 | 0 | 0 | 0 | 0 | 0 |
| Exudation | No | 0 | 0 | 0 to 3 | 3 | 2 | 1 |
| Itching | No | 0 | 0 | 0 | 0 | 0 | 2 to 3 |

N.B. The range of severity of the sign is indicated by 0 (absent) to 3 (severe).

# ANNEX 13: BODY SURFACE AREA

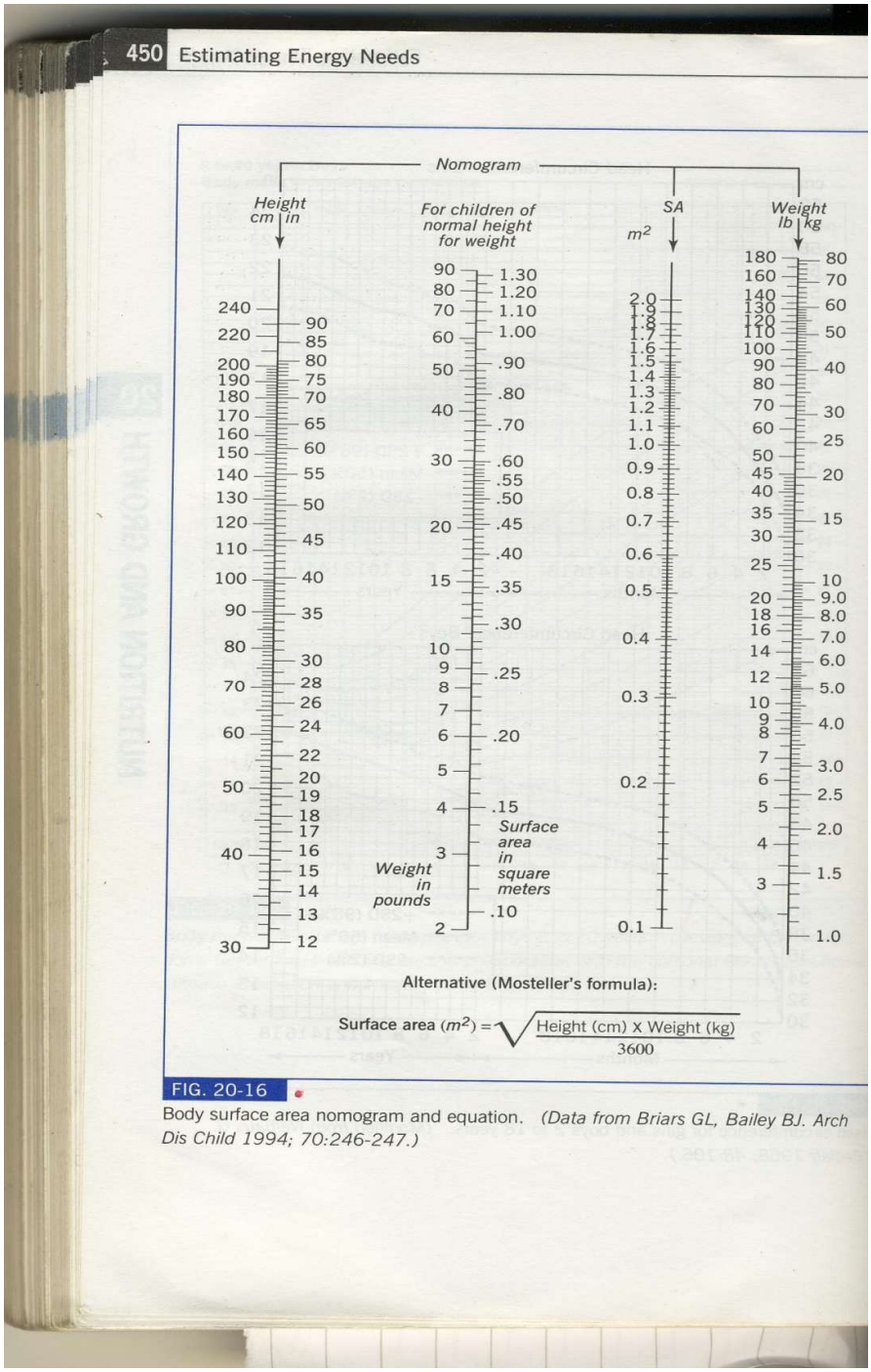



FIG. 20-16

Body surface area nomogram and equation. *(Data from Briars GL, Bailey BJ. Arch Dis Child 1994; 70:246-247.)*

## ANNEX 14: FDA MEDICINE USE IN PREGNANCY

The five categories of Food and Medicine Administration (FDA) for medicine use in pregnancy:

**Category A:** Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester, and the possibility of foetal harm appears remote.

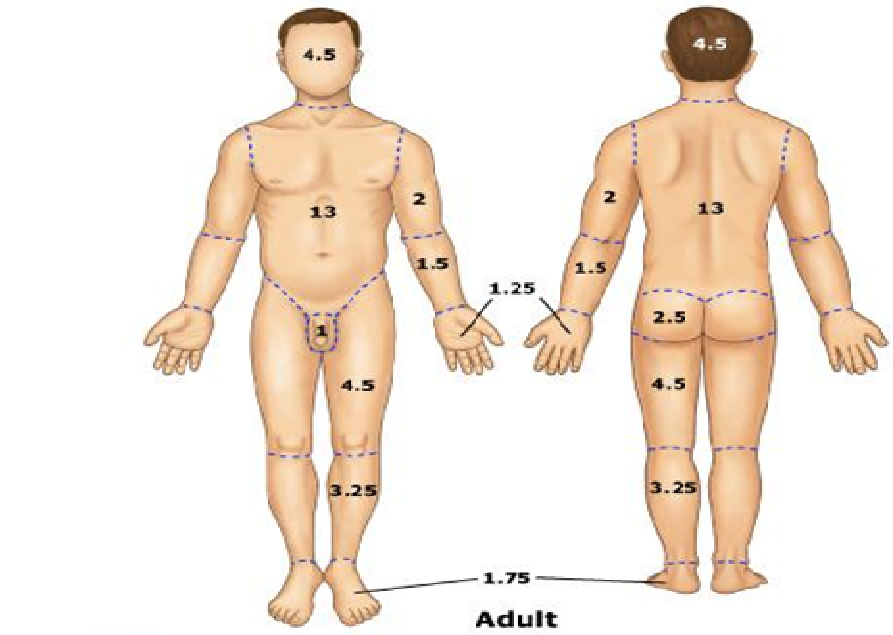
**Category B:** Animal studies do not indicate a risk to the fetus, and there are no controlled human studies or animal studies to show an adverse effect on the fetus, but well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.

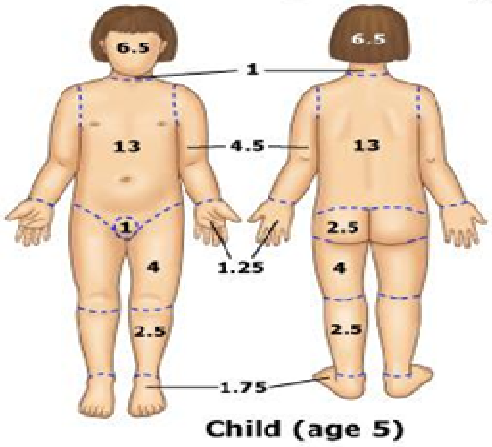
**Category C**: Studies have shown the medicine to have animal teratogenic or embryocidal effects, but there are no controlled studies in women or no studies are available in animals or women.

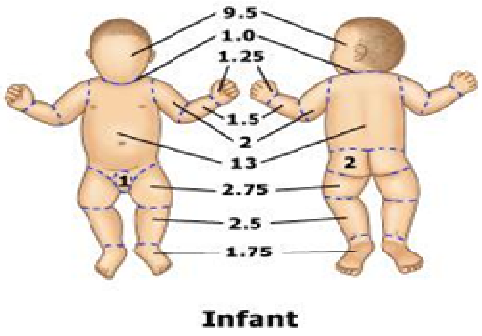
**Category D:** Positive evidence of human foetal risk exists, but benefits in certain situation (e.g, life threatening situations or serious diseases for which safer medicines can not be used or are ineffective) may make use of the medicine acceptable despite its risks.

**Category X:** Studies in animals or humans have demonstrated foetal abnormalities, or there is evidence of foetal risk based on human experience, or both, and the risk clearly out weighs any possible benefit.

## ANNEX 15: BODY SURFACE AREA



## ANNEX 16: ASSESSMENT OF ADRS

**The Naranjo ADRs Assessment Algorithm**

| **Questions** | **Yes** | **No** | **Don't know** |
|---|---|---|---|
| Are there previous *conclusive* reports on this reaction? | +1 | 0 | 0 |
| Did the adverse event occur after the suspected medicine was administered? | +2 | -1 | 0 |
| Did the adverse reaction improve when the medicine was discontinued or a *specific* antagonist was administered? | +1 | 0 | 0 |
| Did the adverse reaction reappear when the medicine was re-administered? | +2 | -1 | 0 |
| Are there alternative causes (other than the medicine) that could have on their own caused the reaction? | -1 | +2 | 0 |
| Did the reaction reappear when a placebo was given? | -1 | +1 | 0 |
| Was the blood detected in the blood (or other fluids) in concentrations known to be toxic? | +1 | 0 | 0 |
| Was the reaction more severe when the dose was increased or less severe when the dose was decreased? | +1 | 0 | 0 |
| Did the patient have a similar reaction to the same or similar medicines in *any* previous exposure? | +1 | 0 | 0 |
| Was the adverse event confirmed by any objective evidence? | +1 | 0 | 0 |

To assess the ADR, the above questionnaire should be answered and score is given.

**Scoring for NARANJO's Algorithm**

- > 9 = definite ADR
- 5-8 = probable ADR
- 1-4 = possible ADR
- 0 = doubtful ADR

**WHO ADRs Assessment Algorithm**

| Term | Description |
|---|---|
| Certain | • A clinical reaction, including laboratory test abnormality, occurring in a plausible time relationship to medicine administration, and which<br>• Cannot be explained by concurrent disease or other medicines or chemicals.<br>• The response to withdrawal of the medicine (dechallenge) should be clinically plausible.<br>• The reaction must be definitive pharmacologically or phenomenologically, (i.e. an objective and specific medical disorder or a recognized pharmacological phenomenon)<br>• Using a satisfactory rechallenge procedure if necessary. |
| Probable/Likely | • A clinical reaction, including laboratory test abnormality, with<br>• A reasonable time sequence to administration of the medicine,<br>• Unlikely to be attributed to concurrent disease or other medicines or chemicals, and which<br>• Follows a clinically reasonable response on withdrawal (dechallenge).<br>• Rechallenge information is not required to fulfill this definition. |
| Possible | • A clinical reaction, including laboratory test abnormality, with<br>• A reasonable time sequence to administration of the medicine, but which could also be explained by concurrent disease or other medicines or chemicals.<br>• Information on medicine withdrawal may be lacking or unclear. |
| Unlikely | • A clinical reaction, including laboratory test abnormality, with<br>• A temporal relationship to medicine administration which makes a causal relationship improbable, and<br>• Other medicines, chemicals or underlying disease provide plausible explanations. |
| Conditional/ Unclassified | • A clinical reaction, including laboratory test abnormality, |
| Unassessable/ Unclassified | • More data is essential for a proper assessment or the additional data are under examination. |

**ANNEX 17: Standard Prescription form**

**PRESCRIPTION PAPER** Code_____
Institution Name: _____Tel. No… ……
Patient's full Name: _____
Sex: ___ Age:___ Weight: _____ Card No. _____
Region: _____Town _____ Woreda_____Kebele _____
House No. ____ Tel. No: _____☐ Inpatient ☐ Outpatient
Diagnosis, if not ICD _____

| Medicine Name, Strength, Dosage Form, Dose, Frequency, Duration, Quantity, How to use & other information | Price (dispensers use only) |
|---|---|
| ℞ | |
| | |
| | |
| | |
| | |
| Total Price | |

| | Prescriber's | Dispenser's |
|---|---|---|
| Full name | _____ | _____ |
| Qualification | _____ | _____ |
| Registration # | _____ | _____ |
| Signature | _____ | _____ |
| Date: | _____ | _____ |

**Please Note the Following Information**

**Prescriptions:**
- May valid only if it has the seal of the health institution.
- filled and blank are legal documents, treat them as fixed assets
- written and verbal information to the client complement one another

**The prescriber:**
- Medicine treatment is only one of the treatment options
- write the prescription correctly and legibly
- diagnosis and other parts of the prescription have to be complete
- abbreviations are NOT recommended
- please accept prescription verification call from the dispenser

**The Dispenser:**
- check legality of the prescription
- check completeness and accuracies before dispensing
- check for whom the medicine is being dispensed: actual client or care taker
- if in doubt about the contents of the prescription; verify with the prescriber
- containers used for packaging must be appropriate for the product
- labels of drugs should be clear, legible and indelible
- Medicines should be dispensed with appropriate information and counseling
- keep filled prescriptions at least for 3 years

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