

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH, COMMUNITY DEVELOPMENT,  
GENDER, ELDERLY AND CHILDREN

**STANDARD TREATMENT GUIDELINES AND  
NATIONAL ESSENTIAL MEDICINES LIST FOR  
TANZANIA MAINLAND**



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Dodoma, Tanzania**

## **FOREWORD**

The Government is committed to ensure adequate availability and accessibility of safe, efficacious and affordable essential medicines at all times to all Tanzanians. To realize this objective, the development and implementation of Standard Treatment Guidelines (STG) and National Essential Medicines List (NEMLIT) is an important step in the health care system for quality diagnosis, treatment and prevention of diseases as well as procurement and supply of essential medicines.

The 2017 edition of STG/NEMLIT has been updated to reflect new therapeutic options and changing therapeutic needs, the need to ensure drug quality, safety issues, medicines for emerging diseases, medicines to meet changing resistance pattern and to reconsider levels of care. A new chapter “approach to patients with emergency conditions” has been added to guide clinicians in the management of patients with emergency conditions and provide initial resuscitation and stabilization. In addition, under notifiable diseases, guidance for the management of COVID-19 has been addressed.

The list of medicines has been selected with due regard to disease prevalence and public health relevance, evidence of clinical efficacy and safety, comparative costs, availability and treatment facilities. The review considered the ongoing expansion of services in primary health facilities; hence, levels of some medicines have been lowered to be available at that level. In particular, special attention has been paid to medicines used to manage non-communicable diseases, such as diabetes and cardiovascular diseases. Also, this new version of STG/NEMLIT adopted the World Health Organization classification of antibiotics into Access, Watch, Reserve (AWaRe) groups, aiming to improve the rational use of antimicrobial agents and minimize the burden of antimicrobial resistance.

The Standard Treatment Guidelines comprise statements to assist practitioners in making decisions about appropriate treatment for specific clinical conditions. Hence, this is a key tool, which should be used to effectively promote access to essential medicines, to achieve maximum therapeutic benefit and optimize patient outcomes. Further, the document will guide the procurement and supply of medicines at the Medical Stores Department (MSD) prescribing and dispensing of medicines in public health facilities as well as the reimbursements of medicines at the National Health Insurance Fund (NHIF).

I therefore urge all responsible institutions and experts to adhere to STG/NEMLIT and to ensure availability of essential medicines at all times, in adequate amounts, in appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. Comments and suggestions that may help us to improve a next edition of STG/NEMLIT are welcome and much appreciated. I am confident that health care workers and responsible institutions will find this document very useful.



Hon. Dr. Dorothy O. Gwajima (MP)

**MINISTER FOR HEALTH, COMMUNITY DEVELOPMENT, GENDER, ERLDERLY AND  
CHILDREN**

## **ACKNOWLEDGEMENTS**

This document was developed through a co-creation process that engaged a broad range of stakeholders. This participatory approach permits ownership of the Standard Treatment Guidelines and Essential Medicines List of Tanzania (STG/NEMLIT) and facilitates its successful implementation. The development process was initiated in December 2019 by identifying key stakeholders. Thereafter, all key stakeholders, including all hospitals were asked to provide their inputs on essential medicines to be added or deleted based on scientific evidence. In addition, stakeholders were asked to recommend stratification for levels of use for specific medicines. I highly appreciate support from Muhimbili National Hospital, Bugando and Mbeya Zonal Referral hospitals as well as Bukoba, Katavi, Njombe and Sekou Toure Regional Referral Hospitals who provided inputs. Your comments were valuable and were incorporated in this STG/NEMLIT edition.

Further, the Ministry in collaboration with Health Promotion and System Strengthening (HPSS) project conducted a survey for the collection of recommendations regarding the review of STG/NEMLIT in 26 health facilities in six regions of Dodoma, Singida, Manyara, Morogoro, Pwani and Dar es Salaam. I thank all health care workers who provided recommendations for STG/NEMLIT improvements; your contributions were consolidated and used to enrich this document.

In a further step, Lead Reviewers for individual chapters were nominated. We thank all Professional Associations who participated in the review through their professional peer reviewers rendering the process fully participatory. I acknowledge the Association of Physicians of Tanzania (APHYTA), Association of Gynecologists and Obstetricians of Tanzania (AGOTA), Association of Pulmonologists-Chest Tanzania, Emergency Medicine Association of Tanzania (EMAT), Nephrology Society of Tanzania (NESOT), Pediatric Association of Tanzania (PAT), Pharmaceutical Society of Tanzania (PST), Tanzania Association for Respiratory Diseases (TARD), Tanzania Cardiac Society (TCS), Tanzania Dental Association (TDA), Tanzania Diabetes Association (TDA), Tanzania Ear Nose & Throat Society (TENTS), Tanzania Gastroenterology and Endoscopy Society (TGES), Tanzania Oncology Society (TOS), Tanzania Ophthalmology Society (TOS), Tanzania Orthopedic Association (TOA), Tanzania Society for Dermatovenerology (TASOD) and Tanzania Surgical Associations (TSA). I also acknowledge the Holistic Approach to Unravel Antibacterial Resistance in East Africa (HATUA-MR/S004785/1)-Tanzania for their preliminary results of patients with urinary tract infections (UTI) which provided insight of the susceptibility patterns of common isolates causing UTI in Tanzania, which was useful to update the relevant chapter. I trust that in the future review you will continue providing technical support.

I sincerely thank the National Medicines and Therapeutic Committee (NMTC), all Lead Reviewers and the NMTC Secretariat who made this a reality. Their names are annexed. Finally, I would like to gratefully acknowledge the financial support provided by the USAID Medicines, Technologies and Pharmaceutical Services (MTaPS) program implemented by Management Science for Health, the Swiss Agency for Development and Cooperation (SDC) through the Health Promotion and System Strengthening (HPSS) project, the Global Fund for AIDS, TB and Malaria (GFATM) and the National Health Insurance (NHIF).



Prof. Abel N. Makubi

**PERMANENT SECRETARY (HEALTH)**

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## ACRONYMS AND ABBREVIATIONS

<b>3D-CRT</b>	Three-dimensional Conformal Radio-Therapy
<b>ACS</b>	Acute Coronary Syndrome
<b>ACS</b>	Acute Chest Syndrome
<b>ACT</b>	Artemisinin Combination Therapy
<b>ADA</b>	Adenosine Deaminase
<b>ADH</b>	Anti-Diuretic Acid
<b>aHUS</b>	atypical Hemolytic Uremic Syndrome
<b>AIS</b>	Acute Ischaemic Stoke
<b>ALU</b>	Artemether Lumefantrine
<b>AMI</b>	Acute Myocardial Infarction
<b>AMPLE</b>	Allergies, Medications, Past medical history, Last meal and Events leading to presentation
<b>bhCG</b>	beta human Chorionic Gonadotropin
<b>BMD</b>	Bone Mineral Density
<b>BP</b>	Blood Pressure
<b>BUN</b>	Blood Urea Nitrogen
<b>C/T/L</b>	Cervical, Thoracic, Lumbar
<b>CAF</b>	cyclophosphamide, doxorubicin hydrochloride (Adriamycin), and fluorouracil
<b>CAH</b>	Congenital Adrenal Hyperplasia
<b>CAP</b>	Community Acquired Pneumonia
<b>CAVE</b>	Cavus, Adductus, Varus, Equinus
<b>CEF</b>	Cyclophosphamide Epirubicin Fluorouracil
<b>CKD</b>	Chronic Kidney Disease
<b>CPP</b>	Cerebral perfusion pressure
<b>CRP</b>	C Reactive Protein
<b>CVA</b>	Cerebral Vascular Accident
<b>CVD</b>	Cardiovascular Disease
<b>CVP</b>	Central Venous Pressure
<b>DIND</b>	Delayed Ischaemic Neurologic Deficit
<b>DKA</b>	Diabetic Keto Acidosis
<b>DME</b>	Diabetic Macular Edema
<b>DNS</b>	Dextrose Normal Saline
<b>DR-TB</b>	Drug Resistance Tuberculosis
<b>DSD</b>	Disorder of Sexual Development
<b>DSM-5</b>	Diagnostic and Statistical Manual of Mental Disorders vol.5
<b>DST</b>	Drug Susceptibility Test
<b>DTLC</b>	District Tuberculosis and Leprosy Coordinator
<b>DWMR</b>	Diffusion Weighted Magnetic Resonance

<b>ECT</b>	Electroconvulsive Therapy
<b>EITB</b>	Enzyme-linked Immune Transfer Blot
<b>EMD</b>	Emergence Medical Department
<b>ENL</b>	Erythema Nodosum Leprosum
<b>ERCP</b>	Endoscopic Retrograde Cholangiopancreatography
<b>ESA</b>	Erythropoietin Stimulating Agent
<b>ESR</b>	Erythrocyte Sedimentation Rate
<b>EVD</b>	External Ventricular Drainage
<b>FAO</b>	Foot Abduction Orthosis
<b>FAST</b>	Focus Assessment with Sonography for Trauma
<b>FAST</b>	Facial drooping, Arm weakness, Speech difficulties and Time
<b>FEIBA</b>	Factor Eight By-passing Agent
<b>FIGO</b>	The International Federation of Gynecology and Obstetrics
<b>FNA</b>	Fine Needle Aspiration
<b>G6PD</b>	Glucose 6 Phosphatase Dehydrogenase
<b>GB</b>	Gall Bladder
<b>GCS</b>	Glasco comma scale
<b>GUS</b>	Genital Ulcer Syndrome
<b>HBA</b>	Haemoglobin Adult
<b>HBS</b>	Sickle Haemoglobin
<b>HD:</b>	Hemo-Dialysis
<b>HDN</b>	Haemolytic Disease of New Bone
<b>HDU</b>	High Dependency Unit
<b>HEENT</b>	Head, Eye, Ear, Nose and Throat
<b>HHS:</b>	Hyperglycemic Hyperosmolar Syndrome
<b>HRCT</b>	High Resolution Computer Tomograph
<b>HVL</b>	HIV Viral Load
<b>IBD</b>	Inflammatory Bowel Syndrome
<b>ICH</b>	Intra Cerebral Haemorrhage
<b>ICP</b>	Intracranial Pressure
<b>ILAE</b>	International League Against Epilepsy
<b>IMCI</b>	Integrated Management of Childhood Illness
<b>IOP</b>	Intraocular Pressure
<b>IPT<sub>P</sub></b>	intermittent preventive treatment in pregnancy
<b>IRIS</b>	Immune Reconstitution Syndrome
<b>ITI</b>	Immune Tolerance Induction
<b>ITP</b>	Idiopathic Thrombocytopenia Purpura
<b>JIA</b>	Juvenile Idiopathic Arthritis
<b>LAMM</b>	Labyrinthine Aplasia, Microtia And Microdontia
<b>LAP</b>	Lower Abdominal Syndrome

<b>LFT</b>	Liver Function Test
<b>LKW</b>	Last Known Well
<b>LLINs</b>	Long Lasting Insecticide Nets
<b>LLQ</b>	Left Lower Quadrant
<b>LMWH</b>	Low Molecular Weight Heparin
<b>LPR</b>	Laryngopharyngeal Reflux
<b>MAP</b>	Mean Arterial Pressure
<b>MDMA</b>	3,4-MethyleneDioxy-MethAmphetamine
<b>MDR-TB</b>	Multi-Drug Resistance Tuberculosis
<b>mRDT</b>	malaria Rapid Diagnostics Test
<b>MSM</b>	Men who have Sex with Men
<b>MTD</b>	Maximum Tolerated Dose
<b>mTOR</b>	mammalian Target Of Rapamycin
<b>MUAC</b>	Mid-Upper Arm Circumference
<b>NGT</b>	Naso Gastric Tube
<b>NIV</b>	Non-Invasive Ventilation
<b>ODS</b>	Osmotic Demyelination Syndrome
<b>OI</b>	Opportunistic Infection
<b>OPG</b>	Orthopantomography
<b>OT</b>	Occupational Therapy
<b>PAD</b>	Peripheral Artery Disease
<b>PCV</b>	Pneumococcal Conjugate Vaccine
<b>PDMPs</b>	Plasma-derived medicinal products
<b>PEFR</b>	Peak Expiratory Flow Rate
<b>PEP</b>	Post Exposure Prophylaxis
<b>PI</b>	Protease Inhibitor
<b>PID</b>	Pelvic Inflammatory Disease
<b>pMDI</b>	Pressurised Metered Dose Inhaler
<b>PPS</b>	Parapharyngeal Space
<b>PPSV</b>	Pneumococcal Polysaccharide Vaccine
<b>PrEP</b>	Pre-Exposure Prophylaxis
<b>PSA</b>	Prostate Specific Antigen
<b>PT</b>	Physio Therapy
<b>PUVA</b>	Psoralens + Ultraviolet radiation
<b>RAM</b>	Resistance Associated Mutation
<b>RBG</b>	Random Blood Glucose
<b>RICE</b>	Rest, Ice, Compression, And Elevation
<b>RR</b>	Rifampicin Resistance
<b>RRT</b>	Renal Replacement Therapy
<b>RTLC</b>	Regional Tuberculosis and Leprosy Coordinator

<b>rtPA</b>	recombinant tissue Plasminogen Activator
<b>SAH</b>	Subarachnoid Haemorrhage
<b>SBCC</b>	Social Behavioural Change
<b>SLE</b>	Systemic Lupus Erythematosus
<b>SMBG</b>	Self-Monitoring Blood Glucose
<b>SMFE</b>	Systemic Marrow Fat Embolism
<b>SpO<sub>2</sub></b>	Oxygen Saturation
<b>SSRI</b>	Selective Serotonin Reuptake Inhibitor
<b>SSS</b>	Scrotal Swelling Syndrome
<b>TBI</b>	Traumatic Brain Injury
<b>TFT</b>	Thyroid Function Test
<b>TIA</b>	Transient Ischaemic Attack
<b>TIVA</b>	Total Intravenous Anaesthesia
<b>TM</b>	Tympanic Membrane
<b>TMD</b>	Temporomandibular Disorders
<b>TMJ</b>	Temporomandibular Joint
<b>TMP</b>	Tympanic Membrane Perforation
<b>TNM</b>	Tumor Nodes and Metastases
<b>TPT</b>	Tuberculosis Preventive Therapy
<b>TURP</b>	Transurethral Resection of the Prostate
<b>UDS</b>	Urethral Discharge Syndrome
<b>UDS</b>	Urine Drug Screen
<b>VAP</b>	Ventilator-Associated Pneumonia
<b>VDS</b>	Vaginal Discharge Syndrome
<b>VTE</b>	Venous Thrombo-Embolism
<b>VWF</b>	Von Willebrand Factor
<b>WfH</b>	Weight for Height
<b>WFNS</b>	World Federation Neurological Surgeon
<b>WHZ</b>	Weight for Height Z score
<b>WPW</b>	Wolff-Parkinson-White Syndrome



# **PART I**

## **THE NATIONAL ESSENTIAL MEDICINES LIST (NEMLIT)**

### **Background Information**

The National Essential Medicines List (NEMLIT) presents essential medicines, for which health facilities at all levels requisite for management of priority diseases. The NEMLIT is based on the concept of essential medicines, defined by the World Health Organization (WHO) as those medicines that meet priority healthcare needs of the population and intended to be available within the context of functioning health systems at all times, with assured quality and at a price the individual and the community can afford. The concept emphasizes carefully and systematically selection of essential medicines using an evidence-based process with due consideration of clear evidence of safety and efficacy and comparative cost effectiveness. The rationale for selecting a limited number of essential medicines is to enhance supply, improve rational use, and lower costs.

### **Categorization of antibiotics**

A new categorization of antibiotics into Access, Watch, Reserve (AWaRe) classification has been introduced to guide their prudent use and reduce antimicrobial resistance.

#### **Access Group Antibiotics**

This group includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. Access group antibiotics are recommended as essential first or second choice empiric treatment options for infectious syndromes. They are essential antibiotics that should be widely available, affordable and quality assured.

#### **Watch Group Antibiotics**

This group includes antibiotic classes that have higher resistance potential. These medicines should be prioritized as key targets of stewardship programs and monitoring. The selected Watch group antibiotics are recommended as essential first or second choice empiric treatment options for a limited number of specific infectious syndromes.

#### **Reserve Group Antibiotics**

This group includes antibiotics that should be reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Reserve group antibiotics should be treated as “last resort” options. While they must be accessible when required, their use should be limited to highly specific patients and clinical settings, when other antibiotic alternatives have failed or are not suitable. They should be protected and prioritized as key targets of national and international AMR stewardship programmes, involving monitoring and utilization reporting, to preserve their effectiveness.

### **Prescribing of Medicines with Regard to Level of Service Provision and Professional Expertise**

Similar to previous editions, the NEMLIT will be used with regard to levels of care. Additionally, a new categorization of prescribing medicines with regards to expertise has been introduced to facilitate reimbursement of medicines by the NHIF. In summary, stocking and prescribing of medicines as per level of care will be: tertiary hospitals (**A, B, C, D & S**); Regional Referral Hospitals (**A, B, C & D**); District Hospitals (**A, B & C**); Health Centers (**A & B**) and dispensaries (**A**). Additional category reflects professional expertise; regardless of level of care: Specialists (**A, B, C, D & S**); Medical Officers (**A, B, C & D**); Assistant Medical Officer (**A, B & C**); Clinical Officers (**A & B**) and Assistant Clinical Officers (**A**).

**Table 1: Restrictions for Prescribing Medicines Listed in the NEMLIT**

Level of Medicines with Regard to Service Provision	Level of Medicines with Regard to Professional Expertise		
Tertiary Hospital	A,B,C,D,S	Specialist	A,B,C,D,S
Regional Referral Hospital	A,B,C,D	Medical Officer (MO)	A,B,C,D
District Hospital	A,B,C	Assistant Medical Officer (AMO)	A,B,C
Health Centre	A & B	Clinical Officer (CO)	A & B
Dispensary	A	Assistant Clinical Officer (ACO)	A

Hence, at tertiary level hospitals (**S**); the National, Zonal Referral and Specialized hospitals, all medicines in the NEMLIT may be stocked; as per hospital needs and specialists may prescribe all medicines listed in the NEMLIT. However, level (**S**) medicines are restricted to other experts. Implying that, a Medical Officers at tertiary hospital will be prescribe medicines listed A, B, C and D and Assistant Medical Officer A, B, & C but not S.

At Regional Referral Hospitals (RRH) level, medicines listed as (**A, B, C & D**) will be stocked. Specialists at that level may prescribe medicines at level (**A, B, C, D, S**) as per their specialty areas e.g. cardiologist may prescribe cardiovascular diseases medicines at that level. Medical officer at RRH will prescribe medicines at level (**A, B, C, D**). If there is an Assistant Medical Officer at RRH allowed to prescribe medicines listed (**A, B, C**) and Clinical Officers (**A & B**).

At District hospitals level, medicines listed as (**A, B & C**) will be stocked. Specialists prescribe medicines listed (**A, B, C, D, S**) as above. Medical Officers will prescribe medicines listed (**A, B, C, D**) and AMO (**A, B, C**). If their Clinical Officers (CO) at that level will be permitted to prescribe medicines listed A & B only. Health Centers stock medicines listed as A & B and dispensaries A, but if there is AMO, MO or specialist will prescribe as above.

#### Note

- Different from previous editions, the arrangement of STG/NEMLIT have changed; the NEMLIT starts followed by chapters of STG to make easy reference of essential medicines by users.
- All medicines indicated for treatment of various diseases in the STG are listed in the NEMLIT.
- Some medicines are listed in some levels for the treatment of specific disease condition e.g. cefixime is level (**D**) but, may be prescribed in lower HFs for treatment of STI only.
- Medicines in the NEMLIT are grouped according to pharmacological groups and written alphabetically, in generic names, with their dosage forms and strengths.
- All health facilities in the public sector will adhere to the NEMLIT in procurement of medicines from MSD and other sources.
- The NHIF will adhere to the NEMLIT for reimbursement of medicines in both public and private health facilities.
- Special arrangement to quantify and procure medicines, which are not managed at specific health facilities but are needed due to presence of expertise as stated above; for that case the Hospital Pharmacists in collaboration with the Office of Chief Pharmacist shall facilitate the process.

Further recommendations, advices and clarifications of the use of this document are much welcome; please, you may communicate with the office of the Director Pharmaceutical Services - Ministry of Health, Community Development, Gender, Elderly and Children. We believe that all medicines stocked in our health facilities are of assured quality. However, for recommendations and advices concerning all aspects of the quality of medicines and any adverse reaction please contact the Tanzania Medicines and Medical Devices Authority at [www.tmda.go.tz](http://www.tmda.go.tz).

**The National Essential Medicines List, 2021 Edition**

Name of drug	Dosage forms and Strengths	Level
<b>1.0 Anesthetics, Preoperative Medicines and Medical Gases</b>		
<b>1.1 General Anaesthetics and Oxygen</b>		
<b>1.1.1 Inhalational Medicines</b>		
Halothane	Liquid for inhalation, 250mL	B
Isoflurane	Liquid for inhalation, 250mMl	B
Nitrous oxide	Cylinder (F gas) for inhalation	C
Oxygen	Cylinder (medical gas) for inhalation	B
Sevoflurane	Inhalation	S
<b>1.1.2 Injectable Medicines and Other Pre-Medication</b>		
Atropine	Injection 1mg (as sulfate in 1mL ampoule)	A
Calcium chloride	Injection 10mcg/mL	D
Clonidine	Injection 500mcg/mL	S
Dexmedetomidine	Injection 100mcg/mL	S
Ephedrine injection	Injection 30mg/mL	B
Flumazenil	Injection 0.2mg (IV)	A
Etomidate	Injection 20mg/mL	S
Glycopyrrolate	Injection 200mcg/mL in 1mL, 600mcg in 3mL	S
Ketamine	Injection (hydrochloride), 10mg/mL in 20mL	B
Labetalol	Injection 10mg/mL	C
Lipid emulsion	Solution 20%	S
Metaraminol	Injection 1mg/mL	S
Midazolam	Injection 1mg/mL, 5mg/mL	D
Noradrenaline	Injection 2mg/mL	S
Ondansetron	Injection 2mg/mL	S
Phenylephrine	Injection 10mg/mL	S
Propofol	Injection 10mg/mL, 20mg/mL	D
Sodium citrate	Solution 0.3 moles	D
Thiopental	Injection (sodium salt), in 20mL	C

## **1.2 Local Anaesthetics**

Bupivacaine	Injection 0.5% (hydrochloride) in 7.5% dextrose spinal	C
Bupivacaine	Injection 2.5mg/mL, 5mg/mL, 7.5mg/mL	C
Lidocaine	Injection hydrochloride 1% & 2%;	A
Lidocaine	Gel 2% & 5%; Spray 10%	B
Lidocaine in Dextrose	Injection (hydrochloride), 5% in 7.5% dextrose	B
Lidoocaine + epinephrine (adrenaline)	Injection (hydrochloride) 2% with adrenaline 1:100,000 in 2mL ampoule for dental use	A

## **1.3 Muscle Relaxants and Cholinesterase Inhibitors**

Atracurium	Injection 50mg/5mL	S
Baclofen	Tablet 10mg	S
Neostigmine	Injection (hydrochloride or hydrogen tartarate), 1mg/mL in 1mL ampoule, Injection (hydrochloride or hydrogen tartarate), 2.5mg/mL in 1mL ampoule	B
Pancuronium	Injection (bromide) 4mg/mL in 2mL ampoule	C
Rocuronium	Injection 50mg/5mL	S
Sugammadex	Injection: 100mg/mL	S
Suxamethonium	Powder for injection (bromide or chloride) 50mg/mL in 2mL vial	C
Tizanidine	Tablet/Capsule: 2mg; 4mg	S

## **2.0 Medicines for Pain and Palliative Care**

### **2.1 Non-opioids and Non-steroidal Anti-inflammatory Medicines (NSAIDs)**

Acetylsalicylic acid	Tablet 300mg	A
Dekketoprofen	Tablet 25mg	S
Diclofenac	Injection 25mg/mL; Recto caps 100mg (slow release); Gel.	A
Diclofenac	Tablet (sodium/potassium salt) 50mg, 100mg;	C
Ketoprofen	Tablet/Capsule: 50mg, 75mg, 200mg; Gel 2.5% w/w	S
Ibuprofen	Tablet 200mg; 400mg ; Syrup 100mg/5ml	A
Mefenamic Acid	Tablet 500mg	B
Meloxicam	Tablet 7.5mg; 15mg	D
Paracetamol	Tablet 500mg; Syrup 125mg/5mL, suppositories 125mg 10 mg/mL Solution for Infusion	A

Piroxicam	Tablet 20mg	A
Sulfasalazine	Tablets 500mg	D
<b>2.2 Opioid Analgesics/Antagonists</b>		
Fentanyl	Injection 100mcg/2mL; Patches	S
Methadone	Tablet: 5mg; 10mg (as hydrochloride); Oral liquid: 5mg/5mL; 10mg/5mL (as hydrochloride); Concentrate for oral liquid: 5mg/mL; 10mg/mL (as hydrochloride)	C
Morphine	Tablet 10mg (morphine hydrochloride or morphine sulfate); Granules (slow-release: to mix with water) 20mg-200mg (morphine sulfate); Oral liquid: (10mg morphine hydrochloride or morphine sulfate)/5mL; Injection: 10mg (morphine hydrochloride or morphine sulfate) in 1mL ampoule	C
Naloxone	Injection (hydrochloride) 0.4mg/mL in 1mL ampoule	B
Pethidine	Injection (hydrochloride) 50mg/mL in 1mL and 2mL ampoule	B
Tramadol	Tablet 50mg; Injection 50mg/mL in 2mL	B
<b>2.3 Medicines for Other Common Symptoms in Palliative Care</b>		
Amitriptyline	Tablet 25mg	A
Haloperidol	Injection: 5mg/1mL ampoule; Tablet 5mg	B
Hydrocortisone	Powder for injection (as sodium succinate) 100mg in vial	A
Hyoscine butyl bromide	Tablet 10mg	A
Hyoscine butyl bromide	Injection: 20mg/mL	B
Loperamide	Tablet 2mg	B
Imipramine	Tablet 25mg	C
<b>3.0 Anti-allergies and Medicines Used in Anaphylaxis</b>		
Betahistine	Tablet as dihydrochloride 16 mg	C
Bethametasone	Injection: 4mg/mL	D
Cetirizine	Oral solution 5mg/5mL; Tablet (hydrochloride) 10mg	A
Chlorpheniramine	Injection (maleate 10mg/mL in 1mL ampoule); Elixir (maleate) 2mg/5mL; Tablet (maleate) 4mg	A
Desloratadine	Tablet: 5 mg film-coated	S

Dexamethasone	Injection: 4mg/mL in 1mL ampoule (as disodium phosphate salt);	B
Epinephrine (Adrenaline)	Injection: 1mg (as hydrochloride or hydrogen tartrate) in 1mL ampoule	A
Loratadine	Syrup 5mg/5mL; Tablet 10mg	C
Promethazine	Injection (hydrochloride) 25mg/mL in 2mL; Syrup 5mg/5mL; Tablet (hydrochloride) 25mg	A

#### 4.0 Antidotes and Other Substances Used in Poisonings

##### 4.1 Antidotes (Non-specific)

Charcoal, activated	Tablet or Powder, 50g	A
Magnesium sulfate	Powder salt, 5g	C

##### 4.2 Antidotes (Specific)

Acetylcysteine	Injection: 200mg/mL in 10mL ampoules	C
Atropine	Injection 1mg (as sulfate in 1mL ampoule)	A
Calcium gluconate	Injection 100mg/mL in 10mL	A
Deferoxamine	Injection 500mg (mesylate)in vial	D
D-penicillamine	Tablet 250mg	D
Dimercaprol	Injectable 50mg/mL in 2mL ampoule	D
Ethylenediaminetetra-acetic acid (EDTA)	Injection 200mg/mL in 5mL	D
Flumazenil	Injection:100mcg/mL in 5mL	D
Pralidoxime	Injection 600mg	S
Sodium bicarbonate 8.4%	Injection 10mLs	C
Sugammadex	Injection 100mg/mL	S
Succimer	Capsule 100mg (2,3-Dimercaptosuccinic acid)	D

#### 5.0 Anticonvulsants and Antiepileptics

Carbamazepine	Syrup 100mg/5mL; Tablet 100mg; 200mg	A
Clonazepam	Tablet 0.5mg, 2mg	D
Diazepam	Tablet 5mg	C
	Injection 5mg/mL in ampoule 2mL	A
Lamotrigine	Tablet 100mg, 200mg	S

Levetiracetam	Injection 5mg/mL, 10mg/mL, 15mg/mL, 100mg/mL, Tablet 250mg, 500mg, 750mg, 1000mg	S
Lorazepam	Injection: 2mg/mL in ampoule; 4mg/mL in ampoule, Tablet 1mg/2mg	C
Magnesium sulfate	Injection 50mg/mL in 10mL vial	A
Phenobarbital	Injection (as sodium salt), 100mg in 2mL ampoule;	A
	Tablet (as sodium) 30mg, 100mg	A
Phenytoin	Suspension (as sodium salt) 30mg/5mL; Tablet/Capsule (as sodium salt) 50mg, 100mg, Injection 100mg/2mL	C
Pregabalin	Tablet/Capsule 75mg, 100mg; 150mg	D
Sodium Valproate	Tablet 200mg, 500mg	C
<b>6.0 Anti-Infective Medicines</b>		
<b>6.1 Antihelminthics</b>		
<b>6.1.1.Intestinal anthelmintics</b>		
Albendazole	Suspension 100mg/5mL in 30mL bottle; Tablet 200mg, 400mg, chewable	A
Mebendazole	Suspension 100mg/5mL in 30mL bottle; Tablet 100mg, chewable	A
<b>6.1.2 Antifilariasis</b>		
Ivermectin	Tablet 3mg, 6mg	A
<b>6.1.3 Anti-schistosomiasis and Other Anti-trematode Medicines</b>		
Praziquantel	Tablet 600mg	A
Albendazole	Tablet 200mg, 400mg	A
<b>6.2 Antibacterial</b>		
<b>6.2.1 Access Group Antibiotics</b>		
Ampicillin	Powder for injection (as sodium salt) 250mg, 500mg in vial	A
Ampicillin + cloxacillin	Capsule 250/250mg, injection	B
Amoxicillin	Capsule (as trihydrate) 250mg; Dispersible tablet 250mg, 125mg	A
Amoxicillin + Clavulanic acid	Powder for suspension (as trihydrate) 125mg+ 31.25mg (as potassium salt) in 5mL AND 250mg amoxicillin + 62.5mg clavulanic acid/5mL; Tablet (as trihydrate) 500mg + 125mg clavulanic acid (as potassium salt)	B
Amoxicillin + Clavulanic acid	Powder for injection 500mg (as sodium), + 100mg (as potassium salt) in vial	C

Benzathine benzyl penicillin	Powder for injection 1.44g (2,400,000 IU) in vial	<b>A</b>
Benzyl Penicillin	Powder for injection (as sodium or potassium salt) 3g (5,000,000 IU) in vial	<b>A</b>
Cephalexin	Capsule 250mg (as monohydrate); Powder for reconstitution 125/5mL; 250mg/mL	<b>B</b>
Cloxacillin	Powder for injection (as sodium salt) 250mg, 500mg in vial	<b>B</b>
Doxycycline	Capsule (as hydrochloride), 100mg	<b>A</b>
Erythromycin	Powder for suspension (as ethylsuccinate), 125mg/5mL in 100mL bottle; Tablet (as stearate or ethyl succinate), 250mg, film coated	<b>A</b>
Flucloxacillin + Amoxicillin	Tablet 500mg (as combination);	<b>C</b>
Flucloxacillin	Injection (sodium) 250mg; 125mg/5mL Oral solution	<b>C</b>
Metronidazole	Suspension as (benzoate) 200mg/5mL in 100mL; Tablet 200mg	<b>A</b>
	Injection (I.V) 5mg/mL in 100mL bottle;	<b>B</b>
Nitrofurantoin	Tablet 100mg	<b>A</b>
Phenoxyethylpenicillin	Powder for suspension 125mg/5mL; (as potassium salt), Tablet 250mg	<b>A</b>
Tetracycline	Capsule 250mg	<b>S</b>
Oxytetracycline	Eye ointment 1% (hydrochloride)	<b>A</b>

#### **6.2.2 Watch Group Antibiotics**

Ampicillin + Sulbactam	Powder for injection (ampicillin 1g/sulbactam 0.5g), (ampicillin 2g/sulbactam 1g), (ampicillin 10g/sulbactam 5g)	<b>C</b>
Azithromycin	Capsule/Tablet (as dihydrate) 250mg, 500mg; Oral liquid 200mg/5mL	<b>B</b> ( level A for STI only)
Clarithromycin	Tablet 250mg, 500mg	<b>C</b>
Chloramphenicol	Oily injection 0.5g (as sodium succinate)/mL in 2mL ampoule; Powder for injection (as sodium succinate) 1g, 125mg/5mL injection (as Phosphate), 150mg/mL in 2mL ampule	<b>B</b> (Reserved for meningitis)
Ceftriaxone	Injection 250mg, 500mg, 1g in vial	<b>B</b> ( level A for STI only)
Ceftriaxone+sulbactam	Injection 1.5g vial	<b>D</b>
Ciprofloxacin	Tablet (as hydrochloride) 250mg, 500mg	<b>A</b>
Ciprofloxacin	Solution for IV infusion 2mg/mL in 100mL	<b>C</b>

Gentamicin	Injection (as sulfate) 40mg/mL in 2mL ampoule, 20mg/mL in 2 mL ampoule	<b>A</b>
Piperacillin + tazobactam	Powder for injection 2g (as sodium salt) + 250mg (as sodium salt); 4g (as sodium salt) + 500mg (as sodium salt) in vial	<b>S</b>
Sulfamethoxazole + triemethoprim	Suspension (Sulphamethoxazole 200 mg/5mL + trimethoprim 40mg/5mL in 100mL bottle; Tablet 480mg; Sulphamethoxazole 400mg/trimethoprim 80mg	<b>A</b>
Ceftazidime	Powder for injection (as pentahydrate) 250mg in vial	<b>D</b>
Cefixime	Capsule 200mg/ 400mg	<b>S (A for STI and Typhoid)</b>
Cefuroxime	Powder for Injection 250mg, 750mg, 1.5g (as sodium salt) in vial	<b>D</b>
	Oral suspension 125mg/5mL, 250mg/5mL; Tablet 250mg, 500mg; injection	<b>D</b>

#### **6.2.3 Reserve Group Antibiotics**

Amikacin	Injection 250mg/mL (as sulfate)	<b>S</b>
Cefepime	Injection 1000mg	<b>S</b>
Clindamycin	Capsule 150mg (as hydrochloride);	<b>S</b>
	Injection (as phosphate) 150mg/mL in 2mL ampule	<b>S</b>
Colistin	Powder for Injection 1MIU per vial	<b>S</b>
Dapsone	Tablet 100mg	<b>S</b>
Meropenem	Injection 500mg, 1000mg	<b>S</b>
Vancomycin	Capsule: 125mg; 250mg (as hydrochloride)	<b>S</b>
	Powder for injection 250mg (as hydrochloride) in vial	<b>S</b>

#### **6.2.3 Antileprosy Medicines**

Clofazimine	Capsule: 50mg; 100mg	<b>A</b>
Dapsone	Dapsone Tablet 50mg, 100mg	<b>A</b>
Rifampicin	Tablet 25mg; 50mg; 100mg	<b>A</b>

#### **6.2.4 Antituberculosis Medicines**

Ethambutol	Tablet (as hydrochloride) 400mg	<b>A</b>
Ethambutol+Isoniazide	Tablet 400mg + 100mg	<b>A</b>
Ethionamide	Tablet 125mg, 250mg	<b>S</b>

Isoniazid	Tablet 100mg	A
Pyrazinamide	Tablet 500mg	A
Rifampicin+Isoniazid	Capsule/Tablet,150mg+75mg, 50mg+150mg	A
Rifampicin+Isoniazid+Pyrazinamide+Ethambutol	Tablet 150mg + 75mg + 400mg + 275mg	A

#### **6.2.5 Reserved Second-line for Treatment of Multidrug Resistance**

##### **Tuberculosis (MDR-TB)**

Cycloserine	Tablet 250mg	S
Bedaquiline	Tablet 100mg	S
Capromycine	Powder for injection 1g (as sulfate) in a vial	S
Delamanide	Tablet 50mg	S
Kanamycin	Powder for injection: 1g (as sulfate) in vial	S
Levofloxacin	Tablet 250mg	S
Linezolid	Injection for intravenous administration: 2mg/mL in 300mL bag; Tablet 400mg; 600mg	S
Moxifloxacin	Tablet 400mg	S
p-Amino salicylic acid (PAS)	Granules 4g in a sachet; Tablet 500mg	S

#### **6.3 Antifungal Medicines**

Amphotericin B	Amphotericin B Powder for injection 50mg in vial	S
Clotrimazole	Clotrimazole Vaginal cream (nitrate) 1%, 10%; Clotrimazole Pessaries 100mg; 500mg ; Topical cream/Ointment	A
Fluconazole	IV infusion 2mg/mL in vial	C
	Tablet/Capsule 150mg, 200mg	A
Flucytosine	Isotonic infusion solution containing flucytosine (1%)and 0.805% sodium chloride	S
	Tablet 250mg, 500mg	S
Griseofulvin	Tablet 500mg	A
Itraconazole	Capsule 100mg	D
Miconazole	Miconazole Oral gel 2%; Vaginal Pessaries, Topical cream/ointment	C
Nystatin	Suspension oral 100,000 IU/mL	A
Terbinafine	Tablet 250mg ; Topical cream	C

#### **6.4 Antiviral Medicines**

##### **6.4.1 Antiherpes Medicines**

Acyclovir	Cream 5%; Tablet 200mg, 400mg,	B
	Injection 500mg/Vial	D
Valganciclovir	Tablet 450mg	S
<b>6.4.2 Antiretrovirals (ARVs)</b>		
<b>6.4.2.1 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors</b>		
Abacavir (ABC)	Tablet: 300mg (as sulfate)	A
Lamivudine (3TC)	Oral Liquid 50mg/mL; Tablet: 150mg	A
Tenofovir disoproxil fumarate (TDF)	Tablet: 300mg	A
Zidovudine (AZT)	Capsule 250mg; Oral liquid 50mg/5mL	A
<b>6.4.2.2 Non-nucleoside Transcriptase Inhibitors</b>		
Efavirenz (EFV)	Tablet: 200mg; 600mg	A
Nevirapine (NVP)	Oral liquid: 50mg/5mL; Tablet 50mg (dispersible); 200mg	A
<b>6.4.2.3 Protease Inhibitors</b>		
Atazanavir	Tablet 100mg; 300mg (as sulfate)	C
Atazanavir + Ritonavir	Tablet: 300mg (as sulfate) + 100mg	C
Lopinavir + Ritonavir (LPV/r)	Capsule 40mg + 10mg; Oral liquid 400mg + 100mg/5mL; Tablet 100mg + 25mg; 200mg + 50mg	C
Ritonavir	Oral liquid 400mg/5mL; Tablet 25mg; 100mg	C
Darunavir	Tablet 75mg, 400mg, 600mg, 800mg	S
<b>6.4.2.4 Integrase Inhibitors</b>		
Raltegravir	Tablet 25mg, 100mg, 400mg	S
<b>6.4.2.5 Fixed Dose Combinations</b>		
Abacavir/Lamivudine	Dispersible Tablet 60/30mg; Dispersible tablet; 120/60mg; Tablet 600/300mg Scored	A
Tenofovir /Emtricitabine	Tablet 300/200mg	A
Tenofovir/Emtricitabine/Efavirenz	Tablet 300/200/600mg	A
Tenofovir/Lamivudine/Efavirenz	Tablet 300/300/600mg	A
Tenofovir/Lamivudine/Dolutegravir	Dispersible tablet 60/30mg; Tablet 300/300/50mg	A
Zidovudine/Lamivudine	Tablet 300/150mg	A

Zidovudine/Lamivudine/Nevirapine	Tablet 300/150/200mg	A
<b>6.4.2.6 Medicines for Prevention of Opportunistic Infections</b>		
Isoniazide	Tablet 300mg	A
Pyridoxine	Tablet 25mg	B
Sulphamethoxazole + trimetoprim	Tablet 400mg + 80mg	A
<b>6.4.3 Antihepatitis Medicines</b>		
<b>6.4.3.1 Medicines for Hepatitis-B</b>		
Entecavir	Tablet 0.5mg	S
Tenofovir disoproxil fumarate (TDF)	Tablet: 300mg	A
<b>6.4.3.2 Medicines for Hepatitis-C</b>		
Ledipasvir	Tablet 90mg	S
Ribavirin	Tablet 600mg	S
Sofosbuvir	Tablet 400mg	S
<b>6.5 Antiprotozoal Medicines</b>		
<b>6.5.1 Antiamoebic and Antigiardiasis Medicines</b>		
Metronidazole	Suspension 200mg/5mL; Tablet 200mg	A
Tinidazole	Tablet 500mg	B
<b>6.5.2 Anti-malarial Medicines</b>		
Artemether/Lumefantrine (ALU)	Tablet 20mg/120mg	A
Artemether	Injection 80mg/mL ampoules	B
Artesunate	Injection: ampoule, containing 60mg anhydrous artesunic acid with separate ampoule of 5% sodium bicarbonate solution	A
Dihydroartemisinin+Piperaquine (DPQ)	Tablet 40mg+320mg, 20mg+160mg	C
Primaquine	Tablet (as phosphates) 2.5mg, 7.5mg, 15mg	A (restricted to few HF under the project)
Sulfadiazine	500mg tablet	D
Pyrimethamine	25mg tablet	D
<b>6.5.3 Malaria Prophylaxis</b>		
Sulfadoxine + Pyrimethamine	Tablet 500mg + 25mg	A

## **7.0 Antimigraine Medicines**

### **7.1 Medicines for Treatment of Acute Attack**

Acetylsalicylic acid	Tablet 300mg	A
Ibuprofen	Tablet 200mg; 400mg	A
Ergotamine tartarate	Tablet 1mg, 2mg	C

### **7.2 Medicines for Prophylaxis**

Propranolol	Tablet 40mg as hydrochloride)	A
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## **8. Antineoplastics, Immunosuppressives and Immunomodulators**

5-fluorouracil	Injection: 250mg; 500mg; 000mg;	S
Abiraterone acetate	Tablet 250mg	S
Actinomycin D	Powder for injection: 500 micrograms in vial	S
Alfuzocin	Tablet 10mg	D
Allopurinol	Tablet 100mg; 300mg	B
Anastrazole	Tablet 1mg	S
Antithymocyte globulin (ATG) (rabbit/horse)	Injection 25mg/mL in 5mL	S
Azacitadine	Injection 25mg/mL	S (with control)
Azathioprine	Tablet 50mg, 75mg, 100mg	S
basiliximab	Injection 20mg	S
Bicalutamide	Tablet 150mg, 50mg	S
Bleomycin	Powder for injection: 15 IU (as sulfate) in vial	S
Bortezomib	Injection 3.5mg/vial	S
Capecitabine	Tablet 500mg	S
Carboplatin	Injection 10mg/mL	S
Chlorambucil	Tablet 2mg	S
Cisplatin	Powder for injection 50 mg; 10mg in vial.	S
Cyclophosphamide	Injection	S
Cyclosporine	Injection: 50 mg/mL in 1-mL ampoule; Capsule: 25 mg; 50mg; 100mg	S
Dacarbazine	Powder for injection: 100 mg in vial; 200mg/; 500mg	S
Danazol	Capsule 100mg	S (hematology special)
Docetaxel	Concentrate for infusion 120mg; 80mg	S
Doxorubicin	Injection 10mg; 20mg, 50mg	S

Dutasteride	Tablet 0.5mg	S
Etoposide	Capsule: 100 mg; Injection 100 mg/mL; Injection 50mg/5mL	S
Everolimus	Tablet 0.25, 0.5mg	S
Febuxostat	Tablet 40mg; 80mg	S
Filgrastim	Injection 5mcg	S
Finasteride	Tablet 5mg	D
Folinic acid	Tablet 15mg, injection 6mg	S
Gemcitabine	Injection 200mg; 500mg; 1000mg	S
Goserelin	Injection 3.6mg, 10.8mg	S
Hydroxychloroquine	Tablet 200mg	S
Hydroxyurea	Capsule 500mg	S
Ifosfamide	Injection 1g/20mL	S
Imatinib	Tablet 400mg	S
Irinotecan	Injection 180mg/mL	S
Lenalidomide	Tablet 25mg	S
Leucovorin	Injection 200 mg/mL	S
Mesna	Injection, 100mg/mL; Tablet 400mg	S
Methotrexate	Tablet 2.5mg; Injection 50 mg/5mL	S
Mycophenolate Sodium	Tablet 360mg	S
Mycophenolate Mofetil	Tablet 500mg	S
Oxaliplatin	Powder for injection 50mg; 100mg in vial;	S
Paclitaxel	Injection 260mg vial	S
Rituximab	Injection 375 mg	S
Sirolimus	Tablet 1mg, 2mg	S
Tacrolimus	Tablet 0.5mg; 1mg; 2mg Ointment 0.1%	S
Tamsulosin	Tablet 0.4mg	D
Tamoxifen	Tablet 20mg	D
Temozolomide	Tablet 200mg	S
Thalidomide	Tablet 200mg	S
Trastuzumab	Injection 440mg; 150mg; 600mg; 500mg	S
Vinblastine	Injection 10mg	S
Vincristine	Powder for injection: 2 mg; 5 mg (sulfate) in vial.	S
Zolendronic acid	Injection 4mg; 5mg	S

## **9.0 Hormones and Antihormones**

### **9.1 Adrenal Hormones and Synthetic Substitutes**

Betamethasone	Injection 4mg/mL	D
Dexamethasone	Tablet 0.5mg; 4mg	D
	Injection (as sodium phosphate) 10mg/mL	B
Hydrocortisone	Powder for Solution for Injection/Infusion 100 mg (as sodium succinate)	A
Methylprednisolone	1000 mg powder and solvent for solution for injection/infusion; Tablet 4mg; 8mg;	D
Metyrapone	Tablet 250mg	S
Prednisolone	Tablet 5mg	A
Triamcinolone	Injection 40mg/mL; Cream 0.1%	S

### **9.2 Oestrogens**

Ethinylestradiol	Tablet 50mcg	A
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### **9.3 Ovulation Inducers**

Clomiphene	Tablet 50mg	C
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### **9.4 Progesterone**

Dydrogestrone	10mg tablet	S
Etonorgestrel	Implant 68mg	A
Levonorgestrel	Tablet 0.03mg, 0.07mg, 0.75mg	A
	Implant 75mg	A
Medroxyprogesterone	Injection acetate (depot) 150mg	A
Norethisterone	Tablet 5mg	C

### **9.5 Androgens**

Testosterone	Injection, 30 mg/1.5mL;100mg/mL; 200mg/mL; Cream	S
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### **9.6 Contraceptives**

Ethinylestradiol + Norgestrel	Tablet 0.03mg + 0.3mg	A
Ethinylestradiol Levonorgestrel	Tablet 0.03mg + 0.15mg	A
Ethinylestradiol Desogestrel	Tablet 0.03mg + 0.15mg	A

### **9.7 Thyroid, Parathyroid Hormones and Antagonists**

Carbimazole	Tablet 5mg	C
Potassium Iodide Solution	Iodine 2mg + Potassium Iodide 4mg/g in water (prepare from raw material)	B

Levothyroxine	Tablet (sodium salt) 0.05g	D
Iodized oil Capsule	Iodized oil Capsule with nipple 240mg/0.5mL and 480mg iodine/mL	A
Iodized oil	Injection	C
Propylthiouracil	Tablet 50mg	D
<b>10. Antiparkinsonism Medicines and Antiprolactenemia</b>		
Benzhexol	Tablet (hydrochloride) 5mg	B
Bromocriptine	Tablet 2.5mg	C
Cabergoline	Tablet 0.5mg	S
Levodopa/Carbidopa	Tablet 100mg + 25mg	D
Selegiline	Tablet 5mg	S
<b>11. Medicines Affecting the Blood</b>		
<b>11.1 Antianaemia Medicines</b>		
Erythropoietin	2000 unit/ML; 4000 units/mL	S
Ferrous	200mg ( sulfate or as fumarate)	A
Ferrous salts	Oral liquid: Equivalent to 25mg iron (as sulfate)/mL; Tablet: Equivalent to 60mg iron	A
Folic acid	Folic acid Tablet 5mg	A
Hydroxocobalamin (Vitamin B <sub>12</sub> )	Injection 1mg/mL	C
<b>11.2 Medicines Affecting Coagulation</b>		
Desmopressin (Move to anti-diuretics)	Injection 4mcg/mL, Tablet 0.2mg	S
Etamsylate	Tablet 500mg	C
Low molecular Weight heparin	Injection 100mg/mL	S
Phytomenadione (Vit K <sub>1</sub> )	Injection 0.5 mg/mL, 2mg/mL in 2mL ampoule;	B
Protamine sulfate	Injection 10mg/mL in 5mL ampoule	B
Rivaroxaban	Tablet 15mg, 20mg	S
Unfractionated Heparin Sodium	Injection (sodium salt) 1,000 IU/mL in 5mL ampoule	B (Under specialist supervision)
Tranexamic acid	Injection 100mg/mL in 5mL ampoule; Syrup 500mg/5mL in 300mL bottle; Tablet 500mg	C
Warfarin	Tablet: 1mg; 2mg; 5mg (sodium salt)	C

**12.0 Blood Products of Human Origin and Plasma Substitute****12.1 Blood and Blood Components**

Fresh frozen plasma (FFP)	Fresh frozen plasma (FFP) Bags	D
Platelets	Platelets	D
Red blood cells.	Packed red blood cells.	D
Whole blood	Whole blood	B

**12.2 Plasma-Derived Medicines****12.2.1 Human Immunoglobulins**

Anti-rabies immunoglobulin		A
Anti-tetanus immunoglobulin		A
Human Immunoglobulin G		S

**12.2.2 Blood Coagulation Factors**

Eltrombopag	Tablet 25mg	S
Factor VIII concentrate	Factor VIII concentrate 500IU	S
Factor IX concentrate	Factor IX concentrate 500 IU	S

**12.3 Plasma Substitutes**

Albumin	Infusion 5%; 25%	S
Polygeline	Polygeline IV solution 3.5%, 500mL bottles	S

**13.0 Cardiovascular Medicines****13.1 Antianginal Medicines**

Bisoprolol	Tablet 5mg; 10mg	S
Glyceryl trinitrate	Spray 400 micrograms/metered dose, sublingual spray	C
Isosorbide Dinitrate	Tablet 10mg, 20mg	C
Labetalol	Tablet 100mg, 200mg ; Injection 5mg/mL	C
Nifedipine	Slow-release Capsule/Tablet 10mg; 20mg	B
Nitroglycerin	Injection/Infusion 25mg/250mL; 50mg/250mL; 100mg/250mL	S
Propranolol	Tablet 40mg	A

**13.2 Antiarrhythmic Medicines**

Adenosine	Injection 3mg/mL in Saline	S
Amiodarone	Injection 30mg/mL in 10mL ampoule; Tablet 100mg	S
Sotalol	Tablet 80 mg, 120 mg, 160 mg, 240 mg; Oral solution 5mg/mL; Injection 15mg/mL	<b>S with control</b>

Verapamil	Injection 2.5mg/mL, 2mL ampoule; Tablet 40mg 80mg	S
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### 13.3 Antihypertensive Medicines

Amlodipine	Tablet 5mg, 10mg	C
Atenolol	Tablet 50mg	B
Candesartan	Tablet 16mg; Tablet in fixed combination	S
Captopril	Tablet 12.5mg, 25mg	B
Carvedilol	Tablet 6.25, 12.5mg	C
Clonidine	Injection 500mcg/mL; Tablet 0.1 mg, 0.2 mg and 0.3 mg	S
Diltiazem	Tablet 60mg	D
Doxazosin	Tablet 2mg, 4mg	S
Enalapril	Tablet 2.5mg, 5mg (as hydrogen maleate)	C
Esmolol	Injection 10g/mL	S
Hydralazine	Tablet 25mg	B
	20mg Powder for Injection/Infusion	C
Irbesartan	Tablet 150mg, 300mg; Tablet in fixed combination	S
Lisinopril	Tablet 5mg, 10mg	C
Losartan	Tablet 50mg; Tablet in fixed combination	C
Nimodipine	Capsule 30mg	S
Methyldopa	Tablet 250mg	A
Metolazone	Tablet 5mg	S
Metoprolol	Tablet 50mg	C
	Injection 1mg/mL	S
Telmisartan	Tablet 40mg, 80mg; Tablet in fixed combination	S

### 13.4 Medicines Used in Heart Failure

Candesartan	Tablet 8mg	C
Dobutamine	Injection 250mg/5mL	S
Dopamine	Injection 250mg	S
Digoxin	Injection 250mg/mL	D
	Tablet 0.25mg	D

Ivabradine	Tablet 5mg	S
<b>13.5 Diuretics</b>		
Furosemide	Injection 10mg/mL; Tablet 40mg	B
Eplerenone	Tablet 25mg, 50mg	S
Bendrofluazide	Tablet 5mg	A
Hydrochlorothiazide	Tablet 25mg; 12.5mg	D
Mannitol	Injectable solution: 10%; 20%	C
Spironolactone	Tablet 12.5mg, 25mg	C
Torsemide	Tablet 2.5mg, 5mg; 10mg	S
<b>13.6 Antithrombotic Medicines</b>		
<b>13.6.1 Anti- Platelet Medicines</b>		
Acetylsalicylic acid	Tablet: 75mg, 100mg	A
Clopidogrel	Tablet: 75mg; 300mg	D
Prasugrel	Tablet 10mg	S (with special permission)
Ticagrelor	Tablet 60mg, 90mg	S (with special permission)
<b>13.6.2 Thrombolytics</b>		
Alteplase	Powder for injection: 50mg vial	S
Streptokinase	Powder for injection: 1.5 million IU in vial.	S
<b>13.7 Lipid Lowering Medicines</b>		
Atorvastatin	Tablet 10mg; 20mg; 40mg	B
Fenofibrate	Capsule 200mg	D
Rosuvastatin	Tablet: 10mg ; 20mg	S
<b>14.0 Dermatological Medicines</b>		
<b>14.1 Antifungal Medicines</b>		
Benzoic acid Compound (whitfield's)	3% salicylic acid and 6% benzoic acid ointment	A
Clotrimazole	Cream 1%	A
Miconazole	Cream (nitrate) 2%	C
Terbinafine	Cream 1%,	C

**14.2 Anti-infective Medicines**

Fusidic acid	Cream 2%	C
Gentian Violet	1%, aqueous solution	A
Mupirocin	Ointment 2%	C
Potassium permanganate	Potassium permanganate Solution 1:4000	A
Povidone iodine	Solution 10%	A
Silver Sulfadiazine	1% Cream	A

**14.3 Anti-inflammatory and Anti-pruritic Medicines**

Betamethasone	cream or ointment 0.1% ( as valerate)	C
Calamine	Lotion 15.0% w/v	A
Clobetasol propionate	Cream 0.05%; 0.1%	D
Fludrocortisone	Tablets 0.1 mg (as acetate)	S
Hydrocortisone	Hydrocortisone Cream 0.5%	A
Mometasone furoate	Ointment/Cream containing 0.1% contains mometasone furoate,	S
Triamcinolone	Injection 40mg/mL as Acetonide	S

**14.4 Medicines Affecting Skin differentiation and Proliferation**

All-trans-retinoic acid (ATRA)	Tablet 10mg, 20mg, injection	S
Benzoyl peroxide	Gel 2.5%, 5% and 10%	A
Coal tar	Solution 5% (prepare from raw materials)	C
Isotretinoin	0.05% cream, Capsule 10mg, 20mg	S
Podophyllin Solution	Solution 10-25% (prepare from raw materials)	D
Salicylic acid	Topical solution 5% (prepare from raw materials)	C
Silver nitrate pencil	Silver nitrate pencil	C
Tretinoin cream	2.5% cream	S

**14.5 Scabicides and Pediculicides**

Benzyl benzoate Emulsion	Emulsion: 25%	A
Lindane	Lotion 1%	C

**14.6 Sunscreen Protector**

Sunscreen protecting factor (SPF 30+)	Sun screen cream 30+	C
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## **15.0 Gastro-Intestinal Medicines**

### **15.1 Antiulcer Medicines**

Antacid Mixture	Antacid Mixture containing magnesium trisilicate + aluminium hydroxide and Simethicone	<b>B</b>
Bismuth Subgallate	Tablet 200mg	<b>D</b>
Esomeprazole	Tablet 20mg; 40mg	<b>S</b>
Lansoprazole	Tablet 30mg	<b>C</b>
Magnesium trisilicate Tablet	Tablet (250mg magnesium trisilicate + 120mg dried aluminium hydroxide)	<b>A</b>
Mesalazine	Tablet 400mg, 500mg, 800mg	<b>S</b>
Octreotide	Injection 50mcg; 100mcg	<b>S</b> (Special permission)
Omeprazole	Tablet 20mg	<b>A</b>
Pantoprazole	Tablet 40mg; Powder for injection 40mg	<b>C</b>
Terlipressin	0.12mg/mL solution for injection (acetate)	<b>S</b>

### **15.2 Drugs affecting Intestinal Secretion and Antispasmodics**

Cholestyramine	Cholestyramine Powder 4g per Sachet	<b>S</b>
Hyoscine butylbromide Tablet	Hyoscine butylbromide Tablet 10mg	<b>A</b>
Hyoscine butylbromide Injection	Hyoscine butylbromide Injection 20mg/mL; 1mL ampoule	<b>C</b>
Infliximab	Injection 100mg	<b>S</b> (Special permit)
Mebeverine	Tablet 135mg	<b>D</b>
Pancreatic	Supplement Enzyme	<b>S</b>
Ursodeoxycholic acid	Tablet/capsule 300mg	<b>S</b>

### **15.3 Anti-emetics**

Domperidone	Tablet 10mg	<b>D</b>
Doxylamine	Tablet 25mg	<b>C</b>
Metoclopramide	Tablet 10mg; Injection 5mg/mL; Suspension 5mg/5mL	<b>C</b>
Promethazine	Tablet (hydrochloride/theoclare) 25mg; Injection (as hydrochloride) 25mg/mL; Elixir 5mg/5mL (as chloral hydrate)	<b>A</b>
Ondansetron	Tablet 8mg, Injection 2mg/mL	<b>S</b>

### **15.4 Cathartics**

Bisacodyl	Tablet 5mg	<b>A</b>
Lactulose	Solution 3.1 - 3.7g/5mL, 200mL bottle	<b>C</b>

L-Ornithine L-Aspartate	Granules; Injection	S
<b>15.5 Anti-Haemorrhoids</b>		
Local anaesthetic + astringent and anti-inflammatory	Suppositories/ointment (zinc oxide 25mg + bismuth oxide+ bismuth subgallate 59 mg + balsam Peru)	B

<b>15.6 Medicines Used in Diarrhoea</b>		
Loperamide	Tablet/Capsule (hydrochloride) 2mg	B
Oral Rehydration Salts (ORS)	Low osmolality sachet to make 1 litre of solution containing Sodium chloride 2.6g, Sodium citrate 2.9g, Potassium chloride 1.5g and Glucose 20.5g)	A
Zinc	Tablet dispersible (equivalent to 20mg elemental zinc)	A
<b>16.0 Insulin and Medicines Used for Diabetes and Related Disorders</b>		
Empagliflozin	Tablet 10mg	S (with special permit)
Glibenclamide	Tablet 5mg	A
Gliclazide	Tablet 40mg; 80mg; 30mg; 60mg	A
Glimepiride	Tablet 1mg; 2mg	C
Glucagon	Powder for reconstitution 10mg/vial	S
Insulin	Rapid acting; Injection: 40 IU/mL; 100 IU/MI	
	Short acting; Injection: 40 IU/mL; 100 IU/mL	A
	Intermediate acting; Injection: 40 IU/mL; 100 IU/mL	A
	Long acting; Injection: 40 IU/mL; 100 IU/mL	A
	Pre-Mixed Insulin; Injection: 40 IU/mL; 100 IU/MI	S
Metformin	Tablet 500mg; 750; 850MG; 1000MG; SR	A
Pioglitazone	15mg	D
Phenoxybenzamine	Tablet 10 mg	S
Sitagliptin	Tablet 50mg; 100mg	S
<b>17.0 Immunologicals</b>		
<b>17.1 Sera and Immunoglobulins</b>		
Anti D immunoglobulin	Injection 150mg; 300mg	C
Antirabies immune globulin	Injection 400IU/mL; 10,000IU/5mL	A

Anti-venom immunoglobulin	Snake venom polyvalent Antiserum injection (Central African type)	<b>A</b>
Diphtheria antitoxin	Injection: 10,000 IU; 20,000 IU vial	<b>A</b>
Tetanus Immunoglobulin	Tetanus Immunoglobulin (human) – 250 IU/mL, 250 IU/2.5mL	<b>A</b>

## **17.2 Vaccines**

### **17.2.1 For Immunization**

BCG Vaccine	Injection 20 doses vial (Bacillus Calmette Guerin)	<b>A</b>
DPT-HepB-Hib Vaccine	Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus Influenza vaccine in vials of 10 doses	<b>A</b>
Hepatitis B	Injection 10mcg/mL, 20mcg/mL, 40mcg/ML	<b>B</b>
Human Papilloma Vaccine (HPV)	Human Papilloma Vaccine (HPV) – 0.5mL per dose	<b>A</b>
Inactivated Polio Vaccine (IPV)	Inactivated Polio Vaccine (IPV)	<b>A</b>
Measles-Rubella Vaccine	Measles-Rubella Vaccine Injection 10 doses in vial	<b>A</b>
Oral Poliomyelitis Vaccine (OPV)	Oral Poliomyelitis Vaccine (Live attenuated) Oral solution 20 doses in vial	<b>A</b>
Pneumococcal Conjugate Vaccine (PCV13)	Pneumococcal Conjugate Vaccine (PCV13) -4 doses vial	<b>A</b>
Pneumococcal polysaccharide vaccine (PPSV-23)	Vial	<b>S</b>
Rota Vaccine	Rota Vaccine Oral solution	<b>A</b>
Tetanus (toxoid) Vaccine	Tetanus (toxoid) Vaccine Injection 20 doses in 10mL vial	<b>A</b>

### **17.2.2 For Specific Groups for Individuals**

Human Diploid Cell Rabies Freeze dried rabies vaccine	Human Diploid Cell Rabies Freeze dried rabies vaccine	<b>A</b>
Meningitis vaccine	Injection	<b>C</b>
Yellow Fever Vaccine	0.5mL dose	<b>C</b>

## **18.0 Muscle Relaxants (Peripherally-Acting) and Cholinesterase Inhibitors**

Neostigmine	Injection: 500microgram in 1mL ampoule; 2.5 (metilsulfate) in 1mL ampoule	<b>C</b>
Suxamethonium	Injection: 50mg (chloride/mL in 2mL ampoule	<b>C</b>

## **19.0 Ophthalmological Preparations**

### **19.1 Anti-infective Agents**

Acyclovir ointment	Acyclovir Eye ointment 3%	C
Ciprofloxacin	Drops 0.3%	C
Chloramphenicol	Drops 0.5%, 1%; Eye ointment 1%	A
Chlorhexidine	Drops 0.2%	S
Dexamethasone+Chloramphenicol	Drops 0.1%, 0.5%	C
Dexamethasone +Gentamicin	Drops 0.1, 0.3%	C
Econazole	Drops 5%	S
Natamycin	Drops 5%	S
Ofloxacin	Drops 0.3%	D
Oxytetracycline t	Eye ointment 3%	A
Iodine	Eye drops, 2.5-5%	A

### **19.2 Anti-allergy, Artificial Tears and Anti-inflammatory Agents**

Dexamethasone eye drops	Drops 0.1%	D
Hydroxypropylmethylcellulose	Drops 0.70%	C
Methylprednisolone acetate	Injection 40mg/mL	D
Prednisolone eye drops	Drops 0.5%, 1%	D
Oxymetazoline	Drops 0.025%	C
Sodium cromoglycate drops	Sodium cromoglycate 2%, 4% eye drops	C
Triamcinolone Acetonide	Injection 40mg/mL	S

### **19.3 Local and Topical Ocular Anaesthetic Agents**

Amethocaine eye drops	Drops 0.5%w/v or 1.0%w/v	A
Tetracaine eye drops	Drops .5%w/v	C

### **19.4 Miotics and Antiglaucoma**

Acetazolamide	Tablet 250mg	C
Acetylcholine	Injection; vial contains 20 mg acetylcholine chloride and 56 mg mannitol	S
Betaxolol	Drops 0.25% -0.5% w/v	D
Brimonidine	Drops 0.15 – 0.2% w/v	D
Dorzolamide	Drops 20 mg/ml	S
Latanoprost	Drops 0.005% w/v	D
Pilocarpine hydrochloride	Drops 2 or 4% w/v	C
Prostamide bimatoprost	Drops 0.03% w/v	D
Timolol	Drops 0.25%, 0.5% w/v	C

<b>19.5 Mydriatics and Anti-vascular Endothelial</b>		
Atropine	Drops 0.5%, 1% w/v; Ointment 1%	B
Cyclopentolate	Drops 0.5%, 1% w/v	C
Tropicamide	Drops 1% w/v	S
Tropicamide with Cyclopentolate	Drops 0.5%, 1% w/v	C
Tropicamide with Phenylephrine	Drops 0.8% / 5% w/v	C
<b>19.6 Other Ocular Preparations</b>		
5 -Fluoro Uracil	1% eye drops	D
Ganciclovir	Injection 2mg; ophthalmic gel, 0.15%	S
Mitomycin C	5mg/vial, 10 mg/vial	D
Silicon Oil	1000 CS, 1500 CS, 5000 CS	S
<b>20.0 Oxytocics and Antioxotocics</b>		
<b>20.1 Oxytocics</b>		
Ergometrine Injection	Injection (maleate) 0.5mg/mL (hydrogen maleate) in 1mL ampoule	C
Misoprostol	Tablet 200mcg (rectal, sublingual)	A
Oxytocin Injection	Injection 10 IU in 1mL ampoule	A
<b>20.2 Antioxotocics (tocolytics)</b>		
Dicyclomine	Tablet 20mg; Injection	B
Nifedipine	Immediate – release capsule: 10mg, 20mg	B
Salbutamol Tablet	Tablet 4mg	A
<b>21.0 Dialysis Solution and Other Related Medicines</b>		
Iron Sucrose	Injection 20mg/ML	D
Intraperitoneal dialysis solution	Parenteral solution (of appropriate composition)	S
<b>22.0 Psychotherapeutic and Related Medicines</b>		
<b>22.1 Medicines used in Psychotic Disorders</b>		
Benzhexol	Tablet 5mg	C
Chlorpromazine	Injection (hydrochloride) 25mg/mL in 2mL ampoule; Tablet (hydrochloride) 25mg, 100mg	A
Donepezil	Tablet 5mg, 10mg	S
Fluphenazine	Injection 25mg/mL (decanoate) in 1mL ampoule	C

Haloperidol	Injection 5mg/mL in 1mL ampoule; Tablet 1.5mg	B
Lorazepam	Tablet 1mg, 2mg	C
Olanzapine	Tablet 5mg; 10mg	S
Risperidone	Tablet 1mg/2mg	S
Zuclopentixol	Injection 50mg/mL (Acetate)	S

## 22.2 Medicines Used in Mood Disorders

### 22.2.1 Medicines used in Depressive disorders

Amitriptyline	Tablet (hydrochloride) 25mg	A
Citalopram	Tablet 20mg	D
Fluoxetine	Capsule 20mg	S
Imipramine	Tablet 25 mg	C
Oxybutynin	Tablet 5mg	S

### 22.2.2 Medicines in Bipolar Disorders

Carbamazepine	Tablet 100mg, 200mg	A
Lamotrigine	Tablet 100mg, 200mg	S
Sodium Valproate	Tablet 200mg, 500mg	C

### 22.3 Medicines Used for anxiety Disorders

Diazepam	Tablet 5mg	C
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### 22.4 Medicines Used for Disorders due to Psychoactive Substance use

Buprenorphine	Sublingual Tablets2mg	S
Methadone	Oral liquid: 5mg/5mL; 10mg/5mL	C
Naltrexone	Tablet 50mg	S

## 23.0 Medicines Acting on Respiratory Tract

### 23.1 Anti-asthmatics

Budesonide inhaler	Inhalation 100mcg, 200mcg	B
Fluticasone propionate	Nasal Spray 50mcg	D
Ipratropium Bromide Aerosol	Inhalation (aerosol): 20 microgram/metered dose; Nebulizer 250-500mcg	S
Montelucast	Tablet 5mg; 10mg	D
Salbutamol	Tablet (as sulfate) 4mg; syrup (as sulfate) 2mg/5mL; Inhalation (as sulfate) 0.1mg per dose (aerosol inhaler)	A
	Nebulizer solution 2.5mg/mL; 5mg/mL; Injection 0.5mg/mL; img/mL	B

Salfolinl	Inhalation 100mcg, 200mcg	C
Tiotropium	Inhalation 1.25mcg/actuation; 2.5mcg/actuation	S ( with special permit)
<b>23.2 Cough Preparations</b>		
Cough syrup	Containing expectorants/Antitussive Lictus	A
<b>24.0 Solutions, Correcting Water Electrolyte and Acid-Base Disturbances</b>		
Dextrose 5%;	Dextrose 5%; 500mL, 1000mL	A
Dextrose 10%;	Dextrose 10%; 500mL	C
Dextrose 25%,	Dextrose 25%, 50mL, 100mL	C
Dextrose 50%,	Dextrose 50%; 50mL, 100mL	C
Polystyrene sulfonate	Solution containing calcium (or sodium)	D
Sodium bicarbonate	Injection 5%,	C
Sodium lactate compound	Sodium lactate compound (Ringer's solution) 500mL, 1000mL.	A
Sodium Chloride solution	0.9% Sodium Chloride 500mL, 1000mL	A
Sodium Chloride solution	3% Sodium Chloride 500mL, 1000mL	C
Sodium chloride+Dextrose	Sodium chloride+Dextrose 0.9%+5%; 500mL, 1000mL	B
Potassium chloride Solution	Potassium chloride Solution 7.4% 10mL Vial	C
Water for injection	5mL, 10mL vial	A
<b>25.0 Vitamins/Minerals</b>		
Ascorbic acid (Vitamin C) Tablet	Ascorbic acid (Vitamin C) Tablet 100mg and 500mg	A
Calcium gluconate	Injection 100mg/mL in 10mL ampoule	A
Calcium Carbonate	Tablet 500mg	S
Calcium	with vitamins	C
Calcium	with amino acids	C
Ergocalciferol (vitamin D)	Capsule 1.25mg (50,000IU); Oral solution 0.25mg/mL (10,000IU/mL)	C
Glucosamine +Chondroitin sulphate	Tablet	S
Iron	with vitamins	C
Iron	with amino acid	C
Nicotinamide (Vitamin B <sub>3</sub> )	Tablet 50mg	C
Potassium chloride	Tablet (slow release) 600mg ; Injections	C

Pyridoxine (Vitamin B <sub>6</sub> )	Tablet (hydrochloride) 25mg	<b>B</b>
Retinol (Vitamin A) Capsule	Retinol (Vitamin A) Gelatin Capsule (with nipple to allow administration drop by drop) 50,000IU, 100,000IU 200, 000IU	<b>A</b>
Sodium Hyaluronate 1%	Injection. 1%	<b>S</b>
Thiamine (Vitamin B <sub>1</sub> )	Tablet (hydrochloride) 100mg	<b>C</b>
Thiamine (Vitamin B <sub>1</sub> )	Injection (hydrochloride) 1000mg/mL in 1mL ampoule	<b>C</b>
Vitamin B complex	Vitamin B complex Tablet BP (contains per Tablet: niacinamide 15mg, riboflavin 1mg, thiamine 1mg)	<b>A</b>
Vitamin B complex	Syrup (contains niacinamide 15mg, riboflavin 1mg, thiamine 1mg/5mL)	<b>A</b>
Vitamin B complex	Injection BP in 10mL vial (contains niacinamide 200mg, pantothenol 30mg, pyridoxine 20mg, riboflavin 20mg, thiamine 50mg per 1 mL)	<b>B</b>
Vitamin E	Tablet/capsule alpha tocopherol acetate 500 mg/5 mL	<b>D</b>

## **26.0 Medicines Used in Ear, Nose & Throat Diseases**

### **26.1 Ear Drops**

Betamethasone	Ear drops; 0.1% w/v	
Boric acid	Ear drop; 3%	<b>A</b>
Ciprofloxacin	Ear drops; 0.3%	<b>C</b>
Clotrimazole	Ear drops; 1%	
Chloramphenicol	Ear drops; 5% w/v	
Dexamethasone + Neomycin	Ear drops: 0.1% + 0.5%	<b>C</b>
Lidocaine + Beclometasone Clotrimazole + Chloramphenicol	+ Ear drop	<b>D</b>

### **26.2 Oral Antiseptics**

Chlorhexidine gluconate Solution	Chlorhexidine gluconate Solution 0.1%; prepare from concentrated solution; gel	<b>B</b>
Potassium permanganate Solution	Potassium permanganate Solution 1:4000; prepare from powder/crystals	<b>A</b>

### **26.3 Nasal Preparations**

Ephedrine	Nasal drops 0.5% and 1%	<b>B</b>
Normal saline	Nasal drop 0.9%	<b>A</b>
Mometasone	Nasal spray 50 micrograms/dose (as furoate)	<b>S</b>
Xylometazoline	Nasal spray 0.05%	<b>S</b>

**27.0 Disinfectants and Antiseptics**

Chlorhexidine + Cetrimide	Solution concentrated containing chlorhexidine digluconate 1.5%+ 15% cetrimide	A
Chloroxylenol	Solution 4.9% BP	A
Cresol saponated	Solution 3% BP	A
Formaldehyde	Solution 36 - 37% stabilized	B
Glutaraldehyde	Activated solution 2%	C
Hydrogen peroxide	Solution 3%	A
Hydrogen peroxide	Solution 6%	A
Methylated spirit	Solution 70%	A
Potassium permanganate	Potassium permanganate Solution 1: 4000	A
Povidone-Iodine	Solution 10%	A
Sodium dichloroisocyanurate	Tablet, 1.67g (equal to 1g available chlorine)	A

**28.0 Miscellaneous**

Sildenafil	Tabet 50mg	S
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## **PART II**

# **THE STANDARD TREATMENT GUIDELINE (STG)**

Standard Treatment Guidelines provide standardized guidance to health professionals on diagnosis and treatments. It provides invaluable assistance to practitioners especially those with lower skills or new in the field. STG are systematically developed statements to assist practitioners/prescribers in making decisions about appropriate treatment for specific clinical conditions. The statements contain information on: clinical conditions, diagnosis criteria, non- pharmacological, medicines of choice (and alternatives) for the medical condition, important prescribing information—dose, duration, contraindications, side effects, warnings, medicine interactions and the referral criteria.

The STGs should be updated regularly to reflect changes in accepted treatment strategies. The 2021 edition of STG have been updated to reflect new therapeutic options and to include new emerging diseases. In the development process, the use of evidence-based medicine was overemphasized and each chapter was revised by a Lead Reviewer, an expert on the specific disease condition. The STG has covered the priority disease conditions in the country arranged in twenty-six chapters namely:

- Emergency and Critical Care
- Anaesthesia
- Haematological Disease Conditions
- Notifiable Diseases
- Malaria
- HIV/AIDS
- TB and Leprosy
- Nervous Disease Conditions
- Respiratory Disease Conditions
- Gastrointestinal Disease Conditions
- Obstetrics, Gynaecology and Contraception
- Sexually Transmitted Infections
- Skin Disease and Allergic Reactions
- Eye Disease Conditions
- Oral and Dental Conditions
- Ear, Nose and Throat Diseases
- Musculoskeletal Disorders
- Trauma and Injuries
- Metabolic and Endocrine Disease Conditions
- Kidney and Urological Disorders
- Malignant Disease Conditions
- Mental Health Conditions
- Nutrition Disorders
- Poisoning

**Note**

- All medicines indicated for treatment of various diseases in the STG are listed in the NEMLIT.
- The referral criteria in the STG meant to refer the patient to the next level of care; with the fact that expertise to manage a patient/diagnosis capacity may lack at that level.

# **CHAPTER ONE**

## **APPROACH TO PATIENTS WITH EMERGENCY CONDITIONS**

### **1.1 The Concept of Emergency Care and Resuscitation**

Emergency care and Resuscitation involves rapid assessment and early intervention. Approach to Emergency care and resuscitation needs to be systematic hence the use of the ABCs approach. The ABCs approach provide the framework for evaluation and treatment of severely ill patients.

#### **Primary survey**

##### **I. Airway**

Assess the airway to establish patency of the airway. This includes:

- Looking for signs of airway obstruction (signs of trauma, swelling, secretions, presence of foreign body).
- Listen for abnormal sounds like stridor, snoring.

If there are signs of airway obstruction intervene by positioning, opening and clearing the airway. Perform chin lift or jaw thrust manoeuvre to open the airway (If suspecting cervical spine injury use the jaw thrust manoeuvre). Use suction to remove the secretions. Airway adjuncts like oropharyngeal or nasopharyngeal airway can be used.

#### **Note**

- Remember to reassess the airway after performing interventions
- Some patient may require use of advance airway devices like endotracheal intubation or surgical airway

##### **II. Breathing**

Upon completing airway assessment and intervention, assess for presence of breathing, signs of respiratory distress such as tachypnea, hypoxia, cyanosis, apnoea and abnormal breath sounds. Provide oxygen when oxygen saturation is below 92% or the patient is dyspnoeic. Oxygen can be administered using the nasal prong, simple face mask, non-rebreather mask or ambu bag. Advance interventions include: mechanical ventilation.

##### **III. Circulation**

Check for pulse (central pulse) for not more than 10 seconds. If absent start CPR (**Refer cardiopulmonary resuscitation section below**). Assess for signs of poor peripheral perfusion (shock) such as cold extremities, prolonged capillary refill, dry mucous membrane and hypotension. If there are signs of shock, establish two (2) IV large bore cannula and give IV fluids (crystalloids) bolus (2lts in adults and 20mls/kg in pediatrics). Limit fluids to individuals whom you suspect to have heart failure, renal failure or malnourished children.

##### **IV. Disability**

This involves rapid assessment of the neurological status. This includes assessment for the level of consciousness (use of AVPU or Glasgow coma scale), signs of convulsions, random blood glucose level, examination of the pupils and presence of focal neurological deficit. Interventions that can be performed during the disability assessment include: correction of hypoglycemia, airway protection, stopping the convulsions by administering anticonvulsant

##### **V. Exposure**

This involves fully exposing the patient and rapid assessment of the body for signs of trauma, rashes or infection.

#### **Secondary survey**

After assessment and stabilization of ABCs during the primary survey, focus is turned into secondary survey. The secondary survey is a systematic assessment of the rest of the body to identify injuries and illnesses. Common approaches include a head to toe or organ –system based assessment. It is important to note that the secondary survey is performed after the primary assessment and interventions. When performing a secondary survey, if the patient condition changes then you must stop immediately and redo the primary survey and necessary interventions.

**Note:**

All patients with compromised airway, breathing, circulation or disability must be attended in the resuscitation rooms. (Refer Triage overview section)

## 1.2 Cardiac Arrest and Cardiopulmonary Resuscitation

Cardiopulmonary resuscitation is an Emergency lifesaving procedure performed when there is sudden cessation of heart beats. It involves the combination of chest compressions and artificial ventilation to preserve blood flow to the organs including the brain function. Early initiation of CPR can double or triple the chances of survival after cardiac arrest.

**Note: HIGH QUALITY CPR**

- Compressions:
  - Infant: 2 finger compression (if alone) or thumb encircling technique (if you have assistance)
  - Child: 1 or 2 hand
  - Adult: Two hands
  - Compression rate: 100-120/min
  - Compression depth: approximately 1/3 antero-posterior diameter of the chest
  - Compression/ventilation ratio: 30:2 (adults and children), 30:2 (If alone) and 15:2 (If you have assistance)
- Allow chest recoil
- Minimize interruptions
- Adequate ventilation

**Clinical presentation**

- Unresponsiveness (sudden loss of consciousness)
- Absence of central pulse (carotid pulse/femoral pulse or brachial pulse in infants)
- Loss of spontaneous respiration

**Investigations**

While continuing with CPR, point of care (POC) tests are conducted while looking for the reversible causes of the cardiac arrest (Hypovolemia, hypoxia, hypo/hyperkalemia, acidosis, hypothermia, hypoglycemia, tension pneumothorax, toxins, thrombi, cardiac tamponade). These includes:

- POC Blood gases
- POC Bicarbonates
- POC Electrolytes- Potassium, sodium, Calcium, Chloride,
- POC Creatinine, POC urea
- POC RBG
- Bedside ultrasound- looking for pneumothorax, cardiac tamponade or thrombi
- POC Toxicology screens (If available)
- POC ECG (if there is return of spontaneous circulation)
- POC lactate
- POC Troponin

**Management**

- **HAZARDS-** ensure safety and use of PPEs
- **HELLO-** Check for responsiveness, Carotid pulse (not more than 10 seconds) and breathing
- CPR starts with early recognition (unresponsiveness, loss of spontaneous breathing and absence of carotid pulse. In infant's CPR is initiated when the heart rate is below 60 beats/min)
- Call for **HELP** and immediately start chest compression. As more members arrives to help assign different roles including airway and breathing management, time recording, documentation, AED/monitor, medications
- Open the airway by performing chin lift or jaw thrust (if suspecting C spine injury). Use airway adjuncts to open the airway.
- Give 2 breaths using bag valve mask connected to oxygen source and observe for chest rise

- Establish IV access for administration of fluids and medications, if failed perform Intraosseous access
- After **FIVE** cycles of compressions/ventilation (**2 minutes**), check for pulse and use AED/Defibrillator to analyze rhythm if there is a need to deliver shock
- If no need for shocking continue with CPR for another **2 minutes** (**FIVE** cycles)

### **Pharmacological Treatment**

**A:** adrenaline (IV) Adult: 1mg, Pediatrics 0.01mg/kg (repeat every 3-5 minutes)

**AND**

**A:** 0.9% sodium chloride (IV): Adult 2000mls, pediatrics 20mls/kg; if suspecting hypovolemia as a cause of the arrest

**AND**

**A:** dextrose 5% (IV) if needed to correct hypoglycemia

**OR**

**C:** dextrose 10%, 25% or 50% (IV) if needed to correct hypoglycemia

**AND**

**C:** sodium bicarbonate 1mmol/kg (IV) push (if needed to correct acidosis)

**\*Additional medications maybe required depending on cause of the cardiac arrest (the reversible cause)**

### **Disposition**

Upon achieving return of spontaneous circulation (ROSC), definitive airway is achieved by performing endotracheal intubation for mechanical ventilation and patient must be admitted to the ICU or transferred to a facility with an ICU capacity.

## **1.3 Approach to Stridor**

Stridor is an abnormal, high-pitched sound produced by turbulent airflow through a partially obstructed airway. Stridor is a dangerous finding and may indicate imminent airway obstruction. It can be inspiratory, expiratory or biphasic.

### **Clinical presentation:**

- Hypoxia
- Respiratory distress
- Altered mental status
- Inability to speak
- Inability to swallow

### **Differential diagnoses**

Infectious causes- croup, epiglottitis, peri-tonsillar abscess, retropharyngeal abscess

Non- infectious causes- Foreign body obstruction, burns, trauma, anaphylaxis, malignancy, laryngotraeheomalacia, stenosis

### **Investigations**

Blood gases analysis, Lateral neck X ray (for foreign body, masses or soft tissue swelling), CXR (foreign body, evidence of aspiration), CT- scan, Blood Sugar, Lactate, Electrolyte analysis and/or Serum creatinine and urea

### **Non pharmacological**

Keep the patient calm by allowing the patient to assume their most comfortable position. Give oxygen if there are signs of increased work of breathing.

### **Pharmacological treatment**

**A:** adrenaline (nebulization) 0.5mls/kg

**AND**

**A:** prednisolone (PO) 1-2mg/kg stat

**OR**

**D:** dexamethasone (PO) 0.6mg/kg stat

**Note**

Administer IV fluids (if signs of shock) – refer section on the management of shock

**Referral:** All patients with stridor whom the cause has not yet been established must be referred to higher health facilities

## 1.4 Approach to Upper Gastrointestinal Bleeding

Upper GI bleeding is any GI bleeding originating proximal to the ligament of Treitz.

### Clinical Presentation

Hematemesis and coffee-ground emesis suggest a UGI source. On physical examination, vital signs may reveal obvious hypotension and tachycardia. Cool, clammy skin is an obvious sign of shock. Abdominal examination may disclose tenderness, masses, ascites, or organomegaly. Perform rectal examination to detect the presence of blood and its appearance, whether bright red, maroon, or melanotic. Other findings include, the presence of spider angiomas, palmar erythema, jaundice, and gynecomastia which may suggest liver disease while petechiae and purpura may suggest an underlying coagulopathy.

### Differential diagnosis

Peptic ulcer disease, upper GI malignancy, oesophageal or gastric varices, esophagitis, Mallory-Weiss tear, Boerhaave syndrome and arteriovenous malformation

### Investigations

ABO Grouping and cross-matching, Complete Blood Count, Hemoglobin Level, Blood Urea Nitrogen and Creatinine, Electrolytes, (Sodium, Potassium, Calcium Chloride), PT, PTT, INR, Liver Function Tests, Lactate levels, Obtain an ECG in patients with underlying coronary artery disease and/or Bedside Ultrasound

### Non Pharmacological treatment

Maintain ABCs, give oxygen if needed

### Pharmacological Treatment

Give blood If severe pallor, ongoing bleeding, Hb < 5g/dl and Hb < 7g/dl (with active bleeding)

- Adults 2 units within 1hour and Paediatric 20ml/kg 1hour (whole blood) or 10ml/kg (pRBC)
- If ongoing indication for blood, start transfusion in the following ratio: 1unit pRBCs (20ml/kg in Paediatric): 1unit FFP (20mls/kg in Paediatric): 1unit PLT (20ml/kg in Paediatric)

Give

**A:** 0.9% sodium chloride (IV)

**OR**

**A:** compound sodium lactate (IV); Adult 2000mls and Paediatrics 20ml/kg

**AND**

**C:** pantoprazole (IV); Adult 80mg stat, then infusion 8mg/hour for 3days, Paediatrics 1mg/kg stat (max 80mg) then infusion 1mg/kg/hour for 3days

**OR**

**S:** esomeprazole (IV) 40mg 24hourly for 3days

For patients with suspected variceal bleeding give:

**S:** octreotide (IV) Adult 50mg slow bolus, then infusion 50mcg/hour for 5days; Paediatrics 1mcg/kg/hour (maximum 50mcg/hour) for 5days

If features suggestive of cirrhosis; give

**C:** ciprofloxacin (IV) 500mg 12hourly for 7days

**OR**

**B:** ceftriaxone (IV) 2g 24hourly for 7days

**DEFINITIVE CARE:** Early Endoscopy and Intensive care unit admission (**Refer Gastrointestinal disease chapter**)

## **1.5 Approach to Seizure and Status Epilepticus**

Status epilepticus is a single seizure ≥5 minutes in length or two or more seizures without recovery of consciousness between seizures. Status epilepticus is a neurologic emergency, and treatment should be initiated in all patients with continuous seizure activity lasting more than 5 minutes.

### **Clinical presentations**

- Abrupt onset seizures
- Altered mental status
- Postictal drowsiness
- Tongue biting

### **Differential diagnoses**

Epilepsy, meningitis, encephalitis, malaria, space occupying lesion, alcohol withdrawal, isoniazid toxicity, intracranial hemorrhage, metabolic abnormalities- hyponatremia, eclampsia, acute hydrocephalus.

### **Investigations:**

Blood Glucose, Electrolytes: (Sodium, Potassium, Chloride, Magnesium and Calcium), ECG, Bedside ultrasound, Blood gases, Malaria Test, Serum creatinine and urea, Lactate levels, Pregnancy test (females), Toxicology screening and/or CT Head

### **Non-pharmacological management**

- Protect patient from injury (If possible place in left lateral position to reduce aspiration risks), Don't place tongue depressor
- Perform both primary and secondary assessment and provide necessary interventions
- Give Oxygen if needed
- Do bedside random blood sugar test
- Establish IV access for administration of anticonvulsants, if unable use the rectal route
- Connect the patient to the cardiac monitor to obtain vital signs

### **Pharmacological management**

#### **I. Active seizure 0-5minutes**

Supportive care:

IV access, monitors, maintain airway, oxygen therapy. Check point-of-care glucose and provide:

**A:** dextrose 5%(IV); if glucose is ≤ 3.5mmol/L

**AND**

**A:** diazepam (IV) 0.15-0.2mg/kg. Maximum 10mg (Rectal dose: 0.2-0.5mg/kg) repeat every 5 minutes up to 3 doses

**OR**

**D:** midazolam (IV): 0.1mg/kg repeat every 5 minutes up to 3 doses

#### **II. Established Status Epilepticus 5-10 min**

**B:** phenobarbitone (IV): Adults 20mg/kg slowly (max 50mg/min); Paediatrics 20mg/kg slowly (max 30mg/min)

**OR**

**C:** phenytoin (IV) Adults 20mg/kg slowly (max 50mg/min); Paediatrics 20mg/kg slowly (max 30mg/min)

Consider **INTUBATION** if patient still seizing

**C:** thiopental (IV): Adult 3-6mg/kg loading dose then 25-100mg infusion as needed; Paediatrics 2-5mg/kg loading dose

**OR**

**D:** propofol (IV): Adults 2mg/kg loading dose then 2-10mg/kg/hour; Paediatrics 3mg/kg loading dose, then 7.5-18mg/kg/hr

**OR**

**D:** midazolam (IV): Adult 0.2mg/kg loading dose then 0.1-0.2mg/kg/hour; Paediatrics 0.1mg/kg then infusion 0.06 – 0.4mg/kg/hour

**Disposition:** Intensive care unit admission or refer to the higher health facility with ICU/HDU capacity

## **1.6 Approach to Altered Mental Status**

This is the acute alteration in brain function and may include alteration of arousal or awareness, thought content, memory or attention.

### **Clinical presentation**

Depending on the cause but may include: agitated, Restlessness, Hemiparesis, visual deficit, dysphasia

### **Differential diagnosis**

The mnemonic **AEIOU TIPS** is widely preferred in the emergency department when considering a broader differential. Alcohol/acidosis, Epilepsy/Electrolytes, Insulin/Inborn Errors of Metabolism, Oxygen/Overdose, Uremia, Trauma, Infection, Psychiatric/Poisoning, Stroke/Subarachnoid Hemorrhage/Shock

### **Investigations**

POC Glucose, Rapid Malaria test, Blood gases, Serum Electrolytes, POC ECG, Bedside ultrasound, Serum Creatinine and Urea, Lactate, Complete Blood Count, Liver function tests, Head CT-scan, Chest Xray and/or Toxicology screening (If highly suspiciousness of intoxication)

### **Non pharmacological treatment:**

- If aggressive/ restless consider restraining- mechanical or chemical (medications)
- Obtain set of vital signs including random blood glucose
- Perform both primary and secondary assessment and provide necessary interventions.
- Give Oxygen if Hypoxic or dyspnoeic
- Connect the patient to the cardiac monitor to obtain vital signs

### **Pharmacological treatment**

**A:** diazepam (IV):Adult 5-10mg loading dose, maintenance 0.03-0.1mg/kg every 30 minutes to 6 hours; Paediatrics 0.1-0.15mg/kg stat, may repeat after 3-5 minutes

**OR**

**B:** haloperidol (IV): Adult 0.5-10mg \*\*\* (If concerned about psychiatric disorder) Child: safety and effectiveness not established

**OR**

**B:** ketamine (IV) 1-2mg/kg and 2-4mg/kg for IM

**OR**

**D:** midazolam (IV): Adults 5mg stat, maintenance 20-100mcg/kg/hr. infusion; Paediatrics 0.05-0.1mg/kg stat

### **Note**

Additional pharmacological treatment will depend on the cause of the altered mental status  
Consult/refer to a higher center with a psychiatrist if concerned about psychiatric disorder

## **1.7 Approach to Difficult in Breathing**

Shortness of breath or breathlessness may result from a range of pulmonary, cardiac and central nervous system causes. It is important to look for the underlying cause for immediate intervention.

### **Clinical presentation**

- Increased work of breathing
- Altered mental status
- Diaphoresis
- Additional sounds- stridor, wheezes

### **Differential diagnosis**

- Pulmonary embolism
- Pulmonary oedema
- Myocardial infarction
- Asthma
- Anaphylaxis
- Airway obstruction
- Tension pneumothorax

- Cardiac tamponade
- Acute chest syndrome
- Pneumonia
- Pericarditis

### **Investigations**

Blood gases, Serum Electrolytes, Serum Creatinine and Urea, Troponins, Chest X-ray, POC ECG, Bedside Ultrasound, Lactate, Troponin, Random blood glucose

### **Non pharmacological treatment**

- Perform both primary survey (ABCs) and secondary survey and provide necessary interventions
- Obtain Vital signs
- Position the patient
- Give Oxygen if hypoxic or increased work of breathing

### **Pharmacological treatment**

Pharmacological management will depend on the underlying cause of difficulty in breathing. (**Refer Asthma-respiratory chapter and Acute chest syndrome and Pulmonary embolism-hematology chapter**)

## **1.8 Anaphylaxis**

Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction characterised by rapidly developing life-threatening airway (pharyngeal or laryngeal edema) and/or breathing (bronchospasm and tachypnea) and/or circulation (hypotension and tachycardia) problems usually associated with skin and mucosal changes.

### **Clinical presentation**

- Hives
- angioedema
- wheezes
- Difficult breathing
- Diarrhoea
- Hypotension

Anaphylaxis is a clinical diagnosis and should be suspected when:

- Acute onset involving skin, mucosal tissue with either respiratory compromise or blood pressure reduction (or syncope)
- Hypotension after exposure to a known allergy for the patient (SBP <90mmHg or >30% from baseline)
- Respiratory compromise (i.e dyspnoea, stridor, wheeze, hypoxemia)
- Exposure to a likely allergen causing involvement of the skin, mucosal, respiratory compromise or blood pressure reduction

### **Investigations**

Blood gases, Serum Electrolytes, POC ECG, Troponin, CXR and/or POC USS

### **Non pharmacological management**

- Perform both primary and secondary assessment. If patient has signs of severe respiratory distress perform early intubation/surgical airway
- Give oxygen if hypoxic (spO<sub>2</sub> below 95%) or severe respiratory distress
- Insert TWO large bore IV cannulas or obtain intraosseous access

### **Pharmacological Management**

A: adrenaline (IM): Adult 0.3-0.5mg (maximum 0.5mg) every 5-15min as soon as possible. If inadequate response, start adrenaline (IV) 2-10mcg/min in 0.9% sodium chloride (IV) OR Ringer lactate (IV) 1-2 litres. If hypotensive. Repeat IV fluids as needed; Paediatric 0.01mg/kg, every 5-15min as soon as possible. If inadequate response, start adrenaline (IV) 0.05-1mcg/kg/min in 0.9% sodium chloride (IV) OR compound sodium lactate (IV) 20mls/kg if hypotensive. Repeat IV fluids as needed

**OR**

**A:** hydrocortisone (IV)200mg stat

**OR**

**B:** salbutamol (nebulisation) 10mg and equal volume of water for injection (This is useful to patients with refractory bronchospasm).

**OR**

**D:** methylprednisolone (IV) 1-2mg/kg/day

**Disposition**

All patient with severe and moderate symptoms which required repeated doses of adrenaline or didn't respond to treatment must be admitted or referred to higher health facility. Those with mild response which responded to IM adrenaline may be discharged after 4 hours' observation at the health facility.

## **1.9 Cardiac Tamponade**

Cardiac tamponade is the result of compression of the myocardium by fluid, gas, pus, blood, or a combination of substances. It occurs in a physiologic continuum reflecting the amount of fluid, the rate of accumulation, and the nature of the heart.

The result is increased pericardial pressure, which causes decreased ventricle compliance and decreased flow of blood into the right ventricle which eventually leads to a decreased cardiac output. Conditions that may predispose a patient to pericardial effusion and tamponade include; trauma, radiation exposure, Tb pericarditis, renal failure (uremic pericarditis), autoimmune diseases, drugs that induce a lupus-like syndrome, hypothyroidism, or ovarian hyperstimulation syndrome.

**Clinical presentations**

- Chest pain and dyspnea
- Pulsus paradoxus >10 mm Hg
- Beck's triad includes low blood pressure, elevated jugular venous distention, and decreased heart sounds.
- In the absence of hypotension and tension pneumothorax in a patient with PEA, consider the diagnosis of cardiac tamponade.

**Investigations**

Bedside ultrasound, POC ECG, Blood gases, Serum Electrolytes, Troponins, Pericardial fluid analysis- biochemistry, microbiology and cytology, Serum creatinine and urea and/or Chest Xray

**Non pharmacological and pharmacological treatment**

- Perform both primary and secondary assessment and provide appropriate interventions.
- Give oxygen if hypoxic or increased work of breathing
- Connect the patient to a cardiac monitor and obtain vital signs
- Pericardiocentesis is the definitive management

**Pharmacological treatment**

**A:** 0.9% sodium chloride (IV): Adults 1-2 lts, Paediatrics 20ml/kg) to increase right sided filling pressure

**Disposition**

All patients with cardiac tamponade require inpatient management in an intensive care unit setting/HDU.

## **1.10 Pulmonary Edema**

Life threatening condition that occurs due to abnormal fluid build-up in the lungs leading to impaired gaseous exchange, acute respiratory distress and may cause respiratory failure. Can be classified as cardiogenic pulmonary edema; due to increased hydrostatic pulmonary pressure (HF) and Non cardiogenic pulmonary edema; due to increased permeability (acute lung injury and allergic alveolitis).

**Note**

Cardiogenic and non-cardiogenic pulmonary edema have no clear cut differences in clinical presentation, however identifying the specific underlying cause of pulmonary edema is significant for therapeutic and prognostic purposes.

**Clinical presentation**

Shortness of breath, use of accessory muscles, diaphoresis, tachypnoea and crepitations

**Investigations**

Chest X-ray, Blood gases, Serum Creatinine and Urea, POC ECG, POC troponin, Serum electrolytes and/or Bedside Ultrasound

**Non Pharmacological management**

- Perform both primary and secondary assessment and provide necessary interventions
- Give high flow oxygen therapy
- Put patient on cardiac monitor (if available) and obtain vital signs
- Position patient at 45° angle or sitting upright position
- Perform ECG (rule out ischemia, dysrhythmia)
- Perform bedside ECHO (to rule out cardiac causes- contractility, pericardial effusion)
- Perform chest ultrasound (comet tails and B lines)

**Pharmacological management****Control hypertension (for SBP>90mmHg)**

**S:** nitroglycerin (IV): Adult loading 100mcg/min titrate rapidly to 400mcg/min over 2 minutes

**CAUTION!**

Beware of preload sensitive condition example inferior or right ventricular myocardial infarction, phosphodiesterase inhibitors use

**Reduce intravascular volume if fluid overloaded**

**B:** furosemide (IV/IM): 0.5-1mg/kg over 20minutes (maximum 120mg) or infusion IV 5-10mg/kg (maximum 120mg)

**CAUTION!**

Beware of renal insufficiency and volume depleted patients, check size of IVC

**Ventilation**

Oxygen therapy (target saturation>95%); CPAP or BiPAP (for persistent respiratory distress, hypoxia or acidosis despite high flow oxygen therapy); Intubation and mechanical ventilation (for respiratory failure despite CPAP/BiPAP)

**Disposition**

Goal of treatment - Relieve hypoxemia (improve oxygenation); Reduction of pulmonary capillary pressure and improve perfusion. Admit all patients with pulmonary edema to HDU/ICU or transfer the patient to a health facility with ICU/HDU capacity

**1.11 Approach to Shock**

Shock is a state of acute circulatory failure leading to decreased organ perfusion, with inadequate delivery of oxygenated blood to tissues and resultant end-organ dysfunction and it is an emergency condition. Adherence to evidence-based care of the specific causes of shock can enhance a patient's chances of surviving.

**Clinical presentation**

- Low blood pressure (systolic BP below 80 mmHg) is the key sign of shock
- Weak and rapid pulse
- Rapid and shallow breathing
- Restlessness and altered mental state

- Weakness
- Low urine output

**Table 1.1: Types of shock & Additional Symptoms**

Type of shock	Description	Additional symptoms	Initial Management
Hypovolemic	Most common type of shock Primary cause is loss of fluid from circulation due to haemorrhage, burns, diarrhoea etc.	Weak thread pulse, cold and clammy skin.	-Ensure patency of the airway - assess breathing and administer oxygen if indicated -Place two large bore cannula and initiate 2lts of saline/crystalloids (20mls/kg in pediatrics). Reassess after giving fluids - Assess for mental status -blood products (RBC,plasma,platelets) 1:1:1 if no improvement then refer
Cardiogenic shock	Caused by the failure of heart to pump effectively e.g. in myocardial infarction, cardiac failure etc. systolic blood pressure less than 80 or 90mmhg	Distended neck veins, weak or absent pulses	-Ensure patency of the airway - Assess breathing and administer oxygen if indicated -Place two large bore cannula and AVOID giving IV fluids, if needed give small volume (adult: 250mls-500mls and pediatrics: 5mls/kg) - Assess for mental status - Inotropes (Dobutamine 2-20mcg/kg/min or vasopressor (Dopamine 1-50mcg/kg/min) - Give blood if needed
Septic shock	Caused by an overwhelming infection, leading to vasodilatation.	Elevated body temperature	-Ensure patency of the airway - Assess breathing and administer oxygen if indicated -Place two large bore cannula and initiate 2lts of saline/crystalloids (20mls/kg in pediatrics) - Assess for mental status -Empirical antibiotic therapy within 1hr
Neurogenic shock	Caused by trauma to the spinal cord, resulting in sudden decrease in peripheral vascular resistance and hypotension.	Warm and dry skin -hypotension -bradycardia -hypothermia	-Ensure patency of the airway - Assess breathing and administer oxygen if indicated -Place two large bore cannula and initiate 2lts of saline/crystalloids (20mls/kg in pediatrics) - Assess for mental status - Inotropes (Dobutamine 2-20mcg/kg/min or vasopressor (Dopamine 1-50mcg/kg/min) - Give blood if needed
Anaphylactic shock	Caused by severe allergic reaction to an allergen, or drug.	Bronchospasm, angioedema and/or Urticaria	Refer anaphylaxis section

### Investigations

The following investigations can be performed depending on the type of shock

- Basic serum chemistry (including renal function)
- Liver function tests
- Blood culture
- POC Ultrasound- lungs, IVC, Cardiac
- Echocardiography
- CSF analysis if a patient is suspected with meningitis
- Troponins
- Blood gases
- Serum Electrolytes
- Lactate
- Hb Level

## **Non-pharmacological Treatment**

Prompt diagnosis of underlying cause is essential to ensure optimal treatment.

- Perform ABCD approach. Intervene when needed
- Maintain open airway
- Administer oxygen with face mask and if needed after intubation with assisted ventilation
- Check for and manage hypoglycemia

## **Pharmacological Treatment**

Treatment depends on the type of shock. Intravenous fluid therapy is important in the treatment of all types of shock except for cardiogenic shock.

**A:** 0.9% sodium chloride (IV): Adult give 2 litres bolus infusion. Repeat bolus until blood pressure is improved. Transfuse blood and plasma expanders in hemorrhagic shock. Paediatrics give 20ml/kg as a slow infusion.

All children with shock which is not obviously due to trauma or simple watery diarrhea should receive antibiotic cover for probable septicemia.

If the pressure doesn't improve after two bolus of IV Fluids (4lts in adults and 40mls/kg in pediatrics), administer inotropes/vasopressors (**Refer Sepsis and septic shock topic section**)

### **CAUTION!**

- Do not administer calcium containing fluids, e.g. Ringer Lactate, within 48 hours of administering ceftriaxone
- Do not administer IV fluids in case of cardiogenic shock but maintain IV line
- If patient develops respiratory distress, discontinue fluids but maintain IV line
- Ceftriaxone is contra-indicated in neonatal jaundice

**Referral:** Refer the patient urgently with the escort of a nurse to high level facility to establish the cause and address all medication given in the referral letter.

## **1.12 Sepsis and Septic Shock**

Septicaemia (Sepsis) is defined as life-threatening organ dysfunction caused by a dysregulated host response to bacterial infection (commonly) and fungal or viral infections (leastly). Organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more, with an in-hospital mortality greater than 10%.

Septic Shock is defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than 40%.

### **Clinical presentation**

- Temperature of  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ ; Heart rate of  $>90/\text{min}$ ; Respiratory rate of  $>20/\text{min}$  or  $\text{PaCO}_2 <32 \text{ mm Hg}$
- Above features plus evidence of organ dysfunction (hypotension, jaundice, oliguria, or altered state of consciousness from altered sensorium like drowsiness/lethargy)

### **Note**

- Septicaemia and septic shock are invariably fatal unless timely investigated and promptly managed using specific antimicrobial therapies and other supportive management.
- Identification of the primary source/focus of infection is mandatory to eliminate the infection and ensure favorable treatment outcomes. Neonates may present atypically with inability to feed, respiratory distress/cyanosis or abdominal distension.

### **Investigations**

Blood gases analysis, Bedside ultrasound- accessing the inferior venacava and the lungs, POC ECG, Urine dipstick, Chest X-ray- if suspecting pneumonia, Complete blood count, Qualitative or quantitative CRP or Procalcitonin in centres available, Serum Electrolytes, Creatinine and Urea, Liver function tests- liver enzymes, bilirubin, clotting time, Blood culture and antimicrobial susceptibility testing. Primary source of infection's clinical sample culture (e.g. urine, pus, sputum,

CSF etc) and antimicrobial susceptibility testing and/or RNA/DNA PCR for viral pathogens (where indicated)

### Diagnostic criteria

**Sepsis:** Q-SOFA in settings with limited laboratory infrastructures: two or more SOFA score namely: Respiratory rate  $\geq 22/\text{min}$ , Altered mentation and Systolic blood pressure  $\geq 100 \text{ mm Hg} \pm$  bacteria or fungal proven blood culture and susceptibility testing are recommended to make a definitive diagnosis.

**Septic shock:** Sepsis diagnostic criteria above and vasopressor therapy needed to elevate MAP  $\geq 65 \text{ mmHg}$  and lactate  $> 2 \text{ mmol/L}$  (18 mg/dL) despite adequate fluid resuscitation.

### Non-pharmacological Treatment

- Nutritional support
- Control measures focused to the primary focus of infection.
- Perform primary and secondary assessment and provide necessary interventions
- Ensure patency of the airway and give oxygen if hypoxic or increased work of breathing
- Connect the patient to the cardiac monitor and obtain vital signs

### Pharmacological Treatments

**A:** 0.9% sodium chloride (IV) (**ADULT:** 2litres; **CHILD:** 20mls/kg)

**OR**

**A:** compound sodium lactate (IV): Adult 2litres; paediatrics 20mls/kg) in 20minutes as first bolus followed by second bolus of 2litres/20mls/kg (use small boluses in CCF).

**OR**

**S:** dobutamine (IV) 2-20mcg/kg/min can be given for patients in shock not responding to fluids or when there is poor cardiac output.

**OR**

**S:** noradrenaline (IV) 5-20mcg/min for patients in septic shock not responding after 4litres of IVF to maintain the mean arterial pressure (MAP) of  $\geq 65\text{mm Hg}$

**AND**

**A:** hydrocortisone (IV) 200mg stat.

**Note:** Transfuse blood (If hemoglobin is  $< 7\text{g/dl}$ )

Antimicrobial therapies (broad spectrum antibiotics must be started within the first hour):

**A:** ampicillin (IV) 150-200mg / kg/day divided 6hourly a day

**AND**

**B:** cloxacillin (IV) 50-100mg / kg/day 6hourly a day

**AND**

**A:** gentamicin (IV) or (IM) 120mg [For children 7.5mg/kg] 24hourly for 5 days.

If no improvement in vital signs within 24 hours (Temp, HR, RR and altered state of consciousness), give:

**B:** ceftriaxone (IV) 1 gm [For children 100 mg/kg (IV) or (IM)] 24hourly for 4-14 days

**AND**

**A:** gentamicin (IV) or (IM) 120mg [For children 7.5mg/kg] 24hourly for 5 days

### Refer immediately.

**D:** ceftriaxone +salbactum (FDC) (IV) or (IM) 75-120 mg/kg 24hourly for 4-14 days

**AND**

**A:** gentamicin (IV) or (IM) 120mg [For children 7.5mg/kg] 24hourly for 5days

**OR**

**S\*\*:** piperacillin+tazobactum (FDC) (IV) (4g+0.5g) administered 8hourly [For children 100 mg Piperacillin+12.5mg Tazobactam per kg body weight 8hourly] for 7-10days

**AND**

**A:** gentamicin (IV) or (IM) 120mg [For children 7.5mg/kg] 24hourly for 5days.

Alternatively, (for patients who have evidence of not improving on the treatment above and referred to a zonal/tertiary hospital with judicious decision from a medical specialist or medical super-specialist):

**S\*\*:** meropenem 2g (IV) 8hourly in adults and adolescents [40 mg/kg 8hourly in children] for 7-14days

**OR**

**S\*\*:** vancomycin (IV) 15 to 20 mg/kg body weight 8 -12hourly (not to exceed 2 g per dose) for 7-14days.

**Note**

In renal insufficiency vancomycin can be adjusted for dose and dose interval. These antimicrobial agents are usually reserved for Gram negative and Gram positive pathogen(s), respectively supported by culture and antimicrobial susceptibility testing

**For suspected co-existing anaerobic infections, an additional to all regimes above of**

**B:** metronidazole (IV) 500mg 8hourly [In children 7.5 mg/kg 8hourly] for 7days

**OR**

**S:** clindamycin 600mg-1.2g/day diluted infusion in two or three doses [In children 15-25mg/kg/day in three equal doses] for 7-10days is recommended.

For the rare cases of sepsis or septic shock due to carbapenem-resistant Gram negative bacteria or vancomycin-resistant Gram positive bacteria, give:

**S\*\*:** colistin (IV) 2.5-5mg/kg/day 8-12 hourly for 5days

**AND**

**S\*\*:** linezolid (PO/IV) 400-600mg 12hourly for 10-14 days respectively or other non-beta lactam antibiotics may be considered *based on culture and antimicrobial susceptibility testing results*.

In case there is/are risk factors for invasive Candida infections like in immunocompromised states, prolonged invasive vascular, necrotizing pancreatitis, then antifungal therapies should be added.

**C:** fluconazole (IV) 800mg 24hourly on the first day then 400mg 24hourly for 14days [In children 6-12mg/kg/day for 14days]

## 1.13 Approach to Pain

Pain is an unpleasant sensation or emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Any pain of moderate or higher intensity is accompanied by anxiety and the urge to escape or terminate the feeling. Pain is subjective and unique perceptual experience with multiple dimensions that may not directly be observed by others or measured by physiological tests. Assesment is almost entirely self-reported.

### Assessment of pain.

Self-report is the key to pain assessment. In non- or pre verbal children, facial expression is the most valid indicator of pain; therefore, use faces pain scale to assess severity. Pain should be assessed by:

- Duration
- Severity, e.g. does the patient wake up because of the pain
- Site
- Characteristics, e.g. stabbing, throbbing, crushing, cramp like
- Persistent or intermittent
- Relieving or aggravating factors
- Accompanying symptoms
- Distribution of pain
- In children pain can be assessed by child's crying voice, posture, movement and colour

### 1.13.1 Approach to Chest Pain

The approach to non-traumatic chest pain requires early recognition of life threatening conditions. Patients with life threatening conditions may have stable initial vital signs.

For a patient presenting with chest pain, the following are the list of differential diagnoses

- Acute coronary syndrome
- Cardiac tamponade
- Pericarditis
- Myocarditis
- Myocardial infarction
- Aortic dissection

- Pulmonary embolism
- Tension pneumothorax
- Acute chest syndrome (sickle cell patients)
- Lung infection (pneumonia)
- Esophageal perforation
- Reflux Esophagitis
- Musculoskeletal pain

## **Investigations**

Depending on the clinical presentation, the following investigations maybe required:

POC ECG, Bedside USS-(cardiac, lungs, pleural, IVC, Abdominal aorta, kidneys etc), Serum electrolytes, POC Troponin, Blood gases, Serum creatinine and urea, Urine pregnancy test, Radiological investigations- Chest X-ray and/or CT scan- chest.

## **Pharmacological Treatments**

Treat the underlying cause as indicated in specific chapters. The following analgesia may be used to relieve the pain:

**A:** paracetamol (PO) 1g6hourly for 24hrs

**OR**

**A:** ibuprofen (PO )400mg 8hourly for 24hours

**OR**

**A:** diclofenac (IM) 50-100mg stat

For those patients who are unable to take oral medications

**B:** tramadol (IV) 50-100mg stat

**OR**

**C:** morphine (IV) 0.1mg/kg stat

**OR**

**D:** paracetamol (IV) 1g stat

If myocardial ischemia is highly suspected give:

**A:** acetylsalicylic acid (PO)325mg stat

**AND**

**D:** clopidrogel (PO) 300mg stat

**Referral:** Refer to higher facility with expertise when failed to establish the cause of the chest pain.

### **1.13.2 Approach to Abdominal Pain**

Abdominal pain is among the common complaints of patients presenting to the Emergency Department. While majority have benign and self-limited etiology, the goal is to identify those with serious or life threatening etiologies so as to perform early intervention.

## **Differential Diagnoses:**

### **Surgical causes:**

- Abdominal aortic aneurysm
- Mesenteric ischemia
- Perforation (PUD, bowel, esophagus, appendix)
- Intestinal obstruction
- Upper GI bleeding
- Lower GI bleeding
- Splenic rupture
- Acute appendicitis
- Pancreatitis
- Gallbladder diseases

### **Genito-urinary causes**

- Ectopic pregnancy
- Torsion (Testicular, ovarian)
- Dysmenorrhoea
- Endometriosis
- Ureteric and kidney stones
- Urinary tract infection
- Pelvic inflammatory disease

### **Medical causes**

- Myocardial infarction
- Peptic ulcer disease
- Gastro esophageal reflux disease
- Inflammatory bowel syndrome
- Gastritis
- Hepatitis

## **Investigations**

Depending on the clinical presentation, the following investigations may be required:

ECG, Bedside USS- (gall bladder, liver, lungs, IVC, Abdominal aorta, kidneys etc), Serum electrolytes, Troponin, Blood gases, Lactate, Serum Creatinine and Urea, Urine pregnancy test, Radiological investigations (Chest and Abdomen X-ray and/or CT scan- Abdomen).

### **Pharmacological Treatments**

For pain control, the following analgesia maybe used:

**A:** paracetamol (PO)1g 6hourly for 24hours

**OR**

**A:** diclofenac (IM) 50-100mg stat.

**OR**

**A:** hyoscine butyl bromide (PO) 10mg 8hourly for 24 hours

For those patients who are unable to take oral medications

**B:** tramadol (IV) 50-100mg stat

**OR**

**C:** morphine (IV) 0.1mg/kg stat

**OR**

**B:** hyoscine butyl bromide (IM) 10mg stat

**OR**

**D:** paracetamol (IV) 1g stat

### **1.13. 3 Headache**

Approach to acute headache

Headache is a challenging complain as it requires balancing symptomatic control with rapid assessment for life threatening diagnoses. Headaches can be categorized into primary and secondary. Primary causes are neurologic and include: tension, cluster and migraine. Secondary headaches are as a results of an underlying pathological process such as malignancies, infections and other organic causes.

### **Differential diagnoses**

#### **Sudden onset severe headache**

- Subarachnoid hemorrhage
- Cerebral venous thrombosis
- Hypertension emergency
- Adrenal and pituitary emergencies

#### **Altered:**

- |   |   |
|---|---|
| <ul style="list-style-type: none"><li>• Meningitis</li><li>• Encephalitis</li><li>• Intracranial tumor</li><li>• Space occupying lesions</li><li>• Stroke</li><li>• Subarachnoid hemorrhage</li></ul> | <ul style="list-style-type: none"><li>• Hypoglycemia</li><li>• Fever</li><li>• Meningitis</li><li>• Malaria</li><li>• Brain abscess</li></ul> |
|---|---|

### **Investigations**

Will be specific basing on the clinical presentation of the patient. These may include:

- |   |   |
|---|---|
| <ul style="list-style-type: none"><li>• Malaria test</li><li>• Random blood glucose test</li><li>• Blood Gases</li><li>• POC Urine dipstick</li><li>• Urinalysis</li><li>• CSF analysis</li><li>• POC ECG</li></ul> | <ul style="list-style-type: none"><li>• Bedside USS</li><li>• Serum Electrolytes</li><li>• Serum Creatinine and Urea</li><li>• POC Lactate</li><li>• Urine pregnancy test</li><li>• Radiological investigations- X-ray, CT scan</li></ul> |
|---|---|

### **Pharmacological Treatment**

**A:** paracetamol (PO): Adult 1g 8hourly for 3days; Paediatrics 15mg/kg 6hourly when required to a maximum of 4doses per 24hours

**OR**

**A:** ibuprofen (PO): Adult 400mg 8hourly for 3days; Paediatrics 5–10mg/kg 8hourly for 24hours

For severe pain or if the patient is unable to take orally, IV/ IM analgesia administration may be administered. These includes:

For those patients who are unable to take oral medications

- B:** tramadol (IV) 50-100mg stat
- C:** morphine (IV) 0.1mg/kg stat
- D:** paracetamol (IV) 1g stat

#### **1.13.4 Other Pains**

Other pains may include:

- Generalized body ache
- Joint pain
- Pain due to local infections
- Pains due to injury
- Eye pains
- Ear pains

#### **Non-pharmacological and Pharmacological Treatments**

Perform the primary and secondary assessment with interventions when needed.

For generalized pain give analgesics, advise the patient to rest and make a follow-up. For joint, infections, injury, eye and ear pains treat as for main disease.

#### **CAUTION!**

- Do not use acetlysalicylic acid for abdominal pain or if a patient is vomiting or has nausea and do not use acetlysalicylic acid in children below 12years. Patients with peptic ulcers should not be given acetlysalicylic acid tablets.
- Refer the patients when pain persists despite of medication given for pain relief for further investigation.

#### **Referral:**

Refer patients if:

- Children with moderate and acute severe pain
- No response to oral pain control
- Uncertain diagnosis
- All acute abdominal pain accompanied by vomiting and no passing of stool
- Pain requiring definitive treatment for the underlying disease
- Pain requiring opioids

#### **1.14 Approach to Fever (Pyrexia)**

Fever is abnormal elevation of body temperature that occurs as part of a specific biologic response that is mediated and controlled by central nervous system and is usually a symptom of an infection. It is characterized by an elevation of body temperature above the normal range of 36.5–37.5 °C

#### **Clinical presentation**

- Depression
- Lethargy
- Anorexia
- Sleepiness
- Hyperalgesia
- Inability to concentrate
- Feeling cold
- Increased muscle tone
- Shivering
- Irritability

#### **Note**

Fever alone is not a diagnosis

#### **Investigations**

Will be specific basing on the clinical presentation. These may include:

- Rapid Malaria test
- Blood slide for malaria parasites
- POC Urine dipstick
- POC ECG
- Bedside USS- Gall bladder, Liver, spleen, Abdominal aorta, kidneys etc
- Serum Electrolytes
- Serum Creatinine and Urea

- Radiological investigations- X-ray, CT scan
- Complete blood count
- Lactate

### **Non-Pharmacological Treatment**

- Perform both primary and secondary assessment. Intervene whenever necessary.
- Advise patient for bed rest
- Ask patient to take plenty of fluids (If able to take orally)

#### **Note**

- In children, temperature  $>40^{\circ}\text{C}$  need urgent lowering. However, lukewarm sponging and evaporative cooling are not recommended.
- Fevers caused by virus are usually self-limiting but all other fevers need treatments.

### **Pharmacological Treatment**

Give antipyretic medicines:

**A:** paracetamol (PO): Adult 1g 6hourly when required, Paediatrics 15mg/kg 6hourly when required **OR** suppository 125mg–250mg, 6hourly

**OR**

**A:** ibuprofen (PO): Adult 400mg 8hourly when required; Paediatrics 5-10mg/kg 8hourly when required

For patient who are unable to take oral medications, give:

**D:** paracetamol 1gm (IV)

#### **Referral**

Refer the patient to the next facility with adequate expertise and facilities.

- If no diagnosis is established
- If no improvement of fever after the use of antibiotics
- Fever that recurs

## **1.15 Cough**

Cough is a common reflex action that clears the throat of mucus, allergens, dusts or other foreign irritants. A cough can be caused by several conditions both temporary and permanent. Frequently coughing indicates the presence of disease.

### **Characteristics of cough/sputum**

- If cough is dry without sputum and fever, it is probable an allergic condition or mild upper respiratory illness (e.g. allergic rhinitis or allergic bronchitis)
- If cough is dry without sputum or fever and is associated with other congestive symptoms it may be due to Congestive Cardiac Failure (CCF)
- If it is a repeated attack cough with wheezing but without fever, it is likely to be bronchial asthma
- If it is a cough with fever, rapid breathing and chest in-drawing, it is likely pneumonia
- If it is cough with sputum which is yellowish pus-like and there is fever, it is likely acute bronchitis or pneumonia
- If it is cough with blood in sputum and/or irregular fever with loss of weight and appetite, it is a suspected tuberculosis
- If it is cough with large quantity of sputum, very foul smelling it is likely lung abscess or bronchiectasis

### **Pharmacological Treatment**

Causative/precipitating factors e.g. CCF, asthma; allergies must be established and treated accordingly. (**Refer respiratory disease condition chapter 9**)

#### **Note**

Refer to high facility with expertise when cough persist and failed to establish the cause or when association with fever.

## 1.16. Approach to the Trauma Patient

Table 1.2: Approach to Trauma Patient

PREPARATION		
Mobilise medical emergency team Prepare equipment, examples; monitors, ultrasound, Consider high-risk mechanisms of injury	<b>High Risk Mechanisms of Injury</b> <ul style="list-style-type: none"><li>• High speed motor vehicle accident</li><li>• Pedestrian accidents</li><li>• Ejection</li><li>• Fall &gt; 3m in height</li><li>• Penetrating injuries</li></ul>	
INITIAL RESUSCITATION		
<b>Airway:</b> Protect as appropriate and ensure Cervical-spine immobilization.		
<b>Breathing:</b> Give oxygen and titrate to SpO <sub>2</sub> (above 92%). If no air entry or if hyper-resonance present, insert chest drain. If patient is showing signs of obstructive shock or deviated trachea, needle decompression can be used initially before definitive decompression with a chest drain.		
<b>Circulation:</b> Insert 2 large bore IV Cannula. Resuscitate with crystalloid solutions according to BP. If not responding to crystalloids, patient should be resuscitated with blood. Control all external bleeding immediately.		
<b>Disability:</b> Check GCS and document this regularly to check for any changes in conscious state. Perform a brief neurological examination. Check pupillary response. Check RBG.		
<b>Exposure:</b> Expose patient to check for other injuries. Prevent against hypothermia.		
SECONDARY SURVEY		
<b>HEENT</b> – check for scalp haematomas, depressed skull fractures, facial bony tenderness, eye injuries, otorrhoea, haemotympanum, tracheal deviation.	<b>Spine</b> – Must log-roll patient and palpate spinous processes of C/T/L-spine and check for any tenderness or stepping.	<b>Chest</b> – look, palpate, auscultate. Check for signs of pneumothorax, haemothorax, ribs fractures, flail chest. If failing to ventilate or oxygenate, consider NIV or intubation.
<b>Pelvis</b> – careful examination for bony pelvic ring movement. If concerns re pelvic fractures, a pelvic binder (sheet) must be placed on the patient.	<b>Abdomen</b> – careful examination for guarding / tenderness / bruising in all quadrants. Ensure FAST examination performed in all trauma patients.	<b>Extremities</b> – examine all peripheries for bony injury, compartment syndrome, muscular or soft tissue damage, neurological changes.

**CHECKLIST :** (Before patient leaves EMD) make sure:

- Airway is patent/protected
- Tension pneumo-haemothorax? SpO<sub>2</sub>>92%
- Large-bore IV placed and fluid given
- Control of external bleeding
- Pelvic fracture assessment done
- Assessment for internal bleeding done
- Spinal immobilization done
- Neurovascular status of all limbs assessed
- Does the patient need chest tube, NGT or catheter?

## 1.17 Approach to Dehydrated Patient

It refers to the loss of body water, with or without salt at a rate greater than the body can replace it. The cause of dehydration is a combination of physiological and disease processes. Persons at

greatest risk for dehydration include persons with diarrhoea, vomiting, fever, diabetes or infections, impaired level status.

**Table 1.3: Types of Dehydration**

	<b>Mild</b>	<b>Moderate</b>	<b>Severe</b>
<b>Consciousness</b>	Is normal	May be irritable but is conscious	Unconscious
<b>Skin pinched up</b>	Becomes normal immediately	Takes two seconds for folds to disappear	Remain in folds for over two seconds
<b>Eyes</b>	Moist and tears are present	Sunken, tears and/or absent	Sunken and tearless
<b>Mouth</b>	Not dry	Is dry	Is dry
<b>Urine output</b>	Decreased	Oliguria	Oliguria/anuria
<b>Fontanel</b>	Normal	Depressed	Sunken
<b>Blood Pressure</b>	Normal	Normal but orthostasis	Decreased
<b>Capillary refill</b>	2s	2-4s	More than 4s

### Investigations

- Blood chemistry (to check electrolytes, especially sodium, potassium, and bicarbonate levels)
- Blood urea nitrogen (BUN) and creatinine
- Bedside USS- IVC
- Complete blood count
- Urine specific gravity
- Blood Gas analysis
- Lactate

Other tests may be done to determine the cause of the dehydration (for example, blood sugar level to check for diabetes).

### Non-pharmacological Treatment

- Perform both primary and secondary assessment and provide the necessary interventions.
- Give oxygen if hypoxic or increased work of breathing
- Put TWO large bore IV cannulas for fluid resuscitations

The treatment for minor dehydration often considered the most effective, is drinking water and stopping fluid loss.

### Pharmacological Treatment

In more severe cases, correction of a dehydrated state is accomplished by the replenishment of necessary water and electrolytes.

**A:** oral rehydration salt (ORS)

**OR**

**A:** 0.9% sodium chloride (IV): Adult 1-2litres; Paediatrics 20mls/kg)

**OR**

**A:** compound sodium lactate (IV): Adult 1-2litres; Paediatrics 20ml/kg

Remember to do reassessment after fluids resuscitations. If there is no electrolyte loss; give

**A:** dextrose (IV) 5%

If the underlying disease condition is diagnosed; treat as per specific condition in guidelines.

Referral: Refer to high center with expertise if no improvement.

### Note

- Dehydration in Children refer to Plan A,B and C in IMCI guideline

## 1.18 Hyponatremia

Defined as serum sodium ( $\text{Na}^+$ ) levels less than 135mEq/L. It can be classified as: Mild hyponatremia (130-135 mEq/L), Moderate hyponatremia (125 -129 mEq/L), Severe hyponatremia (< 125mEq/L).

### Clinical presentation

Clinical signs generally will occur once levels are <125mEq/L. The following are symptoms related to hyponatremia:

- Nausea and vomiting
- Fatigue
- Dizziness
- Headache or confusion
- Tremulousness or seizures
- loss of consciousness or coma
- Cramps or muscle spasms
- Irritability and restlessness
- Weakness
- Thirst and anorexia

### Investigations

Based on classification and patients' clinical findings, the following investigations maybe necessary:

- POC RBG
- Urine dipstick
- Electrolytes
- Creatinine and Urea
- LFTs
- Serum Osmolality
- Urine  $\text{Na}^+$
- Urine Osmolality
- Thyroid profile
- CT brain (suspected cerebral process)
- CXR (suspected pulmonary infection/edema – related to renal failure, CCF)

**Non-pharmacological Treatment:** Nutritional measures adjusted to patients need

- Salt containing foods
- Rehydration therapy
- Dietary modification

The goal of acute management is treatment of serious complications and careful restoration of serum sodium concentration. Management depends on the cause, severity and time course. Based on duration of development, hyponatremia can be (i) acute or (ii) chronic

**Table 1.4: Pharmacological Treatment for Hyponatremia**

ACUTE HYPONATREMIA	CHRONIC HYPONATREMIA
usually symptomatic and onset <48 hours Symptoms: neurologic deficit, seizures, coma and confusion	usually asymptomatic and onset > 48hours
<b>Requires immediate treatment</b> Give: <b>C:</b> 3% sodium chloride (IV) at rate of 1-2mEq/L/hr <b>Alternative:</b> <b>C:</b> sodium bicarbonate (IV) 8.4% 50ml over 5min Do <b>NOT</b> raise serum Sodium by > 6mmol/L in 6hrs Stop infusion when symptoms have resolved Manage seizures and coma as appropriate	No specific treatment if mild and asymptomatic <b>If moderate to severe:</b> Give: <b>A:</b> 0.9% sodium chloride (IV) Do <b>NOT</b> raise serum Sodium by over 12mmol/L in the first 24 hours Stop correction when Sodium reaches 130mEq/L
<b>Once symptoms have resolved</b> Assess volume status using point of care Ultrasound (POCUS) for IVC as well as vitals assessment and quantify as either (i) Hypovolemic hyponatremia, (ii) Euvolemic hyponatremia and (iii) Hypervolemic hyponatremia	



(i) HYPOVOLEMIC	(ii) EUVOLEMIC	(iii) HYPERVOLEMIC
<b>Possible causes:</b> -Dehydration (vomiting, diarrhea, sweating, third spacing, hydration with hyperosmolar fluids)	<b>Possible causes:</b> -Psychogenic polydipsia -Iatrogenic -Syndrome of inappropriate ADH secretion)	<b>Possible causes:</b> -Renal Failure -Cirrhosis -Nephrotic syndrome -Congestive Cardiac Failure -MDMA (Ecstasy use) -Hypothyroidism -Pseudohyponatremia
-Give compound sodium lactate or 0.9% sodium chloride (IV) 250 – 500mls or 0.5-1ml/kg/hour (guided by BP response)	-Prevent further exacerbation of hyponatremia -Prevent rapid overcorrection -Insert Foleys catheter to monitor output	-Nil per oral, restrict fluids - Furosemide (IV) 40mg daily until fluid volume is corrected.

**Note**

- Look for complications of over-correction such as Osmotic demyelination syndrome (ODS)
- Hyponatremia can also lead to cerebral edema which may lead to increased Intra cranial pressure (ICP)
- Exercise associated hyponatremia is common in athletes and the cause is over hydration and not excessive water loss
- Psychogenic polydipsia caused by over ingestion of large quantity of water in psychiatric patients or those on SSRI's.

**Severe Hyponatremia:** (seizures, coma, signs of brainstem herniation), consider treatment for cerebral edema and elevated ICP; give:

- 3% Sodium Chloride 3-5mls/kg over 15 to 60minutes to increase sodium by 2-4mmol/l
- Close monitoring of Serum sodium initially hourly with target correction rate of no more than 8-10mmol/l/day and less than 0.5mmol/l/hour over 1-2hours

**Hypovolemic Hyponatremia:**

- **Determine Sodium deficit:** Total body Sodium deficit = (Desired sodium – actual plasma Sodium) x Total body water{0.6 x weight (kg) Men OR 0.5 x weight (kg) women}
- Replace with 0.9% sodium chloride (IV)
- Correct at no more than 0.5mmol/l/ hour

### Disposition

Symptomatic Hyponatremia, Severe hyponatremiamust be admitted to the HDU/ ICUfor continuous biochemical and clinical monitoring. If not available refer the patient to a higher health facility with HDU/ ICU capabilities.

### 1.19 Hypokalaemia

Is defined as plasma potassium below 3.5mmol/l. It includes: Weakness, constipation, paralysis, bradycardiaand reduced tendon reflexes.

### Investigations

POC ECG, serum creatinine and urea, serum electrolytes and/or bedside ultrasound

Additional investigations may be required basing on the clinical presentation.

### Non-pharmacological Treatment

- Perform both primary and secondary assessment and provide necessary interventions needed.
- Give oxygen if hypoxic or increased work of breathing
- Connect the patient to the monitor and obtain Vital signs
- Place IV access

## **Pharmacological management**

### **Mild (3.0-3.5mmol/l)**

**C:** potassium chloride (PO): Adult 20-40 mEq 8hourly (dissolved in 100-150mL water); Paediatrics 2 mEq/kg 8hourly diluted in oral fluids or food. In case of diarrhea, give ORS (5ml/kg/hr)

### **Moderate (2.5-2.9mmol/l)**

**C:**potassium chloride (IV): Adult 10mEq/hour; Paediatrics 0.5 mEq/kg/hour diluted in 25-50mls of 0.9% sodium chloride or DNS or 5% dextrose solutions via peripheral vein. Do not exceed 10 mEq/hour.

### **Severe (<2.5mmol/l)**

Both IV & Oral Replacement

**C:** potassium chloride(PO): Adult (28mmol K+) per hour if tolerated (dissolved in 100-150mL water) dilutedpotassium; Paediatrics (PO) 2mEq/kg 8hourly.

**OR**

**C:**potassium chloride (IV): Adult 20 mEq in 100mL fluid over 1 hour via cubital fossa vein. Continue to measure serum potassium every 1 to 2 hours until K+ > 2.8 mmol/L. Paediatrics 1mEq/kg/hour.

The calculated hourly dose is multiplied by 12.5ml volume for dilution with NS/DNS/D5%. Do not exceed 10 mEq/hr

#### **Note**

- 20 mEq of Potassium will raise K+ by 0.25 mEq/L. Aim to replace 25% of K+ deficit in 6 hours
- potassium chloride must never be given as IM or IV push
- Oral potassium (Slow K) 600mg tab is equivalent to 8 mEq
- Injection potassium chloride 7.5% 1ml = 1 mEq

## **Role of Magnesium**

Magnesium should be checked. IF LOW, give Magnesium as follows:

**A:** magnesium sulphate 50% (IV): Adult Initially give 4ml diluted to 10ml with 0.9% sodium chloride run over 20 minutes, then potassium chloride infusion, then magnesium sulphate 50% (IV) 0.12ml/kg/day; Paediatrics 0.1 ml/kg/dose administered over 2hours

Hypokalemia in CARDIAC ARREST in Adults: KCl 10 mEq IV over 5 min; the dose may be repeated once

#### **Note: ECG changes in hypokalemia**

- Increased P wave amplitude, Prolonged PR interval,
- ST segment depression,
- QT prolongation, flattening or T wave inversion, and prominent U waves.

## **1.20 Triage Overview**

Triage is the process of determining the priority of a patient to medical care based on the acuity (severity of condition) and capacity of the system to address the condition, so as to optimize outcome.

### **Importance of triage**

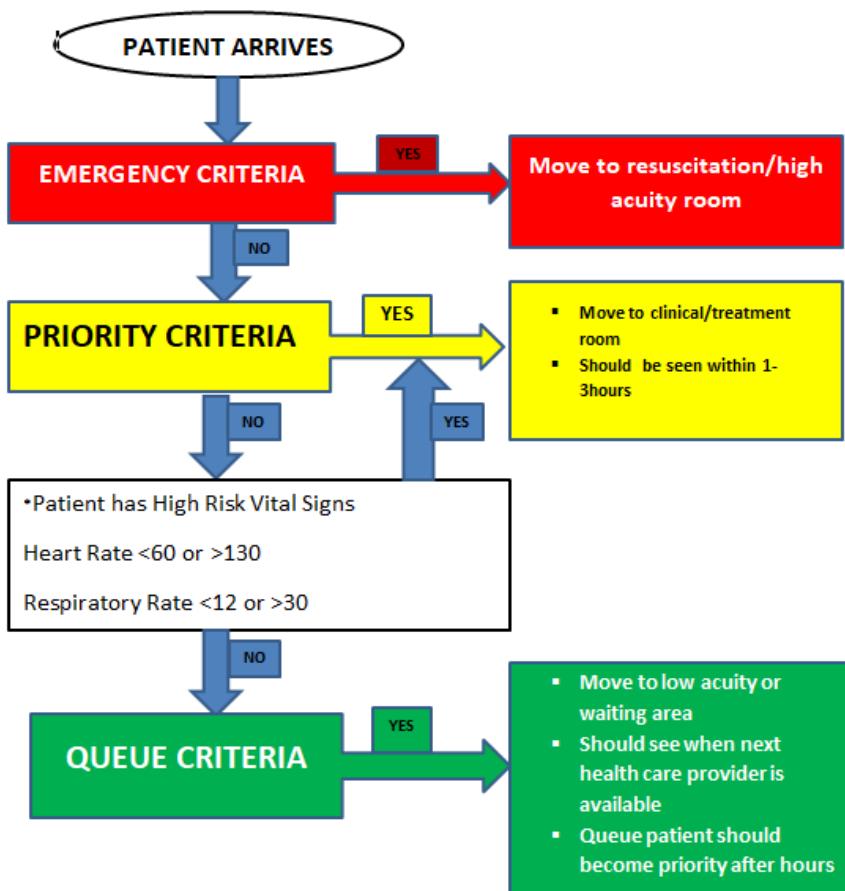
Triage enables quick identification of patients who need immediate attention, and can thus improve patient outcomes by avoiding potential delays. It helps in organizing, monitoring, evaluating and determining the department resources that patients might need.

## Triage system

The triage system is based on recommendation of Emergency Medicine expert's basic principles of triage, which uses specific criteria to categorize patients into three main levels of acuity:

- **Emergency**: all patients with immediate life or limb threats who are deemed salvageable, but likely to further decompensate without immediate intervention will be triaged in this level. This category can also be labeled as **RED**.
- **Priority**: those seriously injured/ill patients with potential to decompensate if not treated within 1 hour are triage as priority cases. This category can also be labeled as **YELLOW**.
- **Queue**: this level includes all the walking wounded or those with less serious injury/sickness who are unlikely to decompensate. Patients in this category can safely wait for their turn. However, they should be monitored as their conditions may change and warrant immediate care. This category is also labeled as **GREEN**.

Figure 1. Summary of triage flow and timelines of care



### EMERGENCY CRITERIA (Tick here if Yes)

Unresponsive	Pregnant with Heavy bleeding
Stridor	Pregnant with Severe abdominal pain
SpO <sub>2</sub> <90%	Pregnant with Seizures
Respiratory distress or cyanosis	Pregnant with Severe headache
Weak pulse or Capillary refill>3 sec	Pregnant with Visual changes
Hear rate <50 or > 150	Pregnant with SBP≥160 or DBP ≥110
Heavy bleeding	Pregnant with Active labour
Active convulsions	Pregnant with Trauma
Hypoglycemia	Age < 2years with Temp <36°C or > 39°C
High-risk trauma*	Child <14 with severe dehydration
Poisoning or dangerous chemical exposure*	Adult with signs of meningitis
Threatened limb*	Acute chest or abdominal pain (>50 years old)
Snake bite	ECG with acute ischaemia
Violent or aggressive	Other (state):

### PRIORITY CRITERIA (Tick here if Yes)

Vomits everything or ongoing diarrhoea (adult)	Severe pain (no Red criteria)
Unable to feed or drink	Visible acute limb deformity
Severe pallor	Open fracture
On-going bleeding (no emergency criteria))	Suspected dislocation
Recent fainting	Other trauma/burns (no Red criteria)
Altered mental status (no emergency criteria))	Sexual assault
Acute general weakness	Acute testicular/ scrotal pain or priapism
Acute focal neurology	Unable to pass urine
Acute visual disturbance	Wheezing (no Red criteria)
New rash worsening over hours or peeling (no emergency criteria)	Exposure requiring time-sensitive prophylaxis (example: animal bite, needle-stick injury)
Any infant 8 days to 2 months old	Child below 14 years old with malnutrition
Child below 14 years old with dehydration	Child below 14 years old with ongoing diarrhoea
Referral patient (no emergency criteria)	Other, state:

### QUEUE CRITERIA (Tick here if Yes)

Patient with no Emergency or priority criteria indicated in above tables
--

## CHAPTER TWO ANAESTHESIA

Anaesthesia is a state of controlled reversible loss of consciousness usually accompanied by analgesia, muscle relaxation, amnesia and areflexia. It is usually induced for the purpose of facilitating surgery and other therapeutic or diagnostic procedures.

### **Anaesthesia may be achieved with either:**

- Regional anaesthesia alone e.g. spinal/epidural anaesthesia, arm block
- General anaesthesia
- A combination of regional and general anaesthesia
- Regional anaesthesia with sedation
- Local anaesthesia through topical application/spray or infiltration of local anaesthetics

#### **Note**

- Anesthetic medicines and sedatives **MUST** be provided by medical practitioners who are properly trained and have appropriate experience with their use
- Medicines and equipment for resuscitation should be immediately available whenever general anaesthesia, regional anaesthesia or sedation is administered.

### **2.1 General Anaesthesia**

Medicines used in general anaesthesia include the following pre-medications:

#### Sedation and Anxiolytics

**A:** diazepam (IV) 0.05 – 0.1mg/kg

**OR**

**C:** diazepam (PO) 0.5 – 0.75mg/kg

**OR**

**C:** lorazepam (IM) 0.05mg/kg or 0.04mg/kg (IV)

**OR**

**D:** midazolam (IV) 0.05–0.1mg/kg

If there is an overdose with benzodiazepines use the following antidote:

**A:** flumazenil (IV): 0.2mg stat over 30 seconds. Repeated dose of 0.2mg may be given at 1minute intervals until desired level of consciousness is achieved; do not exceed 4doses (1mg).

If there is bradycardia, salivary secretion or other muscarinic side effects give

**A:** atropine (IV) 0.01mg/kg

**OR**

**S:** glycopyrrolate (IV) 0.2–0.4mg (0.2mg for every 1mg of neostigmine). Alternatively, a dose of 10–15 µg/kg (0.01–0.015mg/kg) (IV) with 50 µg/kg (0.05mg/kg) neostigmine or equivalent dose of pyridostigmine

Antiemetics are indicated for prevention of Post-Operative Nausea and Vomiting (PONV)

**B:** dexamethasone sodium phosphate (IV) 4–5mg for PONV prevention

**OR**

**C:** metoclopramide (IV) 10mg

**OR**

**S:** ondansetron (IV)4mg administered over 2–5minutes

Antacids are given to patients at risk of aspiration, such as pregnant women, before Caesarean section.

**B:** sodium citrate (PO) 0.3moles, 30ml. Not more than 30 minutes pre-induction of anaesthesia

**OR**

**C:** pantoprazole (IV) 40 mg as soon as the possibility of surgery is known in cases of emergency procedures

General anaesthetics are used for induction of anaesthesia as boluses or for maintenance of anaesthesia as continuous infusions in Total Intravenous Anaesthesia (TIVA).

**B:** ketamine (IV) 1–2mg/kg (For induction, however can be used for maintenance under TIVA, but contraindicated in those who a significant rise in BP/IOP/ICP would constitute a serious hazard)

**OR**

**C:** thiopental (IV) 3–5mg/kg (For induction, however can be used for maintenance under TIVA)

**OR**

**D:** propofol (IV) 1.5–2.5mg/kg for induction of anaesthesia and 6–12mg/kg/hour infusion for maintenance in TIVA.

propofol is contraindicated to Patients with risk of *hypotension*, use volatile agent for maintenance of anaesthesia

**OR**

**S:** etomidate (IV) 0.3mg/kg (between 0.2–0.6mg/kg) for induction (cardiostable, it affects cortisol production)

#### Inhalational anaesthetic agents (for induction and/or maintenance)

**B:** halothane 2–4% in air, oxygen or oxygen/nitrous oxide and maintenance 0.5–1.5% (Nitrous oxide is delivered in a ratio of 70:30 Mix with oxygen, reduce the requirement of a more toxic anaesthetic/ potent agent)

**OR**

**B:** isoflurane 1.2–2.5% titrates to desired effect

**OR**

**S:** sevoflurane 5–7%

Maintenance: 0.5–3% sevoflurane with or without the concomitant use of nitrous oxide.

#### Muscle Relaxants

**B:** suxamethonium (IV) 1–1.5mg/kg for induction

**OR**

**C:** pancuronium (IV) 0.04–0.1mg/kg for maintenance.

**OR**

**S:** atracurium (IV) 0.4–0.5mg/kg over 60 seconds followed by 0.08–0.1mg/kg 20–45minutes after initial dose for maintenance or infusion at 0.05–0.1 mg/kg/min (For patients with renal impairment)

**OR**

**S:** rocuronium (IV) 0.6 -1 mg/kg can be used for induction if sugammadex (reversal agent) is available, it has minimal side effects, can be used in case suxamethonium is contraindicated.

#### Contraindications

Suxamethonium is contraindicated in patients with risk for developing hyperkalaemia or with upper/lower motor neuron defect, prolonged chemical denervation, direct muscle trauma, tumour or inflammation, thermal trauma, disuse atrophy, severe infection

#### Medicines for Reversal of Neuromuscular Blockade

**B:** neostigmine (IV) 50µg/kg with atropine (IV), 20µg/kg (maximum 1.2mg)

**OR**

**S:** glycopyrrolate (IV) 10 µg/kg

**OR**

**S:** sugammadex (IV) 2–4mg/kg

## **Analgesics for Pain Management in Peri-operative Period**

### **Non-Opioid Analgesics**

**B:** paracetamol (IV) 15mg/kg 8hourly

### **Opioid analgesics**

**B:** tramadol (IM/IV) 50mg 6hourly

**OR**

**C:** morphine (IV/IM) 3–5mg as a single dose, then further boluses of 1–2mg/minute.

Maximum dose of morphine 0.1–0.2mg/kg, and monitor vitals closely

**OR**

**B:** pethidine (IV/IM) 1–2mg/kg (used for analgesia during anaesthesia, and during labour)

**OR**

**S:** fentanyl (IV) 1–2 $\mu$ g/kg

### **Antagonists of Opioids**

#### **For opioid over-dosage**

**B:** naloxone (IV) 0.4mg–2mg, alternatively may be given intramuscularly or subcutaneously. For reversal of opioid sedation initial dose 0.1–0.2mg (IV) at 2–3 minutes' intervals to the desired degree of reversal.

## **2.2 Local Anaesthesia**

Medicines used as local anaesthetics cause revisable absence of pain sensation, although other senses are often affected as well. Also, when it is used on specific nerve pathways, paralysis can also be achieved.

**A:** lidocaine (site): Maximum 4.5mg/kg without vasoconstrictors (adrenaline) or 7mg/kg with vasoconstrictors (Not for Spinal Anaesthesia)

**OR**

**C:** bupivacaine (site): 625 $\mu$ g/ml(0.0625%)1.25mg/ml(0.125%)

**OR**

**C:** bupivacaine + glucose: bupivacaine hydrochloride 5mg/ml (0.5%) with 80 mg/ml glucose (specific gravity of 1.026). The addition of glucose produces a hyperbaric solution relative to cerebrospinal fluid.

### **Medicines for Local Anaesthetics Overdose**

**S:** Lipid emulsion (intralipid 20% or 30% solution) for severe local anaesthetic toxicity with cardiovascular or neurological impairment.

**Dose:** 1.5ml/kg (IV) over 1min, then continuous infusion 0.25ml/kg/min. Repeat bolus 1–2times for persistent cardiovascular collapse. Double infusion rate to 0.5ml/kg/min if BP remains low. Continue infusion for at least 10 minutes after cardiovascular stability attained. Recommended upper limit: approximately 10ml/kg lipid emulsion over the first 30 minutes.

### **Epidural and combined spinal-epidural anaesthesia Techniques**

Epidural anaesthesia is a type of neuraxial anaesthesia; local anaesthetic (LA) is injected into the epidural space to anaesthetize the spinal nerve roots that traverse the space. Epidural anaesthesia is used for anaesthesia of abdominal, pelvic, and lower extremity procedures and, less commonly, thoracic procedures.

**A:** lidocaine 1 to 2 %(Epidurally)

**OR**

**C:** bupivacaine 0.25 to 0.75% (Epidurally)

### **Epidural Labour Analgesia (Local Anaesthetics, Adjuvant Drugs)**

**D:** bupivacaine 0.1-0.25% with or without Fentanyl 50 – 100 $\mu$ g (Epidurally). e.g. (Bupivacaine 0.1% Plus Fentanyl 2 $\mu$ g/ml at infusion rate of 0-12mls/hour)

### **Peripheral nerve blocks**

Peripheral nerve blocks are widely used for surgical anaesthesia as well as for both postoperative and nonsurgical analgesia.

Blocks are often used to avoid the effects of alternative anaesthetics or analgesics. The most common rationale for their use is to avoid side effects and complications of general anaesthesia (GA), particularly respiratory-related effects, and to provide analgesia while minimizing opioid use.

#### **Local Anaesthetics**

**B:** lidocaine (Perineurally) 1 to 2%

**OR**

**C:** bupivacaine (Perineurally) 0.25 to 0.75%

**OR**

**C:** bupivacaine+glucose(Perineurally) 0.25 to .75%

#### **Adjuvants**

**A:** adrenaline (Perineurally) Typical Concentration 5-10 $\mu$ g

**OR**

**B:** dexamethasone (Perineurally) 4-10mg

**OR**

**S:** clonidine (perineurally) 0.5-2 $\mu$ g

#### **Topical Anaesthesia**

**B:** lidocaine gel (Topically) 2 to 5%

**OR**

**B:** lidocaine topical spray 2% and 10% solutions for topical anaesthesia of the upper airway (i.e., oropharynx and vocal cords), the trachea, and nasal passages.

### **2.3 Sedation**

The aim of providing sedation is to reduce anxiety, agitation and pain so as to tolerate unpleasant medical procedures or intervention while the patient retains control of airway, breathing and blood pressure. This procedural sedation and analgesia is commonly used in emergency units, radiological /diagnostic units, dentistry and for certain endoscopic and gynaecological procedures.

#### **Minimal Sedation/Anxiolysis (no analgesic effect is required)**

**A:** diazepam (IV) 0.1mg/kg (In a 60kg patient, give boluses of 2mg every minute; may require up to 10mg)

**OR**

**C:** nitrous oxide inhaled 20 to 50%, in oxygen (will also provide some analgesia)

**OR**

**D:** midazolam (IV) 0.05mg/kg (In a 60 kg patient, give boluses of 1 mg every minute; may require up to 3mg)

#### **Medicines for moderate sedation & analgesia**

If analgesia is required, one of the above is usually combined with an opiate. However, ketamine has analgesic activity and can be used on its own or combined with a benzodiazepine.

**B:** ketamine (IV) 0.5mg/kg. Repeat doses of 0.5mg/kg as required, every 5-10minutes

**OR**

**C:** morphine(IV) 0.1mg /kg in increments of 2mg every 5minutes

**OR**

**S:** fentanyl (IV) 0.25 $\mu$ g/kg

#### **Alternative medicines**

**D:** propofol (IV) 0.5mg/kg. Repeated as 0.25mg/kg boluses every 5minutes as required

**OR**

**S:** etomidate (IV) 0.1mg/kg. Repeat doses of 0.05 mg/kg (IV) every 5minutes, as required. But it is more likely to cause myoclonus

**Medicines for Deep Sedation & Analgesia:** This is usually achieved with either higher doses of medications used for moderate sedation, or by combining an opiate, a benzodiazepine, and either Propofol or Etomidate. When agents are combined, lower doses may be adequate.

**Supplemental Analgesia:** Simple analgesics can be given before or after the procedure:

**A:** paracetamol (PO): 1g 4-6 hourly when required to a maximum of 4 doses per 24 hours.

Maximum dose: 15mg/kg/dose. Maximum dose: 4 g in 24 hours.

**OR**

**A:** ibuprofen (PO) 400mg 8 hourly with meals after the procedure.

### Note

#### Sedation in intensive care

- Indications for sedation in intensive care needs to be defined for each patient, and may include one or more of anxiolysis, analgesia, agitation control, or to help patients tolerate uncomfortable situations or procedures (e.g. intubation and ventilation)
- Sedation requirements fluctuate rapidly so, it warrants regular review
- Adequate pain control is often more efficacious than sedatives for reducing agitation. Delirium should be considered and managed appropriately.

#### Short-term and long-term sedation

##### Medicines for short-term sedation (less than 24 hours)

**C:** midazolam (IV) 0.05–0.2mg/kg/hour.

**OR**

**D:** propofol (IV) 0.5mg/kg/hour.

Due to high fat solubility, midazolam also becomes 'long acting' after infusions of more than 24 hours

##### Medicines for longer-term sedation (72 hours or more)

**C:** lorazepam (IV) 0.1mg/kg/hour.

**OR**

**D:** midazolam (IV) 0.2mg/kg/hour.

Lorazepam (0.1 mg/kg/hour) is as effective (and as easy to wean) as midazolam 0.2 mg/kg/hour but more difficult to titrate.

#### Supplemental analgesia

**C:** morphine (IV) 0.1–0.2mg/kg/hour.

**OR**

**S:** fentanyl (IV) 1 µg/kg/hour (also becomes long acting after prolonged infusion due to fat solubility)

## 2.4 Anaesthesia in Special Conditions

### 2.4.1 Surgery in Diabetic Patient

Diabetes leads to increased surgical morbidity, mortality and length of hospital stay. Perioperative Hyperglycemia is associated with increased risk of infection, medical complications and death. The following shall be considered:

- Ideally, the elective patient should have a preoperative glycated haemoglobin less than 9% or blood glucose fasting 10 mmol/l or random 13 mmol/l.
- Screen for nephropathy, cardiac disease, retinopathy and neuropathy and inform surgical team.
- If on oral hypoglycemic therapy and well controlled and surgery is minor, omit therapy on morning of surgery and resume therapy when eating normally.
- If on insulin adjust depending on the type of surgery and expected fasting period as follows:

#### Minor surgery (duration < 3 hours)

Insulin: in the morning intermediate-acting insulin, 1/2 to 2/3 of total daily dose.

- If blood glucose is above 20 mmol/l, give a small dose short-acting insulin.
- In the evening give intermediate-acting insulin, 1/3 of daily dose.

Fluid: 5% dextrose (IV), volume according to age.

Blood glucose monitoring: every 1–2 hours' values between 10–14 mmol/l.

**Major surgery (duration > 3hours)** Involve a general anesthesia and therefore a period of fasting.

- Insulin and fluid: infusion solution containing 5% glucose and 20 mmol/l potassium chloride (maintenance volume)
- Insulin infusion 0.05 IU/kg/hour.
- Blood glucose monitoring: every 1–2 hours; values between 6–14 mmol/l, if < 5 mmol/l reduce infusion rate, continue infusion therapy intraoperatively.
- Post operatively: give 5–10% dextrose (IV) 1 Litre + 20ml potassium chloride + 2/3 of total daily dose of insulin over 8hours and repeat to maintain infusion therapy until food intake is re-established.

#### **2.4.2 Surgery in Hypertensive Patient**

- Monitor BP, scan monitors for HR, ECG rhythm, EtCO<sub>2</sub>, temperature
- Provided the patient is adequately oxygenated & ventilated, deepen anesthetic
- Examine patient:
  - Pupils (high ICP)
  - Diaphoresis & flushing (carcinoid, pheochromocytoma, hyperthyroidism)
  - Rigidity (malignant hyperthermia, serotonin syndrome)
  - Bladder distension
  - Hot (thyroid storm, malignant hyperthermia, serotonin syndrome)
- Examine drugs & equipment:
  - Potential drug error
  - Possible TIVA or circuit disconnect (awareness)
  - Tourniquet (pain)
  - Equipment error (falsely high reading)

Give

**C:** hydralazine (IV) 5-20mg (max 30mg) slow IV push every 20minutes

**OR**

**C:** labetalol (IV) 5-20mg every10min (max total 300mg)

**OR**

**S:** esmolol (IV) 0.5mg/kg over 1minute; start infusion at 50mcg/kg/min

**OR**

**S:** nitroglycerin (IV) 50-100mcg; start infusion at 10mcg/min

- Treat underlying cause i.e., pain.

#### **2.4.3 Surgery in Asthmatic Patient**

##### **Considerations**

- Risk of perioperative respiratory complications:
  - Bronchospasm, mucous plugging, pneumothorax, atelectasis, pneumonia
- Possible pulmonary hypertension & RV failure
- Need for preoperative optimization:
  - Treatment of bronchospasm, infection, atelectasis
- Avoidance of triggers & exacerbating factors:
  - Avoid general anesthesia, endotracheal intubation, histamine releasing medications, light anesthesia
- Medication management:
  - Continue usual inhalers pre-operatively
  - Stress dose steroids (STEROID COVER) if recent high dose steroid use

#### **Severe Asthma Exacerbation Treatment Options**

Refer to asthma section.

##### **Anesthetics**

**B:** ketamine (briochodilator effect)

**OR**

**D:** propofol(bronchodilator effect)

- Volatiles all are bronchodilators but **sevoflurane** is likely best choice
- Always consider noninvasive PPV as rescue before intubation
- If intubation & ventilation:

- Use permissive hypercapnia
- Use low respiratory rates: start at 10-12 breaths/minute but may need lower rates
- Use prolonged expiratory time (e.g. I: E ratios 1:3, 1:4, or even 1:5)
- Tidal volume 6-8cc/kg
- FiO<sub>2</sub> to achieve PaO<sub>2</sub>>60mm Hg

#### **2.4.4 Surgery in Sickle Cell Patient**

- Avoid precipitants of sickle cell crisis:
  - Hypoxia
  - Vascular stasis
  - Hypothermia
  - Hypovolemia/hypotension
  - Acidosis
- Optimize perioperative pain control
- Monitor for:
  - Vaso-occlusive crisis
  - Acute chest syndrome
  - Aplastic crisis
  - Splenic sequestration syndrome
  - Right upper quadrant syndrome

#### **Optimization (in consultation with hematology)**

Risk factors for acute pain crises:

- Age, frequency of hospitalizations &/or transfusions for episodes of crisis, evidence of organ damage (e.g., low baseline oxygen saturation, elevated creatinine, cardiac dysfunction), history of central nervous system events, concurrent infection
- Procedural risk for complications:
  - Low: minor surgery (e.g., inguinal hernia & extremity surgery)
  - Intermediate: intra-abdominal operations (e.g., cholecystectomy)
  - High: intracranial & intrathoracic procedures, hip surgery
- Hematology consult, optimize treatment:
  - Hydroxyurea to ↑ fetal hemoglobin production
  - Cancel non-emergent cases if patient experiencing a crisis
  - IV fluid to avoid dehydration while NPO
- Preoperative transfusion therapy:
  - Controversial without good evidence
  - Purpose is to correct pre-existing anemia, ↓ hemoglobin S concentration & ↑ adult hemoglobin
  - Consider target hemoglobin 6 -10 for surgery & always have blood available for any surgery
  - Exchange transfusions are not routinely recommended
- Treatment of Pain:
  - Rest, warmth, reassurance, analgesia, fluid replacement
  - Oral analgesics may be sufficient for minor attacks
  - Opioids (IM, SC, IV, PO)
  - PCA opioids with baseline analgesia provided by background infusion or fentanyl patch
  - Paracetamol & NSAIDs
  - NSAIDS particularly good for bone pain
  - Ketamine as adjunct
  - Regional blocks as appropriate, epidural use has been reported

# CHAPTER THREE

## HAEMATOLOGY AND BLOOD TRANSFUSION

### 3.1 Anaemia

#### 3.1.1 Iron Deficiency Anaemia

A lack of iron in the body (mainly due to nutritional deficiency, chronic blood loss, malabsorption and hookworm infestations and increased demand such as during pregnancy).

**Clinical presentation:** fatigue, palpitation, dizziness, glossitis, koilonychias (spoon shaped nails) and pica

#### Investigations

- Full blood picture (FBP)
- Peripheral smear
- Iron studies- serum iron levels, total iron binding capacity, serum ferritin
- Stool analysis for hookworm ova and occult blood. If stool for occult blood is positive, do Oesophagoduodenoscopy (OGD) to confirm upper gastrointestinal bleeding

#### Non-Pharmacological Treatment

- To prevent iron deficiency;
  - Eat a variety of iron rich foods like meat, eggs, legumes (dried beans, lentils, peas), spinach and dark green leafy vegetables, iron fortified breads and cereals, nuts and seeds.
- To help in iron absorption from diet;
  - Avoid drinking tea/coffee with meals
  - Increase intake of vitamin C rich foods (e.g. citrus fruit, broccoli, cauliflower, guavas, tomatoes, bell peppers and strawberries) with meals to maintain iron in its reduced state

#### Pharmacological Treatment

Treat the underlying cause of iron deficiency anaemia.

##### Adults

**A:** ferrous sulfate (PO) 200mg 8hourly for 3months.

##### Children:

**A:** ferrous sulphate (PO) 5mg/kg 8hourly. Continue for 3months after the normal hemoglobin has been achieved.

**OR**

**B:** Blood transfusion (is only indicated if anaemia is life threatening; e.g anaemia in failure, hypoxia.)

**OR**

**D:** Iron sucrose (IV) 200mg in 100ml 0.9% sodium chloride running for 15 minutes once a day three times a week for 2 weeks.

PARENTERAL IRON IS INDICATED IN PATIENTS WHO CAN NOT TOLERATE OR ARE REFRACTORY TO ORAL IRON.

- Total cumulative dose = number of 100mg ampoules for Hb increase
- Divide the total cumulative dose in 200mg doses, given 24hourly

**Table 3.1: Number of 100mg/ampoules of iron sucrose needed for Hb increase based on the body weight.**

		Increase in Hb required (g/dL) ie Target Hb minus Actual Hb							
		1g	2g	3g	4g	5g	6g	7g	
Body weight (kg)		40	6	7	8	9	10	11	12
	45	6	7	8	9	10	11	12	
	50	6	7	9	10	11	12	13	
	55	6	8	9	10	12	13	14	
	60	6	8	9	11	13	14	16	
	65	7	8	10	11	13	14	16	
	70	7	8	10	12	13	15	17	
	75	7	9	10	12	14	16	18	
	80	7	9	11	13	15	17	18	
	85	7	9	11	13	15	17	19	
	90	7	9	11	14	16	18	20	
	95	7	10	12	14	16	19	21	
	100	7	10	12	15	17	19	22	

- Duration of treatment may extend to 4 weeks based on the total cumulative dose required.
- Monitor blood counts and clinical assessment monthly.

#### Note

Formulations of iron combined with other nutritional supplements (vitamins, 0.4mg-5mg folic acid, zinc and amino acids) are recommended to enhance absorption of iron and correct combined nutritional deficiencies.

### 3.1.2 Megaloblastic Anemia

This is a condition whereby the bone marrow usually produces large, structurally abnormal, immature red blood cells (megaloblasts) often due to inadequate intake or malabsorption of vitamin B<sub>12</sub> or folate.

#### Clinical presentation

Pallor, depression, hair loss, pins and needles, numbness in hands or feet, tremors and palsies, mildly jaundiced (lemon yellow tint), beefy tongue, darkening of palms and ataxic gait.

#### Investigations

- FBC-Low Hb, sometime pancytopenia, raised mcv but maybe low or normal if coexisting with iron deficiency (combined deficiency anaemia)
- Peripheral smear
- Serum vitamin B<sub>12</sub>,
- Serum folate level,
- TSH
- Reticulocyte count
- Bone marrow aspiration may be indicated

#### Pharmacological Treatment

Vitamin (B<sub>12</sub> deficiency anaemia) and other macrocytic without neurological involvement.

**C:** hydroxycobalamin (IM) initially 1mg 3times a week for 2weeks then 1mg (IM) every 3months.

Review the patient's blood counts and clinical assessment every 3months.

#### Pernicious Anaemia (B<sub>12</sub> deficiency) with neurological symptoms and signs

**C:** hydroxycobalamin (IM) initially 1mg on alternate days until no further improvement (maximum reversal or neuro-psychiatric signs and symptoms are achieved) then 1mg every 2-3months

**AND**

**A:** folic acid (PO) 5mg 24hourly for at least 3months this must be started simultaneously with injection vitamin B<sub>12</sub>

**AND**

**A:** ferrous sulphate (PO) 200mg 8hourly for at least 3months.

### **3.1.3 Haemolytic Anaemia**

Haemolytic anaemia results from an increase in the rate of red cell destruction in the intravascular or in the reticuloendothelial system in some pathological disorders

#### **Clinical presentation:**

- Pallor, jaundice, splenomegaly
- Anaemia, Reticulocytosis, indirect hyperbilirubinemia, and haemoglobinuria

#### **Pharmacological Treatment**

##### **Immunosuppressants**

**A:** prednisolone (PO) 1–1.5mg/kg/day for 1-3 weeks until Hb > 10g/dl

**AND/OR**

**S:** cyclophosphamide (IV) 50mg/kg/day for 4days

If no response;

**A:** folic acid (PO) 5mg 24hourly should be given for 1to 3months.

**OR**

**B:** blood transfusion if anaemia is severe

**OR**

**S\*:** High dose human immunoglobulin G (IV) 400mg/kg/day for 5days

#### **Surgical Management**

Splenectomy may be considered in those who fail to respond to pharmacological treatment.

### **3.1.4 Sickle Cell Disease (SCD)**

#### **Clinical presentation**

The clinical manifestations of SCA are variable;

- Symptoms usually occur after 6 months of life.
- acute onset of unexplained illness, including acute pain, anaemia, acute neurological symptoms, loss of vision, respiratory infections, hepatosplenomegaly, jaundice, swollen limbs and sepsis.
- Four types of crises occur in SCD; vaso-occlusive crisis, hemolytic crisis, sequestration crisis, aplastic crisis.

#### **Investigations**

Screening test: sickling test, isoelectric focusing (electrophoretic separation)

Confirmatory Tests: Sickle Scan, haemoglobin electrophoresis, HPLC (High performance Liquid Chromatography)

Other ancillary laboratory investigations useful in detection and monitoring of the disease include:

- FBP, Reticulocyte count, Peripheral blood film,
- Blood culture and sensitivity,
- LDH, total and indirect bilirubin, liver and renal profile,
- POC blood gases, ECG,
- mRDT, RBG,
- Blood grouping and cross match,
- Imaging eg CXR, ECHO, Ultrasounds (abdominal and transcranial doppler TCD USS), and CT Scan head if suspicious of stroke.

**Note**

Confirmatory test should be done to all patients with positive screening tests and those with negative screening test results but have clinical presentation suggestive of SCD.

**Screening**

From the age of 10 years, screen for renal disease (proteinuria by urine dipstick) and retinopathy annually

Annual screening for risk of stroke by transcranial Doppler from the age of 2 years to 16 years.

**Pharmacological Treatment**

**A:** folic acid (PO) 5mg 24hourly

**Prophylaxis against Pneumococcal Infection**

**A:** phenoxyethyl penicillin (PO) 125mg for children younger than 3 years; phenoxyethyl penicillin (PO) 250mg for children 3 years and older twelve hourly until 5 years of age in all children with SCA.

Immunisation against pneumococcal infection

**A:** pneumococcal conjugate vaccine (PCV-13) from two months of age, 3 doses 8 weeks apart (i.e at age 2 months, 4 months and 6 months) and a booster dose between 12-15 months. If the child has not previously received this vaccine, then at least one dose should be given between 6-18 years. PCV-13 and vaccine against *H. influenza* is incorporated in Tanzania EPI schedule.

**S:** pneumococcal polysaccharide vaccine (PPSV-23) - at 2 years then after every 5 years for life.

**Table 3.2: Analgesia for General Pain Relief**

Severity	Management
Mild	Reassurance, hot packs, reposition, massage, distraction (stories, play) <b>Child:</b> <b>A:</b> paracetamol (PO) 15mg/kg 6hourly <b>Adult:</b> <b>A:</b> paracetamol (PO) 1g 6hourly
Moderate	As for mild pain, <b>PLUS</b> <b>Child:</b> <b>A:</b> ibuprofen (PO) 5mg/kg 8hourly <b>Adult:</b> <b>A:</b> ibuprofen (PO) 400mg 8hourly
Severe	As for moderate pain <b>PLUS</b> <b>Child:</b> <b>C:</b> morphine (PO) 0.5mg/kg 3-4 hourly as needed <b>Adult:</b> <b>C:</b> morphine (PO) 5-10mg, 3-4 hourly as needed If unable to take orally, administer paracetamol (IV) 1g 6-8hourly and morphine 0.1mg/kg 8-12hourly If morphine is not available, tramadol may be used. <b>B:</b> tramadol (PO) 50-100mg 6hourly as needed

**Hydration:** Encourage oral fluids first; it should be used whenever possible. Give IV fluids, preferably normal saline, if the patient is unable to drink well, has severe pain, or abdominal symptoms.

Body weight (kg)	Fluids (ml/kg/day)
<10 kg	150ml/kg/day
11 – 20kg	75ml/kg/day for every kilogram above 10kg ADDED to 1500ml for the first 10kg of weight
> 20kg	30ml/kg for every kilogram above 20kg ADDED to 2250ml for the first 20kg of weight

Divide the total daily volume by 24 hours to obtain hourly fluid rate

**Indications for use of Hydroxyurea Include:**

All children older than nine months with proven SCD; and

In adolescents and adults with the following;

- Recurrent vaso-occlusive crisis (3 or more severe episodes requiring admission in the last 12 months),
- Severe and/or recurrent acute chest syndrome (ACS) (2 or more episodes in a lifetime),
- Severe symptomatic chronic anemia that interferes with daily activities or quality of life,
- Where chronic transfusion therapy is not feasible use it as an alternative to prevent new or recurrent stroke,
- Silent infarcts, stroke and in patients with abnormal TCD (199cm/sec),
- Recurrent priapism,
- Chronic kidney disease on erythropoietin to improve anaemia.

#### **Principle of Dosage Initiation and Monitoring:**

**S:** hydroxyurea (PO) 15 mg/kg/day 24hourly; (5–10 mg/kg/day if patient has chronic kidney disease).

**S:** hydroxyurea (PO) 20mg/kg/day, starting dosage for infants and children.

Increase the dose by 2.5–5 mg/kg/day every 3 months, Maximum tolerated dose (MTD) should not exceed 30mg/kg/day.

#### Blood work monitoring

- Bi-monthly FBP, reticulocyte count for 1 month, then monthly for 3months, then once every 3months if blood counts remain stable.
- HbF % analysis, liver function test, serum creatinine and urea every 6months.
- Weigh patient every three months and adjust the dosage accordingly.

#### Threshold for dose reduction

- Neutrophil ANC < 1.5 X10<sup>9</sup>/L
- Reticulocyte count < 80 X10<sup>12</sup>/L
- Platelet count < 80 X10<sup>9</sup>/L
- Hb < 6g/dl

#### If haematologic toxicity occurs;

- Discontinue hydroxyurea until counts recover, usually 1-2 weeks,
- Reinitiate hydroxyurea at a dose 2.5 mg/kg/day less than the dose given before onset of cytopenias to achieve the maximum tolerable therapeutic dose,
- Do FBP according to the initiation schedule.

#### **Note**

- Clinical response to treatment with hydroxyurea may take 3-6months. A 6month trial on MTD is required before considering discontinuation due to treatment failure.
- Hydroxyurea should be stopped at least three months prior to conception in both males and females
- Hydroxyurea should be discontinued in all pregnant women
- Hydroxyurea should be discontinued in all breastfeeding women

#### **Blood transfusion in SCA**

##### **Simple (Top-Up) Blood Transfusion:**

Indicated in symptomatic anaemia, orhaemoglobin level has dropped by > 2g/dl below the steady-state value.

##### **Exchange Blood Transfusion:**

Aim to reduce HbS to 30%.

##### **Indications for Exchange Blood Transfusion**

- Cerebrovascular Accidents (CVAs)
- Acute Chest Syndrome (ACS)
- Prior to major surgery
- Multi-organ failure, including Systemic Marrow Fat Embolism (SMFE)
- Multiple pregnancies
- Prevention of recurrent stroke.

## **Relative Indications for Exchange Blood Transfusion**

- Intractable or very frequent severe crises
- Major priapism unresponsive to other therapy.

### **Note**

- Because the cardiovascular system adjusts to the chronic anaemia, blood transfusion is not routinely indicated in steady state SCD simply for the reason that haemoglobin level is below 8–10g/dl.
- Packed red cells transfusion is preferred to minimize the risk of fluid overload

## **SCD in pregnancy**

- Stop hydroxyurea 3 months before conception
- Educate the patient about the risks associated with pregnancy in SCD.
- Determine the haemoglobinopathy status of the partner.
- Document pre-pregnancy baseline results if any.
- Refer the patient to a high-risk antenatal clinic for proper follow up
- Prescribe routine prenatal vitamins, see under Obstetric and gynaecology chapter
- Prophylactic blood transfusion is not recommended.
- Vaginal delivery is preferred unless there is indication for caesarian section.
- Prescribe prophylaxis for venous thromboembolism (VTE) for patients with additional risk factors for VTE e.g history of VTE. See details under coagulation disorders section 3.5
- Monitor hydration status, warmth and give analgesia as needed after delivery.
- Assess and manage neonatal opioid dependency and withdrawal all infants with history of in utero opioid exposure.

## **Pharmacological Treatment.**

**A:** acetylsalicylic acid (PO) 75mg 24hourly, starting from the second trimester to reduce the risk of pre-eclampsia.

## **SCD emergency conditions**

### **Acute chest syndrome**

- Life threatening – admit the patient in a high dependency unit or ICU,
- Diagnostic criteria – respiratory distress (fast breathing,  $\text{SPO}_2 < 95\%$  on air) and/or pleuritic pain, cough, fever, tachycardia, infiltrates on CXR,
- Investigations – arterial blood gases, creatinine, electrolytes, ALT, FBP, malaria test, blood and urine culture and sensitivity, CRP, CXR, HPLC,
- Management – Give supplemental oxygen to maintain  $\text{SPO}_2 > 95\%$ , analgesia for pain relief, fluids per hydration protocol, broad spectrum antibiotics while awaiting culture and sensitivity results, top up blood transfusion or exchange transfusion if expertise available.

### **Acute anaemia**

- Haemoglobin < 5g/dl or recent acute drop in Hb >2g/dl below steady state.
- Causes – infection, splenic sequestration, haemolytic crisis and aplastic crisis.
- Investigations – do FBP, reticulocyte count, creatinine, bilirubin, ALT, LDH, malaria test, urine and blood culture and sensitivity, blood grouping and cross-matching,
- Management – immediately transfuse packed red cells 10mls/kg over 4hours, repeat transfusion as needed as per transfusion protocol, treat the underlying cause, document size of liver and spleen.

### **Stroke**

- See management details under central nervous system chapter,
- Exchange transfusion or top up transfusion to prevent recurrent stroke.

### **3.1.4 G6PD Deficiency**

G6PD is an inherited X-linked recessive genetic disorder, haemolysis results from oxidative damage to RBCs due to loss of protective effect of the enzyme G6PD.

#### **Clinical presentation**

- Usually asymptomatic but liable to haemolysis (acute anaemia) if infection, incriminated drugs (e.g. sulphonamides, chloroquine, primaquine or proguanil), or foods (e.g. fava beans) are taken.
- Pallor,
- Jaundice and
- Dark urine (Coca-colored urine)

#### **Investigations:**

- FBP, peripheral smear, reticulocyte count,
- Methaemoglobin reduction (G6PD) test.

#### **Pharmacological Treatment**

**A:** folic acid (PO) 5mg 24hourly for 1 to 3 months.

**AND**

**B:** Transfusion of packed red blood cells in severe anaemia. Give 10ml/kg body weight. Then assess the level of haemoglobin and clinical presentation.

### **3.1.5 Aplastic Anaemia (Bone Marrow Failure)**

Aplastic anaemia is defined as pancytopenia resulting from aplasia of the bone marrow. It can be inherited (Fanconi anaemia) or acquired (idiopathic, chemical or drug induced). It is one of haematological emergency.

#### **Clinical presentation**

Vary with severity but include;

- Anaemia, easy bruising/bleeding, recurrent infection;
- splenomegaly is not a feature.

#### **Diagnostic Criteria**

- Pancytopenia,
- Bone marrow hypocellularity of < 30% hematopoietic cells.

#### **Investigations**

- FBP, peripheral smear, reticulocyte count,
- Viral screening (HIV, Hepatitis B and C),
- Bone marrow aspiration and trephine biopsy.

#### **Pharmacological Treatment**

##### **Supportive treatment**

**B:** blood transfusion (preferred irradiated, leucodepleted) when Hb<7g/dl

**OR**

**S:** platelet transfusion if bleeding or if platelet count is  $<10 \times 10^9/L$ . see dosage under blood transfusion section 3.6

**AND**

Prophylactic antibiotics, hygiene, isolation of the patient, and use of masks to prevent neutropenic sepsis in patients with ANC of less than  $0.5 \times 10^9/L$ .

#### **Note**

Culture and sensitivity in patients with neutropenic sepsis. Refer to management of neutropenic sepsis under malignant diseases chapter.

#### **Definitive treatment**

Allogeneic haematopoietic stem cell transplantation is indicated in patients younger than 45yrs.

##### **Immunosuppressive Therapy**

**S:** anti-thymocyte globulin (ATG) (IV) 40mg/kg/daily 4-10days

**AND**

**S:** cyclosporine (PO) 2-10mg/kg/day 12hourly for 6-24months

**AND**

**S:** eltrombopag (PO): Children <5years; 2.5mg/kg 24hourly, 6-11years; 75mg 24hourly, >12 years; 150mg 24hourly for 6months

For patients who develop cyclosporine toxicity (nephrotoxicity, hypertension, gingival hypertrophy and hirsutism), the following drugs may be used although the response rate is low.

**D:** methylprednisolone (PO) 5-10mg/kg for 3-14days

**OR**

**S:** cyclophosphamide (IV) 45mg/kg /day for 4days

**OR**

**S:** danazol (PO) 5mg/kg/day for 6months

**Note**

Give supportive therapy and refer patients to higher health facility with adequate expertise and facilities.

Monitor blood counts bi-monthly for outpatients, and as needed for admitted patients.

### **3.1.6 Myelodysplastic syndrome (MDS)**

Pre-malignant condition, primarily disease of the old people.

**Investigations:** similar to aplastic anaemia, plus analysis of 5q deletion.

#### **Pharmacological treatment**

**B:**blood transfusion for symptomatic treatment

**AND**

**S:** azacitidine (SC) 75mg/m<sup>2</sup> 24hourly for 7days, repeat after every 28days

## **3.2 Bleeding Disorders**

### **3.2.1 Hereditary Bleeding Disorders**

Hereditary bleeding disorders includes haemophilia A and B, Von Willebrand disease

#### **3.2.1.1 Haemophilia**

Haemophilia is an inherited, X-linked lifelong bleeding disorder which affects males almost exclusively.

#### **Clinical presentation**

- Spontaneous muscle and joint bleeding without injury,
- Prolonged bleeding after injury,
- Epistaxis and easy bruising.
- Complication includes arthropathy and disability.

#### **Haemophilia A (Factor VIII deficiency)**

Is the most common of the hereditary clotting factor deficiencies and are caused by deficiency of factor VIII.

#### **Haemophilia B (Factor IX deficiency)**

- It is caused by deficiency of clotting factor IX
- Presentation as in Haemophilia A, this is less common 20%.

#### **Classification of Haemophilia**

Haemophilia is classified as mild, moderate or severe according to the levels of circulating factor VIII or IX and indicates the expected frequency of bleeding.

**Table 3.3: Classification of Haemophilia**

Classification	Haemophilia A Factor VIII level	Haemophilia B Factor IX level	Clinical features
Severe	<1% of normal ≤ 0.01 U/ml	≤ 1% of normal ≤ 0.01U/ml	<ul style="list-style-type: none"> <li>• Spontaneous haemorrhage</li> <li>• Frequent spontaneous haemarthrosis</li> </ul>
Moderate	2-5% of normal 0.01-0.05 U/ml		<ul style="list-style-type: none"> <li>• Haemorrhage secondary to trauma or surgery</li> <li>• Occasional spontaneous haemarthrosis</li> </ul>
Mild	5-40% of normal	5-40% of normal	<ul style="list-style-type: none"> <li>• Haemorrhage post trauma or surgery</li> <li>• Rare spontaneous</li> </ul>

**Investigations**

- Prolonged aPTT but normal PT and Platelets counts
- Confirm by factor VIII or IX assay

**Non-pharmacological Treatment**

- Avoid I.M injections and use small gauge needles if necessary
- Inform the patient and parents thoroughly on the problem, and provide means of alerting other medical/pharmaceutical personnel
- Genetic counselling
- For Acute Bleeding episodes (RICE): Rest, Ice/cold pack – 5 minutes on, 10 min off, Compression and Elevate the joint.

For haemarthrosis – AVOID incising or aspiration of the affected joint. Treat by replacing the specific factor e.g factor 8 or 9 concentrate if available or FFP (10 - 15ml/kg), joint support and tabs Paracetamol for pain.

**Pharmacological Treatment**

Avoid use of NSAIDs, instead use paracetamol

**Haemophilia A (Factor VIII Deficiency) no Inhibitor**

Dose depends on bleeding severity

**Minor bleed:**

S: Factor VIII (IV) 20–40IU/kg.

**Major bleed:**

S: Factor VIII (IV) 50–100 IU/kg 12hourly for 3-5days or until bleeding stops

**Expected response:** 1IU/kg = 2% rise in factor VIII level

Half life Factor VIII: 8–24hours

**Haemophilia B (Factor IX deficiency) no inhibitor**

Dose depends on bleeding severity

**Minor bleed:**

S: Factor IX (IV) 20-50IU/kg

**Major bleed:**

S: Factor IX (IV) 100IU/kg

**Expected response:** 1IU/kg= 1.5 rise in the factor IX level

Half-life Factor IX: 16–24 hrs

D: Fresh frozen plasma (FFP) can be used where factor concentrate is unavailable.

Average dose 10-15mls/kg

**Note**

- If there is no response to appropriate replacement therapy tests for inhibitors (an inhibitor is formed when one develops antibodies against factor concentrates)
- Detection of inhibitor is by aPTT mix study and confirmed by Bethesda assay (BU)

**Factor VIII Inhibitor Management Options**

- High dose factor concentrate infusion
- Use by-pass agent like FEIBA (Factor Eight Inhibitor By-passing Agent)

- Immune tolerance induction therapy (ITI)
- In case of emergency surgery consider plasmapheresis
- Adjuvant antifibrinolytic agents eg Tranexamic acid can be used with either of the above

**Note**

- All patients suspected with haemophilia A or B refer to higher facility with adequate expertise or consult haematology Unit.
- Children with severe haemophilia are recommended to be on low dose prophylaxis of factor concentrate
- Male circumcision should be done at a hospital where factor concentrate is available. Concentrate should be given before and after the procedure.

### **3.2.2 Von Willebrand Disease (VWD)**

Von Willebrand Disease is inherited disease due to deficiency of vWF. It is the commonest bleeding disorder in the population especially in women.

#### **Clinical presentation**

- History of easy bruising,
- Menorrhagia
- Gum bleeding
- Joint bleeding in severe cases

#### **Investigations**

- Confirmatory test: VWF level assay.
- PT, aPTT, and platelet count are normal except in severe cases.

#### **Pharmacological Treatment**

**C:** etamsylate (PO) 500mg 8hourly until the bleeding stop

**OR**

**C:** tranexamic acid (PO) 500mg 8hourly until bleeding is stopped.

If no response

**S:** Desmopresin (IV) 0.3µg/kg IV stat. Max. Dose20µg.

**Note:**

- Patient unresponsive to DDVAP may be treated with virus-inactivated vWF containing FVIII concentrate.
- Never give Etamsylate or Tranexamic acid to patients bleeding per urethral

### **3.2.3 Acquired Bleeding Disorders/Platelet Disorders**

#### **3.2.3.1 Disseminated Intravascular Coagulation (DIC)**

#### **Clinical features**

- Usually are related to the underlying disorder.
- Bleeding manifestation,
- Extensive organ dysfunction,
- Shock, renal cortical ischemia, coma, delirium and focal neurological symptoms.

#### **Pharmacological Treatment**

Rapid and appropriate treatment of the underlying disorder including;

- Antibiotics for infection,
- Surgical debridement of necrotic tissues,
- Chemotherapy for malignant causes,
- Evacuation of dead fetus;
- Platelets transfusion for thrombocytopenia,
- Fresh frozen plasma (FFP) for coagulation factor depletion.
- Monitor prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin (aPTT), platelet count and fibrinogen.

**Note:** If patient is not bleeding Platelets concentrate is contraindicated. If DIC is severe enough to cause multiorgan dysfunction, management in an intensive care unit is required.

### **3.2.3.2 Idiopathic Thrombocytopenic Purpura (ITP)**

Clinical features:

- long history of Purpura, menorrhagia, epistaxis and gingival haemorrhage.
- Intracerebral haemorrhage occurs infrequently but is the most cause of death
- overt bleeding is rare unless thrombocytopenia severe (less than  $10 \times 10^9/L$ )

#### **Note**

A palpable spleen strongly suggests that ITP is **NOT** the cause for thrombocytopenia.

### **Non-pharmacological Treatment**

- Patients with platelet counts over  $50 \times 10^9/L$  usually do not have spontaneous bleeding and may undergo invasive procedure.
- Emergency treatment of acute bleeding caused by severe thrombocytopenia need immediate platelet transfusion

### **Pharmacological Treatment**

**A:** prednisolone (PO)  $1mg/kg/day$  for 3–6 weeks, then taper  $10mg$  weekly (For all patients with platelet counts below  $30 \times 10^9/L$ )

**OR**

**B:** dexamethasone (IV)  $40mg$  in  $500ml$  Normal saline running for 4hours once a day for 4days.

If no response;

**S:**human Immunoglobulin G (IV)  $0.4g/kg/day$  for 5days,

**OR**

**S:**human Immunoglobulin G (IV)  $1g/kg/day$  for 2days followed by immediately platelets transfusion

## **3.3 Coagulation Disorders**

Venous thromboembolism (VTE) is a common disorder that comprises deep vein thrombosis (DVT) and pulmonary embolism (PE). In most cases, pulmonary embolism arises from proximal deep vein thrombosis i.e. popliteal, femoral or iliac veins in at least 90%.

### **3.3.1 Deep Vein Thrombosis (DVT)**

#### **Clinical presentation**

- Leg pain, tenderness and swelling.
- A palpable cord representing thrombosed vessels.
- Discoloration, venous distention and prominence of superficial veins and cyanosis.
- The clinical diagnosis of DVT is highly nonspecific.

#### **Investigations**

- D-dimer,
- Doppler USS,
- PT, INR, Aptt

#### **Pharmacological Treatment**

Long term anticoagulation is required to prevent a frequency of symptomatic extension of thrombosis and/or recurrent venous thromboembolic events. Warfarin is started with initial unfractionated heparin or enoxaparine therapy and then overlapped for 5days.

**C:** warfarin (PO)  $5mg$  24hourly for 5days, then adjust the dose according to INR levels for 3-6 months.

**AND**

**S:** Low Molecular weight heparin (SC)1mg/kg 24hourly for 5days

**OR**

**S:** Unfractionated heparin (IV) by 75units/kg followed by continuous infusion of 18units/kg/hr.

Adolescents or children: loading dose 75units/kg then 15–25 Units /kg/hr by IV infusion or 250units/kg 12hourly by SC injection.

**S:** rivaroxaban (PO) 15mg 12hourly for 21days, then rivaroxaban (PO) 20mg 24hourly for the remaining duration of treatment.

### Pregnant women

Warfarin is teratogenic, therefore low molecular weight heparin is recommended during pregnancy.

**D:** Low Molecular weight heparin (SC) 1mg/kg 12hourly for the whole duration of treatment.

### 3.3.2 Pulmonary Embolism (PE)

It is a medical emergency.

#### Clinical presentation

- Transient dyspnea and tachypnea in the absence of other clinical features
- Pleuritic chest pain, cough, haemoptysis, pleural effusion, and pulmonary infiltrate
- Severe dyspnea and tachypnea and right-side heart failure
- Cardiovascular collapse with hypotension, syncope, and coma
- Several less common and nonspecific presentation including unexplained tachycardia or arrhythmia, resistant cardiac failure, wheezing, cough, fever, apprehension and confusion.

#### Investigations

- PT, INR, aPTT, D-dimer, CXR and CT angiography

#### Pharmacological Treatment

Treat as Deep Vein Thrombosis

#### Note

- Warfarin therapeutic INR ranges from 2 to 3 for VTE, and 2.5 -3.5 for patients with mechanical heart valves
- Warfarin therapy should be monitored by INR after 5–7 days of treatment, then as needed throughout the duration of treatment.
- If the cause of VTE is acquired thromboembolism, treatment lasts for 3-6 months, BUT if the cause is inherited thrombophilia, treatment is lifelong.
- Warfarin interacts with many drugs therefore precaution should be taken when administered with other drugs.
- If warfarin overdose/toxicity occurs, stop warfarin and give FFP 10-15mls/kg and vitamin K 5mg IV stat. Reinitiate warfarin after bleeding has stopped and INR is within therapeutic range, using the lower dosage.
- For VTE prophylaxis in bedridden patients, give enoxaparin 40mg SC OR Rivaroxaban 10mg orally once a day until ambulation resume.
- Unfractionated heparin should be monitored by aPTT before and during treatment.

### 3.4 Blood Transfusion

#### Blood components

A single donation of blood can be separated into several blood components. Currently in Tanzania the following blood components are available for transfusion: packed red blood cells, Fresh Frozen Plasma, single unit platelet (plasma rich) and whole blood units.

##### I. Whole blood

One unit contains 450mls of blood. It is poor in platelets and clotting factors and can be stored for 35days at 2-6°C.

**Indications:** Exchange transfusion, open heart surgery, and in the absence of PRBCs in patients with acute blood loss and hypovolaemia.

## **II. Packed red blood cells (PRBCs)**

It can be stored for 35days at 2-6°C. One unit increases haemoglobin (Hb) level by approximately 1g/dl in adult, whereas in children, a dose of 10-15mls/kg will increase the Hb by about 3g/dl.

**Indications:** acute blood loss, exchange transfusion, cardiac patients with Hb level <8g/dl, chronic symptomatic anaemia with Hb <5g/dl, preoperative patients with Hb level <8g/dl, pre-radiotherapy patients with Hb level <10g/dl, pre and post chemotherapy patients with Hb <9g/dl, and patients admitted to ICU with Hb <7g/dl.

## **III. Platelets**

A single random donor platelet (RDP) from one whole blood unit and contains about  $5.5 \times 10^9$ /L platelets in 50ml unit. It is stored at room temperature (20-24°C) and has a life span of 5days.

**Dosage:** 50mls per 10kg i.e 5-6 RDP units in adults. In infants < 10kg, the dose is 5mls/kg, one adult therapeutic dose increases platelet counts by approximately  $20-40 \times 10^9$ /L.

### **Indications**

- Therapeutic: thrombocytopenia of platelet counts <  $50 \times 10^9$ /L with clinical evidence of bleeding.
- Prophylactic in patients with platelet counts of:  $<10 \times 10^9$ /L,  $<20 \times 10^9$ /L with additional risk factor of bleeding,  $<50 \times 10^9$ /L and planned for minor surgery,  $<100 \times 10^9$ /L with multiple injuries, or microvascular bleeding, or planned for major surgery. Also, in massive transfusion to maintain a platelet count of  $>50 \times 10^9$ /L.

**Contraindications:** Absolutely contraindicated in heparin induced thrombotic thrombocytopenia (HITT) and thrombotic thrombocytopenic purpura (TTP). Relatively contraindicated in idiopathic thrombocytopenia (ITP) unless a life-threatening bleeding is anticipated.

## **IV. Fresh frozen plasma (FFP)**

FFP prepared from one unit of whole blood contains about 200-300mls of plasma. It is stored at -18°C and contains all clotting factors in physiological levels except factors V and VIII which are present in slightly reduced amount. It has a life span of 12 months. Thaw FFP in water bath at 30-37°C and transfuse within 30 minutes after thawing. It expires 24 hours after thawing.

**Dosage:** 10-20ml/kg, approximately 4-6 units for adult, this will raise a minimum of 30% of plasma clotting factors.

**Indications:** haemophilia if factor concentrates not available, patients with significant coagulopathy eg DIC, Vitamin K deficiency and massive transfusion, thrombotic thrombocytopenic purpura (TTP) or haemolytic uremic syndrome (HUS) as top up or exchange plasma transfusion, scoline apnoea, haemorrhagic disease of the newborn.

### **Investigations**

- Before transfusion:FBC, ABO and Rh-blood grouping and crossmatch (cross matching not needed for platelets and FFP transfusion),
- If transfusion adverse reaction occurs: Assess for haemolysis (FBC, peripheral smear, direct antiglobulin test, serum bilirubin, serum LDH), re-grouping and crossmatch, other tests depending on the type of transfusion reaction.

## **Types of blood transfusion**

### **I. Acute simple/episodic transfusion**

Used in management of symptomatic patients with anaemia or bleeding tendencies

### **II. Chronic/top up transfusion**

Used as prophylactic to prevent complications, eg. In patients with sickle cell anaemia (SCA)

### **III. Exchange blood transfusion**

Used in management of severe neonatal jaundice, in patients with SCA with acute chest syndrome, suspected acute stroke or transient ischaemic attack.

#### IV. Massive blood transfusion

Transfusion of blood volume to patient equivalent to his/her total blood volume in less than 24 hours, or 10 units or more in 24 hours. Administer in parallel a 1:1:1 ratio of 6 Units of RBCs, 6 Units of FFP and 6 Units of Platelets. The target is to achieve 1:1:1 ratio over 6 hours. Aim the PT, PTT <1.5x control mean, fibrinogen >1 g/L, target platelet > 100x10<sup>9</sup>/L if pts has CNS trauma, eye and > 50x10<sup>9</sup>/L for other type of injuries.

#### Plasma Derived Medicinal Products (PDMPs) available from commercial outlets

- Haemostatic factors VIII and IX used in management of haemophilia
- Immunoglobulins used in immune-mediated conditions
- Albumin used in management of hypovolaemia, hypoalbuminaemia and in therapeutic plasma exchange.

#### Therapeutic phlebotomy

Indications: Polycythaemia, and in hereditary iron overload.

**Table: 3.4 Adverse effects of blood transfusion**

Reaction	Transfusion	Management
Acute immunologic reactions	Acute haemolytic transfusion reaction	Stop transfusion, supportive care to maintain hemodynamics. Regroup and crossmatch donor and recipient's samples. Assess for haemolysis.
	Allergic reactions	Stop transfusion, administer antihistamine eg Chlorphenamine 4mg PO as needed +/- steroid eg Hydrocortisone 100mg IV stat, resume transfusion if symptoms subside. If anaphylactic reaction, add vasoactive drugs eg epinephrine and supportive care.
	Febrile non-haemolytic transfusion reaction	Stop transfusion, administer antipyretics A: Paracetamol 1g PO as needed +/- steroid eg Hydrocortisone 100mg IV stat, resume transfusion if symptoms subside
	Transfusion-related acute lung injury (TRALI)	Stop transfusion, oxygen supplementation and mechanical ventilation if required.
	Transfusion associated graft-versus-host disease (TA-GVHD)	Supportive care
Delayed immunologic reactions	Delayed hemolytic transfusion reaction	Symptomatic treatment, request extended cross match for additional transfusions.
	Post-transfusion purpura	Self limiting, <b>S:</b> IV immunoglobulin 0.4g/kg/day IV for 5 days or plasma exchange may be needed in severe cases.
Acute non-immunologic reactions	Transfusion-related circulatory overload (TACO)	Stop transfusion, administer diuretics, manage as cardiac failure. See details under cardiovascular diseases chapter.
	Bacterial contamination	Stop transfusion, antibiotics and supportive care
Delayed non-immunologic reactions	Infectious disease transmission	Manage the infection accordingly eg HIV, Hepatitis B & C. see details under respective chapters
	Iron overload	Iron chelation with deferoxamine

#### Blood transfusion in Jehovah's witness

- Blood transfusion is a medical treatment, and therefore patients have the right to refuse treatment.
- Inform the patient of the benefits and risks of transfusion.
- Enable the patients to understand the consequences of not receiving blood.
- Inform the patients of any alternatives to transfusion available eg autologous transfusion and plasma derived medicinal products.
- Guarantee strict clinical confidentiality

## **Haematological malignancies**

Include the following;

- Leukaemia – acute and chronic leukaemia
- Lymphomas – Hodgkin's and Non-Hodgkin's lymphoma
- Multiple myeloma

These are discussed in details under malignant disease chapter.

## CHAPTER FOUR

### NOTIFIABLE DISEASES

Notifiable Diseases, conditions and events usually pose a great public health threat, with a potential of international spread. They require immediate notification by health personnel (clinical, laboratory, environmental, etc.), to health authorities, as required by the International Health Regulations (IHR 2005). Notification is mandatory, in order to ensure prompt and effective response, to avoid further spread and to prevent deaths.

**Note:**

- Immediately notify the Public Health Authorities using the electronic reporting system for priority diseases, i.e. the electronic Integrated Disease Surveillance and Response (e-IDSR) System
- Ensure that the disease, condition or event is recorded in the Health Facility e-IDSR reporting booklet
- Manage patients on site, in an isolation ward/room or an established isolation centre
- Use Personal Protective Equipment (PPE) before attending a suspected patient
- Strictly apply principles of IPC during patient management and waste disposal

#### **4.1 Bacterial Infections**

##### **4. 1.1 Cholera**

Cholera is an acute gastrointestinal infection caused by *Vibrio cholerae*. Infection occurs through ingestion of contaminated water or food by *Vibrio cholerae* leading to severe diarrhoea and emesis associated with body fluid and electrolyte depletion.

**Note**

Rational approaches to case management of cholera with oral and intravenous rehydration therapy have reduced the case fatality of cholera from more than 50% to much less than 1%. When a case of cholera is suspected at home, advise to rehydrate the patient using ORS if available while preparing to take the patient to the nearest health facility or Cholera Treatment Centre

#### **Clinical Presentation**

- A sudden onset of painless watery diarrhoea that may quickly become severe with profuse watery stool, vomiting, severe dehydration and muscular cramps, leading to hypovolemic shock and death

#### **Case Definition**

- Suspected cholera case: In areas where a cholera outbreak has not been declared: Any patient aged two years and older presenting with acute watery diarrhoea and severe dehydration or dying from acute watery diarrhoea
- In areas where a cholera outbreak is declared: any person presenting with or dying from acute watery diarrhoea
- Confirmed cholera case: A suspected case with *Vibrio cholerae* O1 or O139 confirmed by culture or PCR (Polymerase Chain Reaction).

#### **Laboratory Investigation**

- Specimen: Liquid stool or rectal swab
- Diagnostic test: Isolate *V. cholerae* from stool culture and determine O1 serotype using polyvalent antisera for *V. cholerae* O1. If desired, confirm identification with Inaba and Ogawa antisera.
- If specimen is not serotypable, consider, *V. cholerae* O139
- Antibiotic Susceptibility Testing before provision of antibiotics; Follow up 48 -72 hours after antibiotic initiation

**Note**

- For confirmation at the beginning of an outbreak, rectal swab or stool specimen should be taken from first 5 to 10 suspected cases.
- If any are positive, every tenth case will be sampled for specimen throughout the

- |  |
|--|
| <ul style="list-style-type: none"> <li>outbreak</li> <li>• Manage a suspected cholera case in an isolation ward or in an established Cholera Treatment Centre</li> </ul> |
|--|

## **Prevention**

- Drink treated or boiled water from safe sources (taps, decontaminated deep wells, bottles)
- Boil water or treat to kill bacteria and make it safe for drinking and for other domestic uses
- Wash hands with liquid soap and running water after visiting the toilet, before preparing foods, and before eating
- DO NOT eat uncooked food from the street and do not eat cooked food that is no longer hot
- DO NOT eat street prepared fruits. Always eat home prepared fresh fruits

## **Management**

### **Pharmacological Treatment**

Cholera requires immediate treatment because the disease can cause death within hours. There are three elements of treatment: Rehydration, Antibiotic Treatment, Zinc and Folic Acid Supplements.

#### **i. Rehydration**

- Assess the patient's level of dehydration as per National Guidelines for Prevention and Control of Cholera. It is of paramount importance to make correct diagnosis and administer the right treatment.
  - plan A: No dehydration,
  - plan B: Moderate dehydration and
  - plan C: Severe dehydration.

#### **For Severe dehydration:**

- Administer intravenous (IV) fluid immediately to replace fluid deficit; Use Ringer Lactate solution or, if that is not available, 0.9% sodium chloride solution. Give 100 ml/kg IV in 3 hours, 30 ml/kg as rapidly as possible (within 30 min) then 70 ml/kg in the next 2.5 hours.
- After the initial 30 ml/kg has been administered, the radial pulse should be strong and blood pressure should be normal. If the pulse is not yet strong, continue to give IV fluid rapidly. Administer ORS solution (about 5 ml/kg/hour) as soon as the patient can drink, in addition to IV fluid.
- If the patient can drink, begin giving **A:** oral rehydration salt solution (ORS) by mouth while the drip is being set up; ORS can provide the potassium, bicarbonate, and glucose that saline solution lacks.

#### **Note**

When using 0.9% sodium chloride solution there is a possibility of hyper-metabolic Acidosis causing kidney injury

#### **ii. Antibiotic treatment**

Antibiotic treatment to patients with severe dehydration is as follows:

##### **Adults (Not for pregnant women)**

**A:** doxycycline (PO) 300 mg or 5mg/kg stat then 200mg (PO) 12 hourly for 7 days

**OR**

**A:** ciprofloxacin (PO) 1g stat then 15mg/kg 12 hourly for 7 days or 500mg (PO) 12 hourly for 7 days

**OR**

**A:** azithromycin (PO) 500mg once a day for 7 days

##### **Expectant mothers:**

**A:** erythromycin (PO) 500mg 8 hourly for 7 days

##### **Children:**

**A:** erythromycin syrup (PO) 12.5mg/kg 6 hourly for 5 days

**OR**

**A:** Azithromycin 250mg (PO) once a day for 7 days

### **For adolescents:**

**A:** ciprofloxacin (PO) 12mg/kg 2 times for 5 days

**OR**

**A:** doxycycline (PO) 300mg as stat or 5mg/kg (PO) stat

**OR**

**A:** azithromycin (PO) 500mg once a day for 7 days

#### **Note**

- Ciprofloxacin was previously contraindicated to children under 12 years. Recent studies have shown it to be safe for use in children
- Start feeding 3-4 hours after oral rehydration begins. Preferably, give antibiotics with food to minimize vomiting

### **For moderate Dehydration**

- Give oral rehydration, approximately 75-100ml/kg in the first four hours
- Reassess after four hours; if improved, continue giving WHO based ORS, in quantity corresponding to losses (e.g. after each stool) or 10 to 20ml/kg. If not improved, treat as severe dehydration.

### **If no signs of dehydration**

- Patients who have no signs of dehydration when first observed can be treated at home
- Give these patients ORS packets to take home, enough for 2 days
- Demonstrate how to prepare and give the solution
- Instruct the patient or the caretaker to return if any of the following signs develop; increased number of watery stools repeated vomiting or any signs indicating other problems (e.g. fever, blood in stool)

For each loose stool or vomiting give;

- 50-100 ml ( $\frac{1}{4}$  -  $\frac{1}{2}$  cup) of ORS solution for a child less than 2 years old.
- 100-200 ml for older children. Adults can take as much as they want

#### **Note**

Prophylactic treatment of cholera contacts with antibiotics is not recommended. Routine treatment of a community with antibiotics, or mass chemoprophylaxis, has no effect on the spread of cholera, can have adverse effects by increasing antimicrobial resistance and provides a false sense of security.

### **iii. Zinc and Folic Acid Supplements**

- Zinc (PO) 20mg once daily decreases diarrhea and shortens the duration of illness in children with cholera.
- Provide zinc supplementation, at a dosage of 20 milligrams per day for children older than six months or 10 mg per day for those younger than six months, for 10–14 days.
- Folic acid (PO) 2.5mg once daily for children < 6 months, or 5mg once daily for children >6 months for the duration of the treatment. For Pregnant women use Folic acid (PO) 5mg once daily for the duration of the treatment.

### **Public Health Control Measures**

- Establish treatment centre in locality where cases occur. Treat cases onsite rather than referring them to treatment centers elsewhere.
- Initiate a line listing of suspected and confirmed cases and ensure laboratory results are linked with cases
- Strengthen case management
- Mobilize community early to enable rapid case detection and treatment.
- Work with community leaders to limit the number of large gatherings, if seen mandatory, establish by-laws
- Ensure availability and continuous access to clean and safe water.
- Promote safe preparation of food, including fruits, and vegetables
- Promote safe disposal of human waste.
- Ensure adequate collaboration with various sectors including water and sanitation to ensure appropriate interventions are addressed.

**Note**

Cholera Vaccine is available however its utilization must be accompanied with strategies to improve water and sanitation

#### **4.1.2 Anthrax**

Anthrax is a bacterial disease caused by the spore forming *Bacillus anthracis*, a gram positive, rod-shaped bacterium. It is a zoonotic disease whereby man is infected directly through contact with infected hides or inhalation of spores in the lungs or ingestion of infected meat. It can be manifest on the skin (Cutaneous Anthrax) in the lungs (Pulmonary / Inhalation Anthrax), and/or intestinal (Gastrointestinal Anthrax and Oropharyngeal anthrax) or CNS (Meningeal Anthrax).

#### **Clinical Presentation**

##### **Cutaneous Anthrax**

- Itching
- Pruritic papule or vesicle
- Characteristic depressed black eschar surrounded by moderate to severe edema
- A malignant pustule,
- Pyrexia

##### **Inhalation Anthrax**

###### **Mild inhalation Anthrax**

- Cough, Fever, Fatigue, Myalgia, can resemble a viral respiratory illness, Pulmonary and gastrointestinal signs may occur together
- 

###### **Severe inhalation Anthrax**

- Diaphoresis, Stridor, Dyspnea, Hypotension, Acute respiratory distress

These patients may develop sepsis accompanied by cyanosis, shock, and hemorrhagic pneumonia. Hemorrhagic pleural effusions often develop.

##### **Gastrointestinal Anthrax**

- Fever, Abdominal pain, Vomiting, Diarrhea Bloody stool.

##### **Oropharyngeal anthrax**

Signs of oropharyngeal anthrax may include Dysphagia with posterior oropharyngeal necrotic ulcers, Unilateral neck swelling, Cervical adenopathy, Edema, Pharyngitis fever.

##### **Meningeal Anthrax**

Hemorrhagic meningoencephalitis that involves both

- Deep brain parenchymal hemorrhagic lesions
- Infection of the cerebrospinal fluid (CSF) in the subarachnoid space

#### **Case Definition**

**Suspected Case:** Any person with acute onset illness characterized by several clinical forms which are:

- **Cutaneous form:** Any person with skin lesion evolving over 1 to 6 days from a papular through a vesicular stage, to a depressed black eschar invariably accompanied by oedema that may be mild to extensive.
- **Gastro-intestinal:** Any person with abdominal distress characterized by nausea, vomiting, anorexia and followed by fever
- **Pulmonary (inhalation):** Any person with brief prodromal resembling acute viral respiratory illness, followed by rapid onset of hypoxia, dyspnoea and high temperature, with X-ray evidence of mediastinal widening
- **Meningeal:** Any person with acute onset of high fever possibly with convulsions, loss of consciousness, meningeal signs and symptoms; commonly noted in all systemic infections, but may present without any other clinical symptoms of anthrax.

#### **AND**

Has an epidemiological link to confirmed or suspected animal cases or contaminated animal products?

- Confirmed case:** A confirmed case of anthrax in a human can be defined as a clinically compatible case of cutaneous, inhalational or gastrointestinal illness that is laboratory-confirmed by:
- (a) Isolation of *B. anthracis* from an affected tissue or site; or
  - (d) Other laboratory evidence of *B. anthracis* infection based on at least two supportive laboratory tests.

### Laboratory Investigation

- Isolation of *Bacillus anthracis* from a clinical specimen (e.g. blood, lesions, discharges)
- Demonstration of *B. anthracis* in a clinical specimen by microscopic examination of stained smears (vesicular fluid, blood, cerebrospinal fluid, pleural fluid, stools)
- Positive serology (ELISA, Western blot, toxin detection, chromatographic assay, fluorescent antibody test).
- Detection of nucleic acid by PCR.

#### Other supporting tests

- Measurement of antibodies or toxin in blood
- Chest X-ray
- Computerized tomography (CT) scan
- Detection of *B. anthracis* by nucleic acid test (NAT) covering the genes coding for capsule and virulence factors;

### Prevention: Post Exposure Prophylaxis

- **A:** Initial 10-day exposure: ciprofloxacin (PO)500 mg 12 hourly for 5 days or doxycycline 100 mg (PO)  
12 hourly (or, if pathogens are documented to be susceptible phenoxy methyl penicillin) may be used  
Adults: phenoxy methyl penicillin (PO) 250-500 mg 6 hourly.  
Children 1-5 years: phenoxy methyl penicillin (PO) 125 mg 6 hourly.  
6-12 years: phenoxy methyl penicillin (PO) 250 mg 6 hourly  
48 hours' exposure:  
**OR**
- **S:** clindamycin (PO) 150 to 300 mg 6 hourly for 5 days  
**OR**
- **S:** levofloxacin (PO) 500 mg 12 hourly for 5 days are alternative antimicrobial prophylaxis to the local population within 48 hours of the initial exposure

### Pharmacological Treatment

**A:** benzylpenicillin (IV) 0.6 MU 6 hourly until local oedema subsides then continue with  
**A:** phenoxy methyl penicillin (IV) 250 mg 6 hourly for 7 days

If not responding change to

**A:** doxycycline (PO) 200 mg initial dose then 100 mg 12 hourly for 7 days

**OR**

**A:** ciprofloxacin (PO) 500 mg 12 hourly for 7 days

**AND**

**A:** paracetamol (PO) 15 mg/kg 8 hourly for 5 days

In severe forms ADD

Dexamethasone (PO) 0.6 mg/kg per day in divided doses every 8 hours for 4 days

### Public Health Control Measures

- Standard infection control precautions (IPC) should be used when managing patients with particular attention to body fluid spills, as organisms which remain on surfaces may form spores which are infectious
- Personal protective equipment should be used in situations where there is potential for splashes and inoculation injuries.
- Mobilize the community for early detection and care.
- Ensure proper burial or cremation (if practiced) of dead bodies (humans and animals)

- Conduct community education on the disease symptoms and signs, early reporting/seeking of medical care, disease transmission and prevention, application of infection prevention and control for home care setting,
- Conduct active search for additional cases that may not come to the health care setting (older women or small children patients, for example) and provide a door to door information about prevention and when to seek care.
- Ensure adequate collaboration with other sectors such as livestock, agriculture, environmental and sanitation, to ensure appropriate interventions are addressed.
- Request additional help from district/regional/national levels as needed

#### **4.1.3 Plague**

A zoonotic systemic bacterial infection caused by *Yersinia pestis* (plague bacillus) usually transmitted to humans by rodent fleas or by handling an infected animal. There are 3 forms of plague infection, depending on the route of infection:

- **Bubonic** plague is the most common, caused by the bite of an infected flea. *Y. pestis*, which enters the body at the bite site and travels through the lymphatic system to the nearest lymph node, replicates itself and causes the lymph node to be inflamed, tense and painful, turning into open sores with pus.
- **Septicaemic** plague occurs when infection spreads through the bloodstream, following untreated bubonic plague causing bleeding, tissue necrosis and shock.
- **Pharyngeal and or Pneumonic** plague is the most virulent form and is rare. It is typically caused by spread to the lungs from advanced bubonic plague. Untreated pneumonic plague can be fatal.

Human to human transmission only occurs with the pneumonic form of plague by infectious droplets. Incubation period is 2 to 6 days and case fatality rate (CFR) may exceed 50-60% in untreated bubonic plague and is nearly 100% in untreated pneumonic or septicaemic plague. However, it is usually <1% with appropriate and timely treatment. Currently, plague is one of the most important reemerging bacterial zoonoses in the world.

The main risk factor is exposure to infected populations of wild or domesticated rodents and their fleas in plague endemic areas.

#### **Case Definition**

##### **Bubonic Plague**

**Suspected case:** Any person with a very painful swelling of lymph nodes – buboes And Fever (or history of fever) or at least 3 of the following: headache or chills or generalized or severe asthenia and consistent epidemiological features, such as exposure to infected animals and/or evidence of flea bites and/or residence in or travel to a known endemic area within the previous 10 days.

**Confirmed case:** Any person with suspected case confirmed by isolation of *Yersinia pestis* from blood or aspiration of buboes, or specific seroconversion or rapid diagnostic test detecting the Ag F1 in endemic areas

##### **Pneumonic Plague**

**Suspected case:** Anyone, of any age, with coughs of less than 5 days with one of the following signs: Striated sputum from blood or dyspnea or chest pain and Fever (or history of fever) or at least 3 of the following: headache or chills or generalized or severe asthenia and Epidemiological context (contact with suspect or confirm pneumonic plague case, etc).

**Confirmed caseof pneumonic plague:** Any suspected case of plague in which *Yersinia pestis* has been isolated in culture

Or Suspect plague case with positive F1 rapid diagnostic test (RDT) and positive PCR or Seroconversion or increase in IgG antibody titre by 4 to 15 days

**Suspicious death of plague:** Anyone who died suddenly without apparent cause but with an epidemiological link to plague established and without biological sampling

**Probable case of plague:** Any suspected case of plague alive or deceased with F1 rapid diagnostic test (RDT) Or

Positive PCR alone

**Note:**

Human plague remains a public health concern in Tanzania despite its quiescence in most foci for years, considering the recurrence nature of the disease. Plague hosts comprises about 50% of all the animals trapped in West Usambara Mountains in north-eastern Tanzania.

**Clinical Diagnostic Criteria**

- Sudden onset of fever, chills, head and body aches
- Weakness, vomiting and nausea.
- Yersinia pestis is identified by laboratory testing from a sample of pus from a bubo, blood or sputum.  
A specific Y. pestis antigen can be detected by different techniques.

**Note:**

Differential diagnosis Bubonic plague may be confused with streptococcal or staphylococcal lymphadenitis, infectious mononucleosis, cat-scratch fever, lymphatic filariasis, tick typhus, tularemia and other causes of acute lymphadenopathy

**Laboratory Investigation**

- Aspiration after an injection of 1-2 ml of saline through an 18-22-gauge needle. Suitable microbiological culture media (e.g. brainheart infusion, broth, sheep blood agar, or MacConkey agar) should be inoculated with a portion of each specimen.
- Smears should be examined with Wayson or Giemsa stain and with Gram=s stain to show Small gram-negative and/or bipolar-staining coccobacilli
- smears should also be submitted for direct fluorescent antibody testing (anti-F1 antibody)
- Serological testing - anti-F1 antigen titre by agglutination
- Molecular biological techniques based on PCR and DNA Hybridization

**Note**

Anti-F1 rapid diagnostic test (RDT) positive alone is not a confirmed case. Culture and PCR tests need to done at the appropriate facility.

**Prevention:**

- Inform people of the presence of zoonotic plague and advised to take precautions against flea bites
- Do not handle animal carcasses and avoid direct contact with infected body fluids and tissues
- Apply standard precautions when handling potentially infected patients and while collecting specimens

**Vaccination:** Not recommended except for high-risk groups (such as laboratory personnel who are constantly exposed to the risk of contamination, and health care workers).

**Pharmacological Treatment**

**A:** streptomycin (IM)30 mg/kg/day (up to a total of 2 g/day) in divided doses, to be continued for 10 days of therapy or until 3 days after the temperature has returned to normal.

**OR**

**A:** erythromycin (PO) 500 mg (or 12.5 mg/kg) 8 hourly for 14 days

**OR**

**A:** doxycycline (PO) 200mg 12 hourly for 14 days

**Public Health Control Measures**

- Remove trash, food sources, and rat harborages to control rodent populations
- Protect against fleas with insect repellent on skin and clothing
- Conduct environmental flea control in houses, seaports and airports
- Isolate patients with pneumonic plague with precautions against airborne spread until at least after 48 hours of appropriate antibiotic therapy.
- Always observe the standard infection prevention and control (IPC) measures.

- Conduct community education on the disease symptoms and signs, early reporting/seeking of medical care, disease transmission and prevention, application of infection prevention and control for home care setting,
- Mobilize community to enable rapid case detection and treatment
- Provide chemoprophylaxis using tetracycline (PO) 15-30 mg/kg or chloramphenicol (PO) 30 mg/kg daily in 4 divided doses for 1 week after exposure ceases.
- Ensure adequate collaboration with other sectors such as livestock, agriculture, environmental and sanitation sectors to ensure appropriate interventions are addressed.

#### **4.1.4 Bacterial Cerebro-Spinal Meningitis**

Bacterial epidemics for Cerebro-Spinal Meningitis are commonly caused by *Neisseria meningitidis*. Other common bacteria are *Haemophilus influenza*, *Staphylococcus aureus* and *Streptococcus pneumoniae*. Human-to-human disease transmission is via large respiratory droplets from the nose and throats of infected people. Incubation period is 2 to 10 days. Attack rates are highest among children aged less than 15 years. Case fatality rates are usually 8-15% among treated patients, and >70% among untreated cases. Many survivors suffer long-term sequelae including mental retardation, hearing loss and loss of limb use. Further information on Meningitis for Nervous system related management

##### **Case Definition**

**Suspected meningitis case:** Any person with a sudden onset of fever (>38.5 °C rectal or 38.0 °C axillary), and neck stiffness or other meningeal signs and in case of infants, a bulging fontanelle.

**Probable meningitis case:** Any suspected case with macroscopic aspects of cerebrospinal fluid (CSF) (turbid, cloudy or purulent); or with a CSF leukocyte count >10 cells/mm<sup>3</sup> or with bacteria identified by Gram stain in CSF; or positive antigen detection (for example, by latex agglutination testing) in CSF

**In infants:** CSF leucocyte count >100 cells/mm<sup>3</sup>; or CSF leucocyte count 10–100 cells/mm<sup>3</sup> and either an elevated protein (>100 mg/dl) or decreased glucose (<40 mg/dl) level.

**Confirmed meningitis case:** Any suspected or probable case that is laboratory confirmed by culturing or identifying (i.e. polymerase chain reaction) a bacterial pathogen (*Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* type b) in the CSF or blood

##### **Clinical Diagnostic Criteria**

- Sudden fever
- Neck stiffness,
- Intense headache, nausea and vomiting,
- Altered consciousness and convulsions, Bulged anterior fontanelle (in infants)

##### **Laboratory Investigation**

- Lumbar puncture for Cerebrospinal Fluid Analysis with a median opening pressure
- CSF leukocyte count in episodes with CSF leak-associated meningitis
- CSF Culture and Sensitivity
- Elevated white blood cell count (WBC) in CSF of over 1000 cells/mm<sup>3</sup>
- Glucose concentration, <1.9 mmol/L
- Ratio of CSF glucose concentration to blood glucose concentration, <0.23;
- Protein concentration
- WBC count, >2000 cells/mL CSF neutrophil count, >1180 cells/mL

**Table 4.1: Cerebrospinal Fluid Analysis Findings**

CSF Characteristic	Normal Range	Suggestive of Bacterial Meningitis	Suggestive of Viral Meningitis
Colour	Clear	Cloudy	Cloudy
RBC Count	None	None	None
Gram stain	Negative	Usually Positive	Usually Negative (60%-90%)
Pressure*	20–30 cmH <sub>2</sub> O (16–24 mmHg or 2.1–3.2 kPa) with the patient sitting up	Above > 42 cm H <sub>2</sub> O	Normal
Protein	15 to 20.2 milligrams per deciliter (mg/dL) or 0.15 to 0.6 milligrams per milliliter (mg/mL)	Above 20.2 milligrams per deciliter (mg/dL), >2.20 g/L	Above 20.2 milligrams per deciliter (mg/dL), >2.20 g/L
Glucose	50–75 mg/dL (around 1.9 mmol/L) 50 to 75 mg/dL (or greater than 2/3 of the blood sugar level).	Below normal (<1.9 mmol/L)	Usually normal or below normal
Lymphocytic pleocytosis	None	Positive with neutrophilic pleocytosis	Positive with lymphocytic pleocytosis

\*Measured by recording the height of CSF in the manometer tube with the patient's leg gently and return the neck to a neutral position with the head supported with a pillow  
Use intravenous tubing sets and a ruler to measure cm of pressure if manometer is not available

### Prevention

- Vaccines targeted against *N. meningitidis* serogroups A or C, or a tetravalent A, C, Y, and W135 vaccine are useful for immunocompromized children.
- Hib conjugate vaccine is useful for immunocompromized children

### Pharmacological Treatment

**A:** benzathine penicillin(IV/IM) 300,000U/kg/day with a maximum dose of 24MU/day for 10-14 days, give 4 million units 4 hourly IV in adults and pediatric patients older than 1 month for 10-14 days.

#### AND

**A:** chloramphenicol (IV) 50 to 100mg/kg/day with a maximum dose of 4 g/day give in divided doses at 8 hourly intervals for 10-14 days.

- Serum concentrations requires monitoring due to chloramphenicol toxicity
- Recommended therapeutic levels include a trough of 5 to 10 mcg/mL and a peak of 10 to 20 mcg/mL

If no improvement in 3 days' give

- **C:** ceftriaxone (IV) 2g (50 mg/kg in pediatric patients older than 1 month) 12 hourly for 10-14 days OR cefotaxime (IV)2 g (50 mg/kg in pediatric patients older than 1 month) 6 hourly for 10-14 days.
- **C:** ceftriaxone (IV or IM) 2g for Adults daily for 10-14 days is preferred for patients with central nervous system involvement

#### AND

**B:** dexamethasone (IV/IM) 0.15mg/kg with a maximum dose of 10mg 8hourly for 3 days

### Public Health Control Measures

- Mass vaccination within 4 weeks of crossing the epidemic threshold\*\*\*
- Mobilize community to permit early case detection, treatment, and improve vaccine coverage during mass vaccination campaigns for outbreak control.
- Conduct community education on the disease symptoms and signs, early reporting/seeking of medical care, disease transmission and prevention.

- Maintain regular collection of 5-10 CSF specimens per week throughout the epidemic season in all affected districts to detect possible serogroup shift. Distribute treatment to health centres
- Treat all cases with appropriate antibiotics as recommended by National protocol.

\*\*\*If a neighbouring area to a population targeted for vaccination is considered to be at risk (cases early in the dry season, no recent relevant vaccination campaign, high population density), it should be included in a vaccination programme.

#### **4.1.5 Neonatal Tetanus**

A neuromuscular toxin-mediated illness caused by the anaerobic spore-forming soil bacterium *Clostridium tetani*. The disease is transmitted when spores enter open wounds (injections, cutting the umbilical cord) or breaks in the skin. While tetanus may occur in adults, infection primarily affects newborns. Neonatal tetanus has decreased dramatically in countries with improved maternal tetanus immunization rates. Maternal and neonatal tetanus is targeted for elimination in the WHO African Region, aiming to achieve neonatal tetanus incidence rates of less than 1 case per 1000 live births. Incubation period is 3 to 21 days, with an average of approximately 6 days. Usually occurs through introduction of tetanus spores via the umbilical cord during delivery through the use of an unclean instrument to cut the cord, or after delivery by “dressing” the umbilical stump with substances heavily contaminated with tetanus spores.

#### **Clinical Diagnostic Criteria**

- Sudden inability of a newborn to suck/feed between 2<sup>nd</sup> and 28<sup>th</sup> day after birth
- Generalized stiffness
- Convulsions

#### **Laboratory Investigation**

- **Diagnosis** is mainly clinical as there are no reliable **laboratory** tests for confirming tetanus
- Blood counts and blood chemical findings are unremarkable.
- Peripheral leukocytosis may be suggestive

#### **Prevention**

- Immunize women of reproductive age with TTCV, either during pregnancy or outside of pregnancy. This protects the mother and also her baby through the transfer of tetanus antibodies to the fetus.
- Good hygienic practices when the mother is delivering a child are also important to prevent neonatal and maternal tetanus.

To be protected throughout life, WHO recommends that an individual receives 6 doses (3 primary plus 3 booster doses) of TTCV through routine immunization.

#### **Non-pharmacological Treatment**

- Rigorously cleanse the umbilical stump to stop the production of toxin at the site of infection

#### **Pharmacological Treatment**

**A:** For children amoxycillin-clavulanate(PO) via Nasal Gastric Tube 20–30 mg/kg/day divided 8 hourly for 7 days

**For Adults** amoxycillin-clavulanate (PO) via Nasal Gastric Tube 500mg 8 hourly for 7days  
**AND**

**A:** metronidazole (PO) 7.5mg/kg for postnatal age ≤7days: Weighing 1200–2000g: 7.5 mg/kg/day(PO) given every 24 hours >2000 g: 15 mg/kg/day (PO) in divided doses every 12 hours. Postnatal age >7days: 1200–2000g: 15 mg/kg/day (PO) in divided doses every 12 hours >2000 g: 30 mg/kg/day(PO) in divided doses every 12 hours for 7 days

For Adults Metronidazole 400mg (PO) 8hourly for 7days

**OR**

**C:** ceftriaxone (IV) 2g (50 mg/kg in pediatric patients older than 1 month) 12hourly for 7days

For Adults ceftriaxone(IV) 2g once or in 2 divided doses for 7days

**OR**

**C:**cefotaxime) (IV) 2g (50 mg/kg) in pediatric patients older than 1 month 6hourly for 5days.  
For Adults Cefotaxime 2g (IV) 24hourly or 1g 12hourly for 7days

**OR**

Immunotherapy to neutralise circulating toxin

**B:** Administer human antitetanus immunoglobulin TIG, (IM) 100–300IU/kg stat, with the dose divided into two different muscle masses to the confirmed infected patients (Don't give vaccine to the confirmed infected patients)

**AND**

**A:** diazepam (PO) 0.5mg/Kg 8hourly as the effective management of muscle spasm, give a sedative cocktail of ALL the following via NGT:

**AND**

**A:** chlorpromazine (PO) 2mg/kg 8 hourly

**AND**

**B:** phenobarbitone (PO) 6mg/kg 12 hourly

**Table 4.2: Guidelines for Dosage Administration\*\***

Time (hours)	0	3	6	9	12	15	18	21	24
Diazepam	*	*		*		*		*	*
Chlorpromazine		*		*		*			
Phenobarbitone	*		*					*	

\*\* These are general guidelines. Frequency of drug administration should be titrated vs clinical condition

- Airway / respiratory control  
Provide mechanical ventilation.
- Provide adequate fluids and nutrition, as tetanus spasms result in high metabolic demands and a catabolic state.

### Public Health Control Mesures

The WHO global target for neonatal tetanus elimination is to reduce the incidence of neonatal tetanus to less than 1 case of neonatal tetanus (NT) per 1000 live births in every district of every country. To meet the target

- Immunize the mother and other pregnant women in the same locality as the case with at least 2 doses of tetanus toxoid.
- Conduct a supplemental immunization activity for women of childbearing age in the locality.
- Improve routine vaccine coverage through IVD and maternal immunization program activities.
- Educate birth attendants and women of childbearing age on the need for clean cord cutting and care. Increase the number of trained birth attendants.

### 4.1.6 Tick-Borne Relapsing Fever (TBRF)

A bacterial infection caused by bacteria*Borrelia duttonii*, are known zoonoses transmitted to humans through the bite of infected "soft ticks" *Ornithodoros* spp that live within rodent burrows feeding on the rodent. Humans typically come into contact with soft ticks when they sleep in rodent-infested cabins.

#### Common Symptoms

- Recurring episodes of fever, Non-specific headache, Non-specific Muscle pain, Non-specific Joint pain, Non-specific Chills, Non-specific Vomiting, and Abdominal pain.

Bacteremia tends to be greater among pregnant women, and may sometimes result in more severe infection. Symptoms tend to develop within 7days after the tick bite. Long-term sequelae of TBRF are rare but include iritis, uveitis, cranial nerve and other neuropathies.

#### Clinical Diagnostic Criteria

- Recurring episodes of high fever, headache, muscle and joint aches, and nausea

- Recurring symptoms, producing a telltale pattern of fever lasting roughly 3 days, followed by 7 days without fever, followed by another 3 days of fever. Without antibiotic treatment, this process can repeat several times.

### **Laboratory Investigation**

- Microscopy from the peripheral blood smear will reveal a long and spiral-shaped bacterium *Spirocheta* (spirochetes in blood) in TBRF patients often reaches high concentrations ( $\geq 10^6$  spirochetes/ml). Direct microscopic observation of relapsing fever spirochetes using dark field microscopy or stained peripheral blood smears

### **Prevention**

- Avoid sleeping in rodent-infested buildings whenever possible. Although rodent nests may not be visible, other evidence of rodent activity (e.g., droppings) are a sign that a building may be infested.
- Prevent tick bites. Use insect repellent (on skin or clothing) or permethrin (applied to clothing or equipment).

### **Pharmacological Treatment**

**A:** erythromycin(PO) 500mg (or 12.5 mg/kg) 8 hourly for 14days

**A:** tetracycline(PO)500mg 6hourly for 14days

**C:** ceftriaxone (IV or IM) 2 grams daily for 10-14days is preferred for patients with central nervous system involvement

### **Public Health Control**

- Provide public education, awareness, preventive control measures, and avoidance of areas where infected ticks are most abundant.
- Assessing evidence of rodent activity in and around structures of infected people
- Removal of rodents and their nests
- Reduce tick exposures by removing tick infested structures with an appropriate pesticide applied by a professional pest control operator who is familiar with the types of "crack and crevice" treatments used to control cockroaches or other wall-dwelling pests

## **4.2 Viral Infections**

### **4.2.1 Viral Haemorrhagic Fevers (VHF)**

Viral Haemorrhagic Fever (VHF) is a general term for a severe illness caused by viruses and sometimes associated with bleeding. Their distribution is dependent on the ecology of reservoir hosts with a potential to cause life-threatening illness in humans. Diagnosis and management is challenging due to the non-specificity of early symptoms, limited laboratory facilities in endemic areas, severity of disease, lack of effective therapy, strict infection control requirements and propensity to cause epidemics with secondary cases in healthcare workers.

Primary transmission is from animal to human, through contact with an infected animal or its product. Secondary transmission is from person to person through:

- Contact with a sick person or direct contact with the blood and/or secretions or with objects, such as needles that have been contaminated with infected secretions of an infected person.
- Breast feeding
- Sexual contact

### **Public Health Control measures**

- Maintain strict viral haemorrhagic disease (VHD) infection prevention and control (IPC) practices throughout the outbreak.
- Mobilize the community for early detection and care and conduct community education about how the disease is transmitted and how to implement IPC in the home care setting and during funerals and burials. Consider social distancing strategies.
- Conduct contact follow-up and active searches for additional cases that may not come to the health care setting.
- Establish an isolation ward or treatment centre to handle additional cases that may come to the health centre and ensure strict IPC measures to avoid transmission in health care settings.

- Suspected cases should be isolated and treated for more common conditions with similar symptoms, which might include malaria, typhoid, louse borne typhus, relapsing fever or leptospirosis. Ensure a barrier is instituted between suspected and confirmed cases.
- Provide psychosocial support for the family, community and staff.
- Consider quarantine for high risk contacts with home support during the incubation period and ensure daily follow up of their movements.
- There are promising vaccine candidates under development for some VHDs that might be useful to be used in the event of outbreak in a ring vaccination approach and for health care workers.
- Treat conservatively the symptoms which might be presented; severe cases require intensive support care; if dehydrated ensure fluid replacement with fluids that contain electrolytes.

#### **4.2.1.1 Ebola**

Ebola Virus Disease (EVD) is a deadly disease in people and non-human primates. The viruses that cause EVD are located mainly in sub-Saharan Africa. People can get EVD through direct contact with an infected animal (bat or nonhuman primate) or a sick or dead person infected with Ebola virus. Symptoms appear from 2 to 21 days after contact with the virus, with an average of 8 to 10 days.

##### **Case Definition:**

**Suspected case:** Illness with onset of fever and no response to treatment of usual causes of fever in the area, and at least one of the following signs: bloody diarrhoea, bleeding from gums, bleeding into skin (purpura), bleeding into eyes and urine.

**Confirmed case:** A suspected case with laboratory confirmation (positive IgM antibody, positive PCR or viral isolation), or epidemiologic link to confirmed cases or outbreak.

##### **Note**

During an outbreak, case definitions are likely to be adapted to new clinical presentation(s) or different modes of transmission related to the local event. In outbreak setting, the following standard case definitions apply:

**Suspected case:** Any person, alive or dead, suffering or having suffered from a sudden onset of high fever and having had contact with: - a suspected, probable or confirmed Ebola case; - a dead or sick animal

OR

- Any person with sudden onset of high fever and at least three of the following symptoms: - headaches - lethargy - anorexia / loss of appetite - aching muscles or joints - stomach pain - difficulty swallowing - vomiting - difficulty breathing - diarrhoea - hiccups;
- OR
- Any person with inexplicable bleeding; OR
- Any sudden, inexplicable death; OR
- A person (alive or dead) suffering or having suffered from a sudden onset of high fever and having had contact with: a dead or sick animal.

##### **Clinical Diagnostic Criteria**

A combination of symptoms suggestive of EVD AND a possible exposure to EVD within 21 days before the onset of symptoms is suggestive of Ebola.

##### **Symptoms**

- Fever
- Aches and pains, such as severe headache, muscle and joint pain, and abdominal (stomach) pain
- Weakness and fatigue
- Gastrointestinal symptoms including diarrhea and vomiting
- Abdominal (stomach) pain
- Unexplained hemorrhaging, bleeding or bruising

Other symptoms may include red eyes, skin rash, and hiccups (late stage)

An exposure may include contact with:

- Blood or body fluids from a person sick with or who died from EVD,
- Objects contaminated with blood or body fluids of a person sick with or who died from EVD,
- Infected fruit bats and non-human primates (apes or monkeys), or Semen from a man who has recovered from EVD.

### **Laboratory Investigations**

Ebola virus can be detected in blood after onset of symptoms. It may take up to three days after symptoms start for the virus to reach detectable levels. Investigations includes:

- Blood for RT-PCR
- Antigen detection or IgM (ELISA)

#### **Note**

Do not take specimen before wearing appropriate PPE and ensuring the patient is in an Isolation Ward/ Centre

### **Pharmacological Treatment**

**A:** paracetamol (PO/IV) 15mg/kg 8 hourly for 3 days

**B:** Give oxygen and manage hypoglycaemia if present

Fluid and electrolyte balance

**A:** compoundsodium lactate OR NS intravenously if cannot take fluids orally

**B:** Give Oxygen therapy to maintain oxygen status.

**A:** compoundsodium lactate (Ringers Lactate), NS intravenously if cannot take fluids orally.

Provide IV fluids and electrolytes (body salts) through infusion into the vein (intravenously)

**A:** Manage hypoglycaemia with 5% DNS or 25% Dextrose Solution if hypoglycaemia is shown by RBG testing

**A:** Using medication to support blood pressure, reduce vomiting and diarrhea and to manage fever and pain.

**A:** Treating other infections or any complicating infection and co-morbid condition

**A:** Psychological support is given to patient and family

**C:** Refer for Provision of Mechanical ventilation, renal dialysis, and anti-seizure therapy may be required.

### **Prevention**

- Isolate person with signs of EVD and has had a possible exposure from other people
- Notify the public health authorities
- Blood samples from the patient should be collected and tested to confirm infection
- Prompt identification of cases, contact tracing, and monitoring of high-risk individuals are essential to stopping Ebola virus from spreading
- Early recognition of EVD is critical for infection control. However, because early symptoms are not specific to EVD, it can be hard to distinguish it from other illnesses, including malaria, leptospirosis, influenza (flu), yellow fever, dengue and other viruses spread by insects, or viral or bacterial infections of the intestines, like typhoid fever.
- EVD should be considered when clinical illness is combined with an epidemiologic risk factor, like direct contact with a suspected or confirmed case or travel to an Ebola-affected area.
- Once a case of EVD is identified, everyone who has come in direct contact with the sick patient is traced
- Contacts are watched for signs of illness for 21 days from the last day they came in contact with the Ebola patient. If the contact develops a fever or other EVD symptoms, they are immediately isolated, tested, and provided care.

#### **4.2.1.2 Marburg Haemorrhagic Fevers**

Marburg virus belongs to the family *Filoviridae*, divided into three genera: ebolaviruses, marburgviruses, and cuevaviruses. The reservoir host of Marburg virus is the African fruit

bat, *Rousettus aegyptiacus*. Fruit bats infected with Marburg virus do not show obvious signs of illness. Primates (including humans) can become infected with Marburg virus, and may develop serious disease with high mortality. The disease can spread rapidly within the health care setting. The virus enters through broken skin, mucous membrane or exchange of bodily fluids or ingestion, inhalation and injection of infectious material

### **Case Definition**

**Suspected case:** Illness with onset of fever and no response to treatment of usual causes of fever in the area, and at least one of the following signs: bloody diarrhea, bleeding from gums, bleeding into skin (purpura), bleeding into eyes and urine.

**Confirmed case:** A suspected case with laboratory confirmation (positive IgM antibody, positive PCR or viral isolation), or epidemiologic link to confirmed cases or outbreak.

In an outbreak setting, the following standard case definitions apply;

**Suspected case:** Any person, alive or dead, suffering or having suffered from a sudden onset of high fever and having had contact with: - a suspected, probable or confirmed Marburg case; - a dead or sick animal

OR

Any person with sudden onset of high fever and at least three of the following symptoms: - headaches - lethargy - anorexia / loss of appetite - aching muscles or joints - stomach pain - difficulty swallowing - vomiting - difficulty breathing - diarrhoea - hiccups; OR

- Any person with inexplicable bleeding OR
- Any sudden, inexplicable death; OR
- A person (alive or dead) suffering or having suffered from a sudden onset of high fever and having had contact with a dead or sick animal

### **Non-Pharmacological Treatment:**

Supportive therapy includes:

- Mechanical ventilation, renal dialysis, and anti-seizure therapy may be required.
- Management of complications symptomatically
- Maintaining Oxygen status and Blood Pressure

### **Pharmacological Treatment**

There is no specific treatment for Marburg Haemorrhagic Fever.

**A:** paracetamol (PO/IV) 15mg/kg 8hourly for 3days

**B:** Give oxygen and manage hypoglycaemia if present

If there is Fluid and electrolyte imbalance:

**A:** compound sodium lactate (Ringers Lactate), NS intravenously if cannot take fluids orally

**B:** Give Oxygen therapy to maintain oxygen status.

**A:** sodium lactate compound (Ringers Lactate), NS intravenously if cannot take fluids orally. Provide IV fluids and electrolytes (body salts) through infusion into the vein (intravenously)

**A:** Manage hypoglycaemia with 5% DNS or 25% Dextrose Solution if hypoglycaemia is shown by RBG testing

**A:** Using medication to support blood pressure, reduce vomiting and diarrhea and to manage fever and pain.

**A:** Treating other infections or any complicating infection and co-morbid condition

**A:** Psychological support is given to patient and family

**D:** Refer for Provision of Mechanical ventilation, renal dialysis, and anti-seizure therapy may be required.

#### **4.2.1.3 Rift Valley Fever**

Rift Valley Fever (RVF) is a viral disease that affects mainly animals and occasionally humans. The virus is a member of the Phlebovirus genus, one of the five genera in the family Bunyaviridae. The disease is frequently reported following heavy rainfall and floods. RVF is mainly transmitted from animals (sheep, cattle, goats, camels) to humans through close contact with infected animals (such as handling meat and body fluids and consumption of raw milk). During established RVF outbreaks in animals, humans can also get infected through bites of infected mosquitoes and other biting insects.

The incubation period of RVF varies from 2 to 6 days. These symptoms usually last from 4 to 7 days. Most of the infected people recover on their own. However, a small proportion gets complications such as vomiting blood, nose bleeding and passing bloody stool. Rift Valley fever is difficult to distinguish from other viral haemorrhagic fevers as well as many other diseases that cause fever, including malaria, shigellosis, typhoid fever, and yellow fever.

### **Case Definitions**

**Suspected case:** Early Disease: Acute febrile illness (axillary temperature  $>37.5^{\circ}\text{C}$  or oral temperature of  $>38.0^{\circ}\text{C}$ ) of more than 48 hours' duration that does not respond to antibiotic or antimalarial therapy, and is associated with:

- Direct contact with sick or dead animal or its products AND / OR
- Recent travel (during last week) to, or living in an area where, after heavy rains, livestock die or abort, and where RVF virus activity is suspected/confirmed AND / OR
- Abrupt onset of any 1 or more of the following: exhaustion, backache, muscle pains, headache (often severe), discomfort when exposed to light, and nausea/vomiting AND / OR:
- Nausea/vomiting, diarrhoea OR abdominal pain with 1 or more of the following:
  - Severe pallor (or Hb  $< 8 \text{ gm/dL}$ )
  - Low platelets (thrombocytopenia) as evidence by presence of small skin and mucous membrane haemorrhages (petechiae) (or platelet count  $< 100 \times 10^9 / \text{dL}$ )
  - Evidence of kidney failure (edema, reduced urine output) (or creatinine  $> 150 \text{ mol/L}$ ) AND / OR
  - Evidence of bleeding into skin, bleeding from puncture wounds, from mucous membranes or nose from gastrointestinal tract and unnatural bleeding from vagina AND / OR
  - Clinical jaundice (3-fold increase above normal of transaminases)

### Late stages of diseases or complications

(2-3 weeks after onset)

- Patients who have experienced, in the preceding month a flu-like illness, with clinical criteria, who additionally develop the following:
  - CNS manifestations which resemble meningo-encephalitis AND/OR:
  - Unexplained visual loss OR
  - Unexplained death following sudden onset of acute flu-like illness with haemorrhage, meningo-encephalitis, or visual loss during the preceding month.

### **Confirmed case:**

Any patient who, after clinical screening, is positive for anti-RVF IgM ELISA antibodies (typically appear from fourth to sixth day after onset of symptoms) or tests positive on reverse transcriptase polymerase chain reaction (RT-PCR).

Transmission to human is mainly through direct or indirect contact with blood or organs of infected animals. The virus can be transmitted to human through;

- Handling of animal tissue during slaughtering or butchering, assisting with animal births, conducting veterinary procedures.
- Inoculation e.g via wound from infected knife or through contact with broken skin or through inhalation of aerosols produced during the slaughter of an infected animals.
- Infected mosquito.

Human become viraemic; capable of infecting mosquitoes shortly before onset of fever and for the first 3–5 days of illness. Once infected, mosquitoes remain so for life.

### **Clinical Diagnostic Criteria**

- Acute febrile illness that does not respond to antibiotic or antimalarial therapy,
- Exhaustion, backache, muscle pains, headache (often severe),
- Photophobia
- Nausea/vomiting
- Evidence of bleeding into skin, bleeding from puncture wounds, from mucous membranes or nose, from gastrointestinal tract and unnatural bleeding from vagina

- Clinical jaundice (3-fold increase above normal of transaminases)

Clinical diagnosis is difficult, because RVF symptoms can be mild and non-specific, especially early in the course of the disease.

### **Laboratory Investigations**

Definitive diagnosis of RVF involves laboratory testing of blood (during illness) or other tissue samples (postmortem tissue).

- The virus detection in the blood then virus isolation in cell culture
- Molecular techniques (reverse transcriptase polymerase chain reaction or RT-PCR).
- Antibody testing using Enzyme-Linked ImmunoAssay (ELISA) confirms infection with RVFV
- IgM antibodies reflect a recent infection and IgG antibodies persist for several years (Detection of anti-RVF IgM suggests an ongoing transmission of RVFV in humans during inter-epidemic periods.).
- FBC
  - Low Hb [ $Hb < 8\text{gm/dL}$ ] - Severe pallor
  - Low platelet  $< 100 \times 10^9 /DI$  (Thrombocytopenia) – small skin and mucous membrane hemorrhages (Petechiae))
- Serum Creatinine

#### **Note**

Acute RVF can be diagnosed using several different methods

1. Serological tests such as ELISA may confirm the presence of specific IgM antibodies to the virus. The virus itself may be detected in blood during the early phase of illness or in post-mortem tissue using a variety of techniques including, antigen detection tests by ELISA, RT-PCR, virus propagation (in cell cultures), Immunohistochemistry in formalin-fixed tissues
2. ELISA IgG can be used for retrospective diagnostic.

### **Management**

Management of RVF in humans is mainly supportive as there is no definitive treatment for RVF. Early detection and management of the disease is important. Human control of RVF is through control of the disease in animals through a sustained vaccination program and limiting human-animal contact. Use of insecticide treated nets and mosquito repellents can also reduce infections in human. In addition to human suffering and death, RVF has far reaching economic implications to the Livestock industry. In outbreak settings, the disease manifestation includes non-haemorrhagic febrile syndromes, and laboratory testing should be considered among persons with milder symptoms suggestive of viral illness.

### **Prevention**

People living in or visiting areas with RVF shall be protected from the RVF infection with these steps:

- Protect people from contact with blood, body fluids, or tissues of infected animals. (Use PPEs like gloves, boots, long sleeves, and a face shield)
- Protect people from unsafe animal products. All animal products (including meat, milk, and blood) should be thoroughly cooked before eating or drinking.
- Protect people from mosquitoes and other bloodsucking insects. Use insect repellents and bed nets, and wear long sleeved shirts and long pants to cover exposed skin.

No vaccines are currently available for vaccination in people at risk of RVF infection.

### **Public Health Control Measures**

- Mobilize the community for early detection and care.
- Conduct community education about the confirmed case, how the disease is transmitted, and how to prevent contact with tissues of infected animals and avoid mosquito bites.
- Provide information about prevention in the home and when to seek care.
- Provide supportive treatment to all cases identified
- Collaborate with the animal health specialists to search and document cases among animals as well.

#### **4.2.1.4 Yellow Fever**

Yellow fever virus is an RNA that belongs to the genus Flavivirus and is related to West Nile, St. Louis encephalitis, and Japanese encephalitis viruses. It is transmitted human-to-human via the domestic species of Aedes mosquitoes (Urban epidemics) or to humans from primate reservoir via a forest mosquito species (Sylvatic cycle). About 15% of infections progress to fever and jaundice. While only the minority of cases are severe, case fatality rate may be 25% to 50% among patients with syndrome of haemorrhage, jaundice, and renal disease. A small proportion of patients develop “toxic phase” with jaundice (yellowing of the skin and eyes, hence the name ‘yellow fever’), dark urine and abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach and half of those die within 7 to 10 days.

**Risk factor:** Sporadic cases often linked to occupation or village location near woods or where monkeys are numerous, also non-vaccinated persons. Infection and disease can be prevented by vaccination. With a vaccine efficacy > 95% and duration of immunity is life time

#### **Case definition**

**Suspected case:** Any person with acute onset of fever, with jaundice appearing within 14 days of onset of the first symptoms.

**Probable case:** A suspected case with one of the following;

- Epidemiological link to a confirmed case or an outbreak
- Positive post-mortem liver histopathology

**Confirmed case:** A probable case with one of the following;

- Detection of YF-specific\* IgM
- Detection of four-fold increase in YF IgM and/or IgG antibody titres between acute and convalescent serum samples
- Detection of YFV-specific\* neutralizing antibodies

\*YF-specific means that antibody tests (such as IgM or neutralizing antibody) for other prevalent flavivirus are negative. This testing should include at least IgM for Dengue and West Nile and may include other flavivirus depending on local epidemiology.

OR

One of the following

- Detection of YF virus genome in blood or other organs by PCR

Detection of yellow fever antigen in blood, liver or other organs by immunoassays Isolation of the yellow fever virus

#### **Laboratory Investigations**

- ELISA for the presence of yellow fever Specific IgM and IgG antibodies.
- Exclusion of Dengue, West Nile virus and other locally prevalent flavivirus will be necessary for the confirmation of yellow fever.
- PCR, YF specific seroneutralization, virus isolation or histopathology

#### **Management**

##### **Non-Pharmacological Treatment**

No specific anti-viral treatment, supportive therapies are recommended. Good and early supportive treatment for dehydration, liver and kidney failure, and fever improves outcomes. Associated bacterial infections can be treated with antibiotics

#### **Prevention**

Prevention and Control involve mosquito control and provision of Yellow Fever vaccine. The yellow fever vaccine is safe, affordable and a single dose provides life-long protection against yellow fever disease.

#### **Indication of Yellow Fever Vaccination**

- Persons ≥ 9 months of age
- Planning travel to or residence in an endemic area
- Planning travel to a country with an entry requirement

Needs to be given ≥ 10 days prior to arrival in endemic area

## **Contraindications of Yellow Fever Vaccination**

- Infants aged less than 9 months;
- Pregnant women – except during a yellow fever outbreak when the risk of infection is high;
- People with severe allergies to egg protein; and  
People with severe immunodeficiency due to symptomatic HIV/AIDS or other causes, or who have a thymus disorder

## **Public Health Control Measures**

- Identify all cases and provide clinical, epidemiological and laboratory evidences
- Identify contacts, screen and test for confirmation
- Educate the communities affected on mosquito control
- Destroy known sources of standing water and any newly discovered sites for the presence of mosquito larvae.
- Surveillance of Mosquito by Mosquito control professionals

### **4.2.1.5 Dengue Fever**

Dengue virus is an arbovirus transmitted by aedes mosquitoes (both Ae. aegypti and Ae. albopictus). Dengue fever is caused by four serologically distinct, but closely related Dengue viruses: dengue virus (DENV) 1, 2, 3, and 4 of the Flaviviridae family. Dengue fever is an emerging pandemic that has spread globally during the past 30 years as a result of changes in human ecology. Dengue haemorrhagic fever (DHF) is a potentially deadly complication that has become a leading cause of hospitalization and death among children in Asia and Africa. There is good evidence that sequential infection with the different serotypes of dengue virus increases the risk of more severe disease that can result in dengue shock syndrome (DSS) and death.

Infected humans are the main carriers and multipliers of the virus, serving a source of the virus for uninfected Aedes aegypti mosquitoes which maintain the urban dengue transmission cycle. The virus circulates in the blood of infected human for 2-7 days, at approximately the same time that they have a fever. A sylvatic transmission cycle has been documented in West Africa where DENV-2 has been found in monkeys. There is no evidence of person-to-person transmission.

DENV is frequently transported from one place to another by infected travelers; when susceptible vectors are present in these new areas, there is the potential for local transmission to be established.

### **Case Definition**

**Dengue Fever Suspected case:** Any person with acute febrile illness of 2-7 days duration with 2 or more of the following: headache, retro-orbital pain, myalgia, arthralgia, rash, haemorrhagic manifestations, leucopenia.

**Dengue Fever Confirmed case:** A suspected case with laboratory confirmation (positive IgM antibody, four-fold or greater rise in IgG antibody titres, positive PCR or viral isolation).

**Dengue Haemorrhagic Fever:** A probable or confirmed case of dengue with bleeding tendencies as evidenced by one or more of the following: positive tourniquet test; petechiae, ecchymoses or purpura; bleeding: mucosa, gastrointestinal tract, injection sites or other; haematemesis or melaena; and thrombocytopenia (100,000 cells or less per mm<sup>3</sup>) and evidence of plasma leakage due to increased vascular permeability, manifested by one or more of the following: 20% rise in average haematocrit for age and sex, 20% drop in haematocrit following volume replacement therapy compared to baseline, signs of plasma leakage (pleural effusion, ascites, hypo-proteinaemia).

**Dengue Shock Syndrome:** All the above criteria, plus evidence of circulatory failure manifested by rapid and weak pulse, and narrow pulse pressure ( $\leq 20$  mm Hg) or hypotension for age, cold, clammy skin and altered mental status.

### **Laboratory Investigations**

- Reverse Transcriptase–Polymerase Chain Reaction (RT–PCR)
- Rapid Tests for Dengue NS1 antigen

Serological methods, such as Enzyme-Linked Immunosorbent Assays (ELISA) for IgM and IgG anti-dengue antibodiesFBP

## **Management**

There is no specific treatment for dengue, but appropriate medical care frequently saves the lives of patients with dengue haemorrhagic fever.

### **Non-Pharmacological Treatment**

No specific treatment is available for Dengue fever.

### **Pharmacological Treatment:**

A: paracetamol (PO/IV) 15mg/kg 8hourly for 3days

A: Maintenance fluid (Ringers lactate, NS) intravenously if one cannot take enough fluid orally

B: Blood transfusion and clotting factors.

B: Oxygen and manage hypoglycaemia if present

#### **Note**

- No antibiotics are of proven value.
- Children below 12 years require close monitoring for dangerous form.
- Steroids should not be used.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as ibuprofen and aspirin should be avoided. These anti-inflammatory drugs act by thinning the blood, and in a disease with risk of hemorrhage, blood thinners may exacerbate the prognosis

## **Prevention**

At present, the only method of controlling or preventing dengue virus transmission is to combat the vector mosquitoes using environmental management and chemical methods.

- Prevent dengue by avoiding mosquito bites by *Aedes. aegypti* and *Aedes. albopictus* bite during the day and night (Using mosquito repellent, bed nets and removing reservoirs).
- All four dengue viruses are spread primarily through the bite of an infected *Aedes* mosquito.
- A dengue vaccine is available for use in some parts of the world

### **Public Health Control Measures**

- Wear full sleeve clothes and long dresses to cover the limbs
- Use mosquito repellents
- Use mosquito nets – to protect babies, old people and others, who may rest during the day. Effectiveness of such nets can be improved by treating them with permethrin (pyrethroid insecticide). Curtains (cloth or bamboo) can also be treated with insecticide and hung at windows or doorways, to repel or kill mosquitoes

#### **4.2.1.6 Chikungunya Fever**

Chikungunya Virus Disease is the arthropod-borne virus caused by Chikungunya Virus (CHIKV), transmitted by the *Aedes aegypti* and *Aedes albopictus* mosquitos the same which transmit Dengue virus, West Nile and Yellow Fever viruses. Chikungunya disease (Seroprevalance 7.7% to 26.9% in Tanzania) does not often result in death, but the symptoms can be severe and disabling. People at risk for more severe disease include newborns, older adults ( $\geq 65$  years), and people with medical conditions such as high blood pressure, diabetes, or heart disease. The word "Chikungunya" is Makonde for "that which bends up," in reference to the stooped posture of patients afflicted with the severe joint pain associated with the disease. Epidemics of fever, rash and arthritis, resembling Chikungunya fever were recorded as early as 1779. However, the virus was first isolated between 1952-1953 from both man and mosquitoes during an epidemic in Tanzania.

## **Case Definition**

### **Acute clinical case**

- Clinical criterion: Fever  $>38.50$  C (101.30F) and joint pain<sup>a</sup> (usually incapacitating<sup>b</sup>) with acute onset<sup>a</sup> AND
- Epidemiological criterion: resident or visitor in areas with local transmission of Chikungunya on the last 15 days (suspected case for epidemiological surveillance)<sup>b</sup> OR
- Laboratory criterion: confirmation by laboratory: PCR, serology or viral culture (confirmed case for epidemiological surveillance)

- Usually accompanied by exanthema, myalgia, back pain, headache and, occasionally, vomiting and diarrhoea (pediatric age group).
- In children aged <3 years, joint pain is expressed as inconsolable crying, irritability, rejection to mobilization and/or walking

### **Atypical case**

Clinical case of laboratory confirmed Chikungunya accompanied by other manifestations: neurological, cardiological, dermatological, ophthalmological, hepatic, renal, respiratory, or haematological, among others.

### **Severe acute case**

Clinical case of laboratory-confirmed Chikungunyapresenting dysfunction of at least one organ or system that threatens life and requires hospitalization

### **Suspected and confirmed chronic cases**

Suspect chronic case: Person with previous clinical diagnosis of chikungunya after 12 weeks of the onset of the symptoms presenting with at least one of the following articular manifestations: pain, rigidity, or edema, continuously or recurrently.

Confirmed chronic case: Every chronic case with a positive chikungunya laboratory test

### **Laboratory Investigations**

**Chikungunya** is a biosafety level-3 (BSL-3)

- Detection of **Chikungunya** virus (CHIKV) viral culture of **blood** in the first 3 days
- RT-PCR for Viral RNA from the serum collected <6 days after onset of illness.

Serological tests show a four-fold rise in antibody titer to Chikungunya virus;

### **Non-Pharmacological Treatment:**

The mainstay treatment for Chikungunya is the supportive symptomatic treatment.

**A:** Assure plenty of rest to patients

### **Pharmacological Treatment**

**A:** Maintain body fluids Sodium Lactate Compound (Ringers Lactate) intravenously.

**A:** Control Fever and Pain by giving paracetamol (PO/IV]15mg/kg 8hourly for 3days

#### **Note**

- No antibiotics are of proven value.
- Steroids should not be used.
- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as ibuprofen and aspirin should be avoided. These anti-inflammatory drugs act by thinning the blood, and in a disease with risk of hemorrhage, blood thinners may exacerbate the prognosis
- Do not use products containing oil of lemon eucalyptus (OLE) or para-menthane-diol (PMD) on children under 3 years old.
- Do not apply insect repellent to a child's hands, eyes, mouth, cuts, or irritated skin

### **Prevention**

The most effective way to prevent infection from Chikungunya virus is to prevent mosquito bites during the day and night.

- Use insect repellent (DEET, Picaridin (known as KBR 3023 and icaridin IR3535, Oil of lemon eucalyptus (OLE), Para-menthane-diol (PMD), 2-undecanone)
- Modification of the mosquito bleeding sites
- Wear long-sleeved shirts and pants,
- Treat clothing and gears with permethrin
- Take steps to control mosquitoes indoors and outdoors

### **Public Health Control Measures**

- Symptomatic treatment for mitigating pain and fever using non-steroidal anti-inflammatory drugs along with rest usually suffices. Persistent joint pain may require analgesic and long-term anti-inflammatory therapy.
- Prevention is entirely dependent upon taking steps to avoid mosquito bites and elimination of mosquito breeding sites.

- To avoid mosquito bites:
  - Wear full sleeve clothes and long dresses to cover the limbs
  - Use mosquito repellents
  - Use mosquito nets – to protect babies, old people and others, who may rest during the day.
  - The effectiveness of such nets can be improved by treating them with permethrin (pyrethroid insecticide). Curtains (cloth or bamboo) can also be treated with insecticide and hung at windows or doorways, to repel or kill mosquitoes

#### **4.2.2 Measles (Rubeola)**

Measles is an acute, highly communicable (contagious) infectious viral disease caused by Measles virus (MeV) which is the member of the family *Paramyxoviridae*, genus *Morbillivirus*. The mode of transmission is airborne, by droplet spread through coughing or sneezing, or by direct contact with nasal or throat secretions of infected persons. It is the fourth leading cause of death in children less than 5 years of age in many African countries.

##### **Case Definition**

###### **Suspected case:**

Any person with fever and maculopapular (non-vesicular) generalized rash and cough, coryza or conjunctivitis (red eyes) or any person in whom a clinician suspects measles.

###### **Confirmed case:**

A suspected case with laboratory confirmation (positive IgM antibody) or epidemiological link to confirmed cases in an outbreak.

##### **Clinical Diagnostic Criteria**

- Generalized, reddish (erythematous), blotchy (maculopapular) rash;
- History of fever usually above 38°C (if not measured, then "hot" to touch);
- Dry cough; Sore throat; Runny nose (coryza);
- Inflamed eyes (conjunctivitis), tiny white spots with bluish-white centers on a red background found inside the mouth on the inner lining of the cheek- also called Koplik's spots.
- In addition, children with measles frequently exhibit a dislike of bright light (photophobia), and often have a sore red mouth (stomatitis).

Symptoms usually develop 10–12 days after exposure to an infected person and last 7–10 days

##### **Laboratory Investigation**

With coordination from the WHO, the Global Measles and Rubella Laboratory Network (GMRLN) performs case-based laboratory surveillance standardized methods to confirm Measles Infection by

- Detection of viral RNA by RT-PCR (increasing role in case confirmation),
- Enzyme Immunoassay (EIA) for immunoglobulin M (IgM)

##### **Pharmacological Treatment**

###### **Note**

No specific antiviral treatment exists for measles virus

Adults: **A:** paracetamol(PO) 1g 8hourly for 5days

**AND**

**A:** vitamin A (PO) 200000 IU stat

In case of ocular involvement, add

**A:** oxytetracycline eye ointment 1% apply once daily for 7 days

Children:

**A:** paracetamol (PO) 10–15mg/kg 8hourly for 5days

**A:** vitamin A if less than 1 year give 100,000IU (PO) start and if over 1 year give 200,000IU

##### **Prevention**

Routine measles vaccination for children combined with mass immunization campaigns

- Administration of the first dose of measles-containing vaccine (MCV) at 9 months and 18 months in measles-endemic regions (Tanzania) and at 12–15 months in non-endemic regions.

- Accelerated immunization activities have had a major impact on reducing measles deaths.
- The World Health Organization (WHO) defines measles elimination as “the absence of endemic measles virus transmission in a defined geographical area (e.g. region or country) for at least 12 months in the presence of a surveillance system that has been verified to be performing well.

### **Public Health Control Measures**

Efforts to reduce the secondary spread of measles include;

- Improve routine vaccine coverage through the IVD, and lead supplemental vaccination activities in areas of low vaccine coverage.
- Mobilize the community early to enable rapid case detection and treatment.
- Provide Vitamin A: Dose 1: immediately, Dose 2: next day

### **4.2.3 Rabies**

Rabies is a zoonotic disease (a disease that is transmitted to humans from animals) that is caused by a virus. Rabies infects domestic and wild animals, and is spread to people through close contact with infected saliva (via bites or scratches). The rabies virus infects the central nervous system, causing disease in the brain and, eventually, death. Early symptoms in people include: fever, headache, and general weakness or discomfort. As the disease progresses, symptoms include; insomnia, anxiety, confusion, slight or partial paralysis, excitable behaviour, hallucinations, increase in saliva, difficulty swallowing, and fear of water (hydrophobia).

In unvaccinated humans, rabies is almost always fatal if post-exposure prophylaxis is not administered before the onset of severe symptoms. Death usually occurs within days of the onset of neurological symptoms. Dogs are the main carrier of rabies in Africa and are responsible for most (approximately 97%) of the human rabies deaths worldwide. WHO estimates approximately 55,000 human deaths worldwide due to rabies each year; in Africa the annual death toll is 24,000.

### **Case Definition**

**Suspected:** A person with one or more of the following: headache, neck pain, nausea, fever, fear of water, anxiety, agitation, abnormal tingling sensations or pain at the wound site, when contact with a rabid animal is suspected.

**Confirmed:** A suspected case that is laboratory confirmed

### **Laboratory Investigation**

Human rabies is confirmed by intra-vitam and post mortem diagnostic techniques that detect whole viruses, viral antigens, or nucleic acids in infected tissues (brain, skin or saliva). E.g. Direct fluorescent antibody (DFA) test, which targets rabies virus antigens in brain tissue, Identification of viral nucleic acid by reverse transcriptase PCR on fixed tissue collected post mortem or in a clinical specimen (brain tissue or skin, cornea or saliva) or Detectable rabies-neutralizing antibody titre in the CSF of an unvaccinated person.

### **Pharmacological Treatment**

Post-exposure prophylaxis (PEP) is the immediate treatment of a bite victim after rabies exposure by

- Extensive washing and local treatment of the bite wound or scratch as soon as possible after a suspected exposure;
- Providing effective rabies vaccine that meets WHO standards
- Administration of rabies immunoglobulin (RIG), if indicated.

Local wound therapy: -wash wound thoroughly with running water and soap for 10 minutes, and repeat process with:

**A: 10% Povidone iodine;** to prevent secondary bacterial infection.

If patient present with Anxiety, Agitation, Seizures,

**A: diazepam** Adults 10mg IV slowly in 3–5minutes (0.1–0.3 mg/kg in 3–5 min) 10mg in 3–5minutes, repeated 1–4 hourly Paediatrics 0.1–0.3 mg/kg in 3–5min, repeated 1–4 hourly to provide (total 2.4–12 mg/kg IV for 24 h)

**OR**

**A: diazepam (IV)** slowly in 3–5minutes, repeated 1–4hourly for 24hours

**OR**

**A:** diazepam (IM) 20mg 2hourly for 24hours

**OR**

**A:** diazepam (Intrarectally) 10mg 1–4 hourly for 24 hours

**OR**

**A:** lorazepam 25–50mcg/kg 6 hourly for 24 hours

**OR**

**C:** midazolam 0.08 – 0.2mg/kg (IV) repeated 1–4 hourly for 24 to 48 hours

**OR**

**C:** midazolam (intrarectally)10–30mg over 24 hours by pump for 24 to 48 hours

If patient present with Anxiety

**A:** Haloperidol 5mg (IM or SC) hourly until calm, then 4 or 6 hourly and when necessary

**OR**

**A:** haloperidol 5 mg (IV) 5–15mg/24 hours

**OR**

**A:** chlorpromazine (IM) 25–50mg/6–8 hourly for 48hours

**Table 4.3: Support for Patient with Fever, Hypersecretion and Pain**

Indication	Drug	Route of administration	Dose: adult	Dose: paediatric
Fever	A: paracetamol	iv infusion over 15 minutes	1 g every 8 h, maximum 3-4 g/24 h	
		intrarectal	1g every 4–6h, maximum 3-4 g/24 h	10–15mg/kg (PO) every 8 hours for 5 days
	A: ibuprofen	intrarectal	300–400 mg 8 hourly	
	A: aspirin	intrarectal	450–900mg 4hourly, maximum 3.6 g/day	
Hypersecretion	A: Hyoscine (scopolamine) hydrobromide	sc or iv injection	400 mcg 4 hourly	10 mcg/kg 4–8hourly
		sc infusion	1.2–2 mg/24 h	40–60 mcg/kg/24h
Pain	C: morphine	slow iv, sc or im	10 mg 4hourly	
		intrarectal	15–30 mg 4hourly	100 mcg/kg
	S: fentanyl	transdermal patch	12–25 mcg/h every 72 h	12 mcg/h every 72h

### Prevention

- Rabies can be prevented by
- Vaccinating pets
- Staying away from wildlife
- Seeking medical care after potential exposures before symptoms start
- Immunization

### Immunization

#### Active Immunization

Pre-exposure immunization is recommended for people in certain high-risk occupations such as laboratory workers handling live rabies and rabies-related (lyssavirus) viruses; and people (such as animal disease control staff and wildlife rangers)

Active immunization: Human Diploid Cell Vaccine (HDCV) –either ID or IM

**A:** anti-rabies Vaccines (2- 3 IU/dose)

- **IM:** 1ml on days 0, 3, 7, 14, 28 (5 doses)

- **ID:** 0.2ml by dividing 0.1 ml on left shoulder and 0.1ml on right shoulder, on days 0, 3, 7 and 28 (4 doses). **Intradermal (ID)** is mostly advised.

In addition, patients should receive rabies immune globulin with the 1st dose (day 0)

### **Passive Immunization**

**B:** anti-rabies human immunoglobulin 20 IU/kg half the dose given parenterally and the other half injected into and around the wound for victims suspected to be infected

**AND**

**A:** tetanus toxoid vaccine, please refer to the section on *Tetanus*

### **Note**

Treat the person immediately after the animal bite, before onset of symptoms

Corticosteroid therapy generally is not considered for the management of brain edema in rabies.

### **Public Health Control Measures**

- Post exposure prophylaxis to prevent rabies
- Isolate patient and immunize contacts to prevent infection of others
- Vaccinate local dogs and cats to prevent outbreaks
- Promote public awareness of rabies
- Target immunization campaign for domestic or wild animals in high-risk areas
- Maintain active surveillance of rabies in animals

#### **4.2.4 Zika Virus Disease**

Zika virus is a flavivirus that is transmitted primarily through the bite of an infected mosquito, primarily Aedes aegypti, and also Aedes albopictus, the same mosquitoes that transmit dengue, chikungunya, and yellow fever. Zika virus can also be transmitted in-utero from mother to fetus, and through sexual contact, blood transfusion, and organ transplantation. Zika virus infections are usually asymptomatic. When symptoms occur, they tend to be mild and include mild fever, rash, conjunctivitis, and muscle and joint pain that last for 2 to 7 days. There is no specific treatment but symptoms can be treated with common fever medicines, rest and drinking fluids.

Zika virus infection during pregnancy can result in preterm birth, fetal loss, stillbirth, and congenital malformations including microcephaly, limb contractures, eye abnormalities, brain calcifications, and other manifestations of Congenital Zika Syndrome.

Zika virus is also associated with an increased risk of Guillain-Barré syndrome, and other neurological complications requiring close medical management and possibly intensive care and mechanical ventilation.

### **Case Definition**

**Suspected Case:** Any person presenting with rash and/or fever and at least one of the following signs or symptoms:

- arthralgia; or
- arthritis; or
- conjunctivitis (non-purulent/hyperaemic).

**Probable case:** A suspected case with presence of IgM antibody against Zika virus and an epidemiological link (with no evidence of infection with other flaviviruses).

**Confirmed case:** Any person with laboratory confirmation of recent Zika virus infection presence of Zika virus RNA or antigen in serum or other samples (e.g. saliva, urine, tissue, whole blood); or IgM antibody against Zika virus positive and Plaque Reduction Neutralizing Test (PRNT90) for Zika virus with titre  $\geq 20$  and Zika virus PRNT90 titre ratio  $\geq 4$  compared to other flaviviruses; and exclusion of other flaviviruses.

### **Clinical Diagnostic Criteria:**

- Fever, skin rashes, conjunctivitis,
- Joint pain, malaise, Headache - usually mild and last for 2–7 days.
- Neurological and auto-immune complications of Zika virus disease, babies born with microcephaly (Observed in northeast Brazil).

## **Laboratory Investigations**

- Reverse transcriptase-polymerase chain reaction (RT-PCR) for viral RNA
- Serology for IgM detection
- Plaque reduction neutralization test (PRNT)

## **Non-Pharmacological Treatment:**

The mainstay treatment for Zika Virus is the supportive symptomatic treatment.

- **A:** Assure plenty of rest to patients

## **Pharmacological Treatment**

- **A:** Maintain body fluids Sodium Lactate Compound (Ringers Lactate) intravenously.
- **A:** Control Fever and Pain by giving Acetaminophen or Paracetamol 15mg/kg (PO/IV) 8 hourly for 3 days

### **Note**

- No antibiotics are of proven value.
- Steroids should not be used.
- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as ibuprofen and aspirin should be avoided. These anti-inflammatory drugs act by thinning the blood, and in a disease with risk of hemorrhage, blood thinners may exacerbate the prognosis
- Do not use products containing oil of lemon eucalyptus (OLE) or para-menthane-diol (PMD) on children under 3 years old.
- Do not apply insect repellent to a child's hands, eyes, mouth, cuts, or irritated skin

## **Prevention**

- Vector control: - removal and modification of breeding sites and reducing contact between mosquitoes and people
- Wearing clothing (preferably light-coloured) that covers as much of the body as possible;
- Using physical barriers such as window screens and closed doors and windows;
- Applying insect repellent to skin or clothing that contains DEET, IR3535 or icaridin

## **Public Health Control Measures**

- Strengthen event-based surveillance to detect the emergence of clusters of cases presenting with rash and febrile syndrome of unknown aetiology.
- Actively engage other sectors (e.g., environment, agriculture, tourism) to respond to Zika virus through a multi-sectoral approach (One Health approach).
- Enhance surveillance of Zika virus disease and of the conditions that may be associated with it, including microcephaly and congenital Zika syndrome and Guillain-Barré syndrome (GBS).
- Enhance surveillance at prenatal and postnatal clinics to monitor possible congenital infections and complications.
- Conduct community-based assessments to determine the abundance of vector mosquitoes, identify the most productive larval habitats, promote and implement plans for appropriate vector control.
- Report any identified unusual increase in the incidence of congenital neurological malformations including microcephaly in neonates and adverse pregnancy outcomes not explained through alternate causes, to the relevant public health authorities using IDSR framework.
- Intensify efforts to reduce mosquito populations including elimination of potential breeding sites (e.g., removal of trash and standing water sites around homes, covering home water storage containers, and use of larvicides) and adult mosquito control methods.
- Promotion of personal protection measures such as use of light-coloured protective clothing (long sleeves and pants), insect repellent, and physical barriers such as screens, closed doors and windows, and sleeping under mosquito nets including during the day when Aedes mosquitoes are most active.
- Develop risk communication messages to address population concerns, enhance community engagement, improve reporting, and ensure application of vector control and personal protective measures targeting reduction of contact with the vector.

- Provide women of childbearing age and particularly pregnant women with the necessary information and materials on family planning and to reducing risk of exposure.
- Provide clinical and psychosocial support services for affected children and families.
- Zika can be transmitted through blood and blood products. Precautions already in place for ensuring safe blood donations, transfusions, and prevention of bloodborne pathogens should be followed.
- Zika can be transmitted sexually. Men and women need to get counselling on safer sexual practices, and be offered condoms and full range of contraceptive methods.
- Ensure that pregnant women who have been exposed to Zika virus be counselled and followed for birth outcomes based on the best available information and national practice and policies.
- Refer most severe cases with complication to hospitalized cares.

#### **4.2.5 COVID-19**

Coronavirus Disease 2019 (COVID-19) is a recently discovered disease, caused by a Coronavirus, named SARS-CoV-2, which is genetically related to the virus causing Severe Acute Respiratory Syndrome (SARS) of 2003 and Middle East Respiratory Syndrome (MERS). This virus belongs to the family *Coronaviridae*, of the order *Nidovirales* suspected to originate from an animal host (zoonotic origin) followed by human-to-human transmission. The disease was first detected in Wuhan, the capital city of Hubei, China, in December of 2019 and declared by the WHO to be a Public Health Emergency of International Concern, in 11 March 2020 due to its evident rapid disease spread worldwide in less than 6 months. Most estimates of the incubation period for COVID-19 range from 1-14 days, most commonly around five days.

Current evidence suggests that COVID-19 spreads between people through direct, indirect (through contaminated objects or surfaces), or close contact with infected people via mouth and nose secretions (saliva, respiratory secretions or secretion droplets).

People with the virus in their noses and throats may leave infected droplets on objects and surfaces (called fomites) when they sneeze, cough on, or touch surfaces, such as tables, doorknobs and handrails. Other people may become infected by touching these objects or surfaces, then touching their eyes, noses or mouths before cleaning their hands.

##### **Case definition**

The case definitions are based on the current information available and might be revised as new information accumulates.

**Suspect case:** A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset.

**OR**

A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case (see definition of contact) in the last 14 days prior to symptom onset;

**OR**

A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.

**Probable case:** Any suspect case for whom testing for COVID-19 is inconclusive or is tested positive using a pancoronavirus assay and without laboratory evidence of other respiratory pathogens.

**OR**

A suspect case for whom testing could not be performed for any reason

**OR**

Any suspect case or death with epidemiologic link to confirmed cases or outbreak

**OR**

Any suspect case with typical appearance of COVID-19 in Chest Computed Tomography (CT) or chest x-rays.

**Confirmed case:** An individual (contact or suspect case) with a laboratory-confirmed COVID-19 by real-time reverse-transcription polymerase chain reaction (rRT-PCR).

## **OR**

A suspect case with a strong epidemiological link to COVID-19 patient and detection of antigen using validated/adequate direct SARS-CoV-2 antigen detection tests.

## **OR**

A suspect case with a strong epidemiological link to COVID-19 patient and detection of exposure to virus (Antibodies – IgM and/or IgG, IgA) using validated/adequate serology tests (indirect antibody detection tests).

### **Clinical Diagnosis**

Most common symptoms:

- Fever, Dry Cough and Tiredness

Less common symptoms:

Headache, Sore throat, Loss of taste or smell, Chills, Runny nose, Headache, Chest pain , Muscle aches, Diarrhea,, Conjunctivitis, Skin rash , or Discoloration of fingers or toes

Serious symptoms- Severe Acute Respiratory Infection (SARI):

- Difficulty breathing or shortness of breath
- Chest pain or pressure
- Loss of speech or movement

The risk of serious illness from COVID-19 includes serious heart diseases, such as heart failure, coronary artery disease or cardiomyopathy, Cancer, Chronic obstructive pulmonary disease (COPD), Type 2 diabetes, Type 1 diabetes, Asthma, Liver Disease, Cystic Fibrosis, Severe obesity, Chronic kidney disease, Sickle cell disease, Immunocompromized patients by solid organ transplants, bone marrow transplant, HIV or cancer medications.

### **Laboratory Investigation**

Rule out Community-Acquired Pneumonia (*Streptococcus pneumonia*, *Haemophilus influenza* type b, *Staphylococcus aureaus*, *Klebsiella pneumoniae*, *Legionella pneumophila*, Influenza viruses, and Respiratory Syncytial virus).

Specimen collection, processing, and laboratory testing shall follow biosafety procedures.

- Collect blood cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy.
  - DO NOT delay antimicrobial therapy while waiting for blood culture results.
  - Collect specimens from BOTH the upper respiratory tract (URT; nasopharyngeal and oropharyngeal) AND lower respiratory tract (LRT; expectorated sputum, endotracheal aspirate, or Broncho alveolar lavage) for SARS-CoV-2 testing by RT-PCR.
- Clinicians may elect to collect only LRT samples when these are readily available (for example, in mechanically ventilated patients).
- Use appropriate PPE for specimen collection (droplet and contact precautions for URT specimens; airborne precautions for LRT specimens).
  - When collecting URT samples, use viral swabs (sterile Dacron or Rayon, not cotton) and viral transport media.

#### **Note**

Do not take sample from the nostrils or tonsils

Where feasible both URT and LRT specimens can be tested for other respiratory viruses like Influenza A and B (including zoonotic influenza A), Respiratory syncytial virus, Parainfluenzaviruses, Rhinoviruses, Adenoviruses, Enteroviruses (e.g. EV-D68), Human meta pneumovirus, and Endemic human coronaviruses (i.e. HKU1, OC43, NL63, and 229E).

## **Testing**

- Routine confirmation of cases of COVID-19 is based on detection of unique sequences of virus RNA by Nucleic acid amplification tests (NAAT) such as real-time reverse-transcription polymerase chain reaction (rRT-PCR).
- Serological testing (indirect antibody detection tests) can aid investigation of an ongoing outbreak and retrospective assessment of the attack rate or extent of an outbreak.
- Viral sequencing to providing confirmation of the presence of the virus, regular sequencing of a percentage of specimens from clinical cases can be useful to monitor for viral genome mutations
- Viral culture is not recommended as a routine diagnostic procedure.

## **Severity of Illness Categories**

- Asymptomatic or Pre-Symptomatic Infection: Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test or an antigen test), but who have no symptoms that are consistent with COVID-19.
- Mild Illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- Moderate Illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have saturation of oxygen ( $\text{SpO}_2$ )  $\geq 94\%$  on room air at sea level.
- Severe Illness: Individuals who have  $\text{SpO}_2 < 94\%$  on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ( $\text{PaO}_2 / \text{FiO}_2$ )  $< 300 \text{ mmHg}$ , respiratory frequency  $> 30$  breaths per minute, or lung infiltrates  $> 50\%$ .
- Critical Illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

## **Management**

- All patients with suspected COVID-19 who have severe acute respiratory infection should be triaged and isolated at the first point of contact with the health care system.
- Emergency treatment should be started based on disease severity.
- For those presenting with mild illness, hospitalization may not be required unless there is concern about rapid deterioration. If there is only mild illness, providing care at home may be considered if available.
- Moderate to severe and critical cases must be admitted for management.
- Admitted cases must be monitored for early identification of deterioration and appropriate treatment offered as per national treatment protocol for moderate to severe COVID-19 patients.
- Oxygen is the mainstay of therapy for those whose  $\text{SpO}_2$  drops according the guideline.
- Recovered patients may be discharged if 2 RT-PCR taken at least 24 hours apart are negative with clinical recovery (temperature resolved for more than 48 hours and no need for oxygen therapy).

### **Note**

- All areas for treatment of COVID-19 patients should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, simple face mask, and mask with reservoir bag).
- Use contact precautions when handling contaminated oxygen interfaces of patients with SARS-CoV-2 infection.

## **Early General Supportive Therapy and Monitoring**

Patients with SARI shall be managed in isolated critical care units

- **Give supplemental oxygen therapy** immediately to patients with SARI and respiratory distress, hypoxemia, or shock.
  - Initiate oxygen therapy at 5 L/min and titrate flow rates to reach target  $\text{SpO}_2 \geq 90\%$  in non-pregnant adults and  $\text{SpO}_2 \geq 92-95\%$  in pregnant patients.
  - Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive oxygen therapy during resuscitation to target  $\text{SpO}_2 \geq 94\%$ ; otherwise, the target  $\text{SpO}_2$  is  $\geq 90\%$ .

- **Use conservative fluid management** in patients with SARI when there is no evidence of shock.
- Treat cautiously with intravenous fluids, because aggressive fluid resuscitation may worsen oxygenation, especially in settings limited availability of mechanical ventilation.
- **Give empiric antimicrobials** to treat all likely pathogens causing SARI.
  - Azithromycin 500mg (PO) day 1 following initial assessment, then followed by 500mg (PO) 8 hourly on Days 2-5 when sepsis or superimposed pneumonia is suspected (based on the clinical diagnosis). Give Steroids
- Prednisolone 10mg to 20mg (PO) once a day for 7 days OR Dexamethasone 6mg (PO/IV) once a day for up to 7 days or until hospital discharge based on patient's conditions in ICU / Critical Care Units

#### **Give Supplements**

- Magnesium 300mg or 400mg (PO) once a day for 7 days
- Zinc 7mg (PO) for children aged 1– years of age, increasing up to 25mg (PO) for adults and females of any age who are pregnant or lactating
- Vitamin C dose of 70-150mg 24 hourly for 7 days

#### **Closely monitor the patient's clinical condition 12 hourly**

- Monitor signs of SARI, clinical deterioration, like rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately.

#### **Note**

- Application of timely, effective, and safe supportive therapies is the cornerstone of therapy for patients that develop severe manifestations of SARS-CoV-2 infection
- Do not routinely give systemic corticosteroids for treatment of viral pneumonia. (No survival benefit and possible harms (avascular necrosis, psychosis, diabetes, and delayed viral clearance).
- Corticosteroid should be used with caution in the treatment of COVID-19 patients < 7 days: corticosteroids are not recommended for patients with mild conditions

### **Focused Supportive Management**

#### **Infection Control:**

- For health care workers who are performing aerosol-generating procedures on patients with COVID-19, Using an N95 respirator (or equivalent or higher-level respirator) rather than surgical masks, in addition to other personal protective equipment (i.e., gloves, gown, and eye protection such as a face shield or safety goggles)
- Endotracheal intubation in patients with COVID-19 to be performed by health care providers with extensive airway management experience, if possible
- Intubation be performed using video laryngoscopy, if possible

#### **Hemodynamic Support:**

- Norepinephrine as the first-choice vasopressor
- For adults with COVID-19 and refractory septic shock who are not receiving corticosteroids to treat their COVID-19,  
Low-dose corticosteroid therapy ("shock-reversal") over no corticosteroid therapy

#### **Ventilatory Support:**

- For adults with COVID-19 and acute hypoxic respiratory failure despite conventional oxygen therapy, high-flow nasal cannula (HFNC) oxygen over noninvasive positive pressure ventilation (NIPPV) (BI).
- For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, considering a trial of awake prone positioning to improve oxygenation
  - For mechanically ventilated adults with COVID-19 and acute respiratory distress syndrome (ARDS), use low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight) over higher tidal volumes (VT >8 mL/kg)
  - For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, prone ventilation for 12 to 16 hours per day over no prone ventilation

## **Acute Kidney Injury and Renal Replacement Therapy:**

- For critically ill patients with COVID-19 who have acute kidney injury and who develop indications for renal replacement therapy, provide continuous renal replacement therapy (CRRT), if available. If CRRT is not available or not possible due to limited resources, provide prolonged intermittent renal replacement therapy rather than intermittent hemodialysis

## **Pharmacologic Interventions:**

- For the therapeutic Management of Patients with COVID-19 use of Dexamethasone and Remdesivir, either alone or in combination.
- In patients with COVID-19 and severe or critical illness, there are insufficient data to recommend empiric broad-spectrum antimicrobial therapy in the absence of another indication.

## **Implementation of additional Precautions for suspected SARS-CoV-2 infections**

Contact and Droplet precautions for suspected SARS-CoV-2 infection:

- Place patients in adequately ventilated single rooms. For naturally ventilated general ward rooms this is considered to be 160 L/second/patient;
- Apply Infection prevention and control measures when providing health care where novel coronavirus (SARS-CoV-2) infection is suspected, the Interim Guidance is to:

- Place patient beds at least 1m apart;
- Where possible, cohort HCWs to exclusively care for cases to reduce the risk of spreading transmission due to inadvertent infection control breaches;
- Use of PPE (medical mask, Use eye/facial protection (i.e. goggles or a face shield); Use a clean, non-sterile, long-sleeved fluid resistant gown; Use gloves)
- Use either single use disposable equipment or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers). If equipment needs to be shared among patients, clean and disinfect between each patient use (e.g. ethyl alcohol 70%);
- Refrain from touching eyes, nose or mouth with potentially contaminated hands;
- Avoid the movement and transport of patients out of the room or area unless medically necessary.
- Use designated portable X-ray equipment and/or other important diagnostic equipment.
- If transport is required, use pre-determined transport routes to minimize exposures to staff, other patients and visitors and apply medical mask to patient;
- Maintain a record of all persons entering the patient's room including all staff and visitors.

## **Prevention**

Application of Standard Precautions for all patients and people at risks in the public include hand and respiratory hygiene; use of Personal protective equipment (PPE) depending on risk; in hospitals use safe waste management; environmental cleaning and sterilization of patient-care equipment and linen. Ensure the following respiratory hygiene measures.

- Offer a medical mask (N95) or double cloth mask in health care settings
- Cover nose and mouth during coughing or sneezing with tissue or flexed elbow for others
- Perform hand hygiene after contact with respiratory secretions.

## **Personal Protective Equipment (PPE)**

Rational, correct, and consistent use of available PPE and appropriate hand hygiene helps to reduce the spread of the pathogens. PPE effectiveness depends on adequate and regular supplies, adequate staff training, proper hand hygiene and specifically appropriate human behavior.

Health care workers and Administrators should ensure that environmental cleaning and disinfection procedures are followed consistently and correctly. Thorough cleaning of environmental surfaces with water and detergent and applying commonly used hospital level disinfectants (such as sodium hypochlorite) is an effective and sufficient procedure. Laundry, food service utensils and medical waste should be managed in accordance with safe routine procedures.

## **Public Health Control Measures**

- Establish an alert management system e.g call center with hotlines
- Verify the alerts to determine if they meet the standard case definition for COVID-19
- Respond as for suspected case if they meet the standard case definition
- Record all alerts in an alert/rumor log sheet.
- Provide epidemiological information to conduct risk assessment at the national, regional and global level.
- Conduct epidemiological investigation to identify risk factors for infection and populations at risk for severe disease.
- Maintain strict acute respiratory disease infection control practices throughout the epidemic.
- Mobilize the community for early detection and care and conduct community education about how the disease is transmitted and how to implement IPC at the home care setting and during funerals and burials. Consider social distancing strategies.
- Conduct contact follow-up and active searches for additional community cases or deaths that may not come to the health care setting.
- Distribute laboratory specimen collection kits to health care facilities
- Establish treatment unit to handle additional cases that may come to the health center in line with the national protocols.
- Maintain strict acute respiratory disease infection control precautions and establish an isolation ward to manage additional cases who may present for care.

# CHAPTER FIVE

## MALARIA

### Malaria case definition

A malaria case is a person with malaria infection, confirmed by microscopy or mRDT, regardless of whether fever and other clinical symptoms are present.

### 5.1 Asymptomatic Malaria Case

Asymptomatic malaria case can be found during Active Case Detection (ACD) by health workers in the community and in households. Therefore, all patients with parasitemia are considered “malaria cases”, regardless of whether clinical symptoms are present or not.

### 5.2 Symptomatic Malaria Case

#### 5.2.1 Uncomplicated Malaria

Uncomplicated malaria is defined as symptomatic malaria without signs of severity or evidence (clinical or laboratory) of vital organ dysfunction.

#### Clinical presentation

- Fever
- Headache
- Joint pains
- Malaise
- Vomiting
- Diarrhoea
- Body ache, body weakness
- Poor appetite
- Pallor, enlarged spleen

#### Investigations

The recommended investigations are:

- Quality malaria microscopy or quality malaria Rapid Diagnostic Tests (mRDTs)

#### Note

- It is compulsory to test and confirm all suspected malaria patients. Give antimalarial only to those who test positive.
- In cases where non-response to malaria treatment (treatment failure) is suspected in patients who initially tested positive, microscopy is the recommended laboratory procedure as mRDTs are not recommended because parasite antigens persist up to 4 weeks after parasitaemia has cleared.

#### Non-Pharmacological Treatment

- Continue with feeding and fluid intake
- Followed up immediately if the condition worsens or on the fourth day if symptoms persist.

#### Pharmacological Treatment

Drug of choice for treatment of uncomplicated malaria is:

**A: Artemether+Lumefantrine (FDC) (PO) 20mg+120mg**

#### Common formulations:

- Fixed formulation Artemether 20mg, Lumefantrine120mg; 6, 12, 18 and 24 tablets blister
- Fixed formulation Artemether 80mg, Lumefantrine 480mg; 6 tablets blister

#### Dispersible tablets:

Fixed formulation for children

**A: Artemether 20mg + Lumefantrine120mg; 6 tablets blister (5–14kg): 1 tablet; 15–24 kg: 2 tablets)**

**Table 5.1: Dosage regimen for ALu (artemether 20mg/lumefantrine 120mg)**

		Day 1		Day 2		Day 3	
Kg	Dose	1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	5 <sup>th</sup>	6 <sup>th</sup>
	Hours	0 (*)	8	24	36	48	60
	Age (years)	Tablets	Tablets	tablets	tablets	tablets	Tablets
up to 15	0 to 3	1	1	1	1	1	1

<b>15 up to 25</b>	3 up to 8	2	2	2	2	2	2
<b>25 up to 35</b>	8 up to 12	3	3	3	3	3	3
<b>35 and above</b>	12 and above	4	4	4	4	4	4

(\*) 0 hours means the time of starting medication

**Table 5.2: The recommended dosing schedule for ALu strength 80/480 mg**

<b>Kg</b>	Dose	1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	5 <sup>th</sup>	6 <sup>th</sup>
	Hours	0 (*)	8	24	36	48	60
	Age (years)	tablets	Tablets	Tablets	Tablets	tablets	Tablets
<b>35 and above</b>	12 and above	1	1	1	1	1	1

(\*) 0 hours means the time of starting medication

For practical purposes, a simpler dosage regimen is recommended in order to improve compliance: the first dose should be given as DOT; the second dose should strictly be given after 8 hours; subsequent doses could be given 12 hourly in the second and third day of treatment until completion of 6 doses

The alternative medicines for the treatment of uncomplicated malaria, where there is no response to Artemether-Lumefantrine or it is contraindicated, is Dihydroartemisinin-Piperaquine.

**C:** dihydroartemisinin+piperaquine (FDC) (PO).

Adult formulation containing 40 mg Dihydroartemisinin + 320 mg Piperaquine. Paediatrics formulation contains a fixed combination of 20 mg of Dihydroartemisinin +160 mg Piperaquine.

**Table 5.3: Dose Schedule for Dihydroartemisinin + Piperaquine**

Body Weight (kg)	Daily dose (mg)		Tablet strength	Number of tablets per dose
	Dihydro artemisinin	Piperaquine		
<b>5 to &lt;8</b>	20	160	20mg / 160mg	1 tablet x 3 days
<b>8 to &lt;11</b>	30	240	20mg / 160mg	1 ½ tablet x 3 days
<b>11 to &lt;17</b>	40	320	40mg / 320mg	1 tablet x 3 days
<b>17 to &lt;25</b>	60	480	40mg / 320mg	1 ½ tablet x 3 days
<b>25 to &lt;36</b>	80	640	40mg / 320mg	2 tablets x 3 days
<b>36 - &lt;60</b>	120	960	40mg / 320mg	3 tablets x 3 days

Body Weight (kg)	Daily dose (mg)		Tablet strength	Number of tablets per dose
	Dihydro artemisinin	Piperaquine		
60 to <80	160	1,280	40mg / 320mg	4 tablets x 3 days
>80	200	1,600	40mg / 320mg	5 tablets x 3 days

#### Management of fever

Patients with high fever ( $38.5^{\circ}\text{C}$  and above) should be given an anti-pyretic medicine like paracetamol (**Error! Reference source not found.**) or acetylsalicylic acid every 4 to 6 hours (maximum 4 doses in 24 hours) until symptoms resolve, usually after two days.

#### Note

Children below 12 years should not be given acetylsalicylic acid because of the risk of developing Reye's syndrome.

**Table 5.4: Treatment Schedule for Paracetamol (500mg) Tablets Children 10mg/kg body weight**

Age (years)	Weight (Kg)	Dose
2 months up to 3 yrs	4 up to 14	$\frac{1}{4}$
3 up to 5	14 up to 19	$\frac{1}{2}$
5 up to 12	19 up to 35	1
12 up to 14	35 up to 45	$1\frac{1}{2}$
14 and above	45 and above	2

#### 5.2.2 Severe Malaria

In a patient with *P. falciparum* asexual parasitaemia and no other obvious cause of symptoms the presence of one or more of features listed below classify the patient as suffering from severe malaria.

#### Clinical presentation

- Prostration/extreme weakness
- Impaired consciousness
- Change of behaviour
- Convulsions
- Respiratory distress (due to lactic acidosis and/or pulmonary oedema)
- Jaundice
- Circulatory collapse/shock
- Vomiting everything
- Inability to drink or breast feed
- Bleeding tendency/DIC

#### Investigations

In severe malaria, blood slide (BS) is a recommended malaria test as it quantifies parasitemia. In severe ill patients receiving injectable antimalarial, serial BS investigations monitors level of parasitemia to verify malaria recovery, or if clinical condition is not improving to rule out another serious condition.

- Blood film for malaria parasites
- Blood glucose estimation in patients with altered consciousness
- Haematocrit and/or haemoglobin estimation
- Lumbar puncture to exclude meningitis (if facilities for LP assessment are available)
- Serum creatinine or urea– to assess Kidney function

- Electrolytes— for early detection of acute renal failure
- Full blood cell count and differential white cell count for additional diagnosis of other infectious diseases
- Blood gases, pH and anion gap— to diagnose acidosis
- Radiological investigation: Chest X-ray; look for pulmonary oedema or lobar consolidation
- Blood culture and sensitivity where feasible

### **Non-Pharmacological Treatment**

A rapid assessment must be conducted including airway, breathing, circulation, coma, convulsion, and dehydration status.

**Referral:** If effective management of severe malaria and supportive care for complications is not possible, patients should be given pre-referral treatment and referred immediately to an appropriate facility for continued treatment.

### **Pharmacological Treatment**

#### **A: Parenteral artesunate**

Dosage:

- 2.4 mg/kg in body weight. (IV) or (IM) given on admission (time = 0 hour), then at 12 hours and 24 hours for a minimum of 3 injections in 24 hours regardless of patient's recovery.
- Children weighing less than 20 kg Dosage: 3 mg/kg/dose (or higher). Same schedule as indicated above (0, 12, 24 hours)
- Complete artesunate injection treatment by giving a complete course (3days) of artemether-lumefantrine (ALU) or other ACT.

Consider broad spectrum antibiotic as treatment of septicemia.

Administration and dosage (30 mg, 60mg and 120mg strength): Injectable artesunate has 2-steps dilutions.

- **Step 1:** The powder for injection should be diluted with 1ml of 5% sodium bicarbonate solution (provided in each box) and shaken vigorously 2–3 minutes for better dissolving until the solution becomes clear.
- **Step 2:** For slow intravenous infusion (3–4 minutes), add 5 ml of 5% dextrose or normal saline, to obtain artesunate concentration of 10 mg/ml. For deep intra-muscular injection, add 2 ml of 5% dextrose or normal saline to obtain artesunate concentration of 20 mg/ml.

**Table 5.5: Dilution of Artesunate for Injection**

Route	IV injection			IM injection		
	Strength	30 mg	60 mg	120 mg	30 mg	60 mg
Sodium bicarbonate 5%	0.5	1	2	0.5	1	2
Normal saline or 5% of glucose	2.5	5	10	1	2	4
Total (ml)	3	6	12	1.5	3	6
Artesunate concentration (mg/ml)	10	10	10	20	20	20

**Table 5.6: Dosage Schedule for Artesunate Injection**

Weight	Dose mg/kg	ml per dose strength 60mg		Vials of Artesunate 60mg needed**	
		IV 10 mg/ml	IM* 20 mg/ml		
<5	3.0	1.5	1	1	
5–8	3.0	2	1	1	
9–12	3.0	4	2	1	
13–16	3.0	5	3	1	
17–20	3.0	6	3	1	
21–25	2.4	6	3	1	
26–29	2.4	7	4	2	
30–33	2.4	8	4	2	
34–37	2.4	9	5	2	
38–41	2.4	10	5	2	
42–45	2.4	11	6	2	

46–50	2.4	12	6	2
51–54	2.4	13	7	3
55–58	2.4	14	7	3
59–62	2.4	15	8	3
63–66	2.4	16	8	3
67–70	2.4	17	9	3
71–75	2.4	18	9	3
76–79	2.4	19	10	4
80–83	2.4	20	10	4
84–87	2.4	21	11	4
88–91	2.4	22	11	4
92–95	2.4	23	12	4
96–100	2.4	24	12	4

\*Half the dose is rounded up to 1ml; \*\*Full vial (s) might not be required for a given weight band. The left-over solution must be discarded within 1hr of preparation and must not be reused

If the patient can tolerate oral medication after 24 hours provide a full treatment course of AL. Initiate the first dose of AL 8 hours after the last injection.

#### Alternative

#### C: Injectable Artemether

Injectable Artemether is to be used when Artesunate is contraindicated (in case of allergy, medicine interaction or non- response) and when not available. Artemether should be administered in a dose of 3.2mg/kg loading dose IM stat (0hour) then 1.6mg/kg (24hours and 48hours).

**Table 5.7: Artemether Injectable Dosage by Weight**

Weight	Loading dose		Second and subsequent doses	
	Kg	Mg	Dose	Strength
			3.2 mg/Kg	80 mg/ml
<5	16	0.2	8	0.1
5–8	26	0.3	13	0.2
9–12	38	0.5	19	0.2
13–16	51	0.6	26	0.3
17–20	64	0.8	32	0.4
21–25	80	1.0	40	0.5
26–29	93	1.2	46	0.6
30–33	106	1.3	53	0.7
34–37	118	1.5	59	0.7
38–41	131	1.6	66	0.8
42–45	144	1.8	72	0.9
>45	160	2.0	80	1.0

If the patient can tolerate oral medication after 24 hours provide a full treatment course of ALu. Initiate the first dose of ALu 8hours after the last injection.

#### Management of complications

To reduce the unacceptably high mortality of severe malaria, patients require intensive care. Clinical observations should be made as frequently as possible. Airway maintenance, nurse on side, fanning if hyperpyrexia is present, fluid balance review:

**Coma (cerebral malaria):** maintain airway, nurse on side, and exclude other causes of coma (e.g. hypoglycemia, bacterial meningitis); avoid giving corticosteroids.

**Dehydration:** Correct dehydration

**Hyperpyrexia:** fanning, paracetamol if patient can swallow

**Convulsions:** maintain airways; treat with

Adult

**A:** diazepam (IV) 0.15 mg/ kg (maximum 10 mg) slow bolus IV injection.

Children

**A:** diazepam (rectal) 0.5–1.0 mg/ kg<sup>1</sup>.

If convulsions persist after 10 minutes repeat rectal diazepam treatment as above. Should convulsions continue despite a second dose, give a further dose of rectal diazepam

**OR**

**A:** phenobarbitone (IM/IV) 20 mg/ kg after another 10 minutes.

**Hypoglycemia:** remains a major problem in the management of severe malaria especially in young children and pregnant women. It should be deliberately looked for and treated accordingly. Urgent and repeated blood glucose screening.

In children:

**B:** dextrose 10% (IV) 5 ml/kg

**OR**

**C:** dextrose 25% (IV) 2.5ml/kg as bolus;

If 50% dextrose solution is available, it should be diluted to make 25% by adding an equal volume of water for injection or normal saline.

In adults:

**B:** dextrose 10% (IV) 125ml

**OR**

**C:** dextrose 25% (IV) 50ml as bolus.

Where dextrose is not available, sugar water should be prepared by mixing 20g of sugar (4-level teaspoons) with 200ml of clean water. 50ml of this solution is given ORALLY or by nasogastric tube if unconscious.

**Severe anaemia:** Refer to haematology chapter

**Acute pulmonary oedema:** Refer to respiratory conditions chapter

**Acute renal failure:** Refer to cardiovascular disease condition chapter

**Shock:** Refer to emergency and critical care chapter

## 5.3 Management of Malaria in Special Groups

### 5.3.1 Malaria in Pregnancy (MIP)

The effects of malaria in pregnancy are related to the malaria endemicity, with abortion more common in areas of low endemicity and intrauterine growth retardation more common in areas of high endemicity.

#### 5.3.1.1 Uncomplicated Malaria in Pregnancy

In high-transmission areas (moderate to high immunity); malaria is usually asymptomatic in pregnancy or is associated with only mild, non-specific symptoms. (See section 5.1 above)

#### Pharmacological Treatment

Artemether/Lumefantrine (ALu) is the recommended treatment of choice of a confirmed uncomplicated malaria to pregnant women in all trimesters.

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<sup>1</sup>Draw the IV preparation into a small syringe and remove the needle. Insert 5 cm of a nasogastric tube into the rectum. Inject the diazepam into the nasogastric tube and flush it with 5 ml of water. If a nasogastric tube is not available, use a syringe without a needle. Hold buttocks together for few minutes to ensure retention and absorption of the medicine

### **5.3.1.2 Severe Malaria in Pregnancy**

In low-transmission areas (low malaria immunity); women in the second and third trimesters of pregnancy are more likely to develop severe malaria than other adults, often complicated by pulmonary oedema and hypoglycaemia.

The following are common features of severe malaria during pregnancy:

- High fever
- Hyperparasitemia
- Low blood sugar
- Severe haemolytic anaemia
- Cerebral malaria
- Pulmonary oedema

Pharmacological Treatment Intramuscular/ intravenous Artesunate is the drug of choice for treatment of severe malaria in all trimesters.

### **5.3.1.3 Intermittent Preventive Treatment in Pregnancy (IPTp)**

Malaria parasites can easily accumulate and multiply in the placenta leading to placenta malaria infections, resulting to complications such as maternal anaemia, low birth weight, premature delivery, congenital infection and/or perinatal death.

#### **Note**

IPTp is an administration of antimalarial in full therapeutic doses at predetermined intervals during pregnancy individuals with no signs/symptoms of malaria. The aim is to prevent above mentioned complications with adverse effects to both mother and fetus<sup>3</sup>

#### **The medicine of choice for IPTp**

A: sulphadoxine+pyrimethamine (FDC) (PO) 500mg +25mg

- The dose is 3 tablets once
- A minimum of 3 doses in entire pregnancy period
- The first dose should be administered from 14 weeks of pregnancy onwards
- Each dose should be given at least 4 weeks apart
- The last dose can be administered up to the time of delivery, without safety concerns

#### **Note:**

- SP should not be administered to women receiving cotrimoxazole prophylaxis or pregnant women who are taking folic acid at a daily dose equal or above 5 mg, as it counteracts its efficacy
- SP can be administered safely with combined ferrous sulphate 200mg + folic acid 0.25mg
- If malaria is diagnosed to a scheduled pregnant woman for IPT with SP; SP should not be given, instead a full treatment with antimalarial should be given

### **5.3.2 Management of Malaria in Neonates**

Neonatal malaria is defined as symptoms attributable to malaria with evidence of ring forms of malaria parasite in the blood of an infant within the first twenty-eight days (4 weeks) of life. Congenital malaria is defined as symptoms attributable to malaria with evidence of ring forms of malaria parasite in the blood of an infant within the first seven days (1 week) of life. The signs and symptoms resemble those seen in the new-born with septicemia

#### **Clinical presentation**

- Fever
- Lethargy
- Unable to breastfeed
- Vomiting
- Irritability
- Respiratory distress
- Seizures
- Jaundice
- Pallor
- Hepatosplenomegaly
- Laboratory findings will include the presence of malaria parasites.

## **Investigations**

- Full blood picture
- blood sugar
- blood culture and sensitivity, blood smear for malaria parasite, serum electrolytes
- CSF for analysis

## **Management of neonatal malaria**

- Neonatal malaria should always be considered as severe malaria
- Neonates with suspected malaria should be admitted to hospital immediately as they can deteriorate quickly and die at home
- Parental Artesunate is recommended treatment of choice for neonates. Injectable Artemether can be used as an alternative if Artesunate is not available
- Broad spectrum antibiotic as majority of severe malaria accompanied with septicemia. Refer septicemia treatment section.

## **Nursing care and monitoring**

- Monitor vital signs (PR, RR & Temperature)
- Monitor input/output
- Check BS for malaria parasite daily
- Ensure feeding
- Advise on use of LLINs

### **5.3.3 Management of Malaria in HIV and AIDS Patients**

If malaria is diagnosed, depending on classification of the malaria diagnosis, a full treatment with antimalarial should be given according to the malaria classification.

However, it should be noted that, clearance of parasitaemia may not necessarily be accompanied by clearance of symptoms (fever) due to the presence of other underlying opportunistic infections. HIV and AIDS infected adults with low CD4 cell counts may be more susceptible to treatment failure of anti-malaria drugs.

#### **Note**

- In suspected cerebral malaria in a HIV and AIDS patient, cerebrospinal fluid (CSF) examination to rule out other life-threatening conditions such as bacterial and cryptococcal meningitis

# **CHAPTER SIX**

## **HIVA ND AIDS**

AIDS is defined as Acquired Immuno- Deficiency Syndrome caused by *Human Immunodeficiency Virus* (HIV). Clinical features are usually due to immune system suppression.

### **Clinical presentation**

- Fever, diarrhoea, weight loss, skin rashes, sores, generalized pruritis, altered mental status, persistent severe headache, oral thrush or Kaposi's sarcoma may be found in patients with advanced disease
- Opportunistic infections e.g. tuberculosis, candidiasis or pyogenic infections, Advanced HIV Disease

### **6.1 Treatment of HIV and AIDS in Adults and Adolescents**

- All HIV infected individuals are eligible for ART. Early initiation of combination treatment (ART) is associated with health benefits in terms of reduced morbidity and mortality in all age groups.
- Antiretroviral therapy (ART) has dramatically reduced HIV-associated morbidity and mortality and has transformed the HIV disease into a chronic, manageable condition. In addition, treatment of HIV infected individuals with ART is highly efficient at preventing transmission to sexual partners and mother to child transmission (MTCT).

#### **Evaluation to be done before Initiating ART**

From the moment a patient tests HIV positive, he/she should be linked to the Care and Treatment Clinic (CTC). In health facilities where ART is being initiated at RCH and TB clinics, patients can be managed at those clinics. Mobile outreach clinics can also be used for key and vulnerable population and hard to reach areas.

#### **6.1.1 First-Line Regimens for Adults and Adolescents**

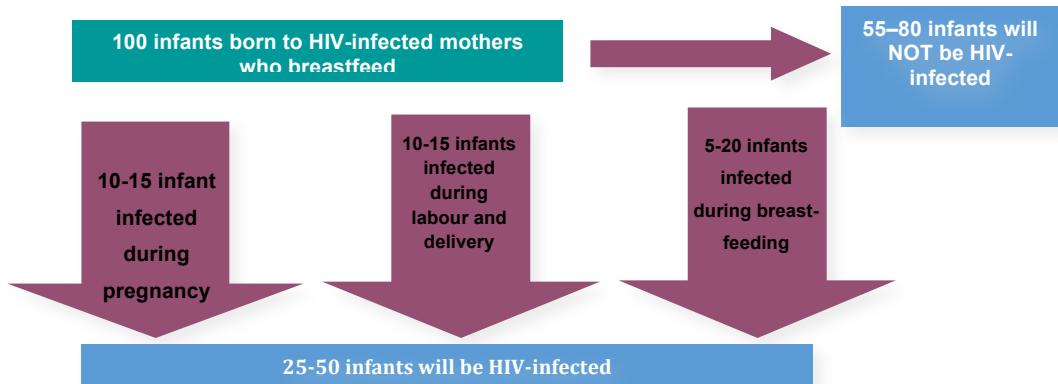
**Table 6.1 Recommended First-Line Regimens for Adults and Adolescents**

Patient group	Preferred (Default) Regimen	Alternative Regimen
Adults and adolescents ( $\geq 15$ years), Pregnant/lactating mothers	A: TDF +3TC +DTG (TLD)	<b>A:</b> ABC + 3TC+ DTG <b>A:</b> TDF + 3TC +EFV (TLE 600 or TLE 400)  <b>Special situations:</b> <b>A:</b> AZT + 3TC + DTG
HIV and TB co-infections	A: TDF + 3TC +DTG (Double dosage of DTG)	<b>A:</b> TDF + 3TC +EFV (TLE600)  <b>A:</b> ABC + 3TC+ DTG (Double dosage of DTG)  <b>Special situations:</b> <b>A:</b> AZT + 3TC + DTG (Double dosage of DTG)
People who Inject Drugs (PWID)	A: TDF + 3TC +DTG	<b>A:</b> ABC + 3TC+ DTG  <b>A:</b> TDF + FTC +ATV/r

#### **6.1.2 ART in Women of Childbearing Potential or Pregnant Women**

Mother-to-child transmission (MTCT) of HIV refers to the transmission of HIV infections from HIV-infected mothers to their infants. MTCT can occur during pregnancy, labour and delivery, and breast-feeding. Without intervention, the overall risk of MTCT is approximately 20%–45%. However, with interventions, this risk can be reduced to less than 5%. Transmission of HIV from mother to her child accounts for over 90% of all HIV infections in children aged below 15 years.

**Figure 6.1 Estimated HIV Outcomes for Infants Born to Mothers Living with HIV**



### 6.1.3 Prevention of Mother to Child Transmission

All HIV infected pregnant women and lactating mothers are eligible for ART regardless of CD4 cell count and clinical stage. The pregnant or breast-feeding women with HIV should be started on lifelong ART at the time of diagnosis.

The recommended first line regimen is once a day fixed dose regimen of TDF + 3TC + DTG. Although TDF+ 3TC + EFV may be an option for use during the pre-conception period through the first eight weeks of pregnancy to avoid potential risk of neural tube defects. Then **TLD** should be continued postpartum

- A women-centered approach is adopted. Women of childbearing potential including those who are using long term effective contraception should be given adequate information to enable making informed decision and choice.
- Women should receive on-going counselling support to continue with HIV care and treatment in order to maintain good health and to reduce the risk of HIV transmission to others.

Available alternative first-line ART regimen includes

**A:**TDF+FTC+EFV600mg (FDC)

**OR**

**A:** ABC+3TC+EFV600 or DTG

**OR**

**A:** AZT+3TC+EFV600 or DTG

#### Prophylaxis for HIV Exposed Infants

- Administer NVP syrup immediately after birth to all HIV exposed infants and continue until six weeks of age
- In case a high risk HIV exposed infant is identified, administer duo prophylaxis containing NVP syrup (once daily) and AZT syrup (twice daily) for the first 6 weeks of life, then continue with daily NVP alone up to 12 weeks of life

*High-risk infants are those who are:*

- Born to women diagnosed to be living with HIV during current pregnancy or breast-feeding period.
- women known to be HIV positive but not yet on ART or
- already on ART but with high viral load ( $\geq 50/\mu\text{L}$  of blood)
- Infant prophylaxis is most effective when given as soon as possible after birth, preferably within 6–12 hours
- HIV exposed infants identified beyond the age of 4 weeks should not be given ARV prophylaxis

**Table 6.2: NVP Dosing Recommendation**

Infant age	NVP daily dosing
Birth to 6 weeks <ul style="list-style-type: none"> <li>▪ Birth weight 2000–2499g</li> <li>▪ Birth weight <math>\geq</math>2500g</li> </ul>	10mg (1 ml) once daily 15mg(1.5ml) once daily

Based on the dosing required to sustain exposure in the infant of >100 ng/mL with the fewest dose changes

Low birth weight infants <2000g should receive mg/kg dosing; suggested starting dose is 2mg/kg once daily.

#### 6.1.4 Second-line ART in Adults and Adolescents

Before treatment failure is confirmed every effort should be made to rule out causes other than drug resistance.

**Table 6.3: Recommended Second-Line Regimens for Adults and Adolescents**

Patient group	Preferred Regimen (Default)	Alternative Regimen
Adults, adolescents ( $\geq$ 15 years) and Pregnant women / breastfeeding mothers	<b>A:</b> AZT+3TC+ATV/r: if TDF was used in first line  <b>A:</b> TDF+FTC+ATV/r: if AZT was used in first line	<b>A:</b> ABC+3TC+ATV/r <b>A:</b> ABC+TC+LPV/r <b>A:</b> TDF+FTC+LPV/r  <b>A:</b> AZT + 3TC + DTG (For patients who did not use DTG in the first line)
HIV and TB co-infection	<b>A:</b> AZT+3TC+LPV/r	<b>A:</b> ABC+3TC+LPV/r <sup>a</sup> <b>A:</b> TDF+FTC+LPV/r <sup>a</sup>  <b>Note:</b> double dosage of LPV/r to 800/200mg for Rifampicin based TB treatment
People Who Inject Drugs (PWID)	<b>A:</b> AZT+3TC + DTG	<b>A:</b> AZT+3TC+ ATV/r <b>A:</b> ABC+3TC +ATV/r

The second line NRTI choice for adults and adolescents depends on the first line regimen. For patients on TDF based regimens in first line, the preferred second line option is AZT plus 3TC combined with a ritonavir-boosted PI, preferably ATV/r because it is dosed once daily and has fewer metabolic complications and side effects. The same NRTIs, with exception of 3TC and FTC used in previous regimens should not be used in subsequent regimens during switching due to treatment failure. LPV/r can be used as an alternative to ATV/r in patients using anti-TB drugs (with ritonavir super boosting) and children below six years. Also, ATV/r (300/100mg) cannot be used in children below 30kg.

For patients who were on AZT and had never used TDF regimen, the default second line option will be TDF or ABC based regimen combined with a boosted PI (TDF+FTC+ATV/r).

For patients who were introduced to TDF in first line due to AZT toxicity, the default second line option is to use ABC plus 3TC combined with a ritonavir-boosted PI ATV/r or LPV/r. (ABC+3TC + LPV/r or ATV/r). However, ABC may be rendered ineffective due to cross resistance with TDF associated resistance mutations.

#### 6.1.5 Third-line Antiretroviral Therapy

Patients failing 2<sup>nd</sup> line regimens may have extensive NRTI and NNRTIs associated resistance mutations (RAMS) which preclude/minimise their use in third-line regimens. Therefore, 3<sup>rd</sup> line

regimens, in order to have at least two or preferably three effective drugs, need to be constructed using other new classes of drugs or second-generation formulations of previous drugs. These second-generation drugs usually have a higher genetic barrier to resistance and their efficacy is not compromised by RAMs associated with the first-generation formulations.

Therefore, this guideline recommends the use of:

- Integrase Strand Transfer Inhibitors (INSTIs) or Integrase Inhibitors Dolutegravir 50mg (DTG) and Raltegravir 400mg (RAL),
- Second generation PIs Darunavir 800mg /Ritonavir 100mg (DRV/r),

**Table 6.4: Recommended Third-Line Regimens for Adults and Adolescents**

Patient group	Preferred Regimen (Default)	Alternative Regimen
Adults, adolescents ( $\geq 15$ years)	S: DTG + DRV/r + AZT/3TC	RAL + DRV/r + AZT/3TC
Pregnant women/breastfeeding mothers	S: (DTG or RAL) + DRV/r + AZT/3TC	DTG + DRV/r (AZT/3TC)
HIV and TB co-infection	S: DTG (BD) + LPV/r + (AZT/3TC or TDF/FTC)	RAL+(AZT/3TC or TDF/FTC) +LPV/r
People Who Inject Drugs (PWID)	S: DTG+DRV/r+ AZT/3TC	DTG+ATV/r+ AZT/3TC

#### Note

- DTG in third line regimen should be given twice daily for clients who were previously exposed to INSTIs.
- For TB and HIV co-infected patients on LPV/r should be switched to DRV/r after completion of TB treatment
- For second- and third-line regimens which are non TDF based, in case of new Hepatitis B co- infection TDF with FTC should be added to the new regimen as treatment of Hepatitis B.

## 6.2 Changing Antiretroviral Therapy

### 6.2.1 Drug Specific Adverse Events-Toxicities

- Intolerable side effects
- Drug interactions

#### Treatment failure

- Clinical failure-occurrence or persistence of HIV related OIs
- Immunological failure
- Virological failure

#### Changing ART due to toxicity

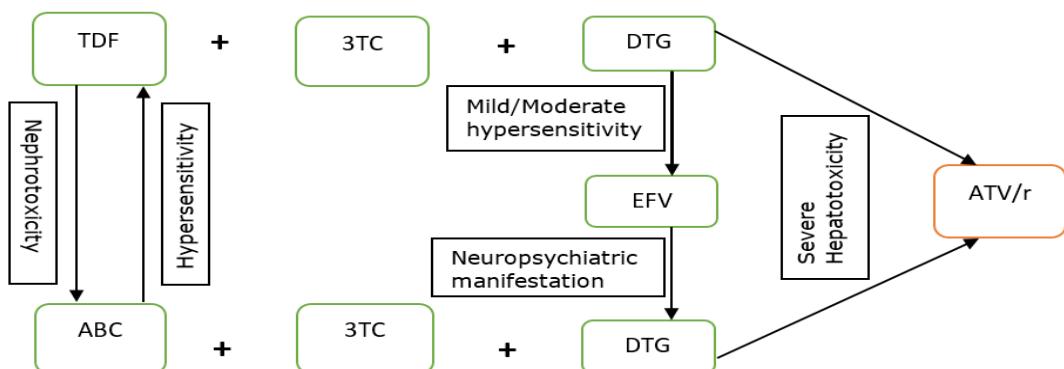
From a clinical perspective, it is generally recommended that when changing a client's regimen due to toxicity, only the toxic drug(s) should be replaced, wherever possible, by a drug without overlapping toxicities. Table 6.5 provides guidance on ARV drug combinations with some common toxicity substitution within first-line regimens.

**Table 6.5: Types of toxicities associated with first and second-line ARV drugs (Refer to National Guidelines for Management of HIV and AIDS 7<sup>th</sup> Edition 2019)**

ARV	Major types of toxicity	Risk factors	Suggested management and substitution
TDF	Tubular renal dysfunction, Fanconi syndrome	Underlying renal disease Older age BMI <18.5 (or body weight <50kg) Untreated diabetes mellitus Untreated hypertension Concomitant use of nephrotoxic drugs or a boosted PI	If TDF is being used in first-line ART, substitute it with AZT or ABC  If TDF is being used in second-line ART (AZT use in first line ART), substitute it with ABC
	Decreases in bone mineral density	History of osteomalacia and pathological fracture Risk factors for osteoporosis or bone loss	
	Lactic acidosis or severe hepatomegaly with steatosis	Prolonged exposure to nucleoside analogues Obesity	
	Exacerbation of hepatitis B (hepatitis flares)	Discontinuation of TDF due to toxicity	No available alternative drug in the country for treatment of hepatitis B e.g. Entecavir
ABC	Hypersensitivity reaction	Genetic predisposition (HLA-B 5701 gene)	If ABC is being used in first-line ART, substitute with TDF or AZT
AZT	Anaemia, neutropaenia, myopathy, lipoatrophy or lipodystrophy	Baseline anaemia or Neutropaenia CD4 cell count ≤200 cells/mm <sup>3</sup>	If AZT is being used in first-line ART, substitute it with TDF or ABC
	Lactic acidosis or severe hepatomegaly with steatosis	BMI >25 (or body weight >75 kg) Prolonged exposure to nucleoside analogues	If AZT is being used in second-line ART, substitute it with ABC
LPV/r	Hepatotoxicity	Underlying hepatic disease HBV and HCV co-infection Concomitant use of hepatotoxic drugs	Replace it with ATV/r
	Pancreatitis	Advanced HIV disease	
	Lipoatrophy or metabolic syndrome dyslipidaemia, severe diarrhea and risk of prematurity	Risk factors unknown	
ATV/r	Indirect hyperbilirubinaemia (clinical jaundice)	Underlying hepatic disease HBV and HCV co infection Concomitant use of hepatotoxic drugs	Indirect hyperbilirunemia is usually transient and ATV/r can be continued, however, if severe jaundice develops and is associated with significantly raised transaminases, then ATV/r should be replaced with LPV/r
	Nephrolithiasis and risk of prematurity	Risk factors unknown	Replace it with LPV/r
EFV	Persistent central nervous system toxicity (such as dizziness, abnormal dreams, depression or mental confusion)	Depression or other mental disorder (previous or at baseline) Taking with high fat meal	Replace it with DTG or NVP. If the person cannot tolerate either INSTI or NNRTI, use boosted PIs
	Hepatotoxicity	Underlying hepatic disease – HBV and HCV co infection	

		Concomitant use of hepatotoxic drug	
	Convulsions	History of seizure	
	Hypersensitivity reaction, Stevens-Johnson syndrome		
	Male gynaecomastia	Risk factors unknown	
NVP	Hepatotoxicity	Underlying hepatic disease HBV and HCV co-infection Concomitant use of hepatotoxic drugs CD4 >250 cells/mm <sup>3</sup> in women CD4 >400 cells/mm <sup>3</sup> for men First month of therapy (if lead-in dose is not used)	EFV. If the person cannot tolerate either NNRTI, use DTG or a boosted PI
	Severe skin rash and hypersensitivity reaction (Stevens-Johnson syndrome)	Risk factors unknown	
DTG	Increase in cholesterol levels; mild elevated liver enzymes; significant rises in creatinine levels; Insomnia and headache may also be experienced.	History of dyslipidemia, diabetes, hypertension	Monitor cholesterol levels; monitor Liver function especially in HBV and HCV. Provide symptomatic treatment
RAL	Increased Cholesterol levels, Glucose, Aspartate Amino Transferase (AST), and Bilirubin. Rash, Cough, Fatigue, dizziness and insomnia	History of dyslipidemia, diabetes, hypertension	In case of severe adverse effects, switch to DTG if patient is >12 years old
DRV/r	Increased Cholesterol levels, triglycerides; Diarrhea, Headache, Rash, Abdominal pain and Nausea	History of dyslipidemia	Monitor severity and occurrence of fever and other symptoms. Provide symptomatic treatment

**Figure 6.2: Substitution within first-line Antiretroviral Regimens**



**Note**

For TB co-infected patients, the dose for DTG should be given twice daily i.e. 50mg

## 6.2.2 Changing ART due to Treatment Failure

**Table 6.6: WHO definitions of treatment failure in chronological order of occurrence: virological, immunological and clinical failure for the decision to switch ART regimens**

Failure	Definition	Comments
Virological	Plasma viral load above 1000 copies/ ml based on two consecutive viral load measurements after 3 months, with adherence support	An individual must be taking ART for at least six months before it can be determined that a regimen has failed.
Immunological	CD4 cell count falls to the baseline (or below) or Persistent CD4 levels below 100 cells/mm <sup>3</sup>	Without concomitant or recent infection or steroid use to cause a transient decline in the CD4 cell count Immunological and clinical characteristics of treatment failure develop much later after virological failure. Immunological and clinical criteria of treatment failure may also misclassify treatment failure and lead to unnecessary ARV switch to subsequent (line of treatment) regimen
Clinical	New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 conditions) after six months of effective treatment.	The condition must be differentiated from IRIS

### Switching to Third-line ARV regimens

It is crucial that before a regimen is declared to have failed, a multidisciplinary switch team is convened to rule out non-adherence which is the commonest cause of reduced CD4 cell count and a VL rise but is often not associated with HIV drug resistance. This team will also plan for enhanced adherence and support, for a period of 3 months before a second VL test. In case of non-adherence, these measures will lower the VL, increase CD4 cell count and avert a switch to a subsequent regimen

Before switching to third-line ARV regimens, genotypic HIV drug resistance is recommended to rule cross resistance between 1<sup>st</sup> and 2<sup>nd</sup> generation drugs and assist in the determination of whether treatment failure is from non-adherence. Genotyping will also inform possibility of recycling drugs used in previous regimens i.e. some drugs used in 1<sup>st</sup> or 2<sup>nd</sup> regimens may still be effective in third-line.

## 6.3 Monitoring Patients on Antiretroviral Therapy

Monitoring of patients on ART is based on clinical and laboratory parameters. Refer table 6.7

**Table 6.7 Clinical and laboratory monitoring of patients on first line drug regimen**

Regimens	Monitoring Tests	Frequency	Rationale
TDF+3TC+DTG ABC+3TC+DTG AZT+3TC+ (EFV or NVP) TDF+FTC+ (EFV or NVP)	HVL (All Clients)	For HVL monitoring, refer to HVL algorithm	ART monitoring
	CD4 (All clients)	Baseline (All) After every six months if CD4 is <350 cells/ml	ART monitoring
	FBP/Hb (All clients) If a client has Hb	Baseline, week 4, thereafter six monthlys	Anaemia monitoring

	<8.5g/dl avoid AZT		
	Serum Creatinine (For patients on TDF)	Baseline, and after every six months and whenever symptomatic	Screening for early renal toxicity
	ALT (For patients on DTG or NVP)	Baseline, one month, after every six months and whenever symptomatic	Liver toxicity
AZT+3TC+ATV/r TDF+FTC+ATV/r ABC+3TC+LPV/r or DTG	Bilirubin (For all clients on ATV/r)	Baseline, 6 months or whenever symptomatic	Indirect hyperbilirubinaemia

**Note**

Clinical evaluation will determine more frequent laboratory tests if required.

**Laboratory monitoring of patients on second line drugs**

The following laboratory tests are recommended for Monitoring of patients on second line drugs:

- FBC, baseline, then monthly for 3 months, then after every 6 months (with CD4 and viral load)
- Fasting cholesterol and triglyceride, baseline, 6 months and thereafter every 12 months
- Liver function tests, (ALT) 6 monthly
- Fasting glucose, every 12 months
- Urinalysis at baseline and after every 3 months
- Serum creatinine at baseline and once a year.

**When changing treatment, the following should be observed:**

- Never change a single drug in the combination if the reason for changing is treatment failure. Change at least two drugs, preferably change all three drugs
- If changing due to toxicity, change only the drug suspected to be causing the problem.
- Never change to monotherapy (i.e. single drug)
- When selecting drugs, choose drugs that have not been used before, drugs which do not have cross-resistance/or no overlapping toxicities or drug-drug interactions.
- Lamivudine has advantage of decreasing viral fitness therefore it may be retained when changing the failing regimen

**6.4 Immune Reconstitution Inflammatory Syndrome (IRIS)**

IRIS is a phenomenon associated with the occurrence or worsening of opportunistic infections/malignancies which can occur early after initiation of ART or at later (several months) during ART. There is an increased risk for occurrence of IRIS in the following situations:

- Treatment naïve patients
- Patients with advanced HIV disease with CD4 cell count < 50 cells/mm<sup>3</sup>
- Patients with undiagnosed and untreated opportunistic conditions
- Patients who have been introduced on ART before or shortly after initiation of treatment of opportunistic infection/malignancy
- In the advent of DTG use, there is increased likelihood for IRIS because of rapid HIV viral load suppression.

**Note**

Any OI, malignancy and autoimmune diseases may present as IRIS

**Diagnostic Criteria:**

The criteria for making a diagnosis of IRIS are delineated below

### **Diagnosis of IRIS would require:**

Both major (A plus B) criteria or criterion A plus 2 minor criteria

#### **Major criteria**

**A.** A typical presentation of “opportunistic infections or tumours” in patients responding to anti-retroviral therapy (ART) includes:

- Localized disease e.g. lymph nodes, liver, spleen
- Exaggerated inflammatory reaction e.g. severe fever, with exclusion of other causes of painful lesions
- Atypical inflammatory response in affected tissues e.g. granulomas, suppuration, necrosis, perivascular lymphocytic inflammatory cell infiltrate
- Progression of organ dysfunction or enlargement of pre-existing lesions after definite, clinical improvement with pathogen specific therapy prior to commencement of ART and exclusion of treatment toxicity and new diagnoses
- Development or enlargement of cerebral space occupying lesions after treatment for cerebral cryptococcus or toxoplasmosis
- Progressive pneumonitis or the development of organizing pneumonia after treatment of pulmonary-TB or PCP
- New onset or worsening of uveitis/vitritis after resolution of CMV retinitis
- Fever and cytopenia after treatment for disseminated *Mycobacterium avium complex* (MAC) disease
- Enlargement of Kaposi's sarcoma lesions and subsequent resolution or partial regression without
- Commencement of radiotherapy, systemic chemotherapy or intralesional therapy

**B.** Decrease in plasma HIV-RNA level by > 1 log base ten copies/ml (1 log drop = 9/10 of Baseline VL copies). This applies in settings where baseline VL is performed.

#### **Minor criteria**

- Increased blood CD4+ cell count after initiation of ART
- Increase in immune response specific to the relevant pathogen e.g. delayed type hypersensitivity to mycobacterial antigens (PPD conversion)
- Spontaneous resolution of disease without specific antimicrobial therapy or tumour chemotherapy with continuation of anti-retroviral therapy.

### **Treatment of IRIS**

Mild to moderate forms:

- Reassure the patient and do not stop ART
- Provide specific treatment for the opportunistic infections/malignancies or other diseases

Severe life-threatening IRIS

- Reassure the patient and Stop ART temporarily
- Provide high doses of prednisolone 1mg/kg for 4 weeks then taper down the dose.
- Provide other appropriate supportive measures such as management of fever, oxygen therapy, i.e. fluids
- Restart ART when the patient stabilizes.

#### **Note**

When using high dose steroids, it is important to rule out *Strongyloides stercoralis* infection to avoid disseminated strongyloidiasis.

## **6.5 Antiretroviral Therapy in Children and Adolescents Living with HIV**

ART in children has been proven to increase survival and decrease HIV-related morbidity and mortality. Children should be started on ART as soon they are diagnosed including those who are presumably diagnosed.

**Table 6.9: When to start ART in Children Under 15 Years**

Age	When you start
Children 0-15 years	Treat all of them regardless of WHO clinical stage or CD4 cell count
Children below 18 months old who qualify for presumptive diagnosis	Start ART while awaiting for DNA-PCR confirmation test results.
Children <18 months of age with a positive DNA/RNA PCR test	Start ART while waiting for the second DNA/RNA PCR test result

**Table 6.10: First-Line ARV Regimens in Infants and Children under 15 years**

Patient group	Preferred 1 <sup>st</sup> Line Regimen	Justification	Alternatives	Comments
Infants and Children weighing <20kg	ABC+3TC+LPV/r	<p>Higher genetic resistance barrier</p> <p>Avoids NNRTI transmitted resistance from mother during PMTCT</p> <p>Potential for malaria prevention</p> <p>Spares AZT for second line</p>	<p>AZT+3TC+LPV/r</p> <p>AZT/3TC+DTG (25mg or 10mg DTG if available)</p>	<p>LPV/r is available in three formulations (syrup, granules and tablets)</p> <ul style="list-style-type: none"> <li>- LPV/r oral solutions for younger infants until they can take granules</li> <li>- LPV/r granules for infants and younger children</li> <li>-LPV/r 100mg/25mg heat stable tablets for children 10kg and above and able to swallow whole tablets</li> </ul>
Children and adolescents weighing ≥20kg	ABC+3TC DTG +	<ul style="list-style-type: none"> <li>-Lowers HIV viral load very fast</li> <li>-Has high genetic barriers to resistance compared to both PIs and NNRTIs</li> <li>-Spares AZT for second line</li> </ul>	ABC+3TC+LPV/r	<p>ABC+3TC Dispensable Tablet 120/60mg plus DTG 50mg</p>
Children and Adolescents weighing ≥30 kg	TDF+3TC+DTG	<p>Higher genetic resistance barrier</p> <p>Avoids NNRTI transmitted resistance from mother during PMTCT</p> <p>Possibility of malaria prevention</p> <p>Spares AZT for second line</p>	<p>ABC+3TC+DTG</p> <p>TDF+3TC+EFV600 or EFV400</p>	TLD Fixed Dose Combination

For TB and HIV co-infected children already on LPV/r-based regimen	ABC+3TC+LPV/r	Continue with ABC+3TC+LPV/r but the dose of LPV/r should be doubled due to the interaction between ritonavir and rifampicin		ABC+3TC+LPV/r in the morning and only LPV/r in the evening
For TB and HIV co-infected children already on DTG based regimen	ABC+3TC+DTG	For children 20-25 kg who get TB/HIV co-infection it is advisable to give them ABC+3TC+EFV for the time of the TB treatment then revert to ABC+3TC+DTG after completion of TB Treatment  For children > 25 kg Continue with ABC+3TC+DTG but the dose of DTG should be doubled due to the interaction between ritonavir and rifampicin		ABC+3TC+DTG in the morning and only DTG in the evening
For TB and HIV co-infected on TLD	TDF+3TC+DTG	For children 20-25 kg who get TB/HIV co-infection it is advisable to give them TDF+3TC+EFV for the time of the TB treatment then revert to TDF+3TC+DTG after completion of TB Treatment  For children > 25 kg Continue with the same regimen, Double dose of DTG		TLD in the morning and only DTG (50mg) in the evening

For dosing of ARV regimens see Annex 6, Paediatric Antiretroviral Dosing

**Note**

Children with weight above 30kg can use TDF as a fixed dose combination with 3TC.

**Special Considerations for LPV/r syrup, granules and tablets**

- The LPV/r liquid requires a cold chain only during storage at the facility
- After dispensing, the liquid is stable at room temperature for 1 month so patients should be given a maximum of 1-month supply
- Patients do not have to refrigerate the LPV/r liquid
- LPV/r granules for infants who can safely swallow LPV/r granules but who are unable to swallow LPV/r tablets whole.

- LPV/r tablet is heat stable but must be swallowed whole and should not be split or crushed as it loses effectiveness

## 6.6. Changing ART in Children Under 15 Years

### I. Drug toxicity

The principles for changing ARVs and the managing drug toxicity in children are like those applied to adults.

### II. Treatment failure

**Virological treatment failure:** Viral load is the most reliable method to detect early treatment failure. Virological treatment failure is recognized if the child is adherent to the current ART regimen, for 6 months or more and has two consecutive viral load measurements over 1000 copies/ml at 3 months apart.

**Immunological treatment failure:** If adherence is good, immunological criteria indicating that a change to second-line therapy is warranted where/when HVL test is not available includes the following:

**Table 6.11: CD4 Criteria Suggesting Immunological Failure<sup>a</sup>**

Immunological failure is recognized as developing or returning to the following age-related immunological thresholds after at least 6 months on ART, in a treatment-adherent child:	
<5 years of age	CD <sub>4</sub> count of <200 cells/mm <sup>3</sup> or CD4 <10%
≥5 years of age	CD <sub>4</sub> count of <100 cells/mm <sup>3</sup>

<sup>a</sup> Preferably, at least two CD4 measurements should be available  
Use of CD4 in children <5 years and absolute CD4 cell counts in those ≥5 years of age is preferred.  
If serial CD4 values are available, the rate of CD4 cell count declines from the peak, CD4 cell count reached should be taken into consideration.

#### Note

CD4 cell percent should not be measured during an inter-current infection but can be determined when the child has recovered.

If there is a modest decline in CD4 cell count or percent (< 5%); and if there is no failure to thrive do not change medication, instead maintain close monitoring.

**Clinical Treatment Failure:** Clinical conditions indicating that a change to second-line therapy is warranted include:

- Poor growth (failure to gain weight, declining or stagnant weight) over a 6-month period, after excluding other causes, such as TB, feeding problems and food insecurity
- No improvement of neuro-developmental milestones
- Development of HIV encephalopathy
- Recurrent infections, such as oral candidiasis, persistent diarrhoea, recurrent severe bacterial pneumonia
- Advancement from one clinical stage to another or new evidence of new WHO stage 3 or 4 disease

#### Note

- Short inter-current episodes of pneumonia, LRTI and gastroenteritis should not be regarded as clinical failure
- Pulmonary or lymph node TB, which are clinical stage 3 conditions, are not indications of treatment failure, and thus may not require consideration of second-line therapy
- The response to TB therapy should be used to evaluate the need for switching therapy
- Before an ARV regimen is thought to be failing based on clinical criteria, the child should have received the regimen for at least 6 months.
- The condition must be differentiated from immune reconstitution inflammatory syndrome.

**Table 6.12: Laboratory parameters for monitoring infants and children under 15 years at baseline, before and during ART**

Laboratory tests for diagnosis and monitoring	Baseline (at entry into care)	At initiation of first-line or second-line ART regimen	Every six months	As required or symptom-directed
HIV diagnostic testing	✓			
Haemoglobin	✓	✓		✓
WBC and differential count	✓			✓
%CD4+ or absolute CD4 cell count	✓		✓ <sup>b</sup>	✓
Pregnancy testing in adolescent girls		✓		✓
Full chemistry (including, but not restricted to, liver enzymes, renal function, glucose, lipids, amylase, lipase and serum electrolytes) <sup>e</sup>		✓	✓ <sub>e</sub>	✓
HIV VL measurement			✓ <sup>d</sup>	✓
OI screening (where possible)	✓	✓	✓	✓
a. HIV re-testing for verification before ART initiation, re-testing is not indicated when switching to 2 <sup>nd</sup> or 3 <sup>rd</sup> line b. For children of <5years continue CD4 monitoring every six months c. CD4 cell count should be taken on emergence of WHO stage 3 or 4 disease d. Viral load monitoring is done annually if the first two VL results 6 <sup>th</sup> month apart are <1000 copies/mL e. Regular monitoring (every six months) of full chemistry, particularly lipid levels, liver enzymes and renal functions, should be considered for infants and children on ART.				

#### **Assessment of Infants and Children receiving ARV Therapy**

Important clinical signs of response to ARV therapy in children include improvement in growth and development and decreased frequency of infections (bacterial infections, oral thrush, and/or other opportunistic infections).

Clinical monitoring of ARV treatment in children should include:

- Feeding practice and nutritional status
- Growth monitoring: weight, height, MUAC (mid-upper arm circumference)
- Head circumference should be monitored in children under 3 years old
- Neurologic symptoms and developmental milestones
- Cotrimoxazole prophylaxis taken daily
- Adjustment of ARV dose based on weight
- WHO disease clinical staging
- Immunization status
- Other medical conditions
- Screening for malaria and TB.

**Table 6.13: Recommended Second-line ARV regimens for children under 15 years**

Patient group	If is on the following first line	Preferred 2L	Comments
Children and adolescents <20kg whose 1 <sup>st</sup> regimen was EFV or NVP based, then transitioned to LPV/r based regimen	ABC/3TC+LPV/r AZT/3TC+LPV/r	Maintain PI AZT/3TC+LPV/r	-Higher genetic resistance barrier -Spare INSTI for third-line
Children and adolescents ≥20kg whose 1 <sup>st</sup> regimen was EFV or NVP based, then transitioned to DTG based regimen	ABC/3TC+DTG AZT/3TC+DTG	AZT/3TC+ATV/r AZT/3TC+DTG ABC/3TC+DTG (for those who cannot tolerate AZT)	Maintain DTG in the 2 <sup>nd</sup> line due to higher genetic barrier than PIs.
Children and adolescents weighing ≥30kg	TDF/3TC/DTG	AZT+3TC+ATV/r ABC+3TC+ATV/r	

**Note**

- Infant and children take longer time to attain adequate viral suppression. Before confirming treatment failure, calculate drop in VL (using 0.5 log two years and above, 0.7log below 2 years- for further details on how to convert VL into numbers).
- ATV/r can be used as an alternative to LPV/r in children above 6 years old if paediatric formulation is available but adolescents >30kg can take adult formulation.

**Third-Line ARV regimens in children under 15 years and adolescents**

Clients failing 2<sup>nd</sup> line regimen have extensive NRTI and NNRTIs associated resistance mutations which minimise their use in third-line regimens. Third-line regimen is constructed using new classes of drugs or second-generation formulations, in order to have at least two or three effective drugs. For examples, Darunavir (DRV) is a second-generation PI without cross resistance to Lopinavir/r used in the previous regimens.

**Criteria for Change to Third line****Failing any 2<sup>nd</sup> line regimen**

- Referral to specialist care is recommended where third line regimen can be chosen according to genotype resistance testing and managed by an expert panel at tertiary care facilities.
- The criteria for diagnosing second-line failure are the same as those used for diagnosing first-line failure.

**Eligibility for Third Line Evaluation:**

All clients should have undergone an Enhanced Adherence Counselling

- Failing 2<sup>nd</sup> line regimens
- Documented virologic failure (VL > 1000) on a PI regimen; except children below 3 years

**Third-line Regimens for Children and Adolescents**

Selection of third-line regimen should consider genotype resistance test results as well as treatment history.

**Table 6.14: Third-line Regimens for Children and Adolescents**

Patient group	3L Options	Justification
Children <20kg	RAL + DRV/r + AZT+3TC	DRV/r -High genetic barrier, Effective for patients with resistance to LPVr and ATVr, cannot be used in children <3 years of age
Children >20kg and above	DTG + DRV/r + AZT+3TC	RAL-Can be used for children <20 kg DTG-Can be used for children ≥20 kg

**Adverse reactions in children and adolescents**

Drug-related adverse reactions while on ART can occur immediately (soon after a drug has been administered), early (within the first days or weeks of treatment) or later (after months of treatment). Adverse reactions can vary in severity from mild to severe to life-threatening and may be specific to the drug or general to the class of drugs in use.

**Table 6.15: Major Types of ARV Toxicity in Children and adolescents**

<b>ABC</b>	ABC is associated with hypersensitivity reactions. Patients may have severe skin rashes or other non-specific symptoms such as fever, arthralgias and lymph node enlargement.
<b>AZT</b>	AZT is associated with risk of haematological toxicity which can include anaemia neutropenia and thrombocytopenia. Measuring haemoglobin is recommended before initiating ART among children with low body weight, low CD4 cell counts and advanced HIV disease. Patients with severe anaemia at baseline (haemoglobin < 7.5 g/dL) should avoid AZT as first line therapy.
<b>TDF</b>	TDF is associated with nephrotoxicity. Nephrotoxicity is more common in elderly patients, but it also occurs in children, especially if co-administered with PI based therapy. Monitoring of creatinine clearance is recommended.
<b>EFV</b>	EFV's main type of toxicity is central nervous system side effects, which typically resolve after few weeks. However, in some cases, they can persist for months or never resolve at all.
<b>NVP</b>	NVP's major toxicities include severe skin rash and hypersensitivity reaction (Steven's Johnson syndrome) and hepatotoxicity. Because of the risk of potentially life-threatening hepatotoxicity associated with NVP, hepatic dysfunction of any aetiology in a child on NVP requires careful consideration of whether NVP should be continued.
<b>LPV/r</b>	LPV/r's major toxicity includes hepatotoxicity, pancreatitis, diarrhoea and lipoatrophy. The risk of hepatotoxicity is increased in patients with underlying hepatic disease and the risk of pancreatitis is increased in patients with advanced HIV disease. Electro-cardiac abnormalities are also possible; patients with pre-existing conduction system disease are at increased risk
<b>ATV/r</b>	Toxicities of ATV/r are like those of LPV/r. ATV/r can cause jaundice (indirect hyperbilirubinemia). Jaundice (indirect hyperbilirubinemia) is usually transient and ATV/r can be continued. If severe jaundice develops and there are significantly raised transaminases, then <del>ATV/r should be replaced with LPV/r</del>
<b>DRV/r</b>	DRV/r's major toxicity is hepatotoxicity. Patients with underlying hepatic disease, hepatitis B or C co-infection or who are taking other hepatotoxic drugs are at higher risk. The other side effect is severe skin and hypersensitivity reactions. Patients with sulphonamide allergy are at higher risk.
<b>RAL</b>	RAL's potential toxicity includes rhabdomyolysis, myopathy and myalgia as well as hepatitis and hepatic failure and severe skin rash and hypersensitivity reactions.
<b>DTG</b>	DTG major toxicity is hepatotoxicity and hypersensitivity reactions. Patients with underlying liver disease or hepatitis B or C co-infection are at higher risk.

**Principles in the management of ARV drug toxicity**

**Severe life-threatening reactions:** Immediately discontinue all ARV drugs, manage the medical event (i.e. provide symptomatic and supportive therapy) and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized

**Severe reactions:** Substitute the offending drug without stopping ART

**Moderate reactions:** Consider continuation of ART if it is feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitution

**Mild reactions:** Reassure a child and caregiver that while the reaction may be bothersome, it does not require a change in therapy; provide counselling and support to mitigate adverse reactions. Emphasize on the maintenance of adherence despite mild and moderate reactions.

**Table 6.16: Suggested ARV Substitutions**

Toxicity events	Responsible ARV	Suggested first-line ARV drug substitution
Acute symptomatic hepatitis	NVP	EFV If the patient cannot tolerate either NNRTI, use boosted PI
Severe or life-threatening rash (Stevens-Johnson syndrome)		boosted PI
Hypersensitivity reaction	ABC	AZT
Lipoatrophy/metabolic syndrome	LPV/r	If LPV/r is used in first line ART for children, use an age appropriate NNRTI (NVP for children below 3 years and EFV for children with 3 years and above)  ATV/r can be used for children above 6 years
Severe anaemia or neutropenia	AZT	Substitute with ABC if < 35 kg
Severe gastrointestinal intolerance		Substitute with TDF if > 35 kg
Persistent and severe central nervous system toxicity	EFV	NVP
Tubular renal dysfunction	TDF	If TDF is being used in first line ART, substitute with AZT or ABC If TDF is being used in second line ART, substitute with ABC

**Note**

Patients on third line ARV regimen who develop toxicities should be referred to next level facility with adequate expertise and facilities

## 6.7 HIV Prevention

### 6.7.1 Post Exposure Prophylaxis (PEP)

Post Exposure Prophylaxis (PEP) is the immediate provision of preventive measures and medication following exposure to potentially infected blood or other bodily fluids in order to minimize the risk of acquiring infection. Several clinical studies have demonstrated that HIV transmission can be reduced by 81% following immediate administration of antiretroviral agents.

Effective post-exposure management entails the following elements:

- Management of exposure site
- Exposure reporting
- Assessment of infection risk
- Appropriate treatment
- Follow-up and counselling.

When an exposure occurs, the circumstances and post exposure management procedure applied should be recorded in the exposed person's confidential form for easy follow up and care.

### Evaluation of the Exposed Individuals

## Evaluation of the Exposed Individuals

Individuals exposed to HIV should be evaluated within two hours and no later than 72 hours. A starter pack should be initiated within 2 hours after exposure and before testing the exposed person. Exposed healthcare workers should be counselled and tested for HIV at baseline in order to establish infection status at the time of exposure. PEP should be discontinued if an exposed healthcare worker refuses to test. Vaccination against Hepatitis B should be considered.

In addition, rape survivors should be:

- Offered counselling, crisis prevention and provision of an on-going psychosocial support to reduce/minimize immediate rape trauma disorder and long-term post-traumatic stress disorder should be offered.
- Referred to mental care, police and legal services, according to the law and regulations.

## Evaluation of the Source Person

Evaluation of the source person should be performed when the exposed individual agrees to take PEP.

- If the HIV, HBV and HCV status of the source person is unknown perform these tests after obtaining consent. The exposed healthcare worker should not be involved in obtaining consent from the source person.
- If the source person is unknown, evaluation will depend on other risk criteria.
- Do not test discarded needles or syringes for viral contamination.

## ARVs used for HIV PEP

Adults

**A:** TDF 300mg+3TC 300mg+DTG 50mg (FDC) (PO) 24hourly for 4weeks

Children (based on body weight)

**A:** AZT+3TC+LPV/r 12hourly for 4weeks

Children whose weight is more than 20kg DTG can be used instead of LPV/r and maintain AZT+3TC as backbone.

### Note

If the source is using PI based regimen, then the PEP regimen should be PI based. (Similar to the source's regimen)

## Follow-up of HIV Exposed individuals

HIV antibody tests should be performed at least after 4–6 weeks' post-exposure (i.e. at 6 & 12 weeks). HIV testing should also be performed for any exposed person who has an illness that is compatible with an acute retroviral syndrome, irrespective of the interval since exposure.

If PEP is administered, the exposed person should be monitored for drug toxicity at baseline and 2 weeks after starting PEP. Minimally, it should include a Full Blood Count (FBC), renal function test (RFT-Serum creatinine and urinalysis) and hepatic function tests (LFT- ALT).

Exposed persons should be re-evaluated within 72 hours, after additional information about the source of exposure including serologic status, viral load, current treatment, any resistance test results (if available) or information about factors that would modify recommendations, is obtained.

PEP should be administered for 4 weeks if tolerated. If not tolerated manage symptoms accordingly and if intolerance persists, change to more tolerable PI based regimen. If the patient seroconverts and the exposed person becomes HIV infected, he/she should be referred to a CTC for proper care and treatment service.

## 6.7.2 Pre-Exposure Prophylaxis (PrEP)

**Pre-Exposure Prophylaxis (PrEP)** is the use of ARV drugs daily by HIV uninfected persons to prevent acquisition of HIV before the person becomes exposed to HIV. PrEP is used by people who are at substantial risk for HIV acquisition to lower their chances of getting HIV infection.

Pre	• Before
Exposure	• Activity that can lead to HIV infection
Prophylaxis	• Prevention

### Eligible clients for PrEP

- Aged 15 years and older
- HIV sero negative
- At substantial risk\* of HIV infection
- No suspicion of acute HIV infection
- Creatinine clearance >60ml/min\*\*
- Willingness to consent for and use PrEP as prescribed

#### \*Substantial risk of HIV infection means:

- Vaginal or anal sex without a condom with more than one partner
- History of a new sexually transmitted infection
- Use of post exposure prophylaxis for sexual exposure
- Has a known HIV positive sexual partner(s) who is not on ART/ on ART less than six months or refuses to report a risk category but still requests PrEP

#### Clients who are not eligible for PrEP include:

- Acute HIV Infection (AHI)
- Client with eGFR\* <60ml/min
- Significantly mobile persons that will not be able to attend visits as prescribed. For example:
  - clients who will not be in a region where PrEP can be provided at the next visit
  - clients who do not have contact information
- Unwilling/unable to take daily medication
- Allergy or contraindication to any medication within PrEP regimen.

#### ARVs used for PrEP

The recommended PrEP regimen in Tanzania is:

A: Emtricitabine 200mg + Tenofovir Disoproxil Fumarate 300mg (PO) 24 hourly.

#### Indications for PrEP discontinuation

Individuals taking PrEP require ongoing risk assessment and PrEP can be discontinued if individuals acquire HIV infection, are no longer at substantial risk for HIV infection or decide to use other effective prevention methods and poor adherence.

Before discontinuation of PrEP, clients should be provided for at least 28 days after the last possible exposure to HIV. The client should return after completing the final prescription for an HIV test to confirm status. Refer the client to other relevant prevention services.

# CHAPTER SEVEN

## TUBERCULOSIS AND LEPROSY

### 7.1 General Management of Tuberculosis

Tuberculosis is chronic airborne infectious disease caused by *Mycobacterium tuberculosis*. It is transmitted from one person to another when a patient is cough, sneezing or singing.

#### Clinical presentation

- Cough of more than two weeks or of any duration in among PLHIV
- Fever
- Excessive night sweats
- Haemoptysis (sputum mixed with blood stains)
- Loss of weight
- Others includes swelling of lymph nodes, ascites, difficulty in breathing, chest pain, swelling of joints etc., depending on the site of the disease

#### Investigations

- Sputum- smears microscopy or sputum for rapid molecular tests like Gene -Expert
- Culture and sensitivity; this is done for diagnosis of drug resistance and surveillance
- Chest X-rays: done to assist clinical diagnosis of TB or in case of triaging presumptive

#### Note.

- Conduct HIV provider-initiated testing and counseling (PITC)for all TB patients
- Conduct Provider Initiated TB screening (PITS) for all health facility outpatients and inpatients

For detailed diagnosis and investigation of TB refer to 'Manual for the Management of Tuberculosis and Leprosy in Tanzania'.

#### Pharmacological Treatment

TB treatment is divided into two phases:

- Initial /intensive phase, which consists of:
- RHZE for 2 months - new and re-treatment cases
- Continuation phase, which consists of:
- RH for 4 months - new and re-treatment cases
- RH for 10 months for severe forms TB such TB meningitis, Miliary TB and TB of the spine

**Table 7.1 Recommended daily doses – regimens of first-line anti-TB drugs for adults and children**

New/Retreatments	Initial Phase	Continuation Phase
New/Retreatments	Rifampicin + Isoniazid + Pyrazinamide and Ethambutol in fixed dose (RHZE) for 2 months	Rifampicin + Isoniazid in fixed dose (RH) for 4 months

**Table 7.2 Daily dosage of anti-TB drugs (FDCs) in new and retreatment adult patients**

Body weight	Number of tablets in initial phase: 2 months (R150/H75/Z400/E275) mg	Number of tablets in continuation phase: 4 months (R150/H75) mg
21–30 kg	2	2
31–50 kg	3	3
51–74 kg	4	4
≥75 kg	5	5

**Table 7.3 Daily dosages of anti-TB Drugs (FDCs) in new and retreatment paediatric patients**

Weight (kg)	Intensive phase * (2 months)		Continuation phase (4 months)
	RHZ (paediatric) 75/50/150 mg	Ethambutol 100mg	RH (paediatric) 75/50 mg
<b>For infants below 2 kg, consult a paediatric specialist, DTLC, and RTLC for treatment advice</b>			
2-2.9kg	½	½	½
3-3.9kg	1	½	1
4-7.9kg	1	1	1
8-11.9kg	2	2	2
12-15.9kg	3	3	3
16-24.9 kg	4	4	4
25 kg+	Go to adult FDCs dosages		

**Note**

- The oral drugs must be swallowed under observation from health facility staff or treatment supporter of his/her choice at home
- The oral drugs should preferably be given on an empty stomach in a fixed dose combination

**7.1.1 Drug Resistance Tuberculosis (DR-TB)**

It is a laboratory diagnosis confirmed after testing *Mycobacterium tuberculosis* strains for resistance using WHO recommended rapid genotypic tests like gene-expert or conventional phenotypic culture and DST.

**Clinical presentation**

The features are the same as susceptible tuberculosis but patient's shows resistance to the first line treatments. Signs and symptoms of DR-TB are like those of drug-susceptible TB (cough, bloody stained sputum, fever, night sweats and weight loss). Patients with the following features have high DR-TB risk (presumptive DR-TB patients)

- History of previous TB treatment
  - Treatment failure after using first-line anti-TB medicines
  - Relapse and return after loss to follow-up, without recent treatment failure
  - Patients who remain sputum smear-positive at month two or later during treatment of TB using first-line anti TB medicines
- Close contact of a known DR-TB case
- Healthcare workers presenting with TB symptoms.
- Vulnerable groups in congregate settings (prisoners, urban poor, miners, PWIDs)

All presumptive DR-TB cases adults and children must receive the Xpert MTB/RIF test as the initial diagnostic test to ensure universal coverage of DST

**Pharmacological Treatment**

When you diagnose RR/MDR TB communicate with DTLC for initiation of treatment.

**Table 7.4 Proposed MDR TB treatment regimens**

Age group	Patient condition	Proposed regimens	
		Intensive phase	If any of the medicines cannot be used, consult the DR-TB consilium to consider replacement if needed using one or more of the following <i>based on DST, prior use and likelihood of efficacy (in order of priority)</i>
Adults and children >12 yrs	MDR/RR-TB susceptible to fluoroquinolone	<b>6</b> Lfx - Bdq - Lzd - Cfz - Cs <b>12</b> Lfx - Cfz - Cs	E, Z, Pto, PAS
	MDR/RR-TB with resistance to fluoroquinolone (pre-XDR) or extensive drug resistance (XDR-TB)	<b>6</b> Bdq - Lzd - Cfz - Cs - Dlm <b>14</b> Lzd - Cfz - Cs	E, Z, Pto, PAS
	Central nervous system disease	<b>6</b> Lfx - Lzd - Cs - Pto - Z <b>14</b> Lfx - Lzd - Cs - Z	INH <sup>HD</sup> (if low-level H resistance - <i>inhA</i> mutation) <sup>1</sup>
	Pregnant RR/MDR-TB	<b>20</b> Lfx - Cs - E - Cfz - Z	<i>Consult consilium on all pregnant cases. Consider strengthening the regimen post-partum with the addition of Bdq and Lzd (for 6 months; to replace Class C medicines if possible).</i>

**Table 7.5: Paediatric treatment regimens for children <12 years with non-severe disease**

Age group	Patient condition	Proposed regimens	
		Intensive phase	If any of the medicines cannot be used, consult the DR-TB consilium to consider replacement if needed using one or more of the following <i>based on DST, prior use and likelihood of efficacy (in order of priority)</i>
Children 6 – 12 yrs	RR/MDR TB susceptible to fluoroquinolone	<b>6</b> Lfx – Bdq – Lzd – Cs <b>3</b> Lfx – Lzd – Cs	Cfz, Dlm <sup>1</sup> (E if documented sensitivity), Z (Cfz preferred over Cs if 50mg capsule available)
	RR/MDR-TB with resistance to fluoroquinolone (pre-XDR) or extensive drug resistance (XDR-TB)	<b>6</b> Bdq - Lzd - Cs - PAS <b>3</b> Lzd - Cs - PAS	Cfz, Dlm <sup>1</sup> (E if documented sensitivity), Z (Cfz preferred over PAS if 50mg capsule available)
3 – 6 yrs	RR/MDR TB susceptible to fluoroquinolone	<b>9</b> Lfx/Mfx - Lzd - Cs - Eto	Cfz, Dlm <sup>1</sup> , PAS (E if documented sensitivity), Z; Eto should not be used if <i>inhA</i> mutation (Cfz preferred over Eto if 50mg capsule available)
	RR/MDR-TB with resistance to fluoroquinolone	<b>6</b> Lzd - Cs - Dlm <sup>1</sup> - Eto <b>3</b> Lzd - Cs - Eto	Cfz, PAS (E if documented sensitivity), Z; Eto should not be used if <i>inhA</i> mutation (Cfz preferred over Eto if 50mg capsule available)
< 3 yrs	RR/MDR-TB susceptible to fluoroquinolone	<b>9</b> Lfx/Mfx - Lzd - Cs - Eto	Cfz, PAS (E if documented sensitivity), Z; Eto should not be used if <i>inhA</i> mutation (Cfz preferred over Eto if 50mg capsule available)
	RR/MDR-TB with resistance to fluoroquinolone	<b>6</b> Lzd - Cs - PAS - Eto <b>3</b> Lzd - Cs - PAS	Cfz, Dlm <sup>1</sup> (E or Z if documented sensitivity) (Cfz preferred over Eto if 50mg capsule available)

**Table 7.6: Modified Short Treatment Regimen**

Age group	Patient condition	Proposed regimens	
		Intensive phase	Continuation phase
15 yrs and above	Patient eligible for short treatment regimen	<b>6</b> Bdq – Lzd – Lfx – Cfz – Cs – Z	<b>3-5</b> Lfx – Cfz – Cs – Z
	Patient eligible for short treatment regimen but cannot tolerate linezolid (Haemoglobin (Hb) < 8 g/dL, neutrophils <0.75 x109/L or platelets <50 x109/L or severe peripheral neuropathy grade ≥2 or optic neuritis grade ≥2 at baseline)	<b>6</b> Bdq – DIm– Lfx – Cfz – Cs – Z	<b>3-5</b> Lfx – Cfz – Cs – Z

### 7.1.2 Treatment of Tuberculosis in Special Cases

#### Treatment of TB/HIV co-infected patients

Consideration is needed when handling a patient with TB/HIV co-infection.

**Table 7.7 Special considerations for ART in TB/HIV co-infected patients**

Start ART for all TB patients living with HIV irrespective of CD4 counts	Treat TB first and start ART as soon as possible, preferably within two weeks of initiating treatment
Already on ART at TB diagnosis	Refer to HIV and AIDS chapter

Also, the following shall be considered in treatment of TB patients:

#### Pregnancy

Anti-TB is safe during pregnancy and breast feeding.

#### TB Prevention;

TPT is offered to:

- Under 5 household contacts of bacteriologically confirmed PTB cases who have no active TB.
- All PLHIV who have no active TB.

#### Dosage

In adult and adolescent

**A:** isoniazid (PO) 300mg 24hourly for 6months to complete one cycle of TPT

In children

**A:** isoniazid (PO) 10mg/kg (10-15 mg/kg) 24hourly for 6months.

#### Note

- TPT should only be given in one cycle in lifetime and no repeat cycle is needed.
- People living with HIV who successfully completed their TB treatment should immediately receive TPT for six months.
- In case of neuropathy due to INH, Pyridoxine should be used for treatment of neuropathy.
- TB Preventive Therapy is not contraindicated in pregnancy and it can be given during any trimester.

**Breast feeding:** In the mothers with pulmonary tuberculosis, the baby should receive INH preventive (5mg/kg) for 6 months followed by BCG vaccination.

**Oral contraceptives:** Rifampicin interacts with oral contraceptives and reduces the efficacy of this contraception.

**Liver disease:** Most of anti-TB medicines can cause liver damage. In case a patient develops jaundice, treatment should be stopped and restarted as soon as the jaundice resolves. In severely ill patients, start moxifloxacin and ethambutol only.

**Renal failure:** Ethambutol is excreted by the kidneys and should either be avoided or given in a reduced dose.

## 7.2 General Treatment of Leprosy

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae*. It mainly affects the skin, the peripheral nerves and the mucous membranes. Leprosy is the commonest cause of peripheral neuritis in the world.

### Clinical presentation

Presence of any one among the three cardinal signs of leprosy below:

- Skin patch with loss of sensation
- One or more enlarged peripheral nerves
- Presence of leprosy bacilli-positive smear

### Classification of Leprosy

#### Multibacillary (MB) Leprosy

- Patients with six or more leprosy skin lesions
- Positive skin smear

#### Paucibacillary (PB) Leprosy

- Patients with one to five leprosy skin lesions
- Negative skin smear

#### Note

- If there is any doubt regarding the classification, the patient should be classified and treated as a multi-bacillary case.

### Pharmacological Treatment

Patients should be treated by multidrug combination therapy; dosage may depend with classification and whether patient is adult or children

**Table 7.8 Treatment of Leprosy**

Classification	Medicine dosage	Duration of treatment
Adult MB: 15years and above	<b>Day 1:</b> Rifampicin 600mg (2x 300mg) +Clofazimine 300mg (3 x 100mg) + Dapsone 100mg. Daily Treatment: Day 2-28, Clofazimine 50mg + Dapsone 100mg	12 blister packs to be taken within a period of between 12–18 months
Child MB: below 15years	<b>Day 1:</b> Rifampicin 450mg (3 x 150mg) + Clofazimine 150mg (3 x 50mg) + Dapsone 50mg. Daily Treatment: Day 2-28 Clofazimine 50mg every other day + Dapsone 50mg daily.	12 blister packs to be taken within a period of between 12–18 months
Adult PB: 15years and above	<b>Day 1:</b> Rifampicin 600mg (2x 300mg) +Clofazimine 300mg (3 x 100mg) + Dapsone 100mg. Daily Treatment: Day 2-28, Clofazimine 50mg + Dapsone 100mg	6 blister packs to be taken within a period of between 6–9 months
Child PB: below 15years	<b>Day 1:</b> Rifampicin 450mg (3 x 150mg) + Clofazimine 150mg (3 x 50mg) + Dapsone 50mg. Daily Treatment: Day 2-28 Clofazimine 50mg every other day + Dapsone 50mg daily.	6 blister packs to be taken within a period of between 6–9 months

### 7.2.1 Treatment of Leprosy in Special Cases

**Tuberculosis:** Patients suffering from both tuberculosis and leprosy require appropriate anti-Tuberculosis therapy in addition to the MDT. Rifampicin must be given in the dose required for the treatment of tuberculosis. Once the intensive phase of anti TB treatment is completed, the patient should continue with his/her monthly rifampicin for leprosy treatment.

**There are two types of reactions**

- Reverse Reaction or type I reaction
- Erythema Nodosum Lepromatous (ENL) or type II reaction (For detail refer Manual for the Management of Tuberculosis and Leprosy in Tanzania)

**Treatment of Reaction:** Depending on severity, treatment of reverse reaction is by giving anti-inflammatory drugs or corticosteroids usually prednisolone for a prolonged period.

**Note**

Health care worker should communicate with DTLC and RTLC when suspect leprosy reaction

# CHAPTER EIGHT

## NERVOUS SYSTEM DISEASE CONDITIONS

### 8.1 Infections of the Nervous System

Infections of the nervous system can arise secondary to bacteria, fungi, protozoa, helminthes or viruses. Clinical features will depend on the site of the nervous system involved.

#### 8.1.1 Bacterial infections

##### 8.1.1.1 Bacterial Meningitis

Bacterial meningitis is a serious infection involving layers (meninges) covering the brain and spinal cord. Causative bacteria differ among different age groups.

##### Clinical presentation

- Headache, high grade fever
- Altered mental status, convulsions, coma.
- Photophobia
- Nausea and vomiting
- Signs of meningeal irritation

##### Investigations

CBC, Blood C/S, Lumbar puncture for CSF analysis

##### Pharmacological Treatment

###### I. Where the organism is not known:

A: benzyl penicillin (IV) 5MU 6hourly for 14days.

AND

B: chloramphenicol (IV) 1000mg 6hourly for 14days

Alternatively

D: ceftriaxone+Subbactam (FDC) (IV) 1.5g 12hourly for 14days

Alternatively

A: ampicillin (IV) 2g 6hourly for 10–14days

AND

S: cefepime (IV) 2g 8hourly for 10–14days

Alternatively, and based on C/S results give

S: meropenem (IV) 2g 8hourly for 10days

###### II. Where the organism is known:

**Meningococcal meningitis** (Refer to notifiable diseases section)

##### Haemophilus influenza meningitis

B: chloramphenicol (IV) 1g 6hourly for 7–10days.

OR

D: ceftriaxone+Subbactam (FDC) (IV) 1.5g 12hourly for 14days

##### Pneumococcal meningitis

A: benzyl penicillin (IV) 5MU 6hourly for 14days

OR

D: ceftriaxone + Salbactam (FDC) (IV) 1.5mg 12hourly for 14days

#### 8.1.1.2 Tuberculous Meningitis

Tuberculous meningitis (TBM) is the most common form of central nervous system tuberculosis, associated with high mortality and morbidity from neurological sequelae.

##### Clinical presentation

- Headache
- Low grade fever
- Altered mental status, coma.
- Seizures
- Nausea and vomiting
- cranial nerve palsies

## **Laboratory investigations**

- CBC
- Blood C/S
- LP for CSF analysis
  - lymphocytic-predominant pleiocytosis usually between 100-500 cells/ $\mu$ L
  - elevated protein levels typically between 100 and 500 mg/dL
  - low glucose-usually less than 45 mg/dL or CSF:Plasma ratio <0.5.
- CSF GeneXpert
- CSF for AFB
- HIV testing

## **Imaging Investigations**

- Contrast head CT scan-can demonstrate multiple ring-enhancing lesions, meningeal and basal cisterns enhancement
- Contrast brain MRI with diffusion weighted sequences (DWI)

## **Pharmacological management**

Refer to TB and leprosy chapter

## **Non-pharmacological management**

- Screen for postinfectious hydrocephalus as it is a common complication of all meningitis cases and can occur early during treatment—monitor for persistent headache, vomiting, papilledema on fundoscopy and parinaud's syndrome.
- Refer all patients presenting with clinical or radiological features of increased ICP from hydrocephalus for neurosurgical evaluation directed at treatment of the associated hydrocephalus by external ventricular drainage (EVD) or VP shunt once CSF is sterile.
- Monitor urine output and serum sodium levels as syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a common complication

### **8.1.1.3 Tetanus**

It is an acute, often fatal disease caused by an exotoxin produced by the anaerobic bacterium *Clostridium tetani*. It is acquired through wounds contaminated with spores of the bacteria and in the case of neonates, through the umbilical stump, resulting in neonatal tetanus.

#### **Clinical presentation**

- Generalized spasms and rigidity of skeletal muscles
- Locked jaws
- Patients are usually fully conscious and aware.
- Dysphagia
- Diaphoresis
- Local spasms may also occur

#### **Non-pharmacological Treatment**

- Admit in **intensive care unit (ICU)**
- Nurse in dark, quiet room to avoid unnecessary external stimuli which can trigger spasms
- Protect the airway (evaluation for early tracheostomy is required)
- Thorough cleaning of the site of entry site (e.g., wound), leaving it exposed without dressing
- Maintenance of fluid balance and nutrition (via NGT)
- Avoid giving medications via IV/IM route as injections can trigger spasms
- Sedation (see below) and care as for unconscious patient

#### **Pharmacological Treatment**

Treatment is generally aimed at the following:

Pain management as the spasms can be very painful

**A:** paracetamol (PO/NGT) 1gm 8 hourly for 5 days

For prevention of further absorption of toxin from the wound

**A:** human tetanus immunoglobulin (IM) Adults give 3000IU stat

**AND**

**A:** amoxicillin (PO/NGT) 500mg 8hourly for 5days

**AND**

**A:** metronidazole (PO/NGT) 400mg 8hourly for 5days

**Control of spasms:** Give a sedative cocktail of the following medications preferably via NGT:

**A:** diazepam (PO/NGT) 10-30mg 4-6hourly for 7-14days

**AND**

**A:** chlorpromazine (PO/NGT) 100–200mg 8hourly for 7-14days

**AND**

**A:** phenobarbitone (PO/NGT) 50–100mg 12hourly for 7-14days

**Table 8.1:Guidelines for Dosage Administration\*\***

Time (Hours)	0	3	4	6	9	12	15	18	21	24
diazepam	*			*		*		*		*
chlorpromazine			*			*			*	
phenobarbitone		*					*			

**Prevention:** tetanus (toxoid) vaccine (IM) 0.5ML; repeat after 4 weeks and after 6-12months, then boost every 10years thereafter.

#### **8.1.1.4 Brain Abscess**

Brain abscess is a focal collection of purulent material within the brain parenchyma, which can arise as a complication of a variety of local cranial or remote systemic infections, trauma, or surgery. The manifestations of brain abscess depend on the site, size, and the immune status of the patient.

#### **Clinical presentation**

- Headache
- Fevers
- Seizures
- Focal neurological deficit
- Altered mental status that may progress to coma

#### **Imaging Investigations**

- Contrast head CT scan--can demonstrate a ring enhancing lesion and possible source of infection e.g., from paranasal sinuses, ear infections
- Contrast brain MRI with diffusion weighted sequences (DWI)
- MR spectroscopy to distinguish from brain tumors where diagnosis is unclear
- CXR
- ECHO in suspected valvular heart disease

#### **Lab Investigations**

- Gram stain, C/S of pus from possible sources
- Purulent aspirate from the abscess for C/S
- Ziehl Neelsen stain

#### **Non-pharmacological Treatment**

- Follow the ABCD protocol
- If unconscious insert NGT for feeding
- insert urethral catheter

#### **Pharmacological Treatment:**

- Control fever and pain with IV Paracetamol
- Manage seizures with antiepileptic drugs
- Prompt initiation of intravenous antibiotics
- Steroids in selected case

**Table 8.2: Pharmacological management of Brain abscess**

Condition	Treatment	Duration
Brain abscess (unspecific bacterial)	<b>A:</b> benzyl penicillin (I.V) 5MU 6hourly <b>OR</b> <b>C:</b> amoxicillin +clavulanate (FDC) (IV) 1.2g 12hourly <b>OR</b> <b>D:</b> ceftriaxone+sulbactam (FDC) (IV) 1.5g 12hourly <b>AND</b> <b>A:</b> metronidazole (IV) 500mg 8 hourly  <b>alternative regimen based on C/S results</b> <b>S:</b> piperacillin+tazobactam (FDC) (IV) 4.5g 8hourly <b>OR</b> <b>S:</b> meropenem (IV) 2g every 8hourly	4-6weeks 4-6 weeks 2weeks 2weeks
Brain abscess ( <i>Staph. aureus</i> )	<b>S:</b> vancomycin (IV) 1g 12hourly (used with cefotaxime or ceftriaxone+Sulbactam)	4-6weeks
Seizures control	<b>C:</b> phenytoin (IV) 15mg/kg loading dose infused at 50mg/min followed by 100mg (IV/PO) 8hourly <b>OR</b> <b>A:</b> carbamazepine (PO/NGT) 200mg 12hourly <b>OR</b> <b>C:</b> sodium valproate (PO) 250mg 12hourly (escalate dose as required based on response)	Until seizure free for at least 6 months
ICP control in selected cases	<b>B:</b> dexamethasone (IV) 0.15mg/kg 6hourly	3-5days

**Note:**

If allergic to penicillin, chloramphenicol 500mg IV every 6hours can be used instead. In case antiepileptic drugs are used for prolonged durations 5mg daily Folic acid supplement should be added for the entire duration of anticonvulsants treatment especially in women of childbearing age.

**Surgical management**

- Refer all patients diagnosed with a brain abscess for neurosurgical evaluation.
- Surgical options include stereotactic abscess aspiration and craniotomy for abscess excision. In cases where the source of infection is paranasal sinuses or ear infection, involve concomitant ENT surgeon evaluation for primary source control interventions.

**8.1.2 Fungal Infections****Cryptococcus Meningitis (CM)**

CM is the most common form of fungal meningitis worldwide. It often develops in patients who are immune compromised e.g., HIV-positive patients with low CD4 cell count, diabetic mellitus and iatrogenic immunosuppression, as in post organ transplant patients.

**Clinical features**

- Headache, fever, intolerance to light and sound,
- Neck stiffness, vomiting, seizures, deafness, impaired vision
- In advanced stages it may present with confusion,
- Altered mental status that may progress to coma.

**Investigations**

- CSF gram stain
- CSF India Ink stain test
- Serum or CSF Cryptococcus antigen (CrAg) test
- CSF cultures
- Contrast brain MRI

- may demonstrate cryptococcomas
- assist to rule out differential diagnoses

### **Pharmacological Treatment**

The treatment should be done in 3 phases:

#### **Phase 1: Induction phase**

**S:** amphotericin B (IV) 0.7-1mg/kg/day

**AND**

**S:** 5 flucytosine (PO)100mg/kg/day for 7days followed by 1 week of

**AND**

**A:** fluconazole (PO): Adult 1200mg/day,

Children/adolescents 2mg/kg/day, up to a maximum dose of 800mg daily

In the absence of flucytosine, alternative therapy should be:

**S:** amphotericin B (IV) if available give 3-6mg/kg for 10days

**AND**

**A:** fluconazole (PO) 1200mg once daily for 14days

**OR**

**C:** fluconazole (IV) 1200mg once daily for 14days

#### **Phase 2: Consolidation phase**

**A:** fluconazole (PO) 800mg/day for 8weeks or until CSF is sterile.

#### **Phase 3: Maintenance phase**

**A:** fluconazole (PO) 200mg 24hourly for 1year

Discontinue maintenance treatment if CD4  $\geq$ 100 with undetectable (<50 copies), viral load or CD4  $\geq$  200 if viral load monitoring not available.

#### **Note**

- It is recommended to initiate ART 5 weeks after initiation of Cryptococcal meningitis treatment in ART naïve patient to prevent IRIS and reduce mortality.
- Monitor creatinine, BUN, serum Potassium and magnesium in all patients on Amphotericin B every 24hours.

### **Non-pharmacological Treatment**

- Refer to section on bacterial meningitis in unconscious patients.
- Perform serial Lumbar puncture for management of increased ICP in cryptococcal meningitis. Opening pressure should be measured during LP and therapeutic CSF drainage done (20-30ml per session) for pressures  $>25\text{cm H}_2\text{O}$ .
- Failure to control ICP after several LPs (recommended 3 attempts) should prompt neurosurgical evaluation for ventriculoperitoneal shunt insertion to divert CSF.

#### **Note**

The usage of Mannitol, Hypertonic saline, acetazolamide, or corticosteroids to manage increased ICP in Cryptococcal meningitis is ineffective and **NOT recommended**.

### **8.1.3 Protozoa infections**

#### **Toxoplasmosis**

Immunocompetent persons with primary infection are usually asymptomatic, but latent infection can persist for the life of the host. In immunosuppressed patients, especially patients with AIDS, the parasite can reactivate and cause disease, usually when the CD4 lymphocyte count falls below 100 cells/mm<sup>3</sup>.

#### **Clinical presentation**

- Altered mental status
- Focal neurological deficits
- Seizures
- Neuropsychiatric manifestations

### **Imaging Investigations**

- Contrast head CT scan-demonstrates ring-enhancing lesions
- Contrast brain MRI with diffusion weighted sequences (DWI)
- CXR

### **Laboratory                  Investigations**

Toxoplasma serology (IgM)

### **Non-pharmacological Treatment**

Similar to bacterial meningitis

### **Pharmacological Treatment For**

acute infection give:

**D:**sulfadiazine (PO) 1g 6hourly for 6weeks

**AND**

**D:** pyrimethamine (PO) 100mg loading dose then 50mg /day for 6weeks

**AND**

**S:** folinic acid (PO) 10mg /day for 6weeks.

After six weeks of treatment give **maintenance treatment** with

**D:** sulfadiazine (PO) 500mg 6hourly

**AND**

**D:** pyrimethamine (PO) 25-50mg /day

**AND**

**S:** folinic acid (PO) 10mg /day until CD4 counts is above 200cells/microlitre and/or undetectable viral load for 3-6months

For those allergic to sulphur replace Sulfadiazine with

**S:** clindamycin (PO) 450mg 6hourly for 6weeks.

### **8.1.4 Helminthic infections**

#### **Neurocysticercosis (NCC)**

NCC is a neurologic infection caused by the larval stage of the tapeworm *Taenia solium*. In the developing world NCC is the most common cause of new onset acquired epilepsy among the adult population. Humans are the definitive hosts for this parasite, and swine are the intermediate hosts. The mature tapeworm develops in humans after they ingest live cysticercus in undercooked pork. NCC develops when humans accidentally ingest eggs from fecal contaminated food.

#### **Clinical presentation**

- Headache
- Seizures
- Focal neurological deficit
- Features of increased intracranial pressure

#### **Imaging Investigations**

- Contrast head CT scan-can demonstrate ring enhancing lesions, calcified lesions
- Contrast brain MRI can demonstrate viable cystic lesions with scolices

#### **Laboratory Investigations**

- FBP, serum electrolytes
- Enzyme-linked immunotransfer blot (EITB)
- Liver function tests

#### **Non-pharmacological Treatment**

- If unconscious, airway and breathing management
- Insert NGT for feeding
- Insert urethral catheter

## Pharmacological Treatment

**Table 8.3: Pharmacological Management of NCC**

Condition	Treatment	Duration
Antihelminthic treatment for single viable lesion	<b>A:</b> albendazole (PO) 15mg/kg/day divided into two daily doses (maximum of 1200mg/day)	2-4weeks
Anthelminthic treatment for multiple viable lesions	<b>A:</b> albendazole (PO) 15mg/kg/day divided in two daily doses (maximum of 1200mg/day) <b>AND</b> <b>A:</b> praziquantel (PO) (50mg/kg/day)	2-4weeks 2weeks
Seizures control	<b>C:</b> phenytoin (IV) 15mg/kg loading dose infused at 50mg/min followed by 100mg (IV/PO) 8hourly <b>OR</b> <b>A:</b> carbamazepine (PO) 200mg 12hourly (can be adjusted based on individual response) <b>OR</b> <b>C:</b> sodium valproate (PO) 250mg 12hourly (escalate dose as required based on response)	Until seizure free for at least 6 months
Control of increased ICP	<b>D:</b> dexamethasone (PO) 0.15mg/kg 6 hourly for 3-5days then taper down. <b>OR</b> <b>B:</b> dexamethasone (IV) 0.15mg/kg 6 hourly for 3-5days then taper down	2weeks

### Note

Fundoscopic examination is **mandatory** for all patients before initiation of anthelminthic therapy.

### Surgical management

- Refer all patients diagnosed with CNS cysticercosis associated with clinical or radiological features of increased intracranial pressure from hydrocephalus for neurosurgical evaluation directed at management of the associated hydrocephalus.
- In patients with untreated hydrocephalus or diffuse cerebral edema, **management of elevated intracranial pressure should proceed anthelminthic treatment.**

### 8.1.5 Viral infections

Viral infections of the nervous system are mainly caused by *Herpes simplex* virus (HSV) and Human immunodeficiency virus (HIV). (Refer to section on viral infections and HIV)

#### Herpes simplex encephalitis

Most of cases in adults are caused by HSV-1, a small number are caused by HSV-2 usually in immunosuppressed states or in neonates. It should be suspected in all patients not responding to antibiotics/other treatments.

#### Clinical presentation

- Early features are fever, headache & altered consciousness which may develop gradually over days or rapidly over hours
- The most common manifestations are personality change, dysphasia, behavioural disturbance, and occasional psychotic features
- Focal or generalized seizures

#### Investigations

- Lumbar puncture--CSF is under increased pressure and may appear normal or show a mild-moderate lymphocytosis, a mild-moderate elevated protein levels and normal or decreased glucose.
- CSF PCR
- HSV1+HSV2 CSF Rapid test
- MRI—demonstrate predominant involvement of the limbic system structures, medial temporal lobes, and insular cortex

## **Pharmacological Treatment**

**B:** acyclovir (IV/PO) 10–15mg/kg 8hourly for 14–21days

## **Non pharmacological treatment**

Provide supportive therapy as for unconscious patients

## **8.2 Initial Management of Stroke**

### **8.2.1 Management of Acute Hemorrhagic Stroke**

Spontaneous, nontraumatic intracerebral hemorrhage (ICH) remains a significant cause of morbidity and mortality throughout the world. However, population-based studies indicate that most ICHs in most patients are survivable with good medical care thus emphasizing the importance of improved clinical care. in determining ICH outcome.

#### **Clinical presentation**

- Severe headache, vomiting,
- Focal neurological deficits
- decreased level of consciousness that may progress to coma
- symptom progression over minutes or hour

#### **Investigations**

- Rapid neuroimaging: plain CT to distinguish ischemic stroke from ICH
- MRI with angiography-useful to evaluate for underlying structural lesions e.g., vascular malformations and tumors in suspicious cases

Admit all patients with ICH in an ICUor **dedicated stroke unit** for initial management and monitoring.

#### **Pharmacological Treatment**

For elevated SBP (150-220mmHg), initiate BP lowering treatment, target at 140mmHg. Consider more aggressive reduction if SBP>220mmHg.

**C:** labetalol (IV) at 1mg/min until target SBP is attained.

Anticoagulation-related ICH: withhold anticoagulants and correct INR, if elevated, start on vitamin K and consider FFP transfusion

**B:** phytonadione (vitamin K) (IV) 1mg slow infusion over 60 minutes

If increased ICP based on clinic radiological features, give

**C:** mannitol (IV bolus) 0.25-1gm/kg 4-6hourly for 24-72hours

**OR**

**C:** hypertonic saline 3% (IV bolus) at 3-5ml/kg 4-6hourly for 24-72hours

Monitor serum osmolarity and renal function when giving Mannitol or Hypertonic saline, stop if osmolarity goes >320mOsm/L

Treat fever with antipyretic medications and/or external cooling methods

**D:** paracetamol (IV) 1g 8hourly for 3-5days then when required

Perform regular monitoring and control of blood glucose to prevent both hyperglycemia and hypoglycemia.

Treat clinical or electrographic seizures associated with decreased loss of consciousness

**S:** levetiracetam (PO/IV) 500mg 12hourly for 2weeks

**C:** phenytoin (IV) 15mg/kg loading dose over 30min, then maintenance at 100mg 8hourly for 2weeks.

#### **Non-pharmacological Treatment**

- Apply compressive stockings or intermittent pneumatic compression at admission to prevent VTE
- LMWH can be started later after cessation of bleeding in immobile patients.
- Consider systemic anticoagulation or IVC filter only in patients with **symptomatic** deep vein thrombosis or Pulmonary embolism.

## Surgical management

- Consider neurosurgical evaluation for **External Ventricular drainage (EVD)** in patients with decreased level of consciousness from resultant hydrocephalus in the setting of intraventricular hemorrhage.
- Refer for **surgical evacuation of hematoma** as soon as possible in patients with **cerebellar hemorrhage** who are deteriorating neurologically or who have brainstem compression and/or hydrocephalus from ventricular obstruction
- For **supratentorial hematomas**, consider evacuation in deteriorating patients with or without decompressive craniectomy as a life-saving measure in selected cases, based on expert neurosurgical clinical judgement.
- Consider minimally invasive clot evacuation via stereotactic or endoscopic aspiration with or without thrombolytic usage, based on expert clinical judgement and available resources.

## 8.2.2 Initial Management of Acute Subarachnoid Hemorrhage from Ruptured Cerebral Aneurysm

Subarachnoid haemorrhage (SAH) refers to presence of blood in the fluid-filled subarachnoid spaces around the brain and spinal cord. The most common presentation is sudden onset of severe novel headache. SAH from ruptured cerebral aneurysms is associated with high mortality and morbidity hence clinician's high index of suspicion and proper initial management is crucial for patient's survival and improved functional outcome.

### Clinical presentation

- Severe headache (worst headache of life)
- Altered mental status that may progress to coma
- Focal neurological deficits
- Seizures

### Laboratory Investigations

- CBC, PT/PTT/INR
- Serial ABGs, electrolytes
- serum and urine osmolality

### Imaging investigations

- CT angiography
- Four vessel catheter angiography/digital subtraction angiography (DSA)
  - Perform 4-vessel catheter angiography to determine source of bleeding
  - The timing of study takes into consideration the patient's condition (unstable or premorbid patients are **not candidates**), the feasibility of early treatment, the likelihood of endovascular therapy (based on patient's age and predicted aneurysm location as well as availability of required resources and expertise)
- CXR—monitor for pulmonary edema if in hyperdynamic therapy

### Principles of initial management of aneurysmal SAH

- Initial hemodynamic stabilization and life support of the patient
  - Prevention of rebleeding through timely coiling or surgical clipping
  - Prevention, identification, and early management of hydrocephalus
  - Prevention and management of delayed ischemic neurologic deficit (DIND) from vasospasm

### Admitting orders

- Admit all aneurysmal SAH patients to **ICU** regardless of their initial GCS score
- Document initial **Hunt & Hess**, **WFNS** clinical scores, and **Fisher CT scan** score
- Bedrest with head of bed elevation at 30°.
- Initiate SAH precautions (low level of external stimulation, restricted visitation, dim light, no loud noises)
- Check neurological status every 1 hour.
- Bed pan, indwelling Foley catheter if patient is lethargic, incontinent with strict Inputs & outputs measurements.
- Keep Nil per Oral (if in preparation for surgery or endovascular intervention)

- Maintain SBP 120–160mmHg in unsecured (unclipped/uncoiled) aneurysm to minimise rebleeding risk, consider
  - D:** labetalol (IV) 1mg/min until target SBP is attained.
- IV fluids: 0.9% NS + 20 mEq KCl/L at 2 ml/kg/hour maintenance fluid

**Prophylactic anticonvulsants:**

**S:** levetiracetam (PO/IV) 500mg 12 hourly while aneurysm is unsecured, continue for 1week post clipping/endovascular intervention

**OR**

**C:** phenytoin (IV) 15mg/kg loading dose at 50mg/min rate then 100mg 8hourly for 2-4 weeks

**Sedation (not over sedation):**

**D:** propofol (IV) (for intubated patients) at 25-75mcg/kg/minute

**Give**

**B:** dexamethasone (IV) 4mg 6 hourly for 3-5days to reduce neck pain

**AND**

**S:** fentanyl (IV) 25–100mcg (0.5–2 ml) every 1–2hours when required in ICU.

**Stool softener: Initiate**

**C:** lactulose (PO) 30mls 8hourly until aneurysm is secured.

**Anti-emetics:**

**D:** ondansetron (IV) 4mg over 2–5minutes, may repeat 8hourly for 1–2days.

**Prevention of vasospasm: Initiate**

**S:** nimodipine (PO/NGT) 60mg 4hourly, continue for 21days

**Stress ulcer prophylaxis:**

**C:** pantoprazole (IV) 40mg 24hourly for 1-2weeks

**Oxygenation goals (for intubated ventilated patients)**

- o PO<sub>2</sub> > 100mm Hg, O<sub>2</sub> saturation 100% in patients at risk for vasospasm, aim for 92% saturation in all others.
- o To achieve above goals, increase FiO<sub>2</sub> and mean airway pressure (PEEP) in ventilated patients
- o in non-intubated patient: Give O<sub>2</sub> 2L per nasal cannula PRN (based on ABG)

- Strive for normocarbia, avoid prophylactic hyperventilation
- Avoid arterial hyperoxia (paO<sub>2</sub> > 300mm Hg)- to avoid risk of vasoconstriction
- maintain normothermia and encourage other cooling measures to reduce and prevent fever.
  - D:** paracetamol (IV) 1g 8hourly for 3-5days then when required
- Hemoglobin and hematocrit: Transfuse whole or PRBC when Hct drops < 40%)
- Monitor serum glucose and maintain normoglycemia

**Surgical management**

Refer to a centre that can handle neurovascular cases for prompt neurosurgical evaluation and subsequent surgical clipping or endovascular intervention (coiling or embolization) to secure the ruptured cerebral aneurysm.

### 8.2.3 Initial management of Acute Ischemic Stroke

Acute ischemic stroke (AIS) is a leading cause of adult disability in the developed world. In AIS, a thrombus impairs cerebral blood flow, resulting in brain tissue infarction. Collateral blood flow gives rise to an area of hypoperfused tissue (ischemic penumbra) that is at risk of infarction if hypoperfusion persists. Prompt reopening of an occluded blood vessel to re-establish blood flow to the ischemic area (reperfusion) in eligible patients, can rescue the ischemic penumbra from death and spare the patient from serious long term disabilities.

## Clinical presentation

- Severe headache
- Focal neurological deficits
- decreased level of consciousness that may progress to coma
- seizures
- symptom progression over minutes or hours

## Investigations

- FBP, PT/PTT/INR,
- Random blood glucose
- serial ABGs, serum electrolytes
- Non contrast CT scan to distinguish AIS from ICH
- DWI for selected patients. (contraindicated with cardiac pacemakers, metal implants)
- Four-vessel catheter angiography
- Baseline ECG and ECHO
- CT angiogram in potential candidates for reperfusion
- CT/MR perfusion studies
- MR angiography (MRA) with

## Prehospital and lower level health facilities

- Provide initial airway management and hemodynamic stabilization
- Exclude stroke mimics like hypoglycemia
- International stroke guidelines recommend rapid identification of all fibrinolytic-eligible and mechanical thrombectomy-eligible patients to facilitate initiation of treatment in the fastest achievable onset-to-treatment time
- Consider prompt referral to a centre that can handle stroke patients including rapid neuroimaging and administration of reperfusion therapy.

## Referral hospital and specialized centres

- Provide initial stabilization of the patient as per ABCDE protocol
- Perform rapid careful neurological examination.
- Order emergency brain imaging evaluation before initiating any stroke specific treatments.
- Screen for reperfusion eligible patients and initiate appropriate treatment protocol.
- In patients with AIS who awake with stroke symptoms or have unclear time of onset > 4.5 hours from last-known-well (LKW) state, perform brain MRI to identify diffusion-positive, FLAIR-negative lesions to aid selecting those who can benefit from IV alteplase administration.
- In potential candidates for mechanical thrombectomy, consider imaging of the extracranial carotid and vertebral arteries, in addition to the intracranial circulation, to provide useful information on patient eligibility and endovascular procedural planning.

## Reperfusion criteria: all must be met

- Onset of stroke or Last known well (LKW) state **<4.5hours**
- No increased bleeding risk contraindications
- Blood pressure controlled to <185/105mmHg target.
- Non contrast brain CT has excluded intracranial hemorrhage and/or established a hypodense zone or hyperdense vessel sign.

## Non-pharmacological Treatment

- Oxygenation—support airway, maintain O<sub>2</sub> saturation >94%
- Monitor BP, if elevated, initiate BP lowering treatment to target BP<185/110 mmHg
- For patients who are non-eligible for fibrinolysis aim to lower BP by 15% in the first 24 hours
- Monitor body temperature and initiate treatment when >38°C
- In immobile stroke patients without contraindications, offer compressive stockings, or pneumatic compression devices for DVT prophylaxis.
- Start on enteral diet (PO/NGT) within 7days of admission after AIS.

## **Pharmacological treatment**

**A:** acetylsalicylic acid (PO) 325mg 24hourly for 4weeks

**AND**

**C:** labetalol (IV) 10-20mg infusion 1-2min, repeated until target BP is attained.

**AND**

**D:** paracetamol (IV) 1g 8hourly for 3-5days then when required.

### **Note**

For those treated with alteplase, acetylsalicylic acid administration should be delayed until 24 hours later

For seizure control

**C:** phenytoin (IV) 15mg/kg loading dose over 30min, then 100mg 8hourly for 4weeks.

**OR**

**S:** levetiracetam (PO/IV) 500mg 12hourly for 2-4 weeks

- Initiate statins in eligible patients and continue statins in patients already taking statins at the time of onset of AIS.

### **Reperfusion treatment:**

In patients qualified for intravenous thrombolysis, benefit of therapy is time dependent, and treatment should be initiated as quickly as possible.

Admit the patient to an **ICU** or designated **stroke unit** for monitoring and initiate,

**S:** alteplase (IV) 0.9mg/kg maximum dose 90mg (given over 60minutes with initial 10% of dose given as bolus over 1 minute)

### **Important precautions:**

- Be prepared to treat potential emergent adverse effects, including bleeding complications and angioedema in patients undergoing fibrinolytic therapy.
- Maintain BP at <180/105mmHg for at least 24 hours following Alteplase infusion.
- Obtain a follow-up CT or MRI scan at 24 h after IV alteplase before starting anticoagulants or antiplatelet agents.
- **For management of intracranial hemorrhage complication within 24 hours following thrombolysis:**
  - Stop alteplase, obtain an emergent non contrast head CT.
  - Obtain hematology and neurosurgery consultations
  - Provide supportive care and initiate

**C:** tranexamic acid (IV) 1g infused over 10 minutes.

**AND**

**D:** cryoprecipitate (includes factor VIII): 10 U infused over 10–30 min

- **In case of angioedema following Alteplase infusion, stop alteplase and provide airway support as required.** Give

**D:** methylprednisolone (IV) 125mg

**AND**

**A:** chlorpheniramine (IV) 10mg stat

If there is further increase in angioedema, administer

**A:** adrenaline (S/C) (0.1%) 0.3 mL or by nebulizer 0.5 mL stat

## **Non-pharmacological Treatment**

### **Mechanical thrombectomy**

- Consider for selected patients who present between **6 and 16 hours** of LKW with an **anterior-circulation large-vessel occlusion** (ICA or proximal MCA) and meet other specified eligibility criteria based on expert assessment, clinical judgement, and availability of required resources.

## **Surgical management of AIS**

- Consider **decompressive craniectomy** in patients ≤60 years of age who deteriorate neurologically within 48 hours from brain swelling associated with unilateral MCA infarctions despite appropriate medical therapy.
- Consider **external ventricular drainage (EVD)** in the treatment of obstructive hydrocephalus following cerebellar infarction.
- Emergency carotid end arterectomy (CEA) in the acute stage is not well established hence **not recommended** in initial management of AIS.

## **8.3 Management of Epilepsy**

Epilepsy is a common neurological disorder characterised by recurring seizures. About two-thirds of people with active epilepsy have their epilepsy controlled satisfactorily with anti-epileptic drugs (AEDs). Other treatment approaches may include surgery and neuromodulation. Optimal management is required to improve patient's health outcomes and minimise detrimental impacts on social, educational, and occupational activities.

### **Clinical presentation**

Recurrent seizures

### **Investigations**

- Serum electrolytes
- Serum antiepileptic drug levels
- Electroencephalogram (EEG)
- Brain CT scan
- Brain MRI with epilepsy protocol

### **Classification of epileptic syndromes**

Classify epileptic seizures and epilepsy syndromes in all patients using a multi-axial diagnostic scheme (refer to ILAE classification) as failure to classify the epilepsy syndrome correctly can lead to inappropriate treatment and persistence of seizures.

### **Pharmacological management**

- Utilize a single AED (monotherapy) and increase dose until seizures are controlled or side effects cannot be tolerated.
- If the initial treatment is unsuccessful, initiate alternative monotherapy with different drugs before resorting to drug combinations.
- Combination therapy (adjunctive or 'add-on' therapy) should only be considered when attempts at monotherapy with AEDs have not resulted in seizure freedom.
- If trials of combination therapy do not bring about worthwhile benefits, revert treatment to the initial monotherapy regimen that has proved most acceptable to the patient and consider referral for expert evaluation.

For management of status epilepticus—refer to **emergency and critical care chapter**

#### **I. Focal seizures**

First Line:

**A:** carbamazepine (PO) 10-20mg/kg 12hourly for 4weeks

**OR**

**S:** lamotrigine (PO) 1-5mg/kg 12hourly for 4weeks

Second line:

**S:** levetiracetam (PO) 10mg/kg 12hourly for 4weeks

Add-on treatment: gabapentin or sodium valproate as adjunctive treatment if first-line treatments are ineffective or not tolerated.

#### **II. Generalised tonic-clonic (GTC) seizures**

**C:** sodium valproate (PO) 10-15mg/kg 12hourly for 4weeks

**OR**

**S:** lamotrigine (PO) 1-5mg/kg 12hourly for 4weeks

Add on treatment: offer levetiracetam as adjunctive treatment if first-line treatments are ineffective or not tolerated.

### **III. Absence seizures**

First Line:

**C:** sodium valproate (PO) 10-15mg/kg 12hourly for 4weeks

Second line: consider levetiracetam

**Note**

**DO NOT** offer carbamazepine, phenytoin or pregabalin for absence seizures.

### **IV. Myoclonic seizures**

First Line:

**C:** sodium valproate (PO) 10-15mg/kg 12hourly for 4weeks

Second line:

**S:** levetiracetam (PO) 10mg/kg 12hourly for 4weeks

### **V. Lenox Gastaut syndrome (LGS)**

First Line:

**C:** sodium valproate(PO) 10-15mg/kg 12hourly for 4weeks

Second line:

**S:** lamotrigine (PO) 1-5mg/kg 12hourly as adjunctive treatment

**Note**

**DO NOT** offer carbamazepine or pregabalin.

### **VI. Idiopathic generalised epilepsy (IGE)**

First Line:

**C:** sodium valproate (PO) 10-15mg/kg 12hourly for 4weeks

Second line:

**S:** lamotrigine (PO) 1-5mg/kg 12hourly for 4weeks

### **VII. Juvenile Myoclonic epilepsy (JME)**

First line:

**C:** sodium valproate (PO) 10-15mg/kg 12hourly for 4weeks

Second line:

**S:** lamotrigine (PO) 1-5mg/kg 12hourly for 4weeks

**OR**

**S:** levetiracetam (PO) 10mg/kg 12hourly for 4weeks

### **VIII. Childhood absence epilepsy**

First Line:

**C:** sodium valproate (PO) 10-15mg/kg 12hourly for 4weeks

Second line:

**S:** lamotrigine (PO) 1-5mg/kg 12hourly for 4weeks

**Add-on treatment:** consider clonazepam, levetiracetam if first-line treatments are ineffective or not tolerated.

### **Management of epilepsy in pregnancy**

The use of antiepileptic drugs (AEDs) is associated with increased baseline risk of fetal malformations during pregnancy. Prescribe Folic acid to all women of childbearing age and girls on AEDs preconception. Attempt to decrease pharmacological treatment to monotherapy and utilize the lowest possible effective dose of drugs that have shown minimal risk of maternal and fetal neural tube defects

**S:** lamotrigine (PO) 1-5mg/kg 12hourly for 4weeks

**OR**

**S:** levetiracetam (PO) 10mg/kg 12hourly for 4weeks

**AND**

**A:** folic acid (PO) 5mg 24hourly for 3-6months

In women who have not had a seizure for at least 2years, attempt complete withdrawal of AEDs.

### **Non-pharmacological Treatment**

- Consider ketogenic diet—based on specialist assessment and expert opinion
- Refer all medically refractory seizures for expert neurosurgical evaluation for epilepsy surgeries
- Consider evaluation for Vagus Nerve Stimulation (**VNS**) as an adjunctive treatment in reducing the frequency of seizures in adults who are refractory to AEDs but who are not suitable for resective surgery

## **8.4. Parkinson's Disease**

Parkinson's disease (PD) is a common chronic, progressive, neurodegenerative disorder in geriatric population, characterized by the loss of dopaminergic neurons from the substantia nigra that subsequently results in the loss of control of voluntary movement over time.

### **Clinical presentation**

**Motor symptoms:** Tremors, rigidity, akinesia or bradykinesia, postural instability

**Non motor symptoms:** drooling, dementia, depression, orthostatic hypotension

Diagnosis is clinical based on United Kingdom Parkinson's Disease Society Brain Bank (UKPDSBB) criteria

### **Pharmacological management of motor symptoms**

First line:

**D:** levodopa+carbidopa (FDC) (PO) 100/25mg 8 hourly (escalate dose based on individual response) for 4 weeks

Give adjunctive treatment for motor symptoms: MAO-B or COMT inhibitors in persistent motor symptoms despite adequate tolerable doses of Levodopa+carbidopa FDC treatment.

**S:** selegiline (PO) 2.5-5mg 24hourly (maximum dose 10mg/day)

### **Pharmacological management of non-motor symptoms**

**Drooling:**

**S:** glycopyrrolate (PO) 0.5-1mg 8hourly for 2weeks

**Orthostatic hypotension:** consider Levodopa dose reduction and give

**S:** fludrocortisone (PO) 0.1mg 24hourly for 2 weeks

**Depression:** Individualize therapy, consider

**S:** fluoxetine (PO) 20mg 24hourly (maximum 60mg/day) for 4weeks

**OR**

**A:** amitriptyline (PO) 50mg 24hourly for 4-12 weeks

**Impulse control disorders:** Consider modification of dopaminergic drug dosages.

### **Non-pharmacological management**

- Provide physiotherapy, occupational, speech and language therapies
- Refer for expert neurosurgical evaluation for **Deep Brain Stimulation (DBS)** in patients with advanced Parkinson's disease whose symptoms are not adequately controlled by best medical therapy.

## **8.5 Congenital Pediatric Nervous System Diseases**

### **8.5.1 Pediatric Hydrocephalus**

Pediatric hydrocephalus (HDC) is a common surgically correctable neurological problem in children with estimated incidence of 1 in every 500 children. HDC can result from various congenital and acquired causes including aqueductal stenosis, Chiari malformations, intraventricular hemorrhage, trauma, tumors, and infection. There are effective surgical interventions that can preserve and improve quality of life in patients with HDC.

### **Clinical presentation**

- Abnormal increase in head size

- Delayed/regressed developmental milestones
- Headache and impaired vision
- Seizure

### **Investigations**

- Cranial Ultrasound
- Non contrast head CT scan
- MRI brain scan

### **Pharmacological management**

Management of associated seizures:

**A:** phenobarbital (PO) 5mg/kg 12hourly for 4weeks

**OR**

**C:** sodium valproate (PO) 10-15mg/kg 12hourly for 4weeks

### **Non pharmacological management**

- Both CSF shunts and endoscopic third ventriculostomy (ETV) are options in the treatment of pediatric hydrocephalus. Refer for expert neurosurgical evaluation.
- Consider **Endoscopic third ventriculostomy** with choroid plexus coagulation (ETV+CPC) as first line option in cases with clear obstruction to CSF flow.
- Consider insertion of ventriculoperitoneal shunt (VP shunt) where ETV+CPC is not available, has failed or is contraindicated. Other alternative CSF shunts include ventriculoatrial (VA) or ventriculopleural shunts.
- Prescribe preoperative antibiotics to prevent shunt infection in patients undergoing shunt surgery.

### **Pharmacological management**

**D:** ceftriaxone+sublactam (FDC) (IV) 100mg/kg stat during anesthesia induction

## **8.5.2 Management of Pediatric CSF Shunt Infections**

### **Clinical presentation**

- CSF leak, purulence, skin erosion,
- Fever, meningismus, erythema,
- exposed or protruding hardware

### **Lab investigations**

- FBP, CRP
- CSF analysis, C/S
- Blood C/S

### **Pharmacological management**

Initiate empirical antibiotic treatment

**C:** amoxicillin +clavulanate (FDC) (IV) 12hourly for 2weeks

**OR**

**D:** ceftriaxone+sublactam (FDC) (IV) 100mg/kg 12hourly for 2weeks

**AND**

**B:** metronidazole (IV) 7.5mg/kg/day 8hourly for 2weeks

### **Alternative regimen based on C/S results**

**S:** piperacillin+tazobactam (FDC) (IV) 300mg/kg/day (of piperacillin component) divided in 4doses per day

**OR**

**S:** meropenem (IV )10mg/kg 8 hourly, (may increase up to 40mg/kg) for 10-14days

Shift to organism's specific regimen after CSF/hardware culture results

For confirmed *Staph spp.* infections add

**S:** vancomycin (IV) 10mg/kg 6hourly for 2weeks or more.

### **Non-pharmacological management**

- Consider partial (externalization) or complete infected shunt hardware removal.

- Insert External ventricular drain (**EVD**) as interim measure for intracranial pressure monitoring and therapeutic diversion of CSF in the setting where an infected internal shunt device has been removed.

### **8.5.3 Congenital Spina Bifida**

Spina Bifida (SB) is one of the commonest complex congenital birth defects in developing countries. Children with SB are faced with multiple medical and psychosocial issues that require a comprehensive multidisciplinary care plan.

#### **Clinical presentation**

- Swelling on the back
- CSF leak
- Lower limb weakness
- Lower limb deformities

#### **Investigations**

##### **Prenatal diagnosis**

- Ultrasound in second trimester of pregnancy
- Amniotic fluid analysis

##### **Postnatal diagnosis**

- Cranial Ultrasound—evaluate for associated hydrocephalus
- Neuraxial MRI—is indicated in complex cases to plan surgical management and evaluate for associated defects—Hydrocephalus, chiari malformations, tethered cord
- Preoperative screening echocardiogram (ECHO)

#### **Pharmacological Treatment**

Initiate antibiotics in children with open infected spinal bifida lesions

**B:** ceftriaxone (IV) 100mg/kg 12hourly for 2 weeks

**OR**

**B:** amoxicillin +clavulanate (FDC) (PO) 15mg/kg 8hourly for 2weeks

**OR**

**C:** amoxicillin +clavulanate (FDC) (IV)15mg/kg 8hourly for 2weeks

**AND**

**A:** metronidazole (PO) 7.5mg/kg/day 8hourly for 2weeks

**OR**

**B:** metronidazole (IV) 7.5mg/kg/day 8hourly for 2weeks

#### **Non-pharmacological Treatment**

##### **Surgical management of SB**

- Refer for expert neurosurgical evaluation for surgical closure of the spinal defect and subsequent evaluation for the need to treat associated hydrocephalus with **CSF shunts** or **ETV+CPC**.

#### **Supportive and preventive and measures**

- Provide routine screenings and testing for specific secondary conditions (HDC, skeletal limb deformities, UTIs) to minimize medical complication rates and help control cost of care.
  - Provide lower limb orthoses (splints, calipers)
  - Provide wheelchair for ambulation
- Track and counsel women about recurrence risk and prescribe 5mg of folic acid beginning at least one month (preferably 3 months) before another conception and continue through the first 3 months of pregnancy.

### **8.6 Cranial Nerve Disorders**

#### **8.6.1 Trigeminal Neuralgia**

Trigeminal neuralgia (TN) is a syndrome characterized by chronic paroxysmal brief episodes of unilateral electric shock-like pains, in one or more divisions of the trigeminal nerve. TN is often mistaken as a dental problem leading to delayed correct diagnosis and appropriate treatment. The diagnosis is based on the characteristic clinical picture.

## Clinical presentation

Unilateral jaw pain exacerbated by cutaneous stimuli,  
e.g., chewing, brushing

## Investigations

- CT scan to exclude structural brain pathologies
- MRI to assess the trigeminal nerve root entry zone (REZ)

## Pharmacological Treatment

First line treatment:

**A:** carbamazepine (PO) 200mg 12hourly for 4-12weeks

## Non-pharmacological management

Refer to neurosurgeon for procedures that involve controlled trigeminal ganglion ablation to alleviate pain

- Radiofrequency ablation
- Gasserian ganglion balloon compression rhizotomy
- Glycerol rhizolysis
- Stereotactic radiosurgery rhizotomy

## Surgical management

Refer all patient with poor response to conservative management for expert neurosurgical evaluation for microvascular decompression (MVD), a surgical procedure undertaken to identify, isolate and separate a vascular loop abutting the trigeminal nerve at the root entry zone (REZ).

## 8.6.2 Bell's Palsy

Bell's palsy, also referred to as idiopathic facial nerve palsy is unilateral paralysis of all the muscles of facial expression of suspected viral etiology. Inflammation and edema of the facial nerve likely play a role in pathogenesis. Reactivation of herpes simplex virus (HSV) is also thought to play an etiologic role. Most patients recover within a few weeks or months.

## Clinical presentation

- Unilateral facial paralysis (sudden onset)
- Inability to close the eye
- Drooping at the affected corner of the mouth
- Decreased tearing
- Hyperacusis

## Investigations

- HIV testing
- RBG
- otoscopic exam

## Pharmacological management

**A:** prednisolone (PO) 60mg 24hourly for 5 days, then taper down to 50mg 24hourly for next 5days.

**AND**

**B:** acyclovir (PO/IV)800mg 4-8hourly for 7-14days.

## Non-pharmacological management

- Provide facial muscle massage and exercises
- Provide eye patch for ocular protection during sleep.
- Refer for ophthalmological evaluation in severe cases

## 8.7 Spinal Cord and Peripheral Nerve Disorders

### 8.7.1 Acute Transverse Myelitis (TM)

Acute onset, usually postinfectious, rapidly progressive neurologic syndrome caused by focal inflammation of the spinal cord. Thoracic spinal cord level is the most commonly involved.

## Clinical presentation

- Rapid progressive bilateral lower limb weakness
- Backache and neuropathic pain
- Numbness and paresthesia
- Bladder and bowel incontinence

## **Investigations**

- FBP, serum electrolytes
- CSF analysis
- Emergency MRI or CT/myelogram to rule out a compressive lesion.
- Brain MRI—may be required to exclude multiple sclerosis

Perform baseline severity score such as American Spinal Injury Association (ASIA) impairment score to assist in clinical management decisions and monitor improvement.

## **Pharmacological management**

Give high-dose steroids

**D:** methylprednisolone (IV) 500-1000mg/day for 3–5days

Consider cyclophosphamide in refractory cases (under the direction of an oncologist)

**S:** cyclophosphamide (IV) 800-1000mg/m<sup>2</sup> pulse dose.

## **Long term management**

Manage generalized pain with

**A:** diclofenac (IM) 75mg 12hourly for 3–5days

**OR**

**B:** tramadol (PO) 50mg 8hourly for 7-14days.

Manage neuropathic pain with

**D:** pregabalin (PO) 75mg 12hourly (maximum dose 300mg) for 2-4weeks

Manage spasticity with

**S:** baclofen (PO) 10mg 8hourly, (maximum dose 120mg/day) for 2weeks

**OR**

**S:** tizanidine (PO) 2mg 8hourly, (maximum dose 36mg/day) for 2weeks

## **Non-pharmacological management**

- Monitor respiratory function, support ventilation where required
- Catheterize bladder and offer stool softeners to aid bowel emptying
- Provide manual position changes 2hourly to avoid pressure sores
- Provide rehabilitation--exercises to assist ambulation
- Offer assisted ambulation devices—e.g., high back wheelchairs

## **8.7.2 Guillan Barre Syndrome**

Guillain–Barré syndrome (GBS) is potentially fatal, immune-mediated acute-onset ascending sensorimotor neuropathy usually triggered by infections. Timely recognition, diagnosis, and prompt referral to a centre equipped to provide ventilatory support is essential to improve mortality and minimize long term morbidity.

### **Clinical presentation**

- Rapid ascending bilateral lower limb weakness
- Little or no sensory deficits
- Evolving respiratory distress
- Cardiac arrhythmias
- Facial or bulbar palsy

### **Investigations**

- FBP, serum electrolytes
- CSF analysis-albuminocytologic dissociation ( $\uparrow$  protein without pleocytosis)
- Emergency MRI to exclude acute spina cord inflammation or compression

## **Pharmacological management**

Admit to **ICU** and provide ventilatory support to all patients with evolving respiratory distress or severe autonomic cardiovascular dysfunction

**S:** human immunoglobulin G (IV) 0.4g/kg 24hourly for 5days (started within 2weeks of disease onset)

For severe cases, consider

**S:** plasma exchange 200-250ml plasma/kg body weight for 5sessions (started within 4weeks of disease onset)

Monitor respiratory function-patient is deemed at risk of respiratory failure if the vital capacity is <20ml/kg, the maximum inspiratory pressure is <30cmH<sub>2</sub>O or the maximum expiratory pressure is <40cmH<sub>2</sub>O

### Non-pharmacological management

- Provide rehabilitation-exercises to assist ambulation
- Assisted ambulation devices—e.g., high back wheelchairs

### 8.7.3 Peripheral Neuropathy

Peripheral neuropathies encompass disorders of peripheral nerve cells and fibers which manifest secondary to a wide range of pathologies that can affect motor, sensory, and autonomic fibers. Peripheral neuropathies can be classified as mononeuropathies, multifocal neuropathies, and poly-neuropathies. Further sub classifications categorize peripheral neuropathies as axonal, demyelinating, or mixed types, which is essential for treatment and management purposes.

#### Clinical presentation

- Numbness and paresthesia,
- Neuropathic pain
- Extremities weakness,
- Loss of coordination
- Orthostatic hypotension
- Cold, pale feet

#### Investigations

- FBP
- Renal function tests
- RBG and HbA1c (Diabetes is a common cause of neuropathy)
- Testing for vitamin and mineral deficiencies such as copper, thiamine, pyridoxine, folate, B12.
- Infectious workup for HIV, and
- Thyroid function testing
- Anti-body testing for specific autoimmune diseases known to cause peripheral neuropathies such SLE and rheumatoid arthritis
- Nerve conduction studies (NCS) and needle electromyography (EMG) to differentiate axonal from demyelinating neuropathies
- MRI or CT scans in suspected nerve compression
- Urine Test for Bence-Jones proteins
- Genetic testing (for inherited neuropathies)
- Nerve biopsy in selected cases where expertise and resources are available

**Table 8.5 Guide to clinical diagnosis of peripheral neuropathies**

Type	Clinical features	Common causes
Distal Symmetric Polyneuropathy	-Length-dependent: diffuse involvement -affects distal segments first -Symptoms occur below the knees prior to affecting fingertips	Most common cause: diabetes, Chronic Idiopathic axonal polyneuropathy, Alcohol, chemotherapy induced.
Mononeuropathy	-Symptoms restricted to distribution of single nerve, myotome, or dermatome -Asymmetric reflexes	Entrapment neuropathies e.g., carpal tunnel, peroneal nerve entrapment. Post traumatic neuropathies, diabetes
Mononeuropathy multiplex	-Occurrence of several concurrent mononeuropathies	Autoimmune vasculitic etiologies
Hereditary neuropathies	-Distal calf atrophy, hammertoes, pes cavus -Motor deficits ≥ sensory deficits -Diffuse areflexia	Genetic diseases

#### Pharmacological management

- Focus on the management of the underlying disease process if identified.

- Ensure glucose control in diabetic neuropathy, alcohol cessation in alcoholic neuropathy and correction of vitamin or mineral deficiencies in nutrition related peripheral neuropathies.
- For drug related neuropathies, stop the offending medicine and give a suitable substitute. e.g., substitute stavudine or didanosine with tenofovir or lamivudine.
- Initial management of symmetric polyneuropathies and postherpetic neuralgia

**D:** pregabalin (PO) 150mg 12hourly for 4-12weeks

**OR**

**A:** amitriptyline (PO) 50-100mg 12hourly for 4-12weeks

**AND**

**B:** vitamin B1, B6, and B12 (FDC) (PO) 12hourly for 4-12weeks

- If the initial treatment is not effective, consider one of the combination therapies.

#### (1) **Gabapentanoid+Tricyclic Antidepressant**

**D:** pregabalin (PO) 150mg 12hourly for 4-12weeks

**AND**

**A:** amitriptyline (PO) 25-50mg 12hourly for 4-12weeks

**AND**

**B:** vitamin B1, B6, and B12 (FDC) (PO) 12hourly for 4-12weeks

#### (2) **Gabapentanoid +Selective Serotonin Reuptake Inhibitors**

**D:** pregabalin (PO) 150mg 12hourly for 4-12weeks

**AND**

**S:** fluoxetine (PO) 20mg 24hourly for 7days then titrate 12hourly for 4-12weeks

**AND**

**B:** vitamin B1, B6, and B12 (FDC) (PO) 12hourly for 4-12weeks

In chronic demyelinating polyneuropathies add steroids

**A:** prednisolone (PO) 20-60mg 24hourly for 6weeks (taper down based on response)

Offer rescue therapy if required, to patients undergoing long term treatment.

**B:** tramadol (PO) 50mg 8hourly for 7-14 days

For localized symptoms, consider topical agents as adjunctive treatment.

**D:** lidocaine 5% patches apply for 60minutes.

For patients on isoniazid related neuropathies, start on

**B:** pyridoxine (PO) 25–50 mg 8hourly for 3weeks, then 25mg 24hourly until completion of TB dose.

#### **Non-pharmacological management**

- Transcutaneous electrical nerve stimulation (TENS) for pain relief.
- Educate patients on increased risk of injury and infection due to loss of sensation
- Recommend wearing socks with closed-toed shoes to decrease the risk of infection.
- Offer support on cessation to patients with alcohol-induced neuropathy

# CHAPTER NINE

## RESPIRATORY DISEASE CONDITIONS

### 9.1 Acute Respiratory Infections (ARI)

It is an infection affecting upper or lower respiratory tract. Commonly caused by bacteria or viruses, other microbes including rickettsia or fungi may be present.

#### 9.1.1 Pneumonia

Pneumonia is the inflammation of the lung tissue. Pneumonia can either be primary (to the causing organism) or secondary to pathological damage in the respiratory system.

##### Clinical presentation

- Fever (typically >38°C)
- Dry or productive cough
- Central cyanosis
- Respiratory distress
- Chest pain and tachypnoea

**Table 9.1: Tool used for assessing Adult Patient with Pneumonia**

CURB 65	Clinical Feature		Points			
	C	U	R	B	65	
C	Confusion				1	
U		Urea >7 mmol/L			1	
R			RR >30		1	
B				SBP <90 mmHg or DBP <60 mmHg	1	
65					Age >65	1
CURB-65 Score	Risk group	30-day mortality		Management		
0-1	1	1.5%		Low risk, consider home treatment		
2	2	9.2%		Probable admission vs close outpatient management		
3-5	3	22%		Admission, manage as severe		

DBP = diastolic blood pressure; SBP = systolic blood pressure. <sup>a</sup> Defined as a Mental Test Score of ≤8, or new disorientation in person, place or time. Predicted 30-day mortality

##### Note

- For patients with pneumonia treatment should be instituted when they have FEVER, COUGH AND CXR with findings suggestive of pneumonia.
- Consider alternative diagnosis when a patient is not responding.
- Pulmonary embolism should be investigated carefully for patient with shortness of breath and not responding to treatment of pneumonia

#### 9.1.1.1 Pneumonia in Children

(For more details, refer to Integrated Management of Childhood Illness (IMCI) guidelines)

**Table 9.2: Important clinical presentation of pneumonia in under-fives**

Age	Signs	Classification
Infants less than 2 months	Severe chest in-drawing or 60 breaths per minute or more	Severe pneumonia (all young infants with pneumonia are classified as severe)
	No severe chest in-drawing Less than 60 breaths per-minute	No pneumonia: Cough or cold
Children from 2 months to 1 year	Chest in-drawing	Severe pneumonia
	No chest in-drawing 50 breaths per minute or more	Pneumonia
	No chest in-drawing Less than 50 breaths per minute	No pneumonia Cough or cold
Children from 1 year to 5 year	Chest in-drawing	Severe pneumonia
	No chest in-drawing 40 breaths per minute or more	Pneumonia
	No chest in-drawing Less than 40 breaths per minute	No pneumonia Cough or cold

## Investigations

- Measure oxygen saturation
- FBC (look for increased WBC, neutrophilia) CRP/ESR (increased), ABG (look for pH, bicarbonate), Blood culture, Sputum culture and sensitivity, Serology for HIV test (if Unknown)
- CHEST X-ray-PA/LATERAL (look for consideration, tap effusion>5cm), Bronchoscopy (Consider if immunosuppression, critically ill, fail to respond, suspected TB or PCP or inadequate)
- CT Scan: if patient is not improving, suspicion of fungal, ILD

## Non-pharmacological Treatment:

- Oxygen therapy if available
- Supportive care
  - Remove clothes
  - If wheezing giving rapid-acting bronchodilator: Nebulized Salbutamol
  - Ensure that the child receives daily maintenance fluid appropriate for the child's age but avoid over-hydration refer to IMCI/ STG & Essential Medicines List for Children

## Pharmacological Treatment

### Non-severe pneumonia

A: amoxicillin (PO) 25mg/kg 8hourly for 5days

AND

A: paracetamol (PO) 15mg/kg 8hourly for 5days(if fever present)

OR

A: paracetamol (supp) 10–15mg/kg (if there is fever)

OR

A: ibuprofen (PO) 15mg/kg 12hourly for 5days

Give the first dose at the clinic and teach the mother how to give the other doses at home.  
Encourage breasting and feeding.

### Severe Pneumonia

A: benzyl penicillin (IV/IM) 50000 units/kg every 6hours for at least 3days

THEN

A: amoxicillin (PO) 40 mg/kg 8hourly for 7days.

Alternatively

A: ampicillin (IV/IM) 50 mg/kg every 6hourly for 5days

AND

A: gentamicin (IV/IM) 7.5 mg/kg 24hourly for 5days

THEN

A: amoxicillin (PO) 40 mg/kg 8hourly for 7days.

### Note

- For children above 5 years, atypical pneumonia should be considered e.g. mycoplasma
- Consider alternative diagnosis after three visit /not responding, refer patient to a pediatrician

### 9.1.1.2 Pneumonia in Adults

#### Community Acquired Pneumonia

CAP refers to a pneumonia that is acquired outside hospital commonly caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, **atypical bacteria** (ie, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella species*) and viral respiratory pathogens (i.e *rhinovirus* and *influenza*)

#### Clinical presentation

- Fever,
- Cough dry or productive with/without purulent sputum,
- Dyspnea,
- Pleuritic chest pain
- Tachypnea
- Crepitation/Rales heard over the involved lobe or segment
- Increased tactile fremitus, bronchial breath sounds may be present if consolidation has occurred.

- Decreased tactile fremitus and dullness on chest percussion

### Investigations

- Measure oxygen saturation use pulse oximetry or Monitor
- FBC (look for increased WBC, neutrophilia),
- CRP/ESR (increased in bacterial infection)
- ABG (look for pH, bicarbonate),
- Serology for HIV test (if Unknown)
- Sputum culture and sensitivity (are indicated for inpatients and those with severe disease (ICU admission),
- Blood culture (are not recommended for ambulatory patients)
- CHEST X-ray-PA/LATERAL (look for one or more focal pulmonary infiltrates, consolidation, tap effusion>5cm),
- Bronchoscopy (Consider if immunosuppression, critically ill, fail to respond, suspected TB or PCP or inadequate
- CT-CHEST Scan Or HRCT: if patient is not improving, suspicion of fungal, ILD etc.

#### Note

Do not use CT chest to diagnose pneumonia

### Non-pharmacological Treatment

- Stop smoking if previously smoking
- Vaccination when indicated, in specialized centre for patient >65yrs and below 5years

### Pharmacological Treatment

#### First line treatment

**Table 9.3: First Line Treatment of Typical Community Acquired Pneumonia**

Condition	Treatment	Duration
Mild CAP (treated on out-patient basis) (common organism S pneumonia and these patients have no comorbidities)	<b>A:</b> erythromycin (PO) 500mg 8hourly <b>OR</b> <b>B:</b> ampicillin + cloxacillin (FDC)(PO) 500–1000mg 8hourly	5-7days
Mild to Moderate CAP (failed to respond to Initial treatment)	<b>A:</b> doxycycline (PO) 100 mg 12hourly (culture guided) <b>OR</b> <b>B:</b> azithromycin (PO) 500mg stat and then 250mg 24hourly <b>OR</b> <b>C:</b> clarithromycin (PO) 500mg 12hourly	5-7days
MILD CAP in patients with comorbidities (i.e. chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; asplenia; immunosuppression; prior antibiotics within 90 days	<b>B:</b> amoxicillin + clavulanic acid (FDC) (PO) 500mg/125mg 8-12hourly or 875mg/125mg 12hourly <b>OR</b> <b>D:</b> cefuroxime (PO) 500mg 12hourly <b>AND</b> <b>A:</b> doxycycline (PO) 100mg 24hourly <b>OR</b> <b>C:</b> clarithromycin (PO) 500mg 12hourly	5-7 days
Severe pneumonia/Aspiration pneumonia (in-patient)	<b>D:</b> ceftriaxone + sulbactam (FDC) (IV) 1.5g 12hourly If suspicion of anaerobes or Aspiration pneumonia <b>Add:</b> <b>B:</b> metronidazole (IV) 500mg 8hourly <b>Do culture and imaging if nonresponse consider second line</b>	7–10days

#### Second line treatment

If no response to first line further investigation is required. If patient is in respiratory distress, or no response after 3 days of first line treatment, or patient's condition deteriorates, then investigate, start empiric treatment while wait for culture and sensitivity

**S:** piperacillin + tazobactam (FDC) (IV) 4.5g 6hourly for 7days

**Table 9.4: Treatment of Typical and Atypical Community Acquired Pneumonias Organism Specific**

Condition	Treatment	Duration
Atypical pneumonias ( <i>Bordetella pertussis</i> , <i>Mycoplasma pneumonia</i> , <i>Chlamydophila pneumonia</i> )	<b>A:</b> erythromycin (PO) 500mg 6hourly <b>OR</b> <b>C:</b> clarithromycin (PO) 500mg 12hourly	7-10days
Pseudomonas pneumonia (Risk factors structural lung disease, COPD, and bronchiectasis)	<b>A:</b> ciprofloxacin (PO) 500mg 12hourly <b>If culture sputum-positive or HRCT suggestive</b> <b>S:</b> piperacillin + tazobactam (FDC) (IV) 4.5g e 6-8hourly <b>OR</b> <b>S:</b> ceftazidime (IV) 2g 8hourly <b>OR</b> <b>D:</b> ceftazidime (IV) 2g 8hourly <b>OR</b> <b>S:</b> meropenem (IV) 1g 8hourly	7-10days
H. influenza	<b>A:</b> amoxicillin (PO) 500mg 8hourly <b>OR</b> <b>D:</b> cefuroxime (PO) 250-500mg 8hourly (culture & sensitivity should be done in order to choose alternativeantibiotics)	7-10days
<i>Pneumocystis jirovecii</i> Pneumonia (PJP) (Refer to Tanzania HIV Guideline for more details)	<b>A:</b> co-trimoxazole (PO) 1920mg 8hourly <b>AND</b> <b>A:</b> folic acid (PO) 5mg 24hourly (if cytopenic) <b>In sulphur allergy:</b> <b>S:</b> clindamycin (PO) 450–600mg 6hourly	21days
<i>Staphylococcus aureus</i> Pneumonia	<b>B:</b> ampicillin + cloxacillin (FDC) (IV) 1g 6hourly <b>OR</b> <b>S:</b> clindamycin (IV/PO) 600mg 6-8 hourly	14days
Klebsiella Pneumonia (due to high mortality observe the duration of antibiotic given not < 10days)	<b>B:</b> chloramphenicol (IV) 500mg 6hourly <b>AND/OR</b> <b>A:</b> gentamicin (IV) 4-5mg/kg 24hourly in 2 divided doses	10-14days
For critical ill patient and those with risk factors for <b>MRSA</b> include hemoptysis, recent, influenza, neutropenia, hemodialysis, and congestive heart failure)	<b>S:</b> vancomycin (IV) 15mg/kg 12hourly	5-7days

**Note**

- In severe *Pneumocystis jirovecii* pneumonia (PCP), add 30 – 40mg prednisolone for 14days consider tapering down after recovery
- Patients with pneumonia should be afebrile for 48-72hours and have improved clinically before antibiotic therapy is stopped. The duration of therapy may need to be increased if the initial empirical therapy has no activity against the specific pathogen or if the pneumonia is complicated by extra pulmonary infection.

Alternative in Staphylococcal and Klebsiella Pneumonia:

**D:** ceftazidime (IV/IM) 2g 8hourly for 7–14days

#### 9.1.1.3 Hospital Acquired Pneumonia/Nosocomial Pneumonia

This is defined as pneumonia that occurs two days (48hrs) or more after hospitalization but that was not incubating at the time of hospital admission.

#### Clinical Presentation

- Fever
- Increase in respiratory rate
- Shortness of breath

## **Pharmacological Treatment**

Empirical treatment until bacteriology available

**C:** ciprofloxacin (IV) 400mg 12hourly for 7days

**OR**

**D:** ceftriaxone + sulbactam (FDC) (IV) 1.5g 12hourly for 7days

### **Note**

In specialized unit management of CAP/HAP can be changed with supportive culture and sensitivity done, this may necessitate use of other broader spectrum antibiotics 48-72hours until the results are obtained

## **9.2 Obstructive Lung Diseases**

It's a chronic airway disease which result in airway flow limitation can be either reversible or irreversible

### **Clinical presentation**

- Wheezing
- Difficulty in breathing or shortness of breath
- Chest tightness
- Cough (dry or productive cough)
- Finger clubbing

### **9.2.1 Asthma**

It is a chronic reversible obstructive inflammatory airways disease in which many cells and cellular element play a role by constriction of bronchial smooth muscle causing bronchospasm, oedema of bronchial mucous membrane and blockage of the smaller bronchi with plug of mucus.

### **Clinical presentation**

- wheeze,
- shortness of breath,
- chest tightness
- cough This presentation particularly at night or in the early morning
- Tachypnea,
- Tachycardia,
- Diffuse musical wheezes,
- Prolonged phase of exhalation,
- Chest hyperinflation.
- Use of Accessory muscle.

### **Investigations**

- FBP (Look for eosinophilia)
- Serum IgE<sup>a</sup>
- ESR
- ABG
- CXR if highly suspicion of pneumonia
- Sputum for cytology <sup>a</sup> (look for eosinophilia),

<sup>a</sup>Very important test to establish diagnosis of asthma

with reversibility test, PEFR measurement with a peak flow meter), Exhaled NO should be done to asses evidence of variable expiratory airflow limitation

### **Non-pharmacological Treatment**

- Avoid polluted environment (both indoors and outdoors)
- Avoid non-selective β-blockers, which can trigger asthmatic attack
- Avoid heavy exercise
- Stop smoking
- Avoid both overweight and underweight

### **Note**

- The management of asthma in children is like that in adult. Infants under 18 months, may not respond well in bronchodilator
- Uncertain in diagnosis should prompt early referral, because asthma-COPD overlap has worse outcome.
- Patient intolerant of NSAIDs or who exhibit any of the high-risk clinical features for intolerance to these drugs (severe asthma, nasal polyps or chronic rhino sinusitis) should use NSAIDs only under close medical supervision.

**Table 9.5: Assessment and Treatment of Asthma attack in Children ≥2years & Adults**

Attack	Clinical Presentation	Treatment (Children & Adults)
<b>MILD-MODERATE ATTACK</b>	Able to talk in sentences or phrases Not agitated Pulse rate 100-120bpm Sat O <sub>2</sub> (on air)-90-95% PEF>50% predicted	<p>I. Salbutamol inhalation (can be given by pMDI or spacer or Nebulization)<sup>2</sup> Give: 4-10 puffs by pMDI/ spacer/ every 20minutes for 1<sup>st</sup> hour  <b>A:</b> salbutamol(nebulization) Adult: Salbutamol respules 5mg 6hrly (2-3cycles and reassess); Pediatric: 2.5mg 6hrly (2-3cycles and reassess).</p> <p>If symptoms completely subside observe for 1-4hours, give Salbutamol for 24-48hours (2-4 puffs every 4-6hours) for 3 days. If attack is only partially resolved give 2-4 puffs of Salbutamol every 3-4 hours if attack is mild; 6 puffs every 1-2 hours if the attack is moderate, until symptoms subside. When attack completely resolved proceed as above.</p> <p><b>II. Prednisolone</b>  <b>A:</b> prednisolone (PO): Adult 40mg am 7/7; Pediatrics 1-2mg/kg max 40mg Do tapering if exceed seven days.</p> <p><b>III:</b> Controlled oxygen (if available): target saturation 93-95% (children: 94-98%)</p> <p><b>Note:</b> If symptoms worsen or do not improve, treat as <b>SEVERE ATTACK</b></p>
<b>SEVERE ATTACK</b>	<ul style="list-style-type: none"> <li>Talks in words i.e. cannot complete a sentence in 1 breath or too breathless to talk/ feed</li> <li>Sits hunched forwards</li> <li>Agitated</li> <li>Respiratory rate &gt;30/min.</li> <li>Accessory muscles being used</li> <li>Pulse rate &gt; 120 bpm</li> <li>O<sub>2</sub> saturation (on air): &lt; 90%</li> <li>PEF ≤ 50% predicted or best</li> </ul>	<p>I. Admit the patient, place in semi-sitting position</p> <p><b>II.</b> Oxygen continuously 5L/min (maintain O<sub>2</sub> saturation for adult 93-95% (children 94-98%)</p> <p><b>III. Inhalation</b>  <b>A:</b> salbutamol (nebulization) 4-10puffs every 20-30min in children &lt;5years, up to 20 puffs in children &gt;5years and adults  <b>Add</b>  <b>S:</b> ipratropium bromide (inhalation)0.25-0.5mg 6-8hourly  <b>AND</b>  <b>A:</b> hydrocortisone (IV) 5mg/kg in children, 100mg in adults 6hourly then switch to oral  <b>A:</b> prednisolone (PO)1-2mg/kg 24hourly to complete 7days of treatment  If attack is completely resolved continue with salbutamol inhalation 2-4puffs every 4hours for 24-48hours and oral prednisolone 1-2mg/kg 24hourly to complete 3-5days of treatment.</p> <p>If not improving or condition worsens, treat as <b>LIFE-THREATENING ATTACK</b></p>

Use a spacer to increase effectiveness. If conventional spacer not available, take a 500ml plastic bottle, insert the mouthpiece of the inhaler into a hole on the bottom of the bottle (the seal should be as tight as possible). The child breathes from the mouth of the bottle in the same way as he would with a spacer

LIFE-THREA TENIN G ATTAC K	Altered level of consciousness (drowsiness, confusion, coma) Exhaustion Silent chest Paradoxical thoracoabdominal movement Cyanosis Collapse Bradycardia in children or arrhythmia/hypotension in adults O <sub>2</sub> saturation<92%	<p><b>I.</b> Admit the patient, place in semi-sitting position</p> <p><b>II.</b> Oxygen continuously 5L/min (maintain O<sub>2</sub> saturation between 94-98%)</p> <p><b>III. A:</b> salbutamol (nebulization) 2.5mg for children &lt;5years and in children &gt;5years &amp; adults 2.5-5mg every 20–30min then switches to salbutamol aerosol when clinical improvement is achieved.</p> <p><b>Add:</b> <b>S:</b> ipratropium bromide (inhalation) 0.25-0.5mg 6-8hourly.</p> <p><b>AND</b> <b>A:</b> hydrocortisone (IV) 5mg/kg in children, 100mg (IV) in adults every 6hours then switch to <b>A:</b> prednisolone (PO) 1-2mg/kg 24hourly to complete 7days of treatment</p> <p>In adult administer a single dose of <b>A:</b> magnesium sulphate (Infusion of 1-2g in 0.9% Sodium Chloride over 20 minutes)</p> <p>In children use continuous nebulization rather than intermittent nebulisation.</p> <p>Patient with life threatening asthma should be managed in HDU/ICU.</p>
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#### Note

Patients who get night attacks should be advised to take their medication on going to bed

#### 9.2.2 Chronic Asthma in Adults

The assessment of the frequency of daytime and nighttime symptoms and limitation of physical activity determines whether asthma is intermittent or persistent. There are 4 categories (see table 9.5)

Therapy is stepwise (Step 1–4) based on the category of asthma and consists of:

- Preventing the inflammation leading to bronchospasm (controllers)
- Relieving bronchospasm (relievers)

#### Controller medicines in asthma

- Inhaled corticosteroids (ICS) e.g. Beclomethasone, Budesonide, Fluticasone
- Leukotriene modifiers: e.g. Montelukast can be added from step 2 patient (should be administer when low ICS or ICS-LABA has failed to achieve desired outcome).
- long acting muscarinic antagonist (LAMA) e.g tiotropium
- Long acting β<sub>2</sub> agonists (LABA) e.g. formoterol, salmeterol

#### Reliever medicines in asthma

- Short acting β<sub>2</sub> agonists (SABA) e.g. Salbutamol
- short acting muscarinic antagonist (SAMA) e.g. ipratropium bromide (should be used in acute asthma attack)

#### Note

- In specialized centre when low dose ICS alone fails to achieve good control for difficult to treat and severe asthma, the addition of **LABA + ICS** should be instituted.
- The most common side effects of **inhaled steroids** are a **sore throat**, hoarseness of voice, and infections/fungal infections in the throat and mouth.

#### Things you can do to avoid or reduce these side effects include:

- Rinsing your mouth and gargling after taking an inhaled steroid
- Using a spacer/holding chamber to reduce the amount of steroid landing in your mouth and throat (For children and elderly patient)

**Table 9.6: Long-Term Treatment of Asthma According to Severity**

Categories	Treatment
<b>STEP 1</b> Intermittent asthma <ul style="list-style-type: none"> <li>• Intermittent symptoms once/week &lt;</li> <li>• Nighttime symptoms &lt; twice/ month</li> <li>• Normal physical activity</li> </ul>	<b>A:</b> As needed low dose ICS <b>OR</b> <b>S:</b> ICS <b>AND</b> LABA <b>B:</b> budesonide (inhalation) 100-200µg 12hourly <b>OR</b> <b>B:</b> budesonide (inhalation) 100-200µg 12hourly <b>AND</b> <b>C:</b> salmeterol 100- 200mcg 2puff 12hourly <b>OR</b> Low dose ICS taken whenever SABA is taken
<b>STEP 2</b> Mild persistent asthma <ul style="list-style-type: none"> <li>• Symptoms &gt; once/ week but &lt; once/ day</li> <li>• Nighttime symptoms &gt; twice/ month</li> <li>• Symptoms may affect activity</li> </ul>	Daily low dose ICS plus as needed SABA <b>OR</b> As needed low dose ICS+ salmeterol <b>OR</b> Low dose ICS taken whenever SABA is taken ICS <b>Add:</b> - LTRA; <b>D:</b> montelukast (PO) 4mg nocte (6month to 6years) or > 6years to 15years (PO) 5mg nocte or >15years (PO) 10mg nocte (for period not less than 3/12)
<b>STEP 3</b> Moderate persistent asthma <ul style="list-style-type: none"> <li>• Daily symptoms</li> <li>• Symptoms affect activity</li> <li>• Nighttime symptoms &gt;once/ week</li> <li>• Daily use of Salbutamol</li> </ul>	Refer these patients to physician/ respiratory physician/ pulmonologist low dose ICS+LABA <b>OR</b> Medium dose ICS <b>OR</b> Low dose ICS +LTRA  LTRA; <b>D:</b> montelukast (PO) 4mg nocte (6month to 6years) or (PO) 5mg nocte > 6-15years or (PO) 10mg nocte >15years (for period not less than 3/12)
<b>STEP 4</b> Severe persistent asthma <ul style="list-style-type: none"> <li>• Daily symptoms</li> <li>• Frequent nighttime symptoms</li> <li>• Physical activity limited by symptoms</li> </ul>	Refer this patient to Respiratory physician/Pulmonologist Medium dose ICS+LABA <b>OR</b> High dose ICS <b>Add</b> <b>S**:</b> tiotropium Mist (inhalation) 6mcg 2puff 24hourly <b>OR</b> <b>Add on</b> LTRA <b>D:</b> montelukast (PO) 4mg nocte (6month to 6years) or (PO) 5mg nocte >6years to 15years or (PO) 10mg nocte>15years (for period not less than 3/12) <b>Add:</b> <b>S:</b> tiotropium mist inhaler 6mcg 2puff 24hourly <b>OR</b> <b>S:</b> ipratropium Bromide (Inhalation) 40 mcg 2puff 12hourly For patient with rhinitis and asthma add sublingual immunotherapy (SLIT) provided FEV <sub>1</sub> >70% predicted
<b>STEP 5</b> Severe asthma <ul style="list-style-type: none"> <li>• Symptoms throughout the day</li> <li>• Night symptoms seven times per weeks</li> <li>• Physical activity extreme limited by symptoms</li> </ul>	Refer to expert opinion (respiratory physician/pulmonologist for phenotypic investigation+- add on treatment)  High dose ICS-LABA Low dose OCS but consider side effects <b>S:</b> tiotropium (inhalation) as step 4 Biologics as indicated <b>S:</b> omalizumab (SC) 75-600mg every 2-4weeks;

**Table 9.7 Low, Medium and High Dose Inhaled Corticosteroids Adults and Adolescents ( $\geq 12$  Years)**

Inhaled corticosteroid	Total daily dose (mcg)		
	Low	Medium	High
Budesonide (DPI)	200-400	>400-800	>800
Fluticasone propionate (DPI OR HFA)	100-250	>250-500	>500
Mometasone furoate	110-220	>220-440	>440
Triamcinolone acetonide	400-1000	>1000-2000	>2000

DPI: Dry powder inhaler, HFA: hydrofluoroalkane, CFC: Chlorofluorocarbon propellant (included for comparison),

**Table 9.8 Low, Medium and High Dose Inhaled Corticosteroids Children 6–11 Years**

Inhaled corticosteroid	Total daily dose (mcg)		
	Low	Medium	High
Budesonide (DPI)	100-200	>200-400	>400
Budesonide (nebuliser)	250-500	>500-1000	>1000
Fluticasone propionate (DPI)	100-200	>200-400	>400
Fluticasone propionate (HFA)	100-200	>200-500	>500
Momentansone furoate	110	>220-≤440	≥440
Triamcinolone acetonide	400-800	>800-1200	>1200

## 9.3 Bronchitis

### 9.3.1 Acute Bronchitis

**Acute bronchitis** was defined as an acute self-limited lower respiratory tract infection manifested predominantly by cough with or without sputum production, lasting no more than 3 weeks with no clinical or any recent radiographic evidence to suggest an alternative explanation. In acute bronchitis some isolated virus (influenza A and B viruses, parainfluenza virus, respiratory syncytial virus, **coronavirus**, adenovirus, and rhinovirus) and bacteria (Bordetella pertussis, Chlamydophila (Chlamydia) pneumoniae, and Mycoplasma pneumonia)

#### Clinical presentation

- Patients with acute bronchitis present with a cough lasting more than five days (typically one to three weeks), which may be associated with sputum production.
- Cough in the absence of fever, tachycardia, and tachypnoea suggests bronchitis,
- Acute bronchitis should be distinguished from chronic bronchitis (see below), it is not a form of COPD

#### Note

When the acute bronchitis persists or worsens, we suggest that the patient is advised to seek reassessment and do below targeted investigation(s).

#### Investigation in COPD (bronchitis and Emphysema)

- FBP
- ESR /CRP OR Procalcitonin
- Serum alpha-1 antitrypsin levels
- Chest radiography (if the patient is elderly or physical findings suggest pneumonia)
- Sputum cytology (if the cough is persistent)
- Blood culture and microbial sensitivity (if bacterial super-infection is suspected)
- Bronchoscopy (to exclude foreign body aspiration, tuberculosis, tumours, and other chronic diseases and patient with worsening symptoms)
- Lung function Test (Spirometry and Peak expiratory flow rate)

#### Note

An exception, however, is cough in elderly patients; pneumonia in elderly patients is often characterized by an absence of distinctive signs and symptoms.

## Symptomatic Treatment

- With non-steroidal anti-inflammatory drugs: paracetamol, acetyl salicylic acid
- Cough management refer section 9.1.1
- There is NO benefit from antibiotic use in acute bronchitis.
- Discourage smoking and other irritating factors.

## 9.3.2 Chronic Bronchitis

It defined by a chronic productive cough for three months in each of two successive years in a patient in whom other causes of chronic cough have been excluded. Patients may get secondary bacterial infection with development of fever and production of thick smelly sputum.

**Table 9.9: Risk Factor for Chronic Bronchitis**

Risk factor	
1. Cigarette smoking	
2. Indoor air pollution	
>Exposure from burning wood	>Exposure to biofuel mass exposure
>Heating in poorly vented dwellings	
3. Occupational exposure	
Coal miners >Tunnel Workers >Hard-rock miners >Concrete manufacture	
>Livestock farming (i.e. to pesticides)	
4. Exposure to agricultural	
5. Use of domestic solid fuel	

## Investigation

As in acute bronchitis

## Non-pharmacological Treatment

- Stop smoking (Reducing loss of lung function) and/or remove from hazardous environment
- Prompt treatment of infective exacerbations
- Controlled oxygen therapy
- Physiotherapy
- Pulmonary Rehabilitation (consist of education, lifestyle modification, regular physical activities, physiotherapy and avoid indoor and outdoor pollutants)
- Nutrition support
- BIPAP in specialized center
- Influenza vaccine in specialized center

## Pharmacological Treatment

- Pharmacologic therapy for Chronic Bronchitis is directed towards 3 major goals
- Relieving symptoms during stable disease

**Mucoactive Agents**-Reduced overproduction and hypersecretion, increases elimination

For pharmaceutical management; refer to emergency and critical care chapter

**Hypertonic saline**-stimulate productive cough and decreases sputum viscoelasticity, increases mucociliary clearance.

7% hypertonic saline or 0.9% saline bd for PRN

**Bronchodilators (Beta-agonists)**-Promotes mucus clearance by increasing airway luminal diameter and ciliary beat frequency, reduces hyperinflation, improve PEF

**A: SABA:** Salbutamol (Inhalation) 100µg 2puff 6hourly

**OR**

**LABA:** salmeterol+fluticasone or in combination with steroids (salmeterol+fluticasone or budenoside fluticasone)

**OR**

**Muscarinic antagonists** -Decrease contractility of smooth muscle in the lung, inhibits bronchoconstriction and mucus secretion

**SAMA: S:** ipratropium bromide (aerosol) 20–80mcg, 6–8 hourly

**LAMA: S:** tiotropium (mist inhaler) 6mcg 2puff 24hourly Preventing exacerbations

## Mucoactive Agents-Refer cough section

**Macrolides- (As indicated)** antibacterial effects; Immune-modulatory and anti-inflammatory effects (Azithromycin/clarithromycin)

### Note

- In specialized center they may use N-acetyl cysteine and carbocysteine as mucolytic agents
- Macrolide should be given in consultation with respiratory physician/Pulmonologist to avoid antimicrobial resistance (Azithromycin and clarithromycin may be used).

**Avoid use of systemic glucocorticoids due to numerous adverse side effects**

## 9.4 Emphysema

It is a destructive process in the gas-exchanging air spaces of the lung that results in perforations, obliteration of airspace walls, and coalescence of small distinct airspaces into much larger ones, leading to enlargement of the gas exchanging units of the lungs. These changes cause loss of elastic recoil of the lungs and abnormal gas exchange.

### Clinical presentation

- Shortness of breath
- Cough, sometimes caused by the production of mucus
- Wheezing
- Slow and prolonged expiration
- Chest wall hyperinflation,
- Limited diaphragmatic motion on auscultation,
- Distant breath sounds, and heart sounds
- Coarse early inspiratory crackles.
- Use of accessory muscles
- Pursed-lip breathing
- Signs of cor pulmonale. (Raised JVP, peripheral oedema, hepatomegaly etc)
- Cyanosis
- Asterixis

### Investigations

- Haematocrit(men>52% and >47men) Or FBP (look at haematocrit)
- ABG(look for bicarbonate-metabolic alkalosis)
- CXR
- Sputum culture and Microbial sensitivity
- Pulmonary function tests
- Six minutes' walk test
- CT SCAN OF THE CHEST/HRCT (for evaluation for Lung Volume Reduction Surgery)

### Non-pharmacological Treatment:

- Stop smoking
- Give oxygen after evaluation

### Pharmacological Treatment

Inhaled bronchodilators relax and open the airways. They may be short-acting (albuterol, ipratropium) or long-acting (salmeterol, tiotropium.). These medicines may be available as inhalers ("puffers") or as a solution. A nebulizer machine aerosolizes the bronchodilator solution, which is then breathed through a tube. For more detail refer Treatment in section 9.2 above

**Table 9.10: COPD Staging and recommended Therapies**

GOLD FEV <sub>1</sub> Stage	Exacerbation Per Year	Mild symptoms	Mod/Severe Symptoms
I: ≥80%	≤2	GROUP A Bronchodilator (SABA-PRN)	GROUP B LAMA OR LABA
II: 50-79%			
III: 30-49%	≥2	GROUP C LAMA+ LABA	GROUP D LAMA or LAMA + LABA or ICS+ LABA
IV: 30%			

## 9.5 COPD Exacerbation

Chronic Obstructive Pulmonary Disease (COPD) exacerbation is a worsening or “flares up” of your COPD symptoms, commonly caused by infection in the lungs but in some cases the cause is unknown.

### Clinical presentation

- Worsening of cough,
- Increase in phlegm production,
- Change in phlegm quality, and increase in dyspnea

**Table 9.11: COPD Exacerbation Management**

AGENT	DOSE
<b>SAMA</b> S: ipratropium bromide (aerosol)	MDI 4-8 puffs every 1-2 hours Nebulizer 0.5mg every 1-2hours
<b>SABA</b> A: salbutamol (inhalation)	MDI 4-8 puffs every 1-2hours Nebulizer 2.5-5mg every 1-2hours
<b>Corticosteroids</b> A: prednisone (PO) If severe A: hydrocortisone (IV) D: methylprednisolone (IV)	40mg AM for 5days  1-2mg/kg 6hourly 125mg 6hourly for 72hours (Then switch oral)
<b>Antibiotic (If infection Presents)</b> (Penicillin/Macrolide/Fluoroquinolone)	
A: amoxicillin (PO)	500mg 8hourly for 7days
OR	
A: ciprofloxacin (PO)	500mg 12hourly for 7days
OR	
A: doxycycline (PO)	100mg every 12hrs 7days
OR	
C: clarithromycin (PO)	500mg 12hourly for 7days
If possible, do culture and sensitivity	
<b>Noninvasive positive pressure ventilation</b>	
<b>Oxygenation if indicated</b>	

## 9.6 Other Respiratory Infections

### 9.6.1 Acute Laryngo-Tracheobronchitis

Laryngo-tracheobronchitis (croup) is acute inflammation of the larynx, trachea and bronchi which occurs in young children (usually between 6 months to 3 years of age). It arises as a result of narrowing of the airway in the region of the larynx. The most common cause is viral infection (particularly parainfluenza viruses) but may also be due to bacterial infection. The obstruction is due to inflammation and oedema.

### Clinical presentation

- The symptoms include paroxysmal “barking” cough, inspiratory stridor, fever, wheezing, hoarseness of voice and tachypnoea
- Such symptoms usually occur at night
- Respiratory failure and pneumonia are potentially fatal complications.

### Non-pharmacological Treatment

- Prevent asphyxiation
- Treat inflammatory oedema
- Humidification of inhaled air
- Hospitalization may be necessary

**Note**

- No stridor at rest, give no antibiotics
- Stridor at rest or chest in-drawing or fast breathing REFER IMMEDIATELY to hospital

**Mild Croup**

- Only stridor when upset, no moderate/severe ARI
- Likely of viral origin

**Severe Croup**

- Likely bacterial origin
- Stridor in a calm child at rest
- Chest in drawing

- Home care – steam inhalation
- Antibiotics NOT required

- Antibiotics are NOT effective and should not be given

**Pharmacological Treatment**

Admit to hospital, give Oxygen therapy to all patients with chest in-drawing (using nasal prongs only, DO NOT use nasopharyngeal or nasal catheter) until the lower chest wall in-drawing is no longer present

**D:** dexamethasone (PO) 0.6mg/kg 24hourly in 1–2 divided doses

**AND**

**A:** adrenaline (inhalation) 400mcg/kg 2hourly if effective; repeat after 30min if necessary.

### 9.6.2 Laryngeal Diphtheria

Is an infection caused by *Corynebacterium diphtheriae*; it is directly transmitted from person to person by droplets. Children between 1–5 years of age are most susceptible although non-immune adults are also at risk. Diphtheria is characterized by grayish-white membrane, composed of dead cells, fibrin, leucocytes and red blood cells as a result of inflammation due to multiplying bacteria.

**Non-pharmacological Treatment**

- Isolate the child
- Gently examine the child's throat – can cause airway obstruction if not carefully done.
- NGT for feeding if unable to swallow
- Avoid oxygen unless there is incipient airway obstruction
- May need tracheostomy if there is incipient airway obstruction

**Pharmacological Treatment:**

Drug of choice

**A:** phenoxyethylpenicillin (PO) 250mg 6hourly for 14days

**OR**

**A:** erythromycin (PO) 125–250mg 6hourly for 14days

**OR**

**B:** azithromycin (PO) 500mg 24hourly for 3days

**OR**

**A:** benzyl penicillin (IV) 25,000–50,000units/kg to a max. of 1.2MU 12hourly until the patient can take oral medicine

**AND**

**A:** diphtheria antitoxin (IM or slow IV) dose depends upon the site and severity of infection:

- First give a test dose of 0.1ml of 1 in 10 dilution of antitoxin in 0.9% Sodium Chloride intradermal to detect hypersensitivity
- It should be given immediately because delay can lead to increased mortality
- The dose should be administered intravenously over 60minutes in order to inactivate toxin rapidly
- 20,000–40,000 units for pharyngeal/laryngeal disease of <48 hours' duration,
- 40,000–60,000 units for nasopharyngeal disease
- 80,000–120,000 units for >3days of illness or diffuse neck swelling "bull-neck"

**Note**

Tracheostomy may be required for airway obstruction

### 9.6.3 Whooping Cough

It is a highly infectious childhood disease caused by *Bordetella pertussis*. It is most severe in young infants who have not yet been immunized.

### **Clinical presentation**

- Paroxysmal cough associated with a whoop
- Fever
- Nasal discharge

### **Non-pharmacological Treatment**

- Place the child head down and prone, or on the side, to prevent any inhaling of vomitus and to aid expectoration of secretions.
- Care for the airway but avoid, as far as possible, any procedure that could trigger coughing, such as application of suction, throat examination
- Do not give cough suppressants, sedatives, mucolytic agents or anti-histamines.
- If the child has fever ( $>38.5^{\circ}\text{C}$ ) give paracetamol.
- Encourage breastfeeding or oral fluids
- Whooping cough is preventable by immunization with pertussis vaccine contained in DPT-HepB-Hib vaccine at week 6, 10 and 14.

### **Oxygen**

- Give oxygen to children who have spells of apnoea or cyanosis, or severe paroxysms of coughing.
- Use nasal prongs, not a nasopharyngeal catheter or nasal catheter which can provoke coughing.

### **Pharmacological Treatment**

**A:** erythromycin (PO) 12.5 mg/kg 6hourly for 10days.

This does not shorten the illness but reduces the period of infectiousness

- If there is fever  
In Children older than age 2 months:

**A:** trimethoprim + sulfamethoxazole (FDC) (PO) 8mg+40mg/kg 12hourly

## **9.6.4 Bronchiectasis**

Bronchiectasis is a progressive respiratory disease characterized by permanent dilatation of the bronchi and associated with a clinical syndrome of cough, sputum production and recurrent respiratory infections.

### **Investigations**

FBP, ESR, Serum IgE and IgG to aspergillus, serum immunoglobulin (IgG, IgA, IgM) CXR, Sputum culture and sensitivity, CT-Chest (CT contrast if suspicion of PE/HRCT, bronchoscopy).

### **Non-pharmacological Treatment**

- Physiotherapy and postural drainage
- Avoid smoking
- Airways clearance technique
- Pulmonary rehabilitation
- Respiratory care during childhood measles helps prevent the development of bronchiectasis in children

### **Pharmacological Treatment**

Consider antibiotics in patients with bronchiectasis with >3 exacerbations per year. (empirical treatment while wait for culture and sensitivity)

Adults:

**A:** ciprofloxacin (PO) 500mg 12hourly for 10days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 10days

Children:

**A:** amoxicillin (PO) 40mg/kg in 2 divided doses for 7days

**AND**

**A:** metronidazole (PO) 7.5 mg/kg 8hourly for 5–7days

If pseudomonas aeruginosa suspicion (should be culture guided)

**D:** ceftazidime (IV) 2g 8hourly for 14days

**OR**

**S:** piperacillin+tazobactam (FDC) (IV) 4.5mg 8hourly for 14days  
**AND**  
**D:** itraconazole (PO) 100mg-200mg 12hourly

#### **Prevention of infection**

**A:** ciprofloxacin 500mg (PO) 24hourly for 7–14days  
**OR**  
**A:** erythromycin (PO) 250–500mg 24hourly for 7–14days

#### **9.6.5 Lung Abscess**

Lung abscess is a cavity within the lung parenchyma filled with necrotic tissues, which occurs as a result of tissue-destroying infection.

#### **Clinical presentation**

It is characterized by high fever, breathlessness, cough productive of large amounts of foul-smelling sputum and haemoptysis.

#### **Investigation**

FBP, ESR, CXR, Sputum Analysis (Gram Stain, Cytology, Gene Xpert, Culture), Blood Culture, CT Chest, Bronchoscopy, Sputum for ova and parasite (if Parasitic cause is suspected).

#### **Non-pharmacological Treatment**

Postural drainage

#### **Pharmacological Treatment**

**B:** ampicillin + cloxacillin (FDC)(IV) 500–1000mg for 7days then (PO) 8hourly for 3–6weeks (children 50mg/kg/dose)

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 7days then (PO) 400mg 8hourly for 4–6weeks (children 7.5mg/kg)

#### **Note**

The duration of antibiotics therapy depends on the clinical and radiographic response of the patient, but completely healing, with radiographic normalization can be seen after two months. Refer patient to specialized unit if Large cavity size (ie, >6cm in diameter), persistent fever.

**D:** ceftriaxone + sulbactam (FDC) (IV) 1.5-3g 6hourly 4-6weeks

**OR**

**S:** clindamycin (IV) 600mg 8hourly for 7days and then (PO) 300mg 8hourly 4-6weeks

**OR**

**S:** piperacillin + tazobactam (FDC) (IV) 4.5g 6hourly 4-6weeks

**OR**

**S:** meropenem (IV) 1g 8hourly for 4-6 weeks

#### **9.6.6 Aspergillosis**

##### **Clinical presentation**

- Cough
- Fever
- Chest pain.
- Difficulty breathing
- Hemoptysis ranging from mild to severe.
- Wheezing may be noted on auscultation.
- Mucous plugs upon coughing.
- Tachypneic and have rapidly progressive worsening
- Hypoxemia.

##### **Investigations**

- Chest X-ray and CT, pulmonary aspergillosis classically manifests as a halo sign and later an air crescent sign
- Sputum Culture.
- Bronchoscopy (BAL)

### **Non-pharmacological Treatment**

- Surgical treatment
- Bronchial artery embolization (for life threatening hemoptysis)

### **Pharmacological Treatment**

D: itraconazole (PO) 100-200mg 24hourly 6-12weeks

### **9.6.7 *Pneumocystis Pneumonia (PCP)***

#### **Clinical presentation**

- Cough dry/productive
- Exertional dyspnoea
- Fever
- Tachypnoea
- Chest pain
- There may be signs of AIDS such as thrush, oral hairy leucoplakia or Kaposi's sarcoma
- Scattered crackles and wheeze may be present, or rarely signs of focal consolidation
- Pulse oximetry may show low SaO<sub>2</sub> at rest
- Extra-pulmonary disease may manifest as hepatosplenomegaly, lymphadenopathy or ocular disease

#### **Investigations**

- Elevated lactate dehydrogenase
- ABG may show hypoxia.
- The alveolar-arterial oxygen tension gradient may be increased.
- Serum (1-->3) Beta-D-glucan levels (high in PCP) is currently being investigated as a diagnostic test.
- Chest X-ray
- CT-CHEST (ground glass infiltrates but has low sensitivity and specificity.)
- Gallium scanning is highly sensitive but with low and variable specificity.
- PFT (Reduction in Vital capacity (VC) and the total lung capacity (TLC).

#### **Management**

Refer table 9.4

### **9.6.8 *Silicosis***

#### **Clinical presentation**

- Asymptomatic
- Chronic cough
- Dyspnea on exertion
- Fine/coarse crackles
- Rhonchi and/or wheezes
- Tachypnea

#### **Investigations**

- Cor pulmonale
- Chest X-ray
- CT Scan (if indicated)
- PFT
- Lung function tests
- Lung biopsy (if indicated)

#### **Non-pharmacological**

- Avoid further exposure to respirable silica
- Smoking cessation
- Bronchodilators (if indicated)
- Vaccination against influenza and pneumococcus
- Oxygen therapy (if indicated)
- Lung transplantation

### **9.6.9 *Coal worker's pneumoconiosis***

#### **Clinical presentation**

- Asymptomatic
- Chronic cough
- Dyspnea on exertion
- Fine/coarse crackles

- Rhonchi and/or wheezes
- Tachypnea

- Cor pulmonale

### **Investigations**

- Chest X-ray
- CT Scan (if indicated)

- Lung function tests
- Lung biopsy (if indicated)

### **Non-pharmacological**

- Avoid further exposure to coal dust
- Smoking cessation
- Bronchodilators (if indicated)

- Vaccination against influenza and pneumococcus
- Oxygen therapy (if indicated)
- Lung transplantation

## **9.6.10 Sarcoidosis**

### **Clinical presentation**

- The common symptoms/signs depend on which organ or system is affected.
- Rales/crepitations
- Jaundice is rare
- Macules, papules, and plaques may arise as single isolated lesions
- Skin lesions frequently leave Scars, pits, and pale, depigmented areas

- Nerve palsies, headache, ataxia, cognitive dysfunction, weakness, and seizures.
- Anterior uveitis
- Tachyarrhythmias and bradyarrhythmias
- Polyarthritis, chronic arthritis

### **Investigations**

- FBP
- ESR
- LFT
- RFT
- RF,
- CPR, S/Electrolytes, LP,
- Auto immune profile
- Biopsy
- Images:
- CXR,
- CT SCAN,
- PETSCAN, FUNDOSCOPY.

### **Pharmacological Treatment**

**A:** prednisolone (PO) 1mg/kg/day

**Referral:** Refer to Specialized center (specialist- physician /dermatologist /rheumatologist /pulmonologist)

## **9.6.11 Obstructive Sleep Apnea Syndrome (OSA)**

Obstructive sleep apnea (OSA) is characterized by episodes of complete or partial collapse of the airway with an associated decrease in oxygen saturation or arousal from sleep. OSA is a sleep disorder that involves cessation or significant decrease in airflow in the presence of breathing effort.

### **Clinical Presentation**

- Daytime sleepiness
- Restless sleep
- Loud snoring
- Morning headaches;
- Insomnia;
- Decreased sex drive;
- Unexplained weight gain;
- Increased urination and/or nocturia.

- Heartburn or gastro esophageal reflux disease; and heavy night sweats
- Trouble concentrating; mood changes such as irritability, anxiety and depression; Forgetfulness; Increased heart rate and/or blood pressure;

## **Investigations**

- Nocturnal polysomnography
- Thyrotropin test
- Cysteine levels
- Multiple Sleep Latency and Maintenance of Wakefulness Tests

## **Non-pharmacological Treatment**

- Lifestyle modification (avoid alcohol, sleeping pills, and other sedatives)
- Continuous positive airway pressure (CPAP)
- The oral appliance (e.g. a mandibular advancement splint)

## **Pharmacological Treatment**

C: acetazolamide (PO) 500mg-1g 24hourly for 3-5days

## **Surgical intervention**

(Maxillomandibular advancement, Tonsillectomy) Uvulopalatopharyngoplasty

## **9.6.12 Cor Pulmonale**

Cor pulmonale is defined as an alteration in the structure (hypertrophy or dilation) and function of the right ventricle (RV) of the heart caused by a primary disorder of the respiratory system resulting in pulmonary hypertension.

## **Clinical Presentation**

- Fatigue
- Tachypnea
- Exertional dyspnea
- Cough
- Anginal chest pain
- Syncope with exertion
- lower limb edema
- Raised JVP
- Wheezes and crackles
- Systolic murmur of tricuspid regurgitation.
- Shortness of breath
- Wheezing
- Chronic wet cough
- Swelling of the abdomen with fluid
- Swelling of the ankles and feet
- Enlargement of the liver
- Bluish discoloration of face

## **Investigations**

- Electrocardiography (ECG)
- Echocardiography
- ABG
- BNP
- CXR
- Chest computed tomography (CT)+/-CTPA
- Ventilation/perfusion (V/Q) scanning
- Cardiac magnetic resonance (CMR) (as indicated)
- Other test to rule out etiology
- FBP/Hematocrit level
- Serum alpha1-antitrypsin
- Antinuclear antibody (ANA)
- Anti-SCL-70 antibodies
- Coagulations studies (serum levels of proteins S and C, antithrombin III, factor V Leyden, anticardiolipin antibodies, homocysteine)

## **Non-pharmacological Management**

- Oxygen therapy when PaO<sub>2</sub> is less 55mmHg
- Pulmonary embolectomy
- Uvulopalatopharyngoplasty (UPPP)
- Surgical embolectomy
- Lung transplant
- Pulmonary rehabilitation

## **Pharmacological Treatment**

Treat Heart Failure (right sided heart failure)

**B:** nifedipine ER (PO) 30mg 12hourly

Pulmonary Hypertension management

**S:** sildenafil (PO) 5mg -20mg 8hourly

**OR**

warfarin or rivaroxaban for indicated patient (For dosage refer to Pulmonary embolism management)

### **9.6.13 Pleural Effusion**

Pleural effusion, is excessive collection of fluid in the pleural space, is rarely a primary disease process but is usually secondary to other diseases.

#### **Clinical presentation**

- Progressive dyspnea
- Cough
- Pleuritic chest pain

**When pleural fluid >300ml you will get these symptoms**

- Dullness to percussion
- Decreased tactile fremitus
- Asymmetrical chest expansion
- Pleural friction rub
- Displacement of the trachea and mediastinum toward the side of the effusion

#### **Investigations**

- CXR
- Full blood picture
- Erythrocyte Sedimentation Rate (ESR)
- Serum ADA
- Point care bed side USS
- Pleural fluid analysis: - (The pleural fluid analysis above will be requested as per indication of suspected diagnosis.)
  - pleural fluid cytology
  - pleural fluid culture
  - pleural fluid Gene x pert, ADA, LDH, glucose, pH
  - pleural fluid cell count.
  - pleural fluid amylase
  - pleural fluid triglycerides and cholesterol
  - pleural fluid bilirubin
- Tumour markers as indicated (e.g. CA-15, CEA, CA-125etc).
- Rheumatoid Factor (if indicated)
- Autoimmune profile or single marker (ANA, ACE etc)
- Renal function (creatinine and BUN)
- Liver function and liver enzymes (Albumin, bilirubin total, direct, PT, PTT, INR ALT, AST, GGT, ALP)
- ECHO
- ECG
- CT-Scan Chest with contrast
- Thoracoscopy
- Pleural Biopsy (when suggestive of malignancy)
- Bronchoscopy

**Table 9.12 Staging Pleural Infections and Recommending Drainage**

Effusion Stage	Pleural Space Features	Bacteriology	Pleural Fluid Chemistry	Thoracentesis/ Drainage
I (uncomplicated parapneumonic)	Minimal, free-flowing effusion (< 10 mm on lateral decubitus)	Culture and Gram stain results unknown	pH unknown	No/No
II (uncomplicated parapneumonic)	Small-to-moderate free-flowing effusion (> 10 mm and less than one-half hemithorax)	Negative culture and Gram stain	pH ≥ 7.20 or glucose ≥ 60 mg/dL	Yes/No
III (complicated parapneumonic)	Large, free-flowing effusion (one-half hemithorax or greater); loculated effusion; effusion with thickened parietal pleura	Positive culture or Gram stain	pH < 7.20 or glucose < 60 mg/dL	Yes/Yes
IV (empyema)		Pus	Tests not indicated	Yes/Yes

#### Non-pharmacological Treatment

- **Serial Thoracentesis**-This approach may require an average of eight thoracenteses in 2 - 4 weeks, this is for non-complicated pleural effusion.
- **Chest Tube Drainage**-Chest tubes vary in size but can be classified as large-bore (24F to 34F) or smallbore (8F to 24F) viscous pleural pus, the surgical tradition recommends the use of large-bore chest tubes (28F to 32F)
- **Fibrinolytic Therapy**-use of streptokinase, urokinase, and rtPA, indicated for patients with empyema and complicated parapneumonic pleural effusions.
- **Thoracoscopy-medical thoracoscopy and video-assisted thoracoscopic surgery (VATS)**, indicated for patient with fibrinopurulent pleural infections and loculated effusion.
- **Thoracotomy, Decortication, and Open Drainage**-Thoracotomy remains the main salvage procedure after unsuccessful thoracoscopy, as defined by the failure of lung expansion to the chest wall

#### Indication for thoracostomy/decortication

- Indicated for Patients with organized empyemas who cannot tolerate thoracotomy or have trapped lungs can undergo rib resection with open drainage
- Chronic empyemas with bronchopleural fistulas or chronic empyemas that are not amenable to surgery
- Critical ill and toxic patients with associated mediastinitis or bronchopleural fistulas who require mediastinal drainage or fistula closure.

#### For Malignant Effusions

Chest tube drainage, radiation, chemotherapy, surgical pleurectomy, pleuroperitoneal shunt, pleurodesis or decortication.

#### Note

- Emergent thoracentesis and/or chest tube placement is necessary in patients with pleural effusion with significant respiratory or cardiac decompensation
- Do consultation with a pulmonologist, interventional radiologist, or thoracic surgeon, depending on the location of the effusion and the clinical situation for patients not responding to treatment.

### **9.6.14 Respiratory Failure**

Respiratory failure is a clinical condition that happens when the respiratory system fails to maintain its main function, which is gas exchange, in which PaO<sub>2</sub> lower than 60 mmHg and/or PaCO<sub>2</sub> higher than 50 mmHg. Respiratory failure is classified according to blood gases abnormalities into type 1 and type 2.

**Hypoxemic respiratory failure** (type I): has a PaO<sub>2</sub> < 60 mmHg with normal or subnormal PaCO<sub>2</sub>. In this type, the gas exchange is impaired at the level of alveoli-capillary membrane. Examples of type I respiratory failures are carcinogenic or non-cardiogenic pulmonary edema and severe pneumonia.

**Hypercapnic respiratory failure** (type II): has a PaCO<sub>2</sub> > 50 mmHg. Hypoxemia is common, and it is due to respiratory pump failure

#### **Investigations**

- ABG
- FBP
- Creatine kinase
- ECHO
- ECG
- Troponin-I
- TSH
- CXR
- Electrolytes
- Creatinine and BUN
- AST/ALT/ALP/GGT, albumin and bilirubin total, direct
- PFT-if patient able to perform

#### **Non-pharmacological Treatment**

Noninvasive Ventilatory Support: Patients with mild-to-moderate acute respiratory failure.

#### **Mechanical Ventilation**

Refer to management of cardiogenic pulmonary edema and acute exacerbations of chronic obstructive pulmonary disease (COPD) in obstructive lung disease

# CHAPTER TEN

## GASTROINTESTINAL DISEASE CONDITIONS

### 10.1 Infections of Gastrointestinal Tract

#### 10.1.1 Amoebiasis

Amoebiasis is an infection caused by the protozoa organism *Entamoeba histolytica*, which can cause colitis and other extra-intestinal manifestations. The infection is primarily acquired through ingestion of contaminated food and water and occasionally can be acquired through oral-anal sexual practices.

#### Clinical presentation

- Bloody diarrhea
- Crampy abdominal pain
- Fever
- Weight loss
- Peritonitis in severe forms
- Evidence of motile trophozoites or cysts on saline wet mount from a stool specimen

#### Pharmacological Treatment

A: metronidazole (PO) 400–800mg 8hourly for 5days

OR

B: tinidazole (PO) 2g 24 hourly for 3days

#### 10.1.2 Amoebic Liver Abscess

It is the most frequent extra-intestinal manifestation of *Entamoeba histolytica* infection which results from the invasion of the portal venous system from the colon leading to inflammation and subsequently abscess formation particularly involving the right lobe of the liver.

#### Clinical presentation

- High grade fever, 39°C
- Right upper quadrant pain,
- Tender and enlarged liver
- Positive imaging evidence of liver abscess
- Serological evidence of *E. histolytica* antibodies or antigens.

#### Pharmacological Treatment

B: metronidazole (IV) 800mg 8hourly for 10days.

OR

B: tinidazole (PO) Adults: 2g once daily for 3days

#### Note

- Metronidazole and Tinidazole should not be given in the first trimester of pregnancy due to potential teratogenic effects.
- Should not be taken with alcohol due to disulfiram like effects

#### Surgery:

Abscess cavity (size >5 cm in diameter) not regressing despite 7days treatment should be aspirated.

#### 10.1.3. Giardiasis

It is the infestation of the upper small intestine caused by the flagellate protozoan *Giardia lamblia* (or *G. intestinalis*), cytopathic effects of which leads to malabsorption and diarrhea. It is more common in immune compromised individuals and is acquired through ingestion of contaminated water

#### Clinical presentation

- Crampy abdominal pain
- Chronic diarrhoea
- Steatorrhea
- Weight loss

## **Investigations**

- Evidence of *Giardia intestinalis trophozoites* or cysts on serial 3 samples of stool examination
- Serological evidence of *G. Intestinalis trophozoites* antigen or antibody
- Evidence of *G. Intestinalis* in duodenal aspirates or biopsy specimen.

## **Pharmacological Treatment**

**A:** metronidazole (PO) 400–800mg 8hourly for 5days

**OR**

**B:** tinidazole (PO) 2g once daily for 3days

### **10.1.4 Ascariasis**

It is a small intestinal infestation caused by *Ascaris lumbricoides* which leads to malnutrition, iron deficiency anaemia, impaired growth and cognition in susceptible hosts. It is most common infestation in children, and it is acquired through ingestion of contaminated food and water.

## **Clinical presentation**

- Chronic Diarrhea
- Steatorrhea
- Malnutrition
- Chronic Cough (Loffler's syndrome)
- Intestinal obstruction
- Obstructive jaundice

## **Investigations**

- Stool examination: evidence of ova or worms on wet mount

## **Pharmacological Treatment**

**A:** mebendazole (PO) 500mg stat or 100mg 12hourly for 3days.

**OR**

**A:** albendazole (PO) 400mg stat

### **10.1.5 Ancylostomiasis**

It is a hookworm disease caused by infestation of the small intestine with *Ancylostoma duodenale* or *Necator americanus* leading to anaemia and malnutrition.

## **Clinical presentation**

- Abdominal pains
- Chronic diarrhea
- Melena stool
- Weight loss
- Chronic cough (Loffler's syndrome) PLUS
- Evidence of ova or worms on wet mount stool examination
- Anaemia

## **Pharmacological Treatment**

**A:** mebendazole (PO) 500mg stat or 100mg 12hourly for 3days.

**OR**

**A:** albendazole (PO) 400mg stat

## **Note**

If persistent, give second course after 4 weeks. Iron replacement and nutritional supplementation (protein and vitamins) should be part of the management strategy. Albendazole is contraindicated in the first trimester of pregnancy

### **10.1.6 Strongyloidiasis**

Small intestinal infestation caused by *Strongyloides stercoralis* usually asymptomatic in immune competent adult but can lead to life-threatening infestation and disseminated strongyloidiasis in an immune-compromised host associated with high mortality rates

#### **Clinical presentation**

- Pruritic papulo-vesicular rash at the site of penetration or urticarial rash involving the perennal region extending to the buttocks, thighs and abdomen
- Chronic cough
- Colicky abdominal pains
- Chronic diarrhea and passage of mucus
- Weight loss
- Hyper-infection syndrome

#### **Investigations**

- Evidence of rhabditiform larva in wet mount stool examination with Serological evidence (ELISA) for anti-strongyloides antibody

#### **Pharmacological Treatment**

**A:** albendazole (PO) 400mg 12hourly for 3days (Repeat after 4 weeks if still positive stool findings)

**OR**

**A:** ivermectin (PO) 200 µg /kg 24hourly for 2days

#### **Note**

Give treatment for 10 days in case of disseminated/super infestation

### **10.1.7 Taeniasis**

Is a tapeworm disease acquired from eating raw or not-well cooked food? Can be due to *Taenia saginata* (beef tapeworm), *Taenia solium* (pork tapeworm), *Diphyllobothrium latum* (fish tapeworm) and *Hymenolepsis nana* (faecal oral contamination from human and dogs) leading to chronic malnutrition (Taeniasis) or multi-organ dissemination and dysfunction (Cysticercosis)

#### **Clinical presentation**

- Taeniasis
- Colicky abdominal pain
- Body Weakness
- Loss of or increased appetite
- Constipation or diarrhea
- Pruritus ani
- Hyperexcitability

#### **Investigations**

- Evidence of characteristic ova, proglottids or scolex in the wet mount stool examination

Cysticercosis - The cysticerci are most often located in subcutaneous and intermuscular tissues, followed by the eye and then the brain. The CNS is involved in 60-90% of patients i.e. Neurocysticercosis which may manifest as

#### **Convulsions and/or seizures:**

- Intracranial hypertension: headache, nausea, vomiting, vertigo, and papilledema.
- Personality and mental status changes (Neuropsychiatric changes)
- Behavioral changes and learning disabilities more marked in children and immunocompromised adults. PLUS
- Head CT scan OR Brain MRI

#### **Note**

Refer the patient to high centers for further investigation and expertise.

## **Pharmacological Treatment**

### **Taeniasis**

**A:** praziquantel (PO) 5–10mg/kg stat

**AND**

**A:** magnesium sulphate (PO) 5–10 g in a glass of water after 2hours

### **Cysticercosis (NCC)**

**A:** praziquantel (PO) 50mg/kg 24hourly for 21days

**OR**

**A:** albendazole (PO) 15mg/kg 24hourly for 30days.

**AND**

**B:** dexamethasone (IV) 4mg 12hourly can be given up to 7days.

**AND**

**A:** carbamazepine (PO) initially 200 mg 12-24hourly, increased slowly to 0.8–1.2 g 24hourly in divided doses

### **Note**

Hydrocephalus should be treated with surgical shunting. Ocular manifestation cysticercosis, should be referred to eye specialist

### **10.1.8 Echinococcosis**

It is a canine tape worm *Echinococcus Granulosus* which is transmitted by dogs, sheep and horses. Human infestation is through contamination of food or water causing visceral cysts (Hydatid Cyst Disease) particularly in the liver and lungs and is usually asymptomatic in susceptible host.

#### **Clinical presentation**

- Upper abdominal discomfort and pain, poor appetite,
- Upper abdominal mass swelling with enlarged liver.
- Cough with features of acute hypersensitivity reaction. (for ruptured cysts)
- Portal hypertension, biliary obstruction or Budd-Chiari syndrome (for complicated cases)

### **Pharmacological Treatment**

**A:** albendazole (PO) 400mg 12hourly for 3months

**OR**

**A:** mebendazole (PO) 500mg 12hourly for 3months

**Referral:** For symptomatic/ complicated cases refer to higher centres with management and expertise.

### **10.1.9 Schistosomiasis**

Parasitic disease caused by blood flukes (trematodes) of the genus *Schistosoma*. Common species found in Tanzania are *S. haematobium* responsible for urogenital schistosomiasis and *S. mansoni* responsible for intestinal schistosomiasis as a result of immune mediated reaction which leads to progressive inflammation and fibrosis of the urinary bladder or portal venous system respectively.

#### **Clinical presentation**

##### ***Schistosoma mansoni***

- Swimmer's itch or katayama fevers in acute infection phase.
- Colicky abdominal pains
- Diarrhoea and dysentery
- Anemia
- Hepatomegaly
- Portal hypertension with bleeding esophageal varices
- Decompensated liver disease

### **Schistosoma hematobium**

- Dysuria and terminal hematuria
- Hematospermia
- Obstructive uropathy  
(hydronephrosis, hydroureters)
- Glomerulonephritis and amyloidosis
- Bladder carcinoma
- Chronic kidney failure

### **Investigations**

- Laboratory evidence characteristic eggs in urine, (*S. Hematobium*) or in stool (*S. mansoni*, *S. japonicum*) examined by kato katz thick smear procedure or PCR assays of both urine and stool samples.

### **Pharmacological Treatment**

**A:** praziquantel (PO) 40mg/kg stat or in 2 divided doses

### **10.1.10 Typhoid and Paratyphoid**

It is an acute systemic disease resulting from infection by *Salmonella typhi* and *S. paratyphi*, serovar group A and B respectively. Infection is acquired through ingestion of contaminated food and water.

#### **Clinical presentation**

- Fever, severe headache, abdominal and muscle pains (myalgia)
- Delirium, obtundation, intestinal hemorrhage, bowel perforation,
- Sequela neuropsychiatric complications

#### **Investigations**

- Laboratory evidence of positive cultures from bone marrow aspirates; blood or stool done within 1 week of acute infection OR
- *Salmonella* stool antigen test
- Indirect fluorescent Vi antibody, ELISA for immunoglobulin M (IgM) and IgG antibodies to *S. Typhi* polysaccharide.

### **Pharmacological Treatment**

#### **Uncomplicated typhoid fever**

**A:** ciprofloxacin (PO) 500mg 12 hourly for 10-14days

**OR**

**B:** azithromycin (PO) Adult 500mg 24hourly for 7days

**OR**

**S:** cefixime 400mg (PO) 24hourly for 7-14days

#### **For complicated typhoid fever**

**C:** ciprofloxacin (IV) 200-400 mg 12hourly daily 7days

**OR**

**B:** ceftriaxone (IV) 1-2gm 24hourly 4-7days

#### **Note**

Definitive treatment of typhoid (enteric fever) is based on susceptibility. For patients with severe or complicated disease (e.g. systemic toxicity, depressed consciousness, prolonged fever, organ system dysfunction or other features that prompt hospitalization), initial therapy with a parenteral agent is appropriate.

### **10.1.11 Shigellosis**

Shigella organisms are a group of gram-negative, facultative intracellular bacteria pathogens. They are grouped into 4 species: *Shigella dysenteriae*, *Shigella flexneri*, *Shigella boydii*, and *Shigella sonnei*, also known as groups A, B, C, and D respectively. Shigellosis is spread by means of fecal-oral, by ingestion of contaminated food or water and leads to bacillary dysentery.

### **Clinical presentation**

- Acute abdominal cramping, high-grade fever, emesis and large-volume watery diarrhea
- Tenesmus, urgency, fecal incontinence, mucoid bloody diarrhea
- Severe headache, lethargy, meningismus, delirium, and convulsions
- Hemolytic uremic syndrome (HUS), microangiopathic hemolytic anemia, thrombocytopenia, and renal failure
- Profound dehydration and hypoglycemia

### **Investigations**

- Laboratory evidence of microscopic isolation of the bacteria from stool or rectal swabs specimens
- Stool culture for suspected cases in early course of infection
- An enzyme immunoassay (ELISA) for shiga toxin detection in stool for *S. dysenteriae* type I.

### **Pharmacological Treatment**

A: ciprofloxacin (PO) 500mg 12hourly for 5days

OR

A: erythromycin (PO) 500mg 6hourly for 5days.

## **10.1.12 Cholera**

For diagnostic criteria, investigations, prevention and treatment refer to under notifiable diseases.

## **10.2. Disorders of Gastrointestinal Tract**

### **10.2.1 Peptic Ulcer Disease**

Refers to acid related peptic ulceration involving the lower esophagus; stomach and duodenum as a result of active inflammation induced by acid –pepsin leading to disruption of the mucosal integrity causing local defect or excavation

#### **10.2.1.1 Gastroesophageal Reflux Disease (GERD)**

It is a disorder resulting from gastric acid-pepsin activity and other gastric contents reflux into the esophagus due to incompetent barriers at the gastroesophageal junction leading to active inflammation of the distal third of the esophagus (prolonged contact with acid can evolve to stricture)

### **Clinical presentation**

- Heartburn and regurgitation are cardinal symptoms.
- Odynophagia, dysphagia, weight loss and bleeding
- Chronic cough, laryngitis, pharyngitis
- Chronic bronchitis, asthma, COPD, pneumonia, chronic sinusitis and dental decay

### **Investigations**

- Endoscopic evidence mucosal ulceration
- Histological evidence of chronic active inflammation
- Positive finding with a gold standard 24-hours esophageal pH testing.

### **Pharmacological Treatment**

#### **Non-erosive, symptomatic**

A: omeprazole (PO) 20mg 24hourly for 8weeks

OR

S: esomeprazole (PO) 20mg-40mg 24hourly for 8weeks.

## **Erosive esophagitis**

**C:** pantoprazole (PO) 40mg 24hourly for 8-16weeks

For refractory cases acid suppression therapy may require continuation up to 6 months. Lifestyle modification and avoidance of triggers is important including avoidance of smoking, alcohol and NSAID use.

**Referral:** Refer to next level center with adequate expertise and facility for refractory cases or cases with alarming symptoms (red flags) such as bleeding, anemia, early satiety, progressive dysphagia or odynophagia, unexplained weight loss, recurrent vomiting or family history of gastrointestinal (GI) cancers, age  $\geq$  40 years.

### **10.2.1.2 Gastroduodenal Ulcers (PUD)**

This is a disorder resulting from breakdown of mucosal defense mechanisms against hydrochloric acid and proteolytic enzymes, most commonly secondary to *H. Pylori* infection or NSAID use.

#### **Clinical presentation**

- Burning epigastric abdominal pains,  
usually relieved by antacids.
- Anorexia, early satiety, bloating,
- Hematemesis or melena stools
- Weight loss

#### **Investigations**

- Endoscopic evidence of gastric or duodenal mucosal ulceration

#### **Pharmacological Treatment**

**A:** omeprazole (PO) 20mg 24hourly for 8weeks

**OR**

**C:** pantoprazole (PO) 40mg 24hourly for 8weeks

**OR**

**S:** esomeprazole (PO) 20mg 24hourly for 8weeks

**AND**

**A:** antiacid liquid (PO) 10-15ml 12hourly to 8hourly for 7-14days

#### **For bleeding PUD: refer to higher centers**

**C:** pantoprazole (IV) 80mg stat then 40mg 12hourly for 2-3days, then (PO) as above if bleeding stops

**OR**

**S:** esomeprazole (IV) 40mg 12hourly for 2-3days, then (PO) as above if bleeding stops

### **10.2.1.3 Helicobacter Pylori Related Peptic Ulcer Disease**

*Helicobacter pylori* is a ubiquitous organism that is present in about 50% of the global population. Chronic infection with *H pylori* causes atrophic and even metaplastic changes in the stomach, and it has a known association with peptic ulcer disease. The most common route of *H pylori* infection is either oral-to-oral or fecal-to-oral contact.

#### **Clinical presentation**

- As above in cap 10.2.1.1

#### **Investigations**

- Positive stool antigen test (Stop PPI 2 weeks before testing)
- Positive urease breath test
- Positive urease test on endoscopic biopsy sample
- Identification of the pathogen by histopathology examination

#### **Pharmacological Treatment**

Triple therapy is indicated for complete eradication of the organism

- A:** omeprazole (PO) 20mg 12hourly for 10-14days  
**AND**
- A:** amoxycillin (PO) 1000mg 12hourly 10-14days  
**AND**
- A:** metronidazole (PO) 400mg 12hourly for 10–14days

Alternatively

- C:** lansoprazole (PO) 30mg 12hourly for 10-14days  
**AND**
- C:** clarithromycin (PO) 500mg 12hourly 10-14days  
**AND**
- B:** tinidazole (PO) 500mg 12hourly for 14days  
**OR**

#### **Concomitant Therapy (all for 7 days)**

- A:** omeprazole (PO) 20mg 12hourly  
**AND**
- A:** amoxicillin (PO) 1000mg 12hourly  
**AND**
- A:** metronidazole (PO) 400mg 12hourly  
**AND**
- C:** clarithromycin (PO) 500mg 12hourly

#### **Treat with Bismuth-based therapy for H. pylori treatment failure**

- C:** pantoprazole (PO) 40mg 12 hourly 10-14days  
**OR**
- S:** esomeprazole (PO) 40mg 12hourly 10-14days  
**AND**
- S:** bismuth subsalicylate (PO) 525 mg 6hourly 10-14days  
**AND**
- A:** metronidazole (PO) 250 mg 6 hourly or 500 mg 8hourly 10-14days  
**AND**
- S:** tetracycline (PO) 500 mg 6hourly for 10-14days.

#### **Note**

*H.pylori* diagnostic tests should be repeated 5 weeks after the last dose of eradication therapy, and the PPI should be stopped 2weeks before testing the *H.pylori* stool antigen test to confirm eradication.

### **10.2.2 Ulcer Related Conditions**

#### **10.2.2.1 Non-ulcer Dyspepsia (Functional Dyspepsia, Indigestion)**

It is a chronic recurrent dyspeptic disorder characterized by upper abdominal symptoms, discomfort, pain, fullness, early satiety, bloating, burning epigastric pain syndrome and post prandial distress syndrome without any organic, systemic or metabolic disease to explain its presence.

#### **Clinical presentation**

- Dyspeptic symptoms present for last 3 months and onset at least months prior to diagnosis
- Bothersome abdominal discomfort post prandial fullness.
- Early satiety
- Epigastric pains
- Epigastric burning

#### **Investigations**

- Lack of evidence of structural disease by upper endoscopic examination.

#### **Pharmacological Treatment**

##### ***H. pylori* eradication (see under *H. pylori*)**

- A:** omeprazole (PO) 20mg 24hourly for 4-8weeks  
**OR**

**C:** pantoprazole (PO) 40mg 24hourly for 4-8weeks

**OR**

**S:** esomeprazole (PO) 40mg 24hourly for 4-8weeks

**AND**

**C:** metoclopramide (PO) 10mg 8hourly when required (bloating and nausea symptoms, delayed gastric emptying)

**OR**

**D:** domperidone (PO) 10mg 8hourly when required to alleviate bloating and nausea symptoms, delayed gastric emptying.

**AND**

**A:** amitriptyline (PO) 25mg at bedtime when required for refractory cases

#### **Note**

Presence of alarm features (see list above under GERD) warrant OGD.

#### **10.2.2.2 Gastritis**

This is an inflammatory mucosal response to injury from variety of agents and mechanisms including infections, drugs, alcohol, acute stress, radiation, allergy, acid and bile, ischemia or direct trauma. The inflammation may involve the entire stomach (pangastritis) or a region of the stomach (antral gastritis) while the severity of inflammation may be erosive or non-erosive.

#### **Clinical presentation**

- Nausea, vomiting, loss of appetite, belching, and bloating
- Acute abdominal pain or abdominal discomfort
- Fever, chills, and hiccups also may be present

#### **Investigations**

- Endoscopic evidence of gastric mucosal inflammation
- Histologic evidence of chronic active inflammation of biopsy specimen.

#### **Non-pharmacological Treatment**

- Reduce the use of drugs known to cause gastritis (e.g., NSAIDs, alcohol)
- Stop smoking
- Reduce fatty, spicy and deep-fried foods

#### **Pharmacological Treatment**

Triple therapy for H. pylori eradication if confirmed present.

Administer fluids and electrolytes as required, particularly if the patient is vomiting.

**C:** pantoprazole (IV) 40mg 6hourly 2-3days

**OR**

**S:** esomeprazole (IV) 40mg 12hourly 2-3days

**AND**

**C:** metoclopramide (IM) 10mg 12hourly when required (for cases presenting with intractable vomiting) in order to relieve symptoms.

#### **Switch to oral PPI once patient can tolerate oral intake.**

#### **Referral**

Refer to next level service with adequate expertise and facilities for complicated case with alarm features (anemia, vomiting blood and weight loss, see complete list under GERD above).

#### **10.2.3 Gastrointestinal (GI) Bleeding**

Intraluminal blood loss anywhere from the oropharynx to the anus. Classification: upper = above the ligament of Treitz; lower = below the ligament of Treitz "Severe" GIB: defined as having associated shock, orthostatic hypotension, fall in hematocrit by 6% (or decrease in Hb by 2 g/dL), or requiring transfusion  $\geq 2U$  PRBCs. Requires hospitalization.

### **10.2.3.1 Upper GI Bleeding (UGIB)**

PUD caused by *Helicobacter pylori* infection or NSAID use is the most common cause of nonvariceal UGI bleeding. Characteristic findings are hematemesis, melena, or (infrequently) bright-red blood per rectum or a high serum BUN/creatinine ratio. Slow and/or chronic bleeding is suggested by iron deficiency and is typical of erosive disease, tumor, esophageal ulcer, portal hypertensive gastropathy, Cameron lesion (erosions found within large hiatal hernias), and angiodysplasia.

**Table 10.1: Differential Diagnosis of Upper GI Bleeding**

<b>Presentation</b>	<b>Diagnosis</b>
Dyspepsia, <i>H. pylori</i> infection, NSAID use, anticoagulation, severe medical illness	Peptic ulcer disease
Stigmata of chronic liver disease, evidence of portal hypertension or risk factors for cirrhosis (alcohol use, viral hepatitis)	Variceal bleeding
History of heavy alcohol use and retching before hematemesis, hematemesis following weightlifting, or young woman with bulimia	Mallory-Weiss tear
Heartburn, regurgitation, and dysphagia; usually small-volume or occult bleeding	Esophagitis
Progressive dysphagia, weight loss, early satiety, or abdominal pain; usually small-volume or occult bleeding	Esophageal or gastric cancer
NSAID use, heavy alcohol intake, severe medical illness; usually small-volume or occult bleeding	Gastroduodenal erosions

#### **Initial management**

**Assess severity:** vital signs including orthostatic changes, JVP. Tachycardia (can be masked by βB use) suggests 10% volume loss, orthostatic hypotension 20% loss, shock >30% loss. After the patient is stabilized, upper endoscopy is required to document the source of bleeding. If upper endoscopy shows an ulcer, test for *H. pylori* infection.

**Resuscitation:** placement of 2 large-bore (18-gauge or larger) intravenous lines, volume replacement: NS or LR to achieve normal vital signs, urine output, and mental status.

#### **Pharmacological Treatment**

For variceal bleeding refer to (10.4.2.3 Bleeding Esophageal Varices)

For bleeding peptic ulcer disease

**C:** pantoprazole (IV) 40mg 12hourly for 2-3days

**OR**

**S:** esomeprazole (IV) 40mg 12hourly for 2-3days

#### **Note**

- Treat high-risk ulcers endoscopically (haemoclips, thermal therapy, or injection therapy) and continuous IV PPI infusion for 72 hours. Blood transfusion to target haemoglobin level of 7 g/dl Repeat endoscopic therapy for continued bleeding
- Surgery or interventional radiology if endoscopic therapy unsuccessful

#### **Laboratory Investigations**

- FBP, LFT, RFT.
- Abdominal ultrasound
- Viral hepatitis screening
- H. pylori* stool antigen

### **10.2.3.2 Lower gastrointestinal (GI) Bleeding**

Acute, painless LGI bleeding in older adult patients is usually due to colonic diverticula or angiodysplasia. Ten percent of rapid rectal bleeding has an UGI source.

Consider outpatient follow-up or early discharge when:

- patient age <60 years
- no hemodynamic instability
- no evidence of gross rectal bleeding
- identification of an obvious anorectal source of bleeding

**Table 10.2: Differential Diagnosis of Lower GI Bleeding**

Presentation	Diagnosis
Painless, self-limited, massive hematochezia	Diverticular bleeding (most common overall cause)
Chronic blood loss or acute painless hematochezia in an older adult patient	Angiodysplasia
Stool positive for occult blood in an asymptomatic patient	Colonic polyp or cancer
Risk factors for atherosclerosis and evidence of vascular disease in an older adult patient; typically, with LLQ abdominal pain	Ischemic colitis
Aortic stenosis	Angiodysplasia (Heyde Syndrome)
History of bloody diarrhea, tenesmus, abdominal pain, fever	IBD
Rapid UGI bleeding	Dieulafoy lesion (large, tortuous, submucosal arteriole)
Large hiatal hernia	Cameron lesion (mucosal erosions)
Recent liver or biliary procedure	Hemobilia
Necrotizing pancreatitis	Hemosuccus pancreaticus (bleeding from pancreas)
Aortic aneurysm repair	Aortoenteric fistula
Painless hematochezia in a young patient and normal upper endoscopy and colonoscopy	Meckel diverticulum
Mucocutaneous telangiectasias	Hereditary hemorrhagic telangiectasia

#### Note

- According to expert opinion, the blood transfusion threshold for patients with colonic bleeding is a haemoglobin value <9 g/dL (note this is different for the evidence-based threshold for UGI bleeding).
- If the patient is hemodynamically unstable, resuscitate the patient before diagnostic studies are performed. Most episodes of LGI bleeding resolve spontaneously.
- Colonoscopy is recommended early, usually within the first 48 hours of admission, and endoscopic therapy is used to control continued bleeding.
- If colonoscopy does not identify a discrete lesion or endoscopic therapy does not control the bleeding, interventional angiography or surgery may be indicated.
- Patients with angiodysplasia in the setting of AS (Heyde Syndrome) may benefit from valve replacement surgery.

#### **10.2.3.3 Bleeding of Obscure Origin**

Obscure GI bleeding is recurrent blood loss without an identified source of bleeding despite upper endoscopy and colonoscopy. Patients aged ≤50 years are more likely to have tumors (leiomyomas, carcinoid, adenocarcinoma, or lymphoma), Dieulafoylesion, or Crohn's disease. Older patients are more likely to have vascular lesions, such as angiodysplasia. Angiodysplasia is the most common cause of obscure GI bleeding overall (40% of all cases). Patients may present with either melena or hematochezia or positive fecal occult blood test (FOBT). The first step is to repeat upper endoscopy and/or colonoscopy, which is diagnostic in approximately 40% of cases.

For patients with obscure active GI bleeding

- nuclear studies (technetium 99m-labeled erythrocyte or sulfur colloid nuclear scan) first, followed by angiography
- if unrevealing, consider push enteroscopy or balloon-assisted enteroscopy (deep enteroscopy)

- surgery and intraoperative enteroscopy is a last diagnostic option

For patients with occult GI bleeding

- capsule endoscopy (first choice GIE 2015; 81:889) or deep enteroscopy
- if unrevealing, repeat endoscopic examinations (upper endoscopy, colonoscopy, capsule endoscopy), or deep enteroscopy

## 10.3 Diseases of the Intestine

### 10.3.1 Inflammatory Bowel Diseases

Inflammatory bowel disease (IBD) is an idiopathic disease involving an immune reaction of the body to its own intestinal tract. The 2 major types of IBD are ulcerative colitis (UC) and Crohn's disease (CD). Pathologically, ulcerative colitis is limited to the colon while Crohn's disease can involve any segment of the gastrointestinal (GI) tract from the mouth to the anus.

#### 10.3.1.1 Ulcerative Colitis (UC)

Inflammatory condition that involves the rectum and extends proximally to affect a variable extent of the colon up to the caecum

#### Clinical presentation

- Diarrhoea
- Rectal bleeding
- Tenesmus, passage of mucus
- Crampy abdominal pain
- Fevers and chills

#### Investigations

- Endoscopic evidence of diffuse and continuous colonic mucosal inflammation with friability and loss of mucosal vascularity characteristic cobble stone appearance.
- Histologic evidence of abnormal crypt architecture and superficial inflammation typical of UC.

#### Pharmacological Treatment

**D:** sulfasalazine (PO) 1000mg 6hourly a day for acute disease, reducing to 1000mg once daily for maintenance

**OR**

**S:** mesalazine (PO) 1.5g–4g/day in divided doses reduced to 0.75–2g g/day in divided doses for maintenance

**AND**

**A:** prednisolone (PO) 30–60mg 24hourly for severe, acute and extensive disease; tapering gradually after induction of remission within 8 weeks.

For severe disease flares give IV corticosteroids,

**D:** methylprednisolone (IV) 16-20mg 8hourly 5- 7days

If unresponsive (i.e. fewer stools, less bleeding) to IV corticosteroids for 5-7days, or acute complications give the following;

**S:** cyclosporine (IV) 2-4mg/kg 12hourly for 7days

**THEN** change to

**S:** azathioprine (PO) 1.5-2.5 mg/kg 24hourly for maintenance.

**OR**

**S:** infliximab (IV) 5 mg/kg at 0, 2, and 6weeks, then every 8weeks

#### Note

Complication of UC may present with massive haemorrhage, toxic mega colon, AND perforation with features of peritonitis necessitates hospitalization. Colonoscopy with random biopsy 8 years after diagnosis to evaluate for dysplasia, every 1-3 years thereafter based on risk factors. Use steroids only when the disease is confirmed and for induction of remission only.

### **10.3.1.2 Crohn's Disease**

Crohn's disease is an idiopathic, chronic, transmural inflammatory process of the bowel that often leads to fibrosis and obstructive symptoms and can affect any part of the gastrointestinal tract from the mouth to the anus.

#### **Clinical presentation**

- Abdominal pain, diarrhea, weight loss, anorexia and fever
- Gross rectal bleeding or acute hemorrhage is uncommon
- Anemia due to ileal disease involvement
- Small bowel obstruction, due to structuring
- Perianal disease associated with fistulization
- Gastroduodenal ulceration

#### **Investigations**

- Endoscopic evidence of rectal sparing skip lesions, cobble stoning with linear ulceration appearance with,
- Histological evidence of transmural disease, aphthous ulcers, and non-caseating granulomas

#### **Pharmacological Treatment**

**S:** methotrexate (PO) 7.5–15mg weekly

**OR**

**S:** azathioprine (PO) 50mg 24hourly for maintenance of remission.

**AND**

**A:** prednisolone (PO) 1–2mg/kg for induction of remission only (Taper in 8 weeks)

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 7–10days

**OR**

**A:** ciprofloxacin (PO) 500mg 12hourly for 7–10days – can be added in presence of perianal disease or evident septic complications.

#### **For severe disease flare or acute complications**

Patients who have had inadequate response to conventional therapy, also for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn disease.

**S:** infliximab (IV) 5 mg/kg at 0, 2, and 6 weeks, **THEN** every 8weeks thereafter

**AND**

**S:** azathioprine (PO) 1.5-2.5 mg/kg 24hourly

#### **Note**

Resuscitative and supportive management should be instituted as for UC section note above.

### **10.3.2 Pseudomembranous Colitis**

This condition is caused by *Clostridium difficile*, a gram positive, anaerobic bacterium causing antibiotic associated diarrhoea as a result of altered bacterial flora and release of enterotoxins.

#### **Clinical presentation**

- Bloody Diarrhea
- Abdominal cramps and tenderness
- Nausea, fever, dehydration

## Investigations

- Lower endoscopic pathognomonic findings of pseudomembranous yellowish plaques overlying the ulcerated and friable rectal sigmoid colon mucosa
- Laboratory evidence of *C. difficile* toxin A-B isolation from cultured stool samples (Toxin B) OR ELISA assay (Toxin A)

## Pharmacological Treatment

Stop the causative antibiotics

**A:** metronidazole (PO) 400mg 8hourly for 10-14days

**OR**

**S:** vancomycin (PO) Adults, 125mg–500mg 6hourly for 10-14days

### Note

Resuscitative and supportive management should be instituted as for UC above. Refer to next level of care with adequate expertise and facilities for all suspected cases for initial evaluation and management and cases presenting with acute complications such as Toxic mega colon

### 10.3.3 Radiation Proctitis

Radiation proctopathy is defined as epithelial damage to the rectum due to radiation that is associated with minimal or no inflammation. Acute radiation proctitis occurs during or within six weeks of radiation therapy. Chronic radiation proctitis has a more delayed onset. The first symptoms often occur 9 to 14 months following radiation exposure but can occur any time post-irradiation up to 30 years after exposure.

## Clinical presentation

- Symptoms of acute radiation proctitis include diarrhea, mucus discharge, urgency, tenesmus, and, uncommonly, bleeding.
- Patients with chronic radiation proctitis have similar symptoms as patients with acute radiation proctitis, but bleeding is usually more severe. In addition, patients may have symptoms of obstructed defecation due to strictures with constipation, rectal pain, urgency, and, rarely, fecal incontinence due to overflow.
- Concomitant injury to the genitourinary tract or small bowel may lead to fistulas, small bowel obstruction, small intestinal bacterial overgrowth, urethral stenosis, and cystitis
- Acute radiation proctitis should be suspected in patients with diarrhea, mucus discharge, urgency, tenesmus, or bleeding during or within six weeks of radiation therapy. Chronic radiation proctitis should be suspected in patients who develop these symptoms nine months or more after pelvic radiation exposure.

## Investigations

- Stool studies for *C. difficile* toxin, routine stool cultures (*Salmonella*, *Shigella*, *Campylobacter*, and *Yersinia*), *Escherichia coli* O157:H7. Microscopy for ova and parasites (three samples)
- Testing for STI, including *C. trachomatis*, *N. gonorrhoeae*, HSV, and *Treponema pallidum*,
- Endoscopy (colonoscopy and biopsy)
- Magnetic resonance imaging

## Pharmacological Treatment

**D:** sulfasalazine (PO) 3g 24hourly for 4weeks

**AND**

**S:** sucralfate enemas (rectal preparation) 2g 12hourly for 4weeks

### Note

Refer to higher level facility with expertise and experience in the management complications such as bleeding. Endoscopic therapy — Argon plasma coagulation (APC) for bleeding. Surgery — Surgery should be reserved for patients who have intractable symptoms such as a stricture, pain, bleeding, perforation, or a fistula

#### **10.3.4 Irritable Bowel Syndrome**

Irritable bowel syndrome (IBS) is a functional GI disorder characterized by abdominal pain and altered bowel habits in the absence of specific and unique organic pathology.

Four bowel patterns may be seen with IBS;

- I. IBS-D (diarrhea predominant)
- II. IBS-C (constipation predominant)
- III. IBS-M (mixed diarrhea and constipation)
- IV. IBS-U (unclassified; the symptoms cannot be categorized into one of the above three subtypes)

#### **Clinical presentation**

- Recurrent abdominal pains or discomfort at least 3 days per month in the last 3 months associated with two or more of the following
- Improvement with defecation
- Onset associated with a change in frequency of stools
- Onset associated with a change in form of stool
- Bloating or feeling of abdominal fullness

#### **Non-pharmacological Treatment**

- Counseling on compelling psycho –social factors, lifestyle modification, avoidance of trigger factors, and reassurance are corner stone of long-term management strategy. Plus, supportive therapies such as:
- High fiber diet and eating a healthy diet.

#### **Pharmacological Treatment**

**A:** hyoscine butyl bromide (PO) 10mg 6hourly when required

**OR**

**D:** mebeverine (PO) 135mg 8hourly when required

**AND**

**A:** amitriptyline (PO) 25mg nocte for one week then 50mg nocte week 2-4.

**AND**

**C:** lactulose (PO) 20mls 12hourly (when required for constipation)

**OR**

**A:** bisacodyl (PO) 5-15mg when required for constipation

For diarrheal predominant IBS

**B:** loperamide (PO) 4mg stat, for diarrhoea followed by 2mg 8hourly or after each unformed stool until diarrhoea is controlled.

#### **10.3.5 Diverticulosis**

Acquired herniations of colonic mucosa and submucosa in areas where vasa recta penetrate, thought to occur in setting of abnormal motility and increased intraluminal pressure.

#### **Clinical presentation**

Asymptomatic but 5–15% develop diverticular hemorrhage (see “GIB” above) and <5% diverticulitis

#### **10.3.6 Diverticulitis**

Retention of undigested food and bacteria in diverticulum leads to fecalith formation with obstruction which compromise diverticulum's blood supply, infection, perforation

**Uncomplicated:** microperforation leading to localized infection

**Complicated:** macroperforation leading to abscess, peritonitis, fistula, obstruction

#### **Clinical presentation**

- LLQ abdominal pain, fever, nausea, vomiting, constipation or diarrhea

- Physical findings range from LLQ tenderness and/or palpable mass to peritoneal signs and septic shock
- Differential diagnosis includes IBD, infectious colitis, PID, tubal pregnancy, cystitis, colorectal cancer

### **Investigations**

- Plain abdominal radiographs to rule out free air, ileus or obstruction
- Abdominal CT scan with contrast, to assess complicated disease (abscess, fistula)
- Colonoscopy contraindicated acutely as increases the risk of perforation; do 6–8 weeks after to rule out neoplasm

### **Pharmacological Treatment**

Mild: outpatient indicated if patient has little comorbidity and can tolerate oral intake

**A:** amoxicillin + clavulanate FDC (PO) 625mg 12hourly daily for 7–10days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 7–10days

**AND**

Liquid diet until clinical improvement

Alternatively

**A:** ciprofloxacin (PO) 500mg 12hourly daily for 7–10days

**OR**

**A:** metronidazole 400mg (PO) 8hourly for 7–10days

**AND**

Liquid diet until clinical improvement

For severe cases

**B:** ceftriaxone (IV) 1-2g 24hourly for 7-10days

**OR**

**S:** piperacillin + tazobactam (IV) 4.5gm 6-8hourly 7-10days (for severe/complicated cases)

**OR**

**S:** meropenem (IV) 1gm 8hourly 7-10days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 7-10days

### **Note**

- Abscesses >4 cm should be drained percutaneously or surgically.
- Surgery:** if progresses despite medical treatment, undrainable abscess, free perforation.
- After source control, 4days antibiotics may be enough.
- Resection for recurrent bouts of diverticulitis on a case-by-case basis.

### **10.3.7 Polyps and Adenomas**

Accumulation of mutations in colonic epithelial cell DNA affecting oncogenes and tumor suppressor genes which leads to tumor initiation (formation of adenoma) tumor progression (adenoma to carcinoma).

**Neoplastic polyps:** adenomas (tubular, villous, tubulovillous dysplasia), sessile serrated adenomas/polyps (concern for interval CRC), carcinomas.

**Non-neoplastic polyps:** hyperplastic, juvenile, Peutz-Jeghers, inflammatory.

### **Investigations**

Colonoscopy is gold standard

### **Note**

- Colonoscopy in all patients starting at age 50 years, then typically every 10years unless pathology found.
- If positive family history, start age 40, or 10 years before age of diagnosis in youngest family member, repeat every 5 years.

### **10.3.8 Hemorrhoids**

Hemorrhoid disease is due to enlargement or thrombosis of the veins in the external or internal hemorrhoidal plexus.

#### **Clinical presentation**

- Painless anal rectal piles
- Painless bleeding –post defecation
- Pain
- Pruritus
- Prolapse

#### **Investigations**

- Endoscopy (Anoscopy, or proctosigmoidoscopy) for evidence of characteristic anal rectal piles.

#### **Treatment**

- Depends on severity of the disease
- **Grade I hemorrhoids** are treated with conservative medical therapy and avoidance of nonsteroidal anti-inflammatory drugs (NSAIDs) and spicy or fatty foods
- **Grade II or III hemorrhoids** are initially treated with nonsurgical procedures (sclerotherapy, band ligation)
- Very symptomatic **grade III and grade IV hemorrhoids** are best treated with surgical hemorrhoidectomy

#### **Pharmacological Treatment**

**A:** benzyl benzoate 1.25%, bismuth oxide 0.875%, bismuth subgallate 2.25%, hydrocortisone acetate 0.25%, Peru balsam 1.875%, zinc oxide 10.75% (PR) suppository one or twice a day

**OR**

**S:** (Euphorbia prostrata extract 100mg + Calcium dobesilate 500mg) (PO) 24 hourly (chewable do not swallow)

**AND**

**S:** (Prednisolone hexanoate 1.3mg +Cinchocaine hydrochloride 1mg) Suppository 24 hourly 5-7days

### **10.3.9 Anal Fissures**

These are painful linear ulcers in the anal canal. Young and middle-aged adults most affected. Primary fissure occurs in the posterior midline. It can also be secondary to Crohn's disease, anal cancer, or infection such as syphilis, TB in which case they occur more lateral. Passage of hard stools is a common predisposition to primary fissures.

#### **Clinical presentation**

- Severe sharp pain during and after defecation with/out bright red bleeding.

#### **Investigations**

- Evidence of linear anal rectal ulceration on proctoscopy examination

#### **Non-Pharmacological Treatment**

- Ensure high fluid intake

#### **Pharmacological Treatment**

- Topical anesthetics and frequent seat baths can reduce sphincter spasm (should be offered before surgery)
- Use non stimulant osmotic laxatives

**Surgery:** Surgical sphincterotomy is definitive treatment.

### **10.3.10 Fistula in Ano**

Is a chronic abnormal communication lined by degree of granulation tissues which runs outward from mucosal lumen.

#### **Risk factors**

- Previous perianal abscess formation
- Chhorn's disease
- Diabetes mellitus
- Tuberculosis
- Trauma
- Radiotherapy
- Immunosuppression-HIV, malignancy

#### **Classifications of fistula in ano**

I.	Intersphincteric	III.	Transphincteric
II.	Suprasphincteric	IV.	Extra sphincteric

#### **Clinical presentation**

- Purulent or bloody discharges
- Pruritis ani
- History of anorectal abscess

#### **Investigations**

- Fistulography
- Endoanal USS
- Pelvic MRI-gold standard
- Surgical Treatment options
- Fistulotomy, Fistulectomy, Seton, Fibrin glue, anal fistula plug, Advancement flap

### **10.3.11 Appendicitis**

This is characterised by inflammation of the appendix, and usually requires urgent surgical intervention.

#### **Clinical presentation**

- Sudden peri-umbilical pain often migrating to the right iliac fossa.
- Nausea and vomiting
- Loss of appetite
- Fever
- Constipation or occasionally diarrhea.
- Bloated abdomen.
- Rebound tenderness
- guarding and rigidity.
- Right iliac fossa tenderness.
- Right iliac fossa rebound pain.
- Severe persistent abdominal pain.

#### **Investigations**

- FBP
- Urinalysis
- Pregnancy test in females
- LFT
- Lipase/amylase excludes pancreatitis
- Abdominal USS
- CT scan

#### **Complications**

- Perforation/peritonitis
- Appendicular abscess
- Appendicular mass

#### **Pharmacological management**

**B:** ceftriaxone (IV) 1g 12hourly for 5-7days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 5-7days

**AND**

**A:** diclofenac (IM) 75mg 8hourly for 3days

## 10.4 Pancreatitis

Pancreatitis is an inflammatory process in which pancreatic enzymes auto digest the pancreatic gland leading to functional and morphologic loss of the gland.

### 10.4.1 Acute Pancreatitis

It is due to sudden inflammation of the pancreas due to pancreatic enzymes auto digestion. Common risk factors which trigger the acute episode are presence of gallstones and alcohol intake.

#### Clinical presentation

- Severe, unremitting epigastric pain, radiating to the back
- Nausea and vomiting
- Signs of shock may be present
- Ileus is also common
- Local complications: inflammatory mass, obstructive jaundice, gastric outlet obstruction
- Systemic complication: sepsis, acute respiratory distress syndrome, acute renal failure

#### Investigations

- Raised Serum levels for lipase and amylase greater than 3 times the upper limit of normal ULN (Lipase is more specific and sensitive than amylase). And,
- Radiological (ultrasound, CT, MRI) evidence of inflamed and/or necrotizing pancreatitis.

#### Treatment

- Principles of management include supportive therapies.
- Intravascular volume expansion (colloids/crystalloid)
- Opiates analgesia usually required (follow WHO analgesic ladder)
- Enteral feeding, (only in absence of ileus) start within 72 hours
- Correction of electrolytes and metabolic deficit accordingly

#### Pharmacological Treatment

**B:** ceftriaxone (IV) 1g 12hourly for 7days

**OR**

**C:** ciprofloxacin (IV) 200-400mg 12hourly for 7days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 7days

**OR**

**S:** meropenem (IV) 1g 8hourly for 7days

#### Note

- Fever can be because of pancreatitis itself; antibiotics should be avoided before 7 days.  
**Pancreatic necrosis:** Nonviable pancreatic tissue. CT-guided FNA if infection suspected.  
**Sterile necrosis:** if asymptomatic, can be managed expectantly, no role for prophylactic antibiotics.  
**Infected necrosis:** high mortality. Treat with carbapenem or metronidazole plus fluoroquinolone
- If stable, defer drainage to >4 weeks. If symptomatic or unstable, percutaneous drainage and minimally invasive surgical debridement or endoscopic necrosectomy superior to open necrosectomy. ERCP + Sphincterotomy may be needed.

### 10.4.2 Chronic Pancreatitis

Chronic pancreatitis is long-term (chronic) inflammation of the pancreas that leads to permanent loss of function and morphology of the gland.

#### Clinical presentation

- Chronic upper abdominal pain associated with nausea, vomiting and loss of appetite.
- Malabsorption diarrhoea (exocrine pancreatic insufficiency (steatorrhoea))

- Recurrent attacks of pancreatitis weight loss
- Diabetes

### **Investigations**

- Radiological (Abdominal Ultrasonography/CT scan) evidence pancreatic calcification and atrophy.

### **Pharmacological Treatment**

Supportive therapies with analgesics in the following order;

**A:** paracetamol (PO) 1g 8hourly daily when required

**OR**

**B:** tramadol (PO) 50mg 12hourly when required for chronic pain relief.

**OR**

**C:** morphine (PO) 5-10mls 6hourly when required

If pain unresponsive to above medications

**ADD**

**A:** amitriptyline (PO) 25mg nocte when required for pain control

**OR**

**D:** pregabalin (PO) 75mg once daily when required for pain relief

### **Manage complications**

Pancreatic enzymes deficiency and steatorrhea

**S:** pancreatic (PO) 1–3tablet 24hourly to supplement digestive enzyme and improve food absorption.

### **Diabetes mellitus**

Refer to metabolic and endocrine disease conditions chapter

#### **Note**

- In patients with persistent or refractory pain look for a dilated pancreatic duct and intraductal calcifications. These patients may benefit from endoscopic stenting, lithotripsy, or surgical drainage (pancreatojejunostomy).

## **10.4 Disorders of The Liver and Biliary Tract**

### **10.4.1 Hepatitis**

This is the term referring to inflammation of the liver, which may result from various causes, both infectious (i.e. viral, bacterial, fungal, and parasitic organisms) and non-infectious e.g. alcohol, drugs, autoimmune and metabolic diseases; this section focuses on viral hepatitis and its sequels.

#### **10.4.1.1 Viral Hepatitis**

It is a systemic infection predominantly affecting the liver caused hepatotropic viral agents namely Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), HBV – associated delta agent or Hepatitis D virus (HDV), and Hepatitis E virus (HEV); in most cases leads to a self-limiting disease but can take a fulminant course and lead to hepatic failure or progress to chronic liver disease (HBV, HBV-HDV and HCV)

#### **Note**

For comprehensive management of viral hepatitis refer to the National Guidelines for Prevention and Management of Viral Hepatitis 2020.

#### **Hepatitis A Virus (HAV)**

HAV is the RNA virus from piconaviridae family under genus hepatovirus. It primarily infects the liver. The disease occurs sporadically or in epidemics and has an incubation period of 14- 28 days. The group most affected is aged between 5-14 years and adults are often infected by spread from children.

### **Clinical presentation**

Mild flulike symptoms of anorexia, nausea and vomiting, fatigue, malaise, low-grade fever (usually < 39.5°C), myalgia, and mild headache, dark urine appears first (bilirubinuria). Pale stool soon follows; Jaundice occurs in most adults. Abdominal pain itching (pruritus), Arthralgias and skin rash, (less frequent than the above symptoms).

### **Investigations**

Specific diagnosis involves serological detection of Hepatitis A specific immunoglobulins IgM or IgG antibodies in blood for acute and resolved infection respectively. Viral RNA detection through PCR is definitive and confirmatory specialized laboratory test. Other tests include FBP, LFT, RFT and tests for other viral hepatitis viruses (HBV±HDV, HCV, and HEV).

### **Treatment**

- Supportive management such as hydration, adequate feeding and avoidance of concomitant use of hepatotoxic medications including herbals is all that is required in mild infections. The disease resolves spontaneously in several weeks or months.
- Hospitalization is necessary in settings of acute liver failure. Therapy is aimed at maintaining fluid replacement, balanced nutritional feeding, relief of pains and fever including specific management for liver failure.

### **Hepatitis B Virus (HBV)**

New-onset hepatitis B infection that may or may not be icteric or symptomatic. Diagnosis is based on detection of hepatitis B surface antigen (HBsAg) and IgM antibodies to hepatitis B core antigen (anti-HBc). Recovery is accompanied by clearance of HBsAg with seroconversion to anti-HBs (antibodies to hepatitis B surface antigen), usually within 3 months.

### **Clinical presentation**

- Fever, anorexia, malaise, jaundice and abdominal pain
- Enlarged and tender liver
- Altered consciousness, coma (hepatic encephalopathy), and bleeding stigmata (in fulminant cases).

### **Investigations**

- Serological evidence of specific viral antigen/ core antibody tests (HBc IgM or HBc IgG); and biochemical alteration of liver transaminases (ALT, AST).

### **Treatment of Acute Viral Hepatitis B**

- No specific antiviral treatment is required.
- Offer supportive management and counselling.
- Offer a follow up plan at 4 or 6 weeks' intervals for a clinical and laboratory re assessment for evidence of symptoms recovery and biochemical remission.
- Re-test at 6 months to assess seroconversion status or progression to chronicity

### **Chronic Hepatitis B infection.**

Defined as persistence of hepatitis B surface antigen (HBsAg) for six months or more after acute infection with HBV.

### **Clinical presentation**

- Usually asymptomatic
- Right upper quadrant abdominal pains.
- Fatigue, malaise, anorexia, low grade fever; jaundice is frequent in severe disease.
- Ascites, variceal bleeding, encephalopathy, coagulopathy, and hypersplenism.
- Urticaria, arthritis, vasculitis, polyneuropathy, glomerulonephritis, thyroiditis

## **Investigations**

- HBsAg, HBsAb, HBeAg, HBeAb, HBV DNA PCR
- LFT, RFT, FBP, HIV,
- Alfa Feto Protein (AFP)
- Colour Doppler ultrasonography or duplex Doppler ultrasonography or real time ultrasonography.
- CT scan
- Fibroscan (if available)

## **Treatment of Chronic Hepatitis B infection**

### **Pre Treatment Considerations – Who to Treat:**

- Patient in chronic active/ Reactivation phase characterized by elevated liver enzymes ALT >2X ULN, HBeAg +ve, viral load >20,000.
- ALT > 2X ULN, HBeAg –ve, HBeAb –ve, viral load>2000(mutant strain).
- Patients with evidence of fibrosis development (APRI score >2)/cirrhosis should receive treatment irrespective of age, and viral loads.
- Adults aged > 30 years with three determinations of persistently abnormal ALT levels above ULN made at unspecific intervals during 6-12month period with DNA viral load > 20,000 IU/ml irrespective of HBeAg status.
- Patients co-infected with HIV

### **Pre Treatment Considerations – Who not treat:**

- Treatment should not be given to patients with persistently normal ALT levels and APRI score < 2 regardless of age and HBeAg status.
- Immunotolerant patients characterized by high viremia with normal liver chemistry, age less than 30 years old require no treatment. Re assess after 24weeks interval.
- Patient in latent or inactive phase characterized by low viremia, normal liver chemistry with or without HBeAg sero-conversion requires no treatment. Re assess after 2 weeks' intervals.

## **Pharmacological Treatment**

(For eligible adults with no contraindications to tenofovir)

**A:** tenofovir (TDF) (PO) 300mg 24hourly; for at least 48weeks;

### **Note**

- Re-asses at 24 weeks for evidence of biochemical and viral replication remission. (Normalization of ALT, viral suppression to undetected level and seroconversion to anti-HBe).
- Offer a consolidated TDF therapy for extended 48 weeks for patients with evidence of HBeAb sero-conversion and biochemical remission at the end of the first 48 weeks. For patients still with detectable viral load and or not yet seroconverted to HBeAb, continue with Tenofovir 300mg daily dose and reassess every 6 to 12 months for HBV DNA, HBeAg/Ab status
- Absolute Contraindications to Tenofovir in patients aged < 12 Years

### **OR**

**S:** entecavir in the following groups: Children and adolescents between age 2 to 18 years weighing between 10kg and 32kg

## **Adults with renal insufficiency (CrCl<49ml/min)**

### **Entecavir dose Considerations**

- Children age 2 to 18 years weighing between 10kg and 32kg - 0.5mg (PO) 24hourly
- Adults naive to nucleoside therapy (PO) 0.5mg 24hourly
- Adults with Lamivudine resistance/previous exposure; and decompensated cirrhosis - 1mg (PO)
- Adults with renal insufficiency (CrCl<49ml/min); dose should be adjusted according to calculated GFR

**A:** Tenofovir (PO) 300mg 24hourly for patients who have treatment failure with other Nucleotides analogues with low resistance barrier (i.e. Lamivudine) **OR** Interferon based therapy.

**Note**

- Lamivudine should not be prioritized due to their low resistance barrier. Interferon based therapy is not recommended in our setting due to undesirable side effects, route of administration and high cost.

**When to Stop Treatment**

- Patient who has been put on Nucleotides analogues therapy without evidence of cirrhosis or APRI< 2 should be given a follow up plan.
- Patients who are HBeAb sero-converted after 48 weeks of consolidation therapy, with persistently normal ALT and undetectable DNA levels should stop treatment and monitored closely
- Patients with evidence of HBsAb sero-conversion after completing consolidated therapy regardless of their DNA and HBeAg status should stop treatment.
- Treatment in patient with Liver cirrhosis or significant Fibrosis is indefinitely

**Monitoring and evaluation of therapeutic response and toxicity.**

- HBsAg, HBeAb, HBeAg, HBV DNA, AFP, ALT should be monitored pre, during, and post treatment patients. PLUS (Fibrosis assessment by APRI scores) at 24/ 48weeks interval
- Renal functions in adults and growth development in children should be monitored annually for renal toxicity for patient on Tenofovir and Entecavir respectively.
- Abdominal Ultrasound (AUS) and Alpha Feto Protein (AFP) should be done at 24- 48 weeks' interval for HCC surveillance.

**Note**

Screening all close contacts is important. All at risk individuals eg. Healthcare workers, men who have sex with men, patients on hemodialysis, prisoners, children born to mothers with HBV and patients requiring multiple transfusions, patients with non-B viral hepatitis should be tested for HBV and vaccinated if found negative for HBsAg and no evidence of natural immunity to HBV.

**HBV in Pregnancy**

All Infants and Neonates should have mandatory vaccination according to the recommended National EPI schedule. Neonates born to mothers infected with HBV and HBeAg positive, should receive at birth dose of hepatitis B immunoglobulin (HBIG) and HBV Vaccine, and then follow up with EPI program schedule at 6weeks. During pregnancy, prevention of HBV transmission from mother to childshould follow similar protocols as per adults with HBV infection.HBsAg positive pregnant mothers with VL >200,000 IU/ml should receive TDF at 3<sup>rd</sup> trimester until 6months post-natal period.

**Pharmacological Treatment**

- First dose for the infant: Hepatitis B vaccine born to HBsAg-negative mothers
- Medically stable infants weighing ≥2,000 grams: 0.5 mL (IM) within 24h of birth
- Preterm infants weighing <2,000 g: 0.5 mL (IM) 1 month after birth or at hospital discharge

First dose for the infant: Hepatitis B vaccine born to HBsAg-positive mothers

**B:** hepatitis B vaccine (HBV) 0.5 mL within 12hours of birth

**AND**

**S:** hepatitis B immune globulin (HBIG) (IM) 0.5 mL within 12hours of birth

**Note**

- Mother's HBsAg status unknown: 0.5 mL IM within 12 hour of birth **AND** HBIG 0.5ml(IM); if newborn wt <2 kg, determine mother's HBsAg status as soon as possible and, if she is HBsAg-positive, also administer HBIG for infants weighing 2 kg or more (no later than age 1 week)

**For the HBV positive pregnant mother**

**A:** tenofovir (PO) 300mg 24hourly (from third trimester to 6 months post-delivery for the mother)

**Post exposure prophylaxis (PEP)**

HBIG and HBV vaccine should be given to individuals who are HBsAg negative exposed to HBsAg positive focus within 24hours followed by active standard schedule to complete 3 doses.

**S:** hepatitis B immune globulin (HBIG) (IM) 0.06 mL/kg once

**AND**

**B:** hepatitis B vaccine (HBV) (IM) 1 mL (20 mcg) at 0, 1, and 6months

**Note:**

- HBIG and HBV Vaccine should be given at different intramuscular sites PEP should be given in <24hours, may not be effective after 72hours of exposure.

**10.4.2.3 Hepatitis C virus (HCV)**

Hepatitis C virus (HCV) is a small enveloped RNA virus and a member of the family Flaviviridae. HCV comprises six genotypes and hundreds of subtypes with variable geographical distribution and bears significance in determining the rate of liver disease progression, development of HCC and specific therapeutic responses.

**Clinical presentation**

- Initial symptoms of HCV are often extrahepatic, most commonly involving the joints, muscle, and skin.
- Arthralgias,
- Paresthesias,
- Myalgias,
- Pruritus,
- Sicca syndrome.
- Sensory neuropathy

Symptoms characteristic of complications from advanced or decompensated liver disease are related to synthetic dysfunction and portal hypertension, such as the following:

- Mental status changes (hepatic encephalopathy), Ankle edema and abdominal distention (ascites), Hematemesis or melena (variceal bleeding)

Signs in patients with decompensated liver disease include the following:

- Hand signs:** Palmar erythema, Dupuytren contracture, asterixis, leukonychia, clubbing
- Head signs:** Icteric sclera, temporal muscle wasting, enlarged parotid gland, cyanosis
- Fetor hepaticus, Gynecomastia, small testes
- Abdominal signs:** Paraumbilical hernia, ascites, caput medusae, hepatosplenomegaly, abdominal bruit, Ankle edema, **Scant body hair**, **Skin signs:** Spider nevi, petechiae, excoriations due to pruritus

Other common extrahepatic manifestations include the following:

- Cryoglobulinemia, Membranoproliferative glomerulonephritis, Idiopathic thrombocytopenic purpura, Lichen planus, Keratoconjunctivitis sicca, Raynaud syndrome, Sjögren syndrome
- Porphyria cutanea tarda, Necrotizing cutaneous vasculitis

## **Investigations**

General baseline studies in patients with suspected HCV include the following:

- FBP, LFT, RFT TSH, T3
- Screening tests for coinfection with HIV or HBV
- Screening for alcohol abuse, drug abuse, or depression
- Pregnancy testing

Tests for detecting HCV infection include the following:

- Hepatitis C antibody testing:
- Qualitative and quantitative assays for HCV RNA PCR
- HCV genotyping
- Serologic testing (essential mixed cryoglobulinemia is a common finding)

## **Treatment**

Use pangenotypic drugs which are efficacious, safe and cost-effective.

### **Who to treat**

- Confirmed cases of Hepatitis C irrespective of clinical stage of the liver disease
- Patients with HCC who are eligible for liver transplant if feasible.
- Liver transplant patients if MELD score is < 18 (pre transplant) or >18 (post-transplant)

### **Who not to treat**

- HCC patients who are not eligible for liver transplant.
- Patient with limited life expectancy due to ESLD (by MELD score or Child-Pugh), or non-hepatic related comorbidities.

## **Pharmacological Treatment**

All individuals diagnosed with HCV infection who are  $\geq$  12 years old are eligible for treatment children (<12 years old), the treatment should be deferred until they reach that age.

**S:** ledipasvir (PO) 90mg 24hourly for 12-24weeks

**AND**

**S:** sofosbuvir (PO) 400mg 24hourly for 12-24weeks

**AND**

**S:** ribavirin (PO) given in two divided doses \* $<75\text{kg}$  of Body weight = $1\text{g/day}$ ;  $>75\text{Kg}$  of Body weight = $1.2\text{g/day}$  for 12weeks (in treatment naive patients) OR for 24 weeks (in treatment experienced patients) for genotypes 1, 4, 5 & 6.

**OR**

**S:** sofosbuvir (PO) 400mg daily **AND** ledipasvir (PO) 90mg daily **AND** ribavirin if a patient has been previously exposed to other antivirals.

### **Note**

- Due to complexity and variability of HCV management, care and treatment should be done at the tertiary level facility
- Ribavirin is contraindicated in patients with anaemia ( $\text{HB} < 8.5\text{g/dL}$ ), and the dose should be reduced if  $\text{HB} < 10\text{g/dL}$   
Sofosbuvir is contraindicated if  $\text{eGFR} < 30\text{ml/min}/1.73\text{m}^2$

## **When to stop medications**

- Ribavirin regimen should be stopped if patients' HB drops to  $< 8.5\text{g/dl}$  during follow up schedules.
- If there's adverse drug reaction
- When there are ALT flares or massively increased ALT ( $>10 \times \text{UNL}$ )
- If there's evidence of drug to drug interactions- consider switching with medication with a less interacting potential

## Clinical monitoring and follow up

- Assess treatment adherence, tolerance and toxicity at 4 weeks after treatment initiation.
- Treatment toxicity
- Stop Ribavirin if HB drops to <8.5
- Stop all DAAs if ALT >10 X ULN and other causes have been ruled out
- Stop Sofosbuvir if eGFR drops to < 30ml/min/1.73m<sup>2</sup>

### 10.4.2.4 Hepatitis D Virus

Hepatitis D virus (HDV) is a defective RNA virus belonging to genus of delta virus that requires the helper function of Hepatitis B (HBV) for virion assembly, release and transmission, and therefore the infection does not occur in the absence of hepatitis B virus. The routes of HDV transmission are similar for HBV the most important being sexually, percutaneous or parenteral exposure to blood or blood products.

#### Investigations

Serology assays for HDV immunoglobulin titres for IgM and IgG are diagnostic for acute and post exposure/chronic infections respectively. Real time PCR for HDV RNA is confirmatory.

#### Treatment

There is no specific treatment for acute or chronic HDV infection.

#### Note

The more risk population includes health care workers, transfusion recipients and haemophiliacs, PWID, and immigrants of endemic areas. Nucleotide sequences of HDV obtained worldwide indicates the existence of eight genotypes, with genotype 1 being detected worldwide. HDV Antiviral nucleotide analogues for HBV have no or limited effect on HDV replication and Pegylated interferon alpha is the only drug effective against HDV now and more than one year of therapy may be necessary as most of patients relapses after discontinuation of therapy.

### 10.4.2.5 Hepatitis E Virus

Hepatitis E virus (HEV) belongs is a RNA virus belonging from a family *Hepadna viridae* under Genus *Hepevirus* and acute liver infection. The virus has at least 4 different types: genotypes 1, 2, 3 and 4. Genotypes 1 and 2 have been found only in humans. Genotype 3 and 4 viruses circulate in several animals (including pigs, wild boars, and deer) without causing any disease, and occasionally infect humans.

#### Clinical presentation

Prodromal-phase symptoms include the following:

- Myalgia, Arthralgia, Fever with mild temperature elevations
- Anorexia, Nausea/vomiting, Weight loss. Dehydration, Right upper quadrant pain

Icteric-phase symptoms may last days to several weeks and include the following:

- Jaundice, Dark urine, Light-colored stool, Pruritus

Other features include the following

- Malaise (most common), Arthritis, Pancreatitis
- Aplastic anemia, Thrombocytopenia
- Neurologic symptoms of polyradiculopathy, Guillain–Barré syndrome, Bell palsy, peripheral neuropathy, ataxia, and mental confusion
- Membranoproliferative glomerulonephritis and membranous glomerulonephritis

#### Investigations

Serology assays for HEV immunoglobulin titres for IgM and IgG are diagnostic for acute and post exposure/chronic infections respectively. Real time PCR for HEV RNA in serum and particularly in stool is confirmatory.

## Treatment

There is no specific treatment for cure or reversing the course of acute hepatitis E. The disease is usually self-limiting; hospitalization is generally not required except for patients with fulminant hepatitis or for symptomatic pregnant women where severity of infection is usually high and associated with high rates of fetal loss and mortality especially in third trimester.

### Note

- The virus is shed in the stools of infected persons and enters the human body through the intestine. It is transmitted mainly through contaminated drinking water. Usually the infection is self-limiting and resolves within 2–6 weeks. Rarely the infection can lead to fulminant hepatitis with acute liver failure.
- The virus causes sporadic cases and major epidemics of viral hepatitis and occurs in resource poor population with unhygienic conditions and through ingestion of contaminated water and food.

## 10.4.2 Portal Hypertension

This is high blood pressure in the hepatic portal system which includes the portal veins and its branches which drains from most of the intestines to the liver. It is indicated when the hepatic venous pressure gradient exceeds 7mmHg, while liver cirrhosis remains the most common cause which in our local setting is commonly caused by chronic viral hepatitis followed by heavy alcohol intake.

### Clinical presentation

- Ascites, Splenomegaly
- Esophageal varices, and hematemesis
- Swollen veins of the anterior abdomen (caput medusa) and hemorrhoids

### Investigations

- Radiological evidence of shrunken liver, with typical features of cirrhosis.

## 10.4.2.1 Ascites

Ascites is the pathologic accumulation of fluid in the peritoneal cavity, and its most common cause is cirrhosis.

### Pharmacological Treatment

**C:** spironolactone (PO) 50mg – 400mg 24hourly incrementally till ascites resolves

**OR**

**S:** eplerenone (PO) 50mg 24hourly

**AND**

**B:** furosemide (PO) 40mg–160 mg 24hourly or in divided doses incrementally till ascites resolves

**AND**

**A:** propranolol (PO) 40mg–160mg 12hourly daily incrementally target heart rate 55-60bpm.

**OR**

**C:** carvedilol (PO) 6.25mg 24hourly, increase to 6.25mg (PO) 12hourly unless persistent arterial hypertension, SBP should not decrease <90mmHg.

**AND**

**S:** albumin 25% (IV) – in refractory ascites and large volume paracentesis. Give 25g stat, repeat at 15–30min Interval at Max Dose of 250g/48hourly

### Note

- Consider discounting βB if SBP <90 or MAP ≤82 mmHg, serum Na <120 mEq/L, AKI, HRS, SBP, sepsis, severe alcoholic hepatitis, poor follow-up.
- Large-volume paracenteses (LVP; >5 L fluid removal): give 6–8g albumin per L fluid removed (above 5 L) as colloid replacement is associated with decreased risk of post-paracentesis circulatory dysfunction and possibly decreased mortality.

#### **10.4.2.2 Spontaneous Bacterial Peritonitis**

Spontaneous bacterial peritonitis is an acute bacterial infection of ascitic fluid in the absence of a contagious cause of infection (e.g., intestinal perforation or abscess)

##### **Clinical presentation**

- Fever and chills
- Abdominal pain or discomfort
- Worsening or unexplained encephalopathy
- Diarrhea
- Ascites that does not improve following administration of diuretic medication
- Worsening or new-onset renal failure
- Ileus

##### **Investigations**

Diagnosis of Spontaneous bacterial peritonitis is based on the demonstration of an absolute number of polymorphonuclear cells in ascitic fluid equal to or greater than 250/mm<sup>3</sup>

##### **Pharmacological treatment**

###### **Community Acquired Spontaneous bacterial peritonitis**

**B:** ceftriaxone (IV) 1g 12-24 hourly for 5- 10days

**OR**

**B:** amoxicillin-clavulanic acid (FDC) (IV) 1-2g 6-8hours for 5-10days

**OR**

**C:** ciprofloxacin (IV) 200mg 12hourly for 5–10days

**AND**

**S:** administration of albumin dose is 1.5 g/kg on day 1 and 1 g/kg on day 3

###### **Nosocomial Spontaneous bacterial peritonitis Treatment**

**S:** meropenem (IV) 1gm 8hourly for 5-7days

##### **Spontaneous bacterial peritonitis prophylaxis**

Prophylaxis should be continuous until the disappearance of ascites (i.e., patients with alcoholic hepatitis), death, or transplant.

**A:** ciprofloxacin (PO) 400mg 24hourly for 10-14days

**OR**

**A:** co-trimoxazole (PO) 960mg 24hourly for 10-14days

#### **10.4.2.3 Bleeding Esophageal Varices**

Esophageal varices are collateral veins within the wall of the esophagus that project directly into the lumen. Acute variceal bleeding is a fatal complication in patients with liver cirrhosis. In patients with decompensated liver cirrhosis accompanied by ascites or hepatic encephalopathy, acute variceal bleeding is associated with a high mortality rate.

##### **Pharmacological Treatment**

**S:** octreotide (SC) 50–100µg 8hourly for 3days (infusion 50µg/hour for 72hours up to 5days)

**OR**

**S:** terlipressin: Adult (body weight up to 50 kg): Initially 2 mg every 4 hours until bleeding controlled, then reduced to 1 mg every 4 hours if required, maximum duration 48 hours. Adult (body weight 50 kg and above): Initially 2 mg every 4 hours until bleeding controlled, reduced if not tolerated to 1 mg every 4 hours, maximum duration 48 hours

**AND**

Band ligation of bleeding esophageal varices (EVL); 3 – 6 shoots per session.

**OR**

Sclerotherapy (Histo Acryl Glue Inj. 5 %;( mixed with Lipiodol at a ratio 1:1) Ethanolamine oleate 5%); given 2 -5ml per varix up to 20ml per session.

**AND**

**B:** ceftriaxone (IV) 1g 24hourly for 7days

**Note**

Blood transfusion (PRBC, PLT concentrates and FFP) when required.

**10.4.2.4 Hepatic Encephalopathy (HE)**

Hepatic encephalopathy (HE) is defined as “a condition which reflects a spectrum of neuropsychiatric abnormalities seen in patients with liver dysfunction after exclusion of other known brain disease.”

**Clinical presentation****Stage      Symptoms**

- |     |   |
|-----|---|
| I   | Mild confusion, agitation, irritability, sleep disturbance, decreased attention |
| II  | Lethargy, disorientation, inappropriate behavior, drowsiness                    |
| III | Somnolent but arousable, slurred speech, confused, aggressive                   |
| IV  | Coma  |

**Pharmacological Treatment**

**S:** L-Ornithine L-Aspartate (IV) 10g 8hourly daily for 3-5days

**THEN**

**S:** L-Ornithine L-Aspartate (PO) 9g 24hourly in divided doses for 4–12weeks

**AND**

**C:** lactulose solution (PO) for bowel cleansing when required

Episode of HE (grade 2 or higher)—**enemas:**

**A:** 0.9% sodium chloride 300mL in 1000mL water 2hourly until there is clinical improvement

Episode of HE (able to tolerate oral administration)—**(PO):** 45mL every hour until there is bowel movement and clinical improvement

Outpatient therapy: 15-45mL 8-12hourly until there are 2-3 bowel movements per day

**AND**

**A:** metronidazole (PO) 400mg 8 hourly for 7days

**AND**

**B:** ceftriaxone (IV) 1g 12 hourly for 7days (if evidence of spontaneous bacterial peritonitis)

Fluid deficit correction and electrolytes replacements as appropriate (screen for and correct all precipitants of HE as shown in the table below).

**Table 10.2: Precipitants of HE**

Hyponatremia	Vomiting
Gastrointestinal bleeding	Diarrhea
Infection	Sedative drugs (narcotics, sleep aids, antihistaminics)
Surgery	Alkalosis
Dehydration	Azotemia
Fluid restriction	Hypokalemia
Diuretics	Excessive protein intake
Excessive paracentesis	Constipation

**10.4.2.5 Hepatorenal Syndrome**

Hepatorenal syndrome (HRS) is the development of renal failure in patients with advanced chronic liver disease and, occasionally, fulminant hepatitis, who have portal hypertension and ascites.

**Table 10.3: Pharmacological treatment**

Vasoconstrictor		Recommended Dosage
<b>S:</b> terlipressin <b>OR</b>	Bolus	Initially 0.5 mg (IV) 4-6hourly. If no response by day 3 can increase the dosage to 1mg 4-6hourly. Maximum dosage is 2mg 4-6hourly. Maximum duration 14days.
	Continuous infusion	Initially 2mg/day. If no response by Day 3, can increase the dosage to 4mg/day. Maximum dosage is 12mg/day. Maximum duration 14days.
<b>S:</b> norepinephrine	Continuous infusion	0.5-3mg/hour continuously to achieve an increase in mean arterial pressure of 10 mmHg. Treatment is to be continued until serum creatinine concentration is < 1.5mg/dL, or < 133µmol/L.
<b>S:</b> Albumin must be given concomitantly with any of the vasoconstrictors at a dosage of 20-40 g/day.		

### 10.4.3 Biliary Tract Diseases

Cholestasis is a pathologic state of reduced bile formation or flow which can be hepatocellular (Intrahepatic), where an impairment of bile formation occurs or ductular (extra hepatic), where impedance to bile flow occurs after it is formed. Intrahepatic causes of cholestasis include viral hepatitis, alcohol, primary biliary cirrhosis, drug toxicity, Hodgkin's lymphoma and pregnancy. Extrahepatic causes include choledocholithiasis, carcinoma, and ascariasis of the biliary tree.

#### Clinical presentation

- Jaundice,
- Dark urine,
- Pale stools, and
- Generalized body itching/pruritis.

#### Investigations

- Laboratory evidence of elevated serum levels of total bilirubin, direct bilirubin, alkaline phosphatase, gamma-glutamyl transferase, and transaminases. WITH
- Supporting radiological evidence of dilated intra or extra hepatic biliary radicles.

#### Pharmacological Treatment

##### Definitive treatment:

Identify and treat specific cause

##### Supportive treatment:

**S:** cholestyramine (PO) 4–16g/day

**OR**

**S:** ursodeoxycholic acid (PO) 20–30 mg/kg/day

#### Note

- Surgical intervention is indicated for extra hepatic cholestasis.

### 10.4.3.1 Cholelithiasis

Cholelithiasis involves the presence of gallstones which are concretions that form in the biliary tract, usually in the gallbladder. Choledocholithiasis refers to the presence of one or more gallstones in the common bile duct (CBD). Treatment of gallstones depends on the stage of disease.

#### Clinical presentation

- Asymptomatic in majority of patients.
- Biliary pain (episodic RUQ or epigastric pain), pain radiating to scapula;
- Pain precipitated by fatty foods; nausea

- Physical exam: afebrile, and/or RUQ tenderness or epigastric pain
- Nonspecific symptoms (eg, indigestion, dyspepsia, belching, or bloating)

### **Investigations**

- Full Blood count
- Liver function panel
- Pancreatic enzymes (Amylase, Lipase)
- Abdominal radiography (upright and supine) – to exclude other causes of abdominal pain
- Ultrasonography
- CT scan –superior for demonstrating stones in the distal CBD
- MRI with MRCP
- Scintigraphy (HIDA) scans
- Endoscopic retrograde cholangiopancreatography (ERCP)
- Percutaneous transhepatic cholangiography (PTC)

### **Complications**

- Cholecystitis
- Choledocholithiasis leading to cholangitis or gallstone pancreatitis
- Mirizzi syndrome
- Cholecystenteric fistula stone erodes through gallbladder into bowel
- Gallstone ileus: SBO (usually at term ileum) due to stone in intestine that passed through fistula
- Gallbladder carcinoma

### **Non-pharmacological Treatment**

- Asymptomatic gallstones – Expectant management
- Symptomatic gallstones – definitive surgical intervention (cholecystectomy)

### **Pharmacological Treatment**

**A:** paracetamol (PO) 1g 8hourly for 5days

**OR**

**A:** ibuprofen (PO) 400mg 4-6hourly for 3-5days

**OR**

**B:** tramadol (PO) 50mg 12hourly for 3-5days

**AND**

**S:** ursodeoxycholic acid 8-10mg/kg/day divided once to three times up to 6months

### **Note**

Cholecystectomy (open or laparoscopic) for asymptomatic gallstones may be indicated in the following:

- Those with large (>2 cm) gallstones
- Nonfunctional or calcified (porcelain) gallbladder on imaging studies and at high risk of gallbladder carcinoma
- Those with spinal cord injuries or sensory neuropathies affecting the abdomen
- Sickle cell anemia patients- difficult to distinguish between painful crisis and cholecystitis
- Cholecystectomy, Cholecystectomy, Endoscopic sphincterotomy, Extracorporeal shockwave lithotripsy

### **10.4.3.2 Choledocholithiasis**

Gallstone lodged in common bile duct (CBD). Occurs in some of patients with gallbladder stones; can form de novo in CBD.

### **Clinical presentation**

- Asymptomatic
- RUQ pain,
- Epigastric pain due to obstruction of bile flow which leads to increase in CBD pressure,
- Jaundice,
- Pruritus,
- Nausea.

## **Investigations**

- LFT,
- Amylase
- Lipase.
- Abdominal (RUQ) Ultrasound
- ERCP, if ERCP unavailable or unsuccessful  
EUS/MRCP

## **Non-pharmacological Treatment**

ERCP & papillotomy w/ stone extraction ( $\pm$  lithotripsy)

Cholecystectomy typically within 6 weeks unless contraindication

## **Pharmacological Treatment**

S: cholestyramine (PO) 4-8g 12hourly when required for itching.

## **Complications**

Cholangitis, cholecystitis, pancreatitis, stricture

### **10.4.3.3 Cholecystitis**

Cholecystitis is inflammation of the gallbladder that occurs most commonly because of an obstruction of the cystic duct by gallstones (stone impaction in cystic duct leads to inflammation behind obstruction causing GB swelling and secondary infection of biliary fluid).

**Acalculous cholecystitis:** Occurs in critically ill. GB stasis and ischemia (without cholelithiasis) leading to necroinflammation.

## **Clinical presentation**

- RUQ/epigastric pain, radiating to right shoulder/back, nausea, vomiting, fever
- Signs of peritoneal irritation may be present
- Patients with acalculous cholecystitis may present with fever and sepsis alone
- RUQ tenderness, Murphy's sign, palpable gallbladder, jaundice
- The absence of physical findings does not rule out the diagnosis of cholecystitis.

## **Investigations**

- FBP, LFT, amylase, lipase
- Ultrasonography RUQ ultrasound: high Sensitivity and specificity for stones but need specific signs of cholecystitis: GB wall thickening  $>4$  mm, pericholecystic fluid and a sonographic Murphy's sign
- Radiography
- Computed tomography (CT)
- Magnetic resonance imaging (MRI)
- Hepatobiliary scintigraphy (HIDA)
- Endoscopic retrograde cholangiopancreatography (ERCP)

## **Pharmacological Treatment**

In acute cholecystitis, the initial treatment includes bowel rest, IV hydration, and correction of electrolyte abnormalities

**A:** paracetamol (PO) 1g 8hourly daily **OR** **D:** paracetamol (IV) 1g 8 hourly daily (for analgesia)

**AND**

**C:** metoclopramide (IV/PO) 10mg 12hourly daily (for intractable vomiting)

**AND**

**S:** piperacillin + tazobactam FDC (IV) 4.5g 6-8 hourly 7-10 days (for severe/complicated cases)

**OR**

**B:** ceftriaxone (IV) 1-2gm 24hourly for 7-10days

**OR**

**C:** ciprofloxacin (IV) 200-400mg 12hourly for 7-10days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 7-10days

In cases of uncomplicated cholecystitis, outpatient treatment may be appropriate.

**A:** ciprofloxacin (PO) 500mg 12hourly for 7days

**AND**

**A:** metronidazole (PO) 400mg 12hourly for 7days

### **Note**

- Laparoscopic cholecystectomy (standard of care for surgical treatment of cholecystitis) others include ERCP.
- Endoscopic ultrasound-guided transmural cholecystostomy, Endoscopic gallbladder drainage.

### **10.4.3.4 Cholangitis**

Bile duct (BD) obstruction leads to infection proximal to the obstruction, etiologies include BD stone, malignant (biliary, pancreatic) or benign stricture, infection with fluke (*Clonorchis sinensis*, *Opisthorchis viverrini*)

### **Clinical presentations**

- Charcot's triad: RUQ pains, jaundice, fever/chills; present in three quarter of patients
- Reynolds' pentad: Charcot's triad + shock and altered mental status; present in 15% of patients

### **Investigations**

- Ultrasound, RUQ USS often demonstrates dilation
- FBP, LFT, amylase, lipase
- Blood cultures
- ERCP; percutaneous transhepatic cholangiogram if ERCP unsuccessful

## **Pharmacologic Treatment**

**B:** ceftriaxone (IV) 1-2g 24hourly for 7-10days

**OR**

**S:** piperacillin+tazobactam FDC (IV) 4.5g 6-8hourly for 7-10days (for severe/complicated cases)

**OR**

**S:** meropenem (IV) 1g 8 hourly for 7-10days

**AND**

**C:** metronidazole (IV) 500mg 8hourly for 7-10days

Alternatively

**C:** ciprofloxacin (IV) 200-400mg 12hourly for 7-10days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 7-10days

**Note**

- About 80% respond to conservative treatment and antibiotics then, 20% require urgent biliary decompression via ERCP (papillotomy, stone extraction and/or stent insertion)
- If sphincterotomy cannot be performed (larger stones), decompression by biliary stent or nasobiliary catheter can be done; otherwise, percutaneous trans hepatic biliary drainage or surgery

# CHAPTER ELEVEN

## OBSTETRICS, GYNECOLOGY AND CONTRACEPTION

### 11.1 Bleeding in Pregnancy

Bleeding during pregnancy is common, especially during the first trimester. Bleeding can sometimes be a sign of something serious, therefore it is important to know the possible causes and take adequate measures.

#### 11.1.1 Abortion

It is a spontaneous loss of a fetus before it is viable (has the potential to survive outside the womb). The World Health Organization (WHO) defines it as expulsion or extraction of an embryo or fetus weighing 500mg or less, approximately at or less than 24 weeks of gestation. In Tanzania abortion is defined as loss of pregnancy before 28 weeks of gestations. Clinical features will depend on the types of abortion.

##### 11.1.1.1 Threatened Abortion

###### Clinical presentation

- Mild vaginal bleeding
- Mild/no lower abdominal pain
- Cervix is closed on digital examination

###### Investigation

Check Hb level

###### Management of threatened abortion in Dispensary & Health Centre

- Adequate bed rest at home
- Avoid strenuous activities and sexual intercourse until all the symptoms have subsided
- Schedule a follow up within 7 days
- Tell the woman to come immediately if:
  - Bleeding becomes heavy
  - Experiences offensive discharge
  - Severe abdominal pain

###### Referral

Refer to higher-level health facility with adequate expertise and diagnostics if:

- Bleeding recurs
- Experiences fever
- Experiences offensive discharge
- Experience severe abdominal pain

###### In higher level health facilities:

- Take thorough history and perform investigations to establish the causes
- Perform ultrasound to confirm pregnancy, gestational age, foetal viability and potential causes of abortion.
- Admit the patient and manage appropriately
- Encourage bed rest
- For unexplained recurrent miscarriage (3 consecutive abortions) or PRL due to luteal phase defect manage with

###### Pharmacological Treatment

S: dydrogesterone (PO) 40mg stat then 10mg 24hourly until the bleeding stops for threatening abortion

OR 10mg 24hourly from conception up to 20weeks for luteal phase defect.

#### 11.1.1.2 Inevitable Abortion

Abortion is said to be inevitable when it is not possible for the pregnancy to continue and the cervix is dilated, but all the products of conception are in situ.

###### Clinical presentation

- Moderate or severe per vaginal bleeding
- Moderate or severe lower abdominal pain

- Membranes may be intact or ruptured with leakage of
- The uterine fundal height may correspond with gestational age
- The cervix is dilated

#### **Management of inevitable abortion in Dispensary & Health Centre (B-EMONC facilities)**

- Apply Airway, Breathing, Circulation and Dehydration (ABCD) principles of resuscitation

**A:** compound sodium lactate (IV) **OR** 0.9% sodium chloride (IV) depending of amount of blood loss.

- Perform Manual Vacuum Aspiration (MVA) if gestation age is below 12 weeks  
Augment the process by administering **A:** oxytocin 20 IU in 500mls RL/NS at 40–60 drops/minute if gestation age is above 12 weeks
- Manage as incomplete abortion if after augmentation some products of conception remain in the uterus
- Manage as complete abortion if all products of conception are expelled

**Referral:** Refer to hospital if MVA is not possible and/or bleeding is persisting or severe to necessitate blood transfusion.

#### **Management of inevitable Abortion in the Hospital**

- Apply Airway, Breathing, Circulation and Dehydration principles of resuscitation
- Obtain blood samples for Hb, grouping and cross-matching
- Give compound sodium lactate (IV)**OR** 0.9% sodium chloride aim at replacing 3 times the amount of estimated blood loss.
- Give blood transfusion if indicated
- Perform Manual Vacuum Aspiration (MVA) if gestation age is below 12 weeks
- Augment the process by administering oxytocin 20IU in 500mls RL/NS at 40–60 drops/minute if gestation age is above 12 weeks
- Manage as incomplete abortion if after augmentation some products of conception remain in the uterus
- Manage as complete abortion if all products of conception are expelled

#### **11.1.1.3 Incomplete Abortion**

Abortion is said to be incomplete when after expulsion some of the products of conception get retained in the uterine cavity.

#### **Clinical presentation**

- Severe Cramping lower abdominal pain
- moderate to severe PV bleeding
- Fundus smaller than dates
- The cervix is dilated and products of conception may be felt on or through the cervix on digital examination

#### **Management of incomplete abortion in dispensary & health centre (B-EMONC facilities)**

- Apply Airway, Breathing, Circulation and Dehydration principles of resuscitation
- Check hemoglobin level
- A:** compound sodium lactate (IV) **OR** 0.9% sodium chloride depending on amount of blood loss
- If feasible Perform digital evacuation of products of conception to minimize the PV bleeding
- Perform MVA if gestation age is below 12 weeks

#### **Pharmacological treatment in place**

##### **In place where uterine evacuation is accessible give;**

**A:** oxytocin (IM) 10 IU

**OR**

**A:** misoprostol (sublingual) 600µg

##### **After evacuation give:**

**A:** erythromycin (PO) 500mg 8hourly for 5days

**OR**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 625mg 8 hourly for 5days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 5days

**AND**

**A:** paracetamol (PO) 1g 8hourly for 5 days

**Referral:** Resuscitate the patient and to hospital level with an escort of a nurse if bleeding continues

**Management in a Hospital**

- If patient is in shock, shout for help, mobilize resources
- Apply ABCD principles of resuscitation
- Obtain blood for HB, grouping and cross-matching
- Blood transfusion if indicated
- Give compound sodium lactate (IV) **OR** 0.9% sodium chloride aim at replacing 3times the amount of estimated blood loss
- Digital evacuation of products of conception if feasible to minimize the PV bleeding
- MVA if gestation age is below 12 weeks
- Evacuate uterus in theatre with sharp curette under general anesthesia if pregnancy was more than 12 weeks

**Pharmacological Treatment**

After evacuation give:

**A:** erythromycin (PO) 500mg 8hourly for 5days

**OR**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 625mg 8hourly for 5 days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 5 days

**AND**

**A:** paracetamol (PO) 1g 8hourly for 5days.

**AND**

**A:** ferrous sulfate + folic acid (FDC) (PO) 1 tab 24hourly for 4 weeks

**Patient education.**

- Counsel and educate the patient on possible reasons for abortion and future fertility
- Provide family planning counseling and give appropriate contraceptive method before the patient leaves the facility premises.
- Provide linkage to other reproductive and non reproductive health services depending on patient needs

**11.1.4 Complete Abortion**

Abortion is said to be complete when the Products of conception are completely expelled

**Clinical presentation**

- Minimal or no PV bleeding
- Uterus smaller than dates and often well contracted.
- Cervix may or may not be closed
- The patient may be in Shock due to severe bleeding

**Pharmacological Treatment**

**A:** erythromycin (PO) 500mg 8hourly for 5days

**OR**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 625mg 8hourly for 5days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 5days

**AND**

**A:** ferrous sulfate + folic acid (FDC) (PO) 1 tablet 24hourly for 4weeks

**If patient is in shock;**

- Shout for help and mobilize resources
- Apply ABCD principles of resuscitation

- Give compound sodium lactate (IV) OR 0.9% sodium chloride (IV) 3 litres or more in the first hour
- Insert an indwelling urethral catheter
- Give ampicillin (IV) 1g and metronidazole (IV) 500mg stat
- Obtain blood for Hb,

**Referral:** Resuscitate the patient and refer to hospital with an escort of a nurse

#### **Management in a hospital**

- If patient is stable continue as above;
- If patient is in shock, perform as above and give blood transfusion if indicated

#### **Patient Education**

Provide counseling, education and FP services as in incomplete abortion above

#### **11.1.1.5 Septic Abortion**

Abortion is said to be septic when it is complicated by infections.

#### **Clinical presentation**

- Moderate to severe abdominal pain following abortion
- Fever may be present
- Foul smelling PV discharge which may be mixed with blood.
- May be in shock
- Tender uterus with or without rebound tenderness
- Cervix is usually open

#### **Management of septic abortion in dispensary & health centre**

- Apply ABCD principles of resuscitation
- Give compound sodium lactate (IV) **OR** sodium chloride (IV) 0.9% in case of hypotension or shock. Avoid IV fluid in case of chronic anaemia.
- Insert an indwelling urethral catheter
- Obtain blood for Hb or FBC
- Perform Ultrasound if feasible

#### **Pharmacological Treatment**

**C:** amoxycillin + clavulanic acid (FDC) (IV) 1.2g 8 hourly for 24–48 hours

**AND**

**B:** metronidazole (IV) 500mg 8 hourly for 24–48 hours

**Referral:** Resuscitate and immediately refer the patient to hospital with an escort of a nurse.

#### **Management in the Hospital:**

- Full Blood Count (FBC)
- Draw Blood for culture and susceptibility testing
- Check abdominal pelvic ultrasound as appropriate
- IV RL/NS depending on individual patient needs
- Give blood transfusion if indicated
- Evacuate the uterus with sharp wide curette under general anesthesia

#### **Pharmacological Treatment**

Treat as above and when the patient is stable continue with;

**B:** amoxicillin+ clavulanic acid (FDC) (PO) 625mg 8 hourly for 7 days

**A:** metronidazole (PO) 400mg 8 hourly for 7 days

If no response with the above antibiotics within 3 days; adjust according to culture and sensitivity results or switch to

**D:** ceftriaxone + sulbactam (FDC) (IV) 1.5g 12 hourly for 5 days

**AND**

**B:** metronidazole 500mg (IV) 8 hourly for 5 days

**AND**

**A:** ferrous sulfate + folic acid (FDC) (PO) 1 tablet daily for 4 weeks then reassess.

## Patient Education

- Counsel educate and provide appropriate contraceptive method.

### 11.1.1.6 Molar Pregnancy

A molar pregnancy is a gestational trophoblastic disease which grows into a mass in the uterus that has swollen chorionic villi. These villi grow in clusters that resemble bunches of grapes. Once diagnosed it should be treated right away.

#### Clinical presentation

- Vaginal bleeding
- Uterus that is bigger than gestational age.
- Exaggerated pregnancy symptoms (Severe nausea and vomiting)
- Vaginal discharge of tissue that resemble grapes
- Heavy PV bleeding when the mole abort spontaneously

#### Management of Molar pregnancy at the dispensary and Health centers

- Apply Airway, Breathing, Circulation and Dehydration principles of resuscitation
- Check hemoglobin level
- If the patient is actively bleeding, catheterize, Establish Iv line and Give IV RL/NS 2lts at a rapid rate

**Referral:** Resuscitate and refer the patient to higher level facility with a nurse escort for appropriate management

#### Management of molar pregnancy at the Hospital

- Apply Airway, Breathing, Circulation and Dehydration principles of resuscitation
- If the patient is patient is actively bleeding or in shock shout for help and mobilize resources
- Check HB, Blood grouping and Cross matching
- Perform quantitative serum Beta Human Chorionic Gonadotropin (bHCG)
- Check abdominal pelvic Ultrasound to confirm the diagnosis (Snowstorm appearance)
- Infuse compound sodium lactate (IV) OR 0.9% sodium chloride (IV) as needed
- Initiate blood transfusion if indicated
- Perform suction curettage in operating theatre
- Perform other investigations as appropriate (chest X ray, RFT, LFT, Chemistry panel)

#### Follow up for Molar pregnancy after Molar Evacuation

- Check weekly bHCG until when it becomes normal(5-10mIU/ml) for 3 weeks consecutively
- Then check monthly bHCG and pelvic ultrasound for 12 months
- Advice the patient to use effective contraception during follow up (preferably COCs)

### 11.1.1.7 Missed Abortion

This happens when a Fetus less than 24weeks die in utero, but it's not expelled out

#### Clinical presentation

- History of amenorrhea
- Regression of the pregnancy symptoms
- Uterine size smaller than dates
- Mild or no PV bleeding

#### Management of a missed abortion at the dispensary and Health center

**Referral:** Referto higher level health facility with adequate expertise and diagnostics/equipment

#### Management of missed abortion at the hospital

##### Investigations

- Abdominal pelvic ultrasound
- Full blood count, Blood Grouping and cross matching
- Clotting indices (PT, APTT, INR)

### **Pharmacological Treatment**

Induce abortion with misoprostol if it is more than 12 weeks

**A:** misoprostol (PV) 100mcg 8hourly to max. 400mcg followed by sharp curettage in case of incomplete abortion

Evacuate by Dilatation and Curettage (D&C) if the GA is less than 12weeks

#### **Note**

Avoid misoprostol in case of previous uterine scar

#### **After evacuation give**

**A:** metronidazole (PO) 400mg 8 hourly for 7days

**AND**

**B:** amoxicillin+ clavulanic acid (FDC) (PO) 625mg 8hourly for 7days

#### **Patient education.**

Counsel and provide appropriate contraception.

## **11.2 Ectopic Pregnancy**

Ectopic pregnancy (EP) is defined as a pregnancy in which the implantation of the embryo occurs outside the uterine cavity, most frequently in one of the two fallopian tubes or, rarely, in the abdominal cavity.

### **11.2.1 Un-ruptured Ectopic Pregnancy**

#### **Clinical presentation**

- History of amenorrhea
- PV Spot bleeding in early pregnancy
- Unilateral Abdominopelvic pain. Unilateral(localized) abdominal tenderness

#### **Management of Un-ruptured ectopic pregnancy**

**Referral:** Patients should be referred to higher level facilities with equipment and expertise

- At higher level facilities un-ruptured EP may be managed surgically or pharmacologically depending GA and available expertise

### **Pharmacological Treatment**

**S:** methotrexate (IV) 50mg/M<sup>2</sup> single dose

**OR**

**S:** methotrexate 2.5mg (PO) 24hourly for 5days (**in case IV methotrexate is not available**)

Perform weekly pelvic ultrasound to ensure regression of Gestation sac

#### **Note**

Contraindications of methotrexate include a ruptured ectopic, ectopic mass greater than 3.5 cm, fetal cardiac activity, high level hCG value (10,000 IU), breastfeeding and immunodeficiency

### **11.2.2 Ruptured Ectopic Pregnancy**

#### **Clinical presentation**

- History of amenorrhea
- Acute generalized abdominal-pelvic pain
- Hypotension
- Fast and weak pulse
- Abdominal distension and tenderness with rebound tenderness

#### **Management of ruptured ectopic at the dispensary and Health Center (B-MONC facilities)**

- Apply ABCD principles of resuscitation
- Perform abdominal pelvic ultrasound if available
- Check Hb
- Start compound sodium lactate (IV) **OR** 0.9% sodium chloride (IV) infuse at a rate of 500mls per hour

**Referral:** Ectopic pregnancy is an obstetric emergency, resuscitate and refer the patient immediately, with an escort by skilled attendant.

### **Management of Ectopic pregnancy at the Hospital (C-EMONC facilities)**

- Perform abdominal pelvic/Transvaginal ultrasonography
- Hb level
- Grouping and cross-matching
- compound sodium lactate (IV) **OR** 0.9% sodium chloride (IV) depending on amount of blood loss
- Blood transfusion if indicated depending on the blood loss
- Perform Emergency laparotomy

### **11.3 Antepartum Hemorrhage**

It is the bleeding from the birth canal after the 28<sup>th</sup> week of gestation but before the onset of labour. The main forms are placenta praevia and abruption placenta. Other rare cause may include VASA previa, heavy show and gynecological malignancies (cervical cancer)

#### **11.3.1 Placenta Praevia**

- It is an obstetric complication in which the placenta embeds itself partially or wholly in the lower segment of the uterus. It is an obstetric emergency which should be managed in a facility offering CEMONC services

#### **Clinical presentation**

- Sudden onset of bright red fresh painless bleeding after 28weeks of gestation

#### **Management**

- If partial PP and asymptomatic – Bed rest at home and follow up every 2weeks
- If complete placenta praevia
  - Admit for close monitoring and observation
  - Perform ultrasound to localize the placenta
  - Perform FBP, Coagulation tests, Blood grouping and cross matching. Keep at least 2 units of blood ready in the bank for transfusion in case of acute bleeding
  - Consider Blood transfusion if indicated
  - Avoid vaginal digital examination
  - If >34weeks and no PV bleeding or contraction, expectant management
  - Deliver by Cesarean section preferably at 37–38 weeks of gestation
  - Deliver by caesarean section by C/S any time incase of onset of labour or severe Pv bleeding
  - Partial or marginal placenta praevia: Carefully perform amniotomy for vaginal delivery if the head is engaged.

#### **Pharmacological management**

**D:** dexamethasone (PO) 6mg 12hourly for 48 hours if pregnancy is <34weeks for fetal lung maturation

**B:** nifedipine (PO) 20mg 8hourly until labour symptoms subside

### **11.3.2. Placental Abruption**

It is PV bleeding due to premature separation of a normally situated placenta in pregnancy after 28 weeks of gestation.

#### **Clinical presentation**

- Vaginal bleeding of dark colored blood or clots. Sometimes bleeding can be concealed
- Abdominal pain is moderate to severe but may be absent in revealed AP
- The uterus may be enlarged and very tender
- Fetal demise or fetal distress may be present

#### **Management of Abruptio Placenta at Dispensary and Health centre.**

- Apply the ABCD principles of resuscitation

- Insert large bore cannula IV line, start rapid infusion with RL/NS
- Insert Urethral catheter

**Refer:** resuscitate and refer immediately to the hospital with an escort of a skilled health attendant

### Management of Abruption Placenta at the hospital

#### Investigations

- Ultrasound: Fetal wellbeing, placenta localization and evidence of retro placental clot
- Full blood count and cross-match
- Renal function test, Liver function test and electrolytes
- Fibrinogen tests if available, D-dimer, PT, PTT, INR

#### Note

The diagnosis of placental abruption is mainly clinical

#### Maternal resuscitation

- Apply the ABCD principles of resuscitation
- Insert two (2) large bore IV lines and give Normal Saline/Ringers Lactate. Replete crystalloids at ratio of 1 unit of blood loss: 3 unit of crystalloids
- Blood Transfusion is usually necessary
- Give oxygen supplementation at a flow of 6L/min
- Insert a urinary catheter to monitor input/output
- If Disseminated Intravascular Coagulation: Give fresh frozen Plasma 1 Unit/hour, give whole blood 2–4 units
- Monitor blood pressure, pulse, bleeding, hourly, full blood count, clotting profile every 2 hours

#### Obstetrical Management

- If the foetus is alive and viable: emergency Caesarean section
- If the foetus is dead: Normal vaginal delivery is preferable if no contraindication for vaginal delivery (eg uterine scar)
- Perform artificial rupture of membrane,

If no spontaneous labour: induce with Oxytocin infusion 5IU in 500 ml NS beginning with 10 drops/min increase the rate after every 20min until optimal contractions are achieved.

- Do active management of third stage of labour and uterine massage
- Emergency Caesarean section should be considered if:
  - Worsening of maternal condition
  - Failure/Non progressing vaginal delivery

#### Prophylactic antibiotics

**C:** amoxycillin + clavulanic acid (FDC) (IV) 1.2g stat

**AND**

**B:** metronidazole (IV) 500mg stat.

#### 11.4 Obstructed Labour

Also known as labour dystocia, is when despite adequate uterine contractions the baby does not exit the pelvis during due to being physically blocked. Obstructed may commonly be caused by; big baby, narrow maternal pelvis, malpresentation and malpositions.

#### Clinical presentations

- Prolonged labour (>8hours of active labour)
- Delayed second stage of labour (>1hour)
- Fetal distress
- Severe moulding (3+)
- Severe caput succedaneum
- Maternal dehydration (neglected obstructed labour)
- Bundl's ring (sign of neglected obstructed labour)

#### Management of obstructed labour at B-EMONC facilities

- Insert IV line with and start RL/ DNS infusion 2L
- Insert urethral catheter
- Check Hb

- Encourage the patient to lay in left lateral position

### **Management of Obstructed labour at the C-EMONC facilities**

- Optimize hydration by RL/NS 2lt before caesarean section
- Ensure the patient is catheterized,
- Perform Hb estimation
- Perform emergency caesarean section.

### **Pharmacological treatment**

**A:** compound sodium lactate (IV)/sodium chloride (IV) 0.9%to ensure adequate hydration

**OR**

**A:** ampicillin (IV) 2g within 30m before CS, continue 2g 24hourly for 3days

**OR**

**B:** ceftriaxone (IV) 1g stat within 30min before CS, continue 1 g 24hourly for 3days

**OR**

**C:** amoxycillin + Clavulinic acid (FDC) (IV) 1.2g within 30min before CS, continue 1.2g 8hourly for 3days

**AND**

**B:** metronidazole (IV) 500mg within 30min before CS, continue 500mg 8hourly for 3days.

### **11.5 Postpartum Hemorrhage (PPH)**

It is abnormal uterine bleeding following delivery through 6 weeks (42 days). It is sub classified in to Primary and Secondary PPH

#### **Primary PPH**

It is typically loss of more than 500 ml of blood from the genital tract after vaginal delivery or more than 1000 ml after Caesarean section in the first 24 hours. OR it is any amount of blood loss after delivery that would result in to haemodynamic instability.

#### **Management of PPH at Dispensary and Health centre**

- Insert 2 large bore cannula IV line, start rapid infusion with compound sodium lactate or sodium chloride
- Start oxytocin (IV) 20IU in 500mls NS at a rate for 20drops per minute
- Ensure no retained placental tissues
- Clamp or ligate bleeding perineal tears if any.
- Massage the uterus
- Insert Urethral catheter

**Referral:** If bleeding continues, immediately refer the patient to the hospital an escort of a skilled health attendant. Maintain IV infusion during transfer.

#### **Management of PPH at the hospital**

- Shout for help and mobilize resources
- Obtain blood samples for Hb, blood grouping and cross matching
- Insert 2 large bore cannulas and start infusing compound sodium lactate or sodium chloride (IV) rapidly
- Blood Transfusion depending on amount of blood loss
- Start oxytocin (IV) 20IU in 500mls compound sodium lactate/0.9% sodium chloride (IV) titrate at 20 drops per minute OR misoprostol (PO) 1000mcg or per rectal
- Perform other manoeuvres (balloon tamponade, TAH, Iliac artery ligation, B-Lynch suture) including surgical interventions depending on patient condition and available expertise.

#### **Prevention of PPH –Active management of Third Stage of Labour (AMSTL)**

Ensure no remaining second twin

**A:** oxytocin (IM)10IU

**OR**

**A:** misoprostol (PO) 600mcg

Controlled cord traction (CCT) is recommended for vaginal births. Sustained uterine massage is not recommended as an intervention to prevent PPH in women who have received prophylactic oxytocin.

#### **Prevention of PPH in Caesarean sections**

**A:** oxytocin (IV/IM) 10IU is the recommended uterotonic drug for the prevention of PPH in Caesarean section

Cord traction is the recommended method for the removal of the placenta in Caesarean section

### **11.6 Prelabour Rupture of Membranes (PROM)**

It is the rupture of membranes (breakage of the amniotic sac) before the onset of labor. If rupture occurs before 37 weeks it is called preterm prelabour rupture of membranes (PPROM). Prolonged PROM is a case of premature rupture of membranes in which more than 24 hours have passed between the rupture and the onset of labour. Prolonged PROM for more than 18 hours is a risk of ascending infection which can lead to chorioamnionitis (infection of chorion, amnion and amniotic fluid).

#### **Clinical presentation**

Leakage of watery fluid per vagina confirmed by performing a sterile speculum examination.

#### **Management of PROM at the dispensary and health center**

Give the following antibiotics for prophylaxis against chorioamnionitis

**A:** erythromycin (PO) 500mg 8hourly for 7days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 7days

**Referral:** Referto the hospital for further evaluation and management

#### **Management of PROM at the hospital**

##### **Investigations**

- Ultrasound for fetal wellbeing, amount of liquor and gestation age.
- Perform a sterile speculum examination to confirm leakage
- Perform HVS for culture and susceptibility testing
- Urinalysis

#### **General Management**

If PROM at term: Delivery within 24 hours

Assess Bishop's Score and Induce Labour accordingly with

**A:** misoprostol (PO) 25mcg 8hourly (Max 3doses) **if unfavorable cervix.**

**OR**

**A:** oxytocin (IV) 5IU in 500ml of D5% titrate beginning with 10dpm **if favourable cervix**

Monitor FHR vigilantly during the process of IOL. Deliver by C/S if vaginal delivery is contraindicated, fetal distress or failed induction of labour.

#### **For Preterm PROM:**

If no sign of infection, wait for foetal maturity and give

**B:** dexamethasone (IM) 6mg 12hourly for 48 hours if pregnancy is <34weeks for fetal lung maturation

**AND**

**B:** nifedipine (PO) 20mg 8hourly for 7 days for tocolysis

Monitor for infection (FBP, RCP, Pulse, Fever) and fetal wellbeing (fetal movement, FHR, obstetric ultrasound)

Administer prophylactic antibiotics

**A:** metronidazole (PO) 400mg 8hourly 10days.

**AND**

**A:** erythromycin (PO) 500mg 8hourly for 10days

## **OR**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 625mg 8hourly for 10days

Deliver irrespective of gestation age in case of infection

**If there are signs of infections-pyrexia, foul smelling liquor (chorioamnionitis)**

**A:** metronidazole (PO) 400mg 8hourly for 5-7 days

**AND**

**C:** amoxycillin + clavulanic acid (FDC) (IV) 1.2g 8hourly for 5-7days

**OR**

**D:** ceftriaxone + sulbactam (FDC) (IV) 1.5g 12hourly for 5-7 days

## **11.7 Antenatal Care**

### **11.7.1 Anaemia in Pregnancy**

It is hemoglobin levels less than 11 g/dl in early pregnancy and less than 10.5 g/dl in the 2nd and 3rd trimester of pregnancy. Mild anemia— hemoglobin: 8–11g/dl; Severe anemia— hemoglobin<7g/dl. Iron deficiency anemia during pregnancy has been associated with an increased risk of low birth weight, preterm delivery and perinatal mortality.

#### **Clinical presentation**

- Tiredness, weakness, palpitations and dyspnea
- Exercise intolerance
- Pallor of skin and mucous membranes
- Dizziness, faintness, headache
- Intermittent claudication (ache, cramp, numbness or sense of fatigue)

#### **Note**

Some patients with anaemia in pregnancy may be asymptomatic

#### **Investigations**

- Full blood count and blood cross-match - red cell morphology
- Red blood cell electrophoresis if haemoglobinopathies suspected
- Blood smear for malaria
- Stool and urine analysis
- HIV test

#### **Non-pharmacological Treatment**

- Iron rich diet (fish, eggs, fruits and vegetables etc.)
- Prevent and early treatment of malaria
- Investigate and treat associated worm infestations

#### **Pharmacological Treatment**

##### **Prophylaxis in Antenatal Care**

**A:** ferrous sulfate(PO) 200mg 8-12hourly

**AND**

**A:** folic acid (PO) 5mg 24hourly

#### **Note:**

- Ferrous sulfate should be taken in a full stomach and avoid taking it with tea/coffee
- Where vomiting is experienced reduce dosage to tolerable level

**If Hb is <7g/dl in 1<sup>st</sup> and second trimester give:**

**A:** ferrous sulphate + folic acid (FDC) (PO) 1 tab 12hourly for 4 weeks.

**AND**

**A:** vitamin B (PO) 12hourly for 4 weeks

**If HB is <7g/dl in 3<sup>rd</sup> trimester or in case of signs for severe anaemia (features of heart failure)**

- Refer/admit the patient for blood transfusion at least 2 units of Packed RBCs

- Continue with ferrous and folic acid as above after blood transfusion

## **11.7.2 Hypertensive Disorders in Pregnancy**

Hypertension is blood pressure (BP) 140/90 mmHg or greater, measured on two occasions at least four hours apart or elevated systolic BP >30mmHg, or diastolic BP 15mmHg from the baseline.

### **Chronic Hypertension**

This is hypertension that is present at the booking visit or before 20 weeks or if the woman is already hypertensive before conception. Most women with chronic hypertension are asymptomatic. New onset chronic hypertension should have further evaluation to find underlying cause e.g. renal artery stenosis, chronic renal disease, Cushing syndrome etc.

### **Pharmacological Treatment**

**A:** methyldopa (PO) 250–500mg 8hourly

**AND**

**B:** nifedipine (PO) 20mg 12hourly

### **Pregnancy induced hypertension (gestation hypertension)**

Gestational hypertension or pregnancy-induced hypertension (PIH) is the development of new hypertension in a pregnant woman after 20 weeks of gestation without the presence of protein in the urine or other signs of preeclampsia. Usually disappears within 12 weeks postpartum

### **Non-pharmacological Treatment**

- Adequate rest at home and avoid strenuous activities
- Eat a normal balanced diet and plenty of oral fluids
- Schedule antenatal visits every 2 weeks up to 32 weeks and every week thereafter
- Recommend to deliver in the hospital and should be delivered at 37 completed weeks of gestation

### **Pharmacological Treatment**

For mild hypertension 140–159 mmHg systolic and/or 90–109 mmHg diastolic.

**A:** methyldopa (PO) 250–500mg 8hourly

**OR**

**B:** nifedipine (PO) 20mg 12hourly

**OR**

**C:** labetalol (PO) 100mg 12hourly a day

### **Severe hypertension**

Severe hypertension is Blood Pressure (BP) of 160/110 mmHg or higher. Admit the patient to hospital

**A:** methyldopa (PO) 500mg 8hourly

**AND**

**C:** hydralazine 10mg (slow IV) stat (over 4–5 minutes); recheck the BP after 20 minutes if DBP is more/equal to 110mmHg give another dose of hydralazine (IV slowly) 5–10mg.

**AND**

**B:** nifedipine (PO) 20mg 12hourly

**OR**

**C:** labetalol (PO) 100mg 12hourly

#### **Note**

Ensure slow administration and monitor closely for hypotension if using hydralazine.

**Referral:** Refer to the next level facility in case there is no improvement

## **11.7.3 Pre-eclampsia**

Is diagnosed when blood pressure is  $\geq$  140/90 mmHg after 20 weeks of pregnancy plus proteinuria of 300 mg per 24 hours or  $>2+$  on urine dipstick. Or elevation of BP in pregnancy with features of end organ damage (eg pulmonary edema, renal or liver damage)

## **Diagnostic Criteria**

- Most patients are asymptomatic, but symptoms may include headaches, dizziness, blurred vision, and epigastric pain.
- Blood pressure of  $\geq 140/90$  mmHg
- Proteinuria ( $\geq 300$ mg per 24 hours)
- Generalized edema may be present (not a necessary criteria)

## **Investigations**

- Urine for Proteinuria (qualitative/quantitative 24-hour urine collection)
- Obstetric Ultrasound and biophysical profile
- Urea, creatinine, electrolytes, liver function test and uric acid
- FBP and clotting profile
- Fundoscopy

## **Non-pharmacological Management**

Pregnancy < 37 weeks of gestation

- Hospitalization and close monitoring
- Bed rest
- Monitoring BP, urine output, proteinuria, fetal movement and fetal heart beats (every day)
- $<34$  weeks

Pregnancy >37 weeks of gestation: admit and deliver accordingly.

## **Pre-eclampsia with Severe Features:**

This is diagnosed when BP  $\geq 160/110$  mmHg (especially diastolic  $\geq 110$  mmHg), or BP of  $\geq 140/90$  mmHg with features of end organ damage eg severe headache, epigastric pain, blurring of vision +/\_ vomiting, pulmonary oedema, renal or liver damage, features of haemolysis and low platelets

## **Pharmacological Treatment**

**C:** hydralazine (IV) 5mg in 10ml sterile water over 4minutes' initial dose. Followed by boluses 5–10mg as needed every 20 minutes until when the diastolic BP is less than 110mmHg)

**AND**

**A:** methyldopa (PO) 500mg 8hourly

**AND**

**A:** nifedipine (PO) 20mg 8hourly until BP is stabilized

**OR**

if hypertension is refractory to hydralazine

**C:** labetalol (IV bolus) 10–20mg stat repeat each 10–20 minutes, with doubling doses not exceeding 80mg in any single dose for maximum total cumulative dose of 300 mg.

Antenatal corticosteroids (dexamethasone Inj. 6mg 12hourly for 48hours) if pregnancy

## **Prophylaxis for Seizures**

Anti-convulsion treatment of choice is magnesium sulfate.

**A:** Magnesium sulfate (IV) 1g hourly in 250mils of RL (OR 5g of 50% MgSO<sub>4</sub> 4 hourly or alternate buttock) for 24 hours if GA is  $\leq 34$  weeks or until 24 hours post-delivery if GA is  $\geq 34$  weeks (Refer to eclampsia section)

## **Obstetrical Management**

If at term deliver immediately when stable, preferably vaginal delivery

## **11.7.4 HELLP syndrome**

It is a life-threatening complications of pre-eclampsia characterized by Haemolysis, Elevated Liver enzymes and Low Platelets

### **Diagnostic criteria**

- **Haemolysis**
  - Abnormal peripheral smear
  - Total bilirubin  $> 1.2$  mg/dL

- Lactic dehydrogenase > 600 U/L
- **Elevated Liver Functions**
  - Serum glutamic oxaloacetic transaminase > 70 U/L
  - Lactic dehydrogenase > 600 U/L
- **Low Platelets**
  - Platelets < 1,000,000/mm<sup>3</sup>

### **Management of HELLP syndrome**

The management is the same as for severe pre-eclampsia

### **11.7.5 Eclampsia**

Eclampsia is a condition peculiar to pregnancy and post-partum periods, characterized by elevated BP and tonic-clonic convulsions which are not caused by epilepsy, severe malaria, meningitis, hypoglycemia or other causes of convulsions. Majority (50%) occur preterm. Eclampsia may occur without prior elevation of BP.

#### **Diagnostic Criteria**

- Signs of severe pre-eclampsia (BP > 160/110mm Hg)
- Loss of consciousness
- Tonic-clonic seizures, coma

#### **Investigations**

- Full blood count and crossmatch
- Ultrasound for GA and fetal viability
- Urea and creatinine + electrolytes
- Liver enzymes tests
- 24h urine collection for proteinuria
- Clotting profile
- Blood smear to exclude malaria
- Blood sugar estimation to exclude hypoglycemia.
- Lumbar puncture may be indicated to exclude meningitis

#### **Pharmacological Treatment**

Manage with antihypertensive as in pre-eclampsia with severe features **AND**

**A:**magnesium sulfate (IV)

**Loading dose:** magnesium sulfate (IV) 4g of 20% (MgSO<sub>4</sub>) slowly over 5minutes.

If having 50% MgSO<sub>4</sub> dilute it to make it 20% MgSO<sub>4</sub> by Drawing 8mls of 50% MgSO<sub>4</sub> and adding 12mls water for injection to make it 20mls of 20% of MgSO<sub>4</sub> and

**OR**

Draw 10mls (5gms) of 50% MgSO<sub>4</sub> into each syringe 1ml of A: 2% lignocaine in each syringe then give deep IM into each buttock. Continue with maintenance dose until 24hours post-delivery or since the last episode of convolution: With MgSO<sub>4</sub> infusion 1g per hour (in 200–300 ml of Ringer's Lactate), or MgSO<sub>4</sub> 5g undiluted 50% of MgSO<sub>4</sub> injection (add 1ml of lignocaine 2%) apply deep intramuscular (IM) injection into each buttock every 4hrs for about 24 hours after delivery or the last seizure whichever come last.<sup>16</sup>

#### **Note**

The magnesium sulfate infusion should only be given if patellar reflexes are present, respiration rate is ≥ 12 per minute, and urine output is >100mls in 4 hours.

#### **If convulsions recur within 15 minutes give;**

**A:** magnesium sulfate 2g. Draw 4mls of 50% of MgSO<sub>4</sub> (2gm), add 6mls of water for injection to make it 10mls of 20% MgSO<sub>4</sub> then give IV slowly over 5 minutes

#### **Features of Magnesium Sulphate toxicity**

- Respiratory depression (<16cycles/min)
- Reduced urine output(<30mls/hour)
- Loss of deep tendon reflexes

#### **In case of magnesium sulphate toxicity**

- Stop magnesium sulphate administration
- A: calcium gluconate (IV) 1g slow bolus in 2 to 3 minutes

### **Obstetrical management**

Patients with eclampsia should be delivered within 12 hours after the onset of seizures, even if the foetus is premature. Expectant management is contraindicated. If not in labour, and no contraindications, induce labour with misoprostol 50 µg (PO), 4 hourly or 25 µg vaginally and repeat 8 hourly up to a total of four doses maximum

- If failure of induction or contraindication to vaginal delivery, immediate Caesarean section is indicated

### **Prevention of pre-eclampsia and eclampsia**

- Ensure effective antenatal care
- Calcium supplementation calcium supplementation at doses of 1.5–2.0 g elemental calcium/day) for those at high risk of developing pre-eclampsia.
- Low-dose acetylsalicylic acid (aspirin, 75 mg) is recommended for the prevention of pre-eclampsia in women at high risk of developing pre-eclampsia.

### **11.7.6 Antiphospholipid Syndrome (APS) in Pregnancy**

It is an autoimmune disease characterized by the presence in maternal circulation of one or more auto antibodies against membrane phospholipids. It is an acquired condition. Antiphospholipid syndrome (APS) is characterized by venous or arterial thrombosis and/or an adverse pregnancy outcome. APS occurs either as a primary condition or in the setting of an underlying disease, usually systemic lupus erythematosus (SLE).

#### **Clinical presentation**

- Recurrent pregnancy adverse outcome e.g. (miscarriages) recurrent miscarriage, intrauterine growth restriction, early severe pre-eclampsia and preterm birth.
- Unexplained venous thrombosis (DVT) or arterial thrombosis (Stroke) or myocardial infarction
- thrombocytopenia (common finding but among the clinical classification criteria)

#### **Classification with APS requires one clinical and one laboratory manifestation:**

##### **Clinical**

- A documented episode of arterial, venous, or small vessel thrombosis
- 1 or more unexplained deaths of a morphologically normal fetus ≥ 10-week GA
- 3 or more unexplained consecutive spontaneous abortions before the 10th weeks of GA with anatomic, hormonal or chromosomal causes excluded
- Eclampsia or severe pre-eclampsia according to standard definitions, or recognized features of placental insufficiency

##### **Laboratory:**

- Anti-cardiolipin IgG and/or IgM measured on 2 or more occasions, not less than 12 weeks apart;
- Anti-β2 glycoprotein I IgG and/or IgM measured on 2 or more occasions, not less than 12 weeks apart
- Lupus anticoagulant detected on 2 occasions not less than 12 weeks apart.

#### **Pharmacological Treatment**

**A:** acetyl salicylic acid (PO) 75–120 mg 24 hourly beginning as soon as the pregnancy is confirmed throughout pregnancy

**AND**

**C:** unfractionated heparin (SC) 5000–10000

**OR**

**S:** low molecular weight heparin (SC) 30–40 mg 24 hourly

**Patients with Thrombosis** such as stroke or pulmonary embolism need therapeutic anticoagulation.

**C:** unfractionated heparin (SC) 5,000 bolus and subsequent 15,000–20,000 doses at 12 hourly intervals

**OR**

**S:** low molecular weight heparin (SC) 1mg/kg 12hourly

**Note**

- Warfarin should be avoided in pregnancy due to the risk of teratogenicity
- The aPTT needs to be checked and is best done midway between the 12hourly doses, 24hourly.
- A target of 1.5–2.5 times the control should be aimed

**Referral**

Refer immediately to a level where expertise and monitoring for treatment through laboratory testing is available.

### **11.7.7 Deep Vein Thrombosis in Pregnancy**

Deep vein thrombosis (DVT) and acute pulmonary embolism (PE) are two manifestations of venous thromboembolism (VTE). The risk of VTE is increased in pregnancy by about five times because of a more hyper-coagulable state. VTE contributes to significant maternal morbidity and mortality. The mainstay of therapy for DVT is anticoagulation, provided there is no contraindication

**Clinical presentation**

- Pain on the affected limb
- Swelling or redness of the calf or thigh
- Homan's sign (pain in the calf in response to dorsiflexion of the foot)

**Investigations**

- Venous doppler ultrasound
- Venography (CT MRI)
- Fibrin degradation product (FDP) or D-dimer

**Prevention of DVT**

- Early passive and active ambulation in women undergoing major obstetric surgery
- Compressive stockings in women  $\geq 100\text{kg}$  undergoing obstetric surgery
- LMWH prophylaxis 5000IU within 1-hour post-surgery to at risk women.

**Pharmacological Treatment**

**B:** unfractionated heparin (SC) 5,000 bolus and subsequent 15,000–20,000 doses at 12hourly intervals (under supervision of a specialist)

**OR**

**S:** low molecular weight heparin (SC) 1mg/kg 12hourly

**OR**

**C:** warfarin (PO) 5mg 24hourly (in delivered women) consider bridging warfarin with Heparin for 5days as it takes longer to act. Warfarin to be continued up to 6weeks postpartum

**Note**

Check PTT every 4hours and PTT should be maintained at 1.5–2.5 X control. Once steady state has been achieved measure PTT levels daily. Change heparin to SC route after 5–10days

**Referral:** Immediate referral to a hospital with expertise and monitoring of the treatment through laboratory testing is recommended.

### **11.7.8 Pulmonary Embolism in Pregnancy**

It is a blockage, usually a blood clot that prevents oxygen from reaching the tissues of the lungs; it can be life-threatening

**Diagnostic Criteria**

- Acute onset of shortness of breath (dyspnea)
- Pleuritic chest pain
- Cough and/or hemoptysis
- Low grade fever
- Tachypnea
- Diminished oxygen saturation
- Diminished breath sounds

### **Investigations**

- Venous Doppler ultrasound
- Pulmonary angiography
- CT scan, MRI
- D-dimer

### **Non-pharmacological Treatment**

Respiratory support and Oxygen supplementation

### **Pharmacological Treatment**

- B:** unfractionated heparin (UFH) is the treatment of choice  
Loading dose 150 U/kg (or minimum of 5000 U) followed by  
Initial infusion 15–25 U/kg/hour (or minimum of 1000U/hourly)

### **Note**

Check PTT every 4 hours and adjust infusion to maintained PTT at 1.5–2.5 x control. Once steady state has been achieved measure PTT levels daily. Change heparin to SC route after 5–10 days to avoid formation of hematoma.

### **Referral**

Immediate referral to a health facility where expertise and monitoring of the treatment through laboratory tests is available is recommended.

## **11.7.9 Vomiting in Pregnancy and Hyperemesis Gravidarum**

It is excessive nausea and vomiting in early pregnancy requiring hospital admission and rehydration.

### **Clinical presentation**

- Weight loss
- Excessive Nausea and vomiting typically in early pregnancy
- Dehydration
- Altered general status (fast pulse, restlessness)

### **Investigations**

- Full blood count
- Blood for urea, electrolytes and serum creatinine
- Urinalysis, micro urine and culture, ketonuria
- Liver function tests
- Thyroid function tests
- Obstetric ultrasound to exclude multiple pregnancy and GTD

### **Non-pharmacological Treatment**

- Nil per oral (nothing by mouth) for 24–48 hrs.
- Input/output monitoring for 24–48 hrs.
- Monitor electrolytes for 24hrs
- Counselling and Reassurance
- Emotional support
- Rest and Lifestyle adjustment
- Ensure adequate hydration and Frequent small carbohydrate meal

### **Pharmacological Treatment**

**A:** compound sodium lactate with 5% dextrose and 0.9% sodium chloride according to daily needs and severity.

**AND**

**C:** vitamin B<sub>1</sub> (IV)100mg 24hourly mix in intravenous rehydration solution

**AND**

**C:** metoclopramide (IM) 5–10 mg 8hourly till vomiting stops.

**OR**

**A:** promethazine (IM) 12.5 mg 12hourly a day

**OR**

**B:** pyridoxine + doxylamine (FDC) (PO) 10mg/10mg 8hourly till vomiting stops

**Referral:** Depends on the status of the patient, refer to a hospital if vomiting is intractable and if there is a need for high volume replacement.

## **11.7.10 Heartburn in Pregnancy**

Heartburn (also called acid indigestion or acid reflux) is a burning sensation that often extends from the bottom of the breastbone to the lower throat. It is caused by some of the hormonal and physical changes in pregnant women.

### **Non-pharmacological Treatment**

#### **Pregnant women should avoid:**

- Food and beverages that cause gastrointestinal distress
- Tobacco and alcohol
- Do not eat big meals, instead eat several small meals throughout the day
- Drinking large quantities of fluids during meals
- Do not eat close to bedtime, they should give themselves 2–3 hours to digest food before they lie down
- Sleep propped up with several pillows or a wedge.

### **Pharmacological Treatment**

**A:** compound magnesium trisilicate (PO) as needed until when the heartburn subsides.

**OR**

**A:** omeprazole (PO) 20–40mg 24hourly

**OR**

**C:** pantoprazole (PO) 40mg 24hourly

## **11.7.11 Other Medical Disorders in Pregnancy**

Other medical disorders in pregnancy/other gynecological disorders include diabetes mellitus, glucose intolerance, malaria, HIV/AIDs complications, Pelvic Inflammatory Diseases (PID) etc. All these complications are discussed under specific disease chapters.

## **11.7.12 Stimulation of Labour and Myometrial Relaxation**

Myometrium stimulants should be used with great care before delivery especially in porous women. Use in obstructed labour should be avoided.

Oxytocic's are indicated for: –

- Augmentation of labour
- Induction of labour
- Active management of third stage of labour.
- Uterine stimulation after delivery for management of PPH due to uterine atony

### **Induction of Labour**

#### **Indications/Contraindications**

- The indication for induction must be documented, and discussion should include reason for induction, method of induction, and risks, including failure to achieve labour and possible increased risk of Caesarean section<sup>5</sup>
- If induction of labour is unsuccessful, the indication and method of induction should be re-evaluated.

#### **Pre-induction assessment**

- Health care providers should assess the cervix (using the Bishop score) to determine the likelihood of success and to select the appropriate method of induction.
- The Bishop score should be documented.
- Care providers need to consider that induction of women with an unfavorable cervix is associated with a higher failure rate and increased rate of operative deliveries.

#### **Post-dates induction**

- Women should be offered induction of labour between 41+0 and 42+0 weeks as this intervention may reduce perinatal mortality and meconium aspiration syndrome without increasing the Caesarean section rate
- Women who chose to delay induction >41+0 weeks should undergo twice-weekly assessment for fetal wellbeing

## **Options for Cervical Ripening/Induction: Unfavorable Cervix**

- Intracervical Foley catheters are acceptable agents that are safe both in the setting of a vaginal birth after Caesarean section and in the outpatient setting
- Double lumen catheters may be considered a second-line alternative

## **Pharmacological Treatment**

**A:** misoprostol (PO) 25µg 2 hourly for 24hours or Misoprostol (PV) 25µg 6hourly for 24hours can be considered a safe and effective agent for labour induction with intact membranes and on an inpatient basis.

**OR**

**S:** dinoprostone (PV) 3mg 6hourly a total of 2doses

### **Note**

- Misoprostol should not be used in the setting of vaginal birth after Caesarean section due to the increased risk of uterine rupture.
- Oxytocin should be started no earlier than 4hours after the last dose of misoprostol.

## **Options for induction with a favourable cervix**

- Amniotomy should be reserved for women with a favorable cervix. Care should be given in the case of unengaged presentation because there is a risk of cord prolapse.
- After amniotomy, oxytocin should be commenced early in order to establish labour.
- In the setting of ruptured membranes at term, oxytocin should be considered before expectant management.
- Women positive for group B streptococcus (GBS) should be started on oxytocin as early as possible after ruptured membranes in order to establish labour within 24 hours.
- Both high- and low-dose oxytocin may be considered within a hospital protocol.
- Because of the various concentrations, oxytocin infusion rates should always be recorded in mU/min rather than mL/hr.
- Oxytocin induction maybe considered in the hospital setting of vaginal birth after Caesarean section.
- For induction of labour use: Oxytocin IV, the dose will depend on parity.

## **Primigravida**

**A:** oxytocin (IV) 5IU in 500mls of 0.9% sodium chloride the initial dose should be 8-10drops/Minute, the titration may be gradually increased at intervals not shorter than 20 minutes and increments of not more than 5drops/minute, until a contraction pattern similar to that of normal labour is established. The recommended maximum rate is 40d/m.

## **Multiparous**

**A:** oxytocin (IV) start with low dose e.g., 2.5IU in 500mls of fluid titrate as above. Regulate the dose according to response.

### **Note**

- Induction of labour with uterotonic drugs requires vigilant monitoring
- Induction of labour should only be attempted at hospitals with capacity to perform Caesarean section

## **Augmentation of Labour**

If labour progress is not optimum labour augmentation is necessary. Can be achieved by:

**A:** oxytocin as above

**OR**

Artificial rupture of membranes (ARM) and oxytocin. If membranes are already ruptured and no labour progress the steps above should be followed; rule out obstruction before augmenting labour with oxytocin.

## **Myometrial stimulation after delivery**

**A:** oxytocin (IM) 10IU after delivery of the infant; when no response give oxytocin (IV infusion) 20 units in 500mls of NS running at 10–20 drops per minute.

**OR**

**C:** ergometrine (IM) 0.25–0.5mg after delivery of the infant, in the absence of myometrium

contraction and to prevent postpartum hemorrhage.

**OR**

**A:** misoprostol (PO/PV) 800–1000µg

**Note**

Use Ergometrine cautiously in cardiac and hypertensive disease patients

**Myometrium relaxation (Tocolysis)**

It is done to relax the uterus in order to:

- Relieve fetal distress immediately prior to Caesarian section
- Stop uterine contractions in premature labour
- Prevent uterine rupture
- Perform external cephalic version

**Pharmacological Treatment**

**B:** nifedipine (PO) 20 mg stat, followed by 10–20mg 6–8hourly

**OR**

**B:** salbutamol (PO) 4mg stat, when required (maximum daily dose 32mg)

**Note**

- $\beta$  -stimulants should never be used if the patient had an antepartum hemorrhage
- $\beta$  -stimulants are contra-indicated for cardiac disease and severe anemia in pregnancy

**11.7.13 Rhesus Incompatibility**

Incompatibility between an infant's blood type and that of its mother, resulting in destruction of the infant's red blood cells (hemolytic anemia) during pregnancy and after birth by antibodies from its mother's blood circulation.

**Investigations**

- Maternal Blood group+ Rhesus factor
- Paternal blood group+ Rhesus factor
- Infant Cord blood at delivery for grouping, FBC, Coombs test to detect maternal antibodies and Total Bilirubin

**Prevention of Rhesus isoimmunisation**

If the mother is Rhesus negative give

**C:** anti D immunoglobulin 300microgram within 72hours of delivery

**Antepartum**

**C:** anti D immunoglobulin (IM)at 28-32weeks of gestation

**Abortion in Rhesus negative mother give**

**C:** anti D immunoglobulin 100microgram (IM) within 72hours of abortion

**Note**

For the management of other medical conditions in pregnancy e.g. Malaria, Peripartum cardiomyopathy, Diabetes and Renal disease in pregnancy refer to specific chapters in this guideline.

**11.8 Postpartum Care**

**11.8.1 Mastitis**

It is the inflammation of the breast usually associated with breastfeeding.

**Clinical Presentation**

- May develop rapidly,
- Breast becomes red and swollen, tenderness, warmth and burning sensation
- Fever

### **Non-pharmacological Treatment**

- Drinking plenty of liquids and resting
- Feed the baby more frequently and ensure adequate emptying.
- Expressing the milk more often in non-breastfeeding mothers.

### **Pharmacological Treatment**

**C:** flucloxacillin + amoxycillin (FDC) (PO) 500mg 12hourly for 5-7days

**OR**

**B:** amoxycillin + clavulanic acid (FDC)(PO) 625mg 12hourly for 5-7days

**AND**

**A:** ibuprofen (PO) 500mg 8hourly for 5days

**OR**

**A:** paracetamol (PO) 500–1000mg 8hourly for 5days

### **11.8.2 Puerperal Sepsis**

It is the infection of the uterus and surrounding tissues within 6 weeks postpartum manifesting as postpartum metritis, postpartum endometritis parametritis, peritonitis or septicaemia.

#### **Clinical presentation**

- Fever
- Foul smelling lochia
- Lower abdominal pain or generalized abdominal pain and tenderness
- Delayed involution

#### **Investigations**

- Full blood picture and Cross Matching
- Check LFT, RFT, Electrolytes
- Blood culture in case of suspected septicaemia
- Abdominal pelvic ultrasound

#### **Management of Puerperal sepsis at Dispensary and Health Center**

**A:** Establish IV line and give compound sodium lactate/0.9% sodium chloride 2l then continue as required

**AND**

**B:** amoxicillin + Clavulanic acid (FDC) (PO) 625 12hourly for 5days

**AND**

**A:** metronidazole (PO) 400mg hourly for 5days

**AND**

**A:** gentamycin (IV) 80mg 12hourly for 24-48hours.

**Referral:** resuscitate and refer immediately to hospital for further investigations and management.

#### **Management of puerperal sepsis at the hospital**

- Blood transfusion in anaemic
- Plan interventions eg (laparotomy, uterine evacuation etc) appropriately.
- Continue with the above antibiotic for 5-7 days
- Adjust drugs depending on the Culture and susceptibility results or if not available and there is no improvement after 3 days of treatment with above antibiotics switch to:

**B:** metronidazole (IV) 500mg 8hourly for 5-7days

**AND**

**D:** ceftriaxone + sulbactam (FDC) (IV) 1.5g 12hourly for 5-7 days

**OR**

**S:** piperacillin + tazobactam (FDC) (IV) 4.5g 12hourly for 5-7days

### **Prevent Puerperal infections by**

Observation of aseptic technique when performing all obstetric procedures including Pelvic examinations during labour. Administration of prophylactic antibiotics within 1hour before performing a caesarean section or manual removal of Placenta.

**C:** amoxycillin + clavulanic acid (FDC)(IV) 1.2g stat

**OR**

**D:** ceftriaxone + sulbactam (FDC) (IV)1.5g stat

**AND**

**B:** metronidazole (IV) 500mg stat

### **11.8.3 Abnormal Uterine Bleeding (AUB)**

It is the uterine bleeding after menopause, in between menstrual periods or abnormally heavy and or prolonged menstrual bleeding. Abnormal uterine bleeding (AUB) is a common condition affecting women that has significant social and economic impact.

**The causes of AUB are classified and summarized into an Acronym; PALM-COEIN**

- P-Polyps
- A-Adenomyosis
- L-Leiomyosma
- M-Malignancy
- C-Coagulopathy
- O-Ovulatory dysfunction
- E-endometrial causes
- I-Iatrogenic
- N-Not yet Classified

#### **Clinical presentation**

##### **Polyps**

- Contact vaginal bleeding
- Abdominal discharge
- Pelvic pain or heaviness

##### **Adenomyosis**

- Premenstrual uterine cramps
- Dysmenorrhea
- Heavy menstrual bleeding

##### **Leiomyoma**

- Abdominal mass and distension
- Heavy or prolonged menstrual bleeding
- Lower abdominal pain and discomfort

##### **Malignancy**

- Presentation depend on type of malignant
- Abnormal intermenstrual or postmenopausal contact bleeding (cervical cancer)
- Foul smelling bloody or mucoid Vaginal discharge
- Weight loss, loss of appetite, early satiety

##### **Coagulopathy**

- History of bleeding tendencies
- Heavy and or prolonged menstruation

##### **Anovulatory dysfunction**

- Irregular bleeding, often heavy
- Infertility or subfertility

##### **Endometrial causes**

- Heavy or prolonged menstruation
- Irregular menstruation associated with endometrial hyperplasia

## **Investigations**

- Investigate according to the possible cause of AUB basing on clinical suspicion
- A complete blood count (CBC)
- Pregnancy test in reproductive age to exclude pregnancy
- Examination under anaesthesia and biopsy in case of malignancy
- Cervical and vaginal swab
- Abdominal pelvic Ultrasound, CT scan, MRI, Xray as indicated
- LFT, RFT, Electrolytes
- Hysteroscopy, Cystoscopy, Proctoscopy in case of suspected malignancy
- Biopsy in case of suspected malignancy
- Specific Tumor markers in certain suspected malignancies e.g. ovarian tumors.
- Testing for coagulation disorders should be considered only in women who have a history of heavy menstrual bleeding beginning at menarche or who have a personal or family history of abnormal bleeding

## **Pharmacological Treatment**

### **The treatment will depend of the causative factor.**

**C:** tranexamic acid (PO) 500 –1000mg 6–8hourly as required until the bleeding is controlled

**OR**

**A:** combined oral contraceptives (PO) Useful for anovulatory bleeding.

**OR**

**A:** medroxyprogesterone acetate (PO) 5–10mg 24hourly for 10–14days initially and repeated for 10days each month thereafter

**OR**

**C:** norethisterone (PO) 5mg 24hourly for 10days. Then 5mg 12hourly from days 19 to 26 of the two subsequent cycles, should be given to prevent recurrence of the condition.

## **Surgical management**

AUB due to organic causes may be amenable to surgical intervention. The decision regarding the approach and the timing for surgical intervention should depend on final diagnosis, expertise and other resources.

## **Referral**

Immediately refer to the next level facility with capable for appropriate evaluation and management recommend

## **11.8.4 Dysmenorrhea**

It is a painful menstruation preventing normal activities and requires medication. There are 2 types of dysmenorrhea:

**Primary (no organic cause).** Typically, pain occurs on the first day of menses, usually about the time the flow begins.

**Secondary (pathological cause)** e.g., usually the pain is due to other underlying causes eg PID, endometriosis, etc.

## **Pharmacological Treatment**

**A:** ibuprofen (PO) 200–600mg 8hourly (maximum 2.4 g/day)

**OR**

**A:** acetylsalicylic acid (PO) 300–600mg 4hourly

**OR**

**A:** diclofenac (PO) 50–100mg 8–12hourly

**OR**

**B:** mefenamic acid (PO) 500mg 8hourly

**AND**

**A:** hyoscine butyl bromide (PO) 20mg 8hourly for 5days

Women with regular complaints can easily detect length of use during their periods (2–3days usually enough). Treat the underlying condition if known

**Note**

For primary dysmenorrhea patients may be advised to start taking ibuprofen one or two days before menses and continue for three to four days during menses to minimize painful menstruation

### 11.8.5 Endometriosis

It is the presence of endometrial glands and stroma in locations other than the uterine endometrium and musculature. The common locations of endometriosis include the pelvis, small intestines, bowels, appendix, anterior abdominal wall and incision scars

**Clinical presentation**

- Chronic pelvic pain, lower back pain and rectal pain
- Dysmenorrhea
- Dyspareunia
- Dysfunctional uterine bleeding
- Infertility

**Management at Dispensary and Health center**

**A:** ibuprofen (PO) 200–600mg 8hourly (maximum 2.4 g/day)

**OR**

**A:** acetylsalicylic (PO) acid 300–600mg 4hourly

**OR**

**A:** diclofenac (PO) 50–100mg 8–12hourly

**OR**

**B:** mefenamic acid (PO) 500mg 8hourly

**OR**

**A:** hyoscine butyl bromide (PO) 20mg 8hourly for 5days

**Referral:** Refer the patient with endometriosis to hospital for further investigations and management.

**Management of endometriosis at Hospital****Investigations**

- Abdominal ultrasound
- pelvic/transvaginal CT scan
- MRI
- Laparoscopy

**Pharmacological treatment of endometriosis**

**A:** combined oral contraceptive pills (PO) 1 tab 24hourly for 3months

**OR**

**A:** medroxyprogesterone acetate (IM) 300mg monthly for 6months.

**OR**

**S:** danazol (PO) 200-400mg 12hourly depending on the severity. Continue RX to maintain amenorrhea.

**OR**

**S:** Goserelin (IM) 3.6mg monthly for 4-6months

### 11.9 Contraception

#### 11.9.1 Short term Contraceptive Methods

**Short-term hormonal contraceptives**

Before initiating hormonal contraceptives:

- Check blood pressure
- Perform vaginal examination (to check normal size of uterus)
- Check for contraindications like deep vein thrombosis

**Follow up:**

- Instruct women always to inform the doctor or nurse that they are on contraceptives while attending clinic or hospital.

- Women on oral contraceptives need regular physical check-ups including blood pressure measurement every six months
- Need to withdraw Contraceptives in:
  - Pregnancy
  - Severe headaches especially associated with visual disturbances
  - Numbness or paresis of extremities
  - Unexplained chest pain or shortness of breath
  - Severe leg pains etc
  - Deep vein thrombosis.

**The recommended short-term hormonal contraceptives are:**

**A:** ethinyloestradiol+norgestrel (FDC) (PO) 0.03mg/0.3mg 24hourly

**OR**

**A:** ethinyloestradiol+levonogestrel (FDC) (PO) 0.03mg/0.15mg 24hourly

**OR**

**A:** ethinyloestradiol+desogestrell (FDC) (PO) 0.03mg/0.15mg 24hourly

**OR**

**A:** medroxyprogesterone acetate (IM) 150mg every three months

**OR**

**A:** levonorgestrel (PO).0.03mg 24hourly

#### Note

- Take the first pill on the 5<sup>th</sup> day of menstruation and then continue every day without any interruptions
- Check blood sugar and hypertension after every 6 months
- Avoid use in women with severe hypertension and women without proven fertility

#### Post-coital contraception

The method is applicable mostly after rape and unprotected sexual intercourse where pregnancy is not desired. Within 3 days (72 hours) of unprotected sexual intercourse, give:

**A:** levonorgestrel (PO) 1.5mg stat

**OR**

**A:** levonorgestrel (PO) 0.75mg 12hourly. 2 doses

**OR**

**B:**CuT380A Intrauterine Contraception Device (IUCD) may also be used.

#### Note

Emergency contraception should not be used as a routine method of contraception. Clients should be advised to use regular effective contraceptive methods of their choice.

#### Barrier methods (condoms)

**A:** Male Condoms

**A:** Female Condoms

A correct use of both male and female condoms is required with every act of sexual intercourse for greatest effectiveness.

#### Note

Condoms are the only contraceptives that can protect against both pregnancy and STIs

### 11.9.2 Long-term Contraceptive methods

#### Implant Contraceptives

Implants are contraindicated to:

- Severe hypertension
- Thromboembolism
- Active liver disease
- Sickle cell anaemia
- Genital bleeding
- Severe headaches

The following are the recommended implants:

**A:** etonogestrel 68mg in single silastic capsule with applicator is implanted in the left upper arm with local anesthesia. Is effective for 3 years

**OR**

**A:** levonorgestrel 75mg in two silastic capsules implanted subdermal in the left upper arm

with local anesthesia. Is effective for 5 years and is recommended for women who have completed their family or not ready for sterilization or those not able to take estrogen containing contraceptives.

**Note**

Implants may be inserted during the immediate postpartum period, or after 4 weeks postpartum

**Intrauterine Contraceptive Device**

It is the device containing copper or Levonorgestrel that is inserted in the uterus to prevent pregnancy

**B:** CuT380A Intrauterine Contraception Device (IUD) may also be used

It can be inserted during the immediate postpartum period, within 48hours postpartum or after 4 weeks postpartum

The contraindication to postpartum IUD includes

- Active postpartum haemorrhage
- Puerperal sepsis/chorioamnionitis, active PID
- Allergy to copper
- Period within 48 hours and 4we

**Note**

Use the WHO Medical eligibility criteria (MEC) wheel on providing FP methods

### **11.9.3 Permanent (surgical) Contraceptive Methods**

The available permanent contraceptive options include;

- Bilateral tubal ligation (female sterilization) for women who will not want more children
- Vasectomy for men who will not want more children

### **11.8.4 Infertility**

Infertility is a condition of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.

A detailed history taking, and physical examination are invaluable for the diagnosis for causes of infertility

**Investigation:** Not every fertility test will be done for every case.

**WOMEN:** For women, fertility testing may include basic gynaecologic examination

- VDRL tests
- Urine routine and microscopic
- Cervical mucus examination
- Abdominal pelvic/Transvaginal USS
- HSG (hysterosalpingogram)for tubal patency
- Hysteroscopy-
- Diagnostic laparoscopy- This test is only done when symptoms point to possible endometriosis, as part of treatment for blocked fallopian tubes, or in some cases of unexplained infertility.
- Hormonal profile- FSH, LH, TSH, AMH, T3 & T4, Testosterone, prolactin, estradiol and progesterone.

**MEN:** Perform the following

- Semen analysis
- VDRL tests
- Hormonal profile-FSH, Testosterone, but sometimes also LH, estradiol, or prolactin

**Treatment** will depend on the underlying cause

**Non-pharmacological Treatment**

- Weight reduction in obese clients.
- Educate the couple on the importance of having sexual intercourse during the fertile window
- Try to avoid smoking/excessive drinking

**Pharmacological Treatment****Ovulation stimulation:**

**C:** clomiphene citrate (PO) 50mg 24hourly for 5days from the 2nd–5th day of menstruation. (maximum 6 cycles)

**Polycystic Ovarian Syndrome (PCOS)**

**A:** metformin (PO) 500mg 8hourly is used for PCOS treatment, alone or along with fertility drugs

**Hyperprolactinemia**

**C:** bromocriptine (PO) 2.5–5mg 24hourly until the prolactin level is within the normal range  
**OR**

**S:** cabergoline (PO) 0.25–0.5mg once or twice weekly initially then the dose is gradually increased monthly until prolactin levels normalize. Doses of less than 3mg per week are usually enough to achieve this goal

**Surgeries:**

- Tubal surgery for Tubal blockage
- Myomectomy for uterine fibroids
- Ovarian drilling is a possible surgical treatment for PCOS-related infertility

**Referral**

Refer all patients with infertility to a gynecologist.

# CHAPTER TWELVE

## SEXUALLY TRANSMITTED INFECTIONS

Sexually transmitted infections (STIs) — are generally acquired by sexual contact with a person who has an STI. The organisms (bacteria, viruses or parasites) that cause sexually transmitted diseases may pass from person to person in blood, semen, or vaginal and other bodily fluids. Reproductive tract infections (RTIs) occur in the genital tract and affect both women and men. Some RTIs, such as syphilis and gonorrhea, are sexually transmitted, but many are not. In women, overgrowth of endogenous microorganisms normally found in the vagina may cause RTIs (yeast infection, bacterial vaginosis).

### Clinical Presentation

- Sores or bumps on the genitals or in the oral or rectal area.
- Painful or burning urination.
- Discharge from the penis.
- Vaginal discharge that is abnormal in colour, odour, amount or consistency.
- Itching or irritation of the vulva or vagina.
- Unusual vaginal bleeding.
- Pain during sex.
- Lower abdominal pain
- Genital ulcers, sores or blisters
- Swelling, lumps or ulcer in the groin area

### 12.1 STIs/RTIs Management Approaches

Management of STIs/RTIs can be done in either of the following approaches:

- **Aetiological laboratory approach:** By identification of causative agents through laboratory methods and sensitivity pattern to the medicine to used, followed by disease-specific treatment.
- **Aetiological clinical approach:** By targeting disease treatment based on suspected causative agents diagnosed clinically. This is not appropriate at any health facility because of its demands on the clinical acumen of the service provider and the danger of incorrect diagnosis and, hence, insufficient treatment.
- **Syndromic approach:** This identifies clinical syndromes (symptoms and signs) followed by syndrome-specific treatment that targets causative agents which cause the syndrome.

#### Management of STIs/RTIs using Aetiological Laboratory Approach

It identifies causative agents through laboratory methods, followed by disease-specific treatment. This is the best approach to be used at a Health Facility (HF) which has a Laboratory capable of doing the Laboratory Investigation and producing timely result(s) so as to enable the clinician to prescribe medicine (s) according to the causative agent(s) and sensitivity pattern.

#### Management of STIs/RTIs using Syndromic Approach

This approach is recommended if the HF is not able to conduct appropriate Laboratory Investigation(s) and producing timely result(s) to enable the clinician to prescribe the medicine in accordance with causative agent(s).

Syndromic management of STIs is based on the diagnosis of defined symptoms and easily recognizable clinical signs. Each syndrome can be caused by several different causative agents. For each syndrome, a well-defined standard treatment which has been proven to be effective against most endemic causative agents for the syndrome are used.

Syndromic approach of managing STIs/RTIs entails the service provider to follow laid down steps in a flow chart which guides him/her in making rational management decisions for treating the client. These are therefore known as treatment flow-charts. They may also be known as treatment algorithms, treatment protocols or treatment decision trees. They guide the provider through a series of decisions and actions that need to be made. Each decision or action is enclosed in a box, with one or two routes leading out of it to another box, with another decision or action. Upon learning a patient's symptoms and signs, the service provider turns to the flow chart for the relevant syndrome

and works through the decisions and suggestions it guides to manage the client accordingly. Each flow chart is made up of a series of three steps. These are:

- The clinical problem (the patients presenting symptoms and signs),
- The decision that needs to be taken,
- The action that needs to be carried out.

## 12.2 Urethral Discharge Syndrome (UDS)

UDS refers to the presence of abnormal secretions in the distal portion of the urethra.

### Causes

- *Neisseria gonorrhoeae* and
- *Chlamydia trachomatis*.

### Clinical Presentation

- Urethral discharge,
- Burning or painful micturition,
- Itchy urethra and increased frequency and urgency of micturition.

### Note

- Persistent or recurrent symptoms of urethritis may be due to drug resistance, poor compliance or re-infection. In some cases, there may be infection with *Trichomonas vaginalis* (TV).
- Male patients complaining of urethral discharge and/or dysuria should be examined for evidence of discharge. If none is seen per inspection, the urethra should be gently milked from the ventral part of the penis towards the meatus.
- Delayed or inadequate treatment may result into orchitis, epididymitis, urethral stricture and/or infertility.

### Investigation(s) if the HF has a Laboratory capable of doing:

- |                           |                                   |
|---------------------------|-----------------------------------|
| • Culture and Sensitivity | • Quantitative or qualitative PCR |
| • Gram stain              | • Genetic sequencing              |
| • ELISA                   |                                   |

Management and Treatment of UDS (*see flow chart 12.1*)

## 12.3 Vaginal Discharge Syndrome (VDS)

VDS refers to change of colour, odour and/or amount of vaginal secretions.

### Causes

- *T. vaginalis*,
- *C. albicans*
- *Bacterial Vaginosis*
- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*

### Clinical Presentation

- |                                   |   |
|-----------------------------------|---|
| • Abnormal vaginal discharge,     | • Increased frequency and urgency of micturition and/or painful coitus. |
| • Burning or painful micturition, |   |
| • Itchy vulva,                    |   |

### Note

- A spontaneous complaint of abnormal vaginal discharge is most commonly due to a vaginal infection.
- *T. vaginalis*, *C. albicans* and *Bacterial Vaginosis* are the commonest causes of vaginal infection while
- *Neisseria gonorrhoeae* and *Chlamydia trachomatis* cause cervical infection.
- The clinical detection of cervical infection is difficult because a large proportion of women with gonococcal or chlamydia infections are asymptomatic.
- vaginal discharge is therefore highly indicative of vaginal infection, but poorly predictive for cervical infection
- Due to the high prevalence of gonorrhea and chlamydia, all women presenting with VDS should receive treatment for both vaginal and cervical infections.

- Delayed or inadequate treatment of VDS may result to endometritis, salpingitis, oophoritis or ectopic pregnancy.
- Gonococcal or chlamydial cervical infection may be asymptomatic

**Investigation(s) if the HF has a Laboratory capable of doing:**

- |                           |                                   |
|---------------------------|-----------------------------------|
| • Wet preparation         | • Pap test (Papanicolaou test)    |
| • Gram stain              | • ELISA                           |
| • Culture and Sensitivity | • Quantitative or qualitative PCR |
| • Fluorescent Microscopy  | • NB starts simple to complex     |

Management and Treatment of VDS (see *flow chart 12.2*)

## 12.4 Lower Abdominal Pain Syndrome or Pelvic Inflammatory Disease (PID)

PID is defined as the inflammation of the uterus, fallopian tubes, ovaries and pelvic peritoneum. It is also known as lower abdominal pain syndrome. It commonly occurs as a result of infection ascending from the cervix. It can also occur as a result of trans-cervical procedure.

**Causes**

- |                                    |             |          |
|------------------------------------|-------------|----------|
| • <i>Neisseria gonorrhoeae</i> ,   | • Anaerobic | bacteria |
| • <i>Chlamydia trachomatis</i> and |             |          |

**Clinical Presentation**

- |  |                      |           |
|--|----------------------|-----------|
| • Lower abdominal pain and tenderness, | • Menometrorrhagia,  |           |
| • Painful micturition,                 | • Fever and sometime |           |
| • Painful coitus,                      | • Nausea and         | vomiting. |
| • Abnormal vaginal discharge,          |                      |           |

**Note**

- Delayed or inadequately treated PID may lead to chronic lower abdominal pain,
- Pelvic abscess,
- Ectopic pregnancy,
- Dysmenorrhea and infertility.

**Investigation(s) if the HF has a Laboratory capable of doing:**

- |                           |                                   |
|---------------------------|-----------------------------------|
| • Wet preparation         | • Pap test (Papanicolaou's test)  |
| • Gram stain              | • ELISA                           |
| • Culture and Sensitivity | • Quantitative or qualitative PCR |
| • Fluorescent Microscopy  |                                   |

Management and Treatment of PID (see *flow chart 12.3*)

**In-patient treatment of PID**

All patients with PID who have fever or body temperature  $\geq 38^{\circ}\text{C}$  should be admitted for closer care. The recommended in-patient treatment options for PID are as follows:

**Regimen 1:**

- A: cefixime (PO) 400mg 12hourly for 7-14days  
**AND**  
A: doxycycline (PO) 100mg 12hourly for 7-14days  
**AND**  
A: metronidazole (PO) 400mg 8-12hourly for 7-14days  
**OR**  
B: metronidazole (IV) 500mg 8-12hourly for 7-14days

**Regimen 2:**

- A: ceftriaxone (IM) 1gm 24hourly for 5-7days  
**AND**  
A: doxycycline (PO) 100mg 12hourly for 7-14days  
**AND**  
A: metronidazole, (PO) 400mg 8-12hourly 7-14days  
**OR**  
A: metronidazole (IV) 500mg 8-12hourly 7-14days

### **Regimen 3:**

**S:** clindamycin (IV) 900mg 8hourly for 7-14days

**AND**

**A:** gentamicin (IV) 1.5 mg/kg 6-8hourly 7-14days

#### **Note**

For all three regimens, therapy should be continued for two days after the patient has improved and then be followed by doxycycline (PO) 100 mg 12hourly for 14days.

- Patients taking metronidazole should be cautioned to avoid alcohol.
- Doxycycline is contraindicated in pregnancy.

## **12.5 Painful Scrotal Swelling (PSS)**

PSS is the inflammation of the epididymis and testis, often accompanied with scrotal pain, swelling and tenderness. It is also known as epididymorchitis.

#### **Causes**

- *Neisseria gonorrhoea* and
- *Chlamydia trachomatis*

#### **Clinical Presentation**

- Scrotal pain,
- Scrotal swelling and tenderness,
- Scrotal oedema
- Fever

#### **Note**

Among the common complications of painful scrotal swelling include infertility and scrotal abscess.

#### **Investigation(s) if the HF has a Laboratory capable of doing:**

- Gram stain
- Culture and Sensitivity
- ELISA
- Quantitative or qualitative PCR
- Genetic sequencing

Management and Treatment of PSS (*see flow chart 12.4*)

## **12.6 Ano-rectal Syndrome (ARS)**

Is defined as soreness, burning, itching or other irritation of the rectum together with redness in the area of anus. Sometimes it is accompanied by diarrhea and it may occur as a toxic side effect of oral administration of certain broad-spectrum antibiotics.

#### **Causes**

- *Neisseria gonorrhoeae*,
- *Chlamydia trachomatis*,
- *Treponema pallidum*
- *Herpes Simplex Virus*.
- *Shigella spp.*, or
- *Entamoeba histolytica*

#### **Clinical presentation**

- Purulent rectal discharge
- Mucous rectal discharge
- Watery rectal discharge
- Soreness, burning, itching or other irritation of the rectum together with redness in the area of anus
- There may also be ineffectual straining to defecate ("tenesmus"), sometimes mistakenly described as "constipation" by patients.
- The anus and rectum may be intensely painful, with external and internal ulceration
- Abdominal pain or cramping, abdominal swelling, distention or bloating;
- Bloody stool (blood may be red, black, or tarry in texture),
- Burning feeling,
- Change in bowel habits, constipation, diarrhea;
- Fecal incontinence (inability to control stools),
- Flatulence; pain, which may be severe, in the abdomen, pelvis, or lower back,

- Urgent need to pass stool and watery diarrhea including multiple episodes.
- A proctoscopic examination (which should be done, if feasible) will reveal rectal pus, bleeding or ulceration.

#### Note

- Proctitis may be caused by *Salmonella spp.*, *Shigella spp.*, or *Entamoeba histolytica* as a part of gastroenteritis, which may manifest as diarrhoea with fever, anorexia, and abdominal cramps.
- Antibiotics that destroy normal intestinal bacteria and allow other bacteria to grow in their place may also cause proctitis.
- Herpes proctitis may be mistaken for the rectal manifestation of ulcerative colitis or Crohn's disease.
- Proctitis typically causes painless bleeding or the passage of mucus (sometimes mistaken for diarrhoea) from the rectum.
- All cases of proctitis in MSM should be treated for gonorrhoea and chlamydia infections.
- Symptoms of diarrhoea, bloody stools, abdominal cramping, nausea, and/or bloating may indicate *Giardia spp* infection or amoebic dysentery.

#### Other non-STI causes of ARS include:

Anal fissure, Fecal impaction, Food intolerance, Gastroenteritis (bacterial and viral), Inflammatory bowel disease (includes Crohn's disease and ulcerative colitis), Neurological damage, and Perirectal or perianal abscess.

Other symptoms might occur with rectal discharge includes gastrointestinal symptoms which vary depending on the underlying disease, disorder or condition. These may include:

- Abdominal pain or cramping, abdominal swelling, distention or bloating; bloody stool (blood may be red, black, or tarry in texture), burning feeling, change in bowel habits, constipation, diarrhea; fecal incontinence (inability to control stools), flatulence; pain, which may be severe, in the abdomen, pelvis, or lower back, urgent need to pass stool and watery diarrhea including multiple episodes.

#### Investigation(s) if the HF has a Laboratory capable of doing:

- |                                  |   |
|----------------------------------|---|
| • Wet preparation                | • <i>Treponema pallidum</i> particle agglutination (TPPA) |
| • Gram stain                     | • ELISA   |
| • Pap test (Papanicolaou's test) | • Quantitative or qualitative PCR                         |
| • Culture and Sensitivity        | • Genetic sequencing                                      |
| • Rapid Plasma Re却n (RPR)        | • Fluorescent Microscopy                                  |

Management and Treatment of ARS(see flow chart 12.5.)

## 12.7 Oropharyngeal Syndrome

Oral sex can lead to oropharyngeal STIs (infections of mouth and throat).

#### Causes

- *Human Papilloma Virus*,
- *Herpes Simplex Virus*,
- *N. gonorrhoea*
- *Chlamydia spp*
- *Treponema pallidum*

#### Clinical presentation

- Pharyngitis,
- History of unprotected oral sex

#### Investigation(s) if the HF has a Laboratory capable of doing:

- |                                  |   |
|----------------------------------|---|
| • Wet preparation                | • <i>Treponema pallidum</i> particle agglutination (TPPA) |
| • Gram stain                     | • ELISA   |
| • Pap test (Papanicolaou's test) | • Quantitative or qualitative PCR                         |
| • Culture and Sensitivity        | • Genetic sequencing                                      |
| • Rapid Plasma Re却n (RPR)        |   |

- Fluorescent Microscopy

Management and Treatment of Oropharyngeal syndrome (see flow chart 12.6.)

## 12.8 Genital Ulcer Disease (GUD)

GUD is a loss of continuity of skin or mucous membrane producing one or more lesions in the genital area.

### Causes

- *Treponema pallidum*,
- *Haemophilus ducreyi*,
- *Chlamydia trachomatis*,
- *Herpes simplex virus type 2 (HSV)*
- *Calymmatobacterium granulomatis*.

### Clinical presentation

- Ulcer
- Sore
- Vesicle

### Investigation(s) if the HF has a Laboratory capable of doing:

- Wet preparation
- Gram stain
- Culture and Sensitivity
- Fluorescent Microscopy
- Treponema pallidum particle agglutination (TPPA)
- Rapid Plasma Reagins (RPR)
- ELISA
- Quantitative or qualitative PCR
- Genetic sequencing

Management and Treatment of GUD (see flow chart 12.7)

## 12.9 Neonatal Conjunctivitis (Ophthalmia Neonatorum)

Ophthalmia Neonatorum (ON) means inflammation of the conjunctiva of a newborn baby of less than 1 month of age.

Is a potentially sight threatening condition. If the baby is older, the cause is unlikely to be an STI.

### Causes

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*.
- Other non-STI causes of neonatal conjunctivitis include:
  - *Staphylococcus aureus*,
  - *Streptococcus pneumoniae*,
  - *Haemophilus and Pseudomonas spp*,
  - Viral, chemical and physical irritation.

### Presentation

- Reddish conjunctiva,
- Oedema/swelling of the eyelids
- Purulent eye discharge

### Prevention and control measures

- Screening of pregnant women,
- Early treatment of VDS in pregnant women
- Routine eye chemoprophylaxis in the newborn by providing A: 1% oxytetracycline eye ointment to all newborns.

### Note

Examine the neonate and exclude other congenital diseases

Management and Treatment of Neonatal conjunctivitis (see flow chart 12.8)

## 12.10 Inguinal Bubo (IB)

Inguinal and femoral bubos are localized enlargements of the lymph nodes in the groin area, which are painful and may be fluctuant.

They are frequently associated with lymphogranuloma venereum and chancroid

### Causes

- *Chlamydia trachomatis*

- *Haemophilus ducreyi*

### Clinical presentation

- Localized enlargements of the lymph nodes in the groin area,
- Painful and may be fluctuant.
- Pain,
- Fever
- Tenderness.

#### Note

- In many cases of chancroid an associated genital ulcer is visible, but occasionally may not be.
- Non-sexually transmitted local and systemic infections (e.g. infections of the lower limb) can also cause swelling of inguinal lymph nodes. These should therefore be ruled out.

### Investigation(s) if the HF has a Laboratory capable of doing:

- Culture and Sensitivity
- ELISA
- Quantitative or qualitative PCR
- Direct Fluorescent Antibody (DFA)

Management and Treatment of Inguinal BUBO (see **flow chart 12.9**)

### 12.11 STI/RTI flow charts

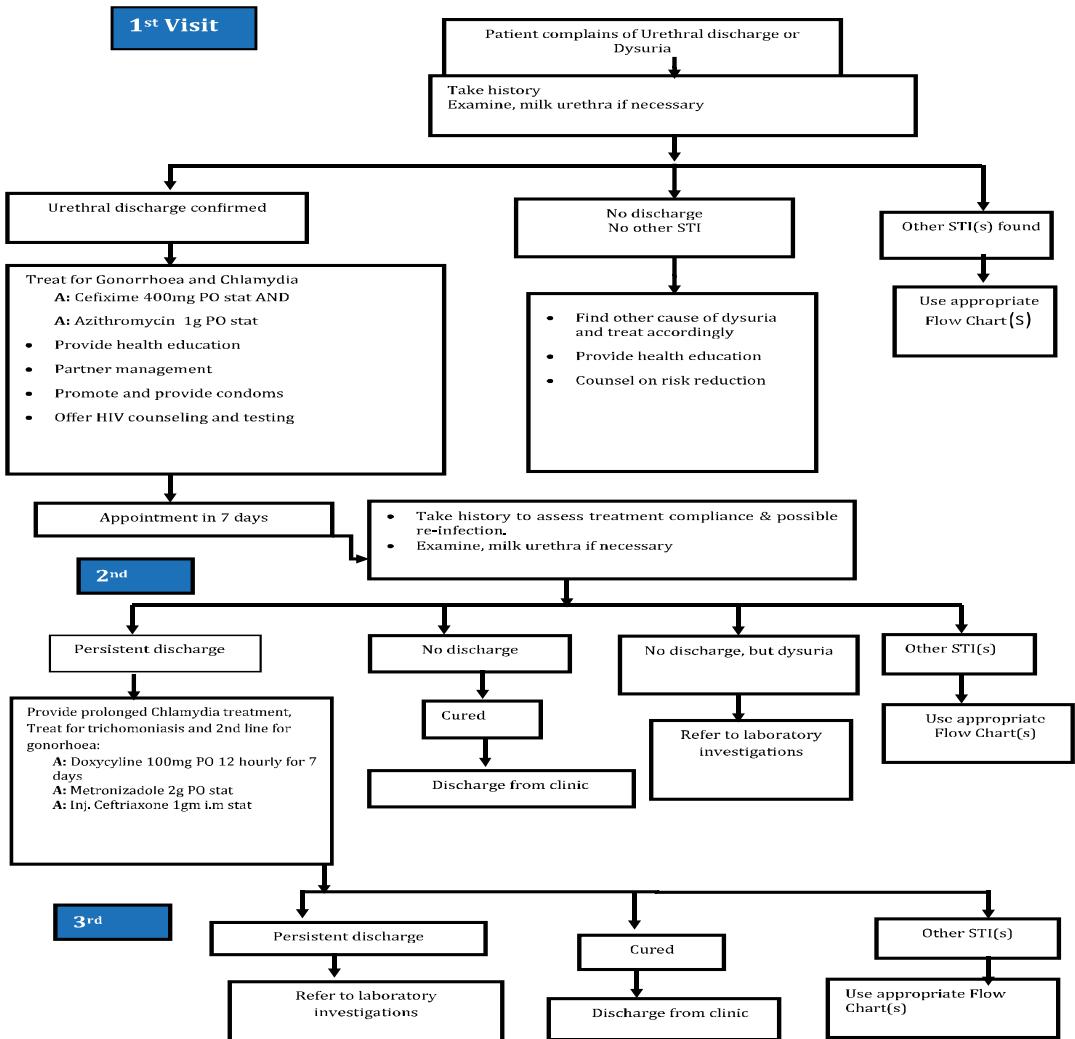
Steps in using the flow charts:

- Start by asking the patient for his/her symptoms.
- Find the appropriate flow chart, stated in the clinical problem box with "Patient Complaints of."
- The clinical problem box usually leads to an action box, which asks you to examine the patient and/or take the history.
- Next, move to the decision box. After taking the history and examining the patient you should have the necessary information to choose Yes or No accurately.
- Depending on your choice, there may be further decision boxes and action boxes.

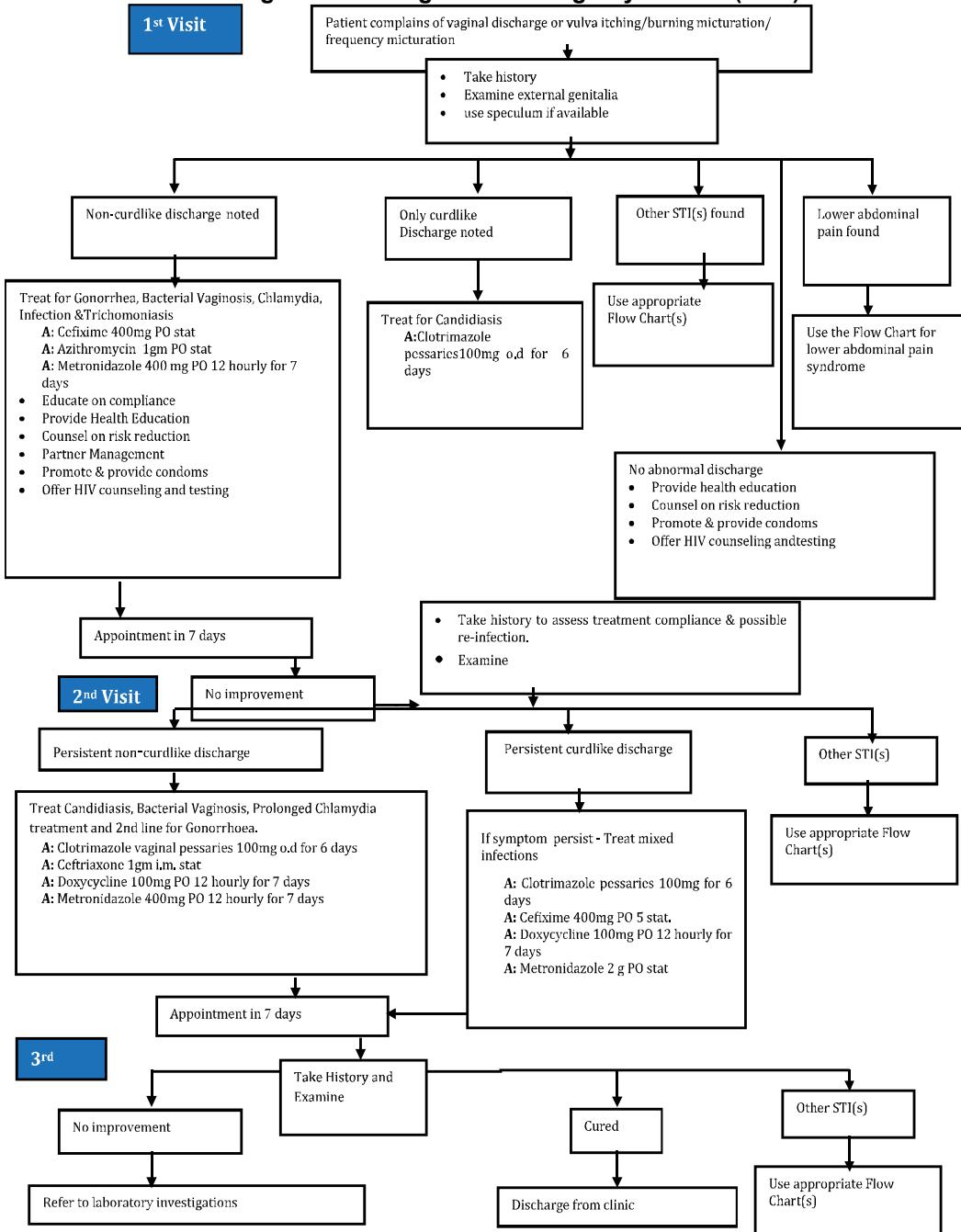
#### Note

For the appropriate management of STIs/RTIs syndrome, drugs in the watch group (azithromycin, cefixime and ceftriaxone) are the standard recommended for use as a first line treatment for the most STIs/RTIs starting at the Dispensary level, therefore, should be used only for STIs/RTIs at Primary HFs)

## Flow Chart 12.1: Management of Urethral Discharge Syndrome (UDS)

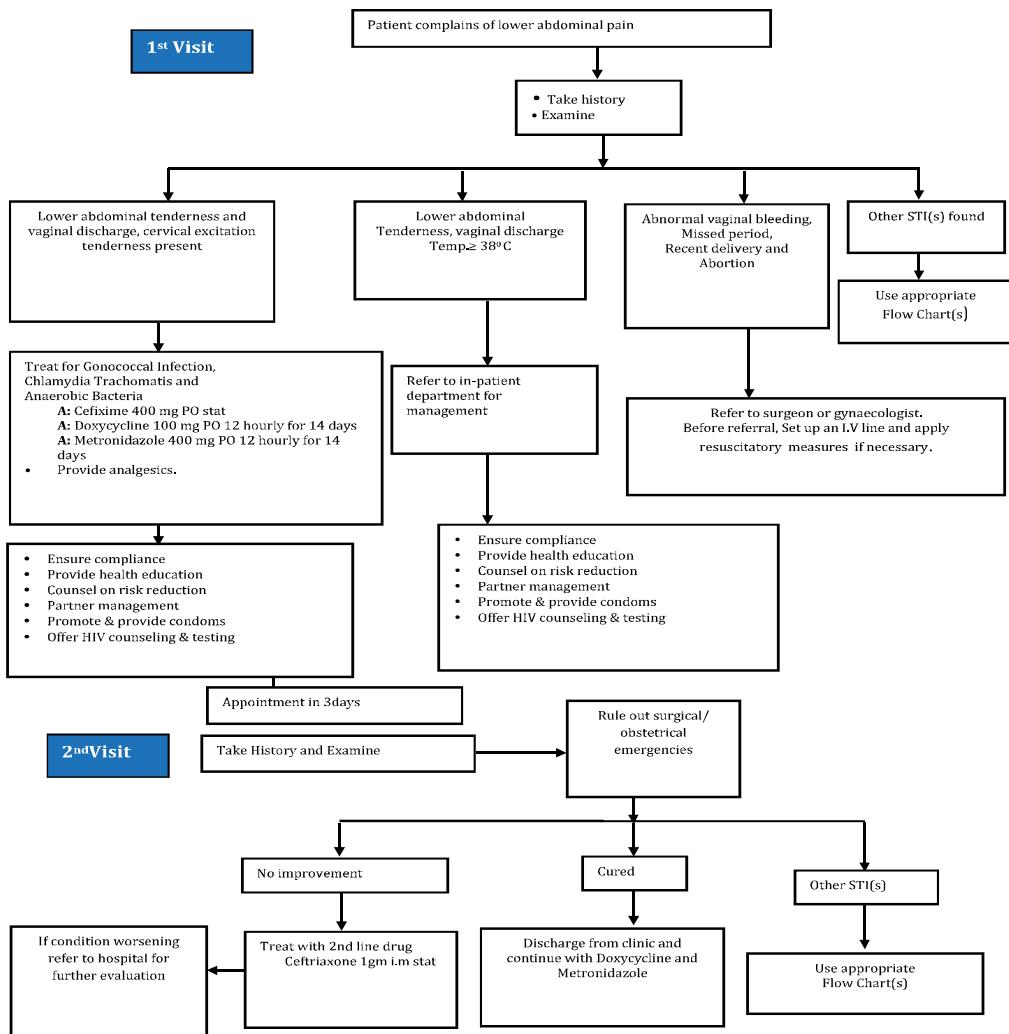


## Flow Chart 12.2: Management Of Vaginal Discharge Syndrome (VDS)

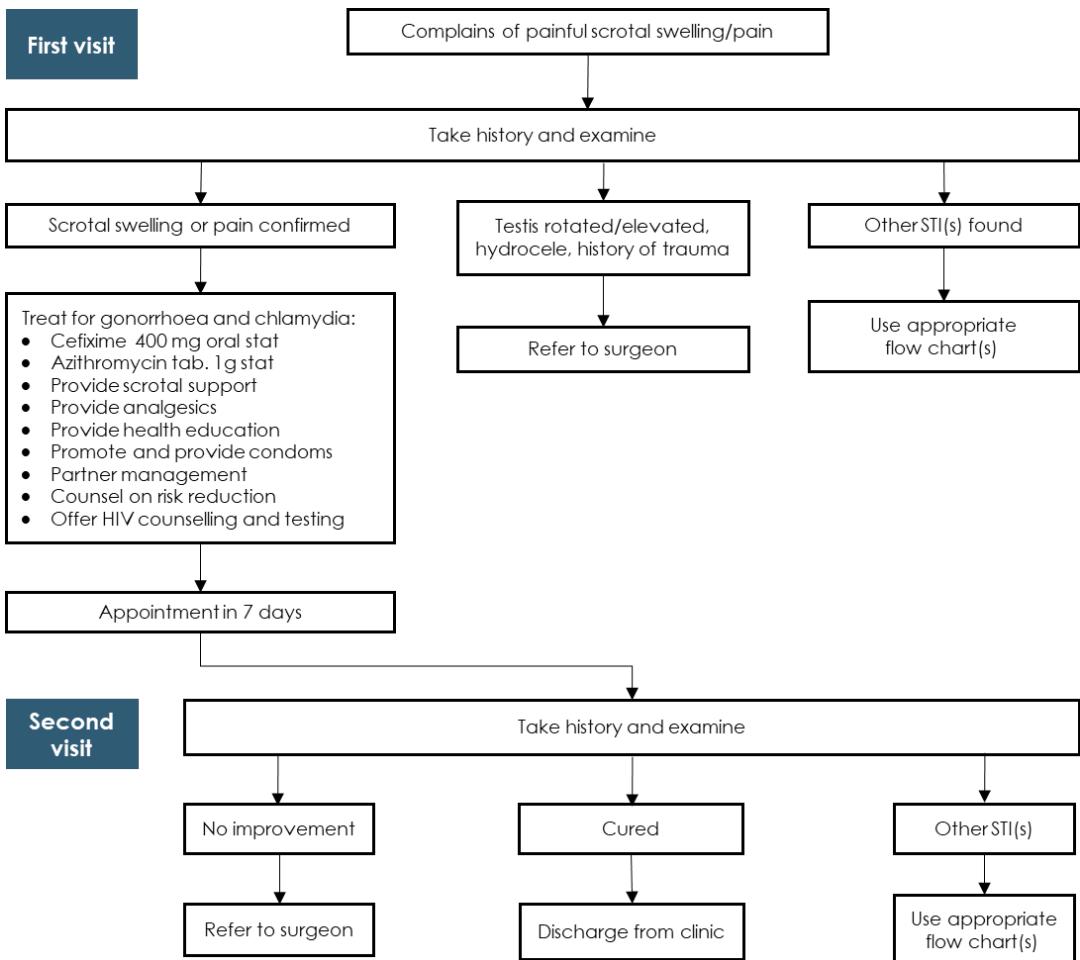


- Do not give Metronidazole in 1st trimester of pregnancy:
- Do not give doxycycline or ciprofloxacin in pregnancy or to lactating mother: Substitute with erythromycin 500 mg 8 hourly for 7 days and ceftriaxone 250 mg i.m. stat.

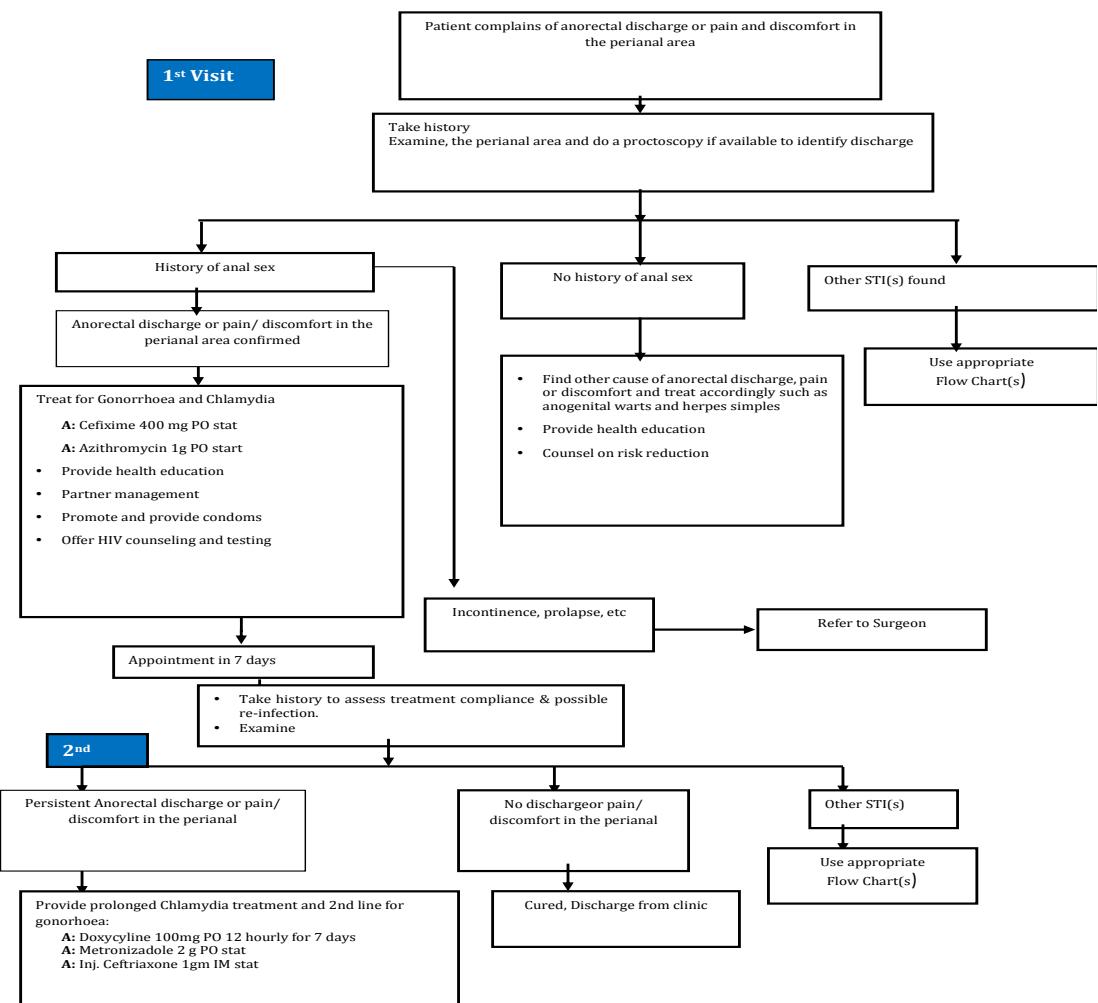
## Flow Chart 12.3: Management Of Lower Abdominal Pain Syndrome (PID)



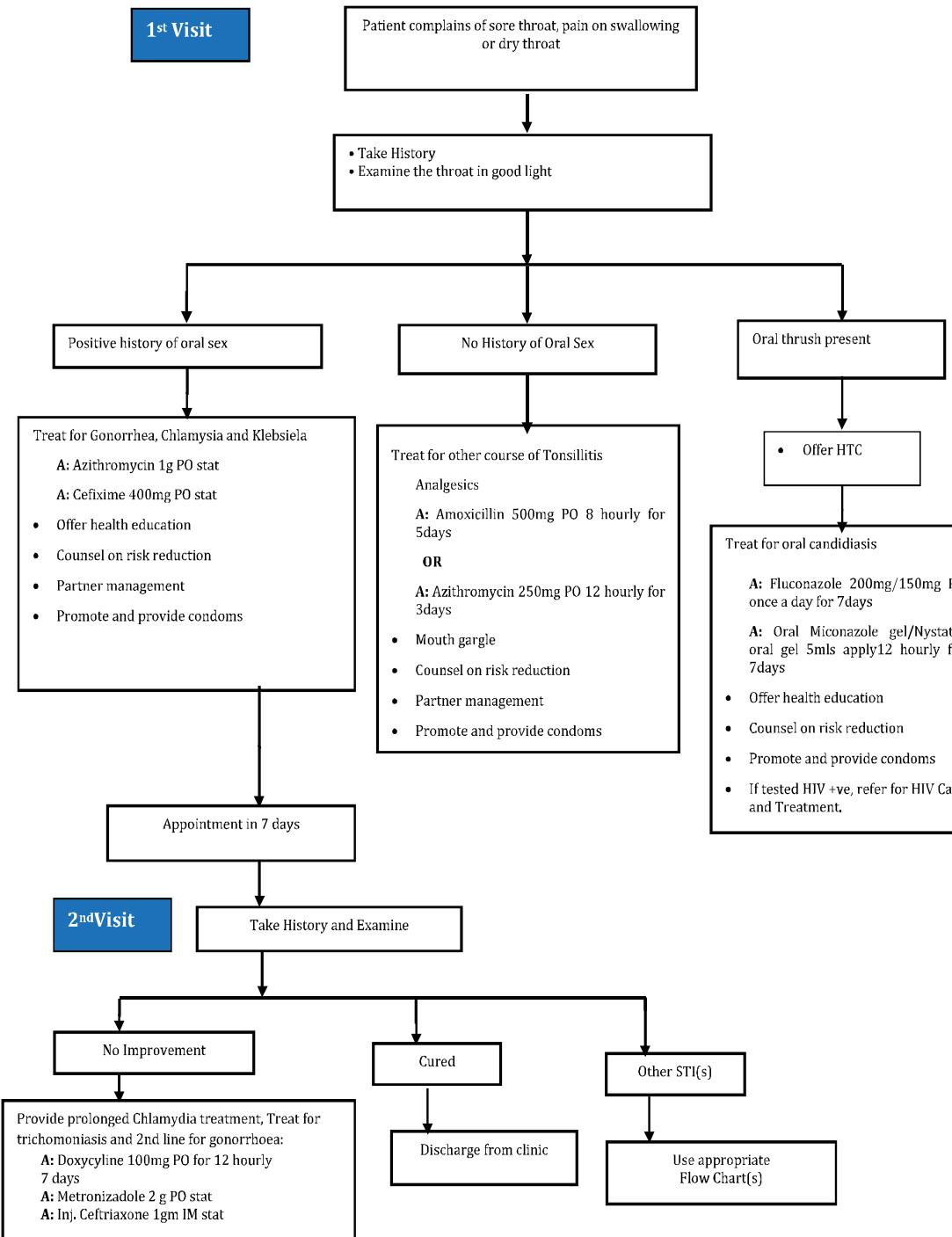
## Flow Chart 12.4: MANAGEMENT OF PAINFUL SCROTAL SWELLING (PSS)



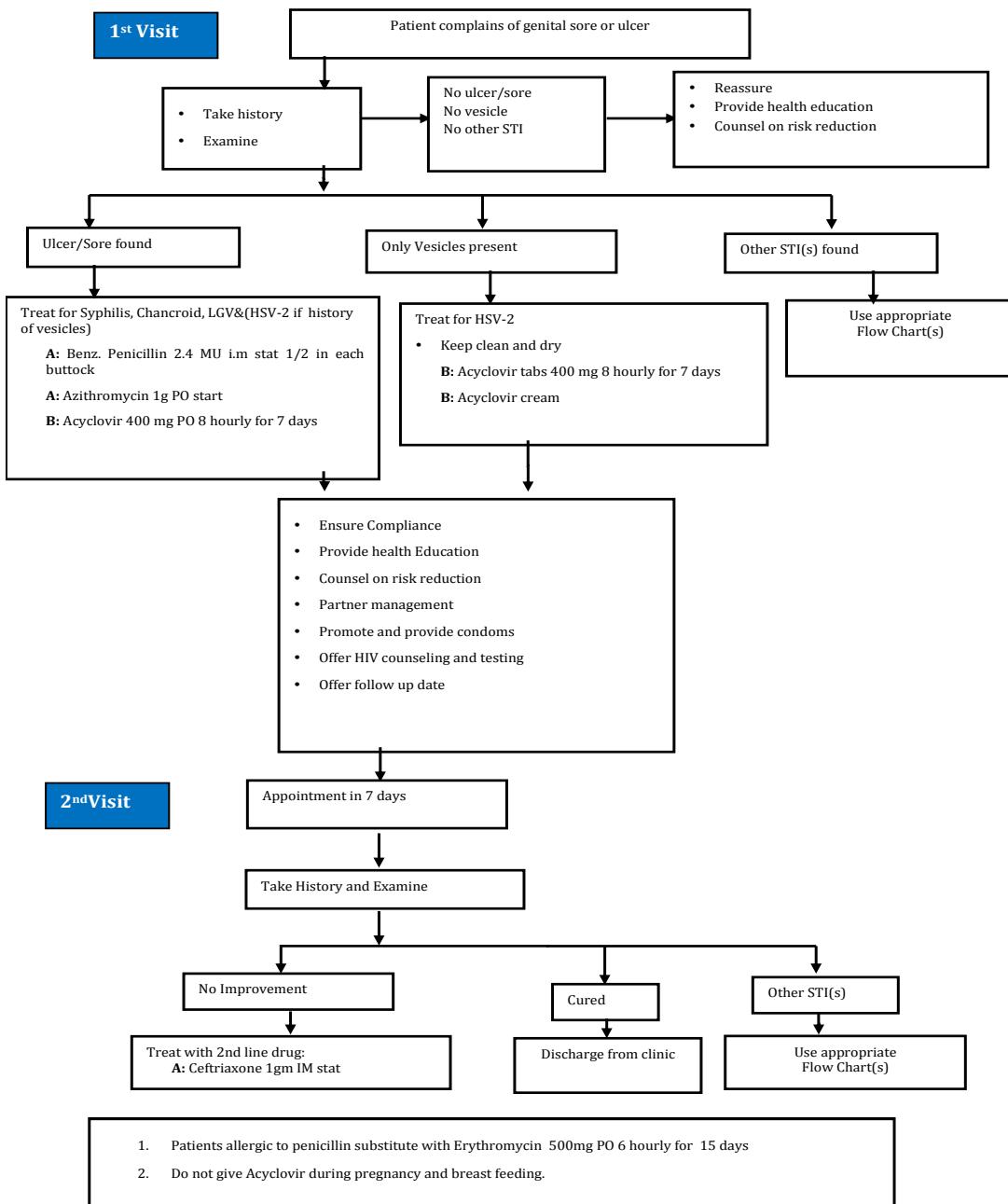
## Flow Chart 12.5: MANAGEMENT OF ANORECTAL SYNDROME (ARS)



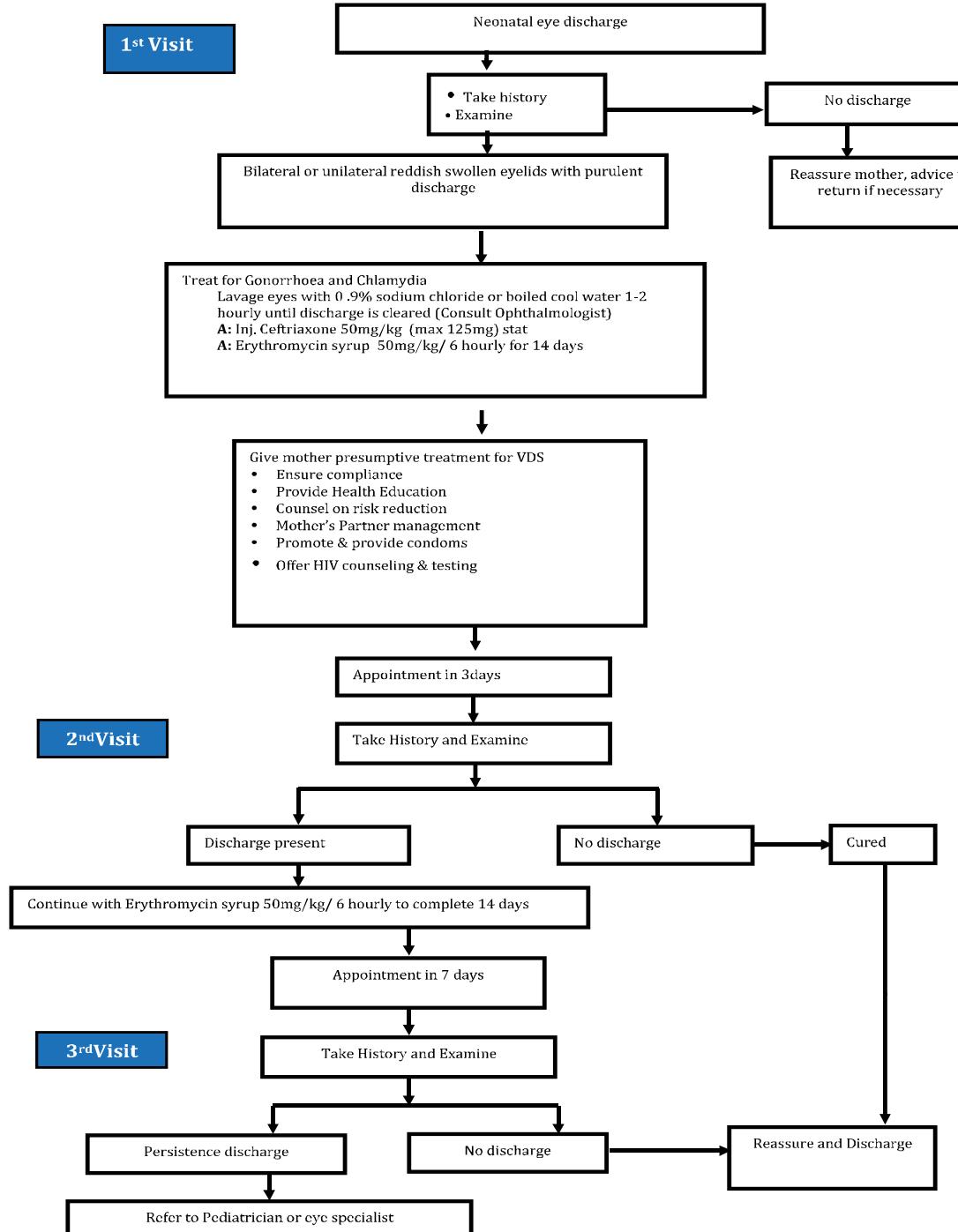
## FLOW CHART 12.6: MANAGEMENT OF OROPHARYNGEAL SYNDROME



## Flow Chart 12.7: MANAGEMENT OF GENITAL ULCER DISEASE (GUD)

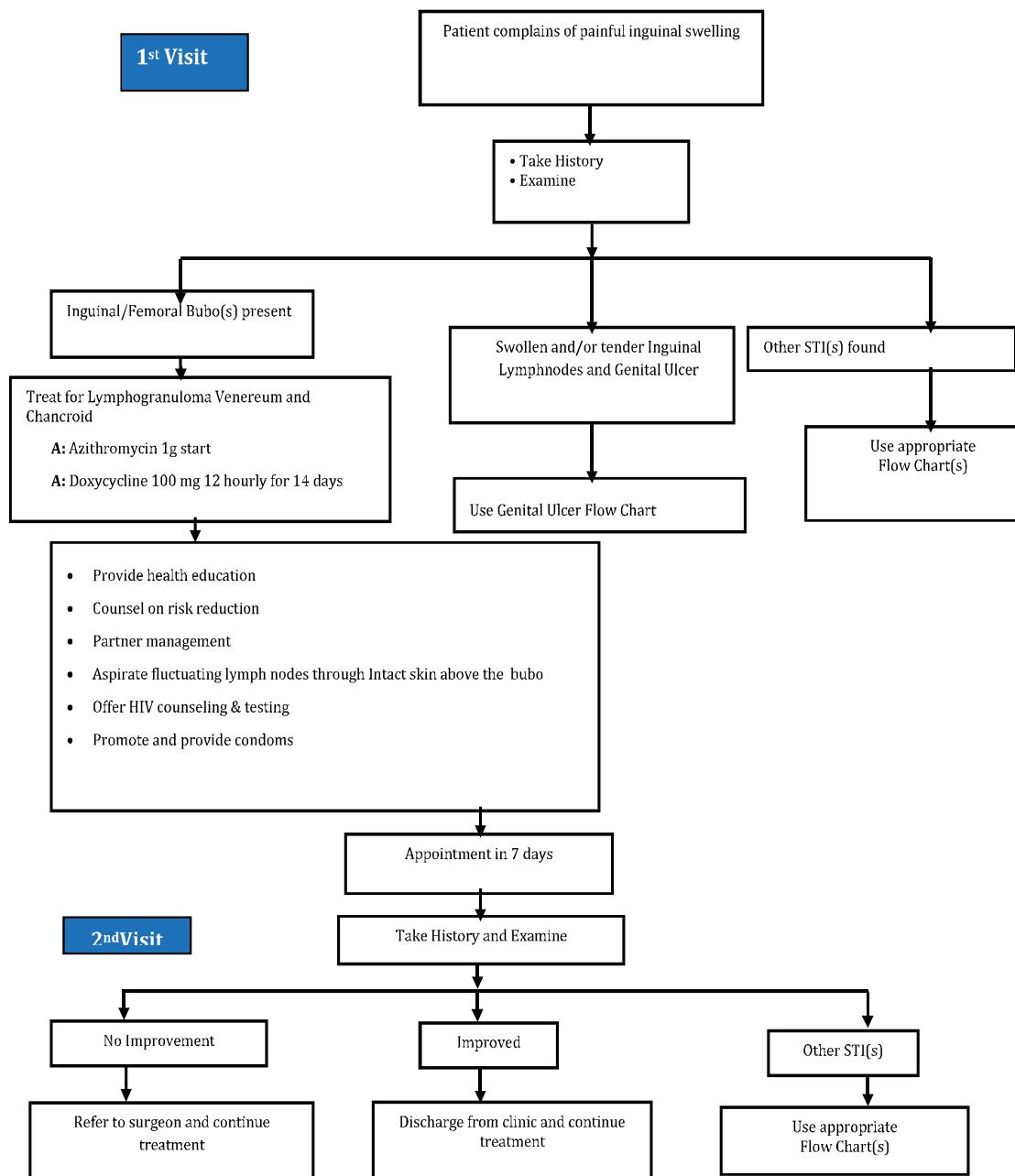


## Flow Chart 12.8: MANAGEMENT OF NEONATAL CONJUNCTIVITIS



- Both parents be examined and treated as per flow chart for genital discharge syndrome.

## FLOW CHART12.9: MANAGEMENT OF INGUINAL BUBOS (IB)



Note: Do not incise the BUBO

**Table 12.1 Management of Mixed Infections**

Mixed Sexually Transmitted Infections	Drug treatment (new episode)
UDS + SSS	Ceftriaxone (IM) 250mg stat <b>AND</b> Azithromycin (PO) 1g per week for 2weeks <b>AND</b> Metronidazole (PO) 2g stat <b>AND</b> Supportive therapy: to reduce pain advice bed rest, scrotal elevation with a scrotal support (T-bandage) and analgesics.
UDS + Balanitis	Cefixime (PO) 400mg stat <b>OR</b> Ceftriaxone (IM) 250mg stat <b>AND</b> Azithromycin (PO) 1g stat <b>OR</b> Doxycycline (PO) 100mg 12hourly for 7days <b>AND</b> Metronidazole (PO) 2g stat <b>AND</b> Clotrimazole cream, local application 12hourly for 7days
UDS + GUS	Cefixime (PO) 400mg stat <b>OR</b> Ceftriaxone (IM) 250mg stat <b>AND</b> Acyclovir (PO) 400mg 8hourly for 7days <b>AND</b> Benzathine Penicillin* (IM) 2.4MU stat <b>AND</b> Azithromycin (PO) 1g stat <b>OR</b> Doxycycline* (PO) 100mg 12hourly for 7days <b>AND</b> Metronidazole (PO) 2g stat
VDS + LAP	Ceftriaxone (IM) 250mg stat <b>AND</b> Azithromycin (PO) 1g per week for 2weeks <b>AND</b> Metronidazole (PO) 400mg 12hourly for 7–14days. Clotrimazole pessary to be added, if vulva oedema, itching, excoriations or curd-like discharge present
VDS + GUS (non-pregnant)	Cefixime 400mg stat <b>OR</b> Ceftriaxone (IM) 250mg stat <b>AND</b> Metronidazole (PO) 2g stat <b>AND</b> Benzathine Penicillin* (IM) 2.4 MU stat <b>AND</b> Azithromycin (PO) 1g stat <b>OR</b> Doxycycline* (PO) 100mg 12hourly for 7days <b>AND</b> Acyclovir (PO) 400mg 8 hourly for 7 days. Clotrimazole pessary to be added, if vulva oedema, itching, excoriations or curd-like discharge present
VDS + GUS (pregnant, breastfeeding)	Cefixime 400mg stat <b>OR</b> Ceftriaxone (IM) 250mg stat <b>AND</b> Metronidazole (PO) 2g stat <b>AND</b> Benzathine Penicillin* (IM) 2.4 MU stat <b>AND</b> Azithromycin (PO) 1g stat <b>OR</b> Erythromycin* (PO) 500mg 6hourly for 7days <b>AND</b> Acyclovir (PO) 400mg 8hourly for 7days. Clotrimazole pessary to be added, if vulva oedema, itching, excoriations or curd-like discharge present
LAP + GUS	Ceftriaxone (IM) 250mg stat <b>AND</b> Metronidazole (PO) 400 mg 12hourly for 7–14days <b>AND</b> Benzathine Penicillin* (IM) 2.4MU stat <b>AND</b> Azithromycin (PO) 1g per week for 2weeks <b>OR</b> Doxycycline* (PO) 100 mg 12hourly for 7–14days <b>AND</b> Acyclovir (PO) 400 mg 8hourly for 7days
SSS + GUS	Ceftriaxone (IM) 250mg stat <b>AND</b> Benzathine Penicillin* (IM) 2.4MU stat <b>AND</b> Azithromycin (PO) 1g per week for 2weeks <b>OR</b> Doxycycline* (PO) 100mg 12hourly for 7–14days <b>AND</b> Acyclovir (PO) 400mg 8hourly for 7days
<b>Note</b>	
In Penicillin-allergic patients: Give Doxycycline (non-pregnant women/men) or Erythromycin (pregnant women) for 14days instead of 7days	

## 12.8 Management of Other Common STI Conditions

### Late Syphilis

This refers to Syphilis infection of more than 2years.

**A:** benzathine benzylpenicillin (IM) 2.4MU once weekly for 3 consecutive weeks.

**AND**

**A:** azithromycin (PO) 2g stat.

### Syphilis in Pregnancy

Pregnant women should be regarded as a separate group requiring close surveillance to detect possible re-infection after treatment has been given. It is also important to treat the sexual partner(s).

**A:** benzathine benzylpenicillin (IM) 2.4MU, as a single dose

In case of late syphilis 3 doses of benzathine benzylpenicillin should be provided.

### **Congenital Syphilis**

All infants born to sero-positive mothers should be treated with a single intramuscular dose of benzathine benzylpenicillin, 50000IU/kg whether the mothers were treated during pregnancy (with or without penicillin).

Treatment regimens for early congenital syphilis (up to 2 years of age), and Infants with abnormal cerebrospinal fluid:

**A:** benzyl penicillin (IV) 100000–150000IU/kg/day administered as 50000IU/kg/dose 12hourly, for the first 7days and every 8hourly thereafter for a total of 10days

### **For congenital syphilis in children 2 or more years**

**A:** benzyl penicillin (IV or IM) 200000 – 300000IU/kg/day administered as 50000IU/kg every 4–6hourly for 10–14days

### **The alternative regimen for penicillin allergic patients, after the first month of life**

**A:** erythromycin (PO) 7.5–12.5 mg/kg 6hourly for 30days.

### **Syphilis and HIV Infection**

All patients with syphilis should be encouraged to undergo testing for HIV because of the high frequency of dual infection and its implications for clinical assessment and management.

### **Genital Warts (Venereal Warts)**

Human papilloma virus (HPV) is a common sexually transmitted pathogen. Genital warts are painless but may lead to serious complications. The removal of the lesion does not mean cure of the infection. No treatment is completely satisfactory. Recommended regimens for venereal warts are as follows:

### **Chemical Treatment (High level Health Facility Management)**

**D:** Podophyllin 10–25% in compound tincture of benzoin, applied carefully to the warts, avoiding normal tissue. External genital and perianal warts should be washed thoroughly 4–6 hourly after the application of podophyllin. Podophyllin applied to warts on vaginal or anal epithelial surfaces should be allowed to dry before removing the speculum or anoscope. Treatment should be repeated at weekly intervals.

### **Other treatment approaches (Available at higher centres)**

Cryotherapy with liquid nitrogen, solid carbon dioxide, or a cryoprobe. Repeat applications every 1-2 weeks

**OR**

Electrosurgery

**OR**

Surgical removal

### **Treatment for Vaginal Warts**

Recommended regimens for treatment of vaginal warts are:

**D:** cryotherapy (with liquid nitrogen)

**OR**

**D:** podophyllin 10–25% (allow to dry before removing speculum)

### **Treatment for Cervical Warts**

Treatment of cervical warts should not be started until the results from a cervical smear test are known

### **Management of Meatal and Urethral Wart**

**D:** Cryotherapy

**OR**

**D:** podophyllin 10–25%

### **Note**

Urethroscopy is necessary to diagnose intra-urethral warts, but they should be suspected in men with recurrent meatal warts.

# CHAPTER THIRTEEN

## SKIN DISEASES AND ALLERGIC REACTIONS

### 13.1 Bacterial Skin Infections

Bacterial skin infections can range from impetigo, folliculitis, furunculosis, erysipelas, cellulitis to recurrent boils. All these skin conditions are caused by either *Staphylococcus aureus* alone or together with *streptococcus*, but rarely *streptococcus* alone.

#### 13.1.1 Impetigo

Is a contagious primary infection of the skin involving the stratum corneum of epidermis. It is particularly common in children and people in disadvantaged areas.

##### Clinical presentation

- Polycyclic vesicles or blisters, which can contain pus
- Early lesions are isolated or confluent Erosions and yellowish crusts ("honey-colored")



Fig 13.1 Impetigo

##### Note

Impetigo is a clinical diagnosis and the typical location in children is around orifices, especially the mouth and nose.

##### Non-pharmacological Treatment

- Improve personal hygiene
- Hand washing
- Wash lesions with soap and water
- Remove crust

##### Pharmacological Treatments

A: Wet dressing with weak potassium permanganate (PP) soaks, 1:40000 (0.025%) solution 12hourly for 3–4days. Each session to last for 15 to 20minutes

A: gentian violet paint (topical) 0.5% 12hourly for 5days

OR

C: mupirocin (topical) 2% 12hourly for 5–7days

OR

C: fusidic acid (topical) 12hourly for 5–7days

If severe or systemic symptoms are present (e.g. pyrexia) add an oral antibiotic:

A: phenoxymethylpenicillin (PO): Adult 500mg; paediatric 25mg/kg given 6hourly for 7days

OR

A: erythromycin (PO): Adult 500mg; paediatric 25–50mg/kg 8hourly for 10days

OR

B: amoxicillin + clavulanic acid 625mg (PO) 8hourly for 5days

### 13.1.2 Folliculitis

Folliculitis is an infection of the hair follicles commonly due to *Staphylococcus aureus*, and Gram-negative bacteria such as *Pseudomonas* and *Candida albicans*.

##### Clinical presentation

Clinical features depend on risk factors, which may result into *Pseudo-folliculitis*, *Carbuncles* aggregation and *Furuncle (boil)*. The following are some of the clinical features:

- Scattered or extensive follicular pustules

- Macular or papulo-erythematous lesions, mainly located on thighs, buttocks, back and bearded area
- Papules and pustules
- Post-inflammatory hyperpigmentation
- Necrosis and suppuration with discharge of necrotic core
- Permanent scars or scarring alopecia
- Firm, broad swollen, painful, fluctuant deep nodules
- Multiple drainage tracts
- Fever and general body malaise

#### **Non-pharmacological Treatment**

- Suspected irritants should be avoided
- In *Pseudo-folliculitis* (*infection of the follicular opening*) of the bearded area, shaving should be stopped for several weeks until improvement occurs. Hair should be left to grow to at least 1 mm long.
- Shaving with electric razors is preferred over manual razors for beard folliculitis. Cleaning with water and soap

#### **Pharmacological Treatment**

**A:** potassium permanganate soaks, 1:40000 (0.025%) solution 12hourly for 3–4days. Each session for 15 to 20minutes

Apply:

**A:** gentian violet paint (topical) 0.5% 12hourly for 5days

**OR**

**C:** mupirocin (topical) 2% 12hourly for 7-14days

**OR**

**C:** fusidic acid (topical) 2% 12hourly for 7-14days

#### **Note**

If severe, or systemic symptoms are present (e.g. pyrexia) add an oral antibiotic as above in impetigo.

#### **Fungal folliculitis**

**A:** clotrimazole cream (topical) 12hourly for 4weeks

**OR**

**C:** miconazole cream (topical) 12hourly for 4weeks

### **13.1.3 Abscess**

Abscess is a collection of pus caused by *Staphylococcus aureus*.

#### **Clinical presentation**

- Painful pus-filled nodule
- Inflammatory erythematous plaque.
- Lymphangitis and satellite nodes may be experienced
- Fluctuant palpable swelling
- Fever is rare

#### **Non-pharmacological Treatment**

- By placing hot compresses over the swelling until it breaks

#### **Surgical Treatment**

- Incision and drainage

#### **Pharmacological Treatment**

**Indicated** in immunosuppressed patient, involvement of the face.

**A:** erythromycin (PO): Adult 500mg; paediatric 25–50mg/kg 8hourly for 7–10days

**OR**

**C:** flucloxacillin + amoxicillin (FDC) (P0): Adult 500mg; paediatric 25mg/kg 6hourly for 7–10days

### **13.1.4 Erysipelas and Cellulitis**

Erysipelas is an acute superficial spreading infection commonly caused by *Streptococci* without pus formation. Could also be due to Gram negative bacilli.

#### **Clinical presentation**

A prodrome of fever, chills, and malaise

- Locally, a large erythematous, swelling, well-demarcated, and usually raised lesion
- Regional adenopathy is frequent
- Superficial blistering secondary to edema,
- Superficial hemorrhage, may be sometimes be observed

#### **Non-pharmacological Treatment**

- Bed rest
- Elevation of the affected part
- Venous compression is recommended during the acute phase and subsequent weeks to reduce the risk of lymphedema
- Prophylaxis of deep venous thrombosis (DVT) should be considered depending on presence of other risk factors

#### **Pharmacological Treatment**

**A:** Weak potassium permanganate soaks, 1:40000 (0.025%) solution 12hourly for 3–4days, with each session lasting for 15–20minutes

**AND**

**A:** silver sulfadiazine cream (topical) 12hourly 24hourly

**OR**

**C:** mupirocin (topical) 2% 12hourly for 5–7days

**OR**

**C:** fusidic Acid (topical) 2% 12hourly for 5–7days

**AND**

**A:** phenoxymethylpenicillin (PO): Adult 250–500mg; paediatric 25mg/kg 6hourly for 5–7days

**OR**

**C:** flucloxacillin + amoxicillin (FDC) (PO): Adult 500mg; paediatric 25–50/kg 6hourly for 5–7days

**AND**

**A:** ibuprofen 400mg (OP) 6hourly for 5days

**Referral:** Refer if there are local or general signs of severity of developing necrotizing fasciitis.

### **13.1.5 Paronychia**

Paronychia is a painful infection that usually occurs at the nail fold. It may occur after injury or minor trauma and is caused by *Staphylococcus aureus*. It may also occur as a result of fungal infection.

#### **Clinical presentation**

- Painful nail
- Redness
- Swelling

#### **Pharmacological Treatment**

##### **Acute Paronychia**

**B:** amoxicillin with clavulanic acid (PO) 625mg 8hourly for 14days.

**AND**

**C:** mupirocin cream (topical) 12hourly for 14days

**OR**

**S:** clindamycin (PO) 300mg 12hourly for 14days

##### **Chronic Paronychia (commonly due to fungal infection)**

**A:** clotrimazole cream (topical) 1%, apply 12hourly for 14days

**AND**

**A:** fluconazole (PO) 200mg 24hourly for 14days

**OR**

**D:** itraconazole tablets (PO) 200mg 24hourly for 14days

**Note**

For acute paronychia incision and drainage may be needed

## 13.2 Fungal Skin Infections

### 13.2.1 Tinea Corporis (Body Ringworm)

Tinea corporis is a superficial fungal infection (dermatophytosis), commonly on the arms and legs, but may occur on any part of the body

#### Clinical presentation

- Enlarging raised annular lesions with a central area of clearing
- Fine scales may be present
- Hair loss in areas of infection



*Tinea corporis- before treatment*



*Tinea corporis- after treatment*

#### Investigation

Scraping edge of lesion for KOH

#### Pharmacological Treatment

**A:** benzoic acid compound ointment (topical) 12hourly up to 2weeks.

**OR**

**C:** miconazole cream (topical) 2%, apply thinly 12hourly a day. Continue for 5-7days after clearing of lesions.

**OR**

**C:** terbinafine cream (topical) 12hourly for 2weeks

#### If extensive, use

**C:** terbinafine (PO) 250mg 24hourly for 2weeks

### 13.2.2 Tinea Capitis

Is a superficial fungal infection (dermatophytosis), on the scalp. It is quite common in children.

#### Clinical features

- Enlarging raised annular lesions with a central area of clearing
- Fine scales may be present
- Hair loss in areas of infection

#### Pharmacological Treatment

**C:** miconazole cream (topical) 2%, apply thinly 12hourly for 2weeks. Continue for 5-7days after clearing of lesions

**AND**

**A:** griseofulvin (PO): Adult 500 mg; Paediatric 10-20mg/kg 24hourly for 6-8weeks

**OR**

**C:** terbinafine (PO): Adult 250mg 24hourly 6-8weeks; paediatric 62.5mg/ 10-20kg 24 hourly; 125mg/ 21-40 kg 24 hourly; 250mg/ 41kg 24hourly

### 13.2.3 Pityriasis Versicolor

It is a common fungal infection caused by yeast.

### **Clinical presentation**

- Hypo/Hyper pigmented macules and confluent patches
- Lesions have fine scales
- Commonly occurs on the chest, back, arms and occasionally neck and face

### **Investigation**

- KOH

### **Pharmacological Treatment**

A: clotrimazole cream (topical) 12hourly for 2weeks

**OR**

C: miconazole nitrate cream (topical) 2% 12hourly for 2weeks

**OR**

C: ketoconazole shampoo 3times per week for 4weeks (if extensive)

**AND**

A: fluconazole (PO) 300mg stat

**OR**

D: itraconazole (PO)200mg 24hourly for 2weeks

### **13.2.4 Tinea Pedis (Athlete's Foot) and Tinea Cruris**

It is a common fungal infection of the toes and is often the source of infection at other sites especially groin.

### **Clinical presentation**

- Tinea pedis presents with erythema and maceration between the toes, sometimes accompanied by painful vesicles.
- The chronic form is characterized by scaling, peeling on the soles.
- **Tinea cruris**-Itching and patches in the groin. Check for interdigital maceration for all with tinea cruris.

### **Prevention and Non-Pharmacological Treatment**

- Frequent change of socks/footwear, underwear.
- Use of cotton socks, underwear.
- Keep as dry as possible the spaces between toes after bathing always. Separating the opposing skin surfaces (e.g. with a piece of gauze) will help speeding healing.

### **Pharmacological Treatment**

A: clotrimazole cream (topical) 1% apply 12hourly for 2weeks

**OR**

C: miconazole cream (topical) 2%apply 12hourly for 2weeks

**OR**

C: terbinafine cream (topical) 24hourly for 14days

**AND**

A: gentian violet 24hourly for 14days for bacterial super infection

Alternatively

C: terbinafine (PO) 250mg 24hourly for 2- 4weeks

**OR**

D: itraconazole (PO) 200mg 24hourly for 2-4weeks

### **13.2.5 Candidiasis**

It is a fungal infection mainly caused by yeast, *Candida albicans*. Candidiasis is usually precipitated by prolonged use of contraceptive pills, AIDS, pregnancy, diabetes, prolonged use of antibiotics, corticosteroid use, and being on immunosuppressive treatment

### **Clinical presentation (depending on the site of infection)**

- Erythematous, moist exudate in the skin folds and accompanying satellite pustules
- Nail affection leads to painful swelling of the nail bed and folds, with pus discharge and is made worse by contact with water
- Oral lesions are characterized by white, adherent mucosal plaques in buccal cavity including the tongue

- Vaginal candidiasis is characterized by itchy, curd-like whitish vaginal discharge, dysuria and dyspareunia
- Gastrointestinal candidiasis may be associated with painful swallowing (odynophagia). Characteristic lesions are seen on endoscopy.

### **Pharmacological Treatment**

#### **Cutaneous candidiasis**

**A:** clotrimazole cream (topical) 1% apply 12hourly for 2weeks

**OR**

**C:** miconazole cream (topical) 2% apply 12hourly for 2weeks

**OR**

#### **Oral candidiasis**

**A:** nystatin oral suspension - gurgle and swallow 6hourly a day

- Newborns: 200,000–400,000 Units for 24 hours

- <2 years old 400,000–1,000,000 Units for 24 hours

- >2 years old 1,000,000–2,000,000 Units for 24 hours

**OR**

**C:** miconazole 2 % oral gel apply every 8hourly for 7days

#### **Vaginal candidiasis**

**A:** clotrimazole vaginal pessaries; insert one at night for 6days

**OR**

**C:** miconazole vaginal pessaries insert one at night for 3day

**AND (if severe)**

**A:** fluconazole (PO) 150mg stat

#### **Gastrointestinal Tract (GIT) candidiasis**

**A:** fluconazole (PO) 150mg 24hourly for 14days

### **13.2.6 Onychomycosis**

It is defined as infection of the nail plate by fungus. Patients with diabetes or peripheral neuropathy may be at a higher risk.

#### **Clinical presentation**

- Yellowish discoloration of the nail
- Subungual hyperkeratosis
- Over time lesions become more prominent and spread until the entire nail is affected

#### **Investigations**

- LFT before starting treatment and monitoring monthly.

### **Pharmacological Treatment**

**A:** fluconazole (PO) 150-300mg once weekly for 6–12months

**OR**

**C:** terbinafine (PO) 250mg 24hourly for 6-8weeks. For toe nails the duration of treatment is generally 12–16weeks.

**OR**

**D:** itraconazole (PO) 200mg 12hourly for 7days is given as pulsed dosing, of each month for 6months

#### **Note**

terbinafine and itraconazole should not be used in pregnancy and while breastfeeding

### **13.2.7 Chromoblastomycosis**

Chronic infection involving inoculated after minor trauma e.g. thorn prick.

#### **Clinical presentation**

- Nodule that progressively increases in into verrucous plaque

## **Pharmacological Treatment**

**D:** itraconazole (PO) 200mg 24hourly for 6-9months

### **13.2.8 Mycetoma (Madura Foot)**

Is a chronic infection of skin and subcutaneous tissue? It can be caused by fungi or bacteria. Once tests have established the etiology, the term Actinomycetoma is used for bacterial form, while Eumycetoma is used for the fungal form. Clinical presentation depends on the affected site and the disease can last for months to years.

#### **Clinical presentation**

- First lesion: nodule
- Localization: feet, legs, arms, buttocks, scalp, trunk
- Discharging sinuses where grains may be visible usually white yellow for Actinomycetoma or black for Eumycetoma
- Pain before rupture of discharging sinus

#### **Investigations**

- KOH
- Biopsy
- Local Xray to rule infiltration of underlying bone.

#### **Treatment of Actinomycetoma (bacteria form)**

##### **Pharmacological Treatment**

**A:** co-trimoxazole (PO) 480mg–960mg 12hourly for 5weeks

**AND**

**S:** amikacin 7.5mg/kg 12hourly for 5weeks

Alternatively

**A:** co-trimoxazole (PO) 480mg–960 mg 12hourly for 5weeks

**AND**

**S:** dapsone (PO): adult 100mg 24hourly for 2–4months; Paediatric 25–50mg 24hourly for 5weeks

#### **Treatment of Eumycetoma (Fungi form) Non-pharmacological Treatment**

- Surgery where indicated
- Footwear and protective clothing in at-risk populations e.g. cattle herders

##### **Pharmacological Treatment**

**D:** itraconazole (PO) 200mg 12hourly for 5weeks or longer (up to a year).

#### **Referral to surgeon**

- Radical surgery for some cases.

## **13.3 Parasitic Infestations**

### **13.3.1 Scabies**

Scabies is an intensely pruritic and highly contagious infestation of the skin caused by mite *Sarcoptes scabiei*.

#### **Clinical presentation**

- Itchy vesicles and papules. Itching worse at night.
- Papules in between finger spaces, wrists, penis and scrotum.
- Someone else in the family is itching.

#### **Non-pharmacological Treatment**

- Treat all members of the household at the same time to prevent reinfection, regardless of presence or absence of itching.
- Advise patients to bathe and dress regularly and change bed linen at the same time of treatment.

#### **Pharmacological Treatment**

**A:** benzyl benzoate emulsion, BBE (25% for adults, 12.5% for children)

Adults and children over 2 years: Apply with fingers, from neck down to cover the whole-

body surface, while paying attention to all skin folds. Leave emulsion in place for 6-8 hours overnight.

#### **Repeat the application after 7 days.**

**OR**

**C:** lindane lotion (1%) to be applied as BBE above (do not use in children less than 1 year)

**AND**

**C:** betamethasone valerate cream (topical) 12hourly for the itch

**AND**

**A:** cetirizine (PO) 10mg 12hourly for 3- 4weeks

**OR (if extensive, Norwegian scabies)**

**A:** ivermectin (PO) 200microgram/kg stat then repeat after 1week

Should be in combination with the topical above

## **13.4 Viral Infections**

### **13.4.1 Herpes Simplex**

It is an acute viral infection caused by Herpes simplex virus hominis (types HSV1, HSV2 acquired by close contact with an infected individual

#### **Clinical presentation**

- Preceding tingling sensation, discomfort and itching,
- Grouped vesicles forming on the skin, and mucous membranes, particularly the buccal area, genitalia, conjunctivae, and cornea,
- **Eczema herpeticum** –herpes simplex infection in Atopic Eczema patients.

#### **Pharmacological Treatment**

**B:** acyclovir cream (topical) applied 4hourly for 7–10days

**OR (especially if severe)**

**B:** acyclovir (PO) 200mg 6hourly for 7–10days

#### **For recurrent cases**

**B:** acyclovir (PO) 400mg 12hourly for 6months up to 1year.

#### **Note**

Benefit of systemic acyclovir is optimum when given within the first 72hours of onset of symptoms

### **13.4.2 Chickenpox**

It is a highly infectious disease caused by *Varicella zoster* virus (VZV)

#### **Clinical presentation**

- Red macular rash with a central vesicle (blister) on the trunk, oral mucosa and scalp
- Pustules and crusting
- Intense pruritus
- Occasional regional lymphadenopathy

#### **Pharmacological Treatment**

**B:** acyclovir (PO) 800mg 6hourly for 7days

**AND**

**A:** paracetamol (PO)1g 8 hourly for 4–5days

**AND**

**A:** calamine lotion (topical) 1% phenol, apply over the whole body 12hourly for 7days.

### **13.4.3 Herpes Zoster (Shingles)**

It is due to resurgence or reactivation of the *Varicella zoster* virus infection which also causes chickenpox.

#### **Clinical presentation**

- Severe burning pain

- Grouped vesicles overlying erythematous skin following a dermatomal distribution; typically, lesions do not cross the midline

### **Pharmacological Treatment**

**B:** acyclovir (PO) 800mg 6hourly for 7–10days

### **Wound care**

**A:** potassium permanganate soaks (1:4000) 12hourly for 3–4days

For Secondary infection (bacterial) apply

**A:** silver sulfadiazine cream (topical) applied 12hourly for 5days

**OR**

**C:** mupirocin 2% cream 12hourly for 5days

### **13.4.4 Post-herpetic Neuralgia**

A complication of shingles (herpes zoster).

### **Clinical presentation**

Intense pain described as burning, stabbing, or gnawing.

### **Pharmacological Treatment**

**A:** amitriptyline (PO) 25mg at night, may be increased to 150mg at nightfor 4 weeks

**OR**

**D:** pregabalin (PO) 75-150mg 24hourly or divided doses for 2-4weeks

**Referral:** Refer immediately to Ophthalmologist in case of herpes zoster ophthalmicus for atropinization

### **13.4.5 Molluscum Contagiosum**

It is viral infection common in children and immunocompromised individuals.

### **Clinical presentation**

- Skin coloured umbilicated papules
- It usually clears without treatment in 12-18months.



*Molluscum contagiosum*

### **Pharmacological Treatment:**

**A:** benzoyl peroxide 24hourly for 4weeks

**OR**

**S:** tretinoin cream (topical) 2.5 % 24hourly for 4weeks

### **Surgical treatment**

- C:** Cryotherapy
- D:** Curatage

### **13.4.6 Viral Warts**

Infection due to Human Papilloma Virus include; common warts, planar warts, and plantar warts, oral warts.

#### **Clinical presentation**

- Verrucous papules on the body, palms, soles, genital and oral mucosa.
- Painful on applying pressure for warts on palms and soles.

#### **Pharmacological Treatment**

**C:** silver nitrate pencil 3times per week for 4weeks for plantar, common warts.

**OR**

**S:** tretinoin cream (topical) 2.5% 12hourly for 4weeks for planar warts.

#### **Surgical treatment**

**C:** Cryotherapy

**D:** Curatage

**D:** Excision of large warts

#### **Note**

For treatment of Genital warts refer to **Sexually Transmitted Infections chapter 12**

## **13.5 Eczema (Dermatitis) Conditions**

### **13.5.1 Contact Dermatitis**

It is a delayed hypersensitivity reaction following skin meeting a chemical. This may be a dye, perfume, rubber, nickel, drugs, skin preparations containing lanolin, iodine, antihistamines, neomycin etc.

#### **Clinical presentation**

- Red papulo-vesicular rash with ill-defined margins
- Itching, which may be severe
- Dry, cracked, scaly skin, if chronic
- Blisters, draining fluid (weeping) and crusting, with severe dermatitis
- Swelling, burning or tenderness

#### **Investigations**

Patch test

#### **Non-pharmacological Treatment**

Avoid contact with allergen

#### **Pharmacological Treatment**

**A:** potassium permanganate soaks, 1:4000 solutions 12hourly for 5days each session lasting 15-20minutes (For weeping lesions weak)

**AND (for mild cases)**

**B:** betamethasone valerate 0.1% cream/ointment 12hourly for 4weeks

**OR(for moderate cases)**

**S:** mometasone furoate cream/ointment (topical) 12hourly for 4weeks

**OR (IF severe cases)**

**D:** clobetasol propionate 0.05% cream/ointment (topical) 12hourly for 4weeks

#### **Note**

A single application with occlusion at night is often more effective than multiple daytime applications.

### 13.5.2 Atopic Eczema

It is a dermatitis/Eczema on a background of atopy. Hence there is often a personal or family history of atopic disease (asthma, hay fever or atopic dermatitis).

#### Clinical presentation

- Pruritus- face in children, flexures, nape
- Chronic or chronic recurrent course
- Positive personal or family history
- of atopy
- Acute forms are weepy, chronic forms are lichenified, scaly



Acute atopic eczema



atopic dermatitis-lichenified and scaly

#### Investigations

FBP, prick test, patch test, Ig E levels

#### Non-pharmacological Treatment

- Education about chronicity of problems
- Remove any obvious precipitant e.g. skin irritants or allergens (avoid irritants e.g. medicated soap, wool and extremes of temperature).
- Generous use of emulsifiers (skin moisturizers)
- Bath oils/soap substitutes

#### Pharmacological Treatment

**A:** promethazine (PO) 25mg at bedtime increased to 50mg if necessary, for 2weeks

**OR**

**A:** cetirizine (PO) 10mg 24hourly for 2weeks

**OR**

**C:** loratadine (PO) 10mg 24hourly for 2weeks

**AND**

**A:** hydrocortisone 1% ointment (topical) 12hourly (if mild disease, or on face)

**OR**

**C:** betamethasone valerate cream/ointment (topical) 0.1% or 0.25% 12hourly for other parts of the body.

**OR (in severe cases)**

**D:** clobetasol propionate cream/ointment (topical) 0.05% 12hourly for up to 8weeks

**OR**

**S:** tacrolimus ointment (topical) 0.03%/ 0.1% 12hourly not less than 1month

#### In case of skin atrophy on the face and in children >1 year

**D:** prednicarbate cream (topical) 0.1 % 24hourly for

#### For severe cases- Erythroderma

##### Extensive involvement of the whole body

- Patient needs admission
- Oral antibiotics **as in impetigo**
- Short course of systemic steroid therapy-

**A:** prednisolone (PO) 0.5 -1mg/ kg 24hourly for 1-2weeks then taper.

- For recalcitrant cases

**S:** methotrexate (PO) 7.5- 20mg weekly for not less than 3months

**OR**

**S:** cyclosporine 3-5mg/kg/day up to 3months

- Phototherapy

Treat any infection (usually bacterial, but occasionally viral- eczema herpeticum).

Choice of skin preparations depends on whether lesions are wet (exudative) or dry/lichenified (thickened skin with increased skin markings).

- If eczema is “weepy”, use saline baths or bathe in:

**A: Potassium permanganate 1:4000 (0.025%) solution 24 hourly for 2-4 days** until dry.

Where large areas are involved give a course of antibiotics for 5-10 days (as for impetigo)

- After the lesions have dried, apply an aqueous cream for a soothing effect.

Start with mild topical steroid cream for wet lesions and use ointment for dry skin lesions.

If the skin starts scaling (condition becomes chronic), add/apply an emollient such as: emulsifying ointment or liquid paraffin.

#### Note

Potent topical corticosteroids may cause harmful cutaneous and systemic side effects especially if the use is prolonged or involves extensive body surface. Striae, acne, hyperpigmentation and hypopigmentation, hirsutism and atrophy may result. Therefore, avoid long term use; don't use on weepy or infected skin. Advise patients NOT to use them as cosmetics (eg for skin lightening purposes)

#### Example of Classes of Topical steroids;

Very Potent (0.05% clobetasol propionate), Potent (0.1% betamethasone valerate Mometasone furoate), Moderately Potent (0.05% clobetasol butyrate), Mild (1% hydrocortisone)

### 13.5.3 Seborrheic Dermatitis

Chronic recurring inflammatory skin disorder associated with *Malassezia species*.

#### Clinical presentation

- Erythematous macules,  
plaques
- Pruritus
- Scalp, face, chest, back axilla  
and groin

#### Pharmacological Treatment

**A:** clotrimazole cream (topical) 12 hourly for 4-16weeks

**OR**

**C:** miconazole cream (topical) 12 hourly for 4-16weeks

**AND**

**A:** hydrocortisone cream (topical) 0.5% 12 hourly for 4-16weeks

**OR**

**C:** ketoconazole shampoo 3 times per week for not less than 3 months

### 13.6 Anaphylaxis

It is an acute and often life-threatening immunologic reaction, frequently heralded by scalp pruritus, diffuse erythema, urticaria, or angioedema. Bronchospasm, laryngeal edema, hyperperistalsis, hypotension, and cardiac arrhythmia may occur. Antibiotics (especially penicillins), other drugs, and radiographic contrast agents are the most common causes of serious anaphylactic reactions.

#### Prevention and Non-Pharmacological Treatment

- If acute (existing for less than 3 months), exclude drug reactions (e.g. penicillin), or infection
- Avoid precipitants

For management refer to emergency and critical care chapter.

### 13.7 Papulosquamous Disorder

#### 13.7.1. Psoriasis

It is an inherited inflammatory condition of the skin

### Clinical presentation

- Thick, silvery white scaly plaques affecting mainly scalp, sacral region and extensor body surfaces
- Usually symmetrically distributed, with a chronic relapsing course.
- Can involve joints

### Note

Exclude precipitating factors e.g. alcohol, deficiencies of B12 or folate, stress, streptococcal infections.

### Non-pharmacological Treatment

Sun exposure to the lesions for half an hour or one hour daily may be of benefit

### Pharmacological Treatment

**C:** crude coal tar 5% in Vaseline in the morning for not less than 3months

**AND**

**C:** salicylic acid 5% in Vaseline to de-scale, apply at night for not less than 3months

**AND**

**C:** betamethasone valerate ointment (topical) 0.25% 12hourly for not less than 12weeks.

**OR**

**C:** betamethasone dipropionate+ salicylic ointment (topical) 12hourly for not less than 4months

In severe disease

**D:** clobetasol propionate cream/ointment (topical) 0.05% 12hourly for not less than 4months

For extensive involvement > 20% body surface area and involvement of joints

**ADD**

**S:** methotrexate (PO) 7.5-20mg weekly for not less than 6months

### Note

Systemic steroids should not be used in psoriasis due to their rebound effect.

## 13.7.2. Lichen Planus

It is an extremely pruritic chronic inflammatory skin condition.

### Clinical presentation

- Primary lesions are violaceous, shiny flat-topped papules
- Coalesce and evolve into scaly plaques
- Distributed over inner wrists, arms and thighs as well as sacral area.
- Post inflammatory hyperpigmentation is common.
- Scarring alopecia may result from lichen planopilaris (severe)

### Pharmacological Treatment

**C:** loratadine (PO) 10mg 24hourly for 2-4weeks

**AND**

**C:** betamethasone valerate ointment (topical) 0.1% 12hrly for 2–4 weeks

**OR**

**D:** clobetasol propionate ointment (topical) 0.05%–0.1% twice daily for 2–4weeks

**AND**

**for extensive involvement**

**A:** prednisolone (PO) 0.5-1 mg/kg 24hourly for 3-4weeks then taper

### For recalcitrant cases

**S:** methotrexate (PO) 7.5- 20mg weekly for not less than 6months

### **13.7.3 Acne**

Acne is a multifactorial disease primarily of teenagers with follicular plugging and inflammation.

#### **Clinical presentation**

- Open and closed comedones
- Pustules, papules
- Nodular and cystic lesions involving the face, chest, shoulder and the back

#### **Non-pharmacological Treatment**

- Avoid underlying precipitating factor e.g. stress, nuts, chocolate, overuse of ointments on skin, steroids, anticonvulsant drugs etc.
- Encourage a healthy lifestyle – exercise, sunshine exposure, etc.
- Use ordinary soap (harsh antibacterial cleansers or iodine-containing preparations may aggravate the acne)
- Do not manipulate pustules and nodules

#### **Pharmacological Treatment**

##### **Mild to moderate acne without scarring**

Apply

- A:** benzoyl peroxide 2.5%–5% once nocte  
OR  
**S:** tretinoic acid cream (topical) 0.05% once nocte

##### **Moderate acne with scarring-**

- A:** doxycycline (PO) 100mg 24 hourly for 1–3 month  
OR  
**A:** erythromycin (PO) 250mg 6 hourly for 1–3 month  
AND  
**A:** benzoyl peroxide or topical retinoid as above.

##### **Nodulocystic and/or conglobate acne**

- S:** isotretinoin (PO) 0.025–0.5mg/kg 24hourly for at least 3–6months  
AND  
**S:** triamcinolone (intralesional) 40mg/ml for cysts stat

##### **Acne fulminans**

- S:** isotretinoin (PO) 0.025–0.5mg/kg 24 hourly for at least 4–6 months  
AND  
**A:** prednisolone (PO) 45mg stat then 5mg reduction daily up to 0mg.

#### **Note**

Isotretinoin is contraindicated in pregnant women.

### **13.8 Drug Reactions**

Drug reactions can be classified in many ways. One useful approach is to separate predictable reactions occurring in normal patients from unpredictable reactions occurring in susceptible patients.

#### **Predictable adverse reactions;**

- Over dosage (wrong dosage or defect in drug metabolism)
- Side effects (sleepiness from antihistamines)
- Indirect effects (antibiotics changing normal flora)
- Drug interactions (altered metabolism of drugs; most commonly involving the cytochrome P-450 enzymes)

#### **Unpredictable adverse reactions**

- Allergic reaction (drug allergy or hypersensitivity; immunologic reaction to drug; requires previous exposure or cross-reaction)

- Pseudo allergic reaction (non-immunologic activation of mast cells).
- Idiosyncratic reaction (unexplained reaction, not related to mechanism of action, without known or suspected immunologic mechanism).

**Note**

- 80% of allergic and pseudo allergic drug reactions are caused by Beta-lactam antibiotics, aspirin, NSAIDs, and Sulfonamides

### 13.8.1 Fixed Drug Eruption (FDE)

It is a cutaneous drug reaction that recurs at the same site with repeated exposure to the agent.

#### Clinical presentation

- Typically, red-brown patch or plaque
- Occasionally may be bullous
- common sites are genitalia, palms, and soles, as well as mucosa
- Often multiple. Starts with edematous papule or plaque later becomes darker
- Resolves with post-inflammatory hyperpigmentation

**Note**

- When confronted with hyper pigmented macule on genitalia, always think of Fixed Drug Eruption

#### Non-pharmacological Treatment

- Avoidance of triggering drug;

#### Pharmacological Treatment

**A:** hydrocortisone (IV) 200mg 12hourly for 24hours

**AND**

**B:** betamethasone valerate cream (topical) 12hourly for 2weeks

**OR**

**D:** clobetasol propionate cream/ointment (topical) 0.05% 12hourly for 2- 4weeks

### 13.8.3 Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

It is a life-threatening condition caused by reaction to drugs e.g. sulphur containing drugs. It causes the skin to blister and peel off. Less than 10% of body surface area involved. Is referred to as SJS. SJS progresses to Toxic Epidermal Necrolysis (TEN) with involvement of more than 2 mucosal surfaces.

#### Clinical presentation

- Patients usually have prodromal with fever, malaise, and arthralgia's
- Erosions, hemorrhage and crusts on lips, and erosions in mouth covered by necrotic white pseudo membrane
- Involvement of the eyes: Erosive conjunctivitis, can lead to scarring
- Involvement of genitalia with painful erosions
- Sudden appearance of diffuse macules or diffuse erythema,
- Early sites of cutaneous involvement are the presternal region of the trunk and the face, but also the palms and soles.
- Then prompt progression with widespread erythema and peeling of skin; skin lies in sheets and folds on the bedding.

#### Pharmacological Treatment

- Identify and discontinue potential offending medications/drugs.
- Transfer patient to intensive care unit or critical care unit or burn unit.
- Wound care
- Keep warm
- Monitor fluid input and output –urine output 0.5-ml/kg/hour. Monitor electrolytes.
- Consultations – **Ophthalmologist, Physician, Dermatologist**

## **SCORTEN SCORE for determining prognosis of patient**

- Age >40years
- Malignancy
- Total body surface area affected >10%
- Heart rate >120 beats/ min
- Blood urea nitrogen >28mg/dl
- Serum glucose >250 mg/dl
- Serum bicarbonate <20mEq per 1

**Calculate SCORTEN on days 1 & 3 of hospital**

### **stay Pharmacological Treatment**

**A:** hydrocortisone (IV) 200mg 12hourly for 48hours

**AND**

**A:** prednisolone (PO) 1–2mg/kg 24hourly for 5–7days

Antibiotics in case of infection (as for treatment of sepsis)

#### **Note**

- Topical sulfur containing medications should be avoided.
- Systemic corticosteroids, if employed, should be used early to attempt to abort the immunologic reaction (**first 24 hours**).

## **13.10 Pellagra**

Is a disease caused by deficiency of nicotinic acid? Cardinal signs: diarrhea, dermatitis (sites exposed to sun) and dementia.

### **Clinical presentation**

- Casal's necklace; hyper-pigmented scaling involving the neck region
- Hyper-pigmented scaly lesions on sun exposed areas

### **Pharmacological Treatment**

Treat both adults and children

**A:** vitamin B complex (PO) 12hourly for 2months

**C:** nicotinamide (PO) 500mg 24hourly for 4weeks or until healing is complete; In children: 5mg/kg 24hourly for 4weeks or until healing is complete.

#### **Note**

The diet should be rich in deficient nutrients i.e. protein (meat, groundnuts, and beans)

## **13.11 Vitiligo**

Is a condition presenting with patchy depigmentation of skin?

### **Clinical presentation**

- Depigmented patches commonly on the face, neck, trunk and extremities
- Mucosal surfaces particularly oral and genital areas can also be depigmented

### **Pharmacological Treatment**

There is no cure for vitiligo, but there are several treatments that can improve the condition.

**C:** betamethasone valerate ointment 0.1% 12hourly for 2–4 months

**OR**

**S:** tacrolimus 0.1% ointment 12hourly for facial lesions and children

**AND**

**D:** clobetasol propionate cream (topical) 0.05% 12hourly

**OR**

**S:** PUVA+ sun exposure

#### **Note**

Counsel the patient about the condition.

## **13.12 Pruritic Papular Eruption (PPE)**

A skin condition characterized by itchy papular eruptions on the extensor area of the upper and lower limbs which is associated with HIV infection.

### **Clinical presentation**

- Papular lesions on the extensor areas
- Extremely itchy
- Excoriation
- Lesions heal with hyperpigmented scars

### **Pharmacological Treatment**

**C:** betamethasone valerate cream (topical) 0.025% 12hourly for 3–4weeks

**AND**

**A:** cetirizine (PO) 10mg 12hourly for not less than 4weeks

**OR**

**S:** dapsone (PO) 100 mg 24hourly for not less than 4weeks

## **13.13 Oculo-cutaneous Albinism and Xeroderma Pigmentosum**

These are recessive inherited oculo-cutaneous conditions.

**Albinism** characterized by the complete or partial absence of pigment (melanin) in the skin, hair and eyes.

### **Clinical presentation**

- Eye problems-photophobia, nystagmus, impaired vision
- Loss of pigment on skin and hair
- Freckles

### **Xeroderma Pigmentosum**

Genetic disorder in which there is a decreased ability to repair DNA damage such as that caused by ultraviolet light.

### **Clinical presentation**

- Freckling in sun exposed areas
- Dry skin
- Changes in skin pigmentation
- Extreme photophobia

### **Non-pharmacological Treatment**

- Counseling of parents that are genetic diseases
- **People with Xeroderma pigmentosum should avoid sunlight as much as possible.**
- Patients are strongly advised to wear sun protective clothing (long sleeved shirt, blouse, skirt and trousers and wide brimmed hats to prevent skin cancers)
- Sun protective glasses with special ultraviolet B (UVB) filters
- Advice on indoor income generating activities
- Cryotherapy of early lesions

### **Pharmacological Treatment**

**C:** Sunscreen applications of SPF 30+ or above, applied twice a day at 8am and noon

**AND**

**S:** 5 Fluoro-uracil topical application of early lesions

### **Surgical treatment**

- Excision of lesions
- Refer to oncologist in extensive involvements

**Note**

Sunscreen lotions and creams contain physical and chemical products that absorb or scatter ultraviolet rays that would otherwise cause damage to skin.

Uses of sunscreen;

- Albinism and xeroderma pigmentosum to prevent sunburn, and reduce risk of squamous cell carcinoma, B cell carcinoma and melanoma.
- Skin conditions e.g. Lupus Erythematosus, dermatomyositis whereby ultraviolet light exacerbates these conditions
- Normal use to prevent photoaging of the skin

### 13.14 Urticaria and Angioedema

Chronic recurrent whealing of the skin, with or without angioedema. Associated with atopy.

**Clinical presentation**

- Wheals which disappear within 24 hours
- With or without Swelling of tongue or lips
- Maybe precipitated by spices, food, food colourants, drugs.

**Investigations**

- FBP and ESR
- Stool for ova and parasite
- Autoantibodies-ANA
- Thyroid function test
- Prick and patch tests

**Non-pharmacological Treatment**

- Avoid precipitating factors e.g. NSAIDs, food, spices
- Treat any infection appropriately fungal, viral if suspect H pylori investigate and treat as per gastrointestinal section.
- Deworm

**Pharmacological Treatment**

Antihistamine can be increased to maximum dose for not less than 12weeks

**A:** cetirizine 10mg 12hourly 4weeks can be increased up to 4 folds

**OR**

**C:** loratadine 10mg 24 hourly dose can be increased up to 4 folds

**OR**

**S:** desloratadine 5mg 24 hourly for not less than 16weeks

**AND**

**D:** montelukast 10mg 24hourly for not less than 16weeks

### 13.15 Connective Tissue Diseases

Are autoimmune diseases of unknown etiology that affects the skin, blood vessels and internal organs.

**Clinical presentation****Scleroderma**

- **Localized scleroderma-** shiny plaques on the extremities, scalp, hands
- **Systemic scleroderma-** skin involvement, Raynaud phenomena, internal organ involvement

**Lupus erythematosus**

- **Discoid Lupus Erythematosus-** hypo/depigmented plaques, follicular plugging on the face mostly
- **Systemic Lupus -** malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disease

**Dermatomyositis**

- cutaneous-gottrons papules, heliotrope rash
- proximal muscle weakness- inability to comb hair
- inability to rise when squats

## **Investigations**

- FBP and ESR
- LFTS
- RFTS
- Urinalysis
- Autoantibodies- ANA, anti-dsDNA, anti-centromere, anti-scleroderma 70, Anti-phospholipids, Anti- SM
- Creatine kinase levels
- Biopsy
- Monitoring liver, renal and blood count 3 monthly
- RBG every 3 months for patients on corticosteroids for long

## **Non-pharmacology Treatment**

- Ophthalmology review before starting hydroxychloroquine and every 6 months after.
- Monitor blood pressure
- Use of sun protective factor (SPF) lotion and clothing especially for dermatomyositis and Lupus.
- Keep extremities warm
- Physiotherapy
- Involve physician

## **Pharmacological Treatment**

### **Deworm- Albendazole 400mg stat**

#### **Localized scleroderma:**

**D:** clobetasol propionate cream / ointment (topical) 0.05% 12hourly

**A:** prednisolone (PO) 0.5-1mg /kg 24hourly for stabilizing then taper slowly

**AND**

**S:** methotrexate (PO) 7.5- 20mg weekly

#### **Discoid Lupus Erythematosus**

**D:** clobetasol propionate cream/ointment (topical) 0.05% 12hourly

**AND**

**S:** hydroxychloroquine (PO) 200mg 24hourly for not less 3months

#### **Systemic Scleroderma**

**D:** clobetasol propionate cream/ointment (topical) 0.05% 12hourly

**AND**

**A:** prednisolone (PO) 0.5- 1 mg 24hourly for 4weeks then taper to lowest level that is effective.

**AND**

**S:** methotrexate (PO) 7.5- 20mg weekly

**AND**

**A:** omeprazole (PO)20mg 24hourly when needed for patients with gastritis, peptic ulcer disease.

#### **Dermatomyositis**

**A:** prednisolone (PO) 1mg/ kg 24hourly for 12weeks till improvement then start tapering to lowest effective dose

**AND**

**S:** methotrexate (PO) 7.5-20mg weekly for at least 6months

## 13:16 Autoimmune Blistering Disease

Conditions in which autoantibodies target components of the skin and mucous membranes, leading to blister and bullae formation. These include pemphigus vulgaris, foliaceous, vegetans, Bullous pemphigoid, Dermatitis herpetiformis, Linear IgA.

### Clinical presentation

- Tense or flaccid Vesicles and bullae on the skin and mucus membranes
- Vegetative plaques in axillae or groin



Linear IgA

### Investigations

- Biopsy
- Immunofluorescence studies
- FBP, LFT, RFT

### Pharmacological Treatment

**C:** betamethasone cream/ointment (topical) 12hourly till improves

**OR**

**D:** clobetasol propionate cream/ointment (topical) 0.05% 12hourly till improves

**AND**

**A:** prednisolone (PO) 0.5-1mg/kg 24hourly for 2months then taper slowly to lowest effective dose

**AND in extensive involvement**

**S:** methotrexate (PO) 7.5 – 20mg weekly for not less than 4months

### Treatment of Dermatitis Herpetiformis /pemphigus foliaceous

**S:** dapsone (PO)100mg 24hourly for not less than 2months

## 13.17 Keloids

Excessive connective proliferation following an injury or spontaneously.

### Clinical presentation

- Skin coloured nodules, plaques extending beyond the scar line commonly on earlobes.

### Pharmacological Treatment

**S:** triamcinolone (intralesional) 2.5-5mg/ml monthly for 4-6months for small – medium sized keloids.

### Surgical treatment

**S:** total excision or debulking of keloids Inj Triamcinolone 20mg intraoperatively and post operatively for 3 months.

## 13.18 Folliculitis Decalvans

Characterized by pustules, papules, keloids and scarring alopecia on the nape of the scalp.

### **Pharmacological Treatment**

**A:** doxycycline (PO) 100mg 12hourly for 2-4weeks

**OR**

**S:** clindamycin (PO) 300mg 12hourly for 3months

**AND**

**D:** clobetasol propionate cream/gel (topical) 0.05% 12hourly for not less than 16weeks

**AND in recalcitrant cases**

**S:** dapson (PO) 100mg 24hourly for 6months

### **13.19 Infantile Haemangioma**

Benign vascular tumor which appears at birth and continues growing till 9 months then starts involuting.

#### **Clinical presentation**

- Red macule at birth
- Grows progressively
- regresses from 9-12 months
- May be part of PHACES syndrome;  
Posterior fossa malformation,

haemangiomas (mainly facial),  
arterial, cardiac, eye, and sternal anomalies

#### **Indications for treatment**

- If interferes with feeding
- If interferes with breathing
- If interferes with vision

#### **Investigations**

- FBG before initiating treatment and serially after
- ECG
- Record heart rate and blood pressure before treatment

### **Pharmacological Treatment**

**A:** propranolol (PO) 1mg/kg divided into 3doses given 8hourly in 24hours.

Monitor heart rate and blood pressure 2hourly for 3days if tolerated

Increase the above-mentioned medication to 2mg/kg/day in 3divided doses till lesion regresses

Adjust with change in weight.

#### **Note**

Request your pharmacist to prepare the syrup.

### **13.20 Cysts**

Slow growing cystic structures.

Include- Epidermoid cysts, Trichilemmal cysts, dermoid cyst

#### **Treatment**

- Excision

### **13.21 Skin Lightening**

Skin lightening or skin bleaching is a cosmetic process that aims at lightening the dark areas of skin. Some of the products used are strong topical corticosteroids e.g. clobetasol propionate, hydroquinone, glutathione, lightening soaps, local concoctions etc. Melasma is a skin condition whereby medical treatment is to lighten dark patches. However, in most situations women and men desiring to have fairer skin go into great lengths to achieve this and end up with some reversible and irreversible changes.

### **Reversible conditions**

- Tinea incognito – refer to treatment of tinea
- Steroid acne – refer to acne treatment
- Scabies – refer to scabies treatment
- Perioral dermatitis- Tacrolimus ointment

### **Irreversible conditions**

- Stria
- Telangiectasia
- Atrophy
- Hirsutism
- Ochronosis
- Poor wound healing

### **Health Education**

- Users should stop before they get permanent irreversible changes.
- Use sunscreen lotion to protect from ultraviolet damage.

# CHAPTER FOURTEEN

## EYE DISEASES AND CONDITIONS

### 14.1 Major Blinding Eye Diseases

Eye Diseases are conditions affecting the eye. Diseases of most importance are those leading to blindness or visual impairment. Blindness is defined as a presenting visual acuity of less than 3/60 or central visual field of less than 10° in the better eye. The definition of blindness in children and infants is the same as that in adults though there are different methods for testing vision in young children until when they are at preschool age when normal visual acuity chart can be used. The common causes of blindness and visual impairment among adults are Cataract, Glaucoma, Cicatricial Trachoma, Vitamin A deficiency (*discussed under nutrition chapter*) and other corneal opacities, diseases of the Retina, uncorrected Refractive Errors and Low Vision. These are diseases that affect both eyes however, they may be asymmetrical in their course. There are other eye diseases that do not lead into blindness or visual impairment, these are also addressed in this section. Patients presenting to eye clinic with unioocular eye complaint must have basic examination of the fellow eye as well.

#### 14.1.1 Cataract

Cataract is clouding of the lens of the eye which prevents clear vision. It may be as a result of ageing process or secondary to trauma or inflammatory diseases. Children may be born with cataract or develop cataract in the early ages of life.

#### Clinical Presentation

- Various degrees of vision impairment unilateral or bilateral
- History of trauma with a sharp object for traumatic cataract
- History of red eye for secondary cataract.
- Glare and haloes around light
- Cloudiness in the lens seen as a white mark behind the pupil and iris seen with slit lamp microscope
- Conjunctiva and cornea are clear and the whole iris can be seen clearly
- Obscured red reflex

#### Note

- Cataract may present in all age groups, blindness due to cataract is reversible
- Treatment is only by surgery
- Early treatment in children is mandatory
- White pupil in children may be a tumor in the eye, late referral may lead to permanent loss of vision, squint, loss of eye or loss of life

#### Investigations

- Visual acuity
- Slit Lamp Biomicroscopy
- Refraction depending on the density of cataract
- Dilated Fundoscopy
- B Scan if no fundal view
- A Scan
- Biometry for Intraocular (IOL) calculation

For congenital cataract, the following additional investigations may be ordered with Paediatrician consultation

- ECG
- Echocardiogram
- Haemoglobin
- Full blood picture
- Chest X Ray
- Blood grouping and Cross-matching

#### Surgical Treatment

The only treatment available for Cataract is surgery. There are different cataract surgical procedures depending on the causes of cataract, age of the patient and surgeons' skills and equipment availability.

## **Pharmacological Treatment**

### **Preoperative Treatment**

**A:** amethocaine hydrochloride 1% Eye drops

**OR**

**C:** tetracaine 0.5% Eye drops

**AND**

**C:** tropicamide 1% +phenylephrine 2.5% (FDC) Eye drops

### **Alternatively**

**C:** tropicamide 1% Eye drops

**AND**

**A:** iodine 2.5 – 5% Eye Drops

**AND**

**A:** lignocaine hydrochloride with adrenaline 2%, *combined* with hyaluronidase 1500IU, 5 mL, retrobulbar or Subtenon injection stat,

**OR**

**A:** lignocaine hydrochloride, *combined* with hyaluronidase 1500IU, 5mL, retrobulbar or subtenon injection stat,

### **Intraoperative Treatment**

**A:** adrenaline 0.5mL infusion in 500mL compound sodium lactate intracameral in during the surgery

**AND**

**C:** trypan blue 0.06% injection, 0.4mL intracameral, stat

**AND**

**S:** sodium hyaluronate 1% Intracameral and topical stat

**AND**

**S:** acetylcholine chloride 1% Injection, 0.5ml intracameral stat

**AND**

**B:** dexamethasone phosphate 1.25mg intracameral injection stat

**AND**

**A:** gentamycin 1.25mg intracameral and subtenon injection stat

**OR**

**B:** ceftriaxone 5mg intracameral and subtenon injection, stat

**In addition to the above intraoperative medicines, in children and patients with preoperative ocular inflammatory conditions, use**

**S:** triamcinolone acetone 20mg injection, Sub tenon, stat

**OR**

**D:** methylprednisolone 20mg injection, Sub tenon, stat

### **Postoperative Treatment**

**C:**dexamethasone + chloramphenicol 0.1 – 0.5%, 1 -2 Drops in the operated eye, 2hourly for 7days then 4hourly for days

**OR**

**C:** dexamethasone + gentamicin 0.1 - 0.3%, 1 – 2 Drops in the operated eye, 2hourly for 7days then 4hourly for 7days

**AND**

**C:** cyclopentolate 1%, 1 – 2 Drops in the operated eye, 12hourly for 14days

**OR**

**B:** atropine 1%, 1- 2 Drops in the operate eye, 24hourly for 14days

**AND**

**C:** acetazolamide (PO) 500mg, stat

**AND**

**A:** paracetamol (PO) 1 gm, 8hourly for 3days

**THEN:**

**D:** prednisolone 0.5%, 1 – 2 Drops, 6hourly for 4weeks

**Note**

- Atropine is given to patients where excessive inflammation is anticipated such as cataract surgeries in children, traumatic cataract and secondary cataract.
- Children may require longer term and more frequent topical steroids depending on their postoperative response

**Referral:** Refer all cases to eye surgeon for cataract surgery, available at some of the Districts, Regional, Zonal and National Hospitals. Children should be referred immediately to a Tertiary Health Facility with capacity to operate children's eyes safely.

### 14.1.2 Glaucoma

Glaucoma is a syndrome characterized by optic nerve damage and peripheral visual field loss which may be associated with raised intraocular pressure. The main classes of glaucoma are open angle glaucoma and angle closure glaucoma.

**Note**

Glaucoma may be congenital, primary or secondary to other secondary to ocular conditions

#### 14.1.2.1 Primary Open Angle Glaucoma

##### Clinical presentation

- Painless loss of peripheral vision leading to absolute glaucoma as the end stage
- Affects mainly adults of 40 years of age and above
- Cornea and conjunctiva are clear
- Pupil in the affected eye does not react with direct light in advanced stage
- The optic nerve is always damaged, this can be seen through fundoscopy
- One eye may be affected more than the other
- First degree relatives of glaucoma patients are at increased risk

**Note**

- Primary Open Angle Glaucoma does not have symptoms in early stages, hence routine intraocular pressure checkup and fundus examinations should be done in all people of 40 years and above by some qualified eye care personnel on annual basis.
- All suspected cases of glaucoma should be referred to qualified eye care personnel for confirmation of diagnosis and commencement of treatment plan
- Surgical treatment is usually preceded by medical treatment
- Refilling of antiglaucoma may be prescribed by a middle cadre eye worker but annual monitoring should be done at a centre where there is an Ophthalmologist
- For advanced and complicated Glaucoma, patients should be referred to a health facility where there are Glaucoma Specialists

##### Investigations:

- Visual Acuity
- Slit Lamp bimicroscopy
- Fundoscopy
- Tonometry
- Gonioscopy
- Refraction
- Visual Field Analysis
- Fundus Photography
- Pachymetry test
- Optical Coherent Tomography

##### Pharmacological Treatment

This is initiated after a diagnosis is reached by an ophthalmologist, refill of some medicines can be done by Assistant Medical Officers in ophthalmology but with regular reviews at a health facility with eye specialist. Medical treatment should be lifelong unless there are conditions necessitating other interventions

**C:** timolol 0.25% or 0.5%, one drop in the affected eye, instill 12hourly.

**OR**

**D:** betaxolol 0.25% or 0.5%, one drop in the affected eye, instill 12hourly. Use lower strength in mild disease and those at risk of complications.

In patients who comply to treatment and there is no good response

**ADD**

**D:** latanoprost 0.005% one drop, 2hourly in the affected eye.

**OR**

**D:** prostamide bimatoprost 0.03%, one drop, 24hourly in the affected eye.

- These may be used as first-line in patients with contraindication of beta-blockers.
- They can be used as a second-line drug in patients on beta-blockers if the target IOP reduction has not been reached.

In patients who are intolerant to prostaglandin analogue or are not responding give:

**D:** brimonidine tartrate 0.15–0.2%, one drop, 12hourly, in the affected eye.

**OR**

**S:** dorzolamide 20mg/mL, one drop, 8hourly in the affected eye

Failure to respond give:

**C:** pilocarpine hydrochloride 2% or 4%, instill one drop in the affected eye 6 hourly.

**Note**

Pilocarpine causes long-standing pupil constriction so it should not be used unless a patient is prepared for glaucoma

surgery or as an alternative topical treatment for patients who are contraindicated for Timolol use.

Consult a specialist

before using it.

In severe cases or while waiting for surgery, use:

**C:** acetazolamide (PO) 250mg 6hourly

**Note**

- $\beta$ -blockers are contraindicated to people who are known to have overt asthma as this group of medication may cause an acute asthmatic attack within a short time following instillation into the eye
- Brimonidine is contraindicated in children below 12years

**Laser Treatment**

- It may be indicated in addition to or instead of eye drops or surgery.
- Laser trabeculoplasty (Argon Laser Trabeculoplasty, Selective Laser Trabeculoplasty) or cyclophotocoagulation are different options among others

**Surgical Treatment**

It is done in all patients with poor compliance and when medical treatment is not useful. There are different surgical techniques depending on the age of the patients, patients' response to surgical treatment, surgeons' surgical skills and availability of equipment. It is recommended that all surgeries are done by Ophthalmologists after thorough assessment of the patients.

**14.1.2.2 Angle Closure Glaucoma**

This is also known as Congestive glaucoma and commonly affect people aged 40 years and above. It affects more females than males.

**Clinical Presentation**

- Acute sudden onset of painful red eye in the affected eye
- Severe headache and cloudiness of the cornea
- Shallow anterior chamber
- Fixed and semi-dilated pupil

- Severe elevated intraocular pressure.
- There is usually dramatic visual impairment and vomiting may be present
- It may be asymptomatic if IOP raises slowly

**Note:**

- Primary acute Angle Closure Glaucoma is an Ophthalmological Emergency
- Refer all patients with Congestive glaucoma to eye specialist after initial medical treatment to lower Intraocular pressure

**Investigations:**

- Visual Acuity
- Slit Lamp bimicroscopy
- Fundoscopy when cornea clear up
- Tonometry
- Gonioscopy when cornea clear up
- Visual Field Analysis for chronic disease

**Pharmacological Treatment**

Institute therapy and then refer the patient to eye specialist at the Regional, Zonal or National Hospital for investigations and proper management.

Try to achieve immediate IOP reduction

**First-Line Treatment**

C: acetazolamide (PO), 500mg immediately as a single dose followed by 250mg 6hourly

**AND**

C: timolol 0.25–0.5% eye drops, instill one drop 12hourly in the affected eye

Use the above combined treatment until you have achieved your target IOP reduction, then continue with only Timolol eye drops for life unless patient has received surgical intervention and the IOP is reduced to normal level.

**Note**

Manage the associated pain and vomiting

**Second-Line Treatment**

If the above measures fail, use as a short-term treatment, givesystemic osmotic agents:

C: mannitol 15–20% (IV)1.5–2mg/kg body weight to run slowly over 30–60minutes

These medicines have diuretic effects, so they are only used as a single dose. They are also used in emergencies to prepare patients with high intraocular pressure for surgery as they lower intraocular pressure rapidly.

**Note**

Acetazolamide is a Sulphur containing medicine, do not use in patients allergic to Sulphur.

**Surgical Treatment**

This is done at a centre with Eye Specialists and necessary diagnostic and treatment equipment. Surgical or Later Peripheral Iridectomy will create a passage for the aqueous fluid from posterior chamber to the drainage angle.

**Referral:** Management of advanced angle closure glaucoma is done by eye specialist. All patients with Angle Closure Glaucoma should be referred to eye specialist for other management modalities.

**14.1.2.3 Childhood Glaucoma**

- Presents from birth to 5 years.
- It is a syndrome whereby the intraocular pressure is raised and cause abnormality of the eyeball and visual disturbances including blindness.

### Clinical Presentation

- Patients presents with eyes bigger than normal for age (buphthalmos)
- Photophobia
- Tearing
- Cloudy cornea,
- Red conjunctiva though not severe.
- Decrease in visual acuity

### Investigations

For children, examination is done under General Anaesthesia

- Tonometry
- Cornea Diameters
- Slit lamp examination
- Fundoscopy
- Gonioscopy depending on corneal visibility

### Surgical Treatment

Treatment for congenital glaucoma is usually surgery, which is done by Pediatric Ophthalmologist or Glaucoma specialist.

**Referral:** Refer any child who has the above-mentioned signs and you suspect that he/she is having congenital glaucoma to a specialist at the National Hospital or Zonal Referral Hospitals where there is Paediatric Eye team.

#### 14.1.2.4 Secondary Glaucoma

This presents as a complication of other eye diseases such as uveitis, hypermature cataract, trauma and retinal diseases. It may also be due to prolonged use of steroids.

### Clinical Presentation

- Poor vision in the affected eye associated with
- High intraocular pressure
- Optic nerve damage
- New vessels on the iris if the cause is retinal diseases

### Investigations

- Visual Acuity
- Slit Lamp bimicroscopy
- Fundoscopy
- Tonometry
- Gonioscopy
- Refraction
- Visual Field Analysis
- Fundus Photography
- Pachymetrytest
- Optical Coherent Tomography

### Pharmacological Treatment

Management of these patients depends on the cause, but it includes medical, surgical and laser. Institute these treatment as you refer these patients:-

**C:** acetazolamide (PO) 500mg immediately stat followed by 250mg 6hourly  
**AND**

**C:** timolol 0.25–0.5% eye drops, instill one drop 12hourly in the affected eye.

Treatment of the preexisting eye disease is highly recommended.

**Referral:** Refer all patients suspected to have secondary glaucoma to a qualified eye specialist available at the Regional, Zonal or National Hospital for proper assessment and definitive management.

#### 14.1.3 Trachoma

It is a chronic conjunctivitis caused by infection with *Chlamydia trachomatis* (bacteria). It is one of the commonest causes of blindness worldwide. There is a chronic inflammation of the conjunctiva leading to scarring of the upper eyelid tarsal plate, entropion and in turn of eyelashes.

### Clinical presentation

- Photophobia in early stages or re-infection
- More than 5 Follicles in the upper tarsal plate seen as round and white nodules in active diagnostic.
- In late stages, in-turned eyelashes rub on the cornea leading to corneal ulcers
- Loss of vision due to corneal scarring.

### Clinical Stages according to World Health Organization

- Trachomatous Inflammation Follicular (TF) - Presence of at least 5 follicles on the upper tarsal plate
- Trachomatous Inflammation Intense (TI) – There is intense inflammation, the conjunctival blood vessels cannot be seen.
- Trachomatous Scarring (TS) – Presence of white scars in the upper tarsal plate
- Trachomatous Trichiasis (TT) – Presence of some eye lashes rubbing against the cornea
- Corneal Opacity (CO) – Presence of corneal opacity (scar) affecting the central cornea

### Investigations

- Visual acuity
- Slit lamp biomicroscopy
- Conjunctival swab for dipstick test and or PCR

### Non-pharmacological Treatment

- Face washing and total body hygiene to prevent transmission of disease from one person to the other
- Environmental improvement/hygiene

### Pharmacological Treatment

**A:** oxytetracycline eye ointment 3% 24hourly for 6weeks

**OR**

**B:** azithromycin (PO)1g stat- for preventive chemotherapy in mass treatment campaign

**Table 14.1: Dosage of Azithromycin in Children**

Weight (kg)	I-day regimen
< 15	20mg/kg 24hourly
15 – 25	400mg 24hourly
26 – 35	600mg 24hourly
36-45	800mg 24hourly
> 45	Dose as per adults

#### Note

Preventive chemotherapy in mass treatment campaign is conducted only once a year

### Surgery

Surgical correction of entropion in TT patients. This procedure can be done at a Dispensary or Health Centre and community level by a trained health worker.

**Referral:** Refer all patients with recurrent TT or lower Eyelid TT to Oculoplastic Surgeon at Regional Referral or Zonal Referral Hospital for proper assessment and surgical management.

### 14.1.4 Diseases of the Retina

Main diseases of the retina that cause blindness are Diabetic Retinopathy, Diabetic Macular Edema, Retinal Detachment and Age-related Macular Degeneration.

#### 14.1.4.1 Diabetic Retinopathy

- It is a complication of diabetes mellitus in the eyes

- It is a chronic progressive sight-threatening disease of the retinal blood vessels associated with the prolonged hyperglycemia and other conditions linked to diabetic mellitus such as hypertension

### Clinical Presentation

- Loss of vision in advanced stages, when there is retinal haemorrhage or cataract
- In early stages it may be asymptomatic
- Regular and annual screening at Diabetic or Eye Clinic is recommended for early diagnosis.

Diabetic retinopathy is mainly grouped into three stages/presentations:

- Background diabetic retinopathy
- Diabetic maculopathy
- Proliferative diabetic retinopathy

### Investigations

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>Visual acuity with and without pinhole</li> <li>Tonometry</li> <li>Dilated fundoscopy (Direct or indirect ophthalmoscopy with or without biomicroscopy)</li> </ul> | <ul style="list-style-type: none"> <li>Fundus photography</li> <li>Fluorescein Angiography</li> <li>Optical Coherence Tomography</li> </ul> |
|---|---|

#### Note

Dilate the pupils with combined

**C:** Tropicamide 1%/Phenylephrine 2.5% eye drops

#### OR

**C:** tropicamide 1% with

**C:** cyclopentolate 1% eye drops to screen

Table 14.2 below gives a summary of the Stages of Diabetic Retinopathy at Eye Clinic, treatment options and Follow up schedule. Treatment is done in consultation with Diabetologist and Physician to ensure a good glycaemic and blood pressure control

**Table 14.2: Treatment options for various grades of DR**

Grade	Treatment Options	Follow-up
No retinopathy	a. Patient counseling b. Strict control of blood sugar, pressure and lipids	9 -12 monthly
Mild or Moderate Non-Proliferative Diabetic Retinopathy (NPDR)	a. No active treatment required b. Patient counseling c. Control of blood sugar, pressure and lipids	6-9 monthly
<b>Pre-proliferative DR</b>		
Severe NPDR *	Close follow up for dilated fundoscopy	2-3 monthly
Very severe NPDR *	Partial scatter PRP therapy (maximum LASER burns 800 spots)	3 monthly
Mild Proliferative DR** (NVD/ NVE No pre-retinal or vitreous hemorrhage No Fibrovascular membrane < FVM >)	Full scatter PRP minimum 1200 shots in one sitting or/ and Anti-VEGF injection***	2 monthly
Moderate PDR ** (NVD/NVE, Moderate to severe Vitreous hemorrhage with visible fundus details for PRP, Pre-retinal Hemorrhage No FVM)	Full scatter PRP up to Ora-serrata sparing the macula and away from the FVM ***	3 monthly

Severe PDR ** (NVD/NVE, Severe Vitreous hemorrhage obscuring fundus details/not visible for PRP, Extensive FVM, Tractional Retinal Detachment <TRD> Macular traction)	REFER To VR clinic	
--	--------------------	--

\* LASER treatment should also be considered in our settings in patients with severe and very severe NPDR with the following situations as it has shown to reduce the rate of vision loss by half: -

- i. Older type 2 diabetics
- ii. Difficult retinal view
- iii. Prior to cataract surgery
- iv. Only eye situation where the first eye was lost due to PDR
- v. Regular attendance to clinic for follow up is likely to be poor
- vi. Difficult to examine patient due to other reasons.

\*\* Monthly intra-vitreal anti-VEGF injections has been found to be effective on treatment for PDR

\*\*\* Mild and moderate PDR should be treated with full scatter PRP (minimum 1200 shots in one sitting) or intravitreal anti-VEGF injection whichever is available, accessible and affordable. If both are available and affordable then anti-VEGF injection is the treatment of choice provided the patient:

- i. Is able to come for follow up at regular intervals- every month for 3 months and then every 2 months for 3 months and then 3 monthly
- ii. Can afford the injections which may total up to 6 injections in the first year
- iii. Has no contraindications to the injections?

If any one of the above does not apply, then the patient should have PRP done.

### Treatment options for DME

Management of DME depends on the clinical stage of DME and treatment options available at the facility where the patient has been attended.

Primary tests are required to be performed in order to grade the DME. Macula OCT for all diabetic patients should be the baseline test to determine presence or absence of DME. Macular thickness of equal or more than 400 microns should be considered as DME. Those facilities without this tool, the clinical assessment will be the baseline test where the best corrected visual acuity will be the key point for grading which will be matched with the clinical findings. Therefore, VA of less than 6/12 should be considered as DME case. It is important to exclude other causes of visual impairment before concluding the presence of DME. Use of anti-VEGF has been found to be effective in the treatment of DME.

**Table14.3: Treatment options for various grades of DME**

Grade	Treatment option	Follow up period
No DME	Close observation	review after 6 to 12months
Non-Centre involving DME	Focal or Grid LASER	3-6months
Centre involving DME	3 intravitreal anti VEGF injections at monthly interval followed by 3 more injections at 6 weekly intervals.  After 6 injections, refer patient to VR clinic if a. VA is not improving b. There is clinically persistent DME  If anti VEGF injection is not available: i. Grid LASER should be given for diffuse, Exudative or edematous macular edema ii. Focal LASER to areas of focal Exudative edema	Every 1 month

## **Pharmacological Treatment**

For glycemic control give antioxidant in non-proliferative diabetic retinopathy

**C:** multivitamin +carotenoids (PO) 24hourly to a maximum of 3months

For intravitreal anti Vascular Endothelial Growth Factor (VEGF) in Proliferative Disease

**S:** bevacizumab, 1.25mg per 0.05ml, intravitreal injection, stat.

**OR**

**S:** ranibizumab, 0.5mg per 0.05ml, intravitreal injection stat.

Repeat after every month to a maximum of 3 months then 6weekly to complete 6 injections. Reassess on 3 monthly basis if there are signs of disease progression, restart treatment if any, with close follow up.

**AND**

**S:** triamcinolone acetonide, 0.05ml, intravitreal injection, stat. Repeat after 3months if it is necessary. This is indicated in Diabetic Macula Edema.

## **Surgical Treatment**

- This is done in the proliferative stage
- It involves removal of vitreous and or blood, peeling of formed fibrovascular tissue and reattachment of retina if the retina is detached
- It is combined with retinal photocoagulation
- The vitreous cavity may be filled with tamponade liquid such as silicon oil or expansile gas like sulfur perfluoropropane or sulphur hexafluoride depending on the level of complication
- It may also be combined with pharmacological treatment (Anti VEGF) mentioned above

## **Laser Treatment**

Laser photocoagulation: Extent and type of this treatment depending on the stage of the disease

- Focal Laser
- Grid Laser
- Pan Retinal Photocoagulation for advanced disease

### **Note**

- Ophthalmologists should work together with Physicians to holistically treat the diabetic patient.
- Poorly controlled diabetes mellitus and diabetic retinopathy can lead to blindness
- All patients with diabetes mellitus regardless of their eye conditions, should have a thorough eye examination by available eye care personnel or an eye specialist at least once a year.
- Dilated eye examination and direct viewing of the retina by an ophthalmologist or qualified eye care personnel is mandatory at initial diagnosis of Diabetes Mellitus and as per recommended schedule by the attending clinician.
- Urgent referral of all diabetic patients with sudden loss of vision to eye specialist

### **14.1.4.2 Age Related Macular Degeneration**

It is a disease condition characterized by progressive macular changes that are associated with increase in age.

## **Clinical Presentation**

- Drusens around macula area (yellowish excrescence in the retina)
- Affects elderly over 60 years
- Poor central vision, later can lead to blindness

## **Investigations**

- Visual Acuity
- Refraction
- Tonometry
- Fundoscopy through a well-dilated pupil,
- Fundus photography

- Optical Coherence Tomography and or
- Fluorescein angiography.

### **Pharmacological Treatment**

- This depends on clinical presentation.
- Intravitreal injection in the affected eye

**S:** bevacizumab 1.25mg per 0.05ml stat

**OR**

**S:** ranibizumab 0.5mg per 0.05ml stat.

Give Antioxidant in non-proliferative Diabetic Retinopathy

**C:** multivitamin + Beta-carotenoids, Zinc Sulfate and Lutein, 1 tablet once daily to a maximum of 3 months

### **Surgical Treatment**

Type of surgery depends on the presentation/ stage of the disease.

**Referral:** Refer patients with Age Related Macular Degeneration to Vitreo-retinal Surgeons for proper management

### **14.1.5 Refractive Errors**

This is a condition where one presents with poor vision either at near or distance at any age. There are mainly 4 types of refractive errors namely presbyopia, myopia, astigmatism and hyperopia. A patient may have more than one type of refractive error.

#### **14.1.5.1 Presbyopia**

This is a disorder of refractive status commonly occurring in older people.

#### **Clinical presentation**

- It usually starts after the age of 40 years
- The main complaint is difficulty in reading/writing or doing near works
- Diagnosis is only through refraction. Attendance to health facility is also a good opportunity for screening of glaucoma and diabetic retinopathy

#### **Investigations**

- |                 |                      |
|-----------------|----------------------|
| • Visual acuity | • Refraction         |
| • Tonometry     | • Stereopsis test    |
| • Fundoscopy    | • Colour vision test |

#### **Non-pharmacological Treatment**

Convex lens spectacles for near vision.

#### **14.1.5.2 Myopia (Short sightedness)**

This is a condition whereby patient has difficulty seeing far objects.

#### **Clinical presentation**

- It is common in young age between 5–25 years
- The condition persists throughout life
- If not treated early, it may progress rapidly and lead to retinal complications
- It is diagnosed through refraction.

#### **Investigations**

- |                   |   |
|-------------------|---|
| • Visual acuity   | • Colour                                |
| • Refraction      | • Strabismus assessment in all children |
| • Fundoscopy      |   |
| • Stereopsis test |   |

#### **Non-pharmacological Treatment**

Concave lens spectacles for constant wear.

#### **14.1.5.3 Hypermetropia (Long sightedness)**

This is a condition where patients have difficulty in seeing near objects. It is less manifested in children as they have a high accommodative power.

##### **Clinical presentation**

- Ocular strain
- Diagnosis in children should be reached after refraction through a pupil that is dilated

##### **Investigations**

- Visual acuity
- Refraction
- Fundoscopy
- Stereopsis test
- Colour
- Strabismus assessment in all children

##### **Non-pharmacological Treatment**

Convex lens spectacles for constant wear

##### **Note**

Spectacles should be given to: -

- Children who have only significant hypermetropia (more than +3.00 Diopter of Sphere both eyes), all children who present with squint and have significant hypermetropia and children with anisometropia
- Elderly who present with signs of ocular strain

#### **14.1.5.4 Astigmatism**

This is a condition where the cornea and sometimes the lens have different radius of curvature in all meridians (different focus in different planes). Some myopic and hyperopic patients may have astigmatism.

##### **Clinical Presentation**

- Poor vision at distance,
- Photophobia
- Headache (sometimes).
- Diagnosis is reached through refraction

##### **Investigations**

- Visual acuity
- Refraction
- Fundoscopy
- Stereopsis test
- Colour
- Strabismus assessment in all children

##### **Non-pharmacological Treatment**

Cylindrical lenses spectacles for constant wear.

##### **Note:**

- Reassessment for all types of refractive errors is done annually and change the spectacles if there are significant variation and improvement with new correction.
- All children with rapid progression of refractive errors need to be seen by Paediatric Optometrist and Paediatric Ophthalmologist for further assessment

#### **14.1.6 Low Vision**

Low vision is irreversible visual loss that cannot be corrected with surgeries or spectacles resulting in reduced ability to perform many daily activities. They have visual impairment even with treatment and or standard refractive correction and

## Clinical presentation

Inability to

- Recognizing people in the streets,
- Reading black boards,
- Writing at the same speed as peers and
- Playing with friends.
- Visual acuity from less than 6/18 to perception of light and a reduced central visual field.

## Investigations

- Visual acuity
- Refraction
- Tonometry
- Fundoscopy
- Low vision assessment
- Orthoptic Assessment

## Non-pharmacological Treatment

- Assessment of the patients' visual function
- Accurate refraction and provision of spectacles if indicated
- Low vision devices such as optical devices (magnifiers, telescopes) and or non-optical devices (reading stands and or reading slits) as per assessment results.
- Surgical intervention is indicated e.g. if a patient has cataract

**Referral:** All children with low vision should be referred to high level health facility for proper assessment and management by a paediatric Eye Team

## 14.2 Painful Red Eyes

The eye conditions shown on Table 14.4 presents with an acute onset of red eyes: ocular trauma, corneal ulcer, uveitis and conjunctivitis. The Table also summarizes the diagnostics of red eyes.

**Table 14.4: Summary on diagnosis of Red Eyes**

Disease Condition	Visual Acuity	Affected Eye	Cornea	Pupil	Pain	Discharge
Allergic/ viral Conjunctivitis	Good	Both	Clear	Normal	No	Watery/mucoid
Bacterial Conjunctivitis	Good	Both	Clear	Normal	No	Purulent
Ophthalmia neonatorum	Poor +/-	One/both	Cloudy +/-	Normal +/-	Yes	Copious purulent
Cornea ulcer	Poor	One/ both	Gray spot	Normal	Yes	Watery/purulent
Uveitis	Poor	One/ both	Clear or cloudy	Small & Irregular	Yes	Watery
Acute glaucoma	Poor	One	Cloudy	Mid dilated	Yes	Watery

### 14.2.1 Ocular Trauma

These are eye injuries that may result from blunt or sharp objects or from chemical substances. The management of these injuries is guided by history from the patient and ocular findings by the clinicians. Classes of ocular trauma are as follows: -

#### 14.2.1.1 Blunt Trauma/Perforating Eye Injury/Foreign Body

Establish the cause to determine the type of injury and whether there is penetration.

## Clinical presentation

- Corneal abrasion/laceration with or without an imbedded foreign body.
- Eye lids may also be involved.

## **Investigations**

This is done after the first aid measures

- Visual acuity
- Examine the injured eye with slit lamp or magnifier
- Fluorescein staining to reveal foreign body or corneal laceration
- Tonometry in blunt injury
- Fundoscopy in blunt injury or embedded foreign body
- B scan in embedded foreign body
- CT Scan in suspected metal foreign body

## **Non-pharmacological Treatment**

- Provide first aid measures to the patients as per presentation
- If no penetration, irrigate the eye with clean water or Ringers Lactate to reduce chemical substance in the eye
- Remove foreign body if visible with a cotton bud or surgical blade if shallow.

## **Pharmacological Treatment**

At the primary care:

### **Corneal Abrasion:**

**A:** chloramphenicol eye ointment 1%, 8hourly to the injured eye until no fluorescein staining

## **Steps Guiding Management of Complicated Blunt Trauma**

Complicated blunt trauma is a trauma where the vision is poor, patient's experiences pain and there is hyphaema. It is best managed by eye specialist as surgery may be required in the management.

**Table 14.5: Steps guiding management of complicated blunt trauma**

<b>Findings</b>	<b>Action to be taken</b>
No hyphema, normal vision	Observe
Hyphema, no pain	Refer
No hyphema, normal vision, pain	Paracetamol, observe for 2 days, refer if pain persist
Poor vision and pain	Paracetamol, refer urgently
Hyphema, pain, poor vision	Paracetamol, refer urgently

### **14.2.1.2 Deep Corneal or Scleral Injuries**

These are corneal or scleral injuries caused by sharp objects.

## **Clinical presentation**

- History of injury with a sharp object such as knife or wire
- Swollen eye
- Eye discharge

## **Investigations**

- Visual acuity
- Examine the injured eye with slit lamp or magnifier
- Fluorescein staining to reveal foreign body or corneal laceration
- Fundoscopy

## **Non-pharmacological Treatment**

- Apply an eye shield or pad with no pressure and refer immediately

While waiting for referral, use the following in the affected eye:

## **Pharmacological Treatment**

**A:** chloramphenicol 1% eye drop, 2 drops stat

**OR**

**A:** chloramphenicol 1% ointment, stat

**AND**

**B:** atropine 1%, 1–2 drops stat

**AND**

**A:** tetanus toxoid (IM) 0.5ml stat as prophylaxis

**AND**

**A:** paracetamol (PO)1gm 4–6hourly to a maximum of 4 doses in 24hours, for 3days in adults, the dosage in children is 10–14mg/kg 4–6hourly for 3days.

#### **Referral indicated if**

- Intraocular foreign body is suspected
- There is globe or intraocular penetration evidenced by:
  - Poor vision,
  - Distorted pupil
  - Ocular contents of foreign body is seen
  - Circumferential subconjunctival hemorrhage
  - Hyphaema with or without raised intraocular pressure
- Conjunctival laceration requiring suturing (>1 cm)
- Laceration/perforation or diffuse damage to the cornea and sclera
- Chemical and thermal injuries
- Damage to ocular adnexa including eyelids
- Limited ocular movements

#### **Surgical Treatment**

This is done by a well-trained eye specialist at the District, Regional, Zonal and National hospitals. It should be done within 48 hours of injury. Post-operative care should be monitored regularly for any signs of endophthalmitis.

#### **Note:**

- Eye ointment should be applied very gently and in the lower fornix (behind the lower eyelid).
- Do not apply pressure on the eye in perforating injuries of the eyeball

Delay in surgical management of the injury may cause irreversible blindness or may necessitate removal of an eye

**Referral:** Immediately refer the patient to a health facility with eye surgeon at the District, Regional, Zonal or National hospital depending on the staff availability.

#### **14.2.1.3 Chemical Injuries/Burn**

This is an Ophthalmological emergency. It occurs when chemicals such as acid or alkali (e.g. household detergents, bleaching agents), snake spit, insect bite, traditional eye medicine, cement or lime cause a damage to the eye.

#### **Clinical presentation**

- Diagnosis relies mostly with patients' history
- Patients may present with photophobia
- Inability to open the eyes
- Excessive tearing/watery eye
- Cloudiness of cornea with blurred vision
- Loss of conjunctival blood vessels
- Traces of chemical substance such as cement or herbs and blisters or loss of eyelid skin in open flame injuries.

#### **Investigations**

- Visual acuity
- Slit lamp bimicroscopy
- Fluorescein staining

#### **Non-pharmacological Treatment**

If a patient gives you history of being in contact with the items mentioned above, the following should be done:

- Irrigate the eye with clean water or Ringers lactate continually for a minimum of 20–30 minutes to reduce chemical substances. Irrigate longer for severe alkali burn.
- Test the patients' vision and examine the patient's eye

#### **Pharmacological Treatment**

**C:** tetracaine 0.5% eye drops, instill 2 drops in the affected eye. Repeat irrigation if possible. Evert the eye lids and remove the debris

**AND**

**A:** chloramphenicol 1% eye ointment, apply 6hourly to prevent infection for 3days.

**AND**

**A:** paracetamol (PO)1gm 4–6hourly to a maximum of 4 doses in 24hours, for 3days in adults, the dosage in children is 10–14mg/kg 4–6hourly for 3days

**Referral:** Refer all cases within 12hours to eye specialist at high level health facilities for more care

#### **14.2.2 Herpes Simplex Keratitis**

It is an inflammatory condition of the cornea caused by Herpes Simplex Virus.

##### **Clinical presentation**

- Acute unilateral painful eye
- Blurring of vision
- Reduced corneal sensation
- Dendritic corneal ulcer seen on staining with fluorescein

##### **Investigations**

- Visual acuity
- Slit lamp bimicroscopy
- Fluorescein staining

#### **Pharmacological Treatment**

**C:** acyclovir 3%, ophthalmic ointment inserted in the lower conjunctival sac, 4hourly. Continue for 3days after ulcer has been healed.

**AND**

**B:** acyclovir, (PO), 400mg 8–4hourly a day for 7–10days depending on initial response as well as the extent of the ulcer.

##### **Note**

Topical corticosteroids are contraindicated in the treatment of dendritic ulcers

#### **14.2.3 Corneal Ulcer**

This is a painful red eye condition resulting from a raw discontinuity to the corneal epithelium. It may be caused by infection (bacterial, viral e.g. Herpes simplex virus and measles, fungal, trauma (physical or chemical) and nutritional (Vitamin A deficiency).

##### **Clinical presentation**

- Painful and red eye of acute onset
- Excessive tearing
- Severe photophobia
- Poor vision
- Gray/white spot on the cornea staining with fluorescein
- Hypopyon (Pus or white cells in anterior chamber)

##### **Investigations**

- Visual acuity
- Slit Lamp bimicroscope
- Corneal scrapping for Gram Stain and
- Corneal scrapping for Potassium Hydroxide staining
- Fluorescein sodium drops or a drop of local anesthetic on a fluorescein strip to assess the pattern of the ulcer and measure the size of corneal defect.

## **Pharmacological Treatment**

While waiting for laboratory results, give:

**C:** ciprofloxacin 0.3%, ophthalmic drops, instill 1–2drops 1–2hourly for 3days then reduce to 3–4hourly.

**OR**

**D:** ofloxacin 0.3%, ophthalmic drops, instill 1 drop 1–2hourly for 3days then reduce to 3–4hourly

Give antifungal, if fungal infection is suspected or confirmed

**S:** natamycin 5%, ophthalmic drops, instill 1 drop 1–2hourly for 3–4days (specialist use only). Then reduce to 1 drop 3–4hourly. Continue for 14–21days until resolution of infection

**OR**

**S:** econazole 2%, ophthalmic drops, instill 1 drop 1–2hourly for 3–4days (specialist use only). Then reduce to 1 drop 3–4hourly. Continue for 14–21days until resolution of infection

**OR**

**S:** chlorhexidine 0.2%, ophthalmic drops, instill 1 drop 1–2hourly for 3–4days (specialist use only). Then reduce to 1 drop 3–4hourly. Continue for 14–21days until resolution of infection

Give antiviral if viral causes are suspected after the examination of the eye

**C:** acyclovir 3% eye ointment 5hourly a day until there is no corneal stain, then continue with treatment 8hourly a day for a maximum of 10–14days

### **Note**

Treatment may be changed depending on corneal scrapping results

**Referral:** Refer to the next level of care where there is an eye specialist when there is hypopyon (white cells in anterior chamber)

## **14.2.4 Uveitis**

This is inflammation of the uveal tissue (iris, choroid and ciliary body) and its adjacent structures. Majority of the cases are idiopathic whereby other cases are due to autoimmune diseases e.g. Rheumatoid Arthritis, Viral and systemic diseases like Tuberculosis, Leprosy, and Syphilis.

### **Clinical presentation**

It has three main clinical presentations namely acute, chronic and acute on chronic. The commonest form is anterior uveitis. In acute type, patients present with: -

- Painful red eye
- Excessive tearing
- Severe photophobia
- Loss of vision
- Cells in anterior chamber
- Irregular pupil with synechiae

### **Investigations**

- Visual acuity
- Slit lamp bimicroscopic examination anterior chamber
- Tonometry
- B scan
- Urinalysis

Laboratory blood tests for bilateral and granulomatous uveitis: -

- FBC
- ESR
- Antinuclear Antibody
- VDRL
- HIV Testing

**Imaging:** Chest X-Rays if Tuberculosis and Sarcoidosis are suspected.

## **Pharmacological Treatment**

Treatment for uveitis is mainly steroids and specific treatment according to the cause. This should be initiated in a facility where workup and close monitoring can be done.

Give:

Steroidal Anti-inflammatory medicines

**D:** dexamethasone 1% eye drops, 1–3hourly in the affected eye for 6weeks

**OR**

**D:** prednisolone 0.5% or 1 % eye drops, 1–3hourly in the affected eye for 6weeks  
**AND**

**A:** prednisolone (PO) 1mg/kg body weight, given in a tapering manner to maximum of 4–6weeks

**AND**

**D:** triamcinolone (subtenon) 20mg stat, it can be repeated after 4 weeks if need arise.  
**AND**

### Pupil dilating eye drops

**B:** atropine eye drops or ointment 1% 12hourly in the affected eye

**OR**

**C:** cyclopentolate 1 % eye drops, 1–2drops 8hourly in the affected eye.

Treatment for uveitis is to be continued for a maximum of 6weeks

#### Note

- Treatment of uveitis must involve various specialists
- Acute uveitis is a serious problem and the patient should be referred urgently for specialist treatment
- Recurrences may occur or acute disease may end up becoming a chronic uveitis

## 14.2.5 Conjunctivitis

This is an inflammation of the conjunctivae and one of the most common causes of red eyes. The cause of conjunctivitis may be bacterial, viral or allergy. Clinical features and treatment guideline depend on the type and cause of conjunctivitis.

#### Note

- If conjunctivitis is due to an infection, counsel on the importance of frequent hand washing, use separate linen, towels and wash towels and avoid direct contact with infected materials or individuals
- Contacts lenses should not be worn in patients with conjunctivitis until the condition has resolved

### 14.2.5.1 Allergic Conjunctivitis

#### Clinical presentation

- Patients present with history of itching of eyes, sand sensation, and sometimes mucoid discharge
- When examined,
  - the eyes may be normal or slightly red,
  - Conjunctival swelling in severe cases,
  - Limbal hyperpigmentation and papillae of the upper tarsal conjunctiva.
  - Normal iris, pupil and visual acuity.
  - Corneal complications in very advanced stages

#### Investigations

- Visual acuity
- Slit lamp bimicroscopy
- Full blood picture
- Skin Allergic test

#### Non-pharmacological Treatment

Treatment of allergic conjunctivitis depends on the severity of the condition and age of the patient. In mild cases where the eyes are white,

- Avoid allergens
- Cold water compresses for 10 minutes four times a day

## **Pharmacological Treatment**

Adults and children > 6 years of age:

**C:** oxymetazoline 0.025% drops 6hourly a maximum of 7days

If no response within 7days, use mast cell stabilizers such as:

**C:** sodium cromoglycate 2% eye drops, instill 6hourly per day (Doctor initiated)

Use may be seasonal (1–3 months) or long term.

Children 2–6 years of age:

**A:** chlorpheniramine (PO) 0.1 mg/kg/dose 6–8hourly

If no response within 7days use

**C:** sodium cromoglycate 2% eye drops, instill 6hourly per day (doctor initiated)

- Use may be seasonal (1–3 months) or long term for the prevention of further attack, depending on the patient's exposure to the allergen.

## **Persistent allergic Conjunctivitis in adults and children of >2 years of age:**

For long term use:

Children 2–6years

**A:** cetirizine (PO) Adult; 10mg. Children below 6year 5mg 24hourly

- Use may be seasonal (1–3 months) or long term

### **Note**

Do not give antihistamine to children under 2 years of age as its effectiveness at this age group has not been proven.

**Referral:** Refer to eye specialist for further specialized care in case of the following:

- Moderate to severe allergic conjunctivitis
- No response
- Persons wearing contact lenses
- Children <2 years of age

At the specialized centre, the following treatment may be added depending on the patient's presentation:

Short term steroid eye drops (in severe cases with involvement of the cornea, apart from mast cell stabilizers, give

**D:** dexamethasone 0.1%, 6hourly for a maximum of 14days.

**OR**

**D:** prednisolone 0.5%, 6hourly for a maximum of 14days.

In very severe form of allergic conjunctivitis, give steroid injection

**D:** triamcinolone acetonide (subtenon) 20mg stat

**OR**

**D:** methylprednisolone sodium acetate (subtenon) 20mg stat

## **14.2.5.2 Viral Conjunctivitis**

The commonest causative organism is adenovirus. It may be unilateral but usually bilateral

### **Clinical presentation**

- It may be associated with upper respiratory tract infection
- Presents with morning crusting and watery eye discharge
- A burning, sandy or gritty feeling in the eyes
- Diffuse pink or red conjunctiva due to subconjunctival hemorrhages
- Photophobia if the cornea is involved
- Normal visual acuity
- Preauricular lymphadenopathy
- It appears in epidemics so there will be history of contact with patients with similar eye condition
- It is usually self-limiting, but the irritation and discharge get worse on 3 – 5 days before getting better and symptoms can persist for 2–3 weeks.

### **Non-pharmacological Treatment**

- Advise on correct cleansing or rinsing of eyes with clean water
- Cold compresses for symptomatic relief

### **Pharmacological Treatment**

Children > 6 years and adults

**C:** oxymetazoline 0.025% eye drops, instill 1–2drops 6hourly for a maximum of 7days.

**AND**

**A:** paracetamol (PO) Adult; 1g. Pediatric 10–15 mg/kg/dose 6hourly when required.

**Note:** Viral conjunctivitis is very contagious so patients and members of the family should be alerted

**Referral:** Refer all patients to a centre with eye specialist if there is

- No response after 5 days
- Unilateral red eye for more than one day
- Suspected herpes conjunctivitis
- Loss of vision
- Irregular pupil
- Hazeiness of cornea
- Persistent painful eye

#### **14.2.5.3 Bacterial Conjunctivitis**

Purulent conjunctival inflammation caused by bacterial infection

### **Clinical presentation**

It is characterized by:

- Mucopurulent discharge from one or both eyes
- Sore, gritty or scratch eyes and swollen lids
- Conjunctiva redness more at the fornices
- Eyelids may be swollen
- Matting of eye lashes in the morning with eyelids stuck shut

### **Non-pharmacological Treatment**

- Educate patient on personal hygiene to prevent spread
- Educate patient correct application of ophthalmic ointment
  - To wash hands thoroughly before applying ophthalmic ointment
  - Not to share the ophthalmic ointment and drops
- Eye swabs for Gram stain and for culture and sensitivity may be needed to tailor down treatment.

### **Pharmacological Treatment**

**A:** chloramphenicol 1%, ophthalmic ointment, applied 8hourly for 5days.

**OR**

**C:** ciprofloxacin 0.3%, ophthalmic drops, instill 1drop, 4hourly for 2days. Then reduce frequency to 1 drop 6hourly for 5days

**OR**

**D:** ofloxacin 0.3%, ophthalmic drops, instill 1 drop 4hourly for 2days. Then reduce the frequency to 1drop 6hourly for 5days

**AND**

**A:** paracetamol (PO) Adult 1g. Children 10–15 mg/kg/dose 6hourly when required. Adults:

**Referral:** Refer to eye specialist if no improvement after 2days of treatment

#### **14.2.5.4 Ophthalmia Neonatorum/Neonatal Conjunctivitis**

This is acute bacterial infection of the eyes that affect newborn baby during the first 28days of life. The infection is acquired from mother's birth canal secretions. It is characterized by inflammation of

the conjunctivae, sticky eyes to abundant purulent discharge and eyelids oedema. Causative organisms are *Neisseria Gonorrhoea*, *Chlamydia spp* and *Staphylococcus spp*.

### Clinical presentation

- Patients present with massive edema and redness of eyelids and with purulent and copious discharge from the eyes, clinical presentation ranges from mild (small amount of sticky exudates) to severe form (profuse pus and swollen eye lids) depending on the causative organism
- There is usually rapid ulceration and perforation of corneal which eventually leads to blindness if treatment is delayed
- It usually presents 3–4 days of life
- Late and mild presentation is due to Staphylococcus or undefined
- Treat parents of a neonate with purulent discharge appropriately

### Investigations

- Pus swab for Gram Stain
- Pus for Culture and sensitivity
- Vaginal swab for Gram stain and culture and sensitivity

### Non-pharmacological Treatment

Cleanse or wipe eyes of all newborn babies with a clean cloth, cotton wool or swab, taking care not to touch or injure the eye

### Pharmacological Treatment

Screen women in the antenatal clinics and treat both parents for Sexually Transmitted Diseases. In Ophthalmia neonatorum, prevention is better than cure.

**A:** Apply chloramphenicol 1% eye ointment, both eyes, to all newborn babies as soon as possible after birth.

**OR**

**A:** povidone iodine 2.5 % Eye Drops, both eyes

### Sticky eye(s) without purulent discharge:

**A:** chloramphenicol 1% eye ointment, apply 6 hourly for 7 days

### Purulent discharge

#### Mild discharge without swollen eyelids and no corneal haziness:

**A:** compound sodium lactate eye wash, immediately then 2–3 hourly until discharge clears

**AND**

**B:** ceftriaxone (IM) 50mg/kg immediately stat

Given at District Hospital (Treatment to be initiated by Clinical Eye Care Professional eg. Assistant Medical Officer in Ophthalmology)

#### Abundant purulent discharge and/or swollen eyelids and /or corneal haziness:

**A:** compound sodium lactate eye wash, immediately then hourly until referral

**AND**

**B:** ceftriaxone (IM) 50mg/kg immediately stat

**Referral:** To high level health facilities for proper management.

### Note

- Ceftriaxone should not be used in neonates that are seriously ill or are jaundiced
- Ceftriaxone should not be administered if calcium containing intravenous infusion e.g Compound Sodium Lactate is given or is expected to be given

Treat both parents of newborns who develop purulent conjunctivitis after 24 hours of birth for N-gonorrhoea and Chlamydia with

**B:** ceftriaxone (IM) 250mg stat

(For ceftriaxone IM injection: Dissolve Ceftriaxone 250mg in 0.9 mL Lidocaine 1% without adrenaline)

**AND**

**B:** azithromycin (PO) 1g stat

**Note:**

For more details on prevention and treatment see the “Neonatal Conjunctivitis (NC) **Flow chart number 12.7** under the Sexual Transmitted disease chapter

**Referral:** Urgently

- Neonates with abundant purulent discharge and/or swollen eyelids and/or corneal haziness and
- Neonates unresponsive to treatment within 2days.

### 14.3 Structural Abnormalities of the Eye

These includes:

- **Squint:** eyes are looking in different directions; one eye appears to be turned in or out, in children or in adult. Refer urgently all children who present with squint to Paediatric Eye Tertiary Centre
- **Ocular surface disease:** The most common ocular surface diseases are pterygium and Squamous cell carcinoma of the conjunctiva.
- **Eyelids abnormalities:** eyelashes rubbing on cornea (trichiasis), inturned eyelids (entropion), eyelids bent out too much (ectropion), drooping eyelids (ptosis), inability to close the eyes (lagophthalmos)

**Referral:** Refer all patients to health facilities with eye specialist for surgical intervention

**Note:** Abnormal tissues excised from eye patients should be subjected to pathology examination for proper diagnosis

### 14.4 Ocular Oncology

#### 14.4.1 Retinoblastoma

It is the commonest childhood malignant tumor of the eyes. It is diagnosed between the first 1–3years of life. It has a lower survival rate after diagnosis hence, monthly screening of all under-five children is important for timely referral and management.

##### Clinical presentation

- White pupil reflex (leukocoria)
- Squint
- Rarely vitreous hemorrhage
- Hyphema
- Ocular/periocular inflammation
- Secondary glaucoma
- In late stages proptosis and hypopyon

##### Investigations

- Visual acuity
- Tonometry
- Fundoscopy
- B Scan
- CT Scan of the head
- Examination under anaesthesia
- Histology of an enucleated eye in advanced disease
- Cerebral Spinal Fluid analysis in advanced disease

##### Non-pharmacological Treatment

Staging and treatment is done in specialized centres in consultation with Pediatrician and Oncologist. The following are treatment modalities:

- Enucleation of the affected eye and the eye is taken for histology
- External beam radiotherapy
- Plaque radiotherapy
- Cryotherapy and laser photoablation

**Table 14.6: Classification of Retinoblastoma and recommended treatment options according to the classification of Retinoblastoma (ICRB)**

Group	Clinical features	Recommended Treatment options
A	All small tumors (3 mm or less) that are only in the retina and are not near important structures such as the optic disc or the foveolar i.e. Not less than 3 mm from the foveolar and 1.5mm from the optic disc.	<ul style="list-style-type: none"> <li>- Focal therapy (cryotherapy or Transpupillary thermotherapy (TTT).</li> <li>- TTT is indicated for posterior located tumors. TTT use Diode Laser (810nm) or 1064nm or 532nm. Tumor is heated until it turns slightly gray. Complete tumor regression can be achieved by using 3-4sessions</li> <li>- Do not exceed 5 minutes per session to avoid complication such as Cataract.</li> <li>- Cryotherapy is done to a small tumor at equatorial and peripheral retina. Under GA place the probe precisely on the sclera, directly behind the intraocular focus of the tumor. apply triple freeze/thaw at 3 week intervals until complete tumor regression.</li> </ul> <p><b>Note:</b> Administer cryotherapy or TTT 3-6 hours prior to chemotherapy if systemic treatment is indicated. Focal therapy synergistically increases drug penetration to the tumor</p>
B	Tumor of >3mm, close to the optic disc or foveola No subretinal fluid	<ul style="list-style-type: none"> <li>- 6cycles of standard dose chemotherapy are indicated to allow adequate tumor reduction.</li> </ul> <p><b>Note:</b> Standard dose is a combination of Carboplatin, Vincristine and Etoposide (VEC). Do not perform focal therapy if tumors are located in the macular and juxtapapillary areas.</p> <ul style="list-style-type: none"> <li>- If focal therapy is indicated chemotherapy should be given within 6hr of focal therapy to increase drug penetration to the eye and tumor</li> </ul>
C	Well-defined tumors with small amounts of subretinal or vitreous seeding (tumor cells floating within the vitreous cavity)  NOTE: Vitreous seeding is one of the most challenging situations for eye-preservation therapy and is the primary reason for treatment failure following conservative management of retinoblastoma.	<ul style="list-style-type: none"> <li>- 6cycle of standard dose Chemotherapy is indicated.</li> <li>- Chemotherapy should be given within 6 hours of focal therapy (cryotherapy or TTT or Subtenon Carboplatin) depending on site and response to treatment.</li> <li>- Chemotherapy cycles are given at 3 weeks intervals, every cycle is preceded by EUA and focal therapy.</li> </ul> <p><b>Note:</b> Do not perform focal therapy if tumors are located in the macular and juxtapapillary areas</p> <ul style="list-style-type: none"> <li>- vitreous seeding can be managed by plaque radiotherapy (need license), External beam Radiotherapy, Enucleation or intravitreal chemotherapy (Melphalan). Melphalan salvage about 60% of eyeball with vitreous seeding (8-10µg is safe dose)</li> </ul>
D	Large or poorly defined tumors occupying up to 50% of the globe with widespread vitreous or subretinal seeding. There is retinal detachment up to 50% of the globe	<ul style="list-style-type: none"> <li>- If unilateral Enucleate.</li> <li>- If bilateral Start 3 cycles of chemotherapy</li> <li>- If no response and no visual potential enucleate the worse eye.</li> <li>- If there is response complete 6cycles of systemic chemotherapy.</li> <li>- Local radiation for persistent vitreous seeds may be indicated (plaque therapy or Intravitreal Melphalan)</li> </ul> <p><b>Note:</b> Focal therapy should be given prior to chemotherapy for every cycle.</p> <ul style="list-style-type: none"> <li>- Chemotherapy should be given within 6 hours of focal therapy to increase drug penetration to the eye and tumor</li> </ul>
E	The tumor is very large with one or more of the following features: -	<p>Enucleation with minimal manipulation is indicated for</p> <ul style="list-style-type: none"> <li>- All group E with no visual potential,</li> <li>- If all known effective treatment has failed</li> </ul>

	<ul style="list-style-type: none"> <li>No visual potential</li> <li>Tumor in the anterior segment</li> <li>Tumor in or on the ciliary body</li> <li>Neovascular glaucoma</li> <li>When there is no direct visualization of an active tumor (Vitreous hemorrhage, cataract or hyphema)</li> <li>Phthisical or pre-phthisical eye</li> <li>Orbital cellulitis-like presentation</li> <li>Total RD of more than 50%</li> </ul>	<p><b>Note:</b> Optic nerve length should not be less than 17mm to minimize the chances of leaving tumor at surgical site. Also, when performing enucleation:-</p> <ul style="list-style-type: none"> <li>Take care not to perforate the globe</li> <li>Use primary orbital implant to achieve excellent cosmetic appearance</li> <li>If histopathology results are positive for high risk factors, 6cycles of Chemotherapy is indicated as for Group D above.</li> </ul> <p>Histopathological features in retinoblastoma are considered high-risk factors (HRF) for tumor progression and metastasis, thus their presence becomes an indication for adjuvant chemotherapy (HRF) includes:</p> <ol style="list-style-type: none"> <li>Scleral extension</li> <li>Post-laminar optic nerve invasion</li> <li>Disease at the cut margin of optic nerve</li> <li>Massive choroidal invasion of more than 3mm</li> <li>Anterior chamber extension</li> </ol> <ul style="list-style-type: none"> <li>If no HRF no need of chemotherapy.</li> <li>Prostheses and protective glasses are indicated for all children who have been enucleated</li> </ul>
EOE	Orbital RB	<ul style="list-style-type: none"> <li>3–6 cycles of high dose chemotherapy- followed by enucleation if tumor regressed significantly</li> <li>External Beam Radiotherapy and adjuvant chemotherapy for a total of up to 12 cycles</li> </ul> <p>NOTE: Exenteration is not encouraged at this stage since aim of treatment is for palliation.</p>
Distance metastasis	CNS involvement RB- where Ct/MRI proved CNS extension or cerebral-spinal fluid is positive for RB cells	Palliative care according to the National Palliative Care Guideline
	Metastatic RB where bone marrow biopsy is positive	Palliative care according to the National Palliative Care Guideline

### Pharmacological Treatment

Systemic chemotherapy is instituted by Oncologists and or paediatrician. Ophthalmologist institute intravitreal chemotherapy if need be.

**Referral:** Refer to Oncology Section in this document for details of Chemotherapy in Retinoblastoma treatment.

#### Note

Close follow up is very important due to the following:-

- There is a chance of developing retinoblastoma in the fellow eye
- The risk is diminished with increase in age
- Also watch for secondary tumors like osteosarcoma

**Referral:** Refer all children presenting with a white pupillary reflex, squint or acute painful red eye to some qualified eye care personnel/ophthalmologist.

### 14.4.2 Squamous Cell Carcinoma of Conjunctiva

Invasive squamous cell carcinoma of conjunctiva is the major and most common ocular malignancy of the eye. The tumor typically occurs on the bulbar conjunctiva, originating at the limbus, and often spreads onto the cornea, globe, orbit and nasolacrimal system. The cancer is a slow growing tumor of middle-aged to elderly people.

#### Clinical presentation

- It manifests usually as a fleshy vascularized mass at the limbus. (temporal or nasally)
- In advanced stage, it may intrude the eyeball and extend to other ocular adnexa structures

- Definitive diagnosis is by histopathological assessment of excised tissue

### **Investigations**

- Visual acuity
- Slit lamp Biomicroscopy
- Tonometry
- Fundoscopy
- Histology examination of the excised mass

### **Non-pharmacological Treatment**

- Check for HIV status of the patient as recurrences occurs most frequently in HIV positive patients
- Close follow up of patients for at least the first 12 months postoperatively to look for residual or recurrent tumors

### **Pharmacological Treatment**

**D:** 5-fluorouracil (5FU) 50mg/mL, on a sponge, on the surgical bed for about 2.5minutes then wash off with compound sodium lactate solution.

**OR**

**D:** mitomycin C 0.2mg/mL, on a sponge, on the surgical bed for about 2.5minutes then wash off with compound sodium lactate solution.

**AND**

**C:** dexamethasone + chloramphenicol eye drops, 0.1%–0.5 %, 6hourly, for 3–4weeks

**OR**

**C:** dexamethasone + gentamicin eye drops, 0.1–0.3%, 6hourly, for 3–4 weeks

(These are post operatively until the wound is healed)

**THEN**

**D:** 5-fluorouracil (5FU) 1% eye drops, 4times daily for 2–3weeks

### **Note**

- 5-fluorouracil (5FU) is used after the excision wound has healed
- 5 FU eye drops may cause watery eye, discomfort or eye inflammation, manage accordingly

### **Surgical Treatment**

- It depends on the tumor size, location, focality, and invasiveness
- Surgical excision of the mass with clear margin of 4 mm without touching the tumor is recommended, followed with topical adjunctive cryotherapy and or chemotherapy to the residual conjunctival and scleral bed
  - Double - four freeze-thaw cycles of cryotherapy to the remaining conjunctival margins, bed and limbus.
  - For tumors that are adherent to the sclera, perform a superficial sclerectomy and use cryotherapy to the base.
- A large or multicentric squamous conjunctival mass should be managed by a surgeon experienced in treating such lesions
- Removal of the eyeball and adnexa may be indicated for advanced stage
- Radiotherapy if required, for palliation after removal of the eye.

### **Referral:**

- All suspicious cases of Squamous Cell Carcinoma of Conjunctiva must be referred to eye specialist for proper evaluation and management.
- Refer all patients with advanced Squamous Cell Carcinoma of the conjunctiva to Oncologist

### **14.5 Dry Eye**

It occurs when there is inadequate tear volume or function.

### **Clinical presentation**

- Feelings of dryness, grittiness, burning and foreign body sensation, usually worse during the day

- Stringy discharge, redness and transient blurring of vision are also common. Exclude allergic conjunctivitis

### **Investigations**

- Visual acuity
- Slit lamp biomicroscopy
- Schirmer Test
- Tear break up test

### **Non-pharmacological Treatment**

- Control symptoms since the condition is not curable
- Educate patients to avoid unprescribed eye medications which may worsen the dryness and control their environmental factors by e.g. blinking frequently during visual attentive tasks, avoid air conditioners

### **Pharmacological Treatment**

Tear substitutes give:

**C:** hydroxypropyl methylcellulose 0.7%, ophthalmic drops, 1drop, 6hourly.

### **14.6 Herpes Zoster Ophthalmicus**

Occurs when Varicella Zoster Virus reactivates in the trigeminal ganglion and passes down the ophthalmic division of the trigeminal nerve

#### **Clinical presentation**

- Presents with painful vesicular rash in the trigeminal V1 area—vesicles on the tip of the nose indicate nasociliary branch involvement and increases the risk of ocular involvement
- Some patients develop conjunctivitis, keratitis, uveitis, retinitis and cranial nerve involvement (oculomotor and optic nerves)
- Later, chronic ocular inflammation, loss of vision, post herpetic neuralgia
- All patients should be offered HIV testing

### **Investigations**

- Visual acuity
- Slit lamp biomicroscopy
- Corneal sensation test
- Fluorescein staining
- HIV Testing

### **Pharmacological Treatment**

**B:** acyclovir (PO) 800mg 4hourly for 7–10days

**AND**

**A:** amitriptyline (PO) 25mg at night for 3months.

#### **Note:**

- Treatment should be initiated within 3 days of the onset of symptoms, except in HIV infected patients who should be treated if there are active skin lesions
- Management of Herpes Zoster is Multidisciplinary so consult physician for proper management of the patient.

### **Referral**

Refer to eye specialist in case of: -

- Vesicles on the tip of the nose
- Fluorescein staining of the cornea shows corneal ulceration
- Decreased vision
- Red eye (uveitis or keratitis)
- Cranial nerve palsies

### **14.7 Endophthalmitis**

It is an infection of the ocular cavity. It is an ophthalmic emergency that can cause blindness that may occur secondary to bacteraemia (endogenous infection) or following penetrating eye injury or surgery

## Clinical presentation

- Loss of vision, may be associated with pain in the affected eye
- Blood culture should be done to identify the source and how it can be treated (for bacteraemia)
- In post injury or surgery, culture of specimens of aqueous or vitreous humour should be done

## Investigations

- Visual acuity
- Slit lamp biomicroscopy
- Tonometry
- Refraction
- B Scan
- Vitreous Tap for Gram stain, Culture and sensitivity

## Pharmacological Treatment

Refer immediately to an ophthalmologist for treatment

### Endogenous Endophthalmitis

Specialist initiated; vitrectomy often required

**B:** ceftriaxone (IV) 2g 24hourly for 7days

### Adjust antibiotics according to culture and sensitivity

**AND**

**D:** ceftazidime (intravitreal) 2.25mg stat repeat after 16–24hours

**AND**

**S:** vancomycin (intravitreal) 1mg stat repeat after 72hours

### Administer using separate 1 ml tuberculin or Insulin syringes

### Post-Surgical endophthalmitis

Specialist initiated; vitrectomy often required

**D:** ceftazidime (intravitreal) 2.25mg stat repeat after 16 – 24hours

**AND**

**D:** vancomycin (intravitreal) 1mg stat repeat after 72hours

Administer using separate tuberculin or Insulin syringes

In addition, if there is soft tissue involvement or as a prophylaxis after a penetrating injury:

**A:** ciprofloxacin (PO) 750mg 12hourly for 7days.

## 14.8 Retinitis

It is seen in advanced HIV infection with CD4 count of less than 100 cells/mm<sup>3</sup>. Management of these patients is done in consultation with treating physicians.

### Diagnostic Criteria

- Presents with characteristic retinal appearance of necrosis (white exudates and haemorrhages at the edge of the exudates)
- Visual loss is irreversible

## Pharmacological Treatment

**S:** ganciclovir (intravitreal) 2mg once a week

Once immune function has been restored with antiretroviral therapy, (CD4 > 100) and the features of active retinitis has been cleared, maintenance Ganciclovir can be stopped but monitor for recurrence.

**Referral:** Refer to Ophthalmologist for confirmation of diagnosis and treatment.

## 14.9 Orbital Cellulitis

Orbital cellulitis is an infection of the soft tissues of the orbit posterior to the orbital septum. It may be a continuum of preseptal cellulitis, which is an infection of the soft tissue of the eyelids and

periocular region anterior to the orbital septum. Orbital cellulitis may result from an extension of an infection from the paranasal sinuses or other periorbital structures such as the face, globe, or lacrimal sac, direct inoculation of the orbit from trauma or surgery or as a haematogenous spread from bacteraemia

### Clinical presentation

- Fever, malaise, and a history of recent sinusitis or upper respiratory tract infection
- Proptosis and ophthalmoplegia are the cardinal signs of orbital cellulitis.
- Conjunctival chemosis, dyschromatopsia, and relative afferent pupillary defect
- Decreased vision
- Elevated intraocular pressure
- Pain on eye movement
- Orbital pain and tenderness are present early
- Swollen eyelids, chemosis, hyperemia of the conjunctiva, and resistance to retropulsion of the globe may be present
- Purulent nasal discharge may be present
- For very ill children, vision may difficult to evaluate in very ill children with marked edema

### Investigations

- Visual acuity
- Slit lamp biomicroscopy
- Tonometry
- Fundoscopy
- Full Blood Count and ESR
- Blood culture
- Assessment of purulent nasal discharge or from the abscess (Swab for Gram Stain)
- CT Scan of the orbits and paranasal sinuses with Contrast and
- MRI will help differentiating it with other diseases but also identifying the source or extension of the disease

### Non-pharmacological Treatment

- Patients must be hospitalized
- Adequate hydration
- Lower the temperature
- Daily evaluation and monitor the vital signs
- Management of orbital cellulitis is done with consultation from other medical team (Neurosurgical (if brain extension is seen), ENT (for involvement of sinuses), Paediatrician (for paediatric patients) and Physicians

### Pharmacological Treatment

The antibiotic will be tailored when the laboratory results are out

Adults, give:

**B:** ampicillin + cloxacillin (FDC) (IV) 1g stat then 500mg 6hourly for 2weeks

**AND**

**A:** gentamicin (IV) 160mg 24hourly for 7days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 7days

**AND**

**S:** vancomycin (IV) 15–20 mg/kg 8–12hourly

Children more than one-month old give:

**B:** ampicillin + cloxacillin (FDC) (IV) 50 mg /kg 8hourly for 7–14days

**AND**

**A:** gentamicin (IV) 7.5mg/kg, 24hourly for 5 -7days

**AND**

**B:** metronidazole (IV) 7.5–15mg/kg 6hourly for 7–10days

**AND**

**S:** vancomycin (IV) 10mg/kg 6hourly for 7–10day

**Note: Individual dose not to exceed 1g**

Children less or equal to one-month old give:

**B:** ampicillin + cloxacillin (FDC) (IV) 25–50mg/kg 8hourly for 7–14days

**AND**

**A:** gentamicin (IV) 5mg/kg 24hourly for 5–7days

**Steroidal anti – inflammatory medicines**

To be given after 48 hours of antibiotic therapy. Give:

**A:** prednisolone (PO) 1–2mg/kg 24hourly to be tapered slowly.

**AND**

Adults:

**A:** ibuprofen (PO) 400–800mg 6–8hourly; not to exceed 3.2 g 24hourly

**OR**

**A:** paracetamol (PO) 1g 4–6hourly to a maximum of 4 doses 24hourly, for 3days

Children:

**A:** ibuprofen (PO) 30–40mg/kg per day in 3–4doses

**OR**

**A:** paracetamol 10–14 mg/kg for 3days

**Note**

Do not use ibuprofen in patients with bleeding disorders or peptic ulcers

**Surgical Treatment**

Surgical drainage is only indicated when there is:

- A decrease in vision
- Development of an afferent pupillary defect
- Progression of Proptosis despite appropriate antibiotic therapy
- The size of the abscess does not reduce on CT scan within 48–72hours after appropriate antibiotics have been administered
- If brain abscesses develop and do not respond to antibiotic therapy, then craniotomy is indicated
- Presence of a drainable fluid collection is evident on CT scan in patients older than 16years

**14.10 Visual Problems**

Visual problems may be due to refractive errors, damage to the eye or optic nerve. This may be an indication of underlying diseases such as diabetes or hypertension.

**Investigations**

- Assess ocular alignment
- Determine visual acuity accurately in both eyes by Snellen chart
- If vision is diminished, (less than 6/12), perform the following:-

**Pin hole test**

- Make a hole of about 1mm wide in a piece of dark/black paper – you can push a hole in a paper or card with a pen tip
- Ask the patient to look through this hole at the Snellen chart
- If vision improves, this means that the patient has a refractive error

**Red Reflex Test**

The patient looks past the examiners head focusing on a distant target.

- With the ophthalmoscope at 0 (zero) the examiner keeps close to his eye and then focuses the beam of light so that it falls on the pupillary area of the cornea
- The examiner stands about 60cm away from the patient.

- In normal individuals, the examiner should be able to see a red or pink colour (reflex) through the pupil which comes from the retina.

### **Significance of absent red reflex**

If there is history of trauma or diabetes, the absence of a red reflex is probably due to:

- Retinal detachment
- A vitreous hemorrhage
- Mature cataract

If there are cataracts, one usually sees:

- Black shadows against the red reflex in immature cataract, or
- Absence of red reflex in mature cataracts

In a >50years of age with no history of trauma, diabetes or previous eye disease, an absent red reflex is often due to cataract formation, especially with decreased visual acuity.

### **Fundoscopy**

#### **Note**

Associated diabetes or hypertension should be adequately managed with referral, as surgery can only be considered with appropriately managed systemic disease

### **Referral**

#### **Urgent within 12–24 hours**

- Sudden loss of vision in one or both eyes
- Pain or redness in one eye only especially with visual and pupillary abnormalities
- Recent proptosis of one or both eyes or enlargement of the eye (buphthalmos) in children
- Hazy cornea in children
- Unilateral watery eye

#### **Within days**

- Squint of recent onset
- Suspected or previously diagnosed glaucoma
- Double vision following recent injury might indicate orbital fracture
- Leukocoria (white reflex from the pupil) especially in children
- Squint at an age if not previously investigated by ophthalmologist
- Visual loss in patients with systemic disease such as diabetes

#### **Non-urgent referral**

- Cataracts in adults
- Refractive errors in teenage and adults
- Longstanding blindness—first visit to health facility

### **14.11 Onchocerciasis (River Blindness)**

Onchocerciasis is a tissue parasitic infestation caused by a filarial worm, *Onchocerca volvulus*. The microfilariae invade lymphatic system, subcutaneous and deep tissues producing acute inflammation and chronic inflammation at a later stage.

#### **Clinical presentation**

- Skin inflammation with papules
- Subcutaneous nodules
- Atypical skin lesions (scarred, saggy, hanging areas of skin, leopard skin)
- Skin nodules under the bony prominent areas
- Microfilaria in anterior chamber
- Scleritis and Keratitis leading to Impaired vision as well as blindness.

#### **Investigations**

- Visual acuity
- Rapid diagnostic test (OV-16 - Onchocerciasis IgG)

- Skin snip for microscopic examination
- Slit lamp eye examination.
- B Scan

### **Pharmacological Treatment**

Treatment is done in consultation with dermatologists and infectious disease specialists.

Apart from WHO recommended mass treatment campaign to community at risk with annual preventive chemotherapy which polarize/paralyze the worm, treatment depends on individual patient presentation.

**A:** ivermectin (PO) 0.15mg/kg once every 12months for 12–15years

**Note:**

- Patients with heavy ocular infestation require retreatment every 3 to 6 months.
- Treatment will only arrest progression of the clinical features but not reverse them.

### **Dosage guidelines based on body weight**

<b>Weight</b>	<b>Dosage</b>
15-25kg	3mg
26-44 kg	6mg
45 -64 kg	9mg
65- 84 kg	12mg
85kg or more	0.15mg/kg

### **Surgical treatment**

Nodulectomy: It is done mostly for nodules located in the scalp to minimize the ocular complications.

# CHAPTER FIFTEEN

## EAR, NOSE AND THROAT DISEASES

Ear, Nose and Throat (ENT) is a specialty in medicine that deals with medical and surgical management of disorders affecting the ear, nose, throat, and the neck. Symptoms and diseases affecting this area are common and commonly lead to patients seeking medical care.

### 15.1 Ear Condition

#### 15.1.1 Circumscript otitis Externa (Furunculosis)

This is a localized infection of the hair follicle on the outer one-third of the external auditory canal. It is caused by *Staphylococcus aureus*.

##### Clinical presentation

- Ear pain that is severe and disproportional to the visible lesion
- Reduced hearing
- Localized swelling on the external auditory canal
- There may be a purulent discharge if the swelling ruptures

##### Non-pharmacological management

- Aural toilet if there is otorrhea (ear suctioning under direct vision).
- Instruct the patient to keep the ear dry and avoiding scratching

##### Pharmacological management

**B:** ampicillin+cloxacillin (FDC) (PO) Adults: 500mg 8hourly for 7 to 10days. Children: 15mg/kg hourly for 7 to 10days

**OR**

**C:** amoxycillin + clavulanic acid (FDC) (PO) Adults: 625mg to 1g 12hourly for 7 to 10days. Children ≤ 3 months: 30mg/kg/day in 2 divided doses for 7-10 days. Children >3 months: 25mg/kg/day in 2 divided doses for 7 to 10 days.

**AND**

**A:** paracetamol (PO) Adults: 500mg to 1g 4 to 8hourly as needed. Children ≤ 10kg: 10mg/kg 4 to 8 hourly as needed. Children >10kg: 15mg/kg 4 to 8 hourly as needed

**OR**

**A:** ibuprofen (PO) Adults: 200 mg to 400mg 4 to 8hourly as needed. Children ≥ 6 months: 5mg to 10mg/kg 4 to 8hourly as needed OR combined ibuprofen and paracetamol

##### Surgical management

- Incision and drainage

#### 15.1.2 Diffusewcer Otitis Externa (Swimmer's ear)

This is an inflammation of the entire external auditory canal. It can be caused by bacteria, fungus or both.

##### Clinical presentation

- Itchy, dry and scaly ear canal and painful ear
- There may be a water or purulent discharge, debris and reduced hearing

Pain may become extreme when the ear canal becomes completely occluded with edematous skin and debris.

##### Non-pharmacological management

- Aural toilet at least once a week (ear suctioning under direct vision using microscope or endoscope).
- Instruct the patient to keep the ear dry and avoiding scratching.

## **Pharmacological management**

**C:** ciprofloxacin ear drops 2 to 4drops each ear 6 to 8hourly for 14days.

**OR**

**C:** cream with combination of gentamicin or Neomycin+ Clobetasol or betamethasone or beclometasone + miconazole or clotrimazole. Dosage: Apply pea size in external auditory canal once per week for 4 to 6weeks.

**OR**

**D:** chloramphenicol+beclomethasone dipropionate+ clotrimazole + lignocaine ear drops (FDC) 2 to 3drops each ear 6 to 8hourly for 14days.

**AND**

**A:** ciprofloxacin (PO) 500mg Adults and children above 12 years 12 hourly 7 to 14 day

**OR**

**B:** amoxycillin +clavulanate (FDC) (PO) Adult 625mg to 1g 12hourly: Paediatric ≤ 3 month 30mg/kg/day in 2 divided doses. Paediatric > 25mg/kg/day in 2 divided doses for 7-14days  
**AND**

**A:** paracetamol (PO) Adult 1g: Pediatric ≤ 10kg 10mg/kg 4. Paediatric >15mg/kg 6 to 8 hourly as needed.

**OR**

**A:** ibuprofen (PO) 200 mg to 400mg 8 hourly as needed. Paediatric ≥ 6 months: 5mg to 10mg/kg 4 to 8hourly as needed

**OR**

**D:** diclofenac+ paracetamol (PO)(FDC)Adults: 50mg diclofenac and 500mg paracetamol 4 to 8hourly as needed.

### **15.1.3 Necrotizing Otitis Externa**

This is a life-threatening infection that affects the external auditory canal and base of the skull. It is common to elderly diabetic patients and other immunosuppressive conditions. Most common causative organism is *Pseudomonas aeruginosa*. Controlling the underlying cause of immunosuppression is of paramount importance.

#### **Clinical presentation**

- Ear pain, discharge, fullness and hearing impairment
- May present with facial nerve paralysis or other cranial nerves palsy.
- Presence of granulation tissues at the junction between the bony and cartilaginous parts of external auditory canal
- Necrosis of external auditory canal

#### **Non-pharmacological management**

- Aural toilet at least once a week (ear suctioning under direct vision using microscope or endoscope).
- Instruct the patient to keep the ear dry and avoiding scratching

#### **Investigations**

- culture and sensitivity of discharge

## **Pharmacological management**

**C:** ciprofloxacin ear drops 2 to 4 drops each ear 6 to 8hourly for 14days

**AND**

**B:** ceftriaxone (IV) 1 to 2 g 12hourly for 7days.

For Children:

**B:** ceftriaxone (IV) 50 to 100mg/kg 24hourly for 7 day

**OR**

**C:** ciprofloxacin (IV) 400mg for 5 to 7days THEN 500mg (PO) 12hourly for 4 to 6weeks days.

**OR**

**S:** meropenem (IV) (**culture and sensitivity test is required**) 500mg to 2g 8 hourly for 7 to 14days.

For Children ≥ 3 months:

**S:** meropenem (IV) (culture and sensitivity test is required) 10mg/kg 8 hourly for 7 to 14days.

**AND**

**A:** paracetamol (IV) 500mg to 1g 4 to 8hourly as needed.

For Children ≤ 10kg:

**A:** paracetamol (IV) 10mg/kg 4 to 8hourly as needed.

For Children >10kg:

**A:** paracetamol (IV) 15mg/kg 4 to 8hourly as needed.

**OR**

**A:** ibuprofen (PO) 200 to 400mg 4 to 8hourly as needed.

For Children ≥ 6 months:

**A:** ibuprofen (PO) 5mg to 10mg/kg 4 to 8hourly as needed

**OR**

**C:** diclofenac+ paracetamol (PO) 50mg diclofenac and 500mg paracetamol 4 to 8hourly as needed

### **Surgical management**

Serial surgical debridement under local anesthesia(LA) or general anesthesia (GA).

**Note:** Necrotizing otitis externa is an emergency therefore treatment should be vigorous including the treatment of underlying immunodeficiency. Consider referral to tertiary facility for specialized care.

### **15.1.4 Herpes Zoster Oticus (Ramsay Hunt syndrome)**

This is a viral infection of external, middle and inner ear caused by reactivation of Varicella Zoster virus in the geniculate ganglion.

#### **Clinical presentation**

- Vesicular rash of the ear
- Facial nerve paralysis
- Ear pain
- Ear discharge

#### **Non-pharmacological management**

Instruct the patient to keep the ear dry and avoiding scratching

#### **Pharmacological management**

**A:** prednisolone (PO) 60mg 24hourly for 5days then taper down to 50mg 24hourly for next 5days. Children: 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

**AND**

**B:** acyclovir (PO) 800mg 4-8hourly for 7-14days.

For Children birth to 3 months:

**B:** acyclovir (IV) 10-20mg/kg 8hourly for 7-14days

For Children from 3 months to 12 years:

**B:** acyclovir (PO) 40-80mg/kg 6hourly for 7-14days

For Children more than 12 years

**B:** acyclovir (PO) 40-80mg/kg 6hourly for 7-14days

**AND**

**B:** acyclovir 5% cream.: Apply on the lesions 12 hourly.

**AND**

**B:** ampicillin+cloxacillin (FDC) (PO) 500mg 8hourly for 10-14 days.

For Children:

**B:** ampicillin+cloxacillin (FDC) (PO) 15mg/kg 6 hourly for 7-14 days

**OR**

**B:** amoxycillin+clavulanate (FDC) (PO) 625mg to 1g 12 hourly for 7-14 days.

For Children ≤ 3 months:

**B:** amoxycillin+clavulanate (FDC) (PO) 30mg/kg/day in 2 divided doses for 7-14 days.

For Children >3 months:

**B:** amoxycillin+clavulanate (FDC) (PO) 25mg/kg/day in 2 divided doses for 7 to 14 days

**OR**

**A:** paracetamol (PO) 500mg to 1g 4 to 8 hourly as needed.

For Children ≤ 10kg:

**B:** amoxycillin+clavulanate (FDC) (PO) 10mg/kg 4 to 8 hourly as needed.

For Children >10kg:

**B:** amoxycillin+clavulanate (FDC) (PO) 15mg/kg 4 to 8 hourly as needed

**OR**

**A:** ibuprofen (PO) 200 to 400mg 4 to 8hourly as needed.

For Children  $\geq$  6 months:

**A:** ibuprofen (PO) 5mg to 10mg/kg 4 to 8hourly as needed

**OR**

**C:** diclofenac (PO) 50 mg 4 to 8hourly as needed.75 mg (IM) 8hourly as needed

**OR**

**A:** paracetamol + ibuprofen (PO) 400mg ibuprofen and 325mg paracetamol 4 to 8hourly as needed.

For Children:

**A:** paracetamol + ibuprofen (PO) 100mg ibuprofen and 162.5mg paracetamol 4 to 8hourly as needed

### 15.1.5 Pre-auricular Sinus Tract Infection

This is an infection of the pre-auricular sinus tract. May present with pre-auricular abscesses. Most common causative organism is *Staphylococcus aureus*.

#### Clinical presentation

- Ear pain, sinus discharge
- Pre-auricular Swelling
- Fever, headache

#### Pharmacological management.

**B:** ampincillin+cloxacillin (FDC) (PO) 500mg 8hourly for 7-10days.

For Children:

**B:** ampincillin+cloxacillin (FDC) (PO) 15mg/kg 6 hourly for 7-10days

**OR**

**B:** amoxycillin+clavulanate (FDC) (PO) 625mg to 1g 12hourly for 7-10days

For Children  $\leq$  3 months:

**B:** amoxycillin+clavulanate (FDC) (PO): 30mg/kg/day in 2divided doses for 7-10days

For Children  $>3$  months:

**B:** amoxycillin+clavulanate(FDC)(PO) 25mg/kg/day in 2divided doses for 7-14days

**AND**

**A:** paracetamol (PO) 500mg to 1g 4-8hourly as needed.

For Children  $\leq$  10kg:

**A:** paracetamol (PO) 10mg/kg 4-8hourly as needed.

For Children >10kg:

**A:** paracetamol (PO) 15mg/kg 4-8hourly as needed

**OR**

**A:** ibuprofen (PO) 200 mg to 400mg 4-8hourly as needed.

For Children  $\geq$  6 months:

**A:** ibuprofen (PO) 5mg to 10mg/kg 4-8hourly as needed

**OR**

**C:** diclofenac (PO) 50 mg 4 to 4-8hourly as needed. **THEN** 75 mg (IM) 4-8hourly as needed

**OR**

**C:** diclofenac+ paracetamol (FDC) (PO) 50mg diclofenac and 500mg paracetamol 4-8hourly as needed

#### Surgical management

- Incision and drainage of the abscess
- Excision of the sinus tract two to three weeks after incision and drainage i.e. when the sinus tract is dry.

## **15.2 Trauma of the Pinna**

### **15.2.1 Hematoma of the Pinna**

#### **Clinical presentation**

- History of trauma
- Fluctuant, tender pinna swelling

#### **Pharmacological Treatment:**

**B:** ampicillin+cloxacillin (FDC) (PO) 500mg 8hourly for 7-10days

Children: **B:** ampicillin+cloxacillin (FDC) (PO) 15mg/kg 6hours for 7-14days

**OR**

**B:** azithromycin (PO) 500mg 24hourly for 3days.

For Children:

**B:** ampicillin+cloxacillin (FDC) (PO) 10mg/kg 24hourly for 3days

**AND**

**A:** paracetamol (PO) 500mg to 1g 4-8hourly as needed.

For Children ≤ 10kg:

**A:** paracetamol (PO) 10mg/kg 4-8hourly as needed

For Children > 10kg:

**A:** paracetamol (PO) 15mg/kg 4-8 hourly as needed

**OR**

**C:** ibuprofen (PO) 200 mg to 400mg 4-8hourly as needed.

For Children ≥ 6 months:

**C:** ibuprofen (PO) 5mg to 10mg/kg 4-8hourly as needed

#### **Surgical management**

- Incision and evacuation of hematoma
- Tight wound dressing to prevent re-accumulation of hematoma

## **15.2.2 Laceration of the Pinna**

Lacerative trauma of the pinna with tear of skin and cartilage through and through.

#### **Non-pharmacological management**

- Skin to skin stitching of the wound, **avoid through and through stitching** this may compromise blood supply to the cartilage.

#### **Pharmacological management**

**B:** ampicillin+cloxacillin (PO) 500mg 8 hourly for 10 -14 days

For Children:

**B:** ampicillin+cloxacillin (PO) 15mg/kg 6hourly for 7 -14day

**AND**

**A:** paracetamol (PO) 500mg to 1g 4-8hourly as needed

For Children ≤ 10kg:

**A:** paracetamol (PO) 10mg/kg 4-8hourly as needed

For Children >

**A:** paracetamol (PO) 10kg: 15mg/kg 4-8hourly as needed

**OR**

**A:** ibuprofen (PO) 200mg to 400mg 4-8hourly as needed

For Children ≥ 6 months:

**A:** ibuprofen (PO) 5mg to 10mg/kg 4-8hourly as needed.

**OR**

**C:** diclofenac+ paracetamol (PO) 50mg diclofenac and 500mg paracetamol 4-8hourly as needed

## **15.2.3 Ear Keloid**

This is abnormal proliferation of scar tissue that forms at the site of cutaneous injury and grows beyond the original margins of the scar. Most common causes are ear piercing, trauma or surgical incisions.

### **Clinical presentation**

- Swelling of the involved area of the ear, most commonly ear lobe

### **Non-pharmacological management**

- Use of pressure therapy e.g. pressure clips

### **Pharmacological management- Intra-lesional steroid injection**

D: betamethasone (Intra-lesional) 6-12mg depending on the size of the lesion weekly for 4 weeks before excision and 4weeks after excision

**OR**

D: triamcinolone acetonide (Intra-lesional) 40mg depending on the size of the lesion weekly for 4weeks before excision and 4weeks after excision

### **Surgical management**

- Total keloidectomy+-Steroid injection. (SHOULD BE DONE BY SOMEONE WITH EXPERTISE)

### **15.2.4 Cerumen Impaction**

Usually occurs following the use of cotton buds which hinder the natural movement of cerumen outwards

#### **Clinical presentation**

- Reduced hearing
- Ear pain
- Ear fullness
- Itching
- Tinnitus

#### **Pharmacological management**

A: hydrogen peroxide 3% ear drops 2-4drops each ear 6-8hourly for 7days.

#### **Non-pharmacological Treatment:**

- Remove using cerumen hook, syringing or suctioning under direct vision

#### **Note**

Patient should be educated on cleansing mechanism of the ear and not to use cotton bud.

### **15.2.5 Foreign Body in the Ear**

Usually happens in children. Common foreign bodies include beads, stones and seeds (bean, maize, orange). In adult's foreign bodies include cotton bud and insect

#### **Non-pharmacological Treatment:**

- Restrain the child
- Remove using a cerumen hook under direct vision (if the child cannot be restrained, sedation is advised)
- An insect should be killed (by soaking the ear canal with normal saline or spirit) before removal

#### **Note**

Do not attempt to remove ear foreign body if you don't have proper instruments and expertise.

### **15.2.6 Traumatic Tympanic Membrane/ Ear Drum Perforation.**

#### **Clinical presentation**

- History of trauma direct or indirect
- Ear bleeding +/- discharge
- Ear pain/otalgia

#### **Non-pharmacological Treatment**

- For indirect trauma avoid ear drops and water in the ear
- For direct trauma aural toilet can be done then ear drops instilled

## **Pharmacological management**

**A:** hydrogen peroxide 3% ear drops 2-4drops each ear 6-8hourly for 7days

**AND**

**A:** ciprofloxacin ear drops, 2-4drops each ear 6-8hourly for 14days

**AND**

**A:** ciprofloxacin (PO) 500mg Adults and children above 12years 12hourly for 5-7days

**OR**

**C:** ciprofloxacin (IV) 400mg 12hourly for 5-7days then for 5-7days

**AND**

**A:** paracetamol (PO) 500mg to 1g 4-8 hourly as needed.

For Children  $\leq$  10kg:

**A:** paracetamol (PO) 10mg/kg 4-8 hourly as needed.

For Children  $>$  10kg:

**A:** paracetamol (PO) 15mg/kg 4-8 hourly as needed

**OR**

**A:** ibuprofen (PO) 200 mg to 400mg 4-hourly as needed.

For Children  $\geq$  6 months:

**A:** ibuprofen (PO) 5mg to 10mg/kg 4-8 hourly as needed

**OR**

**C:** diclofenac+paracetamol (PO) 50mg diclofenac and 500mg paracetamol 4-8hourly as needed

## **15.3 Otitis Media (Acute or Chronic)**

It is an inflammation of the middle ear cavity. It is considered acute when the inflammation is of less than 2 weeks' duration, and chronic when the inflammation is of more than 2 weeks' duration with tympanic membrane perforation.

### **Clinical presentation**

- Examine the pinna
- Using an otoscope carefully examine the external auditory canal and the tympanic membrane

### **15.3.1 Acute Otitis Media**

#### **Clinical presentation**

- Previous upper respiratory tract infection
- Painful ear
- Restlessness
- Fever
- Hearing often reduced
- Inflamed, bulged tympanic membrane

#### **Non-pharmacological Treatment:**

- Acute otitis media should be treated with analgesics, antibiotics and/or paracentesis/ (Myringotomy) to reduce pain and to obtain pus for culture and sensitivity)

#### **Pharmacological Treatment:**

**B:** amoxicillin+clavulanic acid (PO) 375–625mg 12hourly for 10days

**OR**

**A:** azithromycin (PO) 500mg 24 hourly for 5days (for patients who are allergic to penicillin) For Children

**A:** azithromycin (PO) 10mg/kg 24hourly for 5days

**OR**

**B:** ceftriaxone (IV) 1 to 2 g 12hourly for 10days.

For Children:

**B:** ceftriaxone (IV) 50 to 100mg/kg 24hourly for 10days

**OR**

**C:** clarithromycin (PO) 500mg 12hourly for 10-14days.

For Children  $\geq$  6 months:

**C:** clarithromycin (PO) 15mg/kg/day in 2divided doses for 10-14days

**OR**

**S:** cefixime (PO) 400mg 24hourly for 10-4days

For Children ≥ 6 months to 12 years (weight below 45kg):

**S:** cefixime (PO) 8mg/kg 24hourly for 10-14days

**AND**

**A:** paracetamol (PO) 500mg to 1g 4-8hourly for 3days.

For Children ≤ 10kg:

**A:** paracetamol (PO) 10mg/kg 4-8hourly for 3days

For Children >10kg:

**A:** paracetamol (PO) 15mg/kg 4-8 hourly for 3days.

**OR**

**A:** ibuprofen (PO) 200mg to 400mg 4-8hourly as needed.

For Children ≥ 6 months:

**A:** ibuprofen (PO) 5mg to 10mg/kg 4-8hourly as needed

**OR**

**C:** diclofenac+ paracetamol (PO) 50mg diclofenac and 500mg paracetamol 4-8hourly as needed

**Note:** For antibiotics, treatment periods shorter than 10 days increase the risk of treatment failure

### **Referral**

- Children with high fever, severe ear pain, headache, altered state of consciousness
- A chronically discharging ear that persists in spite of proper treatment.
- Foul smelling ear discharge
- Mastoiditis
- Otitis in the normal (or better hearing) ear combined with permanent hearing loss in the other ear

### **15.3.2 Chronic Suppurative Otitis Media**

This is a perforated tympanic membrane with persistent drainage from the middle ear for more than 2-6 weeks. Most common causative organisms are *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus* species, *Klebsiella pneumonia*, and diphtheroids.

#### **Clinical presentation**

- Discharge of pus from the ear
- Perforated tympanic membrane
- Reduced hearing

#### **Non-pharmacological Treatment:**

- Keep ear dry/avoid water into the ear
- Aural toilet – ear suctioning under direct vision(otomicroscopy/endoscopy), removal of debris
- Ear wicking regularly, with a dry cotton wick at home

#### **Pharmacological Treatment**

**C:** ciprofloxacin ear drops, three drops 12hourly for 14days

**A:** hydrogen peroxide 3% ear drops: 2 to 4 drops each ear 6-8hourly for 14days

**OR**

**A:** boric acid ear drops: 2-4 drops each ear 6-8hourly for 14days

**OR**

**D:** ofloxacin ear drops: 2 to 4 drops each ear 6-8hourly for 14days

**AND**

**A:** ciprofloxacin (PO) 500mg 12hourly for 10days

For Children:

**A:** ciprofloxacin (PO) 10–20mg/kg 12hourly for 10days

#### **Surgical management**

- Mastoidectomy
- Endoscopic tympanoplasty
- Tympano-mastoidectomy
- Ossiculoplasty

**Note**

Treatment of shorter than 10 days will result into treatment failure

Avoid ototoxic drugs(gentamycin , neomycin and quinine) if there is TM perforation

### **15.3.3 Mastoditis with Sub-Periosteal Abscess**

It is due to infection of the mastoid air cells in the middle ear, a complication of chronic suppurative otitis media. It presents as a fluctuant painful swelling on the post auricular area. The overlying skin is also inflamed.

#### **Non-pharmacological Treatment**

Aspirate the swelling before incision and drainage, and then refer for mastoidectomy at a zonal/national hospital

#### **Pharmacological Treatment:**

**C:** ciprofloxacin ear drops, 3drops, 12hourly for 14days

**AND**

**A:** ciprofloxacin (PO) 500mg 12hourly for 10days; Children 10–20mg/kg 12hourly for 10days

#### **Investigations**

- Culture &sensitivity
- CT SCAN-Temporal Bone

#### **Surgical management**

- Incision and drainage
- Mastoidectomy/Drainage
- mastoidectomy
- Tympano-mastoidectomy
- Ossiculoplasty

**Note**

Treatment shorter than 10days will result into treatment failure

### **15.3.4 Otitis Media with Effusion**

It is a multifactorial, inflammatory condition in the middle ear with serous or mucous accumulation without ear discharge. It is a residual condition after acute otitis media and rhino sinusitis with Eustachian tube dysfunction.

#### **Diagnostic Criteria**

It is often discovered by chance.

- Little or no ear pain
- Gradual loss of hearing
- No ear discharge
- Aural fullness

#### **Non-pharmacological Treatment**

- Close follow-up
- Valsava maneuver
- Encourage chewing

#### **Pharmacological Treatment**

**D:** fluticasone propionate (50mcg/spray) nasal spray. Adults and adolescents more than 12years: 2sprays in each nostril 24hourly as needed. Children 4-1years: 1spray in each nostril 24hourly as needed.

**OR**

**S:** mometasone (nasal spray) Adults and adolescents from 12years: 1 sprays in each nostril 24hourly as needed. Children 6-11years: 1spray in each nostril 24hourly as needed

**AND**

**B:** ephedrine (0.5% and 1%) nasal drop, Adults and children above 12years: Instill 1 to 2 drops in each nostril, not more than 4 times a day for 3 to 5 days

**Note**

Otitis media with effusion with hearing loss that does not improve after 3months should be referred to a specialist for myringotomy and grommets insertion

**Surgical management**

Myringotomy+grommet insertion (microscopic/endoscopic) +Adenotonsilectomy (In children)

**15.4 Hearing Loss**

A child with hearing loss should be detected and intervention started immediately after delivery. New born hearing screening is done using an otoacoustic emission machine. Any child suspected of hearing loss (usually presenting with delayed speech development) should be referred to a zonal/national hospital immediately since early intervention has a better outcome.

**15.4.1 Sensorineural Hearing Loss (SNHL)**

Loss of hearing that results from defective function of cochlea or auditory pathway. It may be congenital or acquired.

**Clinical presentation**

- Hearing impairment as confirmed by hearing assessment tests.

**Investigation**

- Distraction Test/Free Field Test – for children
- Tympanometry
- Audiometry
- Otoacoustic emission(OAE)
- Auditory Brainstem Response (ABR)
- CT-Scan/MRI for bone cochlea and auditory nerve assessment for pre cochlea implantation

**Non-pharmacological management (Rehabilitation)**

- Avoiding exposure to noises
- Avoiding unnecessary use of ototoxic drugs
- Digital programmable hearing aid-for mild to moderate SNHL
- Super power digital programmable hearing aid-for severe and profound SNHL
- Bone-anchored hearing Aid(BAHA)
- Cochlea Implantation (C.I), with interval programming/troubleshooting –for severe and profound SNHL.
- Speech therapy
- Sign language/lip reading

**Pharmacological management**

**C:** calcium +vitamins 1tablets 24hourly for not less than 3months

**Surgical management**

Posterior tympanotomy for cochlear implantation

**15.4.2 Sudden Sensorineural Hearing Loss****Clinical presentation**

- Sudden onset of hearing loss 24-72 hours from onset, unilateral or bilateral.
- Tinnitus

**Investigations**

- Tympanometry
- Audiometry

**Pharmacological management**

**A:** prednisolone (PO) 60mg 24hourly for 5days then taper down to 50mg 24hourly for next 5days.

For Children:

**A:** prednisolone (PO) 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

**AND**

**C:** calcium and vitamins 1tablet 24hourly for not less than 3months

### **15.4.3 Otosclerosis**

Otosclerosis is a bony overgrowth that involves the footplate of the stapes. As the overgrowth develops, the stapes can no longer function as a piston, it becomes fixated. Conduction gradually becomes worse until a maximal conductive hearing loss of 60 dB is reached.

#### **Clinical presentation**

- Hearing loss
- Dizziness
- Tinnitus

#### **Investigations**

- Tympanometry
- Pure tone Audiometry (PTA)
- CT- Scan of temporal bone

#### **Non-pharmacological management**

- Hearing aids (H/A)-Digital Programmable Hearing Aids
- Cochlea implantation

#### **Surgical management**

- Stapedectomy
- Posterior tympanotomy for Cochlea Implantation

### **15.4.4 Peripheral Vertigo (Meniere's disease and Benign Paroxysmal Positional Vertigo(BPPV))**

#### **Clinical presentation**

<b>Meniere's disease</b>	<b>Benign Paroxysmal Positional Vertigo( PPPV)</b>
Vertigo	Vertigo
Nausea	Nausea
Vomiting	Vomiting
Tinnitus	Directional specificity
Aural Fullness	
Reduced Hearing	
Reduced Hearing	

#### **Investigation**

- Audiometry
- Vestibular test
- Video nystagmogram (vNG)
- Video head impulse test (vHIT)
- MRI Brain-to rule out cerebellopontine angle (**CPA**) tumours

#### **Non-pharmacological management (FOR BPPV)**

- Epley maneuver
- Berbucure maneuver
- Vestibular rehabilitation therapy
- Stabilometer

#### **Pharmacological management (FOR MENIERES)**

**C:** betahistidine (PO) 24-48mg 1 hourly for 14days. Maintenance dose 24mg 24hourly for 14days.

**AND**

**B:** intratympanic dexamethasone (IV) 4mg

**AND**

**C:** acetazolamide (PO) 250mg 24hourly for 14days

### **15.4.5 Vestibular Neuritis /Vestibular Neuronitis and Labyrinthitis**

#### **Clinical presentation**

- Rapid onset severe vertigo, nausea, vomiting
- Spontaneous vestibular nystagmus

- Gait instability

### **Pharmacological management**

**A:** prednisolone (PO) 60mg 24hourly for 5days then taper down to 50mg 24hourly for next 5days.

For Children:

**A:** prednisolone (PO) 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

**OR**

**D:** methylprednisolone (IV) 100mg 24hourly then taper to 10mg over 3weeks.

### **15.4.6 Vestibular Migraine**

#### **Clinical presentation**

- Dizziness/Vertigo
- Moderate to severe temporal headache
- Sensory amplification e.g. hyperacusis

#### **Investigations**

- Audiometry
- Vestibular test
- Video nystagmogram(vNG)
- Video head impulse test(vHIT)
- MRI Brain-to rule out cerebellopontine angle (**CPA**)tumours

### **Pharmacological management**

**A:** propranolol (PO) 40mg 12hourly for 14days

**OR**

**C:** amlodipine (PO) 10mg 24hourly for 14days

### **15.4.7 Tinnitus**

#### **Clinical presentation**

- Perception of sound in proximity to the head in the absence of an external source

#### **Non-pharmacological management**

- Tinnitus masking

### **Pharmacological management**

**C:** betahistidine (PO) 16-24mg 8hourly for 14days

For Children 5-12 years:

**C:** acetazolamide (PO) 250mg 24hourly 14days

### **15.4.8 Glomus Tumours**

Paragangliomas are rare neuroendocrine tumors that arise from the extra-adrenal autonomic paranganglia, small organs consisting mainly of neuroendocrine cells that are derived from the embryonic neural crest and have the ability to secrete catecholamines

#### **Clinical presentation**

- Neck mass (at angle of mandible)
- Pulsatile tinnitus
- Hearing loss(conductive)
- Rising sun signs

#### **Investigations**

- Audiometry
- CT-Scan-head & neck
- CT-angiogram
- MRI-neck

## **Surgical management**

- Glomus Tumour excision

### **15.4.9 Vestibular Schwannomas**

Also known as acoustic neuromas, acoustic schwannomas, acoustic neurinomas, or vestibular neurilemmomas) are Schwann cell-derived tumors that commonly arise from the vestibular portion of the eighth cranial nerve.

#### **Clinical presentation**

- Hearing loss
- Tinnitus

#### **Investigations**

- Audiometry
- MRI-brain (with gadolinium as contrast)

#### **Non-pharmacological management**

- Observation/watchful waiting
- Radiotherapy

#### **Surgical management**

- Tumour (schwanoma) excision

## **15.5 Nose/Paranasal Sinuses Conditions**

### **15.5.1 Acute Rhinitis**

It is a viral inflammatory condition in the nasal mucous membrane, usually part of a more widespread infection of the upper respiratory tract.

#### **Non-pharmacological Treatment**

- Bed rest& warm drinks

#### **Pharmacological Treatment**

**A:** ephedrine nasal drops (1% for adults and 0.5% for children) 1–2drops into each nostril 6hourly for not more than 5days

### **15.5.2 Acute Non-Allergic Rhinitis**

#### **Clinical presentation**

- Nasal blockage
- Post nasal drip
- Erythematous turbinate

#### **Pharmacological management**

**B:** ephedrine (0.5% and 1%) nasal drop, Adults and children above 12years: Instill 1-2drops in each nostril, not more than 4times a day for 3-5days

#### **OR**

**C:** oxymetazoline (0.05%) nasal drops/spray Dosage for adults and children above 6years: Instill 2 -3drops or sprays in each nostril 12hourly for 3-5days

#### **AND**

**D:** fluticasone propionate (50mcg/spray) nasal spray, Adults and adolescents more than 12years: 2sprays in each nostril 24 hourly as needed. children 4-11years: 1 spray in each nostril 24hourly as needed

#### **OR**

**S:** mometasone nasal spray, Adults and adolescents from 12years: 1sprays in each nostril 24hourly as needed, children 6-11 years: 1spray in each nostril 24hourly as needed

**A:** prednisolone (PO), Adults: 60mg 24hourly for 5days then taper down to 50mg 24hourly for next 5days. Children: 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

**Note**

Oral drugs to reduce swelling of the mucous membrane, antihistamines and antibiotics are not indicated

### 15.5.3 Allergic Rhinitis

It is an irritation of the nasal mucosa by an allergen in a previously sensitized individual. Common allergens include house dust (mite's feaces), pollens, cockroach antigen, animal dander, molds (in-door)

**Clinical presentation**

- Itchy nostrils, throat, eyes
- Watery nasal discharge
- Nasal congestion
- Sneezing
- Post nasal drip
- Cough

**Investigations:**

- Anterior rhinoscopy – watery nasal discharge, nasal congestion
- Total or specific IgE
- Skin prick Allergy test

**Non-pharmacological management**

- The main treatment of allergic rhinitis is the Avoidance of the triggers.
- Steaming
- Immunotherapy

**Pharmacological Treatment:**

**A:** ephedrine (0.5% and 1%) nasal drop, Adults and children above 12years: Instill 1 to 2drops in each nostril, not more than 4 times a day for 3-5days

**OR**

**C:** oxymetazoline (0.5%) nasal drops/spray, Adults and children above 6 years: Instill 2- 3 drops or sprays in each nostril every after 12 hours for 3-5days

**AND**

**D:** fluticasone propionate (50mcg/spray) nasal spray, Adults and adolescents more than 12years: 2sprays in each nostril 24 hourly as needed. children 4-11years: 1spray in each nostril 24hourly as needed

**OR**

**S:** mometasone nasal spray, Adults and adolescents from 12years: 1 sprays in each nostril 24 hourly as needed. children 6 to 11 years: 1 spray in each nostril 24 hourly as needed.

**AND**

**A:** prednisolone (PO): 60mg 24hourly for 5days then taper down to 50mg 24 hourly for next 5days. Children: 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

**AND**

**C:** loratadine (PO), Adults: 10mg 24hourly for 30days. Children 2-6years: 5mg 24hourly for 14days. Children above 6 years: 10mg 24 hourly for 14 days

**OR**

**S:** desloratadine (PO)Adults: 5mg 24hourly for 30days. Children 2-5 years: 1.25mg 24hourly for 14days. Children 6 to 12 years: 2.5mg 24hourly for 30days

**AND**

**S:** montelukast, Adults: 10mg 24hourly for 30days.Children 1-15 years: 5mg 24hourly for 14days

### 15.6 Granulomatous Diseases of the Nose

#### 15.6.1 Rhinoscleroma

**Clinical presentation**

- Rhinitis, Fetid rhinorrhea
- Crusting, Nasal bleeds
- Intranasal rubbery nodules
- Dysphonia

- Fibrosis, Nasal deformity

#### **Non-pharmacological management**

- nasal douching with saline solution

#### **Pharmacological management**

**A:** ciprofloxacin (PO), Adults and children above 12years: 500mg 12hourly for 4-12weeks.

Continue treatment for at least 2days after signs and symptoms have disappeared.

**OR**

**S:** cefixime (PO), Adults: 400mg 24hourly for 4-12weeks. Children  $\geq$  6months to 12years (weight below 45kg): 8mg/kg 24hourly for 4-12weeks

**AND**

**A:** prednisolone (PO) Adults: 60mg 24hourly for 5days then taper down to 50mg 24hourly for next 5days. Children: 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

#### **Surgical management**

- Rhinoplasty

### **15.6.2 Tuberculosis of the Nose**

#### **Clinical presentation**

- Nasal pain
- Nasal bleeding
- Mass in the nose
- Nasal deformity

#### **Investigations**

- Nasal mucosal scraping for AFB/gene expert
- Skin biopsy for Histology and AFB

#### **Pharmacological management**

Refer TB Program

### **15.6.3 Syphilis of the Nose**

#### **Clinical presentation**

- Nasal discharge
- Nasal crusting
- Epistaxis
- Ulceration of nose
- Saddle nose

#### **Investigations**

VDRL

#### **Non-pharmacological management**

- Crusts Removal-Endoscopic

#### **Pharmacological management**

Refer STI chapter

### **15.6.4 Rhinosporidiosis**

Nasal disease caused by rhinosporidium seeberi

#### **Clinical presentation**

- Unilateral nasal obstruction
- Epistaxis
- Local pruritus
- Rhinorrhea
- Pink or deep red polyp, strawberry like appearance, Bleeds easily on manipulation

### **Pharmacological management**

**S:** dapsone (PO), Adults: 100mg 24hourly for 6months. Children 1-2mg/kg 24hourly, not to exceed 100mg 24hourly

### **Surgical management**

Wide excision with wide area electro-coagulation of the lesion base

## **15.6.5. Mucormycosis**

This is fungal infection of nose, caused by mucor, rhizopus species.

### **Clinical presentation**

- Fever, Headache
- Nasal congestion, Purulent nasal discharge
- Facial numbness
- Eshar of nasal mucosa
- Proptosis, Blindness

### **Pharmacological management**

**S:** amphotericin B (IV): Adults, Test dose of 1mg IV infused over 20-30 minutes. Loading dose of 0.25-0.5mg/kg infused over 2-6hours. Maintenance dose of 0.25-1mg/kg IV 24hourly for 3-6weeks. Dosage for children: Test dose of 0.1mg/kg not to exceed 1mg: infused over 20-60minutes. Loading dose of 0.25mg/kg infused over 2-6hours. Maintenance dose of 0.25/kg 24hourly to ensure a total dose of 30-40mg/kg is given over 3-6weeks

### **Surgical management**

Endoscopic debridement of the necrotic tissues under general Anastasia(GA)

#### **Note**

High index of suspicion in patient with DKA and nasal symptoms

## **15.7 Other Conditions of the Nose**

### **15.7.1 Nasal septal Abscess and Hematoma**

#### **Clinical presentation**

- Nasal pain
- Fever
- History of trauma for septal hematoma
- Nasal swelling
- Bilateral nasal blockage with boggy septal mass
- Aspiration will confirm the diagnosis

### **Pharmacological management**

**B:** ampicillin+cloxacillin (FDC) (PO) Adults: 500mg 8hourly for 10-14days. Children: 15mg/kg 6hourly for 7-14days

**OR**

**B:** amoxycillin+clavulanate (PO) Adults: 625mg to 1g 12hourly for 7-14days. Children ≤3 months: 30mg/kg/day in 2 divided doses for 7-14 days. Children >3 months: 25mg/kg/day in 2 divided doses for 7-14 days

**AND**

**A:** paracetamol (PO/IV), adults: 500mg to 1g 4-8hourly as needed. Children ≤10kg: 10mg/kg 4-8hourly as needed. Children >10kg: 15mg/kg 4 to 8hourly as needed.

**OR**

**A:** ibuprofen (PO) Adults: 200-400mg 4-8hourly as needed. Children ≥6 months: 5-10mg/kg 4-8hourly as needed

**OR**

**C:** diclofenac+ Paracetamol (PO) Adults: 50mg diclofenac and 500mg paracetamol 4-8hourly as needed

### **Surgical management**

- Intranasal Incision and drainage
- Tight bilateral nasal packing or Suturing of mucoperichondrial to prevent re-accumulation

### **15.7.2. Choanal Atresia**

This is failure of canalization of choanal OR is obliteration or blockage of the posterior nasal aperture.

It can be unilateral or bilateral. If bilateral it is surgical emergency.

### **Clinical presentation**

- New born presenting with cyanosis while at rest which improve on crying
- Thick nasal discharge on the defective nostril
- Failure to pass nasogastric tube
- Thread/cotton test

### **Investigation**

- CT-SCAN-Paranasal sinuses(PNS)

### **Non-pharmacological management**

- For bilateral choanal atresia put oropharyngeal airway then refer to specialized hospital.

### **Surgical management**

- Choanal atresia release (open or endoscopic)

### **15.7.3 Nasal Turbinate Hypertrophy**

Turbinate hypertrophy is a complication of allergic rhinitis

### **Clinical presentation**

- snoring
- Nasal obstruction
- Nasal irritation
- Enlarged inferior or middle turbinate on rhinoscopy

### **Pharmacological Management**

As for Allergic Rhinitis

### **Surgical management**

Partial submucosal Turbinectomy – (open or endoscopic)

### **15.7.4 Nasal Bone Fracture**

#### **Clinical presentation**

- History of nasal trauma
- Deviation of nose or septum
- Nasal bleeding
- Nasal obstruction

**Pharmacological management** (antibiotics & analgesics)-As for nasal septal abscess and hematoma

**Surgical Management**-Closed reduction and alignment of nasal structures under LA or GA this should be 1-2weeks if there is edema. Can be done using nasal speculum or endoscopically.

### **15.7.5 Nasal Septal Deviation (Non-Traumatic)**

#### **Clinical presentation**

- nasal obstruction
- nasal dryness
- +/\_ Nasal bleeding

## **Surgical management**

- Septoplasty –open or Endoscopic

### **15.7.6 Adenoid Hypertrophy**

It is hypertrophy of the lymphoid tissues in the nasopharynx; presenting with mouth breathing, snoring sleep apnea and otitis media with effusion. It is reported mainly in children.

**Investigations:** Nasopharynx lateral view X-ray.

#### **Pharmacological Treatment:**

**A:** cetirizine (PO) 10mg nocte for 2weeks. Children: 5mg nocte for 2weeks

**AND**

**A:** 0.9% sodium chloride nasal spray/drops 4hourly for 2weeks

**AND**

**B:** azithromycin (PO) 500mg 24hourly for 3days. Children: 10mg/kg 24 hourly for 3days

**OR**

**B:** amoxicillin+clavulanic acid (PO) (FDC) Adults: 625mg (500mg amoxicillin+125mg Clavulanic acid) 8hourly for 7days

Children: 375mg (250mg amoxicillin+ 125 Clavulanic acid) 12hourly for 7days;

**OR**

**S:** cefixime (PO) Adults: 400mg 24hourly for 7-14days. Children  $\geq$  6months to 12years (weight below 45kg): 8mg/kg 24hourly for 7-14days

**OR**

**C:** clarithromycin (PO), Adults: 500mg 12 hourly for 7-14days. Children  $\geq$  6months: 15mg/kg/day in 2divided doses for 7-14days

**AND**

**A:** paracetamol (PO) 1gm 8hourly until fever is controlled: Children 10mg/kg body weight 8hourly until fever is controlled.

## **Surgical management**

Adenotonsilectomy/Adenotomy+/-Myringotomy and Gromet insertion

#### **Note**

An adult with snoaring upper aerodigestive tumours and Obstructive Sleep Apnea (OSA)should be considered.

### **15.7.7 Acute Rhinosinusitis**

It is the inflammation of the mucosal lining of the nose and paranasal sinuses of not more than 12 weeks' duration. In sinusitis of dental origin, anaerobic bacteria are often found.

#### **Acute Purulent Rhinosinusitis**

Bacterial infection with pus accumulation in one or more of the paranasal sinuses

#### **Clinical presentation**

- Nasal discharge (watery or purulent)
- Nasal congestion
- Post nasal dripping
- Headache worsening on bending forward and more in the morning
- Fever
- Facial pain
- Ear pain and blockage
- Anterior rhinoscopy – watery/purulent nasal discharge occasionally foul smelling
- Nasal congestion
- Plain paranasal sinuses X ray (Water's, Caldwell views)
- Mucosal thickening; air fluid levels

#### **Pharmacological Treatment:**

**B:** azithromycin (PO) 500mg 24hourly for 3days. Children: 10mg/kg 24hourly for 3days

**OR**

**B:** amoxicillin+clavulanic acid (PO) 625mg 8hourly for 7days Children: 375mg 12hourly for 7days;

**OR**

**C:** clarithromycin (PO), 500mg 12hourly for 7-14days. Children  $\geq$  6 months: 15mg/kg/day in 2divided doses for 7-14days

**OR**

**B:** ceftriaxone (IV) Adults: 1-2 g12hourly for 7 days. Children: 50 to 100mg/kg once for 7days

**OR**

**S:** cefixime (PO) Adults: 400mg 24hourly for 7-14 days. Children  $\geq$  6 months to 12years (weight below 45kg): 8mg/kg 24hourly for 7-14days

**AND** (for fungal rhinosinusitis)

**D:** itraconazole (PO) Adults: 200mg 24hourly for 30days. Children: 50-100mg/kg once for 7days

**OR**

**S:** amphotericin B (IV) Adults: Test dose of 1mg IV infused over 20-30minutes. Loading dose of 0.25-0.5mg/kg IV infused over 2 to 6 hourly. Maintenance dose of 0.25-1mg/kg 24hourly for 3-6weeks for children: Test dose of 0.1mg/kg not to exceed 1mg: infused over 20-60minutes Loading dose of 0.25mg/kg infused over 2-6hours. Maintenance dose of 0.25/kg 24hourly to ensure a total dose of 30-40mg/kg is given over 3-6weeks

**AND**

**B:** ephedrine (0.5% and 1%) nasal drop, Adults and children above 12years: Instill 1 to 2drops in each nostril, not more than 4 times a day for 3 to 5days

**OR**

**S:** xylocaine (0.05% and 0.1%) nasal drops/spray, Adults and children above 6years: Instill 2 to 3drops in each nostril 8hourly for 3 to 5days or1 to 2sprays in each nostril 8hourly for 3 to 5days

**OR**

**D:** fluticasone propionate (50mcg/spray) nasal spray, Adults and adolescents more than 12years: 2sprays in each nostril 24hourly as needed. Children 4-11years: 1spray in each nostril 24hourly as needed

**OR**

**S:** mometasone nasal spray, Adults and adolescents from 12years: 1sprays in each nostril 24hourly as needed. Children 6-11years: 1spray in each nostril 24hourly as needed.

**AND**

**A:** paracetamol (PO) Adults: 500mg to 1g 4-8hourly as needed. Children  $\leq$  10kg: 10mg/kg 4-8hourly as needed. Children >10kg: 15mg/kg 4-8hourly as needed

**OR**

**A:** diclofenac (IM) Adults: 75mg 8hourly as needed

**OR**

**C:** diclofenac (PO) Adults: 50mg 4-8 hourly as needed

**OR**

**C:** ibuprofen (PO) Adults: 200-400mg 4-8 hourly as needed. Children  $\geq$  6 months: 5-10mg/kg 4-8hourly as needed

### **Non-pharmacological management**

- Saline nasal wash
- Steaming with or without Vicks

**Note:** Treatment periods shorter than ten days increase the risk of treatment failure

### **Referral:** To ENT Specialists

- Children with ethmoiditis presenting as an acute periorbital inflammation or orbital cellulitis must be hospitalized immediately (ophthalmology consultation should be sought)
- Adults with pronounced symptoms despite treatment
- If sinusitis of dental origin is suspected
- Recurrent sinusitis (>3 attacks in a year) or chronic sinusitis (duration of illness of >12 weeks)

## **Surgical management**

Surgery if associated with complications eg orbital/periorbital abscess, pottys puffy tumour, Brain abscess and nasal polyposis etc.

- Frontal Trephination
- Open ethmoidectomy
- Functional Endoscopic Sinus Surgery (FESS)

## **15.7.8 Chronic Rhinosinusitis**

Can be caused by Bacterial or Fungal

### **Clinical presentation**

- Anterior and/or posterior nasal mucopurulent drainage
- Nasal obstruction/nasal blockage/congestion
- Facial pain, pressure and/or fullness
- Hyposmia or Anosmia
- Halitosis

### **Investigations**

CT Scan of paranasal sinuses (PNS)-gold standard-should be done after adequate medical treatment with persistent symptoms.

### **Non-pharmacological management**

- Saline nasal wash
- Steaming with or without vicks

**Pharmacological Treatment:** as for acute sinusitis BUT should be for 4-6 weeks

**Surgical Management-**Surgery if associated with complications eg orbital/periorbital abscess, pottys puffy tumour, Brain abscess and nasal polyposis etc and Failure of disease resolution after adequate medical treatment.

Frontal Trephination

**OR**

Caldwell Luc operation

**OR**

Open ethmoidectomy

**OR**

Functional Endoscopic Sinus Surgery (FESS)

## **15.7.9 Nasal Polypsis**

This is mucosal change due to chronic mucosal inflammation. Ethmoidal polyp- This is a complication of allergic rhinitis or chronic rhinosinusitis. Antrochoanal polyp benign tumor of the maxillary sinus that prolapse to the nasal cavity.

### **Clinical presentation**

- History of allergy or asthma
- Nasal congestion/blockage
- Nasal discharge
- Snoaring and mouth breathing
- Post nasal dripping

## **Investigations**

- Direct nasal Endoscopy (DNE) or Fiber optic nasopharyngoscopy
- Serum Total/specific IgE
- CT-Scan of paranasal sinuses (CT-PNS)

## **Pharmacological Management**-As for allergic rhinitis/acute rhinosinusitis

### **Surgical management**

- i. Intranasal polypectomy
- ii. Partial/Medial maxillectomy
- iii. Functional Endoscopic Sinus surgery(FESS)

### **15.7.10 Nose Bleeding (Epistaxis)**

Nose bleeding is a condition which is common in adults. It may be due to a local cause in the nasal cavity (e.g. trauma, tumor, foreign body, septal varices, or septal deviation); or a systemic cause (e.g. blood disorders, vascular disorders, renal failure, hepatic failure, or use of anticoagulants (warfarin, heparin). Most cases of epistaxis are minor; do not require hospitalization. Patients with significant nose bleeding do require hospitalization.

### **Non-pharmacological Treatment**

- Stabilize the patient: put an open intravenous line, do blood grouping and cross matching
- Put the patient in a sitting position and advise the patient to pinch the soft part of the nose gently for 5minutes
- Put on a gown, glasses, head light and sterile gloves and evacuate clots.Do a thorough head and neck examination
- Cauterize septal varices (if any) using a silver nitrate pencil
- Do an anterior nasal packing by introducing into the nasal cavity as far posterior as possible sterile Vaseline gauzes (or iodine soaked gauzes if not available) or special merocele pack,using a dissecting forcep (if bayonet forcep is not available)
- Put rolled dry gauze on the columella and plaster it

If the patient is still bleeding

- Do a posterior nasal packing using a Foley's catheter introduced through the nasal cavity into the oropharynx, balloon it with normal saline up to 10–15cc while pulling it outward to impinge on the posterior nasal choana, then do anterior nasal packing as above
- Put dry gauze on the nose to prevent necrosis of the columella and fix the catheter on the nose with an umbilical clamp
- Almost all of the nasal bleedings will be controlled by this way

**Note:** Remove the packs after 72 hours

### **Pharmacological Treatment (to prevent rhinosinusitis)**

**B:** azithromycin (PO) 500mg 2 hourly for 3days. Children: 10mg/kg 24hourly for 3days  
**OR**

**B:** amoxicillin+ clavulanic acid (PO) Adults: 625mg 8hourly. Children: 375mg 12hourly for 7days

**AND**

**A:** paracetamol (PO) 1gm 8hourly until fever is controlled Children 10 mg/kg body weight 8 hourly until fever is controlled

**AND**

**A:** ephedrine (0.5% and 1%)nasal drops, Adults and children above 12 years: Instill 1 to 2drops in each nostril, not more than 4times a day for 3-5days

**OR**

**S:** xylometazoline (0.05% and 0.1%) nasal drops/spray. Adults and children above 6 years: Instill 2 to 3drops in each nostril 8hourly for 3 to 5days or 1 to 2sprays in each nostril 8hourly for 3 to 5days.

**AND**

**C:** tranexamic acid (PO/IM) Adults: 500mg 8hourly for 5 to 8days. Children: 25mg/kg 6 or 8hourly for 5-8days

**AND**

**C:** silver Nitrate Stick-Apply on the lesion once IF the bleeding area is identified.

**Note**

Putting an ice cube on the forehead, extending the neck or placing a cotton bud soaked with adrenaline in the vestibule will not help

**Referral:** refer the patient to the next facility with adequate expertise and facilities if:

- The patient is still bleeding repack and refer immediately
- Failure to manage the underlying cause, refer the patient

**Surgical management**

- Endoscopic electrical cauterization of the lesion for posterior nasal bleeding
- Ligation/Clipping/cauterization of bleeding vessel (open or endoscopic)

**Note**

Rule out systemic causes of epistaxis eg. renal, blood dyscrasias and liver failure.

### 15.7.11. Foreign Bodies in the Nose

This situation usually occurs in children.

**Non-pharmacological Treatment:**

- Restrain the child before removal using a cerumen hook, if the child cannot be restrained sedation is advised

**Note**

A unilateral foul smelling nasal discharge in a child is due to a foreign body until proven otherwise

## 15.8 Throat Conditions

### 15.8.1 Pharyngotonsilitis

Pharyngotonsilitis is an acute inflammation of the pharynx and tonsils, which is characterized by fever and a painful throat.

**Pharmacological Treatment**

**B:** azithromycin (PO) 500mg 24hourly for 3days. Children: 10mg/kg 24hourly for 3days

**OR**

**B:** amoxicillin+ clavulanic acid (PO)(FDC) Adults: 625mg 8hourly for 7days Children: 375mg 12hourly for 7days;

**OR**

**C:** clarithromycin (PO), Adults: 500mg 12hourly for 7-14days. Children  $\geq$  6 months: 15mg/kg/day in 2divided doses for 7-14days

**OR**

**S:** cefixime (PO) Adults: 400mg 24hourly for 7-14days. Children  $\geq$  6 months to 12 years (weight below 45kg): 8mg/kg 24hourly for 7-14days

**AND**

**A:** paracetamol (PO) Adult 1gm 10mg/ kg body weight 8 hourly until the fever is controlled

**OR**

**A:** ibuprofen (PO) Adults: 200-400mg 4-8hourly as needed. Children  $\geq$  6 months: 5-10mg/kg 4-8hourly as needed

**OR**

**A:** diclofenac (IM) Adults 75 mg 8hourly as needed

**OR**

**C:** diclofenac (PO) Adults: 50 mg 4-8hourly as needed

**OR**

**C:** diclofenac+ paracetamol (PO) (FDC) Adults: 50mg diclofenac and 500mg paracetamol 4-8hourly as needed

**Note**

Refer the patient with tonsillitis to the specialist for tonsillectomy if

- Chronic tonsillitis
- Recurrent tonsillitis (>5 attacks in a year or 3 or more attacks in 2 consecutive years)
- Obstructive tonsillitis (causing an upper airway obstruction)

**Surgical management**

- Tonsillectomy

**15.8.2 Laryngitis**

This is an infectious or non-infectious, acute or chronic inflammatory condition of the larynx. It becomes chronic when the condition lasts for more than 3 weeks. The picture of the disease is different in children and adults due to the small size of the larynx in children.

- Acute subglottic laryngitis occurs mainly in children under the age of seven, it is a viral infection
- Edema of the mucous membrane of the subglottic space causes breathing difficulties, especially on inspiration
- Laryngitis in children may require active treatment

**15.8.3 Acute Laryngitis**

Acute subglottic laryngitis occurs mainly in children under the age of seven, it is a viral infection.

**Non-pharmacological Treatment**

- Parents should behave calmly and avoid frightening the child
- Bed rest
- Keep the air damp and cool
- Give extra fluid

**Pharmacological Treatment**

**A:** adrenaline inhalation/nebulization effectively reduces symptoms

**Table 15.1: Doses of adrenaline Preparation**

Age	adrenaline(20 mg/ml)	0.9% Saline
0-6 months	0.1 ml	2 ml
6-12 months	0.15 ml	2 ml
>12	0.2 ml	2 ml

**Note**

The total fluid volume is inhaled in 5 minutes with the use of inhalator

**AND**

**A:** prednisolone (PO) Adults: 60mg 24hourly for 5days then taper down to 50mg 24hourly for next 5days. Children: 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

**OR**

**A:** hydrocortisone (IV/IM) Adults and children  $\geq$  12years: 100-500mg/dose IV/IM 4hourly as needed. Children <12 years: 1-5mg/kg/day IV/IM divided 12hourly as needed

**AND**

**B:** amoxycillin + clavulanate (PO) (FDC) Adults: 625mg to 1g 12 hourly for 7-14 days. Children  $\leq$  3 months: 30mg/kg/day in 2divided doses for 7-14days. Children >3 months: 25mg/kg/day in 2 divided doses for 7-14days

**AND**

**A:** cough suppressant Syrups-Dosage for adults: as instructed by a physician or pharmacist.

**Hospitalization**

If severe symptoms persist or worsen after epinephrine inhalation, hospitalization is indicated.

## **15.8.4 Chronic Laryngitis**

### **Non-pharmacological Treatment:**

- Voice rest
- Stop smoking
- Rehydration
- Refer to specialist for Rigid laryngoscopy (Endoscopy) OR Fiber optic Nasolaryngoscopy

## **15.8.5 Acute Epiglottitis (AE)**

Epiglottitis is an acute infectious inflammation of the epiglottis, supraglottic and hypopharynx which occurs both in children and adults. It is commonly caused by *Haemophilus influenzae*. Epiglottitis is a potentially lethal condition especially in children. Edema of the epiglottis may cause acute airway obstruction.

### **Clinical presentation**

- Throat pain and difficulty in swallowing
- Drooling
- Husky voice
- Fever often high and with chills
- Patient prefers sitting posture with an extended neck
- Laborious inspiration
- Cough in some cases
- Anxiety

**Investigations:** Plain X-ray of the neck, lateral view characteristically presents with a positive thumb sign (edematous epiglottis).

### **Non-pharmacological Treatment:**

- Immediate hospitalization, preferably in the ICU
- Transportation: sitting, with oxygen supplementation
- Be prepared to treat respiratory failure (intubation or tracheotomy)

### **Pharmacological Treatment**

**B:** azithromycin (PO) 500mg 24hourly for 3days. Children: 10mg/kg 24hourly for 3days

**OR**

**B:** amoxicillin+ clavulanic acid (PO)(FDC) Adults: 625mg 8hourly Children: 375mg 12hourly for 7days;

**AND**

**A:** paracetamol (PO) 1gm 8hourly until fever is controlled. Children: 10 mg/kg body weight 8hourly

## **15.8.6 Non-infectious Chronic Laryngitis**

[Laryngopharyngeal reflux disease (LPR) with Vocal cord nodules or Laryngeal polyp]

### **Clinical presentation**

- Dysphonia or hoarseness
- Dry Cough
- Globus sensation, Frequent throat clearing
- Dysphagia

**Investigations -** Rigid laryngoscopy (Endoscopy) OR Fiber optic Nasolaryngoscopy

### **Non-pharmacological Treatment**

- Dietary modification, spice foods and feeding times
- Life style changes; avoid alcohol, tobacco
- Voice rest

### **Pharmacological Treatment**

**C:** pantoprazole (PO) Adults: 40mg 24hourly for 8-12 weeks

Children  $\geq$  5 year:

**C:** pantoprazole (PO) 20mg 24hourly for 8-12 weeks

For <40kg

**C:** pantoprazole (PO) 20mg 24hourly for 8-12 weeks

For >40kg

**C:** pantoprazole (PO) 40mg 24hourly for 8-12 weeks

**OR**

**C:** Lansoprazole (PO) Adult 30mg. Paediatric ≥ 1 to 12years: <30kg 15mg;>30kg give 30mg 24hourly for 8 – 12 weeks.

**OR**

**S:** esomeprazole (PO) Adult 40mg. Paediatric ≥ 1 to 12 years 10-20mg. Paediatric >12 years 20-40mg 24 hourly for 8-12weeks.

**C:** antacid liquid/mixture10-15mls 12hourly for 10-14days.

**AND**

**A:** prednisolone (PO): Adult 60mg 24hourly for 5days then taper down to 50mg 24hourly for next 5days.

For Children:

**A:** prednisolone (PO): 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

**OR**

**D:** triamcinolone acetonide. Adult (IM) 40-80mg stat. Children 6-12years: 0.2mg/kg stat

**AND**

**C:** loratadine (PO) Adults: 10mg 24hourly for 14days. Children 2-6years: 5mg 24hourly for 14days. Children above 6years: 10mg 24 hourly for 14days

**OR**

**S:** desloratadine (PO) Adults: 5mg 24hourly for 14days. Children 2-5years: 1.25mg 24hourly for 14days. Children 6-12 years: 2.5mg 24hourly for 14days

**Surgical management**

Direct laryngoscopy+microlaryngeal surgery (D/Scopy+MLS) to remove polyp or cyst-using microscope or Endoscope with microdebrider/shaver

**15.8.7 Recurrent Respiratory Papillomatosis (Laryngeal Papillomas)**

It is the commonest benign laryngeal tumor of the larynx caused by Human papilloma virus (HPV), occurring in both children and adults. It has a higher recurrence rate in children than in adults, among adults it may turn into a malignancy.

**Clinical presentation**

- Hoarse voice, audible respiration (inspiratory stridor)
- Progressive difficulty in breathing
- Progressive inspiratory stridor
- On and off cough

**Investigations**

- Perform a thorough respiratory system examination
- Indirect laryngoscopy for papilloma croups on the larynx
- Rigid laryngoscopy (Endoscopy) OR Fiber optic Nasolaryngoscopy

**Non-pharmacological Treatment**

- If in distress, perform a tracheostomy first then refer

**Referral:** Refer the patient to the next facility with adequate expertise and facilities

**Surgical management**

- Tracheostomy if there is upper airway obstruction
- Direct Laryngoscopy under GA+microlaryngeal surgery(D/Scopy+MLS)
- D/Scopy+microdebridment

**15.8.8. Foreign Bodies in the Throat**

If the foreign body is suspected to be in the hypopharynx, esophagus, trachea or bronchus

- Take a thorough history and do a thorough physical examination
- Do chest X ray to confirm your diagnosis (though some foreign bodies are radiolucent)
- Refer to a next level hospital with facility for removal

### **Surgical management**

- Oesophagoscopy for oesophageal foreign body(FB)
- Bronchoscopy for airway FB

### **15.8.9 Subglottic Hemangioma**

Congenital subglottic hemangiomas are vascular lesions that undergo a phase of rapid growth that is initiated during the first few weeks to months of life. They may present as solitary lesions or as part of a segmental hemangioma syndrome.

#### **Clinical presentation**

- Hoarseness of voice
- Inspiratory stridor
- Cough
- Cyanosis
- Concomitant cervical facial hemangioma

#### **Pharmacological management**

**A:** prednisolone (PO) Children: 1mg/kg 24hourly for 5days then taper down by half for the next 5days.

#### **AND**

**A:** propranolol (PO) for children: Starting dose of 0.6mg/kg 12hourly for 1week, then increase dose to 1.1mg/kg 12hourly for 2weeks; then Maintenance dose 1.7mg/kg 12hourly for at least 6months.

**Surgical Management-Tracheostomy-** if severe inspiratory stridor is present.

### **15.8.9 Laryngomalacia**

This is the most common congenital anomaly of the larynx, characterized by partial or complete collapse of supraglottic structures on inspiration. This is the most common cause of noisy breathing in infancy. Gastroesophageal reflux disease (GERD) has been implicated.

#### **Clinical presentation**

- Inspiratory stridor relieved by lying prone
- Difficult breathing/dyspnoea
- Difficult feeding
- Choking on feeding

#### **Investigations**

- Fiber optic nasolaryngoscopy
- Microlaryngoscopy and bronchoscopy

#### **Non-pharmacological management**

- Sleep prone rather than supine
- Feeding modification
- Close observation of upper respiratory tract infections

#### **Pharmacological management**

For children 1-12years

**S:** esomeprazole (PO) 10-20mg 24hourly

For children >12years give

**S:** esomeprazole (PO) 20 - 40mg 24hourly

#### **Surgical management**

- Supraglottoplasty
- Tracheostomy for severe cases

### **15.8.10 Vocal Cords Paralysis**

It is due to total interruption of nerve impulse resulting in no movement of laryngeal muscles. Vocal cord paralysis is a sign of disease and not a diagnosis by itself, vocal cord paralysis can be unilateral or bilateral.

#### **Clinical presentation**

- Change in voice/hoarseness (for unilateral vocal cord paralysis)
- Vocal fatigue
- Dyspnoea/upper airway obstruction
- Stridor
- Cough and aspiration
- History of neck surgery(thyroidectomy)
- Neck or mediastinal tumors

#### **Investigation**

- Fiber optic nasolaryngoscopy
- Video stroboscopy

#### **Non-pharmacological management**

- Speech therapy

**Surgical management:** depends on the severity and desired outcome.

- Tracheostomy
- Arytenoidectomy
- Vocal cord lateralisation through endoscopy
- Cordectomy
- Thyroplasty type i& ii
- Injection of Teflon paste
- Muscle or cartilage implant

### **15.8.11 Infection of Thyroglossal Duct Cyst, Dermoid Cyst, Branchial Cleft Cysts**

#### **Clinical presentation**

- For Thyroglossal cyst- Midline upper neck mass which is cystic just below the hyoid bone. If infected my present with tenderness. My also present as discharging sinus
- For branchial cleft cysts mass or discharging sinus along the anterior border of the sternocleidomastoid muscle.

#### **Investigation**

- Neck USS

#### **Pharmacological management**

**B:** ampicillin+cloxacillin (PO) Adult 500mg. Paediatric 15mg/kg 6-8hourly for 10-14days.

**AND**

**B:** cephalaxin (PO) Adult 500mg 8hourly. Paediatric 75-100mg/kg/day divided in 4doses for 7-14days

**OR**

**B:** amoxycillin + clavulanate (PO): 625mg to 1g 12hourly for 7-14days.

For Children ≤3 months:

**B:** amoxycillin + clavulanate (PO) 30mg/kg/day in 2divided doses for 7-14days.

For Children >3 months:

**B:** amoxycillin + clavulanate (PO) 25mg/kg/day in 2divided doses for 7- 14days

#### **Surgical management**

- Thyroglossal duct cyst excision (Sistrunk procedure)
- Branchial cyst/fistula excision

## 15.8.12 Deep Neck Spaces Infections

### Clinical presentation

- Truisms
- Induration and swelling below the angle of mandible
- Medial bulging of the pharyngeal wall
- Difficult swallowing (dysphagia/odynophagia)
- Difficult breathing
- Neck stiffness/torticollis
- Neck swelling, mass, or lymphadenopathy
- Systemic toxicity with fever and rigors

### Pharmacological management

**B:** azithromycin (PO) Adult 500mg 24hourly. Paediatric  $\geq$  6 months 10mg/kg/day for 2 to 5 days

**OR**

**A:** metronidazole (PO) 400mg 8hourly for 7-14day. Children: 7.5-15mg/kg 8 hourly for 20–30days

**OR**

**B:** metronidazole (IV) 500mg 8hourly. Children: 7.5-15mg/kg 8 hourly for 7-14days

**OR**

**B:** amoxycillin + clavulanate (PO) 625mg to 1g 12hourly for 7- 14days

For Children  $\leq$  3 months:

**B:** amoxycillin + clavulanate (PO) 30mg/kg/day in 2divided doses for 7-14days.

For Children  $>3$  months:

**B:** amoxycillin + clavulanate (PO) 25mg/kg/day in 2 divided doses for 7-14days.

**OR**

**C:** clarithromycin (PO) 500mg 12hourly for 7-14 days.

For Children  $\geq$  6 months:

**S:** clarithromycin (PO) 15mg/kg/day in 2 divided doses for 7-14days

**OR**

**C:** ceftriaxone (IV) Adult 1-2g 12 hourly. Paediatric 50-100mg/kg 24hourly for 7days

**AND**

**A:** paracetamol (PO) 500mg to 1g 4-8hourly as needed.

For Children  $\leq$  10kg:

**A:** paracetamol (PO) 10mg/kg 4-8hourly as needed.

For Children  $>$

**A:** paracetamol (PO) 10kg: 15mg/kg 4-8hourly as needed

**OR**

**A:** diclofenac (IM) 75mg 8hourly as needed

**C:** diclofenac (PO) 50mg 4-8hourly as needed,

## 15.8.13 Peritonsillar Abscess (Quincy)

Peritonsillar abscess is a collection of pus located between the capsule of the palatine tonsil and the pharyngeal muscles.

### Clinical presentation

- Severe sore throat (usually unilateral) with Fever
- "Hot potato" or muffled voice
- Pooling of saliva or drooling may be present
- Trismus, neck swelling and pain and may have ipsilateral ear pain
- Fatigue, irritability
- Swollen and/or fluctuant tonsil with deviation of the uvula to the opposite side

### Pharmacological management

**B:** amoxycillin + clavulanate (PO) 625mg to 1g 12hourly for 7-14days.

For Children  $\leq$  3 months:

**B:** amoxycillin + clavulanate (PO) 30mg/kg/day in 2divided doses for 7-14days.

For Children >3 months:

**B:** amoxycillin + clavulanate (PO) 25mg/kg/day in 2divided doses for 7-14days

**OR**

**B:** ceftriaxone (IV) 1- 2 g 12 hourly for 7days.

For Children:

**B:** ceftriaxone (IV) 50-100mg/kg 24hourly for 7days

**OR**

**C:** clarithromycin (PO) 500mg 12hourly for 7-14days.

For Children ≥ 6 months: 15mg/kg/day in 2divided doses for 7-14days

**OR**

**S:** cefixime (PO) 400mg 24hourly for 7-14days.

For Children ≥ 6 months to 12years (weight below 45kg):

**S:** cefixime (PO) 8mg/kg 24hourly for 7-14days

### **Surgical management**

- Needle Aspiration
- Incision and drainage (LA/GA)
- Drainage/quincy tonsillectomy
- Interval tonsilectomy

## **15.9 ENT Neoplasms**

### **15.9.1 Juvenile nasopharyngeal angiofibromas (JNA)**

Are rare vascular tumors exclusively seen in adolescent males.

#### **Clinical features**

- Nasal bleeding
- Nasal blockage
- May present with eye protrusion

#### **Investigation**

**CT-Scan (with contrast) PNS/Skull base-**will show widening of sphenopalatine fissure and anterior bowing of posterior wall of maxillary sinus.

#### **Note**

Never take biopsy for suspected case of JNA

#### **Surgical treatment**

#### **Embolization of internal maxillary artery THEN**

Excision of Angiofibroma (Open or Endoscopic/modified Denkers operation)

## **15.9.2 Salivary Gland Tumors**

Salivary gland tumors include a heterogeneous group of lesions. Most salivary gland tumors are composed of more than one cell type. Tumours may arise from major or minor salivary glands. (Parotid, Submandibular, Lingual and minor salivary gland tumours)

#### **Clinical presentation**

- Painless progressive swelling of a given salivary gland.

#### **Investigation**

- Fine needle aspiration cytology (FNAC)
- **Do not take incisional biopsy unless lesion is ulcerative.**

#### **Surgical management**

- Partial or Total parotidectomy-for parotid tumours
- Submandibular gland tumor excision-for submandibular gland
- Sub lingual gland tumor excision
- Minor salivary gland tumors excision

### **15.9.3 Parapharyngeal Tumours**

Both benign and malignant tumors may arise from any of the structures contained in this space. Among parapharyngeal space (PPS) tumors; 70-80% are benign, and 20-30% are malignant. Most PPS tumors are of salivary or neurogenic origin.

#### **Clinical presentation**

- Sore throat
- Dysphonia
- Otalgia
- Snoaring
- Tonsilar/pharyngeal mass
- Neck/submandibular mass

#### **Investigation**

- Fine needle aspiration cytology (FNAC)
- CT SCAN-Neck&skull base
- MRI –Head and neck

#### **Surgical Management**

- Parapharyngeal tumour excision

### **15.9.4 Cancer of the Larynx**

It is the commonest ENT malignancy. Risk factors include cigarette smoking, alcohol intake, gastroesophageal reflux disease and human papilloma virus.

#### **Clinical presentation**

- Progressive hoarseness of voice
- Difficulty in breathing (inspiratory stridor)
- Hemoptysis

**Referral:** Refer the patient to the next facility with adequate expertise and facilities

#### **Investigations**

- Rigid Laryngoscopy (endoscopy) or Fiberoptic nasolaryngoscopy(diagnostic)

#### **Surgical management**

1. Direct Laryngoscopy +Biopsy under General Anaesthesia (GA)
2. Tracheostomy
3. Total/Partial laryngectomy +/- neck dissection

#### **Note**

Any patient with progressive hoarseness of voice for more than two weeks should undergo laryngoscopy

### **15.9.5 Sino-Nasal Malignancy**

Is a malignancy of the nose and paranasal sinuses? Risk factors include wood dust (both soft and hard), welding dust, leather industry fumes, hydrocarbons fumes, and aflatoxin dust.

#### **Clinical presentation**

- Nasal bleeding
- Nasal discharge
- Nasal obstruction
- Teeth loosening
- Cheek swelling
- Proptosis
- Hearing loss

**Referral:** Refer the patient to the next facility with adequate expertise and facilities

#### **Investigations**

- Biopsy-transnasal biopsy/Endoscopic
- CT-Scan –paranasal sinus (PNS)
- Chest x –ray
- Urinalysis-bence -Jones proteins

## **Surgical management**

Total Maxillectomy-Open OR

Partial Maxillectomy-Open/Endoscopic

### **Note**

Refer patient for adjuvant chemo and radiotherapy

## **15.9.6 Naso-Pharyngeal Malignancy**

It is a malignancy which arises from the nasopharynx. Risk factors include genetic predisposition, Epstein Bar virus, smoked and/or salted foods.

### **Clinical presentation**

- Cervical lymphadenopathy, usually bilateral
- Nose bleeding
- Nasal blockage
- Hearing loss, tinnitus or ear pain

**Referral:** Refer the patient to the next facility with adequate expertise and facilities

### **Note**

A patient presenting with cervical lymphadenopathy has nasopharyngeal carcinoma until proven otherwise

## **Investigations**

- Biopsy-Transnasal/Endoscopic
- Fine needle aspiration cytology for neck mass
- CT-Scan-head and neck
- Chest x-ray
- Serology for Epstein Bar virus(EBV)

## **Treatment**

- Radiotherapy

### **15.9.7 Oropharyngeal Malignancy**

Oropharyngeal squamous cell carcinomas arise in the soft palate, tonsils, base of tongue, pharyngeal wall, and vallecula.

## **Clinical presentation**

- Sore throat
- Throat pain/painful swallowing
- Voice change ("hot potato" voice)
- Difficulty in breathing
- Oropharyngeal mass/ulcer

## **Investigations**

- Rigid endoscopy
- Transoral biopsy
- Serology for HPV (human papilloma virus)
- CT-Scan or MRI -Neck

## **Management**

- **Surgery:** open or transoral
- **Definitive Management:** Refer Malignancy chapter.

### **15.9.8 Hypo-Pharyngeal Malignancy**

It is a malignancy which arises from the hypopharynx. Risk factors include cigarette smoking, alcohol intake and gastroesophageal reflux disease.

## **Clinical presentation**

- |                               |   |
|-------------------------------|---|
| • Progressive dysphasia       | • Difficulty in breathing (inspiratory stridor) |
| • Progressive odynophagia     | • Excessive salivation/Pooling of saliva        |
| • Hematemesis/hemoptysis      |   |
| • Ear pain (referred otalgia) |   |
| • Cervical lymphadenopathy    |   |

**Referral:** Refer the patient to the next facility with adequate expertise and facilities

## **Investigations**

- Rigid Laryngoscopy (endoscopy) or Fiber optic nasolaryngoscopy(diagnostic).
- CT-Scan-head and neck
- Chest x-ray

## **Surgical management**

1. Direct Hypopharyngoscopy +Biopsy under general anesthesia(GA)

## **Definitive Management**

- Chemoradiotherapy depending on histological results –Refer to oncology chapter

## **15.9.9 Metastatic Lymphadenopathy and Neck Masses**

Cervical lymph nodes are a common site of metastases for malignant tumors that originate at primary sites in the head and neck. Primary lymphoma in neck nodes must be considered in any differential diagnosis.

### **Clinical presentation**

- Neck mass unilateral or bilateral
- Neck ulcer

### **Note**

- An adult patient with neck mass, should be approached with a presumption of malignancy until proven otherwise.
- Once the diagnosis of metastatic squamous cell carcinoma is made, a search for the primary tumor must be performed. The probable primary site can often be identified by history and physical examination; panendoscopy and directed imaging may be required.

### **Investigations**

- Neck ultrasound
- Fine needle aspiration cytology(FNAC)
- Panendoscopy of upper aerodigestive areas (nose and paranasal sinuses, nasopharynx, oropharynx, larynx, hyponasal) and oesophagoscopy.
- Direct nasal endoscopy (DNE)
- Fiber optic nasolaryngoscopy
- Rigid laryngoscopy (endoscopy)

**Note:** Do not treat patient with cervical lymphadenopathy as a case of TB adenitis until malignancy is ruled out and TB adenitis is proved.

### **Surgical management**

- Biopsy for histology from suspected site
- Neck dissection: Radical or Modified Neck Dissection

## **15.10. Speech Disorders**

Speech disorder refers to any condition that affects a person's ability to produce sounds that create words. This includes stuttering, apraxia, dysarthria can be caused by brain damage/stroke, muscle weakness, hearing loss, dementia etc.

### **Investigations**

- Audiometry
- Otoacoustic emission (OAEs)
- Auditory brainstem response
- Fiber optic nasolaryngoscopy

### **Non-pharmacological management**

- Auditory verbal training-for post cochlea implantation
- Speech therapy for aphasia, stuttering, apraxia and dysarthria.
- Hearing Aids
- Cochlea implantation

### **Surgical management**

- Posterior tympanotomy-for cochlea implantation.

# CHAPTER SIXTEEN

## ORAL AND DENTAL CONDITIONS

Oral diseases and conditions are common and range from dental caries, periodontal conditions, dental abscess, acute bacterial infections, viral infections, fungal infections, traumatic injuries, tumors, and lesions affecting the maxillofacial region (periportal, jaws and face). Before doing oral examination or any dental procedures, patients should gurgle with hydrogen peroxide 3% or povidone iodine 2% to minimize infectious agent's contamination between patient and oral health care provider.

### 16.1 Periodontal Conditions

#### 16.1.1 Gingivitis

Inflammatory changes in the gingival develop within a couple of days of undisturbed bacterial growth on the gingival margin of the erupted tooth in the oral cavity

##### Clinical presentation

- Gingival redness
- Swollen and shiny gingival tissue
- Increased tendency of the gingival to bleed on gentle probing or spontaneously, during tooth brushing or even on touch and on biting bread and fruits.
- Bad breath from the mouth

##### Prevention and non-pharmacological Treatment

Proper oral hygiene care counselling.

Remove accumulated plaque and teach oral hygiene on systematic tooth brushing and other adjuvant means of oral hygiene (dental flossing, tongue cleaning on the dorsal part, use of mouth washes including saline mouth wash).

#### 16.1.2 Periodontitis

This is the progression of the inflammation of gingival into the deep tissue affecting the periodontal membrane causing periodontal pockets, introduction of infection and destruction of periodontium.

##### Clinical presentation

- Reddened, swollen gingiva
- Easily bleeding gingival on gently probing
- Periodontal pocket
- Loose/mobile teeth
- Bad breath from the mouth
- Gingival recession

##### Investigation

Orthopantomography (OPG) to determine extent of bone loss

##### Non-pharmacological Treatment

Instruct and guide the patients on proper oral hygiene for proper plaque control.

Plaque control by scaling and root planning.

##### Pharmacological Treatment

Mouth wash: Do not swallow

A: hydrogen peroxide (PO) 3% 6hourly for at least for 5days

OR

B: chlorhexidine gluconate (PO) 0.1% 12hourly at least for 5days

OR

Use antibiotics only in severe cases

A: metronidazole (PO) 400mg 8hourly for 8days

AND EITHER

A: amoxicillin (PO) 500mg 8hourly for 8 days

OR

A: doxycycline (PO) 100mg 12hourly for 10days

### **16.1.3 Acute Necrotizing Ulcerative Gingivitis (ANUG)**

It is a severe form of gingivitis and is characterized by rapid destruction of gingival tissue, particularly in the interdental papilla. Patients usually present with soreness and bleeding of the gums and foul smell test (fetor-ex ore/halitosis). It is common in malnourished children and immunocompromised individuals especially patients with diabetes and HIV/AIDS.

#### **Clinical presentation**

- Painful swollen gingiva which bleeds easily and erythema of the gingival margins
- Yellowish-white ulceration of the gingival
- Fever, malaise, and regional lymphadenitis
- In some patients (especially malnourished children), ANUG may presents with extensive destruction of the face and jaws in the severe form known as Cancrum Oris

#### **Pharmacological Treatment**

Professional cleaning with hydrogen peroxide 3% (under local anesthesia)

**A:** metronidazole (PO) 400 mg 8hourly for 5days

**AND**

**A:** amoxicillin (PO) 500mg 8hourly for 5days

### **16.1.4 Stomatitis**

This is generalized inflammation of the oral mucosal (including the gingiva) due to different etiologies such as infections, chemical burn, radiation, and allergy.

#### **Clinical presentation**

- Oral sores and ulceration

#### **Pharmacological Treatment**

Mouth wash (do not swallow)

**A:** hydrogen peroxide solution 3% (PO) 6hourly for at least 5days

**OR**

**B:** chlorhexidine 0. % topical oral gel 12hourly

#### **Note**

Mouth wash should not be used at the same time with the gel. Also, should not be swallowed.

Oral analgesics can be added

**A:** paracetamol (PO) 1gm 8hourly for at least 3days

**OR**

**A:** ibuprofen (PO) 400 mg 8hourly for at least 3days

**OR**

**C:** diclofenac (PO) 50 mg 8hourly for at least 3days

## **16.2 Dental Caries**

Dental caries is caused by bacteria of the dental plaque which feed on sugary food substrates producing acid as by-products which dissolve the minerals of the tooth surface.

#### **Clinical presentation**

Early stage—asymptomatic

- Intermediate stage: black/brown spot which may be visible on any surface of tooth
- Cavities developing on tooth surface
- Pain/toothache elicited by hot, cold, or sweet foods/drinks

### **Late stage**

- Pain may be spontaneous, intermittent, sharp, and severe, even interfering with sleep.
- Tenderness on percussion of the tooth

### **Investigation**

Periapical x-ray of tooth/teeth may need to be done specially to confirm extent of caries for treatment decision e.g. the caries contained in the dentine can be distinguished from pulpal caries.

### **Prevention**

- Proper counseling to avoid frequent use of sugary foods and drinks
- Use fluoridated toothpaste to brush teeth at least twice a day
- Provide preventive measures to early lesions presenting as a spot on the enamel without cavitation and softening

### **Non-pharmacological Treatment**

Lesion with cavitation but confined to dentine—filling/restoration of teeth with suitable filling materials (e.g. amalgam, composite, glass ionomer)

Perform endodontic treatment with combination of antibiotics wherever possible for tooth with lesion involving the pulp (with or without periapical abscess otherwise tooth extraction is done

### **Pharmacological Treatment**

Analgesics: for toothache

**A:** paracetamol (PO) 1gm 8hourly for 3days

**OR**

**A:** ibuprofen (PO) 400mg 8hourly for at least 3days

**OR**

**C:** diclofenac (PO) 50 mg 8hourly for at least 3days

Antibiotics for endodontic treatment

**B:** ampicillin + cloxacillin (FDC) (PO) 500mg 8hourly for 5days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 5days

## **16.3 Odontogenic and Non-Odontogenic Orofacial Infections**

### **16.3.1. Periapical abscess**

This clinical condition arises as a complication of inflammation of the dental pulp or periodontal pocket. The condition may be acute and diffuse, chronic with fistula or localized and circumscribed. It is in the apical aspect of the supporting bone.

#### **Clinical presentation**

- The patient complains of tooth ache
- Pain during intake of hot or cold foods/drinks
- Pain on bringing the tooth on occlusion
- Tenderness on percussion (vertical percussion)
- Swelling of gingiva around the affected tooth

#### **Non-pharmacological Treatment**

- For posterior teeth: Extraction of the offending tooth under local anesthesia (can perform root canal treatment for posterior teeth instead of tooth extraction under good clinical judgement)
- Perform Incisional and drainage under local anesthesia followed by analgesics.

For anterior teeth (incisors, canine and premolars): extraction is carried out only when root canal treatment is not possible

## **Pharmacological Treatment**

**A:** paracetamol (PO) 1gm 6hourly for 3days.

**AND**

**A:** amoxicillin (PO) 500mg 8hourly for at least 7days

**OR**

**A:** erythromycin (PO) 500mg 8hourly for 7days (if allergic to penicillin)

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 7days

### **16.3.2 Dental Abscess (Odontogenic Abscess)**

Dental abscess is an acute lesion characterized by localization of pus (caused by polymicrobial infection) in the structures that surround the teeth.

#### **Clinical presentation**

- Fever and chills
- Throbbing pain of the offending tooth
- Swelling of the gingiva and sounding tissues
- Pus discharge around the gingiva of affected tooth/teeth
- Trismus (inability to open the mouth)
- Regional lymph nodes enlargement and tender
- Aspiration of pus

#### **Investigation**

Pus for Gram stain, culture, and sensitivity if the patient doesn't respond to initial antibiotic treatment.

#### **Non-pharmacological Treatment**

- Incision and drainage and irrigation (irrigation and dressing is repeated daily). Irrigation is done with 3%hydrogen peroxide followed by 0.9% sodium chloride.
- Supportive therapy carried out depending on the level of debilitation. Most patients need rehydration and detoxification using 0.9% sodium chloride (IV) or compound sodium lactate (IV).

#### **Pharmacological Treatment**

**A:** amoxicillin (PO) 500mg 8hourly for 5days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 5days.

#### **In severe cases,**

**B:** amoxicillin+ clavulanic acid (FDC) (PO) 625mg 8hourly for 5days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 5days.

#### **If a patient is allergic to penicillin**

**A:** erythromycin (PO) 500mg 8hourly for 5days

Where parenteral administration of antibiotics is necessary (especially when the patient cannot swallow and has life threatening infection), consider the following

**B:** ceftriaxone (IV) 1gm once daily for 5days

**AND**

**B:** metronidazole (IV) 500 mg 8hourly for 5days

**AND**

**A:** gentamicin (IV) 80mg 8hourly for 5days

#### **Note**

Incision and drainage is mandatory in cases of deeper spaces involvement followed by a course of antibiotics. The practice of prescribing antibiotics to patients with abscess and denying referral for definitive care until pus has established or resolved has been found to lead to more problems for orofacial infections therefore early referral for definitive care is important.

### 16.3.3 Ludwig's Angina

This is a serious life threatening generalized septic cellulitis of the fascia spaces found on the floor of the mouth and tongue. It is an extension of infection from mandibular molar teeth into the floor of the mouth covering the submandibular, sublingual, and submental spaces bilaterally.

#### Clinical presentation

- Brawny induration
- Tissues are swollen, board like, not pitted and no fluctuance
- Respiratory distress
- Dysphagia
- Tissues may become gangrenous with a peculiar lifeless appearance on cutting
- Three fascia spaces are involved bilaterally (submandibular, submental, and sublingual)

#### Non-pharmacological Treatment

- Incision and drainage is done (even in absence of pus) to relieve the pressure and allow irrigation
- Only when the airway distress is significant and there is evidence that it is not relieved by incision and drainage then tracheostomy is needed. Supportive care includes high protein diet and fluids for rehydration and detoxification. During incision and drainage pus should be taken for culture and sensitivity. Offending tooth should be removed at the same sitting if the patient can open the mouth.

#### Pharmacological Treatment

**B:** ceftriaxone (IV) 1g 24hourly for 5days

**OR**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 625mg 8hourly for 5days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 5days

#### If allergic to penicillin use

**A:** erythromycin (PO) 500mg 6hourly for 5days

Once the patient can swallow, replace IV medication with oral treatment.

#### Note

For this condition and other life-threatening oral conditions consultation of available specialists (especially oral and maxillofacial surgeons) should go parallel with life saving measures.

### 16.3.4 Pericoronitis

Inflammation of the soft tissues covering the crown of erupting tooth and occurs more commonly in association with the mandibular third molar (wisdom) teeth.

#### Clinical presentation

- High temperature
- Discomfort in swallowing and chewing
- Well localized dull pain, swollen and tender gum flap
- Signs of partial tooth eruption
- Bad smell (Foetor-ox oris)
- Trismus

#### Non-pharmacological Treatment

Excision of the operculum/flap (flapectomy) under local anesthesia.

Extraction of the third molar associated with the condition.

Grinding or extraction of the opposing tooth.

#### Pharmacological Treatment

**A:** hydrogen peroxide solution 3% (PO) 6hourly for 5days (Gurgle /rinse)

**A:** amoxicillin (PO) 500mg 6hourly for 5days

## **AND**

**A:** metronidazole (PO) 400mg 8hourly for 5days

If severe (rare) refer to treatment of dental abscess section

### **16.3.5 Osteomyelitis of the Jaw**

Osteomyelitis is an infection involving all layers of bone in which widespread necrosis may occur. It is rare in the maxilla due to the rich blood supply, but on occasions may affect the anterior palate where the bone is thicker. It is more common in the mandible, usually because of dental infection, trauma, or a blood-borne infection.

#### **Clinical presentation**

- In the initial stage there is no swelling
- Malaise and fever
- Enlargement of regional lymph nodes
- Teeth in the affected area become painful and loose.
- Later as the bone undergoes necrosis the area becomes very painful and swollen
- Pus ruptures through the periosteum and discharged outside the skin surface through a sinus

#### **Investigation**

X-ray – OPG (Orthopantomography) or mandibular lateral oblique, water's view for maxilla/midface. The x-ray will show sequestra formation in chronic stage. In early stage features seen in x-ray include widening of periodontal spaces, changes in bone trabeculation and areas of radiolucency. Perform culture and sensitivity of the pus aspirate to detect the specific bacteria.

#### **Non-pharmacological Treatment**

Incision and adequate drainage to confirmed pus accumulation which is accessible.

Removal of the sequestrum by surgical intervention (sequestrectomy) is done after the formation of sequestrum has been confirmed by X-ray.

#### **Pharmacological Treatment**

For acute osteomyelitis of the jaw

**B:** ampicillin + cloxacillin (FDC) (PO) 500mg 8hourly for 4-6weeks

## **AND**

**A:** metronidazole (PO) 400mg 8hourly for 4-6weeks. If culture is available treat according to results.

For chronic osteomyelitis of the jaw which sequestrectomy has been done

**A:** doxycycline (PO) 100mg 12hourly for 5days

## **OR**

**A:** metronidazole (PO) 400mg 8hourly for 5days

## **AND**

**S:** clindamycin (PO) 500mg 8hourly for 5days

### **16.4. Fungal Infections**

#### **16.4.1 Oral Candidiasis**

This is a fungal infection of the oral mucosa caused by Candida infection mainly *Candida albicans*.

#### **Clinical presentation**

Features of candidiasis are divided according to the types as follows:

#### **Pseudomembranous**

- White creamy patches/plaque
- Cover any portion of mouth but more on tongue, palate, and buccal mucosa

- Sometimes may present as erythematous type whereby bright erythematous mucosal lesions with only scattered white patches/plaques

### **Hyperplastic**

- White patches leukoplakia-like which are not easily rubbed-off.

### **Angular cheilitis (angular stomatitis)**

- Soreness, erythema and fissuring at the angles of the mouth
- Commonly associated with denture mastitis but may represent a nutritional deficiency or it may be related to orofacial granulomatosis or HIV infection

### **Pharmacological Treatment**

**A:** nystatin suspension (PO) 100,000IU (1 ml) mixture held in the mouth for at least 3minutes before swallowing, 6hourly

**OR**

**C:** miconazole gel (PO) 25mg/ml 5–10mls in mouth –hold in the mouth for 60 seconds before swallowing. The treatment should be continued for 5days after cure/clearance. Where topical application has failed, or candida infection has been considered severe use.

**A:** fluconazole (PO) 150mg 24hourly for 7days

**OR**

**D:** itraconazole (PO) 200mg 24hourly for 7days

### **Note**

Candidiasis has several risk factors; it is recommended that for HIV/AIDS patients with candidiasis, refer to the Tanzania HIV/AIDS Guidelines.

## **16.5 Viral Infections**

### **16.5.1 Herpes Simplex Virus**

This is a viral infection commonly affecting the lips and perioral soft tissues presenting as papulovesicular lesions which ultimately ulcerate. The primary infection affects mainly the gingiva and palate.

#### **Clinical presentation**

- A prodromal of tingling, warmth or itching at the site usually precedes the recurrence
- About 12 hours later, redness appears followed by papules and then vesicles
- These vesicles then burst, weep, dry, scab and then heal
- The length of the cycle is variable 5–12days mean time being 7days

#### **Non-pharmacological Treatment**

- Adequate hydration
- Avoid salty and acidic drinks
- Cover lesions on the lips with Petroleum jelly and control any underlying cause

#### **Pharmacological Treatment**

This is an otherwise self-limiting condition but if persistent for 10days or recurrent infection use medication:

#### **For Herpes Labialis**

**B:** acyclovir cream applies 4hourly for 5days

#### **For Herpes Stomatitis**

**B:** acyclovir (PO) 200mg 6hourly for 5days

**AND**

**B:** acyclovir cream 12hourly for 5days

### **In immunocompromised patients**

**B:** acyclovir (PO) 400mg 6hourly for 5days

### **For oral facial lesions of herpes zoster treat with**

**B:** acyclovir (PO) 400–800mg 6hourly for 5days

### **Pain control by analgesics**

**A:** paracetamol (PO) 1g 8hourly for 3days

**OR**

**C:** diclofenac (PO) 50mg 8hourly for 3days

**OR**

**A:** ibuprofen (PO) 400mg 8hourly for 3days

## **16.6 Aphthous Ulceration**

Aphthous or recurrent aphthous stomatitis (RAS) are painful recurrent mucous membrane ulcerations. Usually affect the non-keratinized oral mucous membrane.

### **Clinical presentation**

#### **Minor Aphthous Ulcers**

- Small round or ovoid ulcers 2–4 mm in diameter, surrounded by an erythematous halo and some edema.
- Occurs in groups of only a few ulcers (i.e. 1–6) at a time.
- Found mainly on the non-keratinized mobile mucosa of the lips, cheeks, floor of the mouth, sulci, or ventrum of the tongue.

#### **Major Aphthous ulcers**

- Painful ulcers on non-keratinized oral mucous membrane, they are large 1–3 cm edged ulcers, and several may be present simultaneously.

#### **Herpetiform ulcers**

These occur in a group of multiple ulcers which are small (1–5 mm) and heal within 7–10days.

### **Pharmacological Treatment**

**B:** chlorhexidine gluconate 0.1% mouthwash used 8hourly for 5days

**OR**

**D:** triamcinolone acetonide cream 0.1% apply 12hourly for 5days

### **If systemic therapy is required:**

**A:** prednisolone (PO) 20mg 8hourly for 3days then dose tapered to 10mg 8hourly for 2days then 5mg 8hourly for other 2 days.

**A:** paracetamol (PO) 1gm 8hourly for 3days when required for pain.

## **16.7 Post Extraction Complications**

### **16.7.1 Bleeding socket**

Commonly due to disturbing the blood clot by the patient through rinsing or inadequate compression on the gauze, though at times may be due to bony/tooth remnants.

### **Clinical presentation**

Bleeding socket can be primary (occurring within first 24 hours post extraction) or secondary occurring beyond 24 hours post extraction.

### **Primary Bleeding Socket**

- Active bleeding from the socket
- Patient may be dehydrated and pale if has lost significant amount of blood
- Features of decreased pulse rate and volume, hypotension also if patient has lost significant amount of blood

### **Secondary bleeding**

- The socket may show features of infection or trauma

### **Non-pharmacological Treatment**

Give local anaesthesia (lignocaine 2% with adrenaline 1 in 80,000 IU).

Clear any clot available and examine the socket to identify source of bleeding.

Suturing of the wound only when necessary (like significantly traumatized gingiva).

Give proper instructions to follow (bite on gauze pack for 30 minutes, not to rinse or eat hot foods on that day at least for 12 hours and avoid disturbance to the wound).

### **Pharmacological Treatment**

Analgesics may be needed:

**A:** paracetamol (PO) 1g 8hourly for 3days

**OR**

**C:** diclofenac (PO) 50mg 8hourly for 3days

**OR**

**A:** ibuprofen (PO) 400mg 8hourly for 3days

**AND**

**C:** tranexamic acid (PO) or (IV) 500 mg 8hourly for the first 24hours.

### **16.7.2 Infected Socket**

A post extraction complication due to infection of the clot due to contamination (infected socket). The condition is painful and if not managed well could lead to osteomyelitis.

#### **Clinical presentation**

- Severe painful socket 2–4days after tooth extraction
- Fever
- Necrotic blood clot in the socket
- Swollen gingiva around the socket
- Sometimes there may be lymphadenopathy and trismus (inability to open the mouth)

#### **Non-pharmacological Treatment**

Socket debridement under local anaesthesia with lignocaine 2% and irrigate with hydrogen peroxide 3% followed with copious amounts of normal saline. The procedure of irrigation is repeated the 2<sup>nd</sup> and 3<sup>rd</sup> day and where necessary can be extended to the 4th day if pain persists.

#### **Pharmacological Treatment**

Patient is instructed to rinse with 3% hydrogen peroxide or 2% povidone iodine 3–4 times a day. antibiotics should be prescribed to prevent progression to osteomyelitis:

**A:** amoxicillin (PO) 500mg 8hourly for 5–7days

**OR**

**B:** azithromycin (PO) 500mg 24hourly for 3days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 5days

#### **Investigation**

Periapical X-ray of the socket may be necessary when there is limited improvement despite treatment.

### **16.7.3 Dry Socket**

This is a post extraction complication due to failure to form a clot (dry socket). The condition is very painful, and it differs from an infected socket by lack of clotting and levels of severity of pain.

#### **Clinical presentation**

- Severe pain 2–4 days' post-extraction
- Pain exacerbated by entry of air on the site
- Socket devoid of clot
- Surrounded by inflamed gingiva

### **Non-pharmacological Treatment**

Treatment is under local anesthesia with lignocaine 2%, socket debridement and irrigation with hydrogen peroxide 3% followed with copious amount of normal saline. The procedure of irrigation is repeated on the 2nd and 3rd day and where necessary can be extended to the 4th day if pain persists.

### **16.7.4 Oro-Antral Communication**

Occasionally, the uncomplicated extraction of a tooth may fracture the thin floor of the sinus and cause an oro-antral communication (OAC). More commonly, the communication is produced by attempts to remove retained tooth root so that the antrum floor is perforated, or the apex displaced into it.

#### **Clinical presentation**

- Air passing from the nose into the mouth and the surgeon will be able to see bubbling through the communication when the patient is asked to breathe out.
- Blood from the wound, drinks and mouthwashes used to rinse the mouth may pass through the sinus into the nose.

#### **Non-pharmacological Treatment**

Immediately on diagnosing a communication the tooth should be checked to ensure that it has been completely extracted. All pieces of loose bone that might form sequestra are then gently removed. The buccal plate of alveolar bone is trimmed if a flap has been raised but is otherwise left alone. Buccal advancement flap is the operation of choice to repair the fistula (oro-antral communication)

#### **Pharmacological Treatment**

**A:** metronidazole (PO) 400mg 8hourly for 5days

**AND**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 625mg 12hourly for 7days

### **16.8 Tooth Sensitivities**

Teeth become sensitive because of worn enamel, or exposed tooth roots, cavity, gingival collapse, a consequence of periodontitis, tartar (calculus) build-up, cracked or chipped tooth and recent filling.

#### **Non-pharmacological Treatment**

- Recommend brushing teeth with desensitizing toothpaste for sensitive teeth
- Desensitizing or bonding – apply bonding resin material or Glass Ionomer Cement to seal the area around the tooth
- Root canal treatment – for severe, prolonged discomfort
- Prevent tooth-grinding (bruxism) by fabricating to the patient a mouth guard

#### **Pharmacological Treatment**

**C:** sodium fluoride 1.1 % +potassium nitrate 5% (fluoride gel or varnish), apply 12hourly

### **16.9 Tooth Eruption, Shedding and Edentulousness**

#### **16.9.1 Eruption of Teeth**

Eruption of deciduous /primary teeth usually starts at five months of age. Symptoms associated with it like fever and diarrhea are normal and self-limiting unless any other causes can be established. The following conditions are usually associated with tooth eruption and should be referred to dental personnel: eruption cysts, gingival cysts of the newborn and pre/natal teeth.

#### **Note**

“Nylon teeth” is a myth/belief existing in some traditions. These are conditions associated with the eruption of deciduous/primary teeth

## **16.9.2 Shedding of Deciduous Teeth**

Phenomenon of losing deciduous/primary teeth occurring between ages of 5–12 years is a normal physiological change. Deciduous teeth should be left to fall out themselves unless the teeth are carious or there is any other indication. Parents should be counseled accordingly and be instructed to assist their children to loosen the already mobile teeth and when there is no success, or the permanent teeth are erupting in wrong direction should consult a dentist.

## **16.9.3 Edentulousness**

It is the partial or full loss of natural teeth and subsequent resorption of the alveolar bone.

### **Diagnosis**

Diagnostic cast, Periapical X-ray, OPG.

### **Non-pharmacological Treatment**

- Design and fabricate dental prosthesis
- Dental prosthesis may be fixed, partial dentures and complete/full dentures
- Materials required in fabrication of these prostheses are: alginate impression materials, silicone impression materials, implant system, gypsum dental stone, Acrylic resins (monomer and polymer), porcelain, ceramic, metal alloys, wax etc.

### **16.9.3.1 Dental implant (s)**

A permanent device that is biocompatible and bio-functional placed on or within the bone to provide retention for fixed or removable prostheses.

### **Indications of Dental Implant(s)**

- Single tooth replacement.
- Multiple teeth replacement.
- Retention of removable prosthesis in partially edentulous patient.
- Retention of over denture in completely edentulous patient (In mandible two 2 implants are required for support and in maxilla 4 implants are needed to support the denture).
- Retention of fixed prostheses completely edentulous patient (In mandible 4 implants needed and in maxilla - 6-8implants required).
- Retention of maxillofacial prosthesis.

### **Investigation**

#### **Radiographic examination**

Maxillary and mandibular bone status may be evaluated in combination of periapical X-ray, occlusal radiograph, panoramic radiograph, lateral cephalography, MRI and CT-Scan.

### **Surgiguids**

They are custom made for each patient. They are used as guides for drilling in the optimum locations implant placement then removed after placement.

### **Study cast**

Evaluate occlusal centric relation, including any premature occlusal contacts, the relationship of the edentulous area to the adjacent natural teeth and opposing arches.

### **Intra-operatively, the following should be observed to have a successful Implant**

- Assess anatomical variation and abnormalities of vital structures so that implant should never touch them.
- Maintain Sterility as interfere with Osseo-integration

### **Surgical technique**

Adequate blood supply (proper incision design and flap reflection. Using sharp gradual series of drill sizes with copious amount of irrigation by normal saline.

## **Pharmacological Treatment after implant insertion**

Mouth wash: Do not swallow

**A:** hydrogen peroxide 3% 6hourly for at least for 5days

**OR**

**B:** chlorhexidine gluconate 0.2% 12hourly at least for 5days

**AND**

**A:** metronidazole (PO) 400mg 8hourly for 8days

**AND**

**A:** amoxicillin (PO) 500mg 8hourly for 8days

## **16.10 Malocclusions**

Malocclusion is any variation in the arrangement of teeth leading to abnormal occlusion to the extent that may be functionally harmful or aesthetically objectionable.

### **Clinical presentation**

- Class I malocclusion: Diagnosed when there is any occlusal abnormality or individual tooth malocclusion in a case with normal arch relationship in anteroposterior plane.
- Class II malocclusion: Mesiobuccal cusp of upper first permanent molar occludes mesial to the buccal developmental groove of the lower first permanent molar
- Class III malocclusion: The upper first permanent molar occludes distal to the buccal developmental groove of the lower first permanent molar
- Skeletal malocclusions: These malocclusions are caused by defects in the underlying skeletal structure itself.

### **Non-pharmacological Treatment:**

#### **• Preventive orthodontics**

It includes parent counselling, caries control, space maintenance, managing exfoliation of deciduous teeth, release of abnormal frenal attachments, treatment of blocked permanent first molars, management of abnormal oral musculature and related habits.

#### **• Interception orthodontics**

- Correction of anterior or posterior cross bite, relieving crowding of the permanent dentition, Space closure, treatment of anterior open bite, Deep bite, reverse overjet, proclination of the upper labial segment and oral habits management by patient education and monitoring or removable and fixed habit breaker
- For skeletal malocclusion: Use of extra oral appliances like reverse pull headgear combined with an RME, high pull head gear and chin cups or functional appliances are indicated for skeletal malocclusion in growing patients

#### **• Definitive Orthodontic**

Alignment of teeth in patient with dental alveolar malocclusion by using removable, clear aligner or fixed appliances. Simple removable appliances are very useful in our local settings especially for mild to moderate malocclusion in teenagers and include retainers or space maintainers.

## **16.11 Management of Maxillofacial Trauma**

### **16.11.1 Traumatic Dental Injuries**

It may result in loosening, displacement and or loss of teeth, fracture of teeth and or bone, lacerations, and bleeding. The commonest causes are falls (in sports and play) at home or school and motor accidents. Most affected are upper incisors.

## Clinical presentation

Type	Presentation
Tooth concussion	Is an injury to supporting tissues of tooth, without displacement
Subluxation	Is the partial displacement, but is commonly used to describe loosening of a tooth without displacement
Intrusion	Is the displacement of tooth into its socket often accompanied by fracture of alveolar bone
Luxation	Is the displacement of tooth laterally, labially or palatally
Avulsion	Is the complete loss of tooth from the socket

### Soft tissue Injuries

#### Abrasion

Where friction between an object and the surface of the soft tissue causes a wound. This wound is usually superficial, denudes the epithelium, and occasionally involves deeper layers.

#### Contusion/Bruising

Indicates that some amount of tissue disruption has occurred within the tissues, which resulted in subcutaneous or sub mucosal hemorrhage without a break in the soft tissue surface.

#### Laceration

Is a tear in the epithelial and sub epithelial tissues? It is perhaps the most frequent type of soft tissue injury, is caused most by a sharp object

## 16.11.2 Facial Bones Injuries

The commonest causes of fractured jaws are fights, road accidents, falls and sport. They occur chiefly in males between 15-35years of age and twice as frequently in the mandible as in the maxilla.

### Initial assessment

The initial assessment should not concentrate on the most obvious injury but involve a rapid survey of the vital functions to allow management priorities to be established.

### The Mandible

The commonest sites of fracture in the mandible are the condyle neck, the angle, and the canine region.

### Middle third of the face

Fractures of the middle third of the face involve a complex of bones, which include the paired bones, the maxilla, palatine, zygomatic, nasal, lachrymal and inferior conchae, together with the single vomer and ethmoid bones.

### Clinical presentation

Fracture site	Clinical presentation
Bilateral condyle	Pain, tenderness and swelling over both joints Gagging on the posterior teeth and an anterior open bite, Restricted lateral movements, Absence of movement of condyle heads
Body of the mandible	Pain on moving jaw, Trismus Movement and crepitus at site of fracture, Step deformity of lower border of mandible, Derangement of the occlusion, Mental anaesthesia, Haematoma in the floor of mouth and buccal mucosa
Zygomatic bone	Depression of the prominence of the cheek, Step deformity in the infraorbital ridge, Subconjunctival haemorrhage and diplopia, Infraorbital nerve anaesthesia, Haematoma intraorally over the malar buttress, Blood in the antrum, Trismus due to the coronoid process impacting against the displaced

	malar or zygomatic arch, Circumorbital ecchymosis
Le Fort I	Floating palate, Blood in the antrum, Bilateral haematoma in buccal sulcus, Deranged occlusion with anterior open bite
Le Fort II	Gross swelling and, after oedema subside, dish – faced deformity, Subconjunctival haemorrhage and diplopia, Bilateral infraorbital nerve anaesthesia, Bilateral haematoma intraorally over malar buttresses, Retroposed upper dental arch with anterior open bite
Le Fort III	Gross swelling and, after oedema subside, dish – faced deformity Subconjunctival haemorrhage and sometimes diplopia Retroposed upper dental arch with anterior open bite Cerebrospinal fluid leak from nose Signs of head injury
Unilateral condyle	Affected side Pain in joint, worse on moving, Tenderness and swelling Absence (or abnormality) of movements of condyle head, Deviation of mandible towards this side, Gagging on molar teeth Opposite side Open bite Limitation of lateral excursion to that side

## Investigation

Fracture sites	Type of Investigation
Mandible	OPG, Skull x-ray (lateral oblique and PA view)
Zygoma	Skull x-ray (Occipitomental and submental vertex view), CT scan
Maxilla	Skull x-ray (Occipitomental, submental vertex, lateral face view), CT scan.
Naso- ethmoidal complex	CT scan

## Non-pharmacological Treatment

- Intra-oral examination: Look for soft-tissue lacerations, dentoalveolar fractures and damage to teeth.
- Check for tooth fragments which may be displaced in soft tissues.
- Examine traumatized teeth for mobility and check mobility.
- Suture for any soft tissue wounds.
- Extraction is a treatment of choice for significantly traumatized primary/deciduous teeth with mobility and or displacement.

## Reduction of fractures

In reducing fractures, the object is to rearrange the bone ends as accurately as possible. Although the surgeon should attempt to get perfect reduction, the aim is to treat not a radiograph, but a patient, and where displacement is acceptable and function is not impaired the patient should not be subjected to unnecessary surgery.

## Open reduction and rigid internal fixation (ORIF)

It is a standard treatment for most facial fractures. The technique relies on exposing the fractures through intra -or extra oral incisions and accurate reduction of the bony fractures, which are then held rigidly in place by the application of titanium plates for facial fractures, 2 mm used in mandibular fractures, 1.7 mm (low profile) and 1 mm used in mid - third fractures.

## Intermaxillary fixation (IMF)

The mandible is immobilized by fixing it to the maxilla using arch bars and flexible wires of different sizes 0.5, 0.6, 0.7 and 0.8mm. This establishes the occlusion and is an accepted part of the treatment of maxillary fractures. It may be employed in mandibular fractures, particularly when one or both condyles are involved.

**Note**

Give tetanus toxoid (0.5% IU) if the patient has not received vaccination in the past 10 years.

**Pharmacological Treatment**

Pain control by analgesics

**A:** paracetamol (PO) 1g 8hourly for 3days

**OR**

**C:** diclofenac (PO) 50mg 8hourly for 3days

**OR**

**A:** ibuprofen (PO) 400mg 8hourly for 3days

Prophylactic antibiotics are indicated in cases of suspected contamination or extensive damage

**B:** ampicillin + cloxacillin (FDC) (PO) 500mg 8hourly for 5days

## 16.12 Tumours and Tumour-Like Conditions of Oral Cavity and Facial Region

### 16.12.1 Benign Odontogenic Tumors

Each tumour presents with different cardinal features radiologically and on histopathological diagnosis.

#### 16.12.1.1 Ameloblastoma

##### Clinical Presentation

- Recognized between ages of 10 to 80 years
- 80% form in the mandible and 70% develop in the posterior molar region and often involve the ramus
- Painless, slow growing tumor that may be solid or cystic
- Loosening of teeth, with roots resorption
- Gradual facial asymmetry due to enlargement and destruction of bone
- Continuous sheet of paper-thin bone covering the tumor

##### Investigation

Radiographically, the tumour presents with multilocular radiolucency, honeycomb, or soap bubble appearance.

**Note**

Diagnostic confirmation of this tumour is through histopathology. Complete excision e.g. total resection of the jaw, segmental resection plus bone grafting is the treatment of choice. Hence refer the patient to a centre where there is oral and maxillofacial surgeon and histopathology Unit.

#### Calcifying odontogenic tumors

##### Clinical Presentation

- Most often found in the mandibular molar/premolar region, but 33% of cases are found in the maxilla
- It is associated with an unerupted or impacted tooth in 50% of cases

##### Investigation

Radiographically these lesions can be radiolucent, but more characteristically are mixed lucent and opaque masses, exhibiting a snow-driven appearance

#### Non-pharmacological Treatment

Complete excision of the tumour with border of normal lobe should be curative, but recurrence follows incomplete excision.

### **16.12.1.2 Ameloblastic Fibroma**

#### **Clinical Presentation**

- Slower growing tumor than the simple ameloblastoma and does not infiltrate between bone trabeculae
- 75% of ameloblastic fibromas are found in the posterior mandible in the area of a developing tooth. It is benign and expansile, growing as a pushing front rather than invading surrounding tissues

#### **Investigation**

Radiographically this lesion appears as a unicocular or bilocular radiolucency, most often in the posterior mandible. The radiographic appearance is identical to that of unicystic ameloblastoma, and both lesions should be differential diagnoses because they affect similar age groups and have similar clinical and radiographic appearances. Histologic examination differentiates the two.

#### **Non-pharmacological Treatment**

Conservative resection is effective, but if incomplete, recurrence follows

### **16.12.1.3. Adenomatoid Tumors (Adenoameloblastoma)**

#### **Clinical Presentation**

- Two thirds of the cases occur in the anterior maxilla, one third occur in the anterior mandible, and it is never found posterior to the premolars
- Two thirds of the cases are associated with an impacted tooth (usually the cuspid)
- Present with mild swelling or in association with a clinically missing tooth

#### **Investigation**

Radiographically this lesion generally appears as a well-demarcated radiolucency. In 75% of cases, it is associated with an unerupted tooth, usually the canine. It may contain radiopaque flecks, which represent calcified material.

#### **Non-pharmacological Treatment**

Enucleation is curative and recurrence is almost unknown.

### **16.12.1.4 Odontogenic Myxoma**

#### **Clinical Presentation**

- Clinically indistinguishable from ameloblastoma
- The radiographic appearance of this lesion is not distinctive. It appears quite like ameloblastoma (eg multilocular radiolucency).

#### **Investigation**

Confirmation is through histopathology

#### **Non-pharmacological treatment**

Wide excision is required.

### **16.12.2 Non Odontogenic Benign Tumours**

(Benign Osteogenic Tumours, Arise from Bone)

#### **16.12.2.1 Ewing's tumor**

#### **Clinical presentation**

- Painful swelling accompanied with fever.
- It is characterized by extraordinarily fast growth.

#### **Investigation**

Radiographically poorly defined solitary osteolytic lesion, irregular moth-eaten appearance which may be undetectable in serial images for a long period. Histological diagnosis is needed.

## **Pharmacological and Non-pharmacological Treatment**

The initial treatment is wide excision, if not possible radiation should be considered. Combination chemotherapy should be given.

### **16.12.2.2 Pregnancy Tumours**

#### **Clinical presentation**

- They most commonly appear after first trimester, grow rapidly, and typically regress after delivery.
- Found on the gingiva and arise predominantly.
- They are exophytic, lobulated, or smooth surfaced lesion with a red to purplish color and a soft, spongy texture.

#### **Non-pharmacological Treatment**

Surgical intervention is often not required. However, pregnancy tumors can be removed during the second trimester if they interfere with occlusion, are painful, bleed excessively, or are excessively large. Lesions excised during pregnancy often recur. After delivery, pregnancy tumors typically recede spontaneously but excision may be necessary for those cases which persist. Other non-odontogenic tumors are Osteomas, Myxomas, Chondromas, Central giant cell and Fibro-osteoma.

### **16.12.3 Benign Soft Tissues Non-Odontogenic Tumours**

#### **Haemangioma**

#### **Clinical presentation**

- Enlarged, vascular hamartoma appears as a painless, soft, smooth, or lobulated, sessile, or pedunculated mass but may ulcerate and possibly hemorrhage if traumatized
- The lesions present with deep red or bluish red in color and moderately firm to palpation.
- May occur on tongue, lips, buccal mucosa, gingiva, palatal mucosa, salivary glands, alveolar ridge, and jawbone.
- They occur early in life and may enlarge rapidly or progressively as the patient grows.

#### **Non-pharmacological Treatment**

Surgery can be beneficial if the lesion is small and has no risk of excessive bleeding. The potential for severe hemorrhage caused by the vascular nature of the lesion must be considered.

#### **Non-pharmacological Treatment of benign tumors**

Enucleation or excision is the treatment of choice depending on the type. Can be hemi mandibulectomy, total mandibulectomy, hemi maxillectomy or total maxillectomy. Followed with reconstruction when necessary.

#### **Pharmacological Treatment**

**S:** bleomycin injection intralesional (sclerotherapy) under ultrasound guidance to cause sclerosis of tissues. Surgery may follow if deemed necessary.

### **16.12.4 Malignant Soft and Bone**

#### **Tumours 16.12.4.1 Squamous cell carcinoma**

#### **Clinical presentation**

- A sore in the mouth that does not heal (most common symptom).
- Pain in the mouth.
- Persistent lump or thickening of mucosa in the cheek.
- Persistent white or red patch on the tongue, gums, tonsils, or lining of the mouth.
- Difficult moving jaw or tongue.
- Difficult chewing or swallowing.
- Enlarged cervical lymph nodes may be present.

**Note**

Take tissue biopsy of the lesion and send for histopathology investigation or refer the patient as early as possible to a centre where there is oral and maxillofacial surgeon and Histopathology unit.

**Treatment**

Palliative; but this depends on stage of the tumor: stage I and II surgical excision (squamous cell carcinoma) with wide margin then curative radiotherapy. Others, surgical excision, radiotherapy followed by chemotherapy.

**16.12.4.2 Lymphomas**

These are group of neoplasms of varying degrees of malignancy which are derived from B-cells of lymphoid tissues, the lymphocytes and histiocytes in any of their developmental stages.

**Burkitt's lymphoma (African Jaw Lymphoma)****Clinical presentation**

- It shows close association and infection with the Epstein Barr virus. Confined almost exclusively to children between 2–14years of age.
- Rapidly growing tumor mass of the jaws, destroying the bone and causing teeth loosening with extension the maxillary, ethmoid and sphenoid sinuses as well as the orbit.
- Visceral organ involvement also occurs.

**Note**

Diagnostic confirmation is through histopathology; hence, it is emphasized to do early detection and referral since Burkitt's lymphoma responds very quickly on chemotherapy. (For detailed management of malignant tumors please refer to the malignancy on chapter twenty-two)

**16.12.5. Odontogenic and Non- Odontogenic Cysts****Odontogenic cysts**

A group of jaw cysts that are formed from tissues involved in odontogenesis (tooth development). Odontogenic cysts are closed sacs filled with fluid, and have a distinct membrane derived from rests of odontogenic epithelium.

**Non-odontogenic jaw cysts**

A group of cysts arising from epithelial remnants of embryonic ducts left behind after embryonal facial and jaw development; they are located deep within the tissues in the region of former epithelial ridges, epithelial walls, and primary facial fissural and cleft structures. Some few examples of frequently encountered cysts I orofacial regions are:

**Dentigerous cyst**

Dentigerous cysts, also called follicular cysts, are slow-growing benign and non-inflammatory odontogenic cysts that are thought to be developmental in origin.

**Clinical presentation**

- Uninfected dentigerous cysts are painless and non - tender on palpation.
- Larger cysts cause a marked, smooth, rounded expansion of the bone, which may be reduced to a thin layer of cortical plate.

## **Investigation**

Radiographically, they usually present as a well-defined and unilocular radiolucency surrounding the crown of an unerupted or impacted tooth within the mandible.

## **Radicular (Apical) cyst**

Radicular cyst is an inflammatory jaw cyst originating from epithelial remnants of the periodontal ligament because of inflammation that is generally a consequence of pulp necrosis. The resulting cyst commonly involves the apex of the affected tooth either by dental caries or trauma.

## **Investigation**

Take OPG or Skull X-ray, the cysts appear as rounded, radiolucent areas sharply demarcated from normal. Apical periodontal cysts are associated with the roots of dead teeth bone by a thin, radiopaque, limiting line of compact or cortical bone.

## **Non pharmacological treatment**

Dental cystectomy under local or general anesthesia.

## **Globulomaxillary cyst**

The globulomaxillary cyst is a cyst that appears between a maxillary lateral incisor and the adjacent canine. The globulomaxillary cyst often causes the roots of adjacent teeth to diverge.

## **Investigation**

It exhibits as an "inverted pear-shaped radiolucency" on radiographs, or X-ray films.

## **Non-pharmacological Treatment**

Dental cystectomy under local or general anesthesia.

## **Dermoid Cyst**

Dermoid cysts are rare masses of the oral cavity derived from ectodermal elements. These are benign, slow-growing tumors that are typically asymptomatic but cause complications of inflammation or dysphagia, dystonia, and airway encroachment due to mass effects.

## **Clinical presentation**

- Massive swelling of the floor of the mouth, which had displaced the tongue cranially.
- Painless slowly growing cystic lesion in the sublingual and or submental spaces.
- A dentigerous cyst may be suspected where a tooth is missing from the arch without any history of previous extraction.

## **Non-pharmacological Treatment**

Enucleation through an external approach below the mandible or intraorally though an incision in the floor of the mouth.

## **Ranular Cyst**

A mucous extravasation cyst involving a sublingual gland and is a type of mucocele found on the floor of the mouth.

## **Clinical presentation**

- Translucent, blue, dome-shaped, fluctuant swelling in the tissues of the floor of the mouth.
- The swelling is not fixed, may not show blanching, and is non-painful unless it becomes secondarily infected.
- The usual location is lateral to the midline, which may be used to help distinguish it from a midline dermoid cyst.

## **Non-pharmacological Treatment**

Excision of sublingual salivary gland which is affected.

## **16:13 Management of Oral Conditions during Pregnancy**

The oral changes which are seen in pregnancy include gingivitis, gingival hyperplasia, pyogenic granuloma, and salivary changes. Gastric acid secretion and the reflux of the acid into the oral cavity leads to worsening of enamel erosion, increased caries risk, increased tooth mobility and loss.

### **For the first trimester (1-12weeks)**

During the first trimester, it is recommended that the patients be scheduled to assess their current dental health, to inform them of the changes that they should expect during their pregnancies, and to discuss on how to avoid maternal dental problems that may arise from these changes.

#### **Recommendations**

Educate the patients about the maternal oral changes which occur during pregnancy.

Emphasize strict oral hygiene instructions and thereby, plaque control.

Limit dental treatment to a periodontal prophylaxis, normal filling, and emergency treatments only.

Avoid routine radiographs. They should be used selectively and only whenever they are needed.

### **For the second trimester (13-24weeks)**

During the second trimester, the organogenesis is complete, and the risk to the foetus is low. The mother has also had time to adjust to her pregnancy, and the foetus has not grown to a potentially uncomfortable size that would make it difficult for the mother to remain still for long periods.

#### **Recommendations**

Maintenance of oral hygiene and plaque control.

It's safe to perform scaling, polishing and curettage if necessary.

Active oral diseases should be controlled.

It's safe to perform elective procedures i.e. Root canal, extraction, restorations.

Avoid routine radiographs. Use selectively and when they are needed.

### **For the third trimester (25-40weeks)**

The fetal growth continues and the focus of the concern now, is the risk to the upcoming birth process and the safety and comfort of the pregnant woman. It is safe to perform a routine dental treatment in the early part of the 3rd trimester.

#### **Recommendations**

Maintenance of oral hygiene and plaque control.

It's safe to perform scaling, polishing and curettage if necessary.

Active oral diseases should be controlled.

It's safe to perform elective procedures.

The radiograph use should be minimized.

Procedures not to be performed after mid time of the third trimester.

#### **Note**

Pregnancy should not be considered as an absolute reason to deny required dental care. Pregnant patients must be educated about the importance of maintaining good oral hygiene, expected changes in the oral cavity and routine dental visits.

## **16.14 Temporal Mandibular Disorder and Chronic Orofacial Pain**

Temporomandibular disorders (TMD) are disorders of the jaw muscles, temporomandibular joints, and the nerves associated with chronic facial pain.

### **16.14.1 Chronic Orofacial Pain other than Temporomandibular Disorders**

#### **16.14.1.1 Trigeminal Neuralgia**

A sudden, usually unilateral, severe, brief, stabbing, recurrent pain in the distribution of one or more branches of the fifth cranial nerve.

### **Clinical presentation**

- Episodes of severe, shooting, or stabbing pain that may feel like an electric shock.
- Spontaneous attacks of pain triggered by things such as touching the face, chewing, speaking, or brushing teeth.
- Pain in areas supplied by the trigeminal nerve, including the cheek, jaw, teeth, gums, lips, or less often the eye and forehead.
- Pain affecting one side of the face at a time.

#### **Note**

For details of the investigation and treatment refer a chapter eight (Central Nervous System).

### **16.14.1.2 Persistent Idiopathic Orofacial Pain (a Typical Facial Pain, a Typical Odontalgia)**

A persistent facial pain that does not have the characteristics of the cranial neuralgias and is not attributed to another disorder.

### **Clinical presentation**

- Poorly localized deep pain that does not follow anatomically defined patterns.
- Patients may have had multiple dental treatments to try and remove the pain.
- There is a female preponderance in the third to fourth decades.

### **Investigation**

Thorough clinical history and examination

Take radiographs of the dentition preferable OPG

### **Non-pharmacological Treatment**

Irreversible or invasive procedures should not be undertaken on teeth to try and relieve the pain if the clinical picture, vitality testing or radiographic examination would not support the procedure.

### **Pharmacological Treatment**

**A:** amitriptyline (PO) 25mg nocte 24hourly for 1month.

**AND**

**A:** carbamazepine (PO) 100mg 8hourly for 1month. Dosage can be increased up to 300mg at the same frequency and duration.

### **16.14.2 Temporomandibular Disorders (TMDs)**

A collective term embracing several clinical problems that involve the masticatory musculature, the temporomandibular joint and associated structures, or both.

### **Clinical presentation**

- Facial pain.
- Limitation of jaw motion.
- Muscle tenderness and stiffness.
- Along with any number of associated symptoms in the head, face, and neck region.

### **Non-pharmacological Treatment**

#### **Reassurance and counseling**

Provide counseling to the patient on the natural history and course of temporomandibular disorders, the role of stress and parafunctional habits such as clenching and grinding of the teeth, the frequency of the problem in the population, and the self-limited nature of the disorder.

### **Heat application**

Application of heat to the sides of the face with a heating pad, hot towel, or hot-water bottle. Vigorous treatment may be achieved with ultrasound or short-wave diathermy heat treatments, which are widely available in physiotherapy units.

## **Fabrication of Intraoral Occlusal Orthotic Appliances**

These devices are worn on the teeth like a retainer or a removable denture and are usually made of processed, hard acrylic.

## **Physiotherapy**

Perform manual manipulation, massage, and ultrasonography, which are helpful in reconditioning and retraining the masticatory and the other cranio-cervical muscles that are usually involved in temporomandibular disorders.

## **Pharmacological Treatment**

**A:** amitriptyline (PO) 25mg nocte for 1month.

If the treatment is successful, maintenance dose should be given for 2-4months.

## **16.14.3 Osteoarthritis and Rheumatoid arthritis of TMJ**

For details management of these two conditions, refer a chapter for disease of musculoskeletal system

# CHAPTER SEVENTEEN

## MUSCULOSKELETAL DISORDERS

### 17.1 Infections

#### 17.1.1 Osteomyelitis

Osteomyelitis is an infection of the bone or bone marrow caused by pyogenic bacteria or mycobacteria or fungi. This condition is most common in children under 12 years. *Staphylococcus aureus* are the most frequent responsible organisms. In patients with sickle cell disease *Salmonella* species become more common pathogens than in healthy hosts. Can be classified as acute or chronic depending on duration of symptoms.

#### Clinical presentation of acute osteomyelitis

- Fever, malaise severe pain at the site of infection, fatigue, irritability, restriction of movement (pseudo paralysis of limb in neonates) local edema, erythema, and tenderness
- A history of recent trauma, surgery, or infection of another organ If the infection is close to a joint there may be a 'sympathetic' effusion or concomitant septic arthritis.

#### Note

Risk Factor: Poor social economic status, immunosuppression and or malnutrition

#### Investigations

- Total and differential White Blood Cell count
- Erythrocyte sedimentation Rate
- C- Reactive protein
- Urinalysis
- Urine for Culture and Sensitivity
- Blood for culture and Sensitivity or
- Aspirated pus for culture and sensitivity
- Bone Biopsy for Culture and sensitivity
- Polymerase Chain Reaction (PCR ) for special case like *Kingella kingae* species
- Bone Scan using Technetium –99 in acute infection
- Ultrasound
- Plain X-ray
- CT scan in complex anatomical regions like shoulder, pelvic, spine

#### Pharmacological Treatment

**B:** cloxacillin (IV) 1–2g 6hourly then continue with ampicillin + cloxacillin (FDC) (PO) 500mg 8hourly to complete 3-6weeks course or until CRP and x ray become negative.

**OR**

**C:** ampicillin+sulbactam (FDC) (IV) 3g 6hourly for two weeks

**THEN**

**B:** amoxicillin+clavulanate (FDC)(PO) 625mg 12hourly for 4weeks.

#### Patients with penicillin allergy consider.

**S:** clindamycin (IV) 60mg 6hourly for 2weeks then orally to complete 4-6weeks

**AND**

**C:** ciprofloxacin (IV) 400mg 12hourly for 2weeks then orally to complete 4-6weeks

#### For sickle cell patient if salmonella spp is suspected consider

**C:** ciprofloxacin (IV) 400mg 12hourly for 4weeks, you may change to oral after 2weeks

#### Surgical management

Surgical drainage and bone window recommended in all cases presenting with history lasting > 24 hours,

#### Clinical presentation of chronic osteomyelitis

A patient with a history of osteomyelitis who is experiencing a recurrence of pain, erythema, and swelling in association with or without pus draining sinus

#### Investigations

- Total and differential White Blood Cell count
- Erythrocyte sedimentation Rate
- C- Reactive protein

- Stop antibiotic for two weeks before bone biopsy for culture and sensitivity
- Polymerase Chain Reaction (PCR) for special case like *Kingella kingae* species
- Bone Scan using Technetium –99 in acute infection
- Plain X-ray
- CT scan in complex anatomical regions like shoulder, pelvic, spine

### **Pharmacological management**

**B:** amoxicillin + clavulanate (FDC) (PO) 625mg 12hourly for 6weeks

### **Surgical management**

Extensive Surgical debridement of all devitalized tissue and dead bone, dead space filled with antibiotic beads,

### **Antibiotics cement mixture**

**S:** vancomycin at a dosage of 2–4g per 40g of cement

## **17.1.2 Septic Arthritis**

Inflammation of a synovial membrane with purulent effusion into the joint capsule, often due to bacterial infection, but can be caused by fungi and mycobacteria species. If not treated within 24 to 48hours may cause irreversible joint erosion, septicemia and can be fatal.

### **Clinical presentation**

As for acute osteomyelitis however this time sign and symptoms will be localized around the affected joint (refers Kocher's criteria in standard text book for clinical diagnosis )

### **Pharmacological Treatment**

Treat like acute osteomyelitis

### **Surgical drainage**

- Open surgery – incision and drainage followed by meticulous irrigation
- Laparoscopic drainage

## **17.1.3: Gonococcal Arthritis**

### **Pharmacological Treatment**

**A:** benzyl penicillin (IV) 2.5–5MU 6hourly for 7days

**AND**

**B:** ceftriaxone (IV) 1g 12hourly for 7days

**OR**

**S:** cefepime (IV) 2g 12hourly for 7days

### **Note**

- Adjust treatment basing on culture and sensitivity results.
- Repeat serial CRP, FBP, ESR starting 48hrs after initiation of appropriate treatment until normalize

### **Surgical drainage**

- Open surgery
- Laparoscopic drainage

## **17.1.4: Post Open Reduction and Internal Fixation or Arthroplasty Infection**

- Early < 4/52 post surgery and late >4/52

### **Clinical presentation of Post arthroplasty infection**

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>• Pain</li> <li>• Loss of ROM</li> <li>• Swelling</li> <li>• Local warmth</li> </ul> | <ul style="list-style-type: none"> <li>• Signs-sinus, effusion, wound erythema</li> <li>• X rays –periosteal reaction, subchondral bone resorption</li> </ul> |
|---|---|

## **Investigations**

- Total and differential White Blood Cell count
- Erythrocyte sedimentation Rate
- C - reactive protein
- Aspirated pus for culture and sensitivity
- Synovial or Bone Biopsy for Culture and sensitivity
- Bone Scan using Technetium –99m in acute infection
- Plain X-ray
- CT scan in complex anatomical regions like shoulder, pelvic, spine
- Magnetic Resonance Imaging (MRI) in Acute Stage

## **Pharmacological management**

**General Principal:** Start empirical treatment while awaiting culture and sensitivity results, adjust drug according to laboratory results, and continue treatment until CRP become negative.

**S:** vancomycin (IV) 1g 12hourly for 6weeks

**OR**

**S:** clindamycin (IV) 600mg 8hourly for 6weeks

**AND**

**D:** ceftazidime (IV) 2g 12hourly for 6weeks

**OR**

**S:** cefepime (IV) 2g 12hourly for 6 weeks

**OR**

**S:** meropenem (IV) 500mg to 1g 8hourly for 6weeks

## **Surgical management:**

- **Post arthroplasty infection**

Stage 1: Removal of prosthesis and replace with cement spacer or postalac and antibiotics for 6/52

Stage 2: Use of cement in re implantation and use -stemmed component

- **Surgical site infection posts open reduction and internal fixation**

Stage 1: Extensive surgical debridement, remove metal implant and replace with external fixation, traction or orthosis

Stage 2: Revision surgery once CRP and other inflammatory marker become negative

## **Supportive treatment for bone and joint infection**

- Rest and splintage of affected joint for 48hrs
- Nutritional support
- Addressing the predisposing condition
- Physiotherapy to improve range of motion of nearby joint
- Walking aid in case of pathological fracture
- Hydration
- Antipyretic for fever
- Analgesics for pain

## **17.1.5: Tropical Pyomyositis**

This is a condition whereby there is pyogenic infection of large muscle/muscles with extensive necrosis of the involved muscle. This condition occurs more commonly in the tropics, affecting immunocompromised individual than normal individual. The cause is uncertain since abscess multiple pockets explored early are sterile but later culture of the pus usually yields *Staphylococcus aureus*.

## **Clinical presentation**

Fever and painful induration/fluctuation of one or more of the large muscles, mostly in the lower extremities.

## **Investigations**

- Complete blood count (CBC)
- Erythrocyte sedimentation rate (ESR)
- C – Reactive Protein test (CRP)
- Ultrasound
- Plain X-ray
- Muscle biopsy for culture and sensitivity

## **Pharmacological Treatment**

Higher level facilities treatment should be guided by C/S results

### **Children**

- B:** cloxacillin (IV) 1–2g 6hourly for 7-14days  
**OR**
- A:** erythromycin (PO) 500mg 6-8hourly for 7-14days  
**OR**
- S:** vancomycin IV 1g 12hourly for 7days  
**OR**
- S:** clindamycin (IV) 600mg 8hourly for 7days

### **Adults**

- A:** erythromycin (PO) 500mg 6-8hourly for 7-14days;  
**OR**
- B:** amoxillin +clavulanate (FDC) (PO) 625mg 12hourly for 7-14days  
**OR**
- S:** clindamycin (IV) 600mg 8hourly for 7days  
**OR**
- S:** vancomycin (IV) 1g 12hourly for 7days

## **Surgical management**

Incision and drainage and irrigation with copious amount of 0.9% sodium chloride

### **17.1.6: Necrotizing Fasciitis**

Life threatening progressive rapidly spreading inflammatory infection located in deep fascia, most commonly caused by Streptococcus species or polymicrobial

#### **Clinical presentation of Necrotizing Fasciitis**

- Early Sign and symptoms mimic acute osteomyelitis.
- Foul smelling discharge
- Late-stage multiple discoloration develops a large area of gangrenous skin,
- Presence of features of toxic shock

#### **Investigations**

- Complete blood count (CBC)
- Erythrocyte sedimentation rate (ESR)
- C – Reactive Protein test (CRP)
- Ultrasound
- Plain X-ray
- Muscle biopsy for culture and sensitivity

## **Pharmacological Treatment**

- A:** gentamycin (IV) 80mg 8hourly for 7days

**AND**

- B:** chloramphenicol (IV) 500mg 6hourly **+/** **S:** clindamycin (IV) 600mg 8hourly for 7days

Alternatively

- A:** benzathine benzylpenicillin (IV) 2-4MU 6hourly for 7days

**AND**

- S:** clindamycin (IV) 600mg 8hourly **+/** ciprofloxacin 400mg (IV) 8hourly for 7days

Alternatively

- A:** benzathine benzylpenicillin (IV) 2-4MU 6hourly for 7days

**AND**

- S:** clindamycin 600mg (IV) 8hourly for 7days

**OR**

- S:** vancomycin 1g 12hourly for 7days

#### **Note**

Adjust treatment basing on culture and sensitivity results Repeat serial CRP, FBP, ESR starting 48hours after initiation of appropriate treatment until normalize.

## **Surgical management**

Serial extensive surgical debridement,

Skin grafting once the wound granulates with no sign of infection

## **Supportive treatment**

- Hydration
- Rest
- Nutritional support
- Addressing the predisposing condition
- Antipyretic for fever
- Analgesics for pain
- Physiotherapy to improve range of motion of nearby joint

## **17.2 Inflammatory Conditions**

These are a group of diverse inflammatory conditions due to different causes which affect joints and other musculoskeletal tissues.

### **General Guidelines**

- The first-line treatment is a non-steroidal anti-inflammatory drug (NSAID). This group includes medicines like aspirin, diclofenac and Ibuprofen, (provide dosage and scientific proof) but does NOT include paracetamol
- NSAIDs should be used cautiously in pregnancy, the elderly, and patients with asthma and liver or renal impairment.
- NSAIDs should be avoided in patients with bleeding disorders
- NSAIDs increases the risk of heart failure and stroke and should be avoided in patients with cardiovascular diseases and those who are at high risk
- NSAIDs should be avoided in patients with current or past peptic ulceration.
- NSAIDs should be taken with food
- If dyspeptic symptoms develop in a patient on NSAIDs, try adding magnesium trisilicate mixture. If dyspepsia persists and NSAID use considered essential antagonist
- Physiotherapy is a useful adjunct treatment in many inflammatory joint conditions

**Referral:** For patients with serious rheumatic disease and peptic ulceration should be referred to higher level health facility with adequate expertise and facilities.

### **17.2.1 Rheumatoid Arthritis**

Rheumatoid arthritis is an autoimmune condition whereby the immune system attacks the synovial membrane of joints, initially of the small joints but progressively involving the big joints. It is a chronic multisystem disease of unknown etiology.

#### **Clinical presentation**

Morning stiffness for >1hr, symmetrical swelling and inflammation of  $\geq 3$  joints (Elbow, Wrist, PIP, MCP, Ankle MTP) Rheumatoid nodule, subluxed joints.

#### **Target population**

Patients who

- Have at least 1 joint with definite clinical synovitis (swelling)
- With synovitis not better explained by another disease

**Table 17.1: Classification criteria for RA (score- based algorithm):**

add scores of categories A-D, A score of  $\geq 6/10$  is needed for classification of patient as having definite RA

Domain	Category	Point score
A	Joint involvement (0–5 points) <sup>a</sup>	
	1 large joint	0
	2–10 large joints	1
	1–3 small joints (large joints not counted)	2
	4–10 small joints (large joints not counted)	3
B	>10 joints including at least one small joint	5
	Serology (at least one test needed for classification: 0–3 points) <sup>b</sup>	
	Negative RF and negative ACPA	0
C	Low positive RF or low positive ACPA	2
	High positive RF or high positive ACPA	3
	Acute-phase reactants (at least one test needed for classification; 0–1 point) <sup>c</sup>	
	Normal CRP and normal ESR	0

D	Abnormal CRP or abnormal ESR	1
	Duration of symptoms	
	<6 weeks	0
	≥6 weeks	1

## Investigations

### Note

No test results are pathognomonic for RA instead they are potential identifier of disease progression and monitoring of response to treatment.

- Full Blood Picture with differential (FBP)
- Erythrocyte Sedimentation Rate (ESR)
- Rheumatoid factor (RF)
- C-Reactive Protein (CRP)
- Synovial Fluid analysis (WBC >@2000/ mm<sup>3</sup>)
- Antinuclear antibody Test
- Liver Function test
- Renal function Test
- Other test depending on stage of the disease and expert opinion.
- Anti-citrullinated protein antibody (more specific for Rheumatoid arthritis)

## Pharmacological Treatment

Non-steroidal anti-inflammatory drugs (NSAIDs) should be used in combination, corticosteroids or with DMARDs and once DMARDs are effective, NSAIDs and corticosteroids can be reduced in dose or discontinued.

### Non selective COX1 and COX2 Inhibitors, until symptoms subside

**A:** ibuprofen (PO) 400–800mg 8hourly for 5days

**OR**

**D:** meloxicam (PO) 7.5mg–15mg 12 hourly for 5-14 days

**OR**

**A:** Piroxicam 20mg (PO) 24hourly or 10mg 12hourly for 5-14days

### Selective COX 2 inhibitors

**S:** ketoprofen (PO) 50-75mg 8hourly for 7-14days

**OR**

**S:** dexketoprofen trometamol (PO) 12.5mg 6hourly or 25mg (PO) 8hrly for 7-14days

**OR**

### Corticosteroid Therapy

**A:** prednisolone (PO) 40mg for 3days then taper over a course of 2 to 4 weeks

**OR**

**D:** triamcinolone (IM) 40mg every 6weeks may be supplemented by additional IM PRN 20-100mg

**OR**

**D:** betamethasone dipropionate (Intralesional) 2mg + betamethasone sodium phosphate (Intralesional) 10mg once ; not to exceed(4ml) 24hourly repeat every after 2 to 12 weeks, maximum of 4 injections per year for a duration of 2years

### Disease-Modifying Ant-rheumatoid Drugs or DMARDs

**S:** hydroxychloroquine (PO) 400-600mg 24hourly for 4-12 weeks followed by (PO) 200-400 mg 24hourly for 12 weeks

**OR**

**D:** sulfasalazine (PO) 0.5 – 1g 24hourly in two divided doses increase weekly to maintenance dose of 2g/day (PO) for 12 weeks

**OR**

**S:** methotrexate (PO) may be taken with or without food 7.5mg dose weekly; increase PO dose to optimum response however should not exceed 20mg/week for 12 weeks.

### Note

- Repeat CRP and ESR after every two weeks to determine whether to increase dose or maintain or taper down.
- Patient who are using NSAIDs for more than 2 weeks should be given proton pump inhibitors
- Combine oral corticosteroid or NSAIDS with one of the DMARDs to control inflammation symptoms before DEMARDs become effective.
- Those on steroid should undergo RBG at least biannual.

### **Surgical treatment**

- Synovectomy
- Tenosynovectomy
- Tendon realignment
- Reconstructive surgery or arthroplasty
- Arthrodesis

### **Rehabilitation**

**Orthotics and splints:** Useful in decreasing pain and inflammation, improve function, reduce deformity, and restore joint alignment. Well-padded shoes

- Walking aids
  - Braces

### **Physiotherapy and occupational therapy**

- 30 minutes of daily aerobic exercises at least four times a week
- Occupational therapy aims at enabling patient to cope with activities of daily life.

## **17.2.2: Juvenile Idiopathic Arthritis**

Juvenile Idiopathic arthritis (JIA) is the most common chronic rheumatologic disease in children and is one of the most common chronic diseases of childhood. JIA should be considered with arthritis lasting for at least 6 weeks in children aged < 16 years. All the other causes should be excluded including infections, malignancies and hematological conditions like sickle cell anemia.

### **Clinical presentation**

History findings in children with JIA may include the following:

- Arthritis present for at least 6 weeks before diagnosis (mandatory for diagnosis of JIA)
- Either insidious or abrupt disease onset, often with morning stiffness or gelling phenomenon and arthralgia during the day
- Complaints of joint pain or abnormal joint use
- History of school absences or limited ability to participate in physical education classes
- Spiking fevers occurring once or twice each day at about the same time of day
- Evanescent rash on the trunk and extremities
- Psoriasis or subtler dermatologic manifestations

### **Types of JIA include the following:**

- Systemic-onset juvenile idiopathic arthritis
- Oligoarticular juvenile idiopathic arthritis
- Polyarticular juvenile idiopathic arthritis
- Psoriatic arthritis
- Enthesitis related arthritis
- Undifferentiated arthritis

### **Investigations**

- ESR and CRP
- Complete blood count (CBC)
- LFT
- Serum creatinine
- Antinuclear antibody (ANA) testing
- ASOT and Anti-DNAse B test
- Urinalysis additional.

### **Non-pharmacological Treatment**

- Psychosocial support
- Physiotherapy once the pain has subsided

### **Pharmacological Treatment**

**A:** ibuprofen (PO) 10mg/kg/dose 6-8hourly (should be given if the duration of arthritis has not reached 6 weeks)

**AND**

**A:** prednisolone (PO) 0.25-0.5mg/kg/day should be given in the initial stage of the treatment, and for patients that are responding slowly to treatment, duration should be not more than 6 months

**OR**

**S:** methotrexate (PO) 0.5mg/kg weekly (maximum 20mg)

Monitor for toxicity with FBP (leucopenia) and ALT (hepatotoxicity) every 1-3months.

Consider tapering and stopping treatment if the patient is in remission.

**OR**

**D:** Sulfasalazine (PO) 20-50mg/kg/day in two divided doses (maximum 2000mg/day)

### **17.2.3. Gout**

Gout is a recurrent acute arthritis of peripheral joints which results from deposition, in and about the joints and tendons, of crystals of monosodium urate from supersaturated hyperuricaemic body fluids. The arthritis may become chronic.

#### **Clinical presentation**

- The main clinical features are those of an acute gouty arthritis, often nocturnal, throbbing crushing or excruciating pain.
- The signs resemble an acute infection with swelling, hot red and very tender joints.
- The first metatarsophalangeal joint of the big toe is frequently involved

#### **Investigation**

- Serum uric acid level.

#### **Non-Pharmacological Treatment**

- In obese patient, reduce weight
- Avoid precipitants e.g. alcohol. Red meat
- Institute anti-hyperuricaemic therapy & adjust the dose depending on response to reduce uric acid synthesis
- Prevention or reversal of deposition of uric acid crystals in males

**Note:** Aim is to maintain serum uric acid level below 8mg/dl (0.48mmol/l)

### **Pharmacological Treatment**

#### **Acute state**

**A:** ibuprofen (PO) 400mg stat then 200mg 8hourly until 24 hours after relief of pain usually 3-5days.

**OR**

**A:** piroxicam 10–20mg (PO) once a day for 5days

**OR**

**A:** prednisolone (PO) is 40mg daily for 3days then taper for 2-4 weeks combined with NSAIDs and proton pump inhibitor

**OR**

**D:** methylprednisolone Injection **OR** triamcinolone **OR** Betamethasone for monoarticular flares (2vials for large joint and 1vial for small joints perday, repeat every after 2-12 weeks, maximum of 4 injections per year for a duration of 2years)

### **Anti –hyperuricemic therapy for chronic cases**

#### **1<sup>st</sup> line**

**B:** allopurinol (PO) 100mg 24hourly. This may be increased every 2-5weeks to until uric acid level reaches 6mg/dl or less. Maximum of 600mg daily continue therapy for 6months.

## 2<sup>nd</sup> line

**S:** febuxostat (PO) 10mg 24hourly for 4weeks then 20mg 24hourly for 4weeks then 40mg 24hourly may increase to reaches 6mg/dl or less. Continue treatment for 6months.

## Nutritional support

To prevent excessive accumulation of uric acid

- Use of low purine diet by restricting consumption red meat, fish, alcohol, stimulants, and high protein foods to avoid exogenous addition of purines to the existing high uric acid load is recommended
- Encourage consumption of alkalizing foods e.g. lemons, tomatoes, green beans, fruits and milk products
- Intake of fluids about 3lts/day to enhance excretion of uric acid based on assessment is recommended
- Moderate protein intake (0.8g/kg/day)
- Maintain adequate CHO intake to prevent ketosis
- Limit fat intake
- Avoid large and heavy meals late in the evening
- Encourage consumption of whole grains

## 17.2.4 Osteoarthritis

It is a common form of arthritis, characterized by degenerative loss of articular cartilage, subchondral bony sclerosis, and cartilage and bone proliferation subsequent osteophyte formation. Gradual onset of one or a few joints involved.

### Clinical presentation

- Pain is the commonest symptom
- Specific clinical features depend on the joint involved e.g. enlargement of distal interphalangeal joint (Bouchard's nodes)

### Investigation

- Plain X-ray of involved joint/ joints.
- Diagnostic arthroscopy
- CT scan
- Synovial fluid analysis

### Non-pharmacological Treatment

- Rest the joint. Use crutches or walkers to protect weight bearing joints in severe cases.
- Crepe bandage or braces also can be worn during the active phase of disease.
- Reduction of weight in obese patients
- Physiotherapy exercise to the affected joints, TENS

### Pharmacological Treatment

**A:** ibuprofen (PO) 400mg stat then 200mg 8hourly 7-14days

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly for 7-14days

**OR**

**D:** meloxicam (PO) 7.5-15mg 12hourly-24hourly for 7-14days

**OR**

**S:** dextketoprofen trometamol (PO) 12.5mg 4-6hourly or 25mg 8hourly for 7-14

**OR**

### Topical non-steroidal anti-inflammatory drugs

**A:** diclofenac gel 12hourly for 2weeks

**S:** ketoprofen gel 12hourly for 2weeks

**Note**

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2 weeks or more

- A:** omeprazole 20mg 24hourly  
**OR**  
**C:** pantoprazole 40mg 24hourly  
**OR**  
**S:** esomeprazole 40mg 24hourly  
**OR**  
**C:** lansoprazole 30mg 24hourly for 2-4 weeks  
**AND**  
**B:** tramadol (PO) 50mg 8hourly for 7-14days  
**OR**  
**B:** tramadol+paracetamol (PO) 550mg 8hourly for 14days  
**OR**  
**A:** ibuprofen+paracetamol (PO) 900mg 8hourly for 14days  
**AND**  
**A:** prednisolone (PO) 5-10mg 24hourly for

**Intra articular injection**

**D:** methylprednisolone (Intra articular) 80mg/ml for large joint and 40mg/ml for small joints per day repeat every after 2-12 weeks, maximum of 4injections per year for a duration of 2years.

**OR**

**S:** triamcinolone (Intra articular) 80mg/ml for large joint and 40mg/ml for small joints per day repeat every after 2-12 weeks, maximum of 4injections per year for a duration of 2years.

**OR**

**D:** betamethasone (Intra articular) 12mg/ml for large joint and 6mg/ml for small joints per day repeat every after 2-12 weeks, maximum of 4injections per year for a duration of 2years.

**AND**

**A:** 1% lignocaine 1-2mls.

**AND**

**S:** hyaluronic acid (Intra articular)16mg once per week for 3 consecutive weeks

**Supplements**

**S:** glucosamine sulfate1500mg +chondroitin sulfate 1200mg (FDC) (PO) taken with meal once a day for 3-6months

**Surgical management for advanced disease**

- High tibia osteotomy for Varus deformities of knee joint
- Fibula osteotomy for medial degeneration of the knee joint
- Total joint replacement
- Joint fusion /arthrodesis for limb salvage
- Excisional arthroplasty

**Note**

For patient who are not fit for surgery consider nerve block option and or radiofrequency ablation. Patient should be assessed every after two or four weeks to evaluate response to treatment and disease progression

## **17.2.5 Heterotopic Ossification**

Heterotopic ossification is defined as bone formation in non osseous tissues. Usually occurs in trauma such as fractures and surgical procedures, the exact cause remains unknown.

### **Clinical presentation**

- Pain and reduced ROM following trauma or post-surgical intervention.
- swelling and tenderness, which can mimic a low-grade infection.
- Bone in soft tissue starts to appear on plain radiographs 4 to 6 weeks after the trauma/surgery,

### **Pharmacological Treatment**

- Indomethacin 75- 150mg per day in single daily dose or divided dose 12hrly

### **Surgical management**

Surgery is delayed for 6 months after the initial trauma/surgery to allow the bone to mature and a distinct fibrous capsule to develop.

## **17.2.6 Tendinopathies**

These are clinical syndrome characterized by chronic, localized tendon pain exacerbated by mechanical loading. Caused mostly by tendon overuse and metabolic factors. Classified as Acute or Chronic.

### **Clinical presentation**

- Pain with palpation of the affected part
- Pain during tendon loading which may be also referred pain.
- Kinetic chain changes (muscle weakness, abnormal movement patterns or joint stiffness)
- Muscle spasm

### **Investigations**

- MRI for tendinopathy involving deep tendon like around the shoulder joint
- Greyscale or color Doppler uss.

### **Non-pharmacological Treatment**

- Physiotherapy (active exercise, stretching)
- Activity modification
- Correction of any biomechanical faults
- Reduction of aggravating activities
- Ice heat (chronic tendinopathy)
- Joint mobilization and friction (massage).

### **Pharmacological Treatment**

Pain management in acute state

**A:** ibuprofen (PO) 400mg stat then 200mg 8 hourly

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly for 7-14days

**OR**

**D:** meloxicam (PO) 7.5-15mg 12-24hourly for 7-14days

**OR**

**D:** tramadol + paracetamol (PO) 550mg 8hourly for 7- 14days

**OR**

**A:** paracetamol + ibuprofen (PO) 900mg 8hourly for 7-14days

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel applies 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

### **Note**

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2 weeks or more.

### **Proton pump inhibitors**

**A:** omeprazole (PO) 20mg 24hourly

**OR**

**C:** pantoprazole (PO) 40mg 24hourly

**OR**

### **Corticosteroid Therapy**

**A:** prednisolone (PO) 40mg 24hourly for 3days then taper down over 2-4weeks

**OR**

**D:** betamethasone (Intralesional) 12mg 24hourly; repeat every after 2-12 weeks, maximum of 4 injections per year for a duration of 2years.

**OR**

**S:** triamcinolone 40mg per injection site once weekly not to exceed 40mg/day maximum of 3 injections in one year at interval of 1-3 weeks between injections.

### **Surgery**

When no improvement after 6month of combined physiotherapy and medical treatment. Open surgery or laparoscopic

## **17.2.7 Plantar Fasciitis**

Planter Fasciitis is a degenerative disease of plantar fascia probably due to overuse trauma that leads to micro tears. Depending on duration of symptoms it can be acute 4-6 weeks, subacute 6-12 weeks and chronic >12weeks with/without refractory.

### **Clinical presentation**

- Pain in the medial side of the heel, most noticeable with initial steps after a period of inactivity
- Paresthesia
- Tightness of Achilles tendon

### **Investigations**

- Plain X-ray
- Ultrasound
- Nerve conduction and Electromyographic studies
- MRI in chronic with refractory.

### **Non-pharmacological Treatment**

- Weight reduction
- Rest and activity modification
- Stretching/massage
- Ice
- Night splints
- custom orthotic (for client with Pes cavus or planus)
- Extracorporeal shock wave therapy (ESWT) (for subacute and chronic)

### **Pharmacological Treatment**

Pain management in acute state

**A:** ibuprofen (PO) 400mg stat then 200mg 8hourly

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly for 7-14days

**OR**

**D:** meloxicam (PO) 7.5-15mg 12-24hourly for 7-14days

**OR**

**D:** tramadol and paracetamol (FDC) (PO) 550mg 8hourly for 14days

**OR**

**A:** ibuprofen and paracetamol (FDC) (PO) 900mg 8hourly for 14days

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel apply 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

**Note**

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2weeks or more.

**Proton pump inhibitors**

**A:** omeprazole 20mg 24hourly for 2weeks or more

**OR**

**C:** pantoprazole 40mg 24hourly for 2weeks or more

**OR**

**Corticosteroid Therapy**

**A:** prednisolone (PO) 40mg 24hourly for 3days then taper down over 2-4 weeks

**OR**

**S:** triamcinolone per injection site 40mg once weekly not to exceed 40mg/day repeat every after 2 to 12 weeks, maximum of 4 injections per year for a duration of 2 years

**OR**

**D:**betamethasone (Intralesional) 12mg 24hourly; repeat every after 2-12 weeks, maximum of 4 injections per year for a duration of 2years

**Surgery**

- Open partial plantar fascia release with simultaneous release of first branch of lateral plantar nerve or
- Endoscopic partial plantar fascia release

### 17.3: Metabolic Bone Diseases

#### 17.3.1 Osteoporosis and Brittle Bone Diseases

Disease which is characterized by low bone mass, microtextural disruption and skeletal fragility and it has no clinical manifestation until there is a fracture. Contrary to Brittle bone disease which are inheritable with many different phenotypic presentation, however medication for the treatment of these two disease are more or less similar.

**Clinical presentation**

- Presence of fragility fracture (spine, hip, wrist, humerus, rib and pelvis)
- Family history of osteoporotic fracture
- Bone pain

**Investigation**

- |  |                                   |
|--|-----------------------------------|
| • Complete blood count   | • Parathyroid stimulating hormone |
| • Dual-energy X-ray absorptiometry (DEXA) to measure spine and hip bone density as reference point | • Thyroid stimulating hormone     |
| • Serum 25-hydroxyvitamin D,   | • Serum creatinine                |
| • Serum Calcium  | • Urea                            |
|  | • Serum electrolyte               |

**Diagnostic criteria**

T-score chart based on the mineral density measurement by DXA. Osteoporosis is diagnosed when a person's BMD is equal to or more than 2.5 standard deviations below this reference measurement.

Status	Hip BMD
Normal	T-score of -1 or above
Osteopenia	T-score lower than -1 and greater than -2.5
Osteoporosis	T-score of -2.5 or lower
Severe osteoporosis	T-score of -2.5 or lower, and presence of at least one fragility fracture

## **Non-pharmacological Treatments**

- Fall prevention.
- Diet containing Calcium/vit D.
- Exercise
- Cessation of smoking
- Exposure to sunlight

## **Pharmacological Treatment**

### Pain management

**A:** ibuprofen (PO) 400mg start then 200mg 8hourly

**OR**

**D:** meloxicam 7.5-15mg (PO) once-twice a day for 7-14days

**OR**

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel applies 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

### Note

- Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2 weeks or more.

### Proton pump inhibitors

**A:** omeprazole 20mg 24hourly for 2weeks or more

**OR**

**C:** pantoprazole 40mg 24hourly for 2weeks or more

**OR**

### Calcium supplementation

**B:** Calcium 600mg + Vitamin D 800IU (PO) 24hourly for 3months then re-evaluate (1mcg of Vitamin D=40IU)

### **Bisphosphonate treatment – should be given for a period of five years.**

**S:** Ibandronate (IV) 3mg every 3months administered over 15-20minutes (treatment only)

## **17.3.2: Hypocholecalciferolemia (Vitamin D Deficiency)**

This disease is characterized by hypocalcemia and or hypophosphatemia. The acceptable concentration of Vitamin D is between 30-60ng/ML.

### **Clinical presentation**

#### **Adult**

Mild cases are generally asymptomatic

Bone pain and tenderness

Difficulty rising from a sitting position due to muscle weakness

Bone deformities (osteomalacia)

Cognitive decline and dementia

Inadequate dietary and supplemental vitamin D intake

#### **Children**

Mild cases are generally asymptomatic

Bone pain and tenderness

Muscle weakness

Delayed achievement of motor milestones

Fatigue and malaise

Rickets

### **Investigations**

- Serum calcium
- Serum alkaline phosphatase
- Parathyroid function test
- Fasting serum phosphate
- Serum 25-hydroxyvitamin D, (25(OH)D) levels
- Renal Function test
- Dual –energy X-ray absorptiometry (Bone density scan)

**Table 17.3: Interpretation of Serum 25-hydroxyvitamin D, (25(OH) D) levels**

Status	Endocrine Society Guidelines
Deficient	Below 20 ng/mL
Insufficient	21-29 ng/mL
Sufficient	30-60 ng/mL
Ideal	40-60 ng/mL
Considered safe	<100 ng/mL

**Non-pharmacological Treatment**

- Sunlight exposure
- Bracing
- Protective waking
- Isometric exercises

**Pharmacological Treatment**

Children 1-18 years

D: colecalciferol 2,000 IU 24 hourly for 6 weeks

**OR**

50,000IU once a week for 6 weeks followed by maintenance therapy of 600-1000IU 24 hourly for 3-6 months then reevaluate by measuring serum 25(OH)D levels

Adults

D: colecalciferol 6000IU 24 hourly or 50000IU once a week for 8 weeks or 6000IU followed by maintenance therapy of 1,500-2,000IU/day.

**17.4: Condition which may require Amputation.**

Amputation is the surgical removal of part of a limb or extremity such as an arm, leg, foot, hand, toe, or finger. This is the treatment of choice for diseased limbs and devastating extremity injuries for which attempts at salvage and reconstruction may be lengthy, emotionally, and financially costly and have a less than satisfactory results.

**Clinical Indication**

- Trauma most common reason for extremity amputation
- Infection
- Tumor
- Vascular disease
- Metabolic diseases
- Congenital anomalies

**Goals of amputation**

- Preserve functional length.
- Preservation of useful sensibility
- Prevention of symptomatic neuromas
- Prevention of adjacent joint contractures
- Early prosthetic fitting

Early return of patient to work and recreation.

**17.4.1: Diabetic Foot Ulcers**

A common surgical complication in diabetic patients. Ulcers can be secondarily infected by staphylococci, streptococci, coliforms, and anaerobic bacteria which can lead to cellulitis, abscess formation, gangrene, and osteomyelitis.

**Clinical presentation**

The three main factors that lead to tissue necrosis in the diabetic foot are:

- Neuropathy
- Infection
- Ischaemia

**Non-pharmacological Treatment**

- Metabolic control
- Relieve pressure: non-weight bearing

- Smoking cessation is essential.
- Wound care
- Frequent (e.g. weekly) removal of excess keratin and allow efficient drainage of the lesion.

### **Pharmacological Treatment**

**B:** ceftriaxone (IV) 1-2g 24hourly for 7-10days

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 7-10days

Depending on culture results

**S:** piperacillin-tazobactam (IV) 4.5g 6-8hourly 7-10days (for severe/complicated cases)

**OR**

**S:** meropenem (IV) 1g 8hourly 7-10days

### **Surgical Management**

- Surgical debridement
- Amputation depending Wagner's classification

**Table 17:4: Wagners Classification for Diabetic Foot Ulcers**

ULCER GRADING	DESCRIPTION
GRADE 0	No ulcer but high-risk foot
GRADE 1	Superficial ulcer
GRADE 2	Deep ulcer, no bony involvement or abscess
GRADE 3	Abscess with bony involvement (as shown by X-ray)
GRADE 4	Localized gangrene e.g toe, heel etc
GRADE 5	Extensive gangrene involving the whole foot

**Note**  
Grade 1-3 ulcers are termed non-gangrenous ulcers and Grade 4 and 5 ulcers are termed gangrenous ulcers

## **17.5 Affection of the Brain and Spine**

### **17.51 Low Back Pain**

Low back pain is a common presenting complaint especially among the adult population. Severity may range from mild, transient symptom to chronic and disabling pain. Causes of low back pain are numerous and clues to the underlying cause can usually be found from a good clinical history and physical examination. In some patients however, no cause will be found, and these people are described as having nonspecific back pain.

#### **Clinical presentation**

Exclude specific causes of low back pain, for example, suspected or confirmed malignancies, spine infection, spine trauma or inflammatory disease such as spondyloarthritis. (flag signs)

#### **Acute low back pain (pain for <6 weeks' duration)**

#### **Investigations**

- Explain to people with acute low back pain with or without sciatica that their pain is likely to resolve on analgesia and bed rest
- Do not routinely offer imaging for people with acute low back pain with or without sciatica in absence of flag signs. Consider imaging only if the result is likely to change management.

#### **Non-pharmacological Treatment**

**Self-management:** Provide people with advice and information, tailored to their needs and capabilities, to help them self-manage their low back pain.

- information on the nature of low back pain and sciatica
- encouragement to continue with normal activities upon pain relief.

**Physical Exercise:** Encourage exercise programmes (biomechanical, aerobics, or a combination of approaches) based on individual needs, preferences, and capabilities.

### **Pharmacological treatment**

The principles of pharmacological treatment include analgesics and muscle relaxants

**A:** ibuprofen (PO) 400mg stat then 200mg 8hourly

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly for 7-14days

**OR**

**D:** meloxicam (PO) 7.5-15mg 12hourly-24hourly for 7-14days

**OR**

For severe pain

**A:** diclofenac (IM) 75 mg 12hourly by deep IM injection for 1-3 days +/-

**B:** tramadol (IM) 100mg 12hourly by deep IM injection for 1-3days

**THEN**

**C:** diclofenac (PO) 50mg 8hourly for 7days +/-

**B:** tramadol (PO) 50mg 8hourly for up to 7days.

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel applies 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

#### **Note**

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2weeks or more

### **Proton pump inhibitors**

**A:** omeprazole 20mg 24hourly for 2weeks or more

**OR**

**C:** pantoprazole 40mg 24hourly for 2weeks or more

**OR**

**S:** esomeprazole 40mg 24hourly for 2weeks or more

**OR**

**C:** lansoprazole 30mg 24hourly for 2-4weeks

### **Muscle relaxant**

**S:** baclofen (PO) 5mg 8hourly initially, increase by 5mg/dose each after 3days up to 20mg 8hourly for up to 2weeks

**OR**

**S:** tizanidine (PO) initially 2mg 8hourly, increase gradually to 4mg per day every after 1-4days, dose may be extended for 4weeks or more, to discontinue taper gradually; decrease by 2-4mg daily.

### **Chronic Low Back Pain (pain for >6 weeks' duration)**

#### **Investigations**

- Plain Spine x rays
- Dynamic spine x Rays-Flexion/extension views
- Spine CT scan
- Spine MRI
- EMG can be considered for patients in whom the diagnosis is unclear after MRI

### **Non-pharmacological Treatment**

#### **Non Invasive treatment for chronic low back pain**

**Self-management:** Provide people with advice and information, tailored to their needs and capabilities, to help them self-manage their low back pain.

- information on the nature of low back pain and sciatica
- encouragement to continue with normal activities upon pain relief.

**Physical Exercise:** Encourage exercise programs (biomechanical, aerobics, or a combination of approaches) based on individual needs, preferences, and capabilities.

**Manual therapies:** Consider manual therapy (spinal manipulation, mobilization, or soft tissue techniques such as massage) for managing low back pain with or without sciatica, but only as part of a treatment package including exercises.

**Orthotics:** Consider belts or corsets for managing chronic low back pain with or without sciatica in selected cases

**Psychological therapy:** Consider psychological therapies using a cognitive behavioral approach for managing low back pain but only as part of a treatment package including exercise, spinal manipulation etc.

### Pharmacological Treatment

The principles of conservative treatment include:

- External spinal immobilization and supportive treatment with analgesics, muscle relaxants, bisphosphonates and bed rest
- Monitor for clinical or radiographic evidence of spinal instability and neurological deterioration.

**A:** ibuprofen (PO) 400mg stat then 200mg 8 hourly

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly for 7-14days

**OR**

**D:** meloxicam (PO) 7.5-15mg 12hourly-24hourly for 7-14days

**OR**

For severe pain

**A:** diclofenac (IM) 75mg 12hourly by deep IM injection for 1-3 days +/-

**B:** tramadol (IM) 100mg 12hourly by deep IM injection for 1-3days

**THEN**

**C:** diclofenac (PO) 50mg 8hourly for 14 days +/-

**B:** tramadol (PO) 50mg 8hourly for up to 14 days.

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel applies 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

#### Note

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2 weeks or more

Proton pump inhibitors

**A:** omeprazole (PO) 20mg 24hourly for 2-4 weeks

**OR**

**C:** pantoprazole (PO) 40mg 24hourly for 2-4 weeks

**OR**

**S:** esomeprazole (PO) 40mg 24hourly for 2-4 weeks

**OR**

**C:** lansoprazole (PO) 30mg 24hourly for 2-4 weeks

For radicular symptoms add neuromodulators, neurovitamins and muscle relaxants:

#### Neuromodulator

**D:** pregabalin (PO) 75-150mg 24hourly for 4weeks (dose can be escalated based on individual response)

**AND**

#### Neurovitamins

**C:** Vit B<sub>1</sub>+B<sub>6</sub>+B<sub>12</sub> (PO) 24hourly for 4weeks

**AND**

### **Muscle relaxant**

**S:** baclofen (PO) 5mg 8hourly initially, increase by 5mg/dose each after 3days up to-20mg 8hourly for up to 2 weeks  
**OR**

**S:** tizanidine (PO) initially 2mg 8hourly, increase gradually (PO) to 4mg 24hourly every after 1-4days, dose may be extended for 4weeks or more, to discontinue taper gradually; decrease by 2-4mg daily

### **Invasive treatments for Chronic Low Back Pain**

#### **Non-surgical interventions**

- Consider epidural injections of local anesthetic and steroid in people with severe refractory pain.
- Consider referral for assessment for radiofrequency (RF) denervation for people with chronic low back pain when non-surgical treatment has not worked for them and the main source of pain is thought to come from structures supplied by the medial branch nerve and they have moderate or severe levels of localized back pain, or surgical treatment is not possible due to other comorbid conditions.

#### **Surgical interventions**

- Spinal decompression: Consider spinal decompression for people with sciatica when non-surgical treatment has not improved pain or function and their radiological findings are consistent with their symptoms. The surgical approach might entail an open or minimal invasive technique based on patient factors, availability of resources and expertise.
- Spinal fusion: Consider spinal decompression and fusion with transpedicular screws and rods, or interbody devices in unstable spine patients when non-surgical treatment has not improved pain or function and their radiological findings are consistent with their symptoms. The surgical approach might entail an open or minimal invasive technique based on patient factors, availability of resources and expertise.

### **17.5.2: Cervical Degenerative Disorders**

Cervical degenerative spine disorders (DSD) are common among the adult population. Clinical characteristics include neck pain radiating to upper extremities related to compression and/or irritation of one or more cervical nerve roots, resulting into varying degrees of sensory, motor and reflex changes. Severity may range from mild, transient symptom to chronic and disabling pain.

#### **Clinical presentation**

- neck pain, dermatomal arm pain, scapular/periscapular pain
- upper limb paresthesias, numbness and sensory changes,
- muscle cramps, weakness, or abnormal deep tendon reflexes

#### **Investigations**

- Plain Spine x rays
- Dynamic spine x-Rays-Flexion/extension views
- Cervical Spine MRI
- EMG can be considered for patients in whom the diagnosis is unclear after MRI

#### **Non-pharmacological Treatment**

##### **Non Invasive treatment for neck pain and radiculopathies**

**Physical Exercise:** Encourage exercise programs based on individual needs, preferences, and capabilities.

**Manual therapies:** Consider manual therapy (spinal manipulation, mobilization, or soft tissue techniques such as massage) for managing pain as part of a treatment package including exercises.

**Orthotics:** Consider neck collars for managing neck pain with or without radicular symptoms

**Psychological therapy:** Emotional and cognitive factors (eg, job dissatisfaction) should be considered when addressing surgical or medical/interventional treatment for patients with cervical radiculopathy from degenerative disorders

#### **Pharmacological Treatment**

##### **For mild to moderate pain**

**A:** ibuprofen (PO) 400mg stat then 200mg 8hourly

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly for 7-14days

**OR**

**D:** meloxicam (PO) 7.5-15mg 12-24hourly for 7-14days

**OR**

#### For severe pain

**A:** diclofenac (IM) 75 mg 12 hourly by deep IM injection for 1-3 days +/-

**B:** tramadol (IM) 100mg 12hourly by deep IM injection for 1-3days

**THEN**

**C:** diclofenac (PO) 50mg 8hourly for 14days +/-

**B:** tramadol (PO) 50mg 8hourly for up to 14days.

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel applies 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

#### Note

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2 weeks or more

Proton pump inhibitors

**A:** omeprazole (PO) 20mg 24hourly for 2-4 weeks

**OR**

**C:** pantoprazole (PO) 40mg 24hourly for 2-4 weeks

**OR**

**S:** esomeprazole (PO) 40m24hourly for 2-4 weeks

**OR**

**C:** lansoprazole (PO) 30mg 24hourly for 2-4 weeks

**For radicular symptoms add neuromodulators, neurovitamins and muscle relaxants:**

#### Neuromodulator

**D:** Pregabalin (PO) 75-150mg24hourly for 4 weeks (dose can be escalated based on individual response)

**AND**

#### Neurovitamins

**C:** Vit B<sub>1</sub>+B<sub>6</sub>+B<sub>12</sub> (PO) once daily for 4 weeks

**AND**

#### Muscle relaxant

**S:** baclofen (PO) 5mg three times a day initially, increase by 5mg/dose each after 3days up to-20 mg 8hourly for up to 2 weeks

- **OR**

**S:** tizanidine (PO) initially 2mg 8hourly, increase gradually to 4mg 24hourly every after 1-4days, dose may be extended for 4weeks or more, to discontinue taper gradually; decrease by 2-4mg daily

#### Invasive treatments for Dervical Degenerative Disease

##### Non-surgical interventions

Consider transforaminal epidural steroid injections for severe symptoms while developing interventional or surgical plan of management.

##### Surgical interventions

- Spinal decompression: Surgical intervention is recommended for cervical myelopathy and suggested for relief of symptoms of cervical radiculopathy from degenerative disorders.
- The surgical technique (minimal invasive v/s open) approach via anterior/posterior or combined, and the appropriate implants required will be guided by patient factors, availability of resources and expertise.

### **17.5.3 Pyogenic Spondylodiscitis**

Spinal infections constitute an important clinical problem that often requires aggressive medical and surgical management to avoid serious complications and long-term sequelae. Common causative agents are *S. aureus*, *E. coli* and *Proteus spp.*

#### **Clinical presentation**

- Back pain,
- Fever,
- Muscle spasms
- Extremities weakness,
- Numbness,
- Paresthesias

#### **Investigations**

- CBC, ESR, CRP
- Blood and urine cultures
- Spine Xrays
- CT-guided biopsy or a surgical biopsy is advisable if diagnosis is uncertain Spine MRI with contrast
- Radionuclide bone scan

#### **Pharmacological treatment**

The principles of conservative treatment include:

- accurate microbiological diagnosis and treatment with appropriate antibiotics
- Treatment should include analgesics, antibiotics, muscle relaxants, bed rest and external spinal immobilization with spinal orthotics
- Monitor for clinical/radiographic evidence of spinal instability and neurological deterioration

#### **Pain management**

**A:** ibuprofen (PO) 400mg stat then 200mg 8hourly

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly

**OR**

**D:** Meloxicam (PO) 7.5-15mg 12-24hourly for 7-14days

**OR**

For severe pain

**A:** diclofenac (IM) 75mg 12hourly by deep IM injection for 1-3 days +/-

**B:** tramadol (IM) 100mg 12hourly by deep IM injection for 1-3days

**THEN**

**A:** diclofenac (PO) 50mg 8hourly for 14 days +/-

**B:** tramadol (PO) 50mg 8hourly for up to 14 days.

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel apply 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

#### **Note**

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2 weeks or more

#### **Proton pump inhibitors**

**A:** omeprazole (PO) 20mg 24hourly for 2-4weeks

**OR**

**C:** pantoprazole (PO) 40mg 24hourly for 2-4weeks

**OR**

**S:** esomeprazole (PO) 40mg 24hourly for 2-4weeks

**OR**

**C:** lansoprazole (PO) 30mg 24hourly for 2-4weeks

## **For radicular symptoms add neuromodulators, neurovitamins and muscle relaxants:**

### **Neuromodulators**

**D:** pregabalin (PO) 75-150mg 24hourly for 4 weeks (dose can be escalated based on individual response)

**AND**

### **Neurovitamins**

**C:** vit B<sub>1</sub>+B<sub>6</sub>+B<sub>12</sub> (PO) 24hourly for 4 weeks

**AND**

### **Muscle relaxant**

**S:** baclofen (PO) 5mg 8hourly initially, increase by 5mg/dose each after 3days up to 20 mg 8hourly for up to 2 weeks

**OR**

**S:** tizanidine (PO) initially 2 mg 8hourly, increase gradually to 4mg 24hourly after 1-4days, dose may be extended for 4weeks or more, to discontinue taper gradually; decrease by 2-4mg daily

### **Antibiotic treatment**

**B:** ceftriaxone (IV) 2g 12hourly for 4-6 weeks

**OR**

**C:** amoxicillin+clavulanate (IV) 1.2g 12hourly

**AND**

**B:** metronidazole (IV) 500mg 8hourly for 4-6 weeks

(shift to organism specific drugs after C/S results)

**Surgical management** for extensive debridement of the disc and vertebral bodies, and subsequent autologous bone grafting via a least disrupting approach to the stabilizing element is preferred in the following situations

- Failure to respond to conservative therapy.
- Significant or progressive neurologic deficits
- Large paraspinal abscess with local mass effect or septic embolization
- Progressive spine deformity with or without incapacitating spinal pain

## **17.5.4: Tuberculous Spondylodiscitis**

Tuberculous spondylodiscitis, also called Pott's disease is a common form of spinal infection that left untreated can result in serious complications and long-term sequelae.

### **Clinical presentation**

- Back pain,
- Fever,
- Muscle spasms
- Extremities weakness,
- Numbness, paresthesia
- Spine deformity

### **Investigations**

- CBC, ESR, CRP
- serology for HIV
- Chest x-rays
- Spine Xrays
- Spine CT scan

CT-guided biopsy or a surgical biopsy is advisable if diagnosis is uncertainSpine MRI with contrast

### **Pharmacological treatment**

The principles of conservative treatment include:

- antituberculous treatment in accordance with current national TB treatment guidelines
- supportive treatment with analgesics, muscle relaxants, bed rest and external spinal immobilization with spinal orthotics

### **Monitoring for clinical and radiographic evidence of spinal instability and neurological deterioration.**

**A:** ibuprofen (PO) 400mg stat then 200mg 8 hourly

**OR**

**C:** diclofenac sodium (PO) 50 mg 8hourly

**OR**

**D:** meloxicam (PO) 7.5-15mg 12-24hourly

**OR**

For severe pain

**A:** diclofenac (IM) 75 mg 12hourly by deep IM injection

**OR**

**B:** tramadol (IM) 100mg 12hourly by deep IM injection for 1-3days

**THEN**

**B:** tramadol (PO) 50mg 8hourly for up to 14days.

For radicular symptoms add neuromodulators, neurovitamins and muscle relaxants:

Neuromodulator

**D:** pregabalin (PO) 75-150mg 24hourly for 4 weeks (dose can be escalated based on individual response)

**AND**

Neurovitamins

**C:** vit B<sub>1</sub>+B<sub>6</sub>+B<sub>12</sub> (PO) once daily for 4 weeks

**AND**

Muscle relaxant

**S:** baclofen (PO) 10-20mg 8hourly for up to 2weeks

**OR**

**S:** tizanidine (PO) 2mg to 4mg 8hourly for up to 2weeks

### **Surgical management**

Surgical management for extensive debridement of the disc and vertebral bodies, and subsequent autologous bone grafting with or without instrumented spine stabilization via a least disrupting approach to the stabilizing element is preferred in the following situations;

- Failure to respond to pharmacological therapy.
- Progressive neurologic deficits from compromised neural structures.
- Large paraspinal abscess with local mass effect or septic embolization
- Progressive spine deformity

### **17.5.5: Osteoporotic Vertebral Compression Fractures (VCFs)**

Osteoporotic fractures are common in the elderly and in particular post-menopausal women. Vertebral compression fractures (VCFs) are among the most common types of osteoporotic fractures. Other causes of VCFs include primary or metastatic vertebrae tumors and chronic steroid usage.

#### **Clinical presentation**

- Severe back pain
- Extremities weakness,
- Numbness,
- Paresthesia
- Muscle spasms, Spine deformity

#### **Investigations**

- CBC, ESR, CRP
- Serum calcium levels
- Spine X-rays
- Spine CT scan
- Spine MRI with contrast
- Radionuclide bone scan

#### **Non-pharmacological Treatment**

Consider referral for image guided vertebral cement augmentation procedures in patients with poor response to medical treatment and spinal support.

- Vertebroplasty
- kyphoplasty

Surgical management—spinal decompression and instrumented stabilization in

- Progressive neurologic deficits from compromised neural structures.
- Progressive spine deformity with disabling pain.

## **Physical and occupational therapy**

- strengthening back muscle, balance training
- consider 3-5sessions of weight bearing exercises such's walking or jogging with each session lasting 45-60minutes
- also encourage aerobic low impact exercises such as walking and bicycling

## **General measures**

### **Behavioral modification**

Counsel on smoking cessations, and moderation of intake of alcohol, caffeine and encouraged to engage in physical activities

### **Fall prevention**

- installing handrails in bathroom, halls, stairways
- ensures hallways,stairwells and entrance are well lighted
- encourage patient to wear sturdy, low heeled shoes.
- Use of walking aid

## **Pharmacological Treatment**

The principles of conservative treatment include:

- External spinal immobilization and supportive treatment with analgesics, muscle relaxants, bisphosphonates and bed rest
- Monitor for clinical or radiographic evidence of spinal instability and neurological deterioration.

For mild pain provide one of the following NSAIDS as 1<sup>st</sup> line treatment

**A:** ibuprofen (PO) 400mg stat then 200mg 8hourly

**OR**

**C:** diclofenac sodium (PO) 50mg 8hourly for 7-14days

**OR**

**D:** meloxicam (PO) 7.5-15mg 12-24hourly for 7-14days

**OR**

For severe pain

**A:** diclofenac (IM) 75 mg 12 hourly by deep IM injection for 1-3 days +/-

**B:** tramadol (IM) 100mg 12hourly by deep IM injection for 1-3days

**THEN**

**A:** diclofenac (PO) 50mg 8hourly for 14 days +/-

**B:** tramadol (PO) 50 mg 8 hourly for up to 14 days.

Topical analgesics can be added in cases of severe pain,

**A:** diclofenac gel applies 12hourly

**OR**

**S:** ketoprofen gel apply 12hourly

### **Note**

Consider concomitant use of gastro protective treatment in patients with preexistent history of peptic ulcers or when giving NSAIDs for a duration of 2 weeks or more

Proton pump inhibitors

**A:** omeprazole (PO) 20mg 24hourly for 2-4weeks

**OR**

**C:** pantoprazole (PO) 40mg 24hourly for 2-4weeks

**OR**

**C:** lansoprazole (PO) 30mg 24hourly for 2-4weeks

**OR**

**S:** esomeprazole (PO) 40mg 24hourly for 2-4weeks

## **For radicular symptoms add neuromodulators, neurovitamins and muscle relaxants:**

### **Neuromodulators**

**D:** pregabalin 75-150mg 24hourly for 4weeks (dose can be escalated based on individual response)

**AND**

### **Neurovitamins**

**C:** vit B<sub>1</sub>+B<sub>6</sub>+B<sub>12</sub> (PO) 24hourly for 4weeks

**AND**

### **Muscle relaxant**

**S:** baclofen 5mg 8hourly initially, increase by 5mg/dose each after 3days up to 20 mg 8hourly for up to 2 weeks

**OR**

**S:** tizanidine initially 2mg 8hourly, increase gradually to 4mg per day every 1-4days, dose may be extended for 4weeks or more, to discontinue taper gradually; decrease by 2-4mg daily

### **Calcium supplementation**

**B:** Calcium 600mg + Vitamin D800IU (PO) 24hourly for 3 months then re evaluate (1mcg of Vitamin D=40 international unit)

Bisphosphonate treatment – should be given for a period of five years.

**S:** ibandronate (IV) 3mg every 3months administered over 15-20minutes (treatment only) for 5years

## **17.6: Common Congenital Anomalies of Musculoskeletal System**

### **17.6.1 Talipes equinovarus (congenital clubfoot)**

Talipes equinovarus is one of the most common musculoskeletal birth defect affecting approx. 1/1,000 live births. If untreated it causes long-term functional disability. The condition can vary in its degree of severity ranging from quite mild to very severe. It may present with other defects such as spina bifida, arthrogryposis, multiplex congenita, congenital myotonic dystrophy, or diastrophic dysplasia.

#### **Clinical presentation**

#### **Birth deformities of the foot with**

- Small foot and calf
- Cavus (tight intrinsics muscles)
- Adductus of forefoot (tight tibialis posterior)
- Varus (tight tendoachilles, tibialis posterior, tibialis anterior)
- Equinus (tight tendoachilles)

#### **Diagnosis**

- Most clinical diagnosis
- Plain X-ray

#### **Management**

##### **Non operative management - Ponseti method of serial manipulation and casting,**

The goal is to rotate foot laterally around a fixed talus, order of correction follows acronym (CAVE) 1. Cavus 2. Adductus 3. Varus 4. Equinus. Heel cord tenotomy needed in at least 80-90% of children. Followed by Foot abduction orthosis (FAO). Non noncompliance to FAO is the biggest risk factor for deformity recurrence

**Table 17:5: Ponseti Method**

Month 1-4	Weekly serial casting (with knee in 90° of flexion ) with forefoot supination, then forefoot abduction	<ul style="list-style-type: none"> <li>• First correct cavus with forefoot SUPINATED (NOT pronated) by aligning the less varus forefoot with the more varus hindfoot (pronation would increase cavus deformity)</li> <li>• Secondly correct adduction and heel varus by rotating calcaneus and forefoot around talus (head of talus acts as a fulcrum) into forefoot ABDUCTION</li> </ul>
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	Tendon Achilles lengthening (Tenotomy) (TAL) at week 8 required in > 80-90%	<ul style="list-style-type: none"> <li>• Equinus correction last with tendon Achilles tenotomy</li> <li>• Perform when foot is at least 60° abducted, heel is in valgus and equinus persists</li> <li>• Cast in maximal dorsiflexion for 3 weeks after tenotomy</li> </ul>
Month 4-8	Foot abduction orthosis (FAO) <ul style="list-style-type: none"> <li>• 23 hours a day for 3 months after correction</li> <li>• night time/nap time only until age 4 years</li> </ul>	<ul style="list-style-type: none"> <li>• With FAO holding affected feet at least 60° external rotation and 30° in normal foot for unilateral cases <input checked="" type="checkbox"/></li> <li>• Feet are measured prior to tenotomy so FAO is available on the day of post-tenotomy cast removal</li> </ul>
2-4 years	Tibialis anterior tendon transfer (TA transfer) at 2-5 yrs of age (30-50% will require)	<ul style="list-style-type: none"> <li>• 30-50% will need TA transfer with or without repeat TAL or gastrocnemius recession for recurrent deformity</li> <li>• Indicated if the patient demonstrates supination during gait</li> </ul>

### Operative management

- I. posteromedial soft tissue release and tendon lengthening for children of <2years
- II. medial column lengthening or lateral column-shortening osteotomy, or cuboid decancellation indicated for children older than 2years
- III. talectomy-n severe, rigid recurrent clubfoot in children between 6-10yeras or those with arthrogryposis

### Note

Surgical management are complemented by serial casting and foot adduction orthosis

## 17.7: Musculoskeletal Tumour

Musculoskeletal tumors are tumors that develop in muscles, bones and nerves. Bone tumors are divided into primary and secondary (metastatic) tumours. Primary tumours arise from cells which constitute the bone and are divided into benign and malignant types. Metastatic type is most common cause of bone cancer, the most common primary sites being renal, thyroid, lung, prostate, and breast.

### Clinical presentation

- Dull and aching pain which worsens at night is deemed a 'red flag' symptom
- Swelling where the tumor is located
- Pathological fracture
- Fever, weight loss, anemia and general body malaise are late symptoms

### Note

For detailed clinical presentations, investigations and management of specific bone tumor refer to malignancy chapter

## 17:8 Angular Deformity of Limbs

### 17.8.1 Rickets

Refers to softening and weakening of bones in children, usually due to inadequate vitamin D. Vitamin D promotes the body's absorption of calcium and phosphorus. Extreme or prolonged lack of vitamin D makes it difficult to maintain proper calcium and phosphorus levels in bones, which can cause rickets.

### Clinical presentation

- delayed growth,
- bow legs,
- weakness and pain in the spine,
- pelvis and leg

## **Pharmacological Treatment**

Treatment may involve adding vitamin D or calcium to the diet,

### **17.8.2 Physiological Bowing/Knocked Knees**

Is considered bending of knees at an early age due to early walking and overweight below the age of 2years

#### **Diagnosis process**

- I. Diagnosis is mainly by physical examination – obvious varus/valgus deformity and metaphysical widening.
- II. Blood tests to measure the levels of calcium and phosphate in the blood (**Refer to table 17:3.**)
- III. Bone X-rays to check for bone deformities.

#### **Treatment**

- First consultation: rule out if it's physiological – bow legs at young age before the age of 3 years without signs of rickets
- If it's physiological then consider follow up every 6 months +/- vitamin d supplements
- At the age of 3 years if deformity more than 8degrees consider-hemiepiphysiodesis at around the age of 3years if the deformity is due to Blount's disease consider hemiepiphysiodesis/corrective osteotomy.

#### **Note**

For details on specific surgical option kindly refer to standard orthopedic text books.

# CHAPTER NINETEEN

## METABOLIC AND ENDOCRINE DISEASE CONDITIONS

### 19.1 Diabetes Mellitus

Diabetes mellitus is a clinical syndrome characterized by persistently high blood glucose values due to deficiency or diminished effectiveness of insulin.

#### Classification

Diabetes mellitus can be classified as follows:

- Type 1 Diabetes Mellitus (T1DM) – due to autoimmune β-cell destruction
- Type 2 Diabetes Mellitus (T2DM) – due to a progressive loss of β-cell insulin secretion frequently with underlying insulin resistance
- Gestational Diabetes Mellitus (GDM) – diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation
- Specific types of diabetes – due to other causes e.g., monogenic, diseases of the exocrine pancreas and drugs or chemicals.

#### Diagnostic Criteria

- Main clinical features of diabetes are thirst, polydipsia, polyuria, tiredness, loss of weight, blurring of vision.
- Many people have no classical symptoms and may only present late with the symptoms related to complications e.g., pruritus vulvae and balanitis due to infections, paraesthesia or pain in the limbs, non-healing ulcers, and recurrent bacterial infections.

#### WHO diagnostic Criteria 2006

- Fasting plasma glucose level  $\geq 7.0 \text{ mmol/L (126 mg/dL)}$
- Plasma glucose  $\geq 11.1 \text{ mmol/L (200 mg/dL)}$  two hours after a 75 g oral glucose load in a glucose tolerance test
- Symptoms of hypoglycaemia and casual plasma glucose  $\geq 11.1 \text{ mmol/L (200 mg/dL)}$
- Glycated hemoglobin (HbA1c)  $\geq 6.5\%$ .

#### Diagnosis of gestational diabetes (WHO criteria 2013)

- Fasting plasma glucose 5.1–6.9 mmol/l
- 2-hour plasma glucose 8.5–11.0 mmol/l following a 75g oral glucose load.

#### Note

Fasting plasma glucose higher than 6.9 mmol/l or 2-hour plasma glucose higher than 11.0 mmol/l are considered overt diabetes rather than GDM

#### At risk screening

Early diagnosis and good control reduce the risk of costly complications and reduces the deterioration of islet function in T2DM. The following people should therefore be screened with fasting blood glucose or HbA1c **at least yearly** when they visit health facilities:

- Those aged  $\geq 40$  years
- Children and adults  $<40$  years who are overweight or obese and who have two or more additional risk factors for diabetes
- Individuals with impaired glucose tolerance or impaired fasting glucose or a history of a cardiovascular event
- People on long-term steroids or immunosuppressants
- Women with a history of gestational diabetes mellitus or polycystic ovary syndrome
- All pregnant women at the first antenatal visit if overweight, have had gestational diabetes, babies with birth weight  $>4$  kg, previous stillbirths or neonatal deaths. Screening should be repeated in the second trimester if negative.
- All women during the 2<sup>nd</sup> or 3<sup>rd</sup> trimester (for gestational diabetes).

#### Impaired glucose tolerance

For people with glucose intolerance the risk of T2DM and its associated mortality may be reduced by:

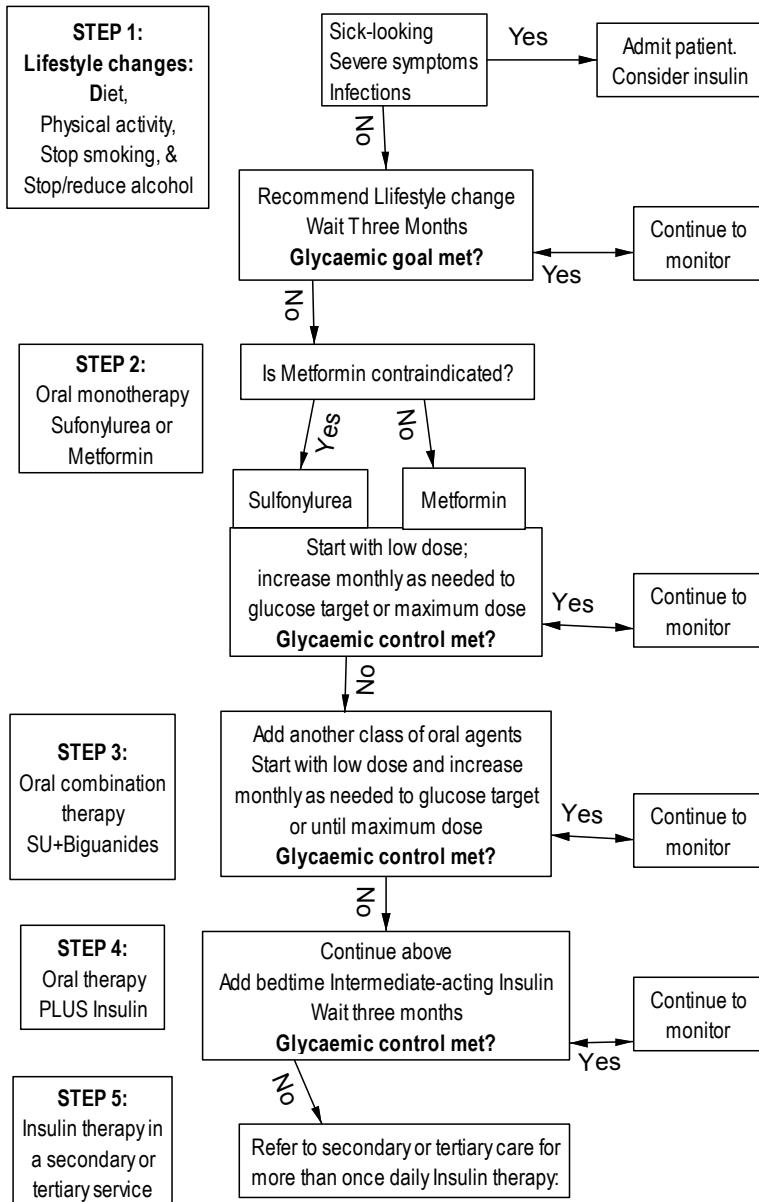
- dietary modification (see chapter on Nutrition)
- physical activity (see chapter on Nutrition)
- weight reduction
- medication with metformin.

### Goals of diabetes management

**Table 19.1: Goals for Optimum Management Of Diabetes**

Diet	Advise same as for people without diabetes
Body mass index	Therapeutic goal is 5–10% weight loss for people who are overweight or obese, but aim for BMI<25 kg/m <sup>2</sup>
Waist circumference	<102 cm for men, <88 cm for women
Physical activity	At least 30 minutes of moderate physical activity on most days of the week (total $\geq$ 150 minutes/week)
Cigarette consumption	0 per day
Alcohol consumption	Not more than 2 standard unit drinks (20 g) per day for men and 1 unit for women
Blood glucose level	Non-pregnant: 4–6 mmol/L fasting; 6–8 mmol/L postprandial Pregnant: $\leq$ 5.0 mmol/L fasting, $\leq$ 6.7 mmol/L postprandial Self-monitoring of blood glucose is essential to improve outcomes
HbA1c	Target $\leq$ 7% (6.5–7.5%). Should be measured every three months until stable, thereafter at least twice a year
Lipids	Total cholesterol: <5.2 mmol/L HDL-C: $\geq$ 1.0 mmol/L LDL-C: <2.6 mmol/L Triglycerides: <1.7 mmol/L
Blood pressure	Target $\leq$ 140/90 mmHg For those with albuminuria/proteinuria $<$ 130/80 mmHg
Urine albumin	Spot collection: <20 mg/L
	Urine albumin-to-creatinine ratio (UACR): women: <3.5 mg/mmol; men: <2.5 mg/mmol

## Algorithm for the Glycemic Management of T2DM



## Non-pharmacological Management

### Healthy lifestyles

#### Dietary control

- Objectives:
  - To meet requirements for growth and development, physical activity, and maintenance of desirable body weight. Majority of people with T2DM are overweight or obese and need to lose weight.
  - Attain and maintain near normal blood glucose levels to prevent hypo- and hyperglycaemia and so minimize the onset of chronic complications.
  - Attain optimum blood lipids and blood pressure control and so reduce the risk of macrovascular disease.
- Appropriate measures

- Each meal should consist of a variety of foods from the core food groups (vegetables, fruits, whole grains, meat and proteins, dairy products)
- Distribute foods evenly throughout the day with small/light meals in between the three main meals.
- Food composition
  - Protein: 15-20% of total energy (1g/kg/day)
  - Energy from carbohydrates: 45-60% of total calories
    - ✓ Less than 100gms carbohydrates per day is not advisable as it leads to ketosis
    - ✓ The distribution and amount of carbohydrates between meals should be synchronized with the action of insulin and drugs.
    - ✓ Distribute the food over three meals with snacks in between rather than 1 or 2 large meals
    - ✓ Give more of carbohydrate as complex starches e.g. whole grain cereals, whole grain bread, roots and stem tubers, because they breakdown more slowly to release glucose.
    - ✓ Avoid simple sugars, sugar-sweetened beverages and honey.
  - Fats should provide < 30% of energy
    - ✓ A lower fat intake of up to 20% or less of the daily energy in case of obese adult with diabetes.
  - Limit salt to less than 1 teaspoonful/day
  - Limit fat intake
- Physical activity
  - Aerobic (e.g. brisk walking) and muscle strengthening activities improve glucose tolerance, energy expenditure, feeling of wellbeing and mood, work capacity, improved blood pressure, lipid profiles and increased functional mobility in older people.
  - Adjust medicine dosages and or food intake to avoid hypoglycaemia.
- No smoking
- Avoid or limit alcohol intake to one drink/day for women, two drinks/day for men.

## **Pharmacological Treatment**

### **Treatment with oral hypoglycemics**

- Review the blood glucose at follow-up clinic and adjust medicines as needed until blood glucose is controlled.
- If lifestyle measures on their own failure achieve blood glucose control or blood glucose levels are persistently high (fasting >11 mmol/l or random >15 mmol/l) initiate:

**A:** metformin (PO) 500mg 12hourly with or after meals. Increase, as required, until a maximum of 2000mg in 2–3 divided doses.

If Metformin is contraindicated, then use

**A:** glibenclamide (PO) 2.5–10mg 12hourly

**OR**

**C:** glimepiride (PO) 1–4mg 12hourly

**OR**

**A:** gliclazide (PO) 40–160mg 12hourly

- If the maximum dose of metformin does not result in adequate glycaemic control, either one of the above sulphonylureas may be added, starting with the lower dose and increasing until control is achieved or the maximum dose is reached.
- If a combination of both medicines is still inadequate, then insulin should be added as detailed below in the section on insulin.

#### **Note**

- Activity of sulphonylureas is prolonged in both hepatic and renal failure
- Metformin is contraindicated in those with severe renal, liver and cardiac failure.
- The lower dosage is appropriate when initiating treatment in elderly patients with uncertain meal schedules, or in patients with mild hyperglycemia
- Sulphonylureas are best taken 15 to 30 minutes before meals

## **Treatment with Insulin Injection in Type 2 Diabetes**

Insulin injections are indicated in T2DM in the following conditions:

- Initial presentation with fasting blood glucose more than 15 mmol/l
- Presentation in hyperglycaemic emergency
- Peri-operative period especially major or emergency surgery
- Other medical conditions requiring tight glycaemic control
- Organ failure: Renal, liver, heart etc,
- Diabetes not well controlled with diet or oral drugs
- Latent autoimmune diabetes of adults (LADA)
- Contraindications to oral drugs

**Note**

The maximum glucose lowering efficacy of oral drugs is usually evident by six months. Therefore, the efficacy of any added therapy must be assessed within six months and an alternative drug instituted in case of failure

Insulin injections should be initiated by a doctor able to fully instruct the patient in its use but insulin will be available at lower health facilities for management of stable patients who require prescription refills.

**Table 19.2: Types of Insulin as per WHO Essential Medicine List**

Type of Insulin	Name	Basal or short acting
Short acting	A: Insulin—short acting (human) soluble	Short acting
Intermediate acting	A: Insulin—intermediate acting (human)	Basal
Pre-mixed insulin	A: Intermediate and short acting insulin (70/30)	Basal + Short acting

**Insulin as substitution therapy**

Oral medicines are discontinued (except metformin if patient is obese)

**S:** Pre-mixed insulin is introduced at a dosage of 0.2 IU/kg body weight and this is split into:  
½ in the morning and ½ in the evening

- Inject 30 minutes before the morning and the evening meals for human insulins
- Inject 0 to 15minutes before meal for analog insulins.

**Insulin as supplemental therapy**

Oral medicines are continued

**A:** neutral protamine hagedorn (isophane) insulin administered at night before 22:00h at a total daily dose of 0.1–0.2 IU/kg body weight.

- The oral medicines are continued (half maximum dose of sulphonylureas and metformin dose of 2 g/day)
- Blood glucose levels are monitored.

**Self-monitoring in patients with T2DM**

Self-Monitoring Blood Glucose (SMBG) is usually recommended in the following patients:

- patients on insulin and glucose lowering agents that can cause hypoglycaemia (sulphonylureas)
- when monitoring hyperglycaemia arising from illness
- with pregnancy and pre-pregnancy planning
- when changes in treatment, lifestyle or other conditions requires data on glycaemic patterns
- when HbA1c estimations are unreliable (eg haemoglobinopathies)

**TYPE 1 Diabetes Mellitus (Childhood diabetes) Non-pharmacological Treatment**

- Nutrition (refer to nutrition chapter)
- Exercise requirements are as for children without diabetes
- Psychological support is important to cope with this chronic illness.

**Pharmacological Treatment**

Total dose of insulin contains soluble and intermediate/long-acting insulin.

- Give total dose of insulin
  - pre puberty 0.5 IU/kg/day subcutaneously for life
  - puberty 1-2 IU/kg/day subcutaneously for life
  - after puberty < 2 IU/kg/day subcutaneously for life
- Divide total insulin dose as per recommended percentage below

**Table 19.3: Recommended Insulin Dosage**

Time	Type of insulin	Proportion
Break-fast	Short acting	30% of total daily dose
Lunch	Short acting	20% of total daily dose
Supper	Short acting	10% of total daily dose
Bedtime	Long/intermediate acting	40% of total daily dose

#### Note

- Diabetes in children is often misdiagnosed as some other condition – e.g. as pneumonia or asthma (laboured breathing),
- Insulin should be given for life and the dose adjusted according to weight and glucose response
- Self-glucose monitoring by glucometer at home 3-4times/day
- Pre-mixed insulins not advised in children

#### Clinical monitoring of people with diabetes

**Table 19.4: Clinical Monitoring of People with Diabetes**

Initial visit	3 Month visit	Annual visit
History and diagnosis Physical examination <ul style="list-style-type: none"> <li>• Height and weight</li> <li>• Waist/Hip circumference</li> <li>• Blood pressure</li> <li>• Detailed foot examination</li> <li>• Tooth inspection</li> <li>• Eye examination</li> <li>• Visual acuity+ Fundoscopy</li> <li>• ECG</li> <li>• Biochemistry               <ul style="list-style-type: none"> <li>◦ Blood sugar</li> <li>◦ Glycosylated Haemoglobin (HbA1c)</li> <li>◦ Lipid profile (TC, HDC, LDLC, TG)</li> <li>◦ Serum creatinine</li> <li>◦ Urine: glucose, ketones, protein</li> </ul> </li> <li>• Education</li> <li>• Nutritional advice</li> <li>• Medication if needed</li> </ul>	<ul style="list-style-type: none"> <li>• Relevant history</li> <li>• Weight</li> <li>• Blood pressure</li> <li>• Foot inspection</li> <li>• Blood Glucose</li> <li>• Urine protein</li> <li>• Education advice</li> <li>• Nutrition advice</li> <li>• Review therapy</li> <li>• HbA1c every six months</li> </ul>	History and examination – as at initial visit  Biochemistry as at initial visit

TC=Total cholesterol, HDLC=high density lipoprotein, LDLC= low density lipoprotein, G=Triglycerides

#### Surgery in diabetes

##### General measures

Correct pre-operative management depends on type of surgery (major or minor), type of diabetes and recent diabetes control.

- Surgery should be delayed if possible if HbA1C >9% or blood glucose fasting >10 mmol/l or random glucose > 13 mmol/l.
- Screen for nephropathy, cardiac disease, retinopathy and neuropathy and inform surgical team.

##### If diabetes is well controlled and surgery is minor:

- If on diet or oral agent therapy, omit therapy on morning of surgery and resume therapy when eating normally
- For T1DM, continue with normal dose of insulin

### If on insulin therapy or poor glycaemic control or major surgery:

- Use continuous IV insulin infusion
- Start at 8 am and stop when eating normally.
- Monitor blood glucose before, during and after surgery: aim for blood glucose levels of 6–10 mmol/l.

### For major surgery (glucose-insulin potassium regimen)

- Once snack is missed, start an IV regimen irrespective of the size of the procedure
- Maintain insulin administration (hourly) to avoid lipolysis and ketoacidosis in patients with restricted oral intake and thus prevent DKA
- Administer 5% dextrose in maintenance IV fluids AND
- Short-acting insulin (16 Units) + KCl 10mmol/L added to 500mls of 10% dextrose.
  - Infuse at 80ml/hr IV.
  - If obese or initial blood glucose is high (>14mmol/l) consider higher dose of insulin (20 Units)
  - If very thin or usual insulin dose is very low, consider lower dose (12 Units)
- Monitor blood glucose levels hourly (aim for 6–10 mmol/l)
  - If blood glucose is low or falling reduce dose by 4 Units
  - If blood glucose is high or raising increase dose by 4 Units
- Patients receiving Multiple Daily Insulin Therapy (MDIT) should receive preoperative basal insulin dose without interruption in the perioperative period. When oral intake is restricted, regular insulin may be given every 4–6 hrs to control hyperglycemia. When a diet is tolerated, the MDIT regimen should be resumed
- Post operatively: give 5–10% dextrose IV 1 litre + KCl 20ml + 2/3 of total daily dose of insulin over 8hrs and repeat until able to take orally. Continue the infusion until 60 minutes after the first meal.
- Resume usual therapy after first meal
- Check electrolytes daily.

## 19.2 Management of Diabetes During Religious Fasting

There are several types of fasting:

- Normal fast (the common fast): the person abstains from all foods but can take water for a limited time.
- Total fast = total abstinence from both food and water. This should not go beyond a maximum of three days and is not recommended for those people taking insulin secretagogues or insulin.
- Partial fast = abstain from selected foods and drinks, or omit a certain meal each of the fasting days.

### Those with very poor glucose control should be discouraged from fasting

- A total fast is not recommended for anyone with diabetes. Adequate hydration is important even during the period of fasting.
- For those on insulin, a partial fast is preferred to total or normal forms of fasting.
- Self-blood glucose monitoring is mandatory for people with diabetes who elect to fast.
  - Once-a-day is adequate for patients on diet only or diet with metformin.
  - At least 3 times a day in patients on insulin secretagogues
  - More frequently if hyperglycaemia is marked and the urine tested for ketones.
- Consider terminating the fast if frequent hypoglycaemia or intercurrent infections.
- Vigorous activity should be avoided during period of fast.
- Ensure ready access to a healthcare provider during the period of fast.

### Management of normal fasting for people treated with oral hypoglycaemic agents

- Fasting is possible in this situation.
- Usual dietary advice should be followed at this time.
- Patients on metformin, alpha-glucosidase inhibitors and thiazolidinediones (glitazones) can continue taking the usual doses at the usual times.
- If on a second or third generation sulphonylurea (glibenclamide, gliclazide, glipizide, glimepiride), this should be taken at the time of breaking the fast and not before dawn.

### **Management of normal fasting for T2DM patients on insulin**

- If on once daily insulin before bed, this can be given as usual
- If on twice daily short- and intermediate-acting insulin:
  - Before the dawn meal, give the usual evening dose of short-acting insulin without any intermediate-acting insulin.
  - Before the evening meal give the usual morning dose of short-acting and intermediate-acting insulin.
- If on basal bolus regimen:
  - Usual doses of the short-acting insulin can be given before the dawn and evening meals, and usual doses of the intermediate-acting insulin can still be given at 10pm.
  - Regular SBGM is essential to ensure prevention of hypoglycaemia
  - Titration of doses should occur according to SBGM results.
- Neither the insulin injection nor the breaking of the skin for SBGM will break the fast.

### **Management of other fasting types**

**Table 19.4: Types of Fasting and Recommended Diabetic Treatment**

Treatment regimen	Fasting regimen	When to take antidiabetic agents
Diet only	Total, normal or partial fast	Not applicable
Metformin, Thiazolidinediones	Normal or partial fast	With meals
Insulin secretagogues Sulphonylureas	Partial fast	Before meals
Daily intermediate or long-acting insulin	Partial fast	Before first meal
Multiple insulin doses using intermediate and short acting insulin	Avoid fasting	Not applicable
Long-acting plus bolus fast acting insulin	Avoid fasting or partial fast	Lantus am and analogue with meals

### **19.3 Hyperglycaemia in Pregnancy**

Gestational Diabetes Mellitus (GDM) is any degree of glucose intolerance first recognized in pregnancy. Diabetes in pregnancy refers to those with pre-existing diabetes, whether diagnosed or not.

#### **Screening at first antenatal visit**

- Perform screening in all women at the first antenatal clinic attendance if they have:
  - BMI > 25 kg/m<sup>2</sup>
  - previous history of GDM
  - previous big baby
  - poor obstetric history
  - family history of DM
  - known impaired glucose tolerance/impaired fasting glucose.
  - grand multipara
  - glycosuria.
- Women in early pregnancy with levels of HbA1c ≥ 6.5% or blood glucose levels fasting ≥ 7.0 mmol/l or two hours ≥ 11.1 mmol/l which are diagnostic of diabetes should be treated as having pre-existing diabetes.
- Women with HbA1c 6.0–6.4%, fasting glucose 5.1–6.9 mmol/l or two-hour glucose 8.6–11.0 mmol/l should be assessed to determine the need for immediate home glucose monitoring and, if the diagnosis remains unclear, assessed for gestational diabetes by 75 g oral glucose tolerance test (OGTT) at 24–28 weeks.

#### **Screening later in Pregnancy**

- All women with risk factors (see above) should have a 75 g OGTT at 24–28 weeks
- A fasting plasma glucose at 24–28 weeks is recommended in low-risk women

#### **Non-pharmacological Treatments**

- All women intending to become pregnant should:

- Be encouraged to achieve excellent glycaemic control using glucose monitoring of both fasting and postprandial values
- Be prescribed high-dose (5mg) pre-pregnancy folate supplementation, continuing up to 12 weeks' gestation
- Have an eye exam and be informed of the risk of developing and/or progression of diabetic retinopathy
- Have a kidney assessment (random urine albumin/creatinine ratio and serum creatinine) and referred if urine protein  $\geq 1\text{ g}$ .
- A combined health-care team (obstetrician, diabetologist or internist, diabetes educator, pediatrician/neonatologist) is required.
- Review SMBG, blood pressure and urine protein and ketones by dipstick at each visit and eye examination in each trimester.
- Target glycaemia:
  - Preprandial blood glucose 3.5–5.5mmol/L
  - Postprandial blood glucose 5–7.5mmol/L
- Lifestyle management is the preferred means of managing gestational diabetes.
  - Diet is based on the principles of optimal nutrition and controlled weight gain.
  - Exercise can be helpful in lowering BG levels: the most acceptable form of exercise for most women is walking in their normal daily routine.
- Glucose-lowering therapy should be considered in addition to diet where fasting or two hours glucose levels are above target, for example, where two or more values per fortnight are:
  - fasting or preprandial  $\geq 5.5\text{ mmol/L}$ , or two hours postprandial  $\geq 7\text{ mmol/L}$  at  $\leq 35\text{ weeks}$
  - fasting or preprandial  $\geq 5.5\text{ mmol/L}$ , or two hours postprandial  $\geq 8\text{ mmol/L}$  at  $> 35\text{ weeks}$
  - any postprandial values are  $> 9\text{ mmol/L}$ .
- When pharmacological treatment of gestational diabetes is indicated, insulin and oral medications are equivalent in efficacy, and either can be an appropriate first-line therapy.

### **Pharmacological Treatment**

**A:** metformin 500 mg 12hourly, maximum 2000mg in 2–3 doses

**OR**

**A:** glibenclamide 2.5mg 24hourly to a maximum of 10mg daily

#### **Note**

Oral hypoglycaemics (except for metformin and glibenclamide) are contraindicated in pregnancy

### **Insulin**

The rapid-acting insulin analogs (lispro and aspart) lower postprandial blood glucose and decrease the risk of nocturnal hypoglycemia. Patients on lispro and aspart prior to conception may continue them during pregnancy. Patients on regular insulin may be switched to lispro or aspart if 1-hour postprandial blood glucose levels are above target and/or the patient is also experiencing pre-meal or nocturnal hypoglycemia.

### **Postnatal Follow Up**

- Women with gestational diabetes should be screened at 6–12 weeks postnatal to ensure return to normal glucose tolerance. Thereafter, a 1–2 yearly follow up is recommended.
- Metformin and glibenclamide may be used even if a woman is breastfeeding. Encourage women to breastfeed.
- If retinopathy, check eyes 1 year postpartum

### **19.4 Diabetes and HIV**

The management of people with both diabetes and HIV need to consider the following:

- ARVs are associated with increased metabolic dysfunction, including insulin resistance, dyslipidemia and lipodystrophy
- Protease inhibitors (PIs) increase insulin resistance and reduce insulin secretion by interfering with GLUT-4 mediated glucose transport
- Standards of treatment and management of diabetes for patients with HIV are generally the same as those for diabetic patients without HIV and patients who acquire HIV may continue to be managed with the same drug therapy as before

- Sulfonylureas may not be effective in the face of severe insulin resistance. In case glycemic control deteriorates, insulin should be initiated, rather than increasing dosage or number of oral medications
- People who are on ARTs need to be screened for diabetes at least once a year and especially if they have other CVD risk factors

## **19.5 Diabetes and Tuberculosis**

Diabetes and tuberculosis are interlinked as follows:

- People attending TB clinics should be screened for diabetes and those attending diabetes clinics should be screened for TB if presenting with symptoms.
- Diabetes may be associated with delayed sputum conversion (>60 days), higher probability of tuberculosis treatment failure, higher recurrence and relapse rates, higher overall mortality, higher rates of multi-drug resistance TB and more atypical presentation in hyperosmolar hyperglycemic nonketotic coma or ketoacidosis
- For both conditions, controlling blood sugar, being more physically active, avoiding chronic stress, getting enough sleep and maintaining ideal weight are recommended.

### **Review Drug Requirements**

- Rifampicin is a potent hepatic enzyme-inducing agent, accelerates the metabolism of oral hypoglycemic agents and shortens the plasma half-life of sulphonylureas
- Isoniazid antagonizes sulphonylureas, impairs insulin release and action and leads to increased requirement of insulin and oral antidiabetic medication
- Therefore, people with diabetes may require an increase in dosage of antidiabetic medication if they develop tuberculosis.

### **Use Oral Antidiabetic Medicines Carefully in Tuberculosis**

- People with diabetes mellitus and tuberculosis should be treated with insulin injection, or in case a diabetic with tuberculosis is on oral hypoglycemic agents, it may be necessary to switch to insulin.
- Tuberculosis affects both the liver and pancreas: oral antidiabetic drugs are contraindicated in hepatic disease, which is a common adverse effect of antituberculous therapy.
- Metformin produces weight loss, particularly in high doses, and it is also an anorectic.
- Marked weight loss and higher insulin and caloric needs in tuberculosis are other important indications for reviewing oral antidiabetic therapy in diabetes mellitus.

## **19.6 Hypoglycaemia**

Hypoglycaemia is defined as blood glucose <3.9mmol/L.

### **Diagnostic Criteria**

- Hunger
- Sweating
- Trembling or shaking
- Anxiety
- Dizziness
- Lightheadedness
- Palpitation
- Numbness around the lips and fingers
- Headache
- Confusion
- Lack of concentration
- Weakness
- Changes in behaviour (e.g. irritability, tearfulness, crying), paraesthesiae.

Patients may also present with convulsions, seizures or coma due to delayed corrective action or impaired hypoglycaemia awareness where the patient loses the ability to detect the early symptoms of hypoglycaemia due to repeated episodes of mild hypoglycaemia or long duration of diabetes leading to loss of adrenergic and glucagon response, with eventual loss of adrenergic and neuroglycopenic symptoms.

### **Non-pharmacological**

#### **Treatment for conscious Patients:**

Quickly take a glass of a sugar-rich drink

**OR**

Eat one table spoon of sugar or honey

**AND**

Have a meal.

If symptoms persist after 5 minutes repeat the above.

#### Treatment for unconscious Patients:

**C:** 50% dextrose (IV) (40–50ml)

**OR**

**C:** 10% dextrose (IV) (200–300ml).

- Repeat if patient is not responsive or if after 15 minutes, the blood glucose is still below 4mmol/l.
- Follow by 8–10 % glucose infusion. Use 5% dextrose if the higher concentrations are not available.

**OR**

**S:** glucagon (IM or SC) 1mg stat

#### Note

If IV access is impossible, consider nasogastric tube or rectal glucose

#### On Recovery

- Give long-acting carbohydrate snack e.g. a piece of bread
- Identify the cause of hypoglycaemia and correct it
- If hypoglycaemia is a result of long acting sulphonylureas, long- or intermediate acting insulin or alcohol, frequently monitor blood glucose (hourly) and give IV dextrose infusion (5–10%) for 12–24 hours
- If patient is not responding look for another cause or refer.

### 19.7 Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic States

These are acute metabolic complications of diabetes mellitus that may lead to severe dehydration, altered level of consciousness and electrolyte imbalance. The presence of acidosis, ketonemia and ketonuria in diabetic ketoacidosis (DKA) differentiates it from hyperglycemic hyperosmolar state (HHS).

#### Symptoms

- |                          |                           |
|--------------------------|---------------------------|
| • Nausea/vomiting        | • Abdominal pain          |
| • Shortness of breath    | • Fever                   |
| • Obtundation/drowsiness | • Altered mental function |
| • Thirst/polyuria        | • Dehydration             |
| • Fruity smelling breath | • Lethargy                |
| • Confusion              | • Coma                    |

#### Note

- When you suspect DKA, confirm diagnosis immediately
- All patients minimum should be admitted in hospital for intensive management

Table: 19.5: Diagnostic Criteria for DKA and HHS

Parameter	Mild DKA	Moderate DKA	Severe DKA	HHS
Blood Glucose	>13.9	>13.9	>13.9	>30
Arterial PH	7.25-7.3	7.00-7.24	<7.00	>7.30
Serum bicarbonate	15-18	10-15	<10	>18
Urine ketones	Positive	Positive	Positive	Small
Serum ketones	Positive	Positive	Positive	Small
Serum osmolality	Variable	Variable	Variable	>320
Alteration in sensorium	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

#### Investigations

Apart from the ones in the table above, check serum electrolytes, urea and creatinine.

#### DKA and HHS Treatment

Treatment of DKA and HHS is similar.

- Frequent monitoring of patients
- Improvement of circulatory volume and tissue perfusion

- Replacement of electrolyte losses (potassium)
- Administration of insulin
- Careful search and management of the precipitating causes

With proper treatment, the average time to resolution is between 10–18 hours for DKA and ~9–11 hours for HHS.

#### I. Fluid management protocol

- The first step - infusion of isotonic saline to expand extracellular volume and stabilize cardiovascular status. Fluid replacement alone results in:
  - Improvement of hyperglycemia, reduce insulin resistance
  - lowering the plasma osmolality,
  - reducing vasoconstriction and improving perfusion,
  - restores renal perfusion
  - Reduce insulin resistance by ↓ stress/counterregulatory hormone levels
- Both DKA and HHS patients have severe volume depletion -- estimated water deficit of 100mls/kg body weight
- Usual initial fluid → isotonic saline (0.9% NaCl)
- Optimal rate of fluid infusion depends on the clinical state of the patient. On average **15 to 20 ml/kg/hour (about 1000 ml/hour) max. <50ml/kg in the first four hours.**

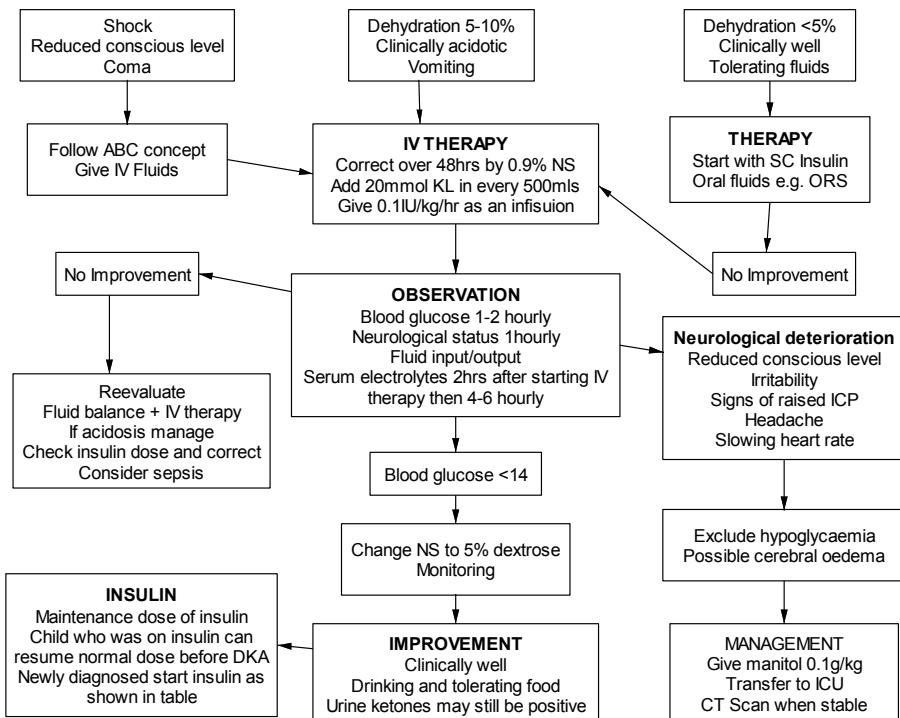
#### For children

- Detailed management of DKA is presented in the algorithm for management of paediatric diabetic ketoacidosis in low resource centre below.
- Give NS or RL for 48 hours
- Fluid Requirements = DEFICIT + 48 hours' maintenance

**Table: 19.6: Maintenance Fluid**

Age (years)	Weight (kg)	Maintenance fluid (ml/kg/hr)
<1	3-9	80
1-5	10-19	70
6-9	20-29	60
10-14	30-50	50
>15	>50	30

## Management of Diabetic Ketoacidosis in Low Resource Centre



## II. Electrolyte management protocol

Almost all patients with DKA or HHS have a substantial potassium deficit.

- Acidosis –shift to extracellular
- Urinary losses related to the glucose osmotic diuresis
- Secondary hyperaldosteronism.
- Loss is high 3-10mEq/kg

**Despite total body potassium deficit, concentration is usually normal or elevated due to**

- insulin deficiency and hyperosmolality
- both result in potassium movement out of the cells
- Insulin treatment reverse distribution

**Good approach checks ECG for signs of hyperkalemia (peaked T wave, QRS widening)**

- Give KCL if signs absent and if  $K^+ < 5.3$
- If Patient oliguric give KCL when  $K^+ < 4$  or ECG signs of hypokalemia (U wave)

**Table 19.7: Potassium Repletion in DKA and HHS**

$K^+ > 5.2 \text{ mEq/L}$	Do not give $K^+$ initially, but check serum $K^+$ with basic metabolic profile every 2 h
$K^+ < 3.3 \text{ mEq/L}$	Hold insulin and give $K^+$ 20-30 mEq/hr until $K^+ > 3.3 \text{ mEq/L}$
$K^+ = 3.3-5.2 \text{ mEq/L}$	Give 20-30 mEq $K^+$ in each L of IV fluid to maintain serum $K^+$ 4-5 mEq/L

**Delay insulin treatment until the serum potassium is above 3.3 mEq/L**

- insulin Rx worsen hypokalemia by driving potassium into the cells.
- To avoid possible arrhythmias, cardiac arrest, and respiratory muscle weakness

### **III. Insulin therapy management protocol**

*Continuous IV infusion of regular insulin is the treatment of choice*

- Correct hypovolemic shock and hypokalemia if present, before starting insulin
- Low dose IV insulin for both DKA and HHS
- Serum potassium <3.3 mEq/L only contraindication for insulin

IV regular/Soluble insulin and rapid-acting insulin analogs are equally effective

### **Insulin therapy**

- Lowers serum glucose concentration ( $\downarrow$  hepatic glucose production  $>>$   $\uparrow$  peripheral utilization)
- Diminishes ketone production (reducing both lipolysis and glucagon secretion)
- Augment ketone utilization.

### **Conventional Insulin Guidelines**

Both HHS and moderate to severe DKA

- IV bolus of regular insulin (0.1 U/kg body weight) followed within 5 minutes by a continuous infusion of regular insulin of 0.1 U/Kg/hour = 7 U/hour in a 70 kg patient
- Alternatively, omit bolus dose → continuous IV infusion of regular insulin at a rate of 0.14 U/kg per hour (equivalent to 10 U/hour in a 70 kg patient)
  - But bolus insulin is a priming dose, saturates insulin receptors full before continuous insulin
  - Avoid lag time in achieving steady state insulin levels
    - ✓ In practice -100iu in 100mls of NS titrate in 5-7cc/h in the first 24hours
    - ✓ Or 60iu in 60mls of NS titrate 6-7cc/hour in 24hours
- Insulin dosing same in DKA and HHS
- If plasma glucose does not decrease by 2.8-4.2mmol/l in the first hour, increase the infusion rate of insulin by 50% to 100%
- Optimal rate of glucose declines 5.5mmol/l/hour
- Glucose drop not allowed to less than 14mmol/l during first 4-5hrs of treatment.
- It takes 12-24 hours to clear ketones from circulation after hyperglycemia is controlled

## **19.8 Diabetes and Cardiovascular Diseases**

Diabetic patients are 2–4 times likely to develop cardiovascular diseases mainly due to atherosclerosis and hypertension.

The clinical spectrum of cardiovascular diseases includes:

- Coronary heart disease
- Angina (which may be silent)
- Acute coronary artery syndrome
- Congestive cardiac failure
- Sudden death
- Cerebral vascular accident (stroke, transient ischaemic attacks and dementia)
- Peripheral vascular disease (intermittent claudication, foot ulcer and gangrene).

### **Assessment (annual)**

- ECG, Chest X-Ray, if with symptoms/signs of heart failure.
- Peripheral vascular disease evaluation includes doppler and angiography of lower limbs.

### **Pharmacological Treatment**

#### **Acute coronary syndrome**

All adults with T2DM and recent acute coronary syndrome and/or coronary stent should receive dual anti-platelet therapy for 12 months after the event or procedure:

**A:** acetyl salicylic acid (PO) 75–100mg 24hourly

**AND**

**D:** clopidogrel (PO) 75mg 24hourly

#### **Note**

- acetyl salicylic acid is also indicated for primary prevention for people with T2DM >40years with family history of ischaemic heart disease (IHD), cigarette smoking, obesity, proteinuria, or dyslipidemia.
- It is contraindicated in peptic/duodenal ulcer, dyspepsia, heartburn, malignant hypertension, haemorrhagic stroke.

## **Hyperlipidaemia**

Statin therapy results in a significant decrease in CVD morbidity and mortality in T2DM and are indicated in Type 2 diabetics > 40 years of age, or diabetes for > 10years

**B:** atorvastatin (PO) 10mg 24hourly. Dose may be increased to 80mg daily if required.

**OR**

**S:** rosuvastatin (PO) 10mg 24hourly. Dose may be increased to 40mg daily if required

Fenofibrate reduces incidence of retinopathy and need for laser surgery, peripheral neuropathy, and improvement in proteinuria, suggesting a more generalized effect on microvascular disease independent of dyslipidaemia.

- **Fibrates:**

- Should be used in mixed hyperlipidemias which have not responded adequately to diet or other therapy.
- Are more effective in lowering triglycerides and increasing HDL, but less effective in lowering cholesterol.
- Should be used with caution in combination with statins.
- Can enhance the effects of warfarin and antidiabetic agents
- Are contraindicated in patients taking Orlistat.

**D:** fenofibrate (PO) 67–267mg 24hourly

## **Hypertension**

In people with T2DM, antihypertensive therapy with an angiotensin receptor blockers (ARB) or angiotensin-converting enzyme inhibitors (ACEI) decreases the rate of progression of albuminuria, promotes regression to normal albuminuria and may reduce the risk of decline in renal function.

Therefore:

- BP-lowering therapy in people with diabetes should preferentially include an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) e.g.

**C:** enalapril (PO) 10 – 40mg 24hourly, taken either as a single dose or two divided doses  
(enalapril (PO) 5 mg–10mg 12hourly)

**OR**

**C:** losartan (PO) initial dose 50mg stat. Maintenance dose; losartan (PO) 25–100mg 24 hourly in single or 2 divided doses.

- The target level for optimum BP is controversial. It is reasonable to target BP levels of <140/90 mmHg for people with diabetes, with lower targets for younger people and those at high risk of stroke. The target BP for people with diabetes and microalbuminuria or proteinuria remains <130/80 mmHg.
- Combining an ARB and an ACEI is not recommended.
- If monotherapy does not sufficiently reduce blood pressure add one of the following:

**C:** amlodipine (PO) 5–10mg 24hourly

**OR**

**A:** bendrofluazide (PO) 5mg 24hourly

- ACE-inhibitors and ARBs should be stopped pre-conception. Diltiazem (PO) 60mg 24hourly may be a useful substitute.

## **19.9 Diabetic Peripheral Neuropathy**

All patients should be screened for distal symmetric polyneuropathy starting at diagnosis of T2DM and at least annually thereafter.

### **Diagnostic Criteria**

- Unsteady gait
- Burning, aching pain or tenderness in legs or feet (occurring at rest or at night, not related to exercise)
- Prickling sensations in legs and feet (occurring at rest or at night, distal>proximal, stocking glove distribution)
- Numbness in legs or feet (distal>proximal, stocking glove distribution)
- History of previous foot ulceration and/or amputation.

### **Investigations** Test for:

- Sensation (10g monofilament or cotton wool)
- Vibration (128Hz tuning fork)
- Postural hypotension and pulse (tibial and dorsalis)
- Inspect foot for structural abnormalities and ulceration.

### **Pharmacological Treatment**

It is difficult to treat. Some of the drugs used include:

**D:** pregabalin (PO) 75-150mg (24hourly–12hourly) for 4weeks

Tricyclic antidepressants may help

**A:** amitriptyline (PO) 25-75mg 24hourly

**OR**

**C:** imipramine (PO) 100mg 24hourly

### **Gastroparesis**

Due to autonomic neuropathy

**C:** metoclopramide (PO) 10mg 8hourly

**OR**

**D:** domperidone (PO) 10mg 8hourly

### **Diabetic Foot:**

Give foot care education and advice on appropriate footwear.

## **19.10 Diabetic Nephropathy**

It is one of the most important causes of chronic renal failure. Persistent microalbuminuria is both a marker for the development of overt nephropathy and cardiovascular risk. Patients with microalbuminuria who progress to macroalbuminuria ( $>300 \text{ mg/24 h.}$ ) are likely to progress to end-stage renal disease over a period of years. Patients with diabetes and chronic kidney disease (CKD) should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease.

### **Non-pharmacological Treatment**

Patients with diabetes and CKD should be advised to:

Intensify management of modifiable risk factors:

- Stop smoking.
- Treat urinary infection aggressively.
- Avoid drugs toxic to the kidney.
- Consume an individualized diet high in vegetables, fruits, whole grains, fiber, legumes, plant-based proteins, unsaturated fats, and nuts; and lower in processed meats, refined carbohydrates, and sweetened beverages
- Undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance

### **Pharmacological Treatment**

- Renin–angiotensin system (RAS) inhibition is recommended for patients with albuminuria and hypertension
- Most patients with T2D, CKD, and eGFR  $\Rightarrow 30 \text{ ml/min per } 1.73 \text{ m}^2$  would benefit from treatment with both metformin and an SGLT2i.
- Patient preferences, comorbidities, eGFR, and cost should guide selection of additional drugs to manage glycemia, when needed, with glucagon-like peptide-1 receptor agonist (GLP-1 RA) generally preferred.

**A:** metformin (PO) 500mg or 850mg (12hourly – 24 hourly); usual maintenance dose: 1g twice daily

### **SGLT-2 Inhibitors**

**S:** empagliflozin (PO) 10–25mg 24hourly

- Advise contraception in women who are receiving ACEI or ARB therapy and discontinue these agents in women who are considering pregnancy or who become pregnant.

- Monitor serum creatinine and potassium annually and more frequently if there is evidence of renal impairment.
- Hyperkalaemia associated with the use of an ACEI or ARB can often be managed by measures to reduce serum potassium levels rather than decreasing the dose or stopping the ACEI or ARB immediately
  - Avoid potassium-containing salt substitute or food products containing the salt substitute.
  - Avoid drugs that can impair kidney excretion of potassium: over-the-counter nonsteroidal anti-inflammatory drugs, supplements, and herbal treatments
  - Avoid constipation by ensuring enough fluid intake and exercise.
  - Consider diuretics treatment to enhance the excretion of potassium in the kidneys especially when there is concomitant volume overload or hypertension.
  - Consider oral sodium bicarbonate especially in patients with CKD and metabolic acidosis.
- Metformin should not be used once the serum creatinine is  $> 200 \mu\text{mol/l}$ .
- Treat blood pressure aggressively with target of  $< 130/80 \text{ mmHg}$ .
- Add diuretics if necessary (but in large doses inhibit insulin release).

## 19.11 Diabetic Retinopathy

It is one of the major causes of blindness. Poor glycaemic control, nephropathy, hypertension and pregnancy, long duration of diabetes are among the risk factors. It is preventable and its progression retarded by improved glycaemic control and blood pressure. Screening for early detection and laser therapy can prevent blindness.

### Screening for Diabetic Retinopathy

For all people with diabetes, yearly screening is necessary for early detection of ocular complications. The screening should begin:

- Comprehensive eye examination in woman planning pregnancy, and during the first trimester, preferably at booking of antenatal clinic (ANC). Further screening should be determined by the degree of retinopathy detected at the initial appointment.
- Five years after the diagnosis of diabetes for individuals with Type 1 diabetes diagnosed after puberty (around 14years).
- At puberty for individuals diagnosed with type 1 diabetes before puberty
- At the time of diagnosis of diabetes for individuals with type 2 diabetes

For each of the scheduled screening visits, detailed patient's assessment should include a complete ophthalmic examination in the following steps:

- a. Take visual acuity (VA) without and with spectacles
- b. If VA less than 6/9 take VA with pin hole
- c. Dilate the pupil by using the mydriatic agents (Tropicamide)
- d. Identify presence of cataract or other causes of media opacification.
- e. Perform retinal evaluation by direct or indirect Ophthalmoscope or Fundus Photography
- f. Identify retinal changes, document and if applicable grade the diabetic retinopathy and maculopathy as shown in Table XX.
- g. Explain the results of screening to the patient and schedule rescreening (Table XX).

**Table 19.8:Grading of Diabetic Retinopathy for Screening at Community/ Diabetic Clinic: Features and Outcome**

Grade	Features	Outcome/action
R0	No disease	Rescreen in 12 months
R1	Mild background DR Including: micro-aneurysms, flame exudates, >4 blot haemorrhages in one or both hemifields and/or cotton wool spots	Rescreen in 12months
R2	Moderate background DR: >4 blot haemorrhages in one hemifield	Rescreen in 6months
R3	Severe non-proliferative or pre proliferative DR: >4 blot haemorrhages in both hemi fields, intra-retinal microvascular anomalies (IRMA),venous bleeding	Refer to Eye Clinic
R4	Proliferative retinopathy, Neovascularization of the Disc (NVD), Neovascularization Elsewhere (NVE), vitreous haemorrhage, retinal detachment	Refer to Eye Clinic
M0	No macular findings	Rescreen in 12months
M1	Hard exudates within 1–2 disc diameters of fovea	Rescreen in 6 months

M2	Blot haemorrhage or hard exudates within 1disc diameter of fovea	Refer to Eye Clinic
P0	Photocoagulation Laser: Absent	Refer to Eye Clinic
P1	Photocoagulation Absent/Present (Any PRP or evidence of Grid Laser)	Refer to Eye Clinic
U	Unclassifiable (When there is Cataract, small Pupil, Vitreous Haemorrhage, Tractional Retinal Detachment or Corneal Opacity)	Refer to Eye Clinic

KEY: R=Retinopathy; M=Maculopathy; P=Photocoagulation, U=Unclassified

At all times, remind patients to stop smoking and intensify blood pressure, lipids and glycaemic control.

## 19.12 Thyroid Disorders

Thyroid disorders are conditions that affect the thyroid gland. There are specific kinds of thyroid disorders that includes hypothyroidism, hyperthyroidism, goiter, thyroid nodules and thyroid cancer.

### 19.12.1 Hypothyroidism

Hypothyroidism is a condition in which a person's thyroid hormone production is below normal. Common causes of the disease are chronic autoimmune thyroiditis, post-surgery and post radioactive iodine.

#### Diagnostic criteria

The symptoms depend on the deficiency of thyroid hormone, but can include:

- Increased cholesterol levels,
- Depression
- Fatigue
- Hair loss
- Memory loss
- Dry, rough skin
- Constipation
- Hoarse voice

#### Investigation

A blood test is used to confirm hypothyroidism

#### Indications for Treatment

- TSH level persistently  $>10\text{mU/L}$ ; treat all patients due to, increased likelihood of progression to overt disease and a higher risk of congestive heart failure, cardiovascular disease and mortality.
- TSH levels ( $4.5\text{--}10\text{mU/L}$ ); consider, treatment in patients younger than 65 with increased cardiovascular risk (e.g., previous cardiovascular disease, hypertension, documented diastolic dysfunction, atherosclerotic risk factors (dyslipidaemia, diabetes mellitus, smoker), goitre, positive antithyroid peroxidase antibodies, evidence of autoimmune thyroiditis by ultrasound, pregnancy, or infertility), particularly when TSH level is persistently  $>7\text{mU/L}$ .
- Levothyroxine therapy could be considered also for symptomatic middle-aged patients for a short period of time. If a clear beneficial effect is observed, levothyroxine therapy could be maintained.
- Persistently mildly increased TSH levels ( $>4.5\text{--}10\text{mU/L}$ ) with positive Thyroid Antibody and thyroid sonographic findings typical of autoimmune thyroiditis.

#### Pharmacological Treatment

Initial dose:

Clinical hypothyroidism—

**D:** levothyroxine  $1.6\text{--}1.8\mu\text{g/kg}$  ideal body weight

Subclinical hypothyroidism—

**D:** levothyroxine  $1.1\text{--}1.2\mu\text{g/kg}$  is recommended

- Take at least after 2hours fast, 30minutes before food intake. Alternatively, at bedtime (3 or more hours after the evening meal).
- When initiating therapy in young healthy adults with overt hypothyroidism, consider beginning treatment with full replacement doses
- Routine use of combined therapy with levothyroxine and triiodothyronine for hypothyroid patients is not recommended

- Assess TSH and adjust dosage when there are large changes in body weight, with aging, and with pregnancy.
- There is no convincing evidence to support routine use of thyroid extracts, L-T3 monotherapy, compounded thyroid hormones, iodine containing preparations, dietary supplementation, and over the counter preparations in the management of hypothyroidism.

### **Monitoring**

- TSH monitoring 6–8weeks after any levothyroxine dose change, and yearly life-long monitoring once euthyroidism is achieved (target TSH 0.2–4.0um/l). FT4 can be measured in early stages of treatment.
- In patients with central hypothyroidism, assessments of serum free T4 should guide therapy and targeted to exceed the mid normal range value for the assay being used.
- Wait for TSH equilibration–TSH equilibration requires eight to 12 weeks after any thyroxine dosage change. Once a stable dose is achieved–yearly TSH is sufficient.

### **In Pregnancy**

When the elevation of the TSH level is confirmed, free T4 should be measured in order to classify the hypothyroidism as clinical or overt (OH) and subclinical (SH).

- TSH > 2.5–10.0mU/L with normal free T4: SH.
- TSH > 2.5 –10.0mU/L with low levels of free T4: OH.
- TSH =10.0mU/L, despite the level of free T4: OH

Women in reproductive period should be euthyroid before conceiving, as the hypothyroidism is associated with neural development. Dose may be doubled during pregnancy and returned to normal dose after delivery

### **19.12.2 Hyperthyroidism**

Hyperthyroidism is a condition in which an overactive thyroid gland is producing an excessive amount of thyroid hormones that circulate in the blood. Graves' disease, multinodular goiter (TMNG), inflammation of the thyroid gland (thyroiditis) and excessive iodine intake are the most common cause of hyperthyroidism.

#### **Diagnostic criteria**

Hyperthyroidism can be suspected in patients with

- Tremors
- Excessive sweating
- Smooth velvety skin
- Fine hair
- A rapid heart rate
- An enlarged thyroid gland
- Frequent bowel movements

#### **Investigations**

- Baseline complete blood count, including white count with differential, and a liver profile (bilirubin and transaminases)
- Differential white blood cell count should be obtained during febrile illness and at the onset of pharyngitis in all patients taking antithyroid medication. Routine monitoring of white blood counts is not recommended
- Test for TSH and T4
- When thyrotoxicosis is confirmed, if cause is not known request thyroid uptake scan

#### **Note**

Management of hyperthyroidism depends on the cause

### **19.12.3 Toxic Multinodular Goitre or Thyroid Antibody Positive**

Patients with overtly Toxic multinodular goitre or Thyroid antibody are treated with either:

#### **Non-pharmacological Treatment**

**S:** Radio iodine (131-I) therapy

**OR**

**S:** Thyroidectomy

#### **Note**

Long term, low-dose carbimazole should not be used for either conditions except in some elderly

## **Surgery**

- Patients with overt hyperthyroidism should be rendered euthyroid prior to the procedure with carbimazole pre-treatment (15–40mg daily, divided into 2–3 doses a day for 4–8 weeks then a maintenance dose of 5–15mg, taken once daily) with or without beta-adrenergic blockade (e.g. propranolol 1–40mg 6 hourly). Preoperative iodine should not be used in this setting.
- Following thyroidectomy for Toxic multinodular goitre, it is suggested that serum calcium or intact parathyroid hormone levels be measured, and that calcitriol and oral calcium supplementation (maximum 1,200mg of calcium per day in two divided doses) be administered based on these results.
- Following surgery for Toxic multinodular goitre, thyroid hormone replacement should be started at a dose appropriate for the patient's weight (0.8µg/lb or 1.7µg/kg) and age, with elderly patients needing somewhat less. TSH should be measured every 1–2 months until stable, and then annually.

## **Radioiodine**

- Radioactive iodine therapy should be used for retreatment of persistent or recurrent hyperthyroidism following inadequate surgery for Toxic multinodular goitre or Thyroid antibody.

### **19.12.4 Grave's Hyperthyroidism**

Patients with overt Graves' hyperthyroidism should be treated with:

Medicine	Initial therapy for 4–6 weeks	Maintenance therapy (gradual reduction over 3–6 months from initial dose)
C: carbimazole	10–60mg/day in 2–3 divided dose	5–10mg/day Continue for approximately 12–18 months, then taper or discontinue if TSH is normal.

Beta Blockers are used for excessive sympathetic symptoms.

**A:** propranolol (PO) 40 to 120mg (24 hourly or 12 hourly)

**OR**

**B:** atenolol (PO) 50–100mg 12 hourly

## **Factors which favour use of antithyroid medicines**

- High likelihood of remission (patients, especially females, with mild disease, small goitres, and negative or low titre TSH-receptor antibody)
- Elderly or others with comorbidities increasing surgical risk or with limited life expectancy or unable to follow radiation safety regulations
- Previously operated or irradiated necks
- Moderate to severe active Graves' ophthalmopathy

## **Radioactive Iodine**

Potassium iodide (**B**) should be given in the immediate preoperative period as 5–7 drops (0.25–0.35 mL) Lugol's solution (8 mg iodide/drop) or 1–2 drops (0.05–0.1 mL) saturated solution of potassium iodide (50 mg iodide/drop) three times daily mixed in water or juice for 10 days before surgery

## **Factors which favour use of radioiodine**

- Individuals with comorbidities increasing surgical risk
- Patients with previously operated or externally irradiated necks
- Lack of access to a high-volume thyroid surgeon
- Contraindications to antithyroid medicines use
- Females who are not pregnant and are not planning a pregnancy in the future (4–6 months) following radioiodine therapy

## **Surgery**

Consider the following factors

- Symptomatic compression or large goitres
- Low uptake of radioactive iodine
- Thyroid malignancy is documented or suspected or large non-functioning nodule
- Coexisting hyperparathyroidism requiring surgery

- Females planning a pregnancy in <4–6months
- Patients with moderate to severe active Graves' ophthalmopathy
- If a patient with Grave's disease becomes hyperthyroid after completing a course of carbimazole, consideration should be given to treatment with radioactive iodine or thyroidectomy. Low-dose carbimazole treatment for longer than 12–18months may be considered in patients not in remission who prefer this approach but evidence is that remission rate in adults is not improved by a course of medicines longer than 18 months
- Whenever possible, patients with Grave's disease undergoing thyroidectomy should be rendered euthyroid with carbimazole.

### 19.12.5 Thyroid Storm (Crisis)

Thyroid storm is one of the most life-threatening endocrine emergencies, resulting from exacerbation of manifestations of thyrotoxicosis.

**Triggers of thyroid storm include:**

- Antithyroid withdraw
- Acute infections
- Thyroidal or nonthyroidal surgeries
- Iodinated contrast dyes
- External beam radiation therapy.
- It should be considered in very sick patients if they present with recent history of thyrotoxicosis and a recent history of precipitating factor.

Patients with thyroid storm (tachycardia, arrhythmias, congestive heart failure, hypotension, hyperpyrexia, agitation, delirium, psychosis, stupor and coma, as well as nausea, vomiting, diarrhoea, and hepatic failure) should receive a multimodal treatment including:

- Beta-adrenergic blockade
- Antithyroid medicine therapy
- Inorganic iodide
- Corticosteroid therapy
- Aggressive cooling with acetaminophen and cooling blankets
- Volume resuscitation
- Respiratory support
- Monitoring in an intensive care unit.

Thyroid storm is not a matter of thyroid levels increased beyond those of uncomplicated thyrotoxicosis, but the systemic decompensation that occurs.

**Table 19.7: Pharmacological Treatment**

Medicine	Dosing	Comment
<b>D:</b> propylthiouracil*	500–1000mg load, then 250mg 4hourly	Blocks new hormone synthesis Blocks T4-to-T3 conversion
<b>C:</b> carbimazole	40–60 mg/day	Blocks new hormone synthesis
<b>A:</b> propranolol	60–80mg every 4hourly	Consider invasive monitoring in congestive heart failure patients Blocks T4-to-T3 conversion in high doses. Alternate medicine: esmolol infusion
<b>B:</b> iodine (saturated solution of potassium iodide)	5drops (0.25mL or 250mg) (PO) 6hourly	Do not start until 1hour after antithyroid medicines Blocks new hormone synthesis Blocks thyroid hormone release
<b>A:</b> hydrocortisone	300 mg intravenous load, then 100mg 8hourly	May block T4-to-T3 conversion Prophylaxis against relative adrenal insufficiency Alternative medicine: dexamethasone

**Note**

In thyroid storm, propylthiouracil is preferred to carbimazole

## **19.13 Cushing's Syndrome**

Cushing syndrome is a clinical condition resulting from prolonged exposure to excessive glucocorticoids from either endogenous or exogenous sources. The most common cause of Cushing's syndrome is from the administration of exogenous sources.

### **Classification**

Cushing syndrome can be divided into two categories based on pathophysiology, ACTH dependent or ACTH – Independent

- ACTH-Dependent States
  - Pituitary Adenoma (Cushing's Disease) 90-95%
  - Ectopic ACTH Syndrome
- ACTH-independent States
  - Adrenal adenoma
  - Adrenal carcinoma
- Exogenous Sources
  - Glucocorticoid intake
- Psychiatric Conditions (Pseudo-Cushing Disorders)
  - Depression
  - Alcoholism
- High Cortisol Secretion Rate without Convincing Clinical Features of Cushing Syndrome
- Pregnancy

### **Symptoms and signs of Cushing's syndrome**

- The symptoms and signs of Cushing's syndrome result directly from chronic exposure to excess glucocorticoid
- Establishing the diagnosis is often difficult because none of the symptoms or signs are pathognomonic of the syndrome.
- An important clinical clue to the presence of glucocorticoid excess is the simultaneous development and increasing severity of several of these symptoms
- Common presenting symptoms include
  - Central obesity
  - Facial plethora
  - Weakness of the proximal muscles
  - Easily bruises and striae
  - Hirsutism
  - Glucose intolerance

### **Diagnosis of Cushing's syndrome**

At least two first-line tests should be abnormal to establish the diagnosis of Cushing's syndrome

- The low-dose dexamethasone suppression tests
- 24hrs urinary cortisol,
- Late night salivary cortisol
- Differential Diagnostic Testing to established, the cause of Cushing's syndrome
  - Morning serum ACTH
  - High dose dexamethasone suppression test

### **Imaging diagnosis**

- Pituitary CT - sensitivity of about 50% for identifying microadenomas
- MRI pituitary sensitivity up to 100%
- Adrenal ultrasonography/CT for suspected Adrenal source

### **Treatment of Cushing's syndrome**

Without therapy, Cushing's syndrome is often fatal.

- Typically, due to CV, HTN or infectious complications.
- With therapy Symptoms improve over 2-12 months.

### **Definitive Therapy**

Surgery by source when possible

- Adrenal source - Adrenalectomy
- Pituitary source - Transsphenoidal resection
- Ectopic source - Tumor Resection

## **Medical therapy**

**S:** metyrapone (PO) 30mg/kg, maximum dose 3,000mg, administered at midnight usually with a snack

## **19.14 Prolactinoma**

Are prolactin – secreting pituitary tumors

### **Classification**

May present as Microprolactinomas (<10mm) or Macroprolactinomas (>10mm)

### **Clinical Presentation**

Symptoms are due to hyperprolactinemia which include galactorhea, oligo/amenorrhea, infertility, reduced libido, impotence and gynecomastia in male, headache and visual abnormality in large adenomas.

### **Diagnosis**

Serum prolactin levels

<100ng/ml possible prolactinoma

100-200ng/ml likely prolactinoma

>200 ng/ml –diagnostic of prolactinoma

### **Treatment**

Proactinomas are unique among pituitary tumors in that first line treatment is medical not surgical.

The mainstays of management for prolactinomas are the dopamine agonist which are:

**C:** bromocriptine (PO) 2.5-20mg (24hourly or 12hourly)

**OR**

**S:** cabergoline (PO) 0.25-1mg (twice a week)

## **19.15 Diabetic Insipidus (DI)**

DI is a disorder of water balance caused by non-osmotic renal loss of water leading to excretion of large volume of dilute urine

### **Classification**

**Central DI:** Is caused by either complete or partial deficiency of antidiuretic hormone (ADH) secretion from the posterior pituitary gland

**Nephrogenic DI:** Is caused by end organ unresponsiveness of the kidney to ADH

**Dipsogenic DI:** Is caused by excessive and inappropriate fluid intake due to a defective in thirsty mechanism

### **Clinical Presentations**

Polyuria especially nocturnal

### **Diagnostic criteria**

- Polyuria and urine osmolality of <300 for a given plasma osmolality
- Volume depletion and orthostatic hypotension may be found
- Plasma Sodium may be normal or elevated

### **Pharmacological Treatment**

In case of water deficit - water replacement. Treating of the underlying defect

Central DI:

**S:** desmopressin (IV) 2-4 µg/day divided 12hourly

**OR**

**S:** desmopressin (PO) Initial dose 0.05mg 12hourly; effective range: 0.1-1.2mg divided 8-12hourly

**OR**

**D:** desmopressin (Intranasal) 10-40µg (0.1-0.4mL) 24hourly, either as a single dose or divided into 2 or 3doses; usual dose is 20µg (0.2mL) 24hourly in 2divided doses

Nephrogenic DI:

**A:** thiazide diuretic (e.g bendrofluazide (PO) 5mg 24hourly OR hydrochlorothiazide 12.5-25mg 24hourly)

## 19.16 Pheochromocytoma

Pheochromocytoma are neuroendocrine tumors arising from catecholamine producing chromaffin cells of the adrenal medullar but about 15–20% are extra-adrenal in origin

### Clinical presentation

- The classic symptoms of pheochromocytoma are due to episodic release of excess catecholamines into circulation (Norepinephrine and Epinephrine)
- Typical symptoms
  - headaches
  - palpitations
  - anxiety and diaphoresis
  - hypertension which can be paroxysmal (~48%) or persistent (~29%).

**Table: Biochemical Tests Comparisons**

Test	Sensitivity	Specificity
Urine Catecholamine	83	88
Urine Total Metanephries	76	94
Urine Catecholamines + Metanephries	90	98
Urine VMA	63	94
Plasma Catecholamines	85	80
Plasma Metanephries	99	89

### Tumor Localization

- Anatomic localization of a catecholamine-secreting tumor should be performed only after biochemical diagnosis has been confirmed
- Approximately 85% of catecholamine-secreting tumors are found in the adrenal glands, and 95% are found in the abdomen and pelvis
- Either CT or MRI are effective for localization of catecholamine-secreting tumors -sensitivity 89 vs 98% resp.

### Management of Pheochromocytoma

- After definitive diagnosis, the mainstay of definitive therapy is complete surgical resection of the tumor
- Prior to planned surgical intervention, the effects of excess catecholamines must be ameliorated in order to avoid perioperative complications and improve outcome, by using  $\alpha$  - adrenergic antagonists

None selective  $\alpha$ -antagonist

**S:** phenoxybenzamine (PO) 10mg 12hourly initially; increase to 20-40 mg 8-12hourly  
**OR**

Selective  $\alpha$ -antagonist

**S:** doxazocin (PO) 1-2mg 24hourly

Combined  $\alpha$  +  $\beta$  blockade

## 19.17 Disorder of Sexual Development (DSD)

DSD formerly known as intersex conditions are classified on the basis of genetics and the state of gonads. They may be caused by virilization 64XX or under virilization 46XY. As well as mosaicism (streak Ovary, Ovotestis, dysgenetic testis). The most common DSD is Congenital Adrenal Hyperplasia (CAH).

### Diagnostic criteria

- Infant born with ambiguous or abnormal genitalia
- Infant with undescended testis, unilateral or bilateral
- Infant with hypospadias

## **Investigations**

- Serum electrolytes
- Chromosomal analysis
- Karyotyping in a male looking male with undescended testis and/or hypospadias whether the genitalia appears normal or not
- Endocrine screening
- Antimüllerian Hormone (AMH)

## **Non-pharmacological Treatment**

Counseling of the parents on

- The condition
- Naming of a child and
- Gender assignment

## **Pharmacological Treatment**

Depends on type of the DSD it is either CAH or other forms of DSD (Non CAH DSD)

### **CAH DSD**

Salt losing in crisis-

- Bolus normal saline (0.9% NaCl) and maintenance,
- Hypoglycemic 2-4 ml of 10% dextrose

Long-term treatment

**S:** fludrocortisone (PO) 0.05-0.3mg 24hourly

### **Non CAH DSD**

**D:** testosterone 50-400mg monthly for 3cycles, then asses +/-

**D:** testosterone cream

## **19.8 Obesity in Adults**

### **Diagnosis**

- Body mass index (BMI) = weight divided by height squared (weight in kg, height in meters)
- Ideal BMI is from 18.5-24.9: less than 18.5 is underweight, 25-29.9 is overweight and 30+ is obese.
- Overweight/obesity increases risk of CVD, type 2 diabetes, pulmonary embolism, gallbladder disease, colorectal cancer, osteoarthritis, chronic back pain and all-cause mortality, especially for those with high blood pressure, hyperlipidemia, and hyperglycemia.
- Individuals living with obesity are subject to considerable stigma, which they may internalize and experience as shame, depression and anxiety.
- As part of prevention of non-communicable diseases, for all adults attending health facilities, height, weight and waist circumference should be measured at least yearly and appropriate action taken:
  - Everyone should be educated on the risks of overweight/obesity and the need to avoid weight gain by adjusting food intake and engaging in regular physical activity
  - Weight loss treatment is indicated for the obese or those overweight with increased cardiovascular risk (e.g. diabetes, prediabetes, hypertension, dyslipidemia, elevated waist circumference) or other obesity-related comorbidities.
  - Evaluate diet, previous and current physical activity, and disorders of sleep, eating and mood
  - Assess the patient's medication regimen for drugs that may contribute to weight gain and consider adjustments
  - Determine diabetes and CVD risk
    - High Blood Pressure
    - Hyperlipidemia
    - Hyperglycemia
    - Elevated liver enzymes (Non-alcoholic liver disease)

### **Non-pharmacological Management**

- Even modest, sustained weight loss of 3%-5% produce clinically meaningful reductions in triglycerides, blood glucose, hemoglobin A1c, and the risk of developing type 2 diabetes.

- Greater amounts of weight loss will reduce blood pressure, improve LDL-Cholesterol and HDL-Cholesterol, and reduce the need for medications to control BP, blood glucose, and lipids as well as further reduce triglycerides and blood glucose.
- Weight loss requires creating an energy deficit through caloric restriction, physical activity, or both
  - Aim for a loss of 5%-10% of baseline weight within 6 months (0·5 kg per week for 6 months: total about 8kg)
  - Prescribe a diet to achieve energy deficit of  $\geq 500$  kcal/d: may be achieved with dietary intake of 1200-1500 kcal/d for women and 1500-1800 kcal/d for men (25-30kcal/kg/day)
  - The choice of diet should address a patient's preference and ease of adherence and be directed towards long-term lifestyle changes that include eating patterns that are practical, achievable, and sustainable
  - Use of very-low-calorie diets (<800 kcal/d) should be advised only under medical supervision
  - Proteins
    - Aim for approximately 20% of total energy from good quality proteins, lean meats and whole pulses
    - Proteins induce a feeling of satiety and any excess is deaminated.
  - Fats
    - Aim for 20% or less of total energy from fats
    - Avoid saturated fats to reduce the risk of heart problems
    - Restrict or avoid fried foods
    - Choose low fat milk.
  - Carbohydrates
    - Aim for 60% of energy from complex carbohydrates
    - Whole grains, roots & tubers, e.g. sweet potatoes, yams
    - Limit sugars and honey.
    - Vegetables e.g. broccoli, mushroom, zucchini, cabbage, lettuce, cucumber, celery
    - Fruits such as pineapple, apples, cherimoya, peach, grapefruit, watermelon
  - Avoid
    - Alcohol as it provides calories without nutrients, and excessive use is harmful in many ways
    - Omit fad diets and other unhealthy practices
- Tailored physical activity program
  - Initially 30 min of moderate intensity 3-5 times per week
  - eventually  $\geq 60$  min on most days; add muscle strengthening on at least two days/week
  - Weight regain following weight loss is reduced by physical activity equivalent to 60 min of brisk walking daily and lifestyle activity that increases energy expenditure throughout the day without concern for the intensity or duration can be as effective for weight control as jogging, swimming, or cycling.
- Offer behavioural support
  - identify cues that prompt overeating or inactivity, and restructure thoughts and behaviours to prompt healthy responses
  - Advise patient to
    - set goals that specify what, when, where, how, and for how long they will engage in a selected activity
    - keep detailed records of food intake, physical activity, and bodyweight
    - eat breakfast regularly and maintain a consistent eating pattern across weekdays and weekends
    - engage family members for ongoing support
    - participate for  $\geq 6$  months in a lifestyle program that assists participants in adhering to a lower-calorie diet and in increasing physical activity
  - For those who have lost weight, prescribe face-to-face or telephone-delivered weight loss maintenance programs that provide regular contact (monthly or more frequently) and helps participants to engage in high levels of physical activity (ie, 200–300 min/wk), monitor body weight regularly (ie, weekly or more frequently), and consume a reduced-calorie diet (needed to maintain lower body weight).
- Facilitate referral to a specialist team (metabolic obesity clinic and/or metabolic surgery) if patient:

- is unable to achieve  $\geq 5\%$  weight loss at 3 months on a lifestyle intervention consisting of reduced energy/low-energy diet, increased physical activity, and/or pharmacotherapy
- has a BMI  $\geq 40 \text{ kg/m}^2$  or BMI  $\geq 35 \text{ kg/m}^2$  with obesity-related comorbid conditions and has not responded to behavioral treatment with or without pharmacotherapy to consider bariatric surgery
- Monitor the patient's requirements for medication as weight loss progresses, particularly for antihypertensive and diabetes medications that can cause hypotension and hypoglycemia.

### **Pharmacological Treatment**

Drug therapy may be considered for those with a BMI  $\geq 30 \text{ kg/m}^2$ , BMI  $\geq 27 \text{ kg/m}^2$  with obesity-related comorbid conditions, or if patient has not lost 0.5kg per week by 3–6months after lifestyle changes

S: orlistat (PO) 120mg 8hourly with each main meal containing fat (during or up to one hour after the meal). It inhibits pancreatic and gastric lipase, reducing fat absorption by approximately 30%

- Anti-obesity pharmacotherapy should be continued beyond 12weeks only if at least 5% of initial body weight has been lost since starting medication and should be prescribed as an adjunct to lifestyle interventions.

### **Innovative strategies for delivery and management of obesity care**

Primary care should be enhanced with:

- patient registries and methods for systematic tracking to assess clinical interventions (electronic health records)
- care teams to manage patients with chronic illnesses
- health information systems that support the use of evidence-based practices at the point-of-care to provide longitudinal care for chronic illnesses.
- Electronic support
  - text messaging to provide outreach, support for behaviour change to patients and educational messages
  - Blood pressure, blood glucose and wi-fi scales, which automatically transmit results from machine to a server
  - smartphones and tablets with weight loss applications to simplify monitoring of food intake, physical activity, and weight
  - interventions by telephone, study-specific website, and email
  - Remote support offers flexibility to patients and practitioners and can be scaled up or down according to patients' needs.

### **Hospitals and health professionals as role models**

- An overweight/obese health worker is less likely to counsel patients with obesity
- Provide healthy food choices for patients, employers, visitors, and communities, with pricing incentives
- Label drinks sold in hospital cafeterias as red, yellow, or green to shift consumption towards healthier beverages
- Prohibit fast food outlets in hospital premises

### **19.19 Physical Activity**

- Physical fitness is the ability to perform physical activities without undue fatigue and is achieved through proper nutrition, moderate to vigorous physical activity, and sufficient rest.
- Physical activity
  - Improves insulin resistance, reduces HbA1c by 0.7% in Type II diabetes and protects against the development of Type II diabetes
  - Improves lipid profile, lowers blood pressure and helps maintain appropriate body weight.
- Physical activities
  - Include:
    - Those associated with the performance of a job e.g. walking, hauling, lifting, pushing, carpentry, farming, shoveling, packing boxes, etc.
    - Those done during free time e.g. structured exercise as well as walking, hiking, gardening, sport, dance, etc.

- Require contraction of skeletal muscle and increased energy expenditure above the resting level.
- The types of physical activity for optimal fitness include aerobic, muscle-strengthening, stretching and coordination.

### **Aerobic Activities**

- These improve the body composition (fat, muscle and bone) and cardiorespiratory fitness
- Examples:
  - brisk walking, climbing stairs, cycling, swimming, dancing, jogging, running, washing windows or car, sweeping floors or carpet, vacuuming, mopping, shoveling, digging ditches, carrying heavy loads such as bricks
  - Sports: badminton, golf, tennis, volleyball, swimming, basketball, football, jumping jacks, jumping rope.
- For optimal effect, the activity has to be:
  - Moderate intensity (a person doing moderate-intensity aerobic activity can talk, but not sing, during the activity) or vigorous (cannot say more than a few words without pausing for a breath).
  - For at least 30 minutes per day at least five days per week.

### **Muscle-strengthening Activities**

- These enable the major muscle groups of the body (the legs, hips, back, chest, abdomen, shoulders, and arms) to do more work than they are accustomed and thus increase muscle mass, strength and endurance.
- Examples: pull-down, pull-ups, push-ups, dips, abdominal crunch/curl-up, calf raises, jumping, carrying heavy loads, and heavy gardening (digging or hoeing).
- For optimal effect:
  - Each activity should consist of at least 8 repetitions of the movement (e.g. 8 push-ups)
  - Each muscle group should be active on at least two days per week.

### **Stretching Activities**

- Improve flexibility such as range of motion, e.g. ability to bend down to tie your shoe.
- Examples: neck flexions, arm rotations, trunk rotations, and stretching of muscles.

### **Coordination Activities**

- Improve neuromuscular fitness such as balance, agility and proprioception necessary for example to prevent falls in the elderly
- Examples: Standing on the toes of one leg.

### **Improving Exercise Adoption and Maintenance**

As part of risk factor assessment in disease prevention, the physical activity level of all patients attending health facilities should be assessed, followed by brief advice, if required, about recommended levels.

# CHAPTER TWENTY

## CARDIOVASCULAR DISEASE CONDITIONS

### 20.1 Prevention of Atherosclerotic Ischaemic Heart Disease and Stroke

Cardiovascular disease (CVD) prevention is a coordinated set of actions, at the population level or targeted at an individual at risk of developing cardiovascular disease, that are aimed at eliminating or minimizing the impact of CVDs and their related disabilities.

#### Diagnostic/screening Criteria

Major risk factors for ischaemic cardiovascular and cerebrovascular disease are:

- Diabetes mellitus
- Hypertension
- Central obesity: waist circumference  $\geq 94\text{cm}$  (men) and  $\geq 80\text{cm}$  (women)
- Dyslipidaemia (fasting levels): Total cholesterol  $> 5 \text{ mmol/L}$ , or LDL  $> 3\text{mmol/L}$ , or HDL  $< 1 \text{ mmol/L}$  in men and  $< 1.2\text{mmol/L}$  in women
- Smoking
- Age: Men  $>50$  years, Women  $>60$  years
- Family history of early onset cardiovascular disease; Male relatives  $<55$  years and Female relatives  $<65$  year

Estimation of total cardiovascular risk is important for prevention of CVD in an individual, should be adapted to his or her total CV risk: the higher the risk, the more intense the management should be (See Table 20.1).

**Table 20.1: Cardiovascular Disease Risk Classification and WHO Risk estimation**

<b>Very High Risk</b>	Subjects with any of the following: <ul style="list-style-type: none"> <li>• Documented CVD, clinical or unequivocal on imaging: previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes plaque on coronary angiography or carotid ultrasound. It does <b>NOT</b> include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery.</li> <li>• DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension.</li> <li>• Severe CKD (GFR <math>&lt;30\text{mL/min}/1.73\text{m}^2</math>).</li> <li>• A calculated CVD Risk Score <math>\geq 10\%</math>.</li> </ul>
<b>High Risk</b>	Subjects with: <ul style="list-style-type: none"> <li>• Markedly elevated single risk factors, in cholesterol <math>&gt;8\text{mmol/L}</math> (<math>&gt;310\text{mg/dL}</math>) (e.g. in familial hypercholesterolaemia) or BP <math>\geq 180/110\text{mmHg}</math>.</li> <li>• Most other people with DM (except for young people with type 1 DM and without major risk factors that may be at low or moderate risk).</li> <li>• Moderate CKD (GFR 30–59mL/min/1.73m<sup>2</sup>).</li> <li>• A calculated CVD Risk Score <math>\geq 5\%</math> and <math>&lt;10\%</math>.</li> </ul>
<b>Moderate Risk</b>	CVD Risk Score is $\geq 1\%$ and $<5\%$ at 10years. Many middle-aged subjects belong to this category
<b>Low Risk</b>	CVD Risk Score $<1\%$

#### Non-pharmacological Treatment

General measures:

- Lifestyle modification (refer to table 20.2)

**Table 20.2: The Summarized Preventive Measures to be Individualized on Targeted Goals**

Risk factor goals and target levels for important cardiovascular disease risk factor reduction		
1	Smoking	No exposure to tobacco in any form.
2	Diet	Reduce dietary sodium intake no more than 1000mmol/L (2.4gm sodium or 6gm sodium chloride per day) Low in saturated fat with a focus on wholegrain products, vegetables, fruit, and fish. Reduce alcohol intake to $\leq 2$ units/day for men and $\leq 1$ unit for women, not more than 5 out of 7days per week (1 unit is equivalent to 25mL of spirits, 125mL of wine, 340mL of beer or sorghum beer, or 60mL of sherry).
3	Physical activity	At least 150minutes a week of moderate aerobic exercise (30minutes for

		5days/week) or 75minutes a week of vigorous aerobic exercise (15minutes for 5days/week) or a combination thereof
4	Body weight	Body weight BMI 18.5–24.9kg/m <sup>2</sup> Waist circumference <94 cm (men) or <80 cm (women)
5	Blood Pressure	<140/90mmHg
6	Lipids LDL-C is the primary target	<b>Very high risk:</b> <1.8 mmol/L (<70mg/dL), or a reduction of at least 50% if the baseline is between 1.8 and 3.5mmol/L (70 and 135mg/dL) <b>High risk:</b> <2.6mmol/L (<100mg/dL), or a reduction of at least 50% if the baseline is between 2.6 and 5.1mmol/L (100 and 200mg/dL) <b>Low to moderate risk:</b> <3.0mmol/L (<115mg/dL)
	HDL-C	No target but >1.0mmol/L (>40mg/dL) in men and >1.2mmol/L (>45mg/dL) in women indicate lower risk
	Triglycerides	No target but <1.7mmol/L (<150mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
7	Diabetes	HbA1c <7%. (<5.3mmol/l)

Recommended to repeat CV risk assessment every 5years, and more often for individuals with risks close to thresholds mandating treatment.

**Pharmacological Treatment:** For specific pharmacological treatment for hypertension, diabetes, dyslipidemia refer specific sections, respectively.

## 20.2 Management of Dyslipidemias

Lowering blood cholesterol levels using statins is recommended to reduce the impact of cardiovascular morbidity and mortality

### Clinical indication for lipid lowering medicine therapy

- Established atherosclerotic disease
- Ischaemic heart disease
- Peripheral vascular disease
- Atherothrombotic stroke

#### Note

Lipid lowering medicines should be administered in this setting even if the level of cholesterol is normal

- Type 2 diabetics >40 years of age, or diabetes for >10 years,
- Existing cardiovascular disease,
- Chronic kidney disease (eGFR < 60mL/min).
- CV risks of more than >20% in 10years Such high-risk patients will benefit from lipid lowering (statin) therapy irrespective of their baseline LDL levels.

### Pharmacological Treatment

**B:** atorvastatin (PO) 20mg to 80mg 24hourly

**OR**

**S:** rosuvastatin (PO) 10mg-40mg 24hourly

**AND**

**D:** fenofibrate (PO) 120mg /160mg /200mg 24hourly

#### Note

- Criteria for initiating lipid lowering therapy are the same as for HIV uninfected patients. Fasting lipid levels should be done 3months after starting lopinavir/ritonavir and atazanavir/ritonavir.
- Patients at high risk (>20% risk of developing a CVS event in 10years) should switch to atazanavir/ritonavir and repeat the fasting lipid profile in 3 months.
- Concomitant use of Ezetimibe and Atorvastatin can lead to liver damage and rhabdomyolysis.
- Fenofibrate indicated Hypertriglyceridemia, in which statin alone is not enough to treat & lower the hypertriglyceridemia.

## **20.3 Chronic Stable Coronary Artery Disease (CSCAD) / ISCHAEMIC Heart Disease (IHD)**

Clinical history characterized by chest pain due to myocardial ischaemia usually inducible by exercise, emotion, or other stress and reproducible, relieved by rest but may occur spontaneously and stable in nature, occurs in high-risk patient.

### **Non-pharmacological Treatment**

#### **General Measures**

- Lifestyle modification (refer to table 20.2).
- Annual control of lipids, glucose metabolism and creatinine are recommended in all patients with known IHD.
- A resting ECG is recommended in all patients at presentation and during or immediately after an episode of chest pain suspected to indicate clinical instability of CAD, Consider immediate referral.
- A resting transthoracic echocardiogram is recommended in some patients for:
  - a) exclusion of alternative causes of angina
  - b) regional wall motion abnormalities suggestive of CAD
  - c) measurement of LVEF for risk stratification purpose
  - d) evaluation of diastolic function.Consider referral if no echocardiogram available or unavailability of skilled personnel to perform transthoracic.
- Stress ECG
- Stress Echocardiography; a) Physical (Exercise) Stress Echo; b) Dobutamine (Pharmacological) Stress Echo performed to Orthopaedic related disorders pt who cannot walk on the Treadmill machine).

### **Pharmacological Treatment**

**A:** acetylsalicylic acid soluble (PO) 75–150mg 24hourly

**AND**

**C:** isosorbide dinitrate (PO) 20mg-40mg 12hourly

If nitrates cannot be tolerated, consider stepwise approach below.

**S:** ivabradine (PO) 2.5mg /5mg 24hourly

Step 1: add β-blocker if not contraindicated:

**B:** atenolol (PO) 12.5/25mg 24hourly

**OR**

**S:** metoprolol tartrate (IV) 5mg 2min for max 3doses, then (PO) 50-100mg 12hourly

**OR**

**C:** metoprolol succinate (SR) (PO) 25–200mg 24hourly

**OR**

**S:** bisoprolol (PO) 2.5mg /10mg 24hourly

Consider long-acting calcium channel blocker, if a β-blocker cannot be tolerated or contraindicated.

Step 2: add long-acting calcium channel blocker.

**S:** verapamil (PO) 60mg -120mg 8hourly 24hourly

**OR**

**D:** diltiazem (PO) 60mg 6 to 8hourlydaily; if suspects Prinzmetal Angina.

### **Key Points**

- All patients with chronic stable angina are high-risk for cardiovascular events, lipid lowering medicines should be initiated (See Section 20.2).
- Consider immediate referral to high level of care where there are adequate resources for the case management.

### **Indications for Referral**

- Angina or chest pain suspected to indicate clinical instability of CAD
- When diagnosis is in doubt/ failed medical therapy; no echocardiogram available or unavailability of skilled personnel to perform transthoracic echocardiogram.

Before referral when high likelihood of clinical instability of stable CAD consider giving:

**A:** acetylsalicylic acid(PO) 300mg stat.

**AND**

**B:** atorvastatin (PO) 80mgstat

**AND**

**D:** clopidogrel (PO) 300mg stat

## 20.4 Acute Coronary Syndrome

### 20.4.1 Unstable Angina (UA)

Unstable angina is a medical emergency and if untreated can progress to Non-ST Elevation Myocardial Infarction (NSTEMI)

#### Diagnostic Criteria

Presents as chest pain or discomfort like stable angina but with the following additional characteristics:

- Angina at rest or minimal effort, occurring for the first time, particularly at rest and prolonged >10minutes, not relieved by sublingual nitrates.
- The pattern of angina accelerates and gets worse.
- The chest pain may be associated with ST segment depression or T wave inversion or normal ECG without rise in cardiac enzymes (biomarkers ie. Total Creatinine, Creatine - MB and Troponin).

### 20.4.2 Non-ST Elevation Myocardial Infarction (NSTEMI)

Non-ST Elevation Myocardial Infarction is a medical emergency characterized with chest pain that is increasing in frequency and/or severity or occurring at rest, associated with elevated cardiac enzymes and ST segment depression or T wave inversion or normal ECG.

#### Diagnostic Criteria

Presents with typical chest pain with the following additional characteristics.

- Electrocardiogram (ECG) may show ST segment depression or transient ST segment elevation, or normal ECG does not exclude the diagnosis (serial ECG is important).
- Raised Cardiac Biomarkers – Total Creatine Kinase (Total-CK), Creatine Kinase - MB (CK-MB) and standard/high sensitive Troponin I or T.

#### Non-pharmacological Treatment

Both UA and NSTEMI are medical emergencies with the same pathophysiological progressive instability of CAD, which share similar management approach.

#### Supportive Therapy

- Admit patient into high dependent ward/ICU/CCU for haemodynamic monitoring, bed rest in Fowler's position and reassurance.
- Oxygen via nasal blog cannula or face mask if saturation < 92%.
- Establish Peripheral Intravenous line for intravenous fluid or drug administration.
- Haemodynamics blood pressure, heart rate and electrocardiogram rhythm monitor.

#### Pharmacological Treatment

##### Adjunctive therapy

Control cardiac pain

**C:** glyceryl trinitrate (Nitroglycerin) sub-lingual/ spray 0.5mg (make sure patient has not taken phosphodiesterase-5 inhibitor).

For persistent pain and if oral therapy is insufficient.

**S:** glyceryl Trinitrate (Nitroglycerin) (IV), 1–2µg/kg/min titrated with chest pain over 8–24hours.

**OR**

**C:** morphine (IV)1–2mg/minute dilute 10mg up to 10mL with sodium chloride solution 0.9%. Total maximum dose10 mg, repeat after 4hours if necessary

**Note**

- If pain is not responsive to this dose, it is suggestive for ongoing unresolved ischaemia. This requires immediate referral to high level of care where resources available to manage Acute Coronary Syndrome or to exclude differential diagnosis.

**Antiplatelet Therapy**

**A:** acetylsalicylic acid (PO) 300mg stat then followed by 75mg/100mg 24hourly

**AND**

**D:** clopidogrel (PO) 300mg /600mg start then followed by 75mg 24hourly

**OR**

**S:** ticagrelor (PO) 180mg stat.

For first year following ACS event: 90 mg 12hourly.

After 1year of maintenance: 60mg 12hourly.

**Statin high dose**

**B:** atorvastatin (PO) 80mg stat then 40mg 24hourly

**OR**

**S:** rosuvastatin (PO) 10mg-40mg 24hourly

**Anticoagulant**

**B:** heparin UFH (IV) 70–100U/Kg body weight a 24hourly

**OR**

**S:** low molecular weight heparin (SC) 1mg/kg body weight 12hourly

**Beta blocker ( $\beta$  –blockers)**

In case of LV dysfunction

**C:** carvedilol initial dose (PO) 6.25mg 12hourly preferred, titrate the dose upward. Max. Dose 25mg 12hourly

**OR**

In the settings of normal LV systolic function

**B:** atenolol 25–50mg (PO) 24hourly,

**OR**

**S:** metoprolol tartrate 5mg (IV) 2min for maximum of 3 doses, then (PO) 50-100mg 12hourly

**OR**

**C:** metoprolol succinate (SR) (PO) 25 – 200mg 24hourly.

**OR**

**S:** bisoprolol (PO) 2.5mg – 10mg 24hourly

**Angiotensin Converting Enzyme Inhibitors (ACEIs)**

**B:** captopril (PO) 6.25mg–25mg 8hourly

**OR**

**C:** enalapril (PO) 10mg 12 hourly

**OR**

**C:** lisinopril (PO) 5mg /10mg 24hourly

**Referral**

High suspicion index of acute coronary syndrome immediate consider referral to high level of care where resources are available to manage. In acute settings before referral from low to high level of care if available consider giving the following **urgently**:

- glyceryl trinitrate (Nitroglycerin) sub-lingual 0.5mg spray prn for intolerable chest pain
- acetylsalicylic acid (PO)300mg stat (chew)
- clopidogrel (PO) 300mg/600mg stat
- High dose statin simvastatin (PO) 80mg stat OR atorvastatin (PO) 80mg stat

**20.4.3 ST Elevation Myocardial Infarction (STEMI)**

STEMI is a medical emergency caused by the complete or partial occlusion of a coronary artery and requires prompt hospitalization and intensive care intervention management.

## Clinical Presentation

Severe chest pain with the following characteristics

- Site: retrosternal or epigastric, quality: crushing, constricting, or burning pain or discomfort.
- Radiation to the neck and/or down the inner part of the left arm.
- Duration: at least 20 minutes and often not responding to sublingual nitrates.
- Occurrence: at rest. May be associated with pulmonary oedema sweating, hypotension or hypertension, arrhythmias.

## Diagnostic Criteria

**Simple recognition triage:** Two out of three points most likely point to STEMI diagnosis

- Symptoms - typical/atypical chest pain
- ECG – ST elevation in two contiguous leads  $\geq 0.1\text{mV}$
- Raised cardiac biomarkers– Total Creatine Kinase (Total-CK), Creatine Kinase -MB (CK-MB) and Standard/Highly Sensitive Troponin I or T

## Non-pharmacological Treatment:

### Supportive therapy

- Consider cardio-pulmonary resuscitation if necessary, before transfer (cardiac arrest– cardiopulmonary resuscitation).
- Oxygen 40% via facemask, if saturation  $< 92\%$  or if in distress
- See section 20.4.2 above on supportive therapy for NSTEMI

### Adjunctive therapy

#### Control cardiac pain

**C:** glyceryl trinitrate sub-lingual/ spray 0.5mg (make sure patient hasn't taken phosphodiesterase-5 inhibitor).

For persistent pain and if oral therapy is insufficient

**S:** glyceryl Trinitrate (IV) 1–2  $\mu\text{g}/\text{kg}/\text{min}$  titrated with chest pain over 8–24 hours.

**OR**

**C:** morphine (IV) 1–2 mg/minute dilute 10 mg up to 10 mL with sodium chloride solution 0.9%. Total maximum dose: 10 mg, repeat after 4 hours if necessary.

#### Anti-platelets therapy

**A:** acetylsalicylic (PO) 300mg stat then followed by 75mg/100mg (PO) 24hourly

**AND**

**D:** clopidogrel (PO) 300mg/600mg stat then followed by 75mg 24hourly

**OR**

**S:** prasugrel (PO) 60mg stat, given after defining coronary anatomy prior to onset of PCI, then 10mg as maintenance dosage.

#### Statin high dose

**B:** atorvastatin (PO) 80mg start then 40mg 24hourly

**OR**

**S:** rosuvastatin (PO) 10mg-40mg 24hourly

#### Anticoagulant

**B:** heparin UFH (IV) 70–100U/Kg 24hourly

**OR**

**S:** low molecular weight heparin (SC) 1mg/kg 12hourly, Reduce dose in renal failure patient to 0.5mg/kg

#### Beta blocker ( $\beta$ –blockers)

In case of LV dysfunction

**C:** carvedilol (PO) initial dose 6.25mg 12hourly daily preferred, titrate dose upward to maximum dose 25mg hourly daily

In the settings of normal systolic function

**B:** atenolol (PO) 12.5mg or 25mg or 50mg 24hourly

**OR**

**S:** metoprolol tartrate (IV) 5mg 2min for max 3doses, then (PO) 50-100 mg 12hourly

**OR**

**C:** metoprolol succinate (SR) (PO) 25 – 200mg 24hourly

**OR**

**S:** bisoprolol (PO) 2.5mg – 10mg 24hourly

**OR**

**S:** verapamil SR (PO) 240 mg – 480 mg daily in 1-2 divided doses

**Note**

Verapamil SR should be initiated from 7 days' post myocardial infarction; any single dose should not exceed 240mg as secondary prevention of myocardial infarction.

Angiotensin-Converting Enzyme Inhibitors (ACEIs)

**B:** captopril (PO) 6.25mg or 12.5mg 8hourly

**OR**

**C:** enalapril (PO) 10mg 12hourly

**OR**

**C:** lisinopril (PO) 5mg-10mg 24hourly

**Definitive management of STEMI – Reperfusion therapy (Myocardial reperfusion)**

Myocardial reperfusion with rapid recanalization of infarct related artery is the key to success in the management of ST Elevation Myocardial Infarction (STEMI). Timely reperfusion is crucial for minimization of infarct size and thereby for preservation of left ventricular function and reduction in mortality in STEMI patients. The two main reperfusion strategies for STEMI patients are;

- Thrombolytic/Fibrinolytic therapy (preferably chest pain duration less 12 hrs)
- Primary percutaneous coronary intervention (PPCI) (preferably less than 90 mins of Door to Needle Time)

Thrombolytic agents

**S:** streptokinase (IV) 1.5 million units diluted in 100 mL sodium chloride 0.9%, infused over 30–60minutes

**OR**

**S:** alteplase (TPA) (IV) 15mg as bolus, 0.75mg/kg over 30min, then 0.5mg/kg over 60min

Absolute contraindication for Thrombolytics

- Previous allergy to streptokinase or used within the last year for streptokinase only.
- Stroke CVA within the last 3 months
- History of recent major trauma
- Bleeding within the last month
- Aneurysms
- Brain or spinal surgery or head injury within the preceding month
- Active bleeding or known bleeding disorder.

Relative contraindication for Thrombolytics

- |  |  |
|--|--|
| <ul style="list-style-type: none"><li>• Refractory hypertension</li><li>• TIA in the preceding 6 months,</li><li>• Subclavian central venous catheter</li><li>• Warfarin therapy</li></ul> | <ul style="list-style-type: none"><li>• Pregnancy</li><li>• Traumatic resuscitation</li><li>• Recent retinal laser treatment</li></ul> |
|--|--|

Referral is urgent for all suspected or diagnosed cases to high level care equipped with cardiac catheterization laboratory for Coronary angiogram (CAG) followed by Percutaneous Coronary Intervention (PCI).

## 20.5 Hypertension

Hypertension is elevation of Blood Pressure SBP  $\geq$  140 mmHg and DBP  $\geq$  90 mmHg measured atleast three separate occasions. Hypertension is a major independent risk factor for the development of CAD, stroke, and renal failure.

### Diagnostic Criteria

Blood Pressure should be measured on three separate occasions, a minimum of 2 days apart and/or taken over period of two months. Minimum of 3 blood pressure readings must be taken at the first visit to confirm hypertension.

Ambulatory Blood Pressure monitoring should be done to exclude Masked or white coat hypertension and monitoring of Blood Presure response to anti-hypetensives.

**Table 20.3: Classification of Hypertension**

Class of hypertension	SBP mmHg	DBP mmHg	Confirm diagnosis
Grade 1	140-159	90-99	After 3 months of life style modification
Grade 2	160-179	100-109	Same visit
Grade 3	>180	>110	Same visit

Consider secondary hypertension with identifiable cause in young patients < 40 years or elderly patient > 60 years presenting for first time with hypertension.

**Note**

- Recommend an alternative contraceptive method for women using oestrogen containing oral contraceptive.
- Evidence of end organ damage, i.e. cardiomegaly, proteinuria or uraemia, retinopathy or evidence of stroke, dictates immediate treatment.

**Treatment goal of Hypertension**

- In patients aged 18 - 59 years without major comorbidities, and in patients 60 years or older who have diabetes, chronic kidney disease (CKD), or both conditions, the blood pressure goal level should be <140/90 mm Hg.
- In patients aged 60 years or older who do not have diabetes or chronic kidney disease, the blood pressure goal level should be <150/90 mm Hg.

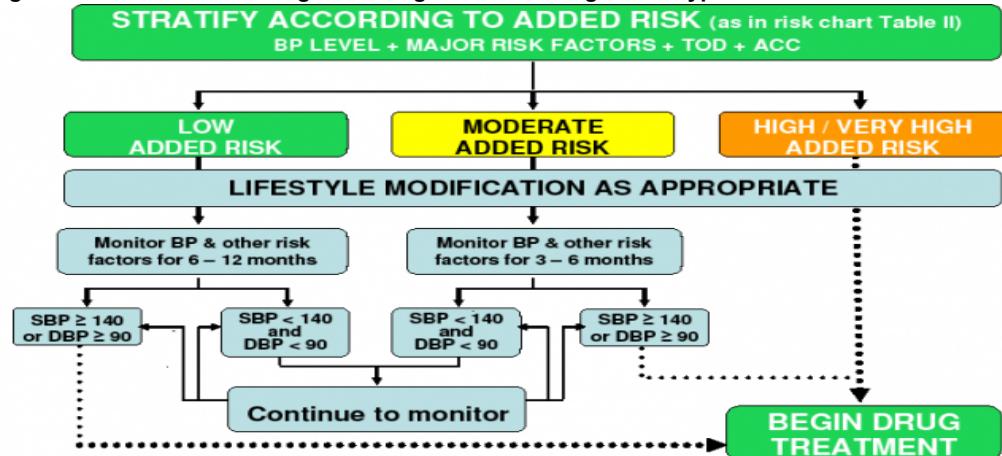
**Non-pharmacological Treatment**

Lifestyle modification:

- Lifestyle modification (refer to table 20.2)

Assess or stratify according to risk factors and target organ damage see figure 20.1 below.

**Figure 20.1: Non-Pharmacological Management flow diagram of hypertension**

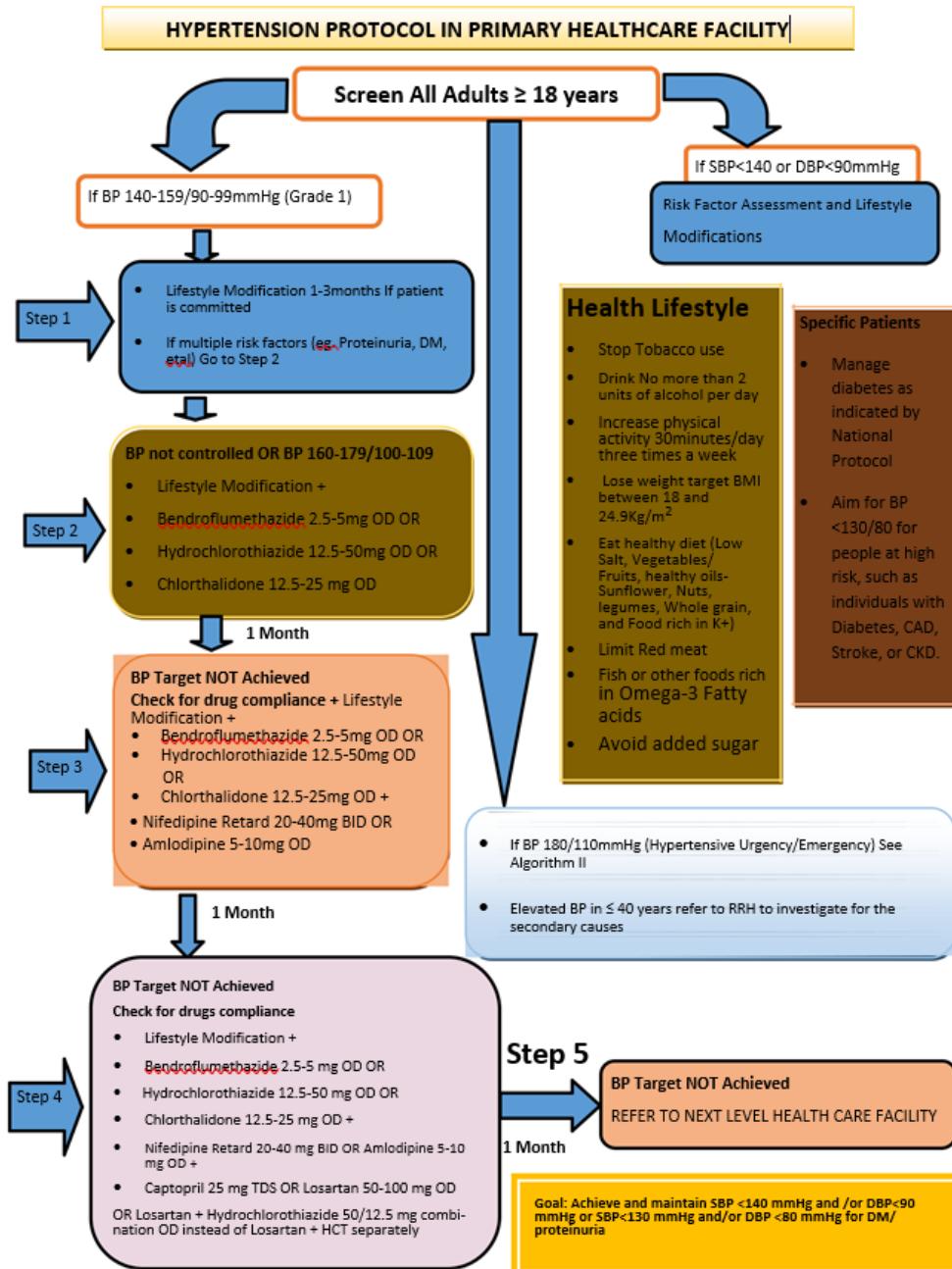


**Pharmacological Therapy**

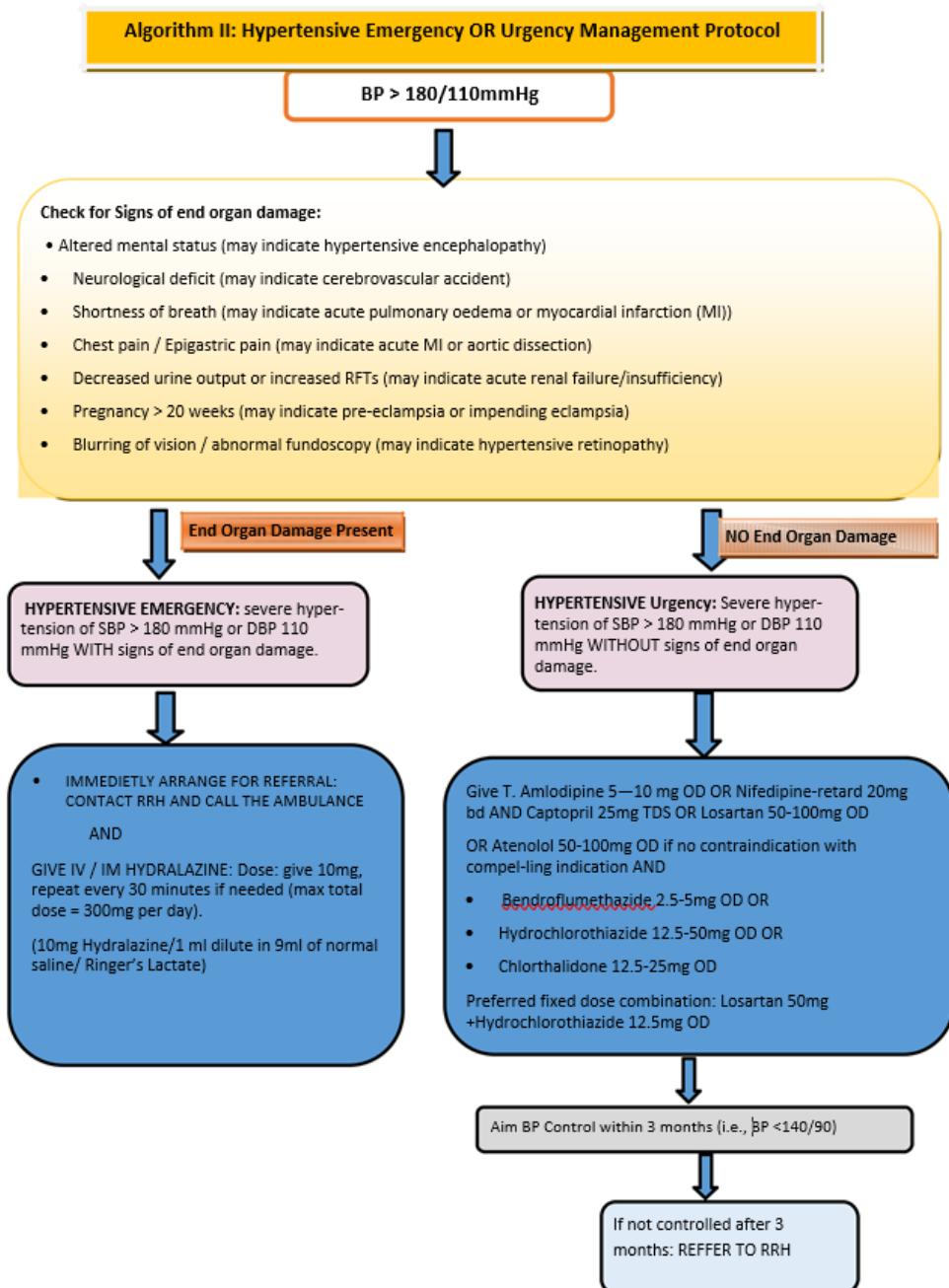
First-line treatment without compelling indications, Thiazide diuretics should be initiated. Combination therapy may be considered if SBP >20mmHg or DBP> 10mmHg above target.

Refer Figure 20.2, Algorithm II and Table 20.4 below show choice of anti-hypertensives.

**Figure 20.2: Approach of Pharmacological Treatment of hypertension in Primary Healthcare Facility.**



**Figure 20.3: Approach of Pharmacological Treatment in Hypertensive Emergency and Hypertensive Urgency.**



**Table 20.4: Compelling Indications and Anti-Hypertensive Drug Combination**

Compelling indications	Drug class
Angina Prior or Post-myocardial infarct	<ul style="list-style-type: none"> <li>• <math>\beta</math>-blocker or Long-acting calcium channel blocker</li> <li>• <math>\beta</math>-blocker and ACEI or ARB if patient sensitive to ACEIs</li> <li>• If <math>\beta</math>-blocker contraindicated: Long-acting calcium channel blocker eg Verapamil Sustained Release / Diltiazem Extended Release.</li> </ul>
Heart failure Volume overload	<ul style="list-style-type: none"> <li>• ACE inhibitor and <math>\beta</math>-blocker eg carvedilol</li> <li>• Diuretics—Loop diuretics eg furosemide and/or spironolactone *(exclude Renal Failure before adding spironolactone)</li> </ul>
Left ventricular hypertrophy (confirmed by ECG or Echocardiography)	ACE inhibitor or ARB if patient sensitive to ACEIs
Stroke: secondary prevention	Hydrochlorothiazide or Indapamide and ACE inhibitor
Diabetic mellitus	ACE inhibitor or ARB, usually in combination with diuretic
Chronic kidney disease	ACE inhibitor, usually in combination with diuretic
Isolated systolic hypertension	Hydrochlorothiazide or Long-acting calcium channel Blocker
Pregnancy	Labetalol, Nifedipine, Methyldopa or Hydralazine (Avoid ACEI/ARB due to teratogenic effect)
Prostatism	alpha-blockers
Elderly	Calcium channel blocker CCB

**Anti-hypertension therapy:**

Thiazide diuretics: Refer Figure 20.2, Step2 above

## Loop diuretics

**B:** furosemide initial dose (PO) 40mg 12hourly  
**OR**

**S:** torsemide (PO) 2.5mg /5mg/10mg 24hourly

*Dose can be up scaled depending on congestive status to maximum dose*

## Mineralocorticoid (Aldosterone) Receptor antagonist

**C:** spironolactone (PO) 25mg 24hourly  
**OR**

**S:** eplerenone (PO) 25mg 24hourly

## Angiotensin Converting Enzyme Inhibitor (ACEI)

**B:** captopril (PO) 6.125mg, 12.5mg or 25mg 8hourly  
**OR**

**C:** enalapril (PO) 10mg 12hourly

## Angiotensin Receptor Blocker–ARB (\*Do not combine with ACEI, indicated in patient sensitive to ACEIs)

**C:** losartan (PO) 25mg/50mg 24hourly  
**OR**

**S:** candesartan (PO) 8mg/16mg 24hourly  
**OR**

**S:** telmisartan (PO) 40mg / 80mg 24hourly  
**OR**

**S:** irbesartan (PO) 150mg / 300mg 24hourly

**Note**

The prescription of ARBs should depend on patient's presenting conditions

## Beta blocker (Beta 1 selective Beta Blocker)

**B:** atenolol (PO) 25mg /50mg/ 100mg 24hourly  
**OR**

**C:** metoprolol succinate (SR) (PO) 50- 200mg 24hourly  
**OR**

**S:** metoprolol injection (IV) 1mg/ml in 5ml stat  
**OR**

**S:** bisoprolol (PO) 2.5mg – 10mg 24hourly

Beta blocker (Non-selective Beta)

**A:** propranolol (PO) 40mg 24hourly

**OR**

**C:** carvedilol (PO) 6.25mg/12.5mg 24hourly

**OR**

**C:** labetalol (PO) 100mg 24hourly

**OR**

**C:** labetalol injection (IV) 5mg/ml in 2ml or 10mg/ml

Calcium Channel Blocker

Dihydropyridines:

**B:** nifedipine (PO) 10mg/20mg 24hourly

**OR**

**B:** nifedipine (Slow Release/Long Acting) (PO) 20mg/30mg/ 60mg/90mg/daily

**OR**

**C:** amlodipine (PO) 5mg or 10mg 24hourly

**OR**

**S:** nimodipine (PO) 30mg 24 hourly (indicated in subarachnoid hemorrhage, less anti-hypertensive effect)

Non-dihydropyridine

**S:** verapamil (PO) 30mg 8-12hourly for 24hours

**OR**

**S:** verapamil (Sustained Release) (PO) 120mg 24hourly (Initial daily dose), Maximum dose: 120mg 12hourly (single dose should not exceed 240mg)

**OR**

**D:** diltiazem (Extended Release) (PO) 60mg / 120mg 24hourly

**OR**

**D:** diltiazem (PO) 30mg 8-12hourly for 24hours

Alpha-2 adrenergic agonists

**A:** methyldopa (PO) 250mg 24hourly

**OR**

**S:** clonidine (PO) 50mcg/100mcg 24hourly

Alpha-1 adrenergic blockers

**S:** doxazocin (PO) 1mg / 2mg 24hourly

**OR**

**D:** tamsulosin (PO) 0.4mg24hourly

Vasodilators

**B:** hydralazine (PO) 25mg 8hourly

**OR**

**C:** hydralazine (IV) 20mg/ml in 1ml injection

**OR**

**S:** nitroglyceride/glyceryl trinitrate Injection (IV) 50mg/ml in 10ml

**Fixed Dose Combination (Poly Pills) - FDCs**

**C:** losartan + hydrochlorothiazide (FDC) (PO) 50mg/12.5mg

**OR**

**S:** candesartan+hydrochlorothiazide (FDC) (PO) 16/12.5 mg

**OR**

**S:** telmisartan + hydrochlorothiazide (FDC) (PO) 40/12.5mg, 80/12.5mg

**OR**

**S:** irbesartan + hydrochlorothiazide (FDC) (PO) 150/12.5mg

**Referral indicated when:**

- Resistant (Refractory) hypertension suspected,
- Secondary hypertension is suspected
- Complicated hypertensive urgency/emergencies,
- Hypertension with Heart failure.
- When patients are young (<30 years).
- Blood pressure is severe or refractory to treatment.

## **20.6 Resistant (Refractory) Hypertension**

Hypertension that remains  $>140/90\text{mmHg}$  despite the use of 3 antihypertensive drugs in a rational combination at full doses and including a diuretic i.e. thiazide. Consider all correctable causes of refractory hypertension before you refer.

## **20.7 Hypertensive Urgency**

Symptomatic severe hypertension SBP  $180\text{mmHg}$  and/or DBP  $>110\text{ mmHg}$  without evidence of target organ damage, such as pulmonary edema, cardiac ischemia, neurologic deficits, or acute renal failure.

### **Note**

All patients with hypertensive urgency should be treated in hospital

### **Pharmacological Treatment**

The goal is to lower DBP to  $100\text{mmHg}$  slowly over 48–72 hours. This can be achieved with two or more oral agents preferably. Refer to Figure 20.3.

## **20.8 Hypertensive Emergency**

A marked elevated systolic blood pressure  $\text{SBP} \geq 180\text{mmHg}$  and/or a diastolic  $\text{DBP} \geq 130\text{mmHg}$  associated with life threatening situations (target end organ damage) one or more of the following:

- Unstable angina/myocardial infarction
- Hypertensive encephalopathy e.g. severe headache, visual disturbances, confusion, coma, or seizures which may result in cerebral haemorrhage
- Acute left ventricular failure with severe pulmonary oedema (extreme breathlessness at rest)
- Excessive circulating catecholamine: e.g. pheochromocytoma – rare cause of emergency; food or drug interaction with monoamine oxidase inhibitors
- Rapidly progressive renal failure
- Acute aortic dissection
- Eclampsia and severe pre-eclampsia

### **Pharmacological Treatment**

**C:** labetolol (IV) 20–80mg bolus every 10 minutes or 0.5–2mg/min infusion stat 20 mg, then 20–80 mg every 10 min as needed, or stat with 0.5 mg/min infusion, then 1–2 mg/min (may be up to 4 mg/min) IV infusion up to 300 mg/d max.

Onset: 5–10 min; duration: 3–6 hours

**AND / OR**

**S:** nitroglycerin (glyceryl trinitrate); highly effective in setting of coronary ischemia, acute coronary syndromes. Dose is (IV) 5–100 $\mu\text{g}/\text{min}$  as infusion

**S:** nitroglycerin (IV) initially 5–10  $\mu\text{g}/\text{min}$  then may be up to  $>200\text{ ug}/\text{min}$  as needed

Onset: immediate; Duration: 1–5 minutes

**AND / OR**

**C:** hydralazine (IV) 5mg slow push over 1–2 minutes, repeat 5–10mg as needed

## **20.9 Heart Failure**

Heart Failure is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress.

### **Heart Failure in Pregnancy**

Symptoms and signs of heart failure in a pregnant woman are an indication for urgent assessment to establish a diagnosis and appropriate management. This is best accomplished through a multidisciplinary approach in which both cardiologists and obstetricians need to participate in order to provide expert counselling and care in pursuit of safe motherhood, as well as to exclude underlying cause of heart failure.

## **Acute Heart Failure (AHF) or Decompensated Acute Heart Failure (ADHF)**

AHF is defined as rapid or gradual onset of signs and symptoms of heart failure that results in urgent unplanned hospitalization or Emergency Medicine Department visits. The clinical signs and symptoms are significantly life threatening if the above features occur in patients with established diagnosis with structurally heart disease categorized as Acute Decompensated Heart Failure (ADHF). The cause and immediate precipitating factor(s) of the AHF must be identified and treated to prevent further damage to the heart.

### **Non-pharmacological Treatment:**

Oxygen therapy and/or ventilatory support.

- Non-invasive positive pressure ventilation includes both CPAP and bi-level positive pressure ventilation (PPV)
- Mechanical ventilation

#### **Note**

In AHF, oxygen should not be used routinely in non-hypoxaemic patients, as it causes vasoconstriction and a reduction in cardiac output

### **Pharmacological treatment**

Recommendations for the management of patients with acute heart failure:

**Diuretics:** Diuretics are a cornerstone in the treatment of patients with AHF. In patients with new-onset AHF or those with chronic, decompensated HF not receiving oral diuretics the initial recommended dose should be 20–40 mg intravenous furosemide (or equivalent); for those on chronic diuretic therapy, initial intravenous dose should be at least equivalent to oral dose.

Diuretics should either be given as intermittent boluses or as a continuous infusion, and the dose and duration should be adjusted according to patients' symptoms and clinical status. Combination of loop diuretic with either thiazide-type diuretic or spironolactone may be considered

Loop diuretic

**B:** furosemide (IV) 20–120mg 24hourly

**OR**

**S:** torsemide (PO) 5–20mg 24hourly

**AND**

Mineralocorticoid (Aldosterone) Receptor Antagonists:

**C:** spironolactone (PO) 25–50mg 24hourly

**OR**

**S:** eplerenone (PO) 25–50mg 24hourly

**Vasodilators:** these are the cornerstone of treatment of AHF and have dual benefit by decreasing venous tone (to optimize preload) and arterial tone (decrease afterload). Consequently, they increase stroke volume

Intravenous vasodilators should be considered for symptomatic relief in AHF with SBP >90 mmHg (and without symptomatic hypotension). Symptoms and blood pressure should be monitored frequently during administration of intravenous vasodilators. In patients with hypertensive AHF, intravenous vasodilators should be considered as initial therapy to improve symptoms and reduce congestion. Intravenous vasodilators for treating AHF are described in table 20.4.

#### **Note**

Vasodilators should be used with caution in patients with significant mitral or aortic stenosis.

Consider oral vasodilators in case intravenous vasodilator not available or unavailability of intensive care or high dependent unit care.

**C:** isosorbide dinitrate (PO) 10–20mg 12hourly

**OR**

**B:** hydralazine (PO) 25mg 6–8hourly. Maximum dose: 200 mg 24hourly

**Inotropes (Inotropic agents):** Indicated in patients with hypotension (SBP <90 mmHg or mean arterial BP < 60mmHg) and peripheral hypoperfusion. Dosage see table 20.5 below.

**Vasopressor (norepinephrine preferably):** Indicated in patients with cardiogenic shock, despite treatment with another inotrope, to increase blood pressure and vital organ perfusion. Dosage see table 20.5 below

**Indication:** Patients with cardiogenic shock, despite treatment with another inotrope, to increase blood pressure and vital organ perfusion.

**Table 20.5: Positive inotropes and/or vasopressors for treat acute heart failure.**

Inotropes / Vasopressors	Bolus	Infusion rate
Dobutamine	No	2–20 µg/kg/min(beta+)
Dopamine	No	3–5 µg/kg/min; inotropic(beta+) >5 µg/kg/min:(beta+), vasopressor(alpha+)
Norepinephrine	No	0.2–1.0 µg/kg/min
Epinephrine	Bolus:1mg can be given iv during resuscitation, Repeated every3–5 min	0.05–0.5 µg/kg/min

**Other Inotropes & inodilators:**

**D:** digoxin injection (IV) 0.25 mg/ml in 2 ml injection

**OR**

**D:** digoxin (PO) 0.125mg / 0.25mg

**Special pharmacological treatment consideration:**

Add ACEI

**B:** captopril (PO) 6.25–25mg 8hourly

**OR**

**C:** enalapril (PO) 5–20mg 12hourly

**OR**

**C:** lisinopril (PO) 5mg – 10mg 24hourly (When patient is out of congestive state)

Add Beta-blocker

**C:** carvedilol (PO) 6.25–25mg 12hourly a day especially in heart failure with reduced systolic function

**Thrombo-embolism prophylaxis**

In Thrombo-embolism prophylaxis, Low Molecular Weight Heparin (LMWH) is recommended in patients not already anticoagulated and with no contra indication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism.

**B:** unfractionated heparin (SC) 5,000IU 12hourly

**OR**

**S:** Low molecular weight heparin (SC) 40mg–80mg 12hourly

**OR**

**S:** Rivaroxaban (PO) 15mg/20mg 24hourly

**Note**

All patients with AHF should be treated at centre/hospital where at least can perform Echocardiographic assessment and Intensive Care Units (ICU) or High care dependent Units (HDUs) are available.

## 20.10 Chronic Heart Failure

Patients who have had HF as defined above for some time are often said to have 'Chronic Heart Failure'. A treated patient with symptoms and signs that have remained generally unchanged for at least 1 month is said to be 'Stable chronic heart failure'

### Diagnostic Criteria

The diagnosis of chronic heart failure requires the following features:

- Symptoms of heart failure, typically breathlessness or fatigue, at rest or during exertion
- Objective evidence of cardiac dysfunction preferably by Echocardiography (Systolic and/or Diastolic)
- A clinical response to treatment is supportive but not sufficient for diagnosis.

Hence diagnosis and management of CHF should be sought at referral centres where at least echocardiography assessment can be performed.

### Treatment of Systolic Heart Failure (LVEF< 45–50%)

#### Goals of treatment

- Prevention of disease leading to cardiac dysfunction and heart failure eg hypertension, coronary artery disease, valve disease etc.
- To achieve maintenance or improvement in quality of life and improve survival

#### Non-pharmacological Treatment

- Avoid excessive fluid intake in severe HF Limit fluid intake to 1–1.5 L/day if fluid overloaded despite diuretic therapy.
- Regular exercise within limits of symptoms and other lifestyle modification (refer to table 20.2).

#### Note

Sexual counselling regarding the risk of pregnancy and the use of oral contraceptives and phosphodiesterase-5 inhibitors (e.g sildenafil) are not recommended in advanced HF, if used nitrates should be avoided <24–48hours of nitrate intakes.

Medicines to avoid or to be used with caution.

- NSAIDs & COXIBS
- Class I anti-arrhythmic
- Calcium antagonists
- Lithium
- Tricyclic antidepressants
- Corticosteroid

#### Pharmacological Treatment (Approach combination therapy)

Diuretics

**B:** furosemide (PO) 40–80mg 12hourly

**OR**

**S:** torsemide (PO) 5–20mg 24hourly

**AND**

Mineralocorticoid (Aldosterone) Receptor Antagonists:

**C:** spironolactone (PO) 25–50mg 24hourly

**OR**

**S:** eplerenone (PO) 25–50mg 24hourly

Thiazide

**D:** hydrochlorothiazide (PO) 12.5–25mg 24hourly

**OR**

**S:** metolazone (PO) 0.1–10mg 12hourly

Angiotensin Receptor Inhibitors ACEI or Angiotensin Receptor Blockers (ARB)

**B:** captopril (PO) 6.25–25mg 8hourly

**OR**

**C:** enalapril (PO) 5–20mg 12hourly

Angiotensin Receptor Blocker-ARB (\*Do not combine with ACEI, Indicated in patient sensitive to ACEIs)

**C:** losartan (PO) 50mg 24hourly

**OR**

**S:** candesartan (PO) 4–16mg 24hourly

Beta blocker (Carvedilol—improve Morbidity & Mortality in CHF).

**C:** carvedilol (PO) 6.25–25mg twice a day especially in heart failure with reduced systolic function

#### Note

Beta Blockers is contraindication to patients with Bronchial Asthma or Severe Pulmonary Disease  
Symptomatic bradycardia or hypotension

## **Heart failure in Type 2 Diabetes Mellitus and Non-DM:**

**S:** empagliflozin (PO) 10mg/ 25mg 24hourly

### **Add on therapy in patient in NYHA class III/IV.**

Vasodilator agents: The combination of hydralazine/nitrate

**C:** isosorbide dinitrate (PO) 10–20mg 12hourly

**AND**

**B:** hydralazine (PO) 25 mg 6–8hourly. Maximum dose: 200 mg/day

Cardiac Glycosides—Digoxin, give with caution as has narrow therapeutic index see below under section of Cardiac Glycosides

**D:** digoxin (PO) 0.125mg–0.25mg 24hourly

#### **Note**

Patients at high risk of digoxin toxicity are: Elderly, patients with poor renal function, hypokalaemia and low body weight

### **Anti-thrombotic agents.**

Heparin &/or warfarin – firmly indicated on congestive heart failure with atrial fibrillation, previous thromboembolic events or a mobile LV thrombus Heparin for DVT prophylaxis for patients admitted to hospital, unless contraindicated:

**B:** unfractionated heparin (SC) 5000 units 8hourly

**OR**

**S:** low molecular weight heparin (IV) 40-60mg/ml 24hourly

**OR**

**C:** warfarin (PO) 5 mg 24hourly (Monitor INR to therapeutic range (2.0–2.5)

**OR**

**S:** rivaroxaban (PO) 15-20mg 24hourly

### Antidote for heparin

**B:** protamine (IV) 10ml/ml in 5mls Ampoule/vial.

1mg of protamine sulphate neutralizes approximately 100units of heparin.

Thiamine Supplement: Consider in all unexplained heart failure

#### **Note**

- Ideally all patients with CHF should be managed in dedicated HF clinics/units with devoted HF expert staffs (nurses & doctors) for further evaluation and Device therapy including CRT, CRT-D and ICD. The following category of patients should be referred for specialized care
  - Severe HF class III/IV
  - HF of unknown origin
- Relative contraindication: asymptomatic bradycardia, low blood pressure, Intolerance to low doses, Previous use of β-blockers and discontinuation because of symptoms, Bronchial asthma, or severe pulmonary disease.

## **20.11 Pulmonary Oedema**

### **Diagnostic Criteria**

Common cause of pulmonary oedema is cardiac/fluid overload, and the common causes

- Systolic heart failure complicating fluid overload
- Renal failure complicating fluid overload
- Iatrogenic fluid overload

### **Other Cause of pulmonary oedema**

- Increased capillary permeability Acute Respiratory Distress Syndrome (ARDS); many causes include Systemic sepsis—gram negative infection, pancreatitis, head injury, aspiration of gastric contents, amniotic embolus.

### **Non-pharmacological Treatment**

#### **Initial management**

- Maintain airway, bed rest in Fowler's position except if hypotensive or comatose.
- Administer oxygen to keep PO<sub>2</sub>> 60 mmHg (O<sub>2</sub> saturation > 90%)

- Correct base–acid & electrolyte disorders, determine and correct arrhythmias,

## **Pharmacological Treatment**

### **Cardiac failure**

- **B:** furosemide (IV) 20mg–80mg may be repeated in 10–15 minutes, If symptoms persist,
- **C:** morphine (IV) 1–3mg diluted form,
- Inotropic support if hypotensive SBP <90mmHg,
- **S:** dobutamine (IV) 2–20 µg/kg/min
- Intravenous vasodilator nitroglyceride if SBP > 100mmHg

### **Non-cardiac (ARDS)**

- Treat the underlying conditions
- Ventilate with PEEP – if RF
- Inotropic support if SBP<90mmHg
- Dialysis if renal failure

### **Note**

- All patients suspected with pulmonary oedema should be referred to high level of care where hospital resourced with high care dependent unit or intensive care unit.
- Patient should be stabilized first at low level of care before referral to the high level of care.

## **20.12 Infective Endocarditis (IE)**

The infective process of endocardial layer of the heart can involve native or prosthetic valve and congenital defects/shunts. Alpha-haemolytic streptococci are the most common causes of native valve endocarditis but *Staphylococcus aureus* is more likely if the disease is rapidly progressive with high fever or is related to a prosthetic valve (*Staphylococcus epidermidis*).

### **Diagnostic Criteria**

Use Modified Dukes Criteria below and consult microbiologist where possible. Three sets of blood cultures should be taken before starting treatment.

### **Modified Dukes Criteria**

#### **Major Criteria**

- Positive blood cultures of typical organism for IE from at least two separate blood cultures
- Evidence of endocardial involvement by echocardiogram (Trans-thoracic Echo/Trans-oesophageal Echo)

#### **Minor Criteria**

- Fever > 38°C
- Presence of Rheumatic heart disease, congenital heart disease
- Vascular phenomena; Major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival hemorrhage, Janeway lesions
- Immunological phenomena; glomerulonephritis, Osler's nodes, Roth's spots,
- Rheumatoid factor.
- Serologic evidence of active infective endocarditis or blood culture not meeting major criterion.

### **Definition of infective endocarditis according to the modified Duke criteria:**

#### **Definitive diagnosis of IE**

##### **Pathological criteria**

- **Microorganisms** demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen  
**OR**
- **Pathological lesions:** vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis.

##### **Clinical criteria**

- Two major criteria OR
- One major and three minor criteria OR
- Five minor criteria

## Possible Diagnosis of IE

- One major and one minor OR
- Three minor criteria

## Rejected IE

Firm alternate diagnosis.

- Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or
- No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days;  
**OR**
- Does not meet criteria for possible IE, as above.

### Note

- Positive blood cultures remain the cornerstone of diagnosis and provide live bacteria for both identification and susceptibility testing.
- To improve yield of culturing bacteria at least three blood sample sets are taken at 30 minutes apart each containing 10mL of blood and should be incubated in both aerobic and anaerobic atmospheres.
- Sampling should be obtained from a peripheral vein using a meticulous sterile technique.

## Pharmacological Treatment

### Empirical Treatment

Consider for negative blood culture or if risk delaying treatment for blood culture outweigh the benefit of starting treatment early

#### Treatment for native valves:

**A:** benzyl penicillin G (IV) 18–24million Units/24hours 4hourly in equally divided dose 4–6weeks

**OR**

**B:** ceftriaxone (IV) 2g 24hourly 4–6weeks

**AND**

**B:** cloxacillin (IV) 2g 6hourly 4–6 weeks

**AND**

**A:** gentamicin (IV) 1–1.5mg/kg 8 hourly for at least 2weeks

**OR**

If methicillin-resistant staphylococci anaerobes (MRSA)

**S:** vancomycin (IV) 30mg/kg 24 hourly in two equally divided dose, not to exceed 2gm in 24hours unless serum levels are monitored 4–6weeks.

### Note

It is important to assay serum gentamicin levels every 3–4days. One-hour peak concentration should not exceed 10mg/l and trough concentration (2-hour pre-dose) should be less than 2mg/l.

#### Prosthetic valve empirical treatment

**A:** benzyl penicillin G (X-Pen) (IV) 18 –24 million Units 4 hourly for 24hours in equally divided dose 6 – 8 weeks

**OR**

**B:** ceftriaxone (IV) 2g 24hourly >6 weeks

**AND**

**B:** cloxacillin (IV) 2g 6 hourly >6 weeks

**AND**

**A:** rifampicin 300 –600mg (IV) 8hourly >6 weeks

**AND**

**A:** gentamicin 1mg/kg (IV) 8hourly 2 weeks.

### Note

- It is important to assay serum gentamicin levels every 3–4days. One-hour peak concentration should not exceed 10mg/l and trough concentration (2-hour pre-dose) should be less than 2mg/L.
- Gentamycin in renal failure should be given based on CrCl.
- Patients with complicated IE should be evaluated and managed in high level of care or centre, with immediate surgical facilities and the presence of a multidisciplinary including an Infectious Disease specialist, a microbiologist, cardiologist, imaging specialists, and cardiac surgeons

## Infective Endocarditis Prophylaxis

- Antibiotic prophylaxis should be considered for patients at highest risk for IE:
- Patients with any prosthetic valve, including a trans catheter valve, or those in whom any prosthetic material was used for cardiac valve repair.
- Patients with a previous episode of IE.
- Patients with Congenital Heart Disease (CHD):
  - Any type of cyanotic CHD.
  - Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.

### Note

Antibiotic prophylaxis is not recommended in other forms of valvular or CHD.

## Prophylaxis of Endocarditis Infective

- To reduce the risk of bacterial endocarditis, antibiotic prophylaxis should be given to patients undergoing dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa.

Antibiotic prophylaxis is not recommended for,

- Respiratory tract procedures including bronchoscopy or laryngoscopy, or trans nasal or endotracheal intubation
- Gastrointestinal or urogenital procedures or Trans-oesophageal Echocardiogram, gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery.
- Skin and soft tissue procedures

**Table 20.6: Recommended prophylaxis for high-risk dental procedures in high-risk patient**

Situation	Antibiotic	Single-dose 30–60 minutes before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	amoxicillin or ampicillin*	2g (PO/IV)	50 mg/kg (PO/IV)
Allergy to penicillin or ampicillin	clindamycin	600 mg (PO/IV)	20 mg/kg (PO/IV)

\*Alternatively, **B**: ceftriaxone (IV) 1g for adults or 50 mg/kg for children. Cephalosporins should not be used in patients with anaphylaxis, angio-oedema, or urticaria after intake of penicillin or ampicillin due to cross-sensitivity.

## 20.13 Acute Rheumatic Fever

It is a non-suppurative sequela of a group A β haemolytic streptococcal (GABHS) pharyngeal infection.

### Diagnostic Criteria Jones See table 20.7 below

#### Definitive Diagnosis

- Two major criteria or
- One major criterion with two minor criteria, with evidence of antecedent streptococcal infection

**Table 20.7: Criteria for Acute Rheumatic Fever Diagnosis**

Major Criteria	Minor Criteria
Carditis Migratory polyarthritis Sydenham's chorea Erythema Marginatum	Clinical Fever Arthralgia Laboratory Elevated Acute Phase Reactants eg CRP Prolonged PR interval
<b>Plus</b>	
Supporting evidence of recent group A streptococcal infection e.g. positive throat culture or antigen detection and/or elevated streptococcal antibody tests*	

\*anti-streptolysin O, anti-deoxyribonuclease B

## **Non-pharmacological Treatment**

### **Acute stage:**

- Bed rest and supportive care until all evidence of active carditis has resolved
- Patient education.
- Intensive health education for prevention of sore throats.

## **Pharmacological Treatment**

Treatment of acute attack for eradication of streptococci in throat: Regardless of the presence or absence of pharyngitis at the time of diagnosis.

**A:** benzathine penicillin (IM) 1.2MU stat

Paediatric > 5 years 0.3MU, 5–10 years 0.6 MU > 10 years 1.2 MU stat

**OR**

**A:** penicillin V (PO) 500mg 8-12 hourly 24 hourly for 10days

Children > 10years 500mg, 5–10 years 250mg, < 5years 125mg (PO) 8-12 hourly for 10 days

### **Patients allergic to penicillin**

**A:** erythromycin (PO) 500mg or 40mg/kg 6hourly for 10days.

### **Treatment of Acute Arthritis and Carditis:**

**A:** acetylsalicylic acid (PO) 25mg/kg 6hourly 24hourly as required.

Acetylsalicylic acid should be continued until fever, all signs of joint inflammation and the ESR have returned to normal and then tapered gradually over 2 weeks. If symptoms recur, full doses should be restarted. \*dose should be reduced if tinnitus or other toxic symptoms develop

**In severe carditis** with development of increasing heart failure or failure of response to aspirin, Add

**A:** prednisolone (PO) 1–2mg/kg 24hourly for 3–4weeks

Then review and gradual reduction and discontinuation of prednisolone may be started after 3–4 weeks when there has been a substantial reduction in clinical disease.

**Heart failure** should be managed in the usual way (see Heart Failure Section 20.9).

### **Treatment of Sydenham's chorea:**

**B:** haloperidol(PO) 1.5–3mg 8hourly for 24 hours as required (Adult).

Paediatrics 50µg/kg for 24 hours in 2 divided doses.

**Referral:** Ideally all patients should be referred to high level of care a specialized hospital care, where surgery is contemplated

### **Antibiotic prophylaxis after rheumatic fever**

Prophylaxis should be given to all patients with a history of acute rheumatic fever and to those with rheumatic heart valve lesions. The optimum duration of prophylaxis should be up to at least 21years of age.

#### **Note**

Specific situations requiring prophylaxis for longer periods (up to 30years as a guide):

- definitive carditis in previous attacks
- high risk of exposure to streptococcal infection at home or work (crowded conditions, high exposure to children)

### **Medicine of choice**

**A:** benzathine penicillin (IM) 2.4MU monthly or every three weeks\*

Paediatrics <12yrs 1.2MU every 4 weeks or 3 weeks\* up to 21–30yrs

**OR**

**A:** phenoxymethylpenicillin (PO) 250mg 12hourly Adult

Paediatric<12yr 125–250mg 12hourly for 24hours up to 21–30years

**OR**

**A:** erythromycin (PO) 250mg 12hourly for 24hours Adult

Paediatric <12yr 125–250mg 12hourly for 24hours up to 21–30yrs\*every 3week regimen is more effective

### Valvular Heart Disease and Congenital Structural Heart Disease

**Valvular Heart Disease** are chronic acquired sequelae of Acute Rheumatic Fever or Acute Sequelae of Infective Endocarditis or Ischaemic Heart Disease, consisting of valvular damage, usually left heart valves, with varied progression of severity and complications.

**Congenital Heart Disease** is a congenital chamber defects or vessel wall anomalies

Valvular Heart Disease and Congenital Structural Heart Disease may be complicated by:

- Heart failure
- Infective endocarditis
- Atrial fibrillation
- Systemic embolism eg Stroke

### General measures

- Advise all patients with a heart murmur regarding the need for prophylaxis treatment prior to undergoing certain medical and dental procedures.
- Advise patients to inform health care providers of the presence of the heart murmur when reporting for medical or dental treatment

**Referral:** Should be considered from low level of care to high level of care where specialized (physician's care) or super-specialized care (Cardiologist's care) can be offered

## 20.14 Pulmonary Embolism

### 20.14.1 Acute Pulmonary Embolism

Clinical Spectrum less than two weeks

- Sudden onset of dyspnoea often with unexplained anxiety (most common)
- Pleuritic chest pain and haemoptysis
- Massive embolism: pleuritic chest pain, cyanosis, right heart failure and shock. Minor emboli or pulmonary infarction may herald massive embolism and must be treated vigorously
- About 90% of emboli are from proximal leg deep vein thromboses (DVTs) or pelvic vein thromboses. DVTs are at risk for dislodging and migrating to the lung circulation. Thus, termed as venous thromboembolism (VTE).

### Diagnostic Criteria

#### Determination pre-test probability of PE

Use validated scoring system: **Wells Score**

- Score > 6.0—High clinical probability proceeds with imaging test to confirm PE and treat,
- Score 2.0 to 6.0—Moderate clinical probability; negative D-dimer, PE is excluded and D-dimer positive, obtain imaging tests to confirm based on result treat.
- Score < 2.0—Low clinical probability negative D-dimer, PE is excluded. Positive D-dimer obtain imaging tests to confirm or rule out and based on result treat

### Alternatively

- Score > 4—PE likely, d-dimer positive proceeds with diagnostic imaging to confirm and treat PE.
- Score 4 or less—PE unlikely, consider d-dimer to rule out PE.

**Table 20.8: Wells Score**

Variable	Score
Clinically suspected DVT	3.0 points
alternative diagnosis is less likely than PE	3.0 points
Tachycardia (heart rate > 100)	1.5 points
Immobilization ( $\geq 3$ d)/surgery in previous four weeks	1.5 points
History of DVT or PE	1.5 points
Hemoptysis	1.0 points
Malignancy (with treatment within six months) or palliative	1.0 points

- ECG – Not reliable test for diagnosis may be normal. However,
- Sinus tachycardia most common feature, acute right ventricular strain – i.e. right axis shift, S1Q3T3 occurs in small percentage of cases, may develop acute bundle branch block – right or left, may simulate right ventricular infarction, may develop arrhythmias – eg atrial fibrillation
- Arterial blood gases; not diagnostic, the  $pO_2$  decreased <60mmHg due ventilation/perfusion mismatch.  $pCO_2$  decreased due to hyperventilation, pH increased but may decrease in shocked patient
- D-dimer test – very sensitive blood test, but not specific. A negative test d-dimer test excludes an embolus in majority of cases (best exclusive test to rule out PE when is negative)
- Chest X-ray – Not very reliable usually normal, diaphragm may be raised on affected area, atelectasis may occur, peripheral wedge-shaped shadow & plural effusion
- Cardiac Echocardiography: Useful in diagnosis, features suggestive or support evidence of massive embolus acute right ventricular strain
- Computer Tomography Pulmonary Angiogram Scan (CTPA); Useful can demonstrate the presence and extent of proximal pulmonary emboli
- Ventilation/Perfusion Scan; Useful in stable patient to confirm the diagnosis. The presence of a perfusion defect with normal ventilation not corresponding to an x-ray abnormality is characteristic
- Pulmonary Angiography: Still gold standard investigation, may be necessary to establish
- Diagnosis and catheter-based embolectomy in the catheterization lab.

### **Non-pharmacological Treatment**

- Administer  $O_2$  – maintain  $pO_2$  > 60mmHg,
- Treat shock
- Correct electrolyte & acid base abnormalities and arrhythmias
- Ventilate if patient in respiratory failure

### **Pharmacological Treatment**

#### **Anticoagulation**

**B:** unfractionated heparin (UFH) (IV) 10,000units then maintenance infusion starts with 6,000U over 6 hours to keep PTT or clotting time 2–3times above baseline. PTT should be performed 12hourly per lab instruction.

**OR**

**S:** low molecular weight heparin (SC) 1mg/kg 12hourly for 24hours

Start warfarin after 24hours of heparin and continue post discharge for long-term. If the aetiology unknown may be for life, if aetiology is established at least for six months. Maintain INR 2.0–3.0

#### **Thrombolytic (Fibrinolysis)**

Indicated in proximal massive pulmonary emboli and haemodynamically unstable if no contraindication exists

**S:** streptokinase (IV)250,000IU over 30minutes, then 100,000IU per hour for 24hours

**OR**

**S:** alteplase (rtPA) (IV) 100mg over 2hours

**Referral:** All cases suspected of pulmonary embolus should be referred to a high level of care – specialized hospital care with HCDU/ICU

### **20.14.2 Chronic Pulmonary Embolism**

Chronic pulmonary embolism is mainly a consequence of incomplete resolution of acute pulmonary thromboembolism. Clinically symptoms and signs may be preceded by Acute Pulmonary Embolism for more than 2weeks.

#### **Pharmacological Treatment**

Long-term oral anticoagulation

**C:**warfarin(PO) 2–10mg 24hourly

**OR**

**S:** rivaroxaban (PO) 15-20mg 24hourly

**Maintain INR 2.0–3.0 for warfarin use individuals.**

**Referral:** All cases suspected of pulmonary embolism should be referred to a high level of care

## **20.15 Cardiac Arrhythmias/ Dysrhythmias**

Always exclude underlying structural cardiac disease in all patients with cardiac dysrhythmias as well as performing Holter ECG monitoring aiding at detecting type of arrhythmia.

### **20.15.1 Tachyarrhythmias**

#### **20.15.1.1 Narrow QRS Complex Tachyarrhythmias (SVTs)**

Definition Sustained (> 30 seconds) or non-sustained narrow QRS ( $\leq 0.1$  seconds) tachycardias.

##### **Atrial Fibrillation**

###### **Acute onset (< 48 hours)**

- Assess clinically, e.g. heart failure, mitral stenosis, thyrotoxicosis, hypertension, age and other medical conditions.
- Consider anticoagulation with heparin or warfarin.
- Synchronized DC cardioversion is occasionally necessary in emergency especially haemodynamic instability or consider if is the first episode.

###### **Non-acute/chronic (> 48 hours)**

- As above, but not immediate DC cardioversion is indicated, unless in hypotensive emergency cases. Anticoagulation with oral warfarin 2-5mg orally once a day for at least a month, then perform elective cardioversion at specialized hospital.

##### **Atrial flutter**

- P waves visible before QRS, commonly occurs, usually 2:1. (150 per minute). P waves, usually negative in Lead II precede QRS, blocked P in ST segment or hidden by QRS.
- Vagal stimulation with ECG may reveal blocked P waves.

##### **AV Junctional Re-Entry Tachycardias**

Usually paroxysmal, often young with normal heart.

- AV nodal re-entry or WPW syndrome. P waves usually not visible (hidden by QRS).

##### **Non-pharmacological Treatment**

###### **Electrical Cardioversion.**

Synchronized DC cardioversion, 200 J, after sedation with:

**A:** diazepam (IV)10–20 mg stat

If flutter has been present longer than 48hours, defer cardioversion for 4weeks after anticoagulation with warfarin, unless severe symptoms or heart failure requires urgent cardioversion.

##### **Pharmacological Treatment**

None is nearly as effective as DC cardioversion.

Consider anticoagulants if Atrial flutter sustained.

**Long term treatment:** Recurrent atrial flutter is an indication for referral. Many can be cured by radiofrequency catheter ablation.

###### **Atrial tachycardias**

- Rare, often incessant P before QRS (often long PR) or hidden in T
- May cause heart failure (tachycardia cardiomyopathy).

###### **Atrial fibrillation**

- I. With fast ventricular response without aberrant conduction.

###### **Pharmacological Treatment, Initial:**

Anticoagulation with warfarin

**OR**

**S:** rivaroxaban (PO)15-20mg 24hourly (in Non-valvular AF)

**Rate control** (Control the ventricular rate with one of the following):

**D:** digoxin (IV) Initial dose: 0.25-0.5mg; then 0.25mg 4-6hourly to maximum of 1mg; Maintenance dose: 0.125-0.25mg 24hourly (IV) or (PO) (Digoxin 0.25mg (PO) daily; use only in heart failure).

**OR**

**B:** atenolol (PO) 50–100mg 24hourly (contraindicated in asthmatics).

**OR**

**D:** diltiazem (IV) initial dose: 15-20mg over 2minutes; may repeat in 15 minutes, Maintenance dose: 5-15mg hourly by continuous IV infusion

**OR**

**S:** verapamil (IV) 5 to 10 mg over 2minutes; may repeat in 30minutes

DC cardioversion in selected cases, after 4weeks of anticoagulation

Digoxin only controls rate at rest and is insufficient on its own. If used for long-term, combine with  $\beta$  – blocker:

**D:** digoxin (PO) 0.125-0.25mg 24hourly

In the elderly and patients with renal impairment: Adjust dosages according to trough levels within the therapeutic range. Do levels only if the patient has been on the drug for at least 10 days.

**AND / OR**

**B:** atenolol (PO) 50–100 mg 24hourly

**OR**

**S:** bisoprolol (PO) 2.5mg – 10mg 24hourly

**OR**

**C:** metoprolol (PO) 25mg -50mg 24hourly

**OR**

**S:** sotalol (PO) 80mg – 160mg 12hourly

**Note**

Avoid use of Digoxin in patients with Accessory pathway.

- II. With fast ventricular response with Aberrant conduction (eg: Wolff-Parkinson-White syndrome, WPW)

Catheter ablation of the accessory pathway in symptomatic patients with preexcited AF, especially if the accessory pathway has a short refractory period that allows rapid antegrade conduction.

**Long – term**

- Continue warfarin anticoagulation long-term, unless contraindicated:

**C:**warfarin (PO) 5mg 24hourly

**OR**

**S:** rivaroxaban (PO) maintance dose; 15mg / 20mg 24hourly

**OR**

Left atrial appendage occlusion (LAAO).

**Note**

- INR monitoring in patients on warfarin. Maintain therapeutic Range INR 2–3: Stable patients check 3 monthly. If INR < 1.5 or > 3.5: do monthly monitoring.
- Left atrial appendage occlusion (LAAO) is indicated in Atrial Fibrillation patients who can not tolerate long-term Anticoagulation or contraindicated to OACs (Oral anticoagulants) and have thrombo-embolic risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$ ), increased risk of bleeding (HASBLED score  $\geq 3$ ) and thrombo-embolic events despite adequate OAC after excluding other plausible causes (eg carotid disease).

## 20.15.2 AV Junctional Re-Entry Tachycardias

### Non-pharmacological Treatment

Vagal manoeuvres: Valsalva or carotid sinus massage. The patient should be supine and as relaxed as possible, to avoid competing sympathetic reflex

### Pharmacological Treatment

If vagal manoeuvres fail:

**S:**adenosine (IV) 6mg over 1-3 seconds (maybe given IO) followed by rapid flush with 20mL NS, if no conversion within 1-2minutes give 12mg, repeat a second time if necessary (30mg total)

If none of the above is effective, and patient is hypotensive, consider DC shock

### **Prevention of recurrent paroxysmal atrial fibrillation**

Only in patients with severe symptoms despite the above measures:

**S:** amiodarone (PO) 200mg 8hourly for 1week, followed by 200mg 12hourly for one week and thereafter 200mg 24hourly. Specialist initiated.

### **Precautions:**

- Halve dosage of warfarin and monitor INR closely if patient on warfarin, until stable
- Avoid concomitant digoxin use.

#### **Note**

Verapamil and digoxin are contraindicated in WPW syndrome.

**Long-term treatment:** Teach the patient to perform vagal manoeuvres, Valsalva is the most effective. For infrequent, non-incapacitating symptoms:

β –Blockers

**B:** atenolol (PO) 50–100mg 24hourly (If asthmatic)

**OR**

**S:** verapamil (PO) 80–120mg 8hourly for 24hours (Normal heart)

**Referral:** Refer to Cardiac specialized center for Mapping and Radiofrequency Ablation (RFA)

### **20.15.3 Wide QRS (Ventricular) Tachyarrhythmias (VTs)**

Sustained (> 30 seconds) or non-sustained wide QRS (> 0.12 seconds) tachycardias

#### **Regular Wide QRS Tachycardias**

These are ventricular tachycardias until proved otherwise. Regular wide QRS supraventricular tachycardias are uncommon.

#### **Non-pharmacological Treatment**

Refer all cases after resuscitation and stabilization. Emergency DC cardioversion is mandatory with a full protocol of Cardiopulmonary Resuscitation (CPR)

- If no cardiac arrest: DC cardioversion, 200J, after sedation with: Diazepam, I.V, 10–20mg If 200J fails, use 360J.
- If cardiac arrest: Defibrillate (not synchronized).

#### **Pharmacological Treatment**

DC cardioversion is first line therapy for regular wide QRS tachycardias.

Medicines are needed if VT recurs after cardioversion or if spontaneous termination/recurrence.

**S:** amiodarone (IV) 5mg/kg (150–300mg) infused over 30minutes then continue with maintenance dose to total dose of 1200mg/24hours

**OR**

**S:** amiodarone (PO) 800 mg 24hourly for 7days, 600mg/day for 3days followed by a maintenance dose of 200–400mg/day

Amiodarone may cause serious long-term side effects due to long half-life. Therefore, patients require regular monitoring by specialist.

**A:** lidocaine (IV) 50–100mg (1–2mg/kg) initially and at 5minute intervals if required to a total of 200–300mg,

Thereafter, for recurrent ventricular tachycardia only

**A:** lidocaine (IV) 1–3mg/minute for 24–30hours. Lidocaine will only terminate ± 30% of sustained ventricular tachycardias, and may cause hypotension, heart block or convulsions.

#### **Note**

- Never give verapamil IV to patients with a wide QRS tachycardia.
- For emergency treatment of ventricular tachycardia, DC cardioversion is first-line therapy, even if stable.

### **Sustained (> 30 Sec) Irregular Wide QRS Tachycardias**

They are usually due to atrial fibrillation with bundle branch block, or pre-excitation (WPW syndrome).

## **Non-pharmacological/Pharmacological Treatment**

- If the QRS complexes have a pattern of typical right or left bundle branch block, with a rate < less than 170/minute, treat as for atrial fibrillation. See the section on atrial fibrillation.
- If the rate is > 170 per minute, and/or the complexes are atypical or variable, the likely diagnosis is WPW syndrome with atrial fibrillation, conducting via the bypass tract, DC conversion.

**Referral:** Refer patient to high care centre for further management including arrhythmia mapping and RFA

## **Non-Sustained (< 30 Sec) Irregular Wide QRS Tachycardias**

They are usually ventricular, commonly in acute myocardial infarction. In acute myocardial infarction, only treat non-sustained ventricular tachycardia if causes significant haemodynamic compromise. Ensure the serum potassium level is above 4 mmol/L.

## **Pharmacological Treatment**

Medicines are needed if VT recurs after cardioversion or if spontaneous termination/recurrence.

**S:** amiodarone (IV) 5 mg/kg (150-300mg) over 30minutes then continue with maintenance dose to total dose of 1200mg for 24hours

**OR**

**S:** amiodarone (PO) 800mg 24hourly for 7days, followed by 600mg 24hourly for 3 days then a maintenance dose of 200–400mg 24hourly

Only in a haemodynamically stable patient:

**A:** lidocaine (IV) 50–100mg (1–2mg/kg) initially and at 5minute intervals if required to a total of 200–300mg

Thereafter, for recurrent ventricular tachycardia only:

**A:** lidocaine (IV) 1–3mg/minute for 24–30hours

In the absence of acute ischaemia or infarction, consider torsade's de pointes.

## **Torsade's De Pointes Ventricular Tachycardia (VT)**

- Has a twisting pattern to the QRS complexes and a prolonged QT interval in sinus rhythm, it is usually due to a QT-prolonging drug, ± hypokalaemia.

## **Non-pharmacological Treatment**

- Cardioversion/defibrillation, as necessary.
- Torsade's complicating bradycardia: temporary pacing

## **Pharmacological Treatment**

Stop all QT-prolonging drugs. Correct serum potassium.

**A:** magnesium sulphate (IV) 2g over 5–10minutes

If recurrent episodes after initial dose of magnesium sulphate:

**A:** magnesium sulphate (IV) 2g over 24hours

Torsade's complicating bradycardia: temporary pacing.

**A:** adrenaline infusion to raise heart rate to >100 per minute  
(if temporary pacing unavailable).

**Referral:** Refer all cases of wide QRS tachycardia, after resuscitation and stabilization for possible arrhythmia mapping and RFA.

## **20.16 Heart Block (Second and Third Degree)**

Most cases occur in patients over 60 years and is idiopathic. Acute, reversible AV block commonly complicated by inferior myocardial infarction, here temporary Pacemaker used as bridge therapy. The condition may also be induced by medicines, metabolic and electrolyte derrangements.

## **Non-pharmacological Treatment**

- Emergency cardio-pulmonary resuscitation.
- External pacemaker should be available in all secondary hospitals and must be preceded by appropriate analgesia.

## **Pharmacological Treatment**

Analgesia if external pacemaker:

**C:** morphine (IM)10–15mg 3–6hourly

For Temporary treatment of complete AV block before referral for pacemaker:

**A:** atropine (IV) bolus 0.6–1.2mg every 3 – 5min (max 3mg) may be repeated until a temporary or permanent pacemaker is inserted.

(Use in an Inferior Infarct patients, hypotension, and second-degree AV block).

For resuscitation of asystole:

**A:** adrenaline (IV) 1:10000, slow 5mL (0.5mg)

#### **Referral**

- All cases with a heart rate below 40 beats/minute after resuscitation and stabilization to high level of care where permanent pacemaker implantation can be performed.
- All cases of second or third-degree AV block, whether myocardial infarct or other reversible cause is suspected, and whether the patient is thought to be symptomatic.

#### **Note**

Complete Heart Block Is a Medical Emergency Refer Urgently

## **20.17 Sinus Bradycardia & Sinus Arrest**

This rhythm does not require treatment, unless they are causing symptoms, i.e. syncope, dizziness, tiredness, and poor effort tolerance. Sinus bradycardia <50/minute or sinus arrest with slow escape rhythm, accompanied by hypotension, strongly suggests a treatable underlying cause:

- Acute inferior myocardial infarct
- Hyperkalaemia, especially if wide QRS and/or peaked T waves
- Drugs, especially combination of verapamil and  $\beta$  -blocker or digoxin
- Hypothermia
- Hypoxia

Treat the cause. Consider atropine if inferior infarct.

#### **Note**

- Refer the patient After stabilization to the Cardiac Specialized centre for thorough evaluation and Pacemaker Implantation [Temporary/Permanent Pacemaker Implantation (single or Dual chamber) depending on the underlying cause], prepare Vancomycin injection for sterilization of Permanent Pacemaker pouch.

# CHAPTER TWENTY-ONE

## KIDNEY AND UROLOGICAL DISORDERS

These are disorders resulting from structural malformation or function of the genitourinary system that may lead to kidney impairment. These disorders include diseases originating from the kidney and systemic diseases, which result in complications affecting the kidney. Hypertension and diabetes mellitus are the commonest conditions causing complications in the kidney, therefore all patients with hypertension and diabetes mellitus should be regularly screened for kidney complications.

### 21.1 Chronic Kidney Diseases (CKD)

It is structural or functional kidney damage present for >3months, with or without a decreased glomerular filtration rate (GFR). Early screening in high-risk groups [hypertension, Diabetes and glomerular diseases] is crucial in improving outcome of CKD. Once cause and plan for care has been established, adults with early CKD stages 0-3 can be managed at primary care level.

#### Clinical Presentation

Clinical features depend on the stage of kidney disease. In advance stage includes:

- Anorexia
- Malaise
- Vomiting
- Oliguria/anuria

#### Investigations

- Kidney function tests (serum creatinine and urea) - at diagnosis check every month for 3months. If active sediment/proteinuria, provider may check more frequently
- FBC (HB)
- Urinalysis (Protein, red blood cells and cast cells) then quantify the amount of protein in urine by Esbach test or Urine albumin-creatinine ration or Urine protein-creatinine ratio
- Kidney-Ureter-Bladder (KUB) ultrasound
- CXR
- ECG
- Serum electrolytes Potassium, Calcium Phosphate and Sodium [CKD stage 3-5: Check monthly]
- Serum albumin (for corrected calcium)
- Serum bicarbonate levels (venous) [CKD stage 3-5: Check monthly]
- Parathyroid hormone levels, Serum Phosphate and Alkaline phosphatase (ALP) [CKD stage 5 on dialysis]

#### Note

Cause of CKD should be determined and addressed. Especially when thinking of kidney transplantation

The general management of the patient with chronic kidney disease involves the following issues

- Treatment of reversible causes of kidney dysfunction
- Preventing or slowing the progression of kidney disease
- Treatment of the complications of kidney dysfunction
- Identification and adequate preparation of the patient in whom kidney replacement therapy will be required

**Table 21.1: Staging of kidney disease for adequate management of CKD stage/glomerular filtration rate (GFR\*) (ml/minute/1.73)**

Stage	Description	Action Includes actions from preceding stages
Stage 0 or GFR >90	Increased risks for CKD e.g. <ul style="list-style-type: none"><li>• Diabetes mellitus</li><li>• Hypertension</li><li>• Glomerular disease</li><li>• HIV</li></ul>	Screening for advanced CKD and CVD disease CKD risk reduction i.e. treat hypertension, diabetes and HIV <ul style="list-style-type: none"><li>• Check creatinine/BUN every month for 3 months then yearly if stable</li></ul>

	<ul style="list-style-type: none"> <li>Hepatitis B/C</li> </ul>	
Stage 1 or GFR >90	Kidney damage with normal GFR	Diagnose and treat comorbid conditions See for Stage 0
Stage 2 or GFR 60-89	Kidney damage with mild GFR reduction	Refer to determine cause and develop care plan While on the care plan, monitor the GFR in these patients and make sure kidney function is not worsening rapidly and watch for stage 3
Stage 3 or GFR 30-59	Moderate GFR reduction	Refer to physician/nephrologist Monitor and manage complication Check creatinine/BUN every 3months
Stage 4 or GFR 15-9	Severe GFR reduction	Refer to nephrologist Prepare for kidney replacement therapy
Stage 5 or GFR <15	Kidney failure requiring kidney replacement therapy End stage kidney disease	Refer to nephrologist

\* Use CKD-EPI formula without the ethnicity factor. This calculator is available freely online.  
Laboratories in Tanzania should report as eGFR.(Delanaye and Mariat, 2013)[1, 2]

### Non-pharmacological Treatment

- Reduce salt intake.
- Low protein diet (not exceed 1g/kg per day) is indicated in the presence of CKD stage 4 and 5. (Evidence)
- Reduce cardiovascular disease risk factors – See section: Prevention of ischaemic heart disease and atherosclerosis.
- Treat underlying conditions.
- Decrease significant proteinuria, if present.

Significant proteinuria = more than +2 protein on urinalysis OR spot urine protein creatinine ratio of > 0.1 g/mmol OR ACR (albumin-creatinine ratio) > 100 g/mol, confirm as positive if raised on at least 2 of 3 occasions, in the absence of infection, cardiac failure and menstruation.

### Proteinuria

- In established chronic kidney disease, decrease proteinuria, irrespective of presence or absence of systemic hypertension.
- Monitor kidney function and potassium especially with impaired kidney function.
- If volume depleted, first rehydrate before commencing ACE-inhibitor.
- ACE-inhibitor are contraindicated in:
  - ✓ Hyperkalaemia
  - ✓ known allergy to ACE-inhibitor

Begin with low dosage of ACE-inhibitor and titrate up ensuring blood pressure remains in normal range and no side effects are present, up to the maximum dose or until the proteinuria disappears – whichever comes first.

### Pharmacological Treatment

#### Adults

C: enalapril (PO) 10–20mg 12hourly

OR

C: lisinopril (PO) 5-10mg 24hourly (titrate max 40mg 24hourly)

Also see other ACEI in hypertension treatment (Cardiovascular Chapter)

### Hyperlipidaemia

If hyperlipidaemia is a co-existent risk factor manage according to section

### 21.1.1 Diabetic Kidney Disease

This is a clinical diagnosis based on the presence of albuminuria, decreased estimated glomerular filtration rate (eGFR) or both in diabetes. This diagnosis includes diabetic nephropathy which has

microalbuminuria (30-300mg/g) and retinopathy in its defining characteristics. In diabetics, optimise control according to section 9.6: Diabetes mellitus type 2, in adults.

### Investigations

- Urinalysis (Dipstick biochemistry + microscopy)
- Kidney biopsy with the following indications – if cause not apparent
  - Albuminuria >300mg/g within 5years of DMT1 onset
  - RBC cell cast, dysmorphic RBC or WBC casts in urine sediment
  - Presence of other systemic illness eg SLE
  - Rapid decline (per year) of eGFR>5mL/min/1.73m<sup>2</sup>
- Ultrasonography kidney ureter and bladder (KUB)

**Table 21.2: Pharmacological Treatment of CKD patients with Diabetes mellitus**

[3-5, 20-25] (Saisho, no date; Wanner *et al.*, 2016; V. Perkovic *et al.*, 2019; Vlado Perkovic *et al.*, 2019; Zou *et al.*, 2019)]

Non-dialysis CKD Adults (Titrate carefully)

eGFR	Medication	Considerations
>90 Stage 1	As in treatment of non-CKD Diabetes: see Diabetes Mellitus Chapter	Strong consideration of including SGLT2-Inhibitors
89-60 Stage 2	For type-2 DM with high cardiovascular risk (an add on) <b>S:</b> empagliflozin (PO) 10mg 24hourly <b>OR</b> <b>S:</b> sitagliptin (PO) 50mg 24hourly	
59-30 Stage 3	<b>A:</b> gliclazide (PO) 40–80mg 12hourly if not available use <b>OR</b> <b>C:</b> glimepiride (PO) 1-8mg 24hourly +/- <b>S:</b> empagliflozin (PO) 10 mg 24hourly	Caution on Metformin and long acting sulphonyl urea Titrate carefully
29-15 Stage 4	<b>C:</b> gliclazide (PO) 40 – 80mg 12hourly <b>OR</b> <b>C:</b> glimepiride (PO) 1-8mg 24hourly +/- <b>S:</b> sitagliptin 25mg 24hourly	If on insulin, dose reduction is needed
< 15 Stage 5 OR On dialysis	Insulin preferred. Reduce dosage with decreasing eGFR <b>D:</b> pioglitazone (PO)15-30mg 24hourly	fluid control

### 21.1.2 Hypertension and CKD

Treat if present. See Cardiovascular chapter

The target blood pressure for CKD patients without proteinuria should be <140/90 and for those with proteinuria should be <130/80.

### Investigation

- Ambulatory blood pressure monitoring
- As for CKD section
- R/o secondary causes and control

### Non-pharmacological Treatment

- Salt restriction (low sodium diet)
- Cardiovascular risk reduction as per Hypertension/CVD section

**Table 21.3: Pharmacological Treatment of Hypertension and CKD**

eGFR STAGE	Medication <b>*At least one medication be taken at bedtime</b>	Considerations
>90 Stage1  And  89-60 Stage2	With Proteinuria >500mg/day <b>C:</b> enalapril (PO) 10–20mg 12hourly <b>OR</b> <b>C:</b> lisinopril) 5-10mg 24hourly (titrate max 40mg 24hourly) <b>OR</b> <b>S:</b> irbesartan (PO) 150-300mg 24hourly If not available, use another ARB as in Hypertension treatment If poorly response + oedema Diuretics as in section on fluid overload +/- <b>D:</b> diltiazem (PO) 60-120mg 12hourly <b>OR</b> <b>S:</b> verapamil (PO) 40–80mg 8hourly	Check K+ level Consider repeat creatinine after 5-7days of starting ACE-Inhibitor
	With no Proteinuria <500mg/day If has oedema Diuretics See section on fluid overload <b>PLUS</b> ACE-Inhibitors/ARB as above ADD if not controlled <b>D:</b> diltiazem (PO) 60-120mg 12hourly <b>OR</b> <b>S:</b> verapamil (PO) 40–80mg 8hourly  Other medications If above fails <b>C:</b> spironolactone <b>OR</b> <b>S:</b> eplerenone as in Hypertension treatment/Portal hypertension +/- <b>B:</b> hydralazine (PO)12.5 mg – 50 mg +/- <b>B:</b> nifedipine (PO) 20-40mg 12hourly <b>OR</b> <b>C:</b> amlodipine 5-10mg 24hourly +/- <b>B:</b> atenolol (PO)25–00mg 24hourly  If not available or intolerable use below <b>C:</b> carvedilol (PO)6.25mg-25mg 12hourly <b>OR</b> <b>S:</b> bisoprolol (PO) 2.5-5 mg 24hourly +/- <b>S:</b> doxazosin (PO) 1mg 24hourly (titrate max 16mg) <b>OR</b> <b>A:</b> methyldopa (PO)250-1000mg 8hourly	
59-30 Stage 3	As above Dose adjustment <b>C:</b> lisinopril (PO) 5-10mg 24hourly	Monitor potassium more frequency
29-15 Stage 4  < 15 Stage 5 OR On dialysis	DO NOT USE ACE inhibitor OR angiotensin receptor blocker. Treatment as above  Dose reduction for <b>S:</b> bisoprolol (PO)2.5mg 24hourly <b>A:</b> methyldopa (PO)250mg – 1 g 24hourly <b>S:</b> doxazosin (PO) 1mg 24hourly (titrate max 16mg 24hourly)	Fluid control may be more important  *Diuretics *Salt restriction *Ultrafiltration volume in dialysis

## **Fluid overload**

Treat fluid overload if present and refer. Exclude other causes of oedema as part of management.

### **Adults**

**B:** furosemide (slow I.V, PO) 40–80mg 12hourly.

**OR**

**D:** torsemide (PO) 10-20mg 24hourly (titrate max 200mg/day)

If poor response, repeat after 1hour.

If diuresis is inadequate and there is no hypokalaemia a combination therapy with thiazide or thiazide-like diuretics could be used

**B:** furosemide (maximal 600mg/day) slow infusion rather than boluses +/-

**D:** hydrochlorothiazide (PO) 25-50mg 12hourly

**OR**

**S:** metolazone (PO) 2.5–20mg 24hourly

### **Note**

Do not give I.V fluids – use heparin lock or similar I.V access.

### **Referral to nephrologist**

- All cases of suspected chronic kidney disease stages 3–5 for assessment and planning
- All children
- All cases of CKD with:
  - haematuria,
  - proteinuria
  - raised blood urea or creatinine initially for assessment and planning
- Uncontrolled hypertension/fluid overload
- CKD associated with hyperlipidaemia
- No resolution of proteinuria with ACE-I therapy

### **Note**

Patients who might qualify for dialysis and transplantation or who have complications should be referred early to ensure improved outcome and survival on dialysis, i.e. as soon as GFR drops below 30 mL/min/1.73m<sup>2</sup>, or as soon as diagnosis is made/suspected

### **21.1.3 Dialysis**

Refer to the National guidelines for Dialysis services from the MOHCDGEC for the detailed indications, procedures and management of patients on dialysis (Haemodialysis or Peritoneal dialysis)

### **21.1.4 CKD Associated Metabolic Acidosis**

(serum bicarbonate below 22mmol/l)

**S:** sodium bicarbonate (PO) 650mg 12hourly. Titrate to serum bicarbonate levels 23–29mmol/l

**OR**

**S:** calcium carbonate (PO) 500mg 12hourly.

### **21.1.5. Hyperkalaemia**

Refers to an elevation in potassium concentration  $\geq 5.5$  mmol/l. Kidney failure and use of medications use are common causes. Severity of hyperkalaemia may be mild (5.5-6), moderate 6.1–6.5 and Severe  $>6.5$ . Severity grading increases once there is ECG changes.

### **Clinical Presentation**

- Muscle weakness (ascending)
- Muscle fasciculation
- Paralysis
- Cardiac conduction abnormalities
- Cardiac arrhythmias

### **Investigation**

- Serum potassium – frequent reassessment 0hr, 1hr, 3hr
- ECG (decreased size of p waves, T waves changes, prolonged PR and
- Serum bicarbonate
- Full blood picture
- Serum creatinine

- Lipid levels – Total cholesterol and LDL
- Uric acid
- Blood glucose

### **Non-pharmacological Treatment**

- Avoid foods rich in potassium; which include potatoes, bananas, green vegetables
- Stop offending medication Renin-angiotensin-aldosterone system inhibitors. NSAIDS and potassium sparing diuretics

### **Pharmacological Treatment**

Cellular membrane stabilization – All patients with potassium >6.5mmol/l or with ECG changes

Adults

**A:** calcium gluconate (IV) 10% 10-30mls stat

Reserve for ICU through a central line.

**D:** 10% calcium chloride (IV) 10mls stat

- may repeat again if ECG abnormal within 5-10minutes
- do not give together with sodium bicarbonate

### **Potassium shift to the intracellular compartment (repeated dosing of insulin may be necessary)**

Adults

**A:** insulin short acting 5-10IU +50mls of 50% Glucose iv injection. Only give glucose if RBG is <11

- Monitor RBG for hypoglycaemia
- Repeat insulin short acting /glucose every 4-6 hours

Children

**A:** insulin short acting 0.1IU/kg + dextrose 0.5g/kg for 30min

**AND**

Adults

**C:** salbutamol nebulized 2.5-10mg every 4-6hours

**OR**

If has metabolic acidosis and not overloaded

Adults and Children

**C:** sodium bicarbonate (IV) 1mEq/kg over 15minutes

### **Removal of Potassium from the body**

**D:** calcium (or sodium) polystyrene sulphonate 15-30g 8hourly for 3days. (Caution: Bowel perforation risk). Can be given 3time a week chronically

**AND**

**B:** furosemide (PO/slow I.V) 40–80mg 12hourly +/- haemodialysis

If above is not available

**C:** lactulose (PO)10-30ml hourly until rapid laxation then 30mls 8hourly per 24hours

### **21.1.6 CKD Associated Anaemia**

Patients with CKD present with anaemia, which may be contributed by several factors including inability to produce erythropoietin, frequent, blood loss (from gastritis, dialysis therapy and poor appetite. [Refer to the national guidelines for dialysis]

Investigations for anaemia for patients with CKD stage 3-5

- Peripheral smear
- Reticulocyte count
- Full blood count
- Iron studies; serum iron, transferrin saturation and serum ferritin
- Stool for occult blood

Patients with CKD stage 3 and below with anaemia should be given erythrocyte stimulating agents (ESA) when Haemoglobin is < 10 g/dL and interrupt or reduce once Haemoglobin level reaches 11g/dL.

**S:** erythropoietin alfa (IV) 50-100 units/kg 3times a week as approximate starting dose,  
May be given with IV iron supplementation

Patients with CKD stage 3 and below with iron deficiency indicated by transferrin saturation <30% or serum ferritin <500ng/ml should be given iron supplementation;

**D:** Iron sucrose (IV) 100mg with each dialysis for 10doses

**Note**

IV Iron is preferred to oral iron and can be given with ESA among patients on dialysis.

### **21.1.7 Mineral Bone Disease (MBD)**

Mineral bone diseases are common among patients with CKD including those undergoing maintenance haemodialysis and these diseases contribute cardiovascular complication and mortality. Clinical features of these disorders include Bone pain, Convulsions, Tetany, Tissue calcification, Fractures. The following investigations should be carried out to identify these disorders among patients with CKD stage 3 and below;

- Serum calcium,
- Albumin (for correction of calcium)
- Phosphate
- Parathyroid hormone (intact)
- Vitamin D Levels
- Lumbar-X-ray (lateral)
- DEXA scan (those suspected)

#### **Non-pharmacological Treatment**

- Nutritional consultation: Low phosphate diet and high calcium diet

#### **Pharmacological Treatment**

Hyperphosphataemia treatment

**S:** calcium carbonate (PO) 500-1500mg 8hourly with meals [For patients with hypocalcaemia]

### **21.1.8 Haemodialysis (HD) Catheter Related Blood Stream Infection**

A common life-threatening complication which needs prompt recognition and response in the dialysis unit.

#### **Clinical Presentation**

- Chills and/or fever  $\geq 37.8^{\circ}\text{C}$
- Tunnel or exit site purulence
- Rigors

#### **Investigations**

- Blood culture
- FBP
- Investigate for metastatic infection when indicated

#### **Non-pharmacological Treatment**

- Refer to management of sepsis if in shock
- Removal of catheter if there is non-response to therapy, exit site infection, tunnel infection, metastatic infection or hemodynamic instability

#### **Pharmacological Treatment**

Usual 14-21days of treatment

- Empirical (while waiting for microbiological results)

Children

**C:** flucloxacillin (IV) 25-50mg/kg/day in 3 divided doses

- Adults**
- D:** ceftazidime (IV) 50mg/kg/dose every 48hourly, give after dialysis or on dialysis days
  - C:** flucloxacillin (IV) 1-6g/d in 3 divided doses  
**AND**
  - D:** ceftazidime (IV) 1g stat immediately after HD and 1g after subsequent HD session  
**OR**
- Adult**
- S:** vancomycin (IV) 20mg/kg loading over last 1 hour then 1g during the last hour of subsequent HD sessions  
**AND**
  - D:** ceftazidime (IV) 1gm STAT immediately after HD and 1g after subsequent HD session
- Children**
- S:** vancomycin (IV) 10mg/kg/dose (consider checking serum levels)  
**AND**
  - D:** ceftazidime 50mg/kg/dose 48hourly, give after dialysis or on dialysis days
- Tailored
    - According to bacteriological results
    - If negative continue with empirical treatment showing clinical improvement

**Note**

In case all above mentioned antibiotics are not available, patients should be treated empirically with antibiotics favouring both gram negatives and gram positives.

Catheter lock (during treatment)

- D:** gentamicin lock
- D:** vancomycin lock

## 21.2 Acute Kidney Disease

Acute kidney disease is a sudden decline in the glomerular filtration rate (GFR) resulting elevation of serum blood urea, creatinine and other waste products. Practically AKI is recognized when there is urine output of less than 0.5ml/kg/hour for >6 hours. Causes of AKI are classified as pre-renal, renal and post-renal causes and usually result in reversible kidney failure, these causes include;

**Table 21.4: Causes of acute kidney injury**

Category	Examples	Intervention
Pre-renal: loss of effective blood flow to the kidneys	Low blood volume <ul style="list-style-type: none"> <li>• Diarrhea, burn, acute blood loss</li> </ul> Heart failure Hepatic failure	Restore blood volume <ul style="list-style-type: none"> <li>• IV fluids</li> </ul> Low blood pressure <ul style="list-style-type: none"> <li>• Use of inotropes</li> </ul>
Renal: caused by intrinsic kidney insult	-Glomerulonephritis -Nephrotoxic medications -Rhabdomyolysis -Tumor lysis syndrome	Treatment of specific Glomerular disorders Omit offending nephrotoxic drugs
Post renal: occurs as a consequence of urinary obstruction	-BPH -Urinary stones -Obstructed urinary catheters -Bladder stones	Relief of obstruction -Urinary catheterization -Nephrostomy

### Clinical Presentation

- Oedema
- Oliguria/anuria
- Convulsions in children

### Investigation

Early disease

- Creatinine [increase of  $\geq$  26micromol/l within 48hrs or  $\geq$  50% increase within 7 days defines AKI]

- Ultrasound KUB
- Urinalysis (Dipstick and microscopy)

Advanced disease defined by urine output of less than 0.5ml/kg/hour for >12 hours.

- Serum electrolytes [potassium, chloride, bicarbonate, Sodium phosphate and calcium]
- Arterial Blood Gases
- Uric acid
- Urine electrolytes – Fractional excretion of Sodium
- Chest X-ray
- ECG
- Kidney biopsy if cause not obvious clinically
- Creatine kinase if Rhabdomyolysis is suspected

### **Non-pharmacological Treatment**

- Give oxygen, and nurse in semi-Fowlers' position if patient has respiratory distress.
- Stop intake of all salt and potassium containing foods and fluids
- Restrict fluid intake to 10 mL/kg/day daily plus visible fluid losses
- Remove nephrotoxic medications
- Adequate nutritional support: sufficient amounts of energy and adequate protein. Consider enteric/parenteral nutrition

### **Pharmacological Treatment**

Treat underlying cause

#### **Adults**

If dehydrated,

**A:** 0.9% sodium chloride (PO/IV) while monitoring urine output

If diastolic blood pressure is greater than **100 mmHg** or systolic blood pressure is above **150 mmHg**:

**C:** amlodipine (PO) 5 mg

If there is respiratory distress (rapid respiration, orthopnoea) and is fluid overloaded [chest crackles and raised JVP]:

**B:** furosemide (IV bolus) 80mg. (higher doses may be tried once)

If there is respiratory distress (laboured breathing with low serum bicarbonate=metabolic acidosis)

**C:** sodium bicarbonate (IV) 150mEq in 1L of 5%Dextrose

Consider Proton pump inhibitors to reduce risk of gastrointestinal bleeding

**C:** pantoprazole (IV/PO) 40mg 24hourly

Treat Hyperkalaemia as in CKD

Haemodialysis or Peritoneal dialysis when indicated

#### **Note**

- Indications for dialysis include pulmonary oedema, Hyperkalaemia, metabolic acidosis not responding to medical therapy and uremic encephalopathy or pericarditis. Acute poisoning with a dialysable substance is another indication.
- Patients with AKD will be followed regularly to monitor and prevent CKD. A weekly kidney assessment (creatinine and/or urinalysis) for one month and then monthly for 2 months and then 6-monthly thereafter is a suggested regime when there is no CKD.
- Do not put up a drip **and do not** give a fluid infusion if the patient is fluid overloaded or urine does not increase with iv. fluids

#### **Referral**

All cases where adequate laboratory and clinical resources exists, management according to the hospital level guidelines may be instituted. Referral to the nephrologist should occur in the following:-

- Glomerulonephritis is a strong possibility – haematuria and proteinuria.
- Worsening despite initial treatment.

### **21.3 Glomerular Diseases (GD)**

Glomerular diseases include a broad array of clinicopathological syndromes which progress to glomerulosclerosis and eventually end stage kidney disease. Glomerular disease may be a result of a primary condition of the kidney or may be secondary to a systemic disorder.

## Clinical Presentation

- Proteinuria
- Reduced GFR (and its effects)
- Haematuria
- Hypertension
- Oedema.

### 21.3.1 Glomerular disease - Nephritic syndrome

A non-infectious inflammatory process that involves the nephron. History and examination should exclude secondary causes.

#### Clinical Presentation:

- Painless macroscopic turbid, bloody or brownish urine
- Peripheral and facial oedema
- Difficulty in breathing
- Hypertension encephalopathy with impaired level of consciousness or convulsions
- Little or no urine excretion

#### Investigations

- Serum Creatinine
- Blood urea nitrogen/Urea
- Urinalysis (Dipstick + microscopy)
- confirm proteinuria by Urine albumin-creatinine ratio (UACR) or Urine protein-creatinine ratio (UPCR)
- Urine culture
- Complete blood count
- Kidney biopsy and histology
- Others on tertiary hospital e.g. ANA, dsDNA, RF, , complements, Syphilis tests (VDRL or RPR)

#### Non-pharmacological Treatment

- Give oxygen, and nurse in semi-Fowlers position if patient has respiratory distress.
- Restrict intake of all salt
- Restrict potassium containing foods and fluids
- Restrict fluid intake to 10 mL/kg/day daily plus visible fluid losses

#### Pharmacological Treatment

##### Adults

Fluid overload

**B:** furosemide (IV bolus) 80mg

If hypertension

If diastolic blood pressure is greater than **100mmHg** or systolic blood pressure is above **150mmHg**:

**C:** amlodipine (PO) 5mg stat before referral to higher facility

Continue with other medications as in hypertension section (caution contraindications)

#### Note

The definitive treatment of nephritis depends on the cause – an assumption of acute post streptococcal nephritis or any other disease cannot be made without specific investigation, which may include kidney biopsy.

### 21.3.2 Nephrotic syndrome

It is a kidney disorder characterized by urinary protein loss leading to generalized body swelling. It is severe proteinuria defined as: Adults: 3.5 g/day,

#### Clinical Presentation

- Oedema
- Hypoalbuminaemia
- Hyperlipidaemia

#### Note

- Diagnosis of nephrotic syndrome requires a kidney biopsy, however in children (1year-18 years) biopsy is indicated for children with steroid resistant nephrotic syndrome
- Children (1-18 years) should be given treatment with steroid, they should be referred for renal biopsy if there is no response.

## Non-pharmacological Treatment

Adequate calories and adequate protein 1g/kg/d

No added salt to limit fluid overload

## Pharmacological Treatment

The management of glomerular disease depends on the type/cause of the disease and is individualized guided by a specialist according to the histology results obtained after renal biopsy.

### Note

Referral to nephrologist may include treatment using immunosuppressant such as prednisolone, mycophenolate mofetil, cyclophosphamide, angiotensin blockade etc

**Table 21.5 Histology based treatment of Glomerular diseases**

S/N	Histological Pattern	Treatment Regime	Special considerations
1	Minimal change disease	<p>Children</p> <p><b>Steroid Sensitive</b></p> <p>Initial: <b>A:</b> prednisolone 60mg/m2/d] or 2mg/kg/d [max 60mg/d] for 6 weeks [complete 6weeks of initial treatment if remission is attained at 4weeks)</p> <p>Continue: <b>A:</b> prednisolone 40mg/m2 or 1.5mg/kg for 6weeks, if the patient has attained remission by 4weeks of initial treatment, after 6weeks of alternate days' therapy taper and stop within 6weeks (taper by 5-10mg a week)</p> <p>Relapsing Steroid Sensitive 0.9% sodium chloride</p> <p><b>A:</b> prednisolone 60mg/m2 or 2mg/kg [max 60mg/d] until in complete remission for 3 days,</p> <p><b>THEN</b></p> <p><b>A:</b> prednisolone single dose on alternate days (40mg/m2 per dose or 1.5mg/kg per dose: maximum 40 mg on alternate days) for at least 4 weeks.</p> <p><b>S:</b> levamisole (PO) 2.5mg/kg on alternate days for 12months</p> <p>Frequent relapse steroid dependent</p> <p><b>S:</b> cyclophosphamide 2mg/kg/d 10-12 weeks [max 168mg/kg cumulative dose] <b>OR</b></p> <p><b>S:</b> cyclosporine 4-5mg/kg/d (starting dose) <b>OR</b></p> <p><b>S:</b> tacrolimus 0.1mg/kg/d (starting dose) <b>OR</b></p> <p><b>S:</b> everolimus 0.5-2mg 12hourly <b>OR</b></p> <p><b>S:</b> sirolimus 1-3mg 12hourly <b>OR</b></p> <p><b>S:</b> mycophenolate mofetil 1200mg/m2/d in two divided doses</p> <p><b>S:</b> rituximab 375-1000mg/m2</p> <p>Steroid resistant Nephrotic syndrome</p> <p><b>S:</b> mycophenolate mofetil 1200mg/m2/d in two divided doses <b>OR</b></p> <p><b>S:</b> mycophenolate sodium <b>AND</b></p> <p><b>A:</b> prednisolone high dose</p> <p>Adults</p> <p><b>D:</b> prednisolone (PO) 1mg/kg 24hourly (maximum 80 mg) <b>OR</b></p> <p>alternate-day single dose of 2 mg/kg (maximum 120 mg – 4-week if remission, continue to 16 weeks if complete remission not achieved</p> <p>Frequent relapse/steroid dependent/resistant</p>	<p>In children biopsy is indicated for</p> <ul style="list-style-type: none"> <li>1. Children with steroid resistant NS</li> <li>2. Late failure to respond following initial response</li> <li>3. Decreasing kidney function</li> </ul> <p>Monitor calcineurin inhibitor toxicity/levels</p>

2	Focal segmental glomerulosclerosis	<p>for idiopathic only</p> <p><b>D:</b> prednisolone (PO) 1mg/kg [max 80mg] daily or alternate day dose 2mg/kg [max 120mg] 4-16weeks  <b>OR</b>            Intolerance for steroids or steroid resistant</p> <p><b>S:</b> cyclosporine 3.5-5mg/kg/d in 2divided doses  <b>OR</b>  <b>S:</b> tacrolimus 0.1mg/kg/day in 2 divided doses (then titrate)</p>	<p>Exclude secondary</p> <p>Slow taper after remission over 6months</p> <p>Monitor levels</p>
3	Membranous nephropathy	<p>For idiopathic membranous nephropathy only</p> <p>Children</p> <p>Alternating monthly treatment with Methyl prednisolone + Prednisolone (month 1, 3 &amp; 5) and oral Cyclophosphamide (month 2, 4 &amp; 6)</p> <p><b>D:</b> methylprednisolone 10mg/kg for 3days, prednisolone 0.5mg/kg for 27 days</p> <p><b>S:</b> cyclophosphamide 2mg/kg for 30 days</p> <p>Alternative regimes</p> <p><b>S:</b> cyclosporine 3.5-5mg/kg in two divided doses with prednisolone 0.15 mg/kg/day for 6 months</p> <p><b>S:</b> tacrolimus 0.2mg/kg in two divided doses without prednisolone</p> <p>Adults</p> <p><b>S:</b> cyclophosphamide</p> <p><b>A:</b> prednisolone 1mg/kg/day</p> <p><b>D:</b> methylprednisolone IV monthly</p> <p>Alternative regimes</p> <p><b>S:</b> tacrolimus 0.1mg/kg/day in 2 divided doses for 6 months <b>OR</b></p> <p><b>S:</b> cyclosporine 3.5-5mg/kg/d in 2 divided doses</p> <p>If albumin is less than 25g/l + thrombosis risk</p> <p><b>C:</b> warfarin 5mg PO [refer to DVT anticoagulation]</p>	<p>Exclude secondary</p> <p>Monitor for 6 months before initiation unless life threatening symptoms OR</p> <p>Raising creatinine</p> <p>-Do not use serum creatinine &gt;309 micromol/l [CKD patient]</p> <p>Kidney biopsy might be repeated</p>
4	Membrano proliferative	<p><b>S:</b> cyclophosphamide <b>OR</b></p> <p><b>S:</b> mycophenolate mofetil 1200mg/m2/d in two divided doses  <b>OR</b></p> <p><b>S:</b> mycophenolate sodium  <b>AND</b></p> <p><b>A:</b> prednisolone</p>	
5	Immunoglobulin A Nephropathy	<p>Initial supportive care for 3-6 month</p> <p><b>C:</b> enalapril (PO)10-20mg 24hourly <b>OR</b></p> <p><b>C:</b> lisinopril (PO)2.5-10mg 24hourly</p> <p>For those persistent proteinuria 1g/d for 6 months</p> <p>Adults and children</p> <p><b>A:</b> prednisolone (PO) 1mg/day for 6 months</p>	<p><b>Note</b></p> <p>Other registered ACEI or ARBs may be used as in Hypertension section</p>
6	Lupus nephritis Adult	<p>All patients</p> <p><b>S:</b> hydroxychloroquine (PO) 6mg/kg/day maintenance</p> <p>Class II with proteinuria &gt;3g/day</p> <p>For those with proteinuria &gt;3g/day</p>	

		<p><b>Class III and class IV</b></p> <p><b>Initial 6 months</b></p> <p><b>D:</b> methylprednisolone (IV slow) 250mg-1000mg 30min 3days monthly</p> <p><b>AND</b></p> <p><b>S:</b> cyclophosphamide (IV) 500-1000mg/m<sup>2</sup> monthly</p> <p><b>OR</b></p> <p><b>S:</b> mycophenolate mofetil (PO) 0.5-1g 12hourly titrating (PO) 1.5g 12hourly if tolerated <b>OR</b></p> <p><b>S:</b> mycophenolate sodium</p> <p><b>Maintenance</b></p> <p><b>S:</b> azathioprine (PO) 1.5-2.5mg/kg/d</p> <p><b>OR</b></p> <p><b>S:</b> mycophenolate mofetil (PO) 0.5-1g 12hourly</p> <p><b>OR</b></p> <p><b>S:</b> mycophenolate sodium <b>OR</b></p> <p><b>S:</b> cyclosporine 4-5mg/kg/d (starting dose) 6 months <b>OR</b></p> <p><b>S:</b> tacrolimus 0.1mg/kg/d (starting dose)</p>	<p>Oral prednisolone less effective 60mg/day may be given</p> <p>Open to use a shorter more frequent regime</p> <p>EURO lupus Cyclophosphamide 500mg every two weeks x 6doses</p>
		Class V + persistent nephrotic range proteinuria As clas II and IV	
7	Pauci-immune focal and segmental necrotizing glomerulonephritis	<p><b>Initial</b></p> <p><b>S:</b> cyclophosphamide (IV) 15mg/kg every 2 weeks x3 doses then every three weeks for 3-6 months <b>OR</b></p> <p><b>S:</b> cyclophosphamide oral 1.5-2mg/kg daily 3-6 months</p> <p><b>AND</b></p> <p><b>D:</b> methylprednisolone (IV) 250mg-1000mg slow 30min 3days as induction then Prednisolone 1mg/kg then taper to 30mg in one week then taper down to 5mg by 4-6months</p> <p><b>Severe disease</b></p> <p><b>S:</b> rituximab 1g followed by 14 days later another 1g</p> <p><b>OR</b></p> <p><b>S:</b> rituximab 375 mg/m<sup>2</sup> per week for 4 weeks</p> <p><b>AND</b></p> <p><b>D:</b> methylprednisolone (IV) 250-1000mg slow 30min 3days as induction then</p> <p><b>A:</b> prednisolone 1mg/kg then taper to 30mg in one week then taper down to 5mg by 4-6months</p> <p><b>Maintenance therapy</b></p> <p><b>S:</b> azathioprine (PO) 1-2mg/kg/d 18months</p> <p><b>OR</b></p> <p><b>S:</b> mycophenolate mofetil 1g 12hourly <b>OR</b></p> <p><b>S:</b> mycophenolate sodium</p>	<p><b>S:</b> Haemodialysis</p> <p><b>S:</b> Plasmapheresis</p> <p>In special indications</p>

## 21.4 Kidney Transplantation

Kidney transplantation is one of the kidney replacement therapies with good outcomes in morbidity and mortality. A Kidney Transplant recipient (KTR) is a fully rehabilitated individual who is capable of contributing to the society.

### 21.4.1: Transplant Donor Evaluation

General principles of preparing a live Kidney Transplant Donor will be outline in this subsection. Risk assessment and communication to ensure the donor candidate is able to decide without undue pressure is one of the early steps in evaluation. The transplant program policies of concerned centre

should be the basis for decision. Post decision for both accepted or excluded, follow up care should be formulated.

## Clinical presentation

A complete history and physical examination should be documented.

## Investigations

Investigations will be based on the following :-

Adults aged 18years and above should be considered for live related donation. Pre-donation evaluation should include

- Psychosocial assessment
- Surgical assessment for suitability
  - Obesity
  - Anticoagulation
  - Vascular anatomy and native kidneys in polycystic kidney disease
  - Urology
- Diabetes screening
- Cancer screening this should proceed even after transplantation.
  - Imaging, cystoscopy even colonoscopy for candidates with specific increased risks
  - Do not exclude patients with cured malignancy. Waiting time will depend on malignancy
- Pulmonary disease assessment
- Cardiovascular disease assessment
  - ECG and ECHO
  - Stress ECG
  - Dobutamine ECHO if above 40 years/ has risk of myocardial arterial disease.
- Peripheral arterial disease
  - All candidates by history and physical examination. Imaging may be necessary. Consult vascular surgeon prior to transplantation.
- Neurological disease screening
  - Wait for 6 months after a stroke or TIA
  - Screen for intracranial aneurysms in high risk autosomal dominant polycystic kidney disease
- Gastrointestinal and Liver disease
  - History and physical examination to exclude active PUD, Diverticulitis, Pancreatitis Cholelithiasis Inflammatory bowel disease and liver disease
    - Specific investigations may be necessary
- Haematological
  - Screen for thrombophilia and antiphospholipid antibodies in high risk individuals
  - Need for anticoagulation is not a contraindication for transplantation
- Immunological assessment
  - Document and communicate all sensitizing events (blood transfusion & miscarriage)
  - Perform HLA antibody testing at transplant evaluation
- Infection screening
  - Hepatitis B/C
  - HIV
  - CMV
- Compatibility testing
  - ABO blood typing
  - Human leukocyte typing for MHC and Class I, II in both donor and recipients
  - Donor specific anti-HLA antibodies in recipients
- Pre-donation Kidney function
  - Serial Serum creatinine, eGFR
  - Measured creatinine clearance
  - OR measured GFR
  - In special situations single kidney GFR (using radio labelled agents eg TC-DTPA - technetium 99mTc-diethylenetriamine pentaacetic acid (DTPA))

## **21.4.2: Transplant Candidate**

All patients with CKD stage 4-5 should be informed of, educated about and considered for kidney transplantation regardless of socioeconomic status, sex, or ethnicity. Pre-emptive transplantation referral should be 6-12 months before anticipated RRT initiation. Active diseases should be controlled first before transplantation.

The following are not recommended for kidney alone transplant

- Multiple myeloma and AL amyloidosis
- Decompensated cirrhosis
- Severe irreversible obstructive or restrictive lung disease
- Severe uncorrectable and symptomatic cardiac disease
- Progressive central neurodegenerative disease

### **Transplant candidate assessment should include the following**

- Psychosocial assessment, Adherence to therapy and Tobacco use avoidance
- Surgical assessment for suitability
  - Obesity
  - Anticoagulation
  - Vascular anatomy and native kidneys in polycystic kidney disease
  - Urology
- Diabetes screening
- Cancer screening this should proceed even after transplantation.
  - Imaging, cystoscopy even colonoscopy for candidates with specific increased risks
  - Do not exclude patients with cured malignancy. Waiting time will depend on malignancy
- Pulmonary disease assessment
- Cardiovascular disease assessment
  - ECG and ECHO
  - Stress ECHO
  - Dobutamine ECHO if above 40 years/ has risk of myocardial arterial disease.
- Peripheral arterial disease
  - All candidates by history and physical examination. Imaging may be necessary. Consult vascular surgeon prior to transplantation.
- Neurological disease screening
  - Wait for 6 months after a stroke or TIA
  - Screen for intracranial aneurysms in high risk autosomal dominant polycystic kidney disease
- Gastrointestinal and Liver disease
  - History and physical examination to exclude active PUD, Diverticulitis, Pancreatitis Cholelithiasis Inflammatory bowel disease and liver disease
    - Specific investigations may be necessary
- Haematological
  - Screen for thrombophilia and antiphospholipid antibodies in high risk individuals
  - Need for anticoagulation is not a contraindication for transplantation
- Immunological assessment
  - Document and communicate all sensitizing events (blood transfusion & miscarriage)
  - Perform HLA antibody testing at transplant evaluation
- Infection screening
  - Hepatitis b/c
  - HIV
  - CMV

## **21.4.3 Transplant Recipient**

This section will cover the management of kidney transplant recipients (KTRs). It includes initial and maintenance immunosuppression, monitoring and management of special conditions. Enhanced investigations and treatment in this group is paramount to ensure kidney graft survival.

#### **21.4.4.1 Induction Therapy**

There is a choice of Interlukin 2 receptor blockers and lymphocyte depleting agents. Patients with high immunologic risk for acute graft rejection should receive lymphocyte-depleting agents instead of IL2-RA. The following factors favor using lymphocyte-depleting agents.

- One or more human leukocyte antigen (HLA) mismatches
- Younger recipient and older donor age
- Panel reactive antibody (PRA) greater than 0 percent
- Presence of a donor-specific antibody (DSA)
- Blood group incompatibility
- Delayed onset of graft function
- Cold ischemia time greater than 24 hours

#### **For low risk patients**

Adults

**S:** basiliximab 20mg (IV) stat within 2hours before transplant and (IV) 20mg stat on day 4

**OR (high risk patients)**

**S:** rabbit anti-thymocyte globulin 1.5 mg/kg/day for 4 to 7 days; the first dose prior to transplant (Intra OP)

**OR**

**S:** Antithymocyte globulin ATG (horse)

Children

For children above 35kg use same dose as adults.

Below 35kg use below

**S:** basiliximab (IV) 10mg stat within 2hours before transplant and 10mg IV stat on day 4

**OR (high risk patients)**

**S:** horse anti-thymocyte globulin 1.5mg/kg/day for 4 to 7days; the first dose prior to transplant

#### **21.4.4.2 Maintenance Immunosuppressive Medication**

A combination of immunosuppressive medication which include a calcineurin inhibitor (CNI) and an antiproliferative agent with or without corticosteroids is recommended at this stage. Except for when mammalian target of rapamycin inhibitors (mTORi) is used, it is recommended to start immunosuppression before or during transplantation without waiting for graft function establishment.

#### **Monthly investigations**

- Serum creatinine and Blood urea nitrogen
- Urinalysis
- Urine biochemistry (Urine dipstick)
- Serum Tacrolimus (12-h trough) or cyclosporin (12-h trough or 2-h post dose) levels according to patient's regime

#### **Pharmacological Treatment**

Adults

**S:** tacrolimus initial 0.1-0.2mg/kg/day in 2divided doses titrate to planned serum levels (immediate release)

**OR**

If tacrolimus is not available

Adults and Children

**S:** cyclosporin (modified) 7-12mg/kg/day in 2divided doses (titrate to serum levels)

In special indications (eg. with Kaposi Sarcoma) or mostly low risk KTRs

Adults

**S:** sirolimus loading dose: 15mg loading dose on day 1. Maintenance: 5mg/day (trough concentration 5-7ng/mL)

**AND**

**S:** mycophenolate mofetil (PO) 1-1.5g 12hourly

**OR**

**S:** mycophenolate sodium 360-1080mg 12hourly

**OR**

**S:** azathioprine Initial following transplant IV/PO 2-5mg/kg stat. Maintenance (PO) 1-3mg/kg 24hourly

**AND**

Glucocorticoids as part of triple-agent immunosuppressive regime

Initial

**D:** methylprednisolone 7mg/kg (maximum of 500mg) IV stat intra (OP) –operation

**OR**

**A:** prednisolone 1mg/kg/day (max 80mg) for first 3 days' post-transplant

Maintenance

**A:** prednisolone 20mg/day 7 days then taper by 5mg weekly maintain at 5mg/kg

After 4months post transplantation efforts to decrease dose of immunosuppression if there has been no acute rejection. Do not stop steroids or CNIs

**Note**

- Use of a non-dihydropyridine CCB to minimize CNI dosage may be economical.
- Assessment for medication adherence is crucial. So education for all KTRs and family members is important.

#### **21.4. 4. 3 Monitoring schedule for the Kidney Transplant Recipients (Routine)**

Kidney transplant recipients have high risk of getting complications including surgical complications (first 3 months), frequent infections (first six months) and complication related to immunosuppressive medications including diabetic mellitus. Some of the immunosuppressive medications have a narrow therapeutic window and have toxic effects including nephrotoxicity. Therefor these patients need regular and frequent follow up as indicated in the table below.

**Table 21.6: Monitoring schedule for the Kidney Transplant Recipients (Routine)**

Test	Screening intervals by time after transplantation					
	1week	1month	2-3months	4-6months	7-12months	>12months
Creatinine + eGFR	Daily	2-3 per week	Weekly	Every 2 weeks	Monthly	Every 2-3 mo
Urine protein (UACR/UPCR )	Once			Every 3 months		
Complete blood count	Daily	2-3/week	Weekly	Monthly		Annually

Diabetes	Weekly		Every 3 months		Annually
Lipid profile	-	-	Once	-	Annually
BKV Nucleic acid testing	monthly		Every 3 months		-
EBV Nucleic acid testing	Once	Monthly		Every 3 months	-
BP/pulse/weight/height	Each clinic visit				

## 21.4.5. Acute Kidney Graft Rejection

An acute rejection is clinically suspected in patients with increased serum creatinine, after the exclusion of other causes of graft dysfunction. Other causes are generally excluded with a biopsy. Acute rejection should be treated after kidney biopsy unless this will substantially delay treatment.

### Clinical presentation

- Occur within the first six months after transplantation
- Fever
- Malaise
- Oliguria
- Graft pain and/or tenderness
- Worsening hypertension

### Investigations

- Kidney biopsy which may be repeated if there is failure of treatment
- Serum creatinine and Blood Urea nitrogen
- Kidney Ultrasound and doppler US of the kidney
- Nuclear medicine renal scans
- Urinalysis – urine biochemistry and microscopy
- BK polyomavirus
- CMV

Acute cellular rejection (Use Banff classification in treatment)

**D:** methylprednisolone (IV) 300-500mg 24hourly for 3-5days followed by prednisolone taper.

If corticosteroids have failed

**OR/AND**

**S:** rabbit Anti-thymocyte globulin 1.5 mg/kg/day for 4 to 7days

**OR**

**S:** anti-thymocyte globulin (ATGam) Children and Adolescents: IV: 10 to 15mg/kg/dose once daily for 14days, then if needed, may administer every other day up to a total of 21 doses in 28 days

Antibody-mediated acute rejection (Histology of injury + vascular endothelium c4d staining + serologic evidence)

**D:** methylprednisolone (IV) 300-500mg daily for 3-5days

**AND**

**S:** plasma exchange 24hourly or alt. day until serum creatinine within 30% of previous (max 5sessions)

**OR**

**S:** rituximab 200 to 375 mg/m<sup>2</sup> after completion of plasmapheresis and IVIG

**OR**

**S:** rabbit Anti-thymocyte globulin 1.5 mg/kg/day for 4-7days

**OR**

**S:** anti-thymocyte globulin (ATGam) Children and Adolescents: IV: 10 to 15 mg/kg/dose 24hourly for 14days, (up to 21 doses in alternate days sometimes)

## 21.4. 6 Other Conditions in Transplantation and their Managements

**Table: 21.6 Other Common Conditions That Are Encountered Among Transplant Recipients and Their Management**

Diagnosis/Conditions	Evaluation	Treatment
Recurrent Kidney Disease	Urine protein Serum creatinine Kidney biopsy +/- ANCA +/- Anti-GBM antibodies CBC, LDH	+/- Plasmapheresis +/- Cyclophosphamide and corticosteroids -/+ ACE-Inhibitor or ARBs
Vaccinations	Check Hepatitis B surface antibodies 12weeks after completing vaccination	All inactivated vaccines (unless not approved) are okay HBV vaccination before transplant Avoid vaccinations in the first 6/12 Influenza vaccine may be given in the first 6months. AVOID live vaccines Pneumococcus
Viral diseases		
BK polyoma virus (BKV)	Kidney biopsy BKV Nucleic acid testing	Reduce immunosuppression
Cytomegalovirus	CMV serologies pre-transplant both donor and recipient  CMV plasma Nucleic acid testing is used for diagnosis and monitoring treatment	Prophylaxis for 3 months <b>S:</b> valganciclovir (PO) 900mg 24hourly  For treatment of life-threatening disease <b>S:</b> ganciclovir (IV) 6mg/kg 12hourly until clinical response Then continue with <b>S:</b> valganciclovir (PO) 900mg bid until symptom resolution
Epstein-Barr Virus and Post-Transplant Lymphoproliferative disease	EBV by nucleic acid testing	Reduce immunosuppressive medication with patients who have raising EBV loads  EBV disease and post-transplant lymphoproliferative disease
Herpes simplex virus 1,2 and varicella zoster virus		Superficial disease Oral acyclovir /valacyclovir until lesions have resolved  Systemic disease 1. Reduce immunosuppressive medication 2. Iv. Acyclovir Frequent attacks Give prophylactic antivirals
Pneumocystis jirovecii	Diagnosis by bronchial alveolar lavage and/or lung biopsy	-Prophylaxis for 3-6 months with <b>A:</b> trimethoprim+sulfamethoxazole -After treatment for acute rejection (6 weeks) -Add corticosteroids for moderate to severe disease
Candida		Prophylaxis with oral clotrimazole lozenges, nystatin or fluconazole
Cardiovascular diseases CVD		
New onset diabetes after transplantation (NODAT)	Fasting plasma glucose and/or HbA1c and/or Glucose tolerance testing  See above schedule or after starting or changing medication	Adult <b>A:</b> acetylsalicylic acid 75mg PO (Balance risk/benefit)-maintenance Oral – check section on DM management in CKD patients.
Atherosclerotic CVD		<b>A:</b> acetylsalicylic acid (PO)75mg per 24hours maintenance
Malignancy		
All malignancies	Education on self-examination and Health care directed screening	See relevant chapter on management
Kaposi Sarcoma		Change to mTOR Inhibitors

## **21.5 Cystic Kidney Disease**

Acquired or hereditary disorders of the kidneys. Autosomal dominant polycystic kidney disease is a common cause of end stage kidney disease. It is progressive and incurable condition.

### **Clinical presentation**

- **Kidney**
  - Nocturia, polyuria and frequency due to concentration defect
  - Hypertension
  - Pain syndrome (infection, bleeding, stones, rupture or compression)
  - Uremic manifestations
- **Extra-kidney manifestations**
  - Polycystic liver disease
  - Intracranial aneurysms
  - Cardiac – valvular heart disease

### **Diagnostic ultrasonographic criteria**

15-39 -years       $\geq 3$  cysts, unilateral or bilateral

40-59 years       $\geq 2$  cysts in each kidney

$\geq 60$  years       $\geq 4$  cysts in each kidney

### **Investigations**

- Ultrasonography – KUB
- Serum creatinine
- Urinalysis – biochemistry and microscopy
- Genetic testing for those who want to be donor (family history)
- CT scan – contrast enhanced has better sensitivity
- ALT, AST and bilirubin if using Tolvaptan

### **Non-pharmacological Treatment**

- Increase fluid intake  $>3$  L if has no fluid retention (eGFR  $<30\text{mL/min}/1.73\text{m}^2$ )
- Kidney transplantation when indicated
  - Might need pretransplant native nephrectomy

### **Pharmacological Treatment**

S: tolvaptan (PO) 45mg in the morning and 15mg 8hours later (titrate to 90mg am and 30mg pm)

- pm dose should be taken before 4pm

### **21.6 Renal artery stenosis**

Renal artery stenosis is narrowing of the one or both renal arteries. Atherosclerosis or fibromuscular dysplasia are the commonest causes. Progression to chronic kidney disease and end-stage disease may be prevented or slowed.

### **Clinical presentation**

- Hypertension, which is resistant, refractory to therapy with three or more drugs.
- Young onset hypertension with no family history
- An acute rise in serum creatinine  $>30\%$  after ACE-inhibitor or ARB use
- Episodes of flash pulmonary oedema
- Asymmetrical kidneys.
- Unexplained hypokalaemia

## Investigations

- Serum creatinine/BUN
- Urine protein creatinine ratio
- Urinalysis
- Duplex Doppler ultrasonography
- Computer tomography angiography
- Magnetic resonance angiography
- ACE-inhibitor Scintigraphy
- Conventional arteriography

## Non-pharmacological Treatment

Revascularization (when >80% stenosis)

## Pharmacological

**A:** acetyl salicylic acid (PO) 75mg 24hourly

ACE-Inhibitors or ARBs as in the section of Hypertension

A pathological description characterized by thrombocytopenia, microangiopathic hemolytic anemia and organ injury. AKI is a common manifestation in the kidney due to the glomerular circulation damage and occlusion. Early recognition is important.

## Clinical presentation

- Haemolysis
- Ischemic organ dysfunction
- AKI
- Extrarenal manifestations include
  - Pancreatitis and Hepatitis
  - Seizures
  - Diarrhoea/vomiting and abdominal pain
  - Digital gangrene

## Investigations

- ADAMTS13 activity (>10% excludes TTP)
- Bacterial culture/serology
  - HIV serology
- ANA, anti-ds DNA, anti-phospholipids, anti Scl70
- Kidney biopsy

## Pharmacological Treatment

Identify and treat the underlying cause. Primary thrombotic microangiopathies includes complement mediated aHUS and Thrombotic thrombocytopenic purpura with decreased ADAMTS13.

**S:** plasma exchange (until ADAMTS13 to exclude TTP) +/- immunosuppression

## 21.8 Reflux nephropathy

A type of chronic interstitial nephritis associated with vesico-ureteric reflux (VUR) in early life with the appearance of scars in the kidney as demonstrated by various imaging modalities. May be associated with renal dysplasia and other congenital abnormalities of the urinary tract. Including urethral valves.

## Clinical presentation

- Usually asymptomatic
- Hypertension
- Frequency of micturition
- Dysuria
- Aching lumbar pain
- Urinalysis shows leucocytes

## Investigations

- Ultrasonography – KUB
- Radionuclide DMSA scans
- Serial imaging by Magnetic Resonance Imaging – MRI

- MCUG- micturating cystourethrography
- Urine analysis – dipstick/biochemistry/microscopy
- Serum creatinine
- Urine culture

### **Non-pharmacological Treatment**

- If recurrent pyelonephritis occurs in an abnormal kidney with minimal function – Nephrectomy
- Hypertension may be cured by removal of a diseased kidney
- Severe reflux may be managed by ureteric reimplantation or sub trigonal injection of Teflon/polysaccharide

### **Pharmacological Treatment**

Treat UTI as in section with Urinary tract infection.

### **21.9 Contrast Induced Nephropathy (CIN)**

Contrast induced nephropathy (CIN), which is also known as Contrast Induced Acute Kidney Injury may occur after administration of iodinated contrast material, which is called contrast-induced nephropathy. Common contrast based studies resulting in CIN include CT scan, MRI and coronary angiography. Contrast induced acute kidney injury is usually characterized by rapid recovery of renal function.

#### **Clinical features**

Major clinical manifestations of CIN include

- Early mild increase in serum creatinine that is generally observed within 24-48 hours after the iodinated contrast exposure and that is usually mild. Serum creatinine starts to decline within 3-7days of exposure
- Nonoliguria, patients with CIN are passing urine normally and if it occurs develop immediately.
  - Oliguria and more severe elevation of creatinine may develop in patients with moderate to severe CKD.
- Urinalysis may show sediments consistent with acute tubular necrosis.
- Other manifestations of reduced GFR including hyperkalaemia, acidosis and hyperphosphataemia

#### **Investigations**

- All patients scheduled for contrast studies should have serum creatinine performed before the study and 24-48hours after contrast study
- For patients with raised creatinine
  - Serial creatinine should be performed until 7 days
  - Potassium, sodium, phosphorus, calcium and urinalysis
  - Kidney ureters and bladder ultrasound

### **Treatment and prevention of CIN**

#### **Non-pharmacologic Treatment**

- Identify all at risk patients; diabetic mellitus, heart failure, patients with CKD
- Stop NSAID 24-48 hours prior to contrast study
- Encourage adequate hydration prior to study
- Use lower possible dose of contrast (<125 ml)
- Use low osmolar (iohexol, ioversol) or iso-osmolar (iodixanol) contrast media

#### **Pharmacologic Treatment**

- Fluid administration should be used if there are no contra-indications. Normal saline should be administered before and continued for few hours after the study
  - Outpatients: 3mL/kg over one-hour pre-procedure and 1-1.5mL/kg/hour during and for four to six hours' post-procedure, with administration of at least 6mL/kg post procedure.

- Inpatients; 1mL/kg/hour for 6-12hours pre-procedure, intra-procedure, and for 6-12hours post-procedure

**Note**

Patient with severe CIN may need to undergo haemodialysis if there is no improvement within 7days.

## 21.10 Urinary Tract Infection (UTI)

Urinary tract infections may involve the upper or lower urinary tract. Infections may be complicated or uncomplicated. Uncomplicated cystitis is a lower UTI in a non-pregnant woman of reproductive age and who has a normal urinary tract. All other UTIs should be regarded as complicated. The commonest causative pathogens for UTIs irrespective of the group of patients involved in Tanzania are *Escherichia coli*, *Klebsiella pneumonia*, *Proteus* spp. and *Staphlococcus aureus*.

**Note**

- Differentiation of upper from lower urinary tract infection in young children is not possible on clinical grounds
- Upper UTI is a more serious condition and requires longer and sometimes intravenous antimicrobial treatment.
- Special considerations should be given in the following groups of patients: children, pregnant women, elderly (>60 years) and other individuals with functional or structural abnormalities in the urinary tract.

### Clinical presentations of lower UTI (cystitis)

- Suprapubic pain/tenderness, dysuria, frequency, and urgency
- Pyuria and occasionally haematuria
- Temperature 38<sup>0</sup>C or higher

### Clinical presentations of upper UTI (pyelonephritis)

- |                                      |   |
|--------------------------------------|---|
| • Flank pain/tenderness              | • Temperature 38 <sup>0</sup> C or higher |
| • Pyuria and occasionally haematuria | • Vomiting                                |

### Clinical presentations of catheter associated UTI (CAUTI)

- Presence of symptoms and signs of UTIs (as stated in cystitis or pyelonephritis above) occurring in a person whose urinary tract is currently catheterized or has had a catheter in place within the past 48 hours.

### Clinical presentations of urosepsis

- Any of the above features of cystitis or pyelonephritis plus two or more of the following: (1) Temperature >38° C or <36° C; (2) tachycardia >90 beats per minute; (3) tachypnoea >20/minute, (3) WBC count>12,000/mm<sup>3</sup> or <4000/mm<sup>3</sup>; confusion, hypotension or any other evidence of organ dysfunction as a sequelae of UTI complications.

### Investigations

- Quantitative or semi-quantitative urinalysis (high protein, low sugar, nitrites positive, leucocyte esterase positive, and low pH) and Urine microscopy (>8–10 WBC/HPF) may be suggestive of UTIs.
- Quantitative urine culture (growth of at least 10<sup>4</sup> or 10<sup>5</sup> colony forming units of bacteria/ml of urine) and antimicrobial sensitivity testing. Concomitant urine and blood cultures are indicated in case of urosepsis.
- Urinary LAMM – in patients with suspected to have genitourinary TB
- Ultrasound (kidney and pelvis) to exclude stones or structural abnormalities in patients with recurrent UTI

**Note**

Positive WBC counts on urinalysis or urine microscopy + compatible 2 or more clinical presentations supported by urine culture in centers where this test is available.

### Non-pharmacological Treatment,

- Ensure adequate hydration

- Voiding of urine whenever an urge to micturate occurs; or after sexual intercourse in adults.
- Removal of indwelling bladder catheter (where indicated)

### **Pharmacological Treatment**

Analgesics in severe dysuria and flank pain

Adult:

**A:** paracetamol (PO) 500-100mg every 6-8hours.

Children:

**A:** paracetamol (PO) 15 mg/kg/dose 4–6hourly when required to a maximum of 4doses per 24hours;

### **Uncomplicated cystitis**

Adults:

**A:** nitrofurantoin (PO) 100mg 12hourly for 5days  
**OR**

**B:** flucloxacillin + amoxicillin (FDC) (PO) 500mg 8hourly for 5days

### **Complicated cystitis**

Adults:

**A:** ciprofloxacin (PO) 500mg 12hourly for 7days  
**OR**

**B:** amoxicillin+ clavulanic acid (FDC) (PO) 625mg 12hourly for 7days

### **For pregnant women and adolescents**

**A:** nitrofurantoin (PO) 100mg 12hourly for 5days  
**OR**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 625mg 12hourly for 7days

### **For children**

**A:** nitrofurantoin (PO) 50mg 12hourly for 5days (Do not give Nitrofurantoin if the child has G6PG deficiency or porphyria)

**OR**

**B:** amoxicillin + clavulanic acid (FDC) (PO) 40mg/kg/day of amoxicillin in 3divided doses (maximum 2000 mg amoxicillin) for 7days

### **Acute Pyelonephritis**

Outpatient therapy is only indicated for women of reproductive age, who do not have any of the danger signs – see referral criteria. All other patients should be referred.

**A:** ciprofloxacin (PO) 500mg 12hourly for 10days

**OR**

**B:** ceftriaxone (IV) 1g [For a child ceftriaxone (80 mg/kg I.V or I.M)] 24hourly for 5days

### **Catheter associated UTI (CAUTI)**

Patients with indwelling or suprapubic catheters and nephrostomy tubes invariably become carriers of potential bacterial pathogens and routine antimicrobial treatment is not indicated. However, judicious evidence from clinical and laboratory evidence is critical to warranty antimicrobial therapies.

**A:** ciprofloxacin (PO) 500mg 12hourly for 7days

### **Urosepsis**

**A:** gentamicin (I.V/I.M) 120mg [For children 7.5mg/kg] 24hourly for 5days (completion of 10days treatment to be guided by culture results)

**AND**

**D:** ceftriaxone + sulbactam (FDC) (IV) 1g [For children 80 mg/kg I.V or I.M] 24hourly for 5days

Alternatively;

**A:** gentamicin (I.V/I.M) 120mg [For children 7.5mg/kg] 24hourly for 5days (completion of 10 days' treatment to be guided by culture results)

**AND**

## **OR**

**S:** Meropenem (IV) 250–500mg 8hry for 5–7days

Once results for urine and blood cultures are available change the antibiotic treatment options accordingly.

### **Referral**

Refer the patient **urgently** to the next facility with adequate expertise and facilities if: -

Acute pyelonephritis with:

- Vomiting
- Features of suggestive of urosepsis
- Diabetes mellitus

Acute pyelonephritis in:

- Pregnant women
- Women beyond reproductive age
- Men

## **21.10 Urology Disorders**

Are diseases that affect urinary system including urinary incontinence, urolithiasis, benign prostatic hyperplasia, prostate cancer.

### **21.10.1 Prostatitis**

It is an inflammation of the prostate usually secondary to bacterial infection caused by urinary or STI pathogens.

#### **Clinical Presentation**

- Perineal, sacral or suprapubic pain
- Dysuria and frequency
- Varying degrees of obstructive symptoms which may lead to urinary retention
- Sometimes fever

#### **Investigations**

- Urine analysis
- Urine culture

#### **Pharmacological Treatment**

##### **Acute bacterial prostatitis**

In men < 35 years or if there are features of associated urethritis (STI regimen):

**S:** cefixime (PO) 400mg as a single dose

Followed by:

**A:** doxycycline (PO) 100mg 12hourly for 7days

In men > 35 years or if there is associated cystitis:

**A:** ciprofloxacin (PO) 500 mg 12hourly for 14days

#### **Referral to Urologist if**

- No response to treatment
- Urinary retention
- High fever
- Chronic/relapsing prostatitis

## **21.10. 2 Benign Prostatic Hyperplasia (BPH)**

Benign prostatic hyperplasia is a noncancerous (benign) growth of the prostate gland. Management of BPH depends on severity of symptoms according to International Prostate Symptom Score (IPSS)

#### **Clinical Presentation**

- Obstructive symptoms: weak, intermittent stream and urinary hesitancy
- Irritative (frequency, nocturia and urgency) voiding symptoms.
- Digital Rectal Examination reveals a uniform enlargement of the prostate with smooth surface and firm in consistence. The median sulcus is also palpable

- Urinary retention with a distended bladder may be present in the absence of severe symptoms, therefore it is important to palpate for an enlarged bladder during examination.
- Pelvic or transrectal USS confirms the prostate enlargement
- Prostatic specific antigen levels are within normal range
- Symptoms should be graded by the IPSS – international prostate symptom score into mild, moderate and severe

### **Non-pharmacological Treatment**

- Patients with mild symptoms should be put under watchful waiting (change of lifestyle and regular follow up)
  - Reduce fluid intake especially in the evening, avoid caffeinated drinks
- Patients with severe symptoms should undergo surgery, transurethral resection of the prostate for prostate weighing up to 75g and those weighing more than 75g should undergo open prostatectomy
- For patients presenting with urinary retention, insert a urethral catheter as a temporary measure while patient is transferred to hospital
- Remove drugs that prevent urinary outflow e.g. tricyclics and neuroleptics.

### **Pharmacological Treatment**

Patients with moderate symptoms according to IPSS should be put under medical therapy unless opt for surgery.

Medical treatment of BPH includes alpha-adrenergic blocker or 5 alpha- reductase inhibitor or a combination of both

#### **Adrenergic Alpha Blockers:**

**D:** tamsulosin (PO) 0.4mg 24hourly  
**OR**

**D:** alfuzosin (PO) 10mg 24hourly

#### **5-alpha Reductase Inhibitors**

**D:** finasteride (PO) 5mg 24hourly  
**OR**

**S:** dutasteride (PO) 0.5mg 24hourly

#### **Anticholinergics**

**S:** oxybutynin (PO) 5mg 8hourly for patients with persistent urgency despite above medications

#### **Note**

All patients with BPH and associated complications like recurrent UTI, Haematuria, Kidney insufficiency, hernia and urinary stones need surgery and should be referred to centres where specialized care can be offered.

## **21.10. 3 Prostate Cancer**

Usually occurs in men over 50years and is most often asymptomatic. Systemic symptoms, i.e. weight loss, bone pain, etc. occurs in 20% of patients. Obstructive voiding symptoms and urinary retention are uncommon in the early stages of the disease.

### **Clinical Presentation**

- The prostate gland is hard and may be nodular with obliterated median sulcus on digital rectal examination and/or PSA elevation
- Verification of prostate cancer is by prostate core biopsy
- As the axial skeleton is the most common site of metastases, patients may present with back pain or pathological fractures.
- Lymph node metastases can lead to lower limb lymphoedema.
- Serum prostate specific antigen (PSA) is generally elevated and may be markedly so in metastatic disease.

#### **Note**

Interpretation of PSA should be interpreted careful, PSA has a low sensitivity therefore some patients may have low PSA value (<4.0ng/mL) and have prostate cancer. There false positivity where PSA is raised in the absence of prostatic cancer

## **Non-pharmacological Treatment**

- Watchful waiting- low risk patients with short life expectancy
- Active surveillance-lowest risk of cancer progression and more than 10years life expectancy
- Radical prostatectomy- patients with localized cancer and life expectancy more than 10years
- Surgical Androgen deprivation therapy (bilateral orchidectomy) for advanced prostate cancer

## **Pharmacological Treatment**

Medical androgen Deprivation Therapy is offered in patients with advanced disease, PSA levels more than 50ng/ml, poorly differentiated tumour and in those who cannot receive any form of local treatment.

For early disease

- Watchful waiting – low risk patients with short life expectancy
- Active surveillance – lowest risk for cancer progression and more than 10 years life expectancy
- Radical prostatectomy – patients with localized cancer and life expectancy more than 10 years

Late disease

Luteinising hormone releasing hormone (LHRH) Agonists

**S:** goserelin (subcutaneous) 3.6mg every week or 10.8mg every 12weeks

**OR**

**S:** bicalutamide (PO) 50–150mg 24hourly

**OR**

**S:** Both LHRH and bicalutamide 50mg 24hourly if above options fail

**OR**

**Castrate resistant prostate cancer**

**S:** docetaxel 75mg/m<sup>2</sup> every 3weeks

**Referral for oncologist:** All patients with suspected cancer (For more detail refer to the Malignant diseases section)

## **21.10.4 Urolithiasis**

Stones formed in the urinary tract are a result of urine, which is supersaturated with respect to a stone-forming salt. Kidney stones have been associated with an increased risk for chronic kidney disease, end-stage kidney failure, and cardiovascular diseases.

### **Clinical Presentation**

- Sudden onset of acute colic, localized to the flank, causing the patient to move constantly.
- Sweating, pallor, nausea and vomiting and blood in urine
- Referred pain to the scrotum or labium (L1) on the same side as the stone moves down the ureter
- Urinalysis with features of infection or microscopic haematuria
- Ultrasound with an acoustic shadow with features of obstructive uropathy eg. Hdrourerter or hydronephrosis
- Plain x-ray can pick up to 90% of calculi as they are radio-opaque
- Conventional intravenous urogram or CT urography confirms upper urinary tract lithiasis.

### **Investigations**

- Plain abdominal X-ray
- Non-contrast CT-Scan of the Kidney Ureter and Bladder (CTKUB) – **GOLD STANDARD**
- Ultrasonography – Kidney Ureter and Bladder (KUB)
- Chemical composition of the stone – most valuable test
- Urinalysis – Dipstick biochemistry +Microscopy

For First Stone

- Serum Calcium, magnesium, phosphate, uric acid, urea, K, Na, Cl, HCO<sub>3</sub>

### Recurrent Stone

- Parathyroid hormone
- Urine dipstick – biochemistry
- 24-HR Urea, creatinine clearance, sodium, calcium, oxalate and uric acid

**Table 21.7: Non-Pharmacological Treatment**

Type of stone	Prevention strategy
All stones	Increase water intake to have at least 2L of urine/day
Hyperoxaluria	Low oxalate diet + increase dietary calcium intake Limit vitamin C supplementation
Calcium stones	Reduce salt intake, Restriction of animal protein (less meat, fish and poultry) Increase intake of fruits and vegetables
Calcium oxalate, cystine and uric acid	Diet high in fruits and vegetables, Prescription citrate,
Uric acid	Control gout
Calcium phosphate and struvite	Acidify urine

- Surgical intervention is indicated (uroscopy, percutaneous nephrolithotomy and extracorporeal shockwave lithotripsy) for
  - obstructive uropathy
  - infection,
  - urgent intervention (surgical or otherwise) if a patient has a solitary kidney emergency decompression is indicated by percutaneous nephrostomy placement or ureteric DJ Stenting
- Stone fragmentation with ureteroscopy stone fragmentation/ ultrasonic disaggregate/extracorporeal shock wave lithotripsy

### Pharmacological Treatment

Analgesia for pain, if needed:

**A:** ibuprofen (PO) 400mg 8hourly for 3 days

**OR**

**A:** diclofenac (IM) 75mg stat then continue (PO) 50mg 8hourly

**OR**

**B:** tramadol (IV) 100mg stat then continue with (PO) 50mg 8hourly

**OR**

**B:** pethidine (IM) 100mg stat

Other management e.g. antiemetic for vomiting may be needed or IV fluids

For distal ureteric calculi less than 7mm

**D:** tamsulosin (PO) 0.4mg 24hourly for a month may be prescribed for spontaneous stone expulsion.

**OR**

**B:** nifedipine (PO)10mg 24hourly for 30days (monitor blood pressure)

For prevention of stone

Thiazide diuretics for calcium stones ANY of the following

**A:** bendrofluazide (PO) 5mg 24hourly

**OR**

**D:** hydrochlorothiazide (PO) 12.5-50mg 24hourly

For low uric acid levels

**AND**

**B:** allopurinol (PO) 50-100mg 24hourly

### 21.10.5 Obstructive uropathy

Obstructive uropathy contribute to the burden of CKD, obstruction may occur anywhere along the urinary tract. Causes of obstruction vary based on the location of obstruction

- Obstruction within the kidney causing dilatation of individual calyces

- Obstruction at or distal to the renal pelvis causes diffuse caliectasis of hydronephrosis. Ureteral obstruction may result from stones, tumors, enlarged lymph nodes and retroperitoneal fibrosis
- Bladder tumors can obstruct one or both ureters or ureteric orifices

### Clinical Presentation

Generally, patients present one or more of the following symptoms

- Pain
- Change in urine output
- Hypertension
- Hematuria
- Increased serum creatinine

### Investigations

- Urinalysis
- Full blood count
- Serum creatinine
- KUB ultrasound
- Intravenous pyelography
- CT IVU
- MRI
- Examination under anaesthesia

### Non-pharmacological treatment

Measures to reduce recurrence risk

- Taking adequate fluids 2L/day for patients with renal stones

### Pharmacological Treatment

- Relief of pain

**C:** diclofenac (PO) 100mg as initial dose followed by 50mg 6-8hourly

**OR**

**C:** morphine (IV/SC) 1-4mg 1-4hourly (may increase up to 10mg 4hourly as needed for acute pain)

### Referral of the patients

- The patient should be referred to the urologist for definitive treatment of the cause of obstruction
- Patient may need long term follow up if there is impaired renal function

## 21.11 Sexual Dysfunction

### 21.11.1 Female Sexual Dysfunction

Sexual dysfunction in women refers to sexual problems associated with personal distress and may take different forms including lack of sexual drive, impaired arousal, failure to achieve orgasm or dyspareunia. Diagnostic criteria are reached when a sexual problem is recurrent/ persistent and result in personal distress.

The causes of sexual dysfunction are multifactorial and may include psychological problem (depression or anxiety), relationship conflicts, fatigue, stress, prior physical or sexual abuse, medications or physical problems that make sexual activity uncomfortable (endometriosis, genitourinary symptoms of menopause).

### **Non-pharmacological Treatment**

Correction of contributing factor (genital lesion, systemic or hormonal factors and drugs e.g. SSRIs)

Psychological therapies

Use of antidepressants

### **21.11.2 Male sexual dysfunction**

It is inability to attain and maintain an erect penis with sufficient rigidity for vaginal penetration and ability to ejaculate. Organic causes include neurogenic, vasculogenic, endocrinological as well as many systemic diseases and medications.

#### **Non Pharmacological Treatment**

- Education counselling
- Consider the removal of drugs that may be associated with the problem.
- A change in lifestyle or medications may resolve the problem, e.g. advise cessation of smoking and alcohol abuse.

#### **Pharmacological Treatment**

- Treat the underlying condition.
- If persist refer the patient

#### **Note**

The use of medication like sildenafil may result to serious problem.

## **CHAPTER TWENTY-TWO**

## **MALIGNANT DISEASE CONDITIONS**

### **22.1 Cancer Prevention, Screening and Early Detection**

Cancer represents a unique public health opportunity, unlike other Non-Communicable disease, it is possible to prevent most of cancers prevails in Sub-Saharan Countries including Tanzania by intervening at both Primary and secondary levels of the natural history of the disease.

Primary prevention is mainly based on educating the public to modify their life styles to avoid risk factors for cancer as well as ensure the availability and affordability of prophylactic vaccines, the secondary prevention focus on the availability of effective screening programs that allow for reducing incidence and downstage cancer.

Early detection detects (or diagnoses) the disease at an early stage, when it has a high potential for cure (e.g. cervical or breast cancer) reduce morbidity, improve quality of life as well as increase survival due to good outcome following treatment.

#### **Key interventions in Cancer Prevention Primary Prevention**

This is the most efficient and cost-effective form of cancer control it involves prevention interventions that keeps a cancerous process from developing which can be through behavior change by health counseling, education and environmental controls or through a biological mechanism, such as Vaccination.

Among the most important modifiable risk factors for cancer are: tobacco use; overweight, and obesity; harmful alcohol use; sexually transmitted human papilloma virus (HPV) infection, HIV/AIDS; air pollution, both outdoor and indoor; and occupational carcinogens.

Public health education and promotion: Public Awareness raising on risk factors for cancer and providing education on ways of avoiding as well as reducing exposure through behavior change is essential. However, this is a long term intervention and may be difficult to quantify. Community education should also focus raise awareness and knowledge on the benefits of early diagnosis, ways of detection and screening. These preventive measures should be highly promoted by also raise awareness of warning symptoms and signs of cancer and taking prompt action, by the general public as well as physicians, nurses and other health care providers, can have a great impact on the disease through early diagnosis and hence more effective management.

#### **Vaccination**

Human papillomaviruses (HPVs) is among the most important infections associated with cancers, which can cause most cervical and anal cancers as well as a fraction of oral cancers; hepatitis B virus (HBV) and hepatitis C virus (HCV), which can cause liver cancer; and Helicobacter pylori, which is a bacterium that can cause cancer of the stomach.

Highly effective vaccines against HBV have been available for several decades and most countries include HBV vaccination in their childhood immunization programs; vaccination is also highly effective in preventing infection with the HPV types that cause the majority of cervical cancers.

Hepatitis Vaccination is recommended to general population and the high risk group such as health care workers, and can be done at all levels. The Vaccine is given in 3 doses in 6 months. Second dose should be given after 1 month after 1<sup>st</sup> dose and 3<sup>rd</sup> dose 6 months after the first dose.

HPV vaccination is recommended to girls between the age of 9 to 14 years. HPV vaccine is given in two doses at 6 months apart.

#### **Secondary Prevention: Early detection and Cancer Screening**

The main aim of cancer screening is to prevent death from cancer. Screening can also make it possible to use less severe treatment methods if the cancer is detected early enough. Cervical, breast, skin, Prostate and bowel cancer, screening can actually prevent the cancer from developing. However only cervical cancer screening is offered as part of an organized program with adequate resources for high quality.

**Breast Cancer:** Screening for breast cancer includes breast self-examination (BSE), clinical breast examination (CBE) and breast imaging (mammogram and/or ultrasound scanning). BSE is recommended at day 10 of the menstrual cycle. For post-menopausal women, a monthly BSE schedule should be established.

All patients with clinical suspicious lesions should have imaging as part of early detection. Mammogram is recommended for women over 40 years, while ultrasound is the imaging of choice for younger women. MRI may be used where possible for screening and early detection in patients at high risk of breast cancer such as those with BRCA1 & 2 gene mutations.

For prevention and early detection, all women aged 25 years and above should be taught on breast self-examination and should be advised to have regular physical check with a health provider and have a regular annual Mammography. They should also be encouraged on physical exercise and proper diet.

**Skin Cancer:** Prevention or early detection is through frequent self-health check-up or screening exercise and prompt treatment of early skin lesions. For light skinned people—avoid UV light especially people with Albinism.

**Colon:** colorectal cancers are usually asymptomatic until advanced stage hence regular screening with annual digital rectal examination, stool for occult blood + colonoscopy and are recommended starting at 50 years of age.

**Prostate:** Routine screening not recommended, but when done should begin with PSA and digital rectal examination at age 50 if life expectancy is >10 years. It is recommended that screening of high risk group should take place starting at age 45.

## 22.2 Gynecological Malignancies

### 22.2.1 Cancer of the Uterine Cervix

It is caused by persistent infection with human papilloma Virus (HPV). Risk factors include early coitus and childbirth, multiple sexual partners, smoking and HIV infection. It is preventable through avoiding risk factors, screening and vaccination. When detected early, it is curable by surgery or radiotherapy hence regular screening is required for all women.

#### Diagnostic Criteria

- Asymptomatic in early stages of the disease.
- Majority present with abnormal vaginal bleeding (post coital, inter-menstrual or postmenopausal vaginal bleeding).
- Foul smelling discharge, pain and incontinence (VVF or RVF) are symptoms of late disease

#### Investigations

- FBC, LFT, RFT and HIV test.
- CXR.
- Abdomen and Pelvis USS.
- Pelvic MRI, CT Scan of the abdomen and pelvis.
- PET/CT
- Bimanual Examination under Anesthesia (EUA) and Biopsy.

**Table 22.1 Management of Cervical cancer by disease stage.**

Stage	Management
Stage IA1:	Simple hysterectomy or if patient desires fertility consider conization
Stage IA2–IB2	Consider Wertheim Hysterectomy plus bilateral pelvic lymph node dissection. RT may be given post operation or alone. No benefit of adjuvant chemotherapy
Stage IB2; IIA and IIB	2.0Gy/Per Fraction to 50Gy external beam + 8.0 Gy x 3 Fractions HDR +/- Chemotherapy depending on renal function
Stage IIIA and IIIB	If stage by CT or MRI and no distant metastasis and good renal function: 2.0Gy to 50 Gy external beam + 8.0 Gy x 3 Fractions HDR
Stage III A and III B	2.5 Gy to 50 Gy external beam only no HDR nor chemotherapy if poor renal function
Stage IV A + good general	Can be given curative dose of 50 Gy external beam

condition, no VVF or RVF:	+ Brachytherapy or palliative dose of 20Gy/5 Fractions or 30 Gy/10 Fractions or 10Gy Single Fraction monthly X 2 Fractions
Stage III B advanced/stage IV B with bad general condition	Palliative care / supportive care

### Pharmacological Treatment

Chemotherapy is given as a radiotherapy sensitizer or on palliative intent.

**S:** cisplatin (IV) 40 mg/m<sup>2</sup> to max of 70 mg is given weekly during radiation therapy.

- If patient is HIV positive or has mild renal impairment consider 30 mg/m<sup>2</sup> to max of 60 mg weekly.
- Available and preferred palliative chemotherapy drugs for metastatic, recurrent or persistent cancer after RT, given in single or combination regimen include: cisplatin, paclitaxel, bevacizumab, carboplatin, docetaxel and gemcitabine.
- Do FBC, urea and creatinine before each cycle of chemotherapy.

### Follow up:

First visit at 4–6 weeks post treatment then 3–6 months in the first 2 years, there after yearly.

**\*This follow-up schedule applies to all malignancies with few exceptions\***

#### Note

- All patients suspected or confirmed to have cervical cancer should be referred to cancer specialized centers for definitive management.
- All women aged 25 years and above are advised to have regular cervical screening with VIA and VILI or Pap smear

## 22.2.2 Endometrial Cancer

This is predominantly a disease of old women. Adenocarcinoma is the commonest histological type. Risk factors for endometrial carcinoma include obesity, diabetes, high fat diet, early age at menarche, nulliparity and late age at menopause, old age and use of tamoxifen.

#### Diagnostic Criteria

- Abnormal Uterine Bleeding for women in the post-menopausal period.
- For Pre-menopausal women; may present with irregular bleeding, intramenstrual bleeding, vaginal discharge, pain during intercourse and unexpected weight loss.

#### Investigations

- FBC, LFT, Urea, Creatinine
- Cancer Antigen 125 (CA 125)
- CXR
- Abdomen and Pelvis USS
- Abdomen and Pelvic CT scan and/or Pelvic MRI
- Endometrial biopsy to confirm the diagnosis
- PET/CT

**Staging:** FIGO and TNM

**Table 22.2 Management of Endometrial cancer by Stage**

Stage	Management
All Patients	Medically operable patients should undergo Surgery. Perform TAH and BSO or radical hysterectomy if cervical stromal involvement and obtain peritoneal cytology. Consider selective pelvic and paraaortic LN dissection for myometrial invasion or if grade 2–3, and include nodes from paraaortic, common iliac, external iliac, internal iliac, and obturator chains.
Stage 1A/1B	Grade 1 - Observation; Grade 2-3 or presence of other adverse features: Offer Vaginal Brachytherapy (VBT) 7Gy x 3 fractions
Stage IA, IB, II clear cell or serous	Offer Adjuvant Chemotherapy + Vaginal Brachytherapy 7Gy x 3 fractions Or Pelvic External Beam Radiation Therapy alone (46Gy)

carcinoma, IB High Grade	
Stage III	Adjuvant Chemotherapy + Radiotherapy (High Risk Disease: EBRT (46Gy) + VBT 7Gy x 3 fractions )
Stage IV	Chemotherapy

**Note**

- For inoperable disease stage IIb – IVA, radiotherapy and or chemotherapy can be offered as neo-adjuvant prior to surgery

### **Pharmacological Treatment**

Cytotoxic therapy for inoperable, metastatic or recurrent disease is given with palliative intent.

Recommended regimens are:

**S:** doxorubicin (IV) 60 mg/m<sup>2</sup> over 30 minutes AND cisplatin (IV) 50 mg/m<sup>2</sup> 1 hour(IV) infusion on day 1; repeat every 21days for 4 – 6 cycles

**OR**

**S:** cisplatin (IV) 50 mg/m<sup>2</sup>1-hour infusion on day 1 AND doxorubicin(IV) 45 mg/m<sup>2</sup> over 20 minutes on day 2 AND paclitaxel (IV) 160 mg/m<sup>2</sup> over 3hours on day 2 AND filgrastim (SC) 5 µg/kg on days 3–12; repeat every 21days for 4-6 cycles

**OR**

**S:** carboplatin (IV) AUC 5–6 1-hour infusion day 1 AND paclitaxel (IV) 175 mg/m<sup>2</sup> over 3hours on day 1 repeat every 21 days for 4-6 cycles

**Note**

- All patients should be referred to a gynecologist for evaluation and surgical management
- All surgical specimens should be sent for histopathology diagnosis and staging.
- After surgery and histopathology report, all patients should be referred to cancer specialized center for management and follow up.

### **22.2.3 Cancer of the Vulva**

Vulva cancer is predominantly a disease of older women. Squamous cell carcinoma is the commonest histological type, usually arising from premalignant lesions—vulva intraepithelial neoplasia (VIN). Risk factors contributing to development of VIN and later vulva cancer include HPV infection, infection with HIV, and cigarette smoking.

#### **Diagnostic Criteria**

- A lump or vulva mass
- Presence of leukoplakia and other dystrophic changes on the vulva
- Itching is a common manifestation and may become ulcerative (“non-healing ulcers”)

#### **Investigations**

- FBC, LFT, Urea, Creatinine, HIV test
- CXR
- Ultrasonography or CT scan of Abdomen and Pelvis
- Colposcopy to determine presence of other lesions in the vagina and cervix
- Biopsy from the vulvar lesion to confirm the diagnosis
- PET/CT

**Staging:** FIGO and TNM.

#### **Management:**

Treatment is individualized, taking into considerations of histological type, disease stage and patient factors

**Primary treatment is surgery.** Wide Local Excision (Radical Vulvectomy) plus Groin Lymphnode dissection.

**Radiotherapy** is indicated in the following conditions:

- As primary therapy for patient with small primary tumors particularly young patients in whom surgical resection would have significant psychological consequences.
- For patients with locally advanced disease where resection is not possible.

- After surgery to treat the pelvic and groin nodes.
- After surgery in patients with positive surgical margins.
- In palliation (Pain, Bleeding etc)

### **Pharmacological Treatment: As for cervical cancer**

#### **22.2.4. Gestational Trophoblastic Disease**

##### **22.2.4.1 Hydatidiform mole**

Two types; complete and partial hydatidiform mole. Treatment is suction curettage or hysterectomy. Careful risk assessment is needed to determine patients who require chemotherapy after surgery. Patient with high risk hydatidiform mole will have to reserve single agent chemotherapy; methotrexate or actinomycin D

**Note:** Patient should be followed up with weekly serum β-hCG after surgery until it is undetectable.

##### **22.2.4.2 Choriocarcinoma**

Choriocarcinoma is extremely chemo sensitive; cure is possible even in metastatic disease. All patients with choriocarcinoma should undergo a careful pre-treatment evaluation for proper staging and risk stratification.

#### **Investigations:**

- Serum β-hCG level
- LFT, RFT, TSH, T3, T3
- CXR and or CT Scan chest
- Abdomen and Pelvis USS or CT Scan
- Brain MRI
- Tissue sample for histology
- CSF hCG level
- PET/CT

#### **Clinical presentation:**

- Persistently raising or plateau BhCG postmolar pregnancy.

#### **Staging: FIGO Staging**

Stage I – Persistently elevated human chorionic gonadotropin (hCG) levels; tumor confined to the uterine corpus

Stage II – Tumors extending to the adnexa or to the vagina, but limited to the genital structures

Stage III – Pulmonary metastases on chest radiograph, with or without uterine, pelvic, or vaginal involvement

Stage IV – Metastatic disease outside of the lungs and pelvis and/or vagina

**Table 22.3 Prognostic Factors required for Stage grouping and Risk score**

	Risk Score				
Prognostic Factor	0	1	2	4	Factor score
Age (years)	<40	>40			
Antecedent pregnancy	Hydatidiform mole	Abortion	Term pregnancy		
Interval months from index Pregnancy	<4	4-6	7-12	>12	
Pretreatment hCG (IU/mL)	<10 <sup>3</sup>	10 <sup>3</sup> to <10 <sup>4</sup>	10 <sup>4</sup> to 10 <sup>5</sup>	>10 <sup>5</sup>	
Largest tumor size, including uterus (cm)	<3	3-5	>5		
Site of metastasis	Lung	Spleen, kidney	Gastrointestinal tract	Brain, liver	
Number of metastasis identified		1-4	5-8	>8	
Previous failed chemotherapy			Single medicine	Two or more medicines	
Total Risk Score					

**Table 22.4 Risk Stratification (FIGO) and Treatment recommendation**

<b>Stage / Score</b>	<b>Recommendation</b>
Low risk: Stage I – III with WHO risk score below VI	Single agent: methotrexate (IV) or actinomycin D (IV)
High risk: Stage IV or II and III with WHO risk score above VI	Combination therapy: 1. EMACO (etoposide, methotrexate, actinomycin D, cyclophosphamide, vincristine) (IV) 2. APE (actinomycin D, cisplatin, etoposide) (IV)
Brain metastasis	methotrexate, dexamethasone and prophylactic anti epileptic to control seizures Or High dose EMACO plus intrathecal methotrexate and leucovorin. Concomitant whole brain radiation: 20-30 Gy in 2Gy daily fraction concurrently with high dose chemotherapy(MTX)

**Note**

Do serial measurement of BhCG at start of treatment and weekly during therapy.

**Table 22.5 Recommended Chemotherapy regimens for Single agent**

<b>Single Agent</b>	
1	<b>S:</b> actinomycin D (IV) 12µg/Kg daily for 5 days  With response: Repeat same dose  Without response: add 2µg/Kg to the initial dose or switch to methotrexate protocol
2	<b>S:</b> methotrexate (IV) or (IM) 0.4mg/Kg daily for 5 days  With response: Repeat same dose  Without response: add 0.6mg/Kg to the initial dose or switch to actinomycin D protocol
<b>Note:</b>	
<ul style="list-style-type: none"> <li>• Do serial measurement of BhCG at start of treatment and weekly during therapy.</li> <li>• Do FBC, Platelet count, LFT daily.</li> <li>• If no response to single agent , give combination drugs.</li> </ul>	

**Table 22.6 Recommended Chemotherapy regimens for Combination therapy**

<b>Combination Therapy (EMACO – Regimen)</b>		
Course 1 (EMA)	Day 1	<b>S:</b> VP – 16 (etoposide) (IV) 100mg/m <sup>2</sup> infusion over 30 minutes AND actinomycin D (IV) 0.5mg bolus AND methotrexate (IV) 100mg/m <sup>2</sup> bolus, followed by a 200mg/m <sup>2</sup> IV infusion over 12 hours
	Day 2	<b>S:</b> VP – 16 (etoposide) (IV) 100mg/m <sup>2</sup> infusion in 200ml of saline over 30 minutes AND actinomycin D (IV) 0.5mg bolus  folinic acid (IM) 15mg OR orally every 12 hours for 4 doses beginning 24 hours after start of methotrexate (IV)
Course 2 (CO)	Day 8	<b>S:</b> vincristine (IV) 1mg/m <sup>2</sup> (IV) bolus AND cyclophosphamide 600mg/m <sup>2</sup> 1 hour (IV) infusion.
	<b>Note</b>	
	<ul style="list-style-type: none"> <li>• Cycles are repeated after every 14 days until β-hCG is normal</li> </ul>	

## **Follow-up**

- Weekly measurement of hcg level until they are normal for 3 consecutive weeks
- Monthly hcg levels until levels are normal for 12 consecutive months
- Effective contraception during the entire period of hormonal follow-up

### **22.2.5 Cancer of the Ovary**

Epithelial tumours comprise 90% of all ovarian malignancies. Due to anatomical location, most patients present with advanced disease.

#### **Diagnostic Criteria**

- Minimal or no symptoms in early stage
- Abdominal distension with palpable mass, pain and ascites are all late signs

#### **Investigations:**

- Inspection and bimanual examination under anesthesia (EUA) recto–vagina are mandatory to exclude primary disease or extension from other sites such as cancer of the cervix
- FBC, RFT, LFT, CA 125 & CEA
- CXR
- Abdomen and Pelvis CT Scan or USS
- Histology of Oophorectomy specimen or biopsy obtained at laparotomy
- Ascitic fluid/peritoneal and pelvic washing cytology

**Staging:** Is based on surgical diagnosis (laparotomy): FIGO: IA, IB, IC, IIA, IIB, IIC, IIIA, IIIB, IIIC, IVA and IVB.

**Table 22.7: Management: Surgery**

Stage 1 and 2	Total hysterectomy with Bilateral Salpingo –Oophorectomy (TAH+BSO) and omentectomy should be performed in resectable tumor.  If total tumor removal is not possible, then maximum debulking (Cyto –reductive) surgery is done. This is followed by adjuvant Chemotherapy. Unilateral salpingo-oophorectomy is only justified for stage IA tumour with favourable histology.
Stage 3	Neoadjuvant chemotherapy followed by Surgery and then Adjuvant Chemotherapy.
Stage 4	As stage 3 +/- Palliative care.

#### **Pharmacological Treatment**

##### **Adjuvant chemotherapy**

Indicated in all patients at high risk i.e. stage IC or II, high grade or clear cell cancers of any stage. Recommended regimens is;

**S:** carboplatin (IV) AUC 6 1 hour infusion Day 1 AND paclitaxel (IV) 175 mg/m<sup>2</sup> over 3 hours day1; repeat every 21days for 6 cycles.

**For recurrent disease:** give same regimen if tumor is platinum sensitive (recurrence after 6 months since last chemotherapy cycle)

For platinum resistant disease give gemcitabine or bevacizumab as single agent or in combination with taxanes. When available, liposomal doxorubicin is active and indicated in recurrent disease.

**S:** gemcitabine (IV) 1000 mg/m<sup>2</sup> 30 minutes infusion Day 1, Day 8 and Day 15;  
Repeat every 4 weeks for 6 Courses

**S:** bevacizumab (IV) 15 mg/kg 1-hour infusion Day1, every 3 weeks until disease progression

**Endocrine therapy** is indicated in selected cases with recurrent disease.

**S:** tamoxifen (PO) 20mg every 12 hourly,daily AND goserelin (SC) 3.6 mg every 4 weeks or 10.8mg every 12 weeks

#### **Note**

All patients must be referred to a gynecologist and cancer specialized center for evaluation and proper management

## **22.3 Breast Cancer**

The etiology of breast cancer is so far unknown, however, age, nulliparity, not breastfeeding, first pregnancy age 35years, previous radiation exposure, family history of breast cancer, smoking and alcohol consumption, are the risks associated with breast cancer.

Screening for breast cancer includes breast self-examination (BSE), clinical breast examination (CBE) and breast imaging (mammogram and/or ultrasound scanning and or MRI Breast). All patients with clinical suspicious lesions should have imaging as part of early detection.

### **Diagnostic criteria**

A solitary hard lump or mass in the breast that may be associated with

- Changes of breast skin appearance or ulceration
- Nipple retraction
- Presence of axillary lymphadenopathy or elsewhere
- Attachment/fixed to chest wall muscles

Other symptoms and signs include cough, bone pain/fracture, or neurological symptoms depending on site of metastasis

### **Investigations**

- FBC, LFT, Urea, Creatinine
- ECHO Mammogram/MUGA (Baseline Ejection Fraction and follow up)
- Bilateral Mammography, Breast Ultrasound as necessary
- CXR
- Abdomen and Pelvic USS
- Bone scan
- CT scan and or PET/ CT where indicated
- Open biopsy for histopathology and Immunohistochemistry (IHC)
- A core needle biopsy done manually, or preferably by ultrasound or stereotactic guidance is recommended.
- Immunohistochemistry (IHC) – ER, PR and Her 2
- FISH/CISH for Equivocal Her 2 for Confirmation of Her 2 OverExpression
- Breast MRI may be of value in select group of women who have had equivocal mammogram/ ultrasound.

### **Staging:** TNM

**Management:** Includes surgery, chemotherapy, radiotherapy, hormonal therapy and targeted therapy

### **Surgery**

Optimal management includes multidisciplinary evaluation by clinical oncologist and breast surgeon.

Options for surgical management include:

- Breast conserving surgery with lumpectomy/quadrantectomy
- Modified radical mastectomy
- Total Mastectomy

As described above, all surgical approaches should include surgical axillary staging with axillary lymph node dissection to level 1 and 2 nodes (>10 lymph nodes dissected).

Surgical approaches aimed at breast conservation should only take place in cases that allow for multi-disciplinary management with access to radiotherapy. If radiotherapy access is limited, mainstay of surgical care should be modified radical mastectomy.

**Radiotherapy** is strongly indicated in the following conditions:

- After BCS
- T3–4 tumor
- Positive surgical margin
- If ≥ 4 sampled lymphnodes are positive
- Palliation for fungating and bleeding tumor, mets to bones, brain etc.

**Radiotherapy dose:** 50Gy/25 Fractions given in 5 weeks or Hypofractionation 40.05Gy/15 Fractions. For palliative intent usually 30Gy/10 Fractions in 2 weeks

### **Pharmacological Treatment**

Chemotherapy is indicated for almost all patients as neo-adjuvant, adjuvant or palliative. Patients, who are planned for surgery and have  $\geq$  T3 tumors, should receive neo-adjuvant chemotherapy before operation.

**Table 22.8 Recommended chemotherapy regimens for Breast cancer**

<b>Dosing schedules for combinations for HER 2 negative disease:</b>	
1	<b>Dose-dense doxorubicin (IV) AND cyclophosphamide(IV) followed by weekly paclitaxel (IV)</b>  <b>S:</b> doxorubicin (IV) 60 mg/m <sup>2</sup> over 30 minutes' day 1 AND cyclophosphamide (IV) 600 mg/m <sup>2</sup> 1-hour infusion day 1 given every 14 days for 4 cycles  <b>Followed by</b>  <b>S:</b> paclitaxel (IV) 80 mg/m <sup>2</sup> by 1-hour infusion weekly for 12 weeks.
2	<b>Dose-dense adriamycin AND cyclophosphamide followed by 3 weekly taxanes</b>  <b>S:</b> doxorubicin 60 mg/m <sup>2</sup> (IV) over 30 minutes on day 1 PLUS cyclophosphamide 600 mg/m <sup>2</sup> 1 hour (IV) infusion day 1 given every 21 days for 4 cycles then  <b>Followed by</b>  <b>S:</b> paclitaxel (IV) 175 mg/m <sup>2</sup> 3 hours infusion day 1, given every 21days for 4 cycles <b>OR</b> <b>S:</b> docetaxel (IV) 100 mg/m <sup>2</sup> 3 hours infusion day 1 given every 21days for 4 cycles.
3	<b>TAC (IV) chemotherapy regimen</b>  <b>S:</b> docetaxel (IV) 75 mg/m <sup>2</sup> 3 hours' infusion day 1 AND doxorubicin (IV) 50 mg/m <sup>2</sup> 30 minutes' day 1 AND cyclophosphamide (IV) 500 mg/m <sup>2</sup> 1-hour infusion day 1 given every 21 days for 6 cycles.

### **Dosing schedule for combinations for HER2-Positive disease:**

1	<b>S:</b> doxorubicin (IV) 60 mg/m <sup>2</sup> 30 minutes' day 1 <b>AND</b> cyclophosphamide (IV) 600 mg/m <sup>2</sup> 1-hour infusion day 1 given every 21 days for 4 cycles <b>followed by</b> paclitaxel (IV) 80 mg/m <sup>2</sup> 1-hour infusion weekly for 12 weeks  <b>AND</b> <b>S:</b> trastuzumab (IV) 4 mg/kg with first dose of paclitaxel (IV) followed by trastuzumab (IV) 2 mg/kg weekly to complete 1 year of treatment.
2	As an alternative, trastuzumab (IV) 6 mg/kg (IV) every 21 days may be used following the completion of paclitaxel (IV) and given to complete 1 year of trastuzumab (IV) treatment.

### **Note**

- All cycles are with myeloid growth factor support.
- FBC, RFT, LFT before each cycle.
- Cardiac monitoring at baseline, 3, 6, and 9 months.

### **Other Regimens are:**

**S:** CAF (cyclophosphamide, adriamycin and 5-flourouracil)/

**S:** CEF (cyclophosphamide, epirubicin and 5-fluorouracil) and

**S:** CMF (cyclophosphamide, methotrexate and 5-fluorouracil) (for elderly patients >65 yrs with poor cardiac function)

### **For Metastatic Breast Cancer (Stage 4):**

Chemotherapy regimens for either combinations ie

**S:** CAF, CEF, gemcitabine/paclitaxel,

**S:** trastuzumab+paclitaxel/carboplatin or trastuzumab+paclitaxel or trastuzumab + docetaxel or trastuzumab+capecitabine; or single agent

**S:** trastuzumab, taxane or capecitabine or gemcitabine.

### **Endocrine therapy**

Premenopausal ER/PR Positive

**S:** tamoxifen (PO) 20 mg daily for 5 years

Post-menopausal ER/ PR Positive

**S:** anastrazole (PO) 1 mg daily for 5 years

**OR**

**S:** tamoxifen (PO) 20 mg daily for 2 years followed anastrazole (PO) 1 mg daily for 3 years.

#### **Note**

- All patients must be referred to a specialized oncology center for proper management

## **22.4 Cancer of The Skin**

Skin cancers are classified into non melanoma and malignant melanoma.

### **22.4.1 Non-melanoma Skin Cancers**

Basal cell carcinoma (BCC) and squamous cell (SCC) are the most common non melanoma skin cancers. SCC is more aggressive than BCC and has the potential to metastasis. The main cause of these skin cancers is overexposure to Ultraviolet radiation. Risk factors include light-coloured skin (e.g albinism), previous burn and immunosuppression eg after transplant or HIV infection

**Prevention or early detection:** is through frequent self-health check-up or screening exercise and prompt treatment of early skin lesions. For light skinned people—avoid UV light especially people with Albinism.

### **Diagnostic Criteria**

The most common warning sign of skin cancer is a change in the appearance on exposed areas of the skin, such as a new growth or a sore that will not heal. Occasionally, such changes may appear on an old burn area.

### **Investigations**

- None if lesion is small
- Local X-ray if bone involvement is suspected
- CXR
- Biopsy – preferably excisional biopsy where possible for histology
- CT or MRI for suspected Nodal and bone involvement.
- PET/CT when indicated

### **Management**

Surgery is the primary treatment. Wide local excision that achieves negative surgical margins is adequate. Skin grafting may be required after surgery. Amputation sometimes is done for palliation. Locally destructive methods such as curetting or cryotherapy may be employed

### **Radiotherapy**

Indication: Positive margin, high grade disease or inoperable tumour.

Dose: 60-66Gy/ in 30-33 Fractions EBRT for Radical Treatment, 30Gy in 10 Fractions for palliative treatment

### **Pharmacological Treatment**

**S:** 5-fluorouracil topical cream apply every after 12 -24 hours, for very superficial lesions or carcinoma in situ

Systemic chemotherapy is given for palliation in advanced stage or as radio sensitizer.

## **22.4.2 Malignant Melanoma**

### **Diagnostic criteria**

History of a pre-existing naevi which has changed recently –itching, colour change, increase in size, satellite lesions, elevated surface, ulceration and/or oozing.

### **Investigations**

- CXR
- Abdomen and Pelvic CT Scan or USS
- PET CT
- Excisional biopsy of suspicious lesion for histopathology

**Staging:** Clark's or Breslow classifications are used. Tumour size closely correlates with prognosis.

**Detection/ prevention:** Frequent self –check up or screening exercise and prompt treatment of naevi

**Management: Surgery** is the primary treatment.

- Wide local excision and graft
- Amputation sometimes for advanced useless limb

### **Pharmacological Treatment**

**S:** cisplatin (IV) 20mg/m<sup>2</sup>/day 30 minutes' infusion day 1-4 AND vinblastine (IV) 1.6mg/m<sup>2</sup>/day bolus day 1-5 AND dacarbazine (IV) 800mg/m<sup>2</sup> 30minutes infusion day 1 repeat every 21 days for 6 cycles

**OR**

**S:** dacarbazine (IV) 250mg/m<sup>2</sup> 30 minutes' infusion Day1–Day 5 every 21 days for 4 cycles

**OR**

**S:** temozolomide (PO) 200mg/m<sup>2</sup> Day 1–Day 5 every 28 days

**Radiotherapy** used for palliation if:

- Lesion is inoperable. May use large fractions: 30Gy/6Fractions/1 week
- Excision margins are involved or very close
- Palliative intent 30Gy in 10 Fractions/ 20Gy in 5 Fractions (brain mets, fungation or profuse bleeding, bone pain etc)

## **22.4.3 Kaposi's sarcoma (KS)**

It is a malignant tumour of angio-formative cells usually starting from the skin but occasionally involving many other organs of the body. Kaposi sarcoma can be primarily categorized into four types: epidemic of AIDS-related, immunocompromised, classic or sporadic, and endemic (African). Here we have Non AIDS related (endemic) KS and AIDS related (epidemic) KS where the late is more common 80–85%.

### **Diagnostic criteria**

- KS presents as a firm, dark brown nodules or plaque in the skin. Usually more on the limbs
- In young children and those with immunodeficiency it presents as wide spread lymphadenopathy with or without skin lesions.
- Presence of B symptoms (fever, sweating and weight loss) is commonly associated with epidemic type.

### **Investigations**

- FBC, LFT, Urea & Creatinine, HIV test (if positive CD4 count and viral load)
- CXR
- Abdomen and Pelvis ultrasound or CT scan
- Chest Scan CT
- Bronchoscopy and Endoscopy
- Skin biopsy for histological confirmation

**Staging of KS:** Epidemic Kaposi sarcoma use AIDS clinical trials group (ACTG) system and for endemic/classical Kaposi sarcoma use Mitsuyasu classification system.

### **Management:**

- Treatment is palliative irrespective of type and stage hence careful assessment and decision is required to choose the best palliative treatment.
- ARVs should be initiated in epidemic KS patients who have not started the treatment.
- Choice of palliation depends on clinical presentation and patient general condition.

**Radiotherapy:** Is the best palliative treatment in symptomatic patient with local or extensive disease.

- 8Gy single fraction for disease on limbs or lower half body
- 6Gy single fraction for upper half body
- Dose of 9Gy/3Fractions or 22Gy/11 Fractions can be prescribed for lesions elsewhere.

### **Pharmacological Treatment**

Palliative chemotherapy is usually given in patient with generalized disease.

Recommended regimens are:

**S:** doxorubicin (IV) 25 mg/m<sup>2</sup> over 30 minutes day1 AND bleomycin (IV) 10 IU/m<sup>2</sup> over 10 minutes' day 1 PLUS vincristine (IV) 1.4mg/m<sup>2</sup> over 10 minutes (max.2mg) day1 given every 21 days for 6 –8 cycles

**OR**

**S:** paclitaxel (IV) 100mg/m<sup>2</sup> day 1 every 14days

**OR**

**S:** docetaxel (IV) 75mg/m<sup>2</sup> day 1 every 21days is given for persistent or recurrent after ABV.

## **22.5 Head and Neck Cancers**

Cancer of the head and neck include the following: The oral cavity, pharynx, larynx, nasal cavity, para nasal sinuses, salivary glands, and thyroid.

These tumours may present with a neck mass due to lymph node metastases, with or without findings from the primary disease site. Important etiological factors are smoking, excessive alcohol, viral infections (eg HPV and EBV), genetic predisposition, previous exposure to radiation and industrial chemicals. Squamous cell carcinoma is the commonest histological type for the malignancies but salivary gland tumors are mostly adenocarcinoma.

### **22.5.1 Nasopharyngeal Cancer**

Nasopharyngeal carcinoma is the predominant tumor type arising in the epithelium of the nasopharynx.

#### **Diagnostic Criteria**

- Neck mass, unilateral hearing loss, tinnitus, nasal obstruction, epistaxis, and cranial nerve palsies

#### **Investigations:**

- FBC, RFT, LFT and HIV
- CXR
- Abdominal ultrasound
- CT scan and/or MRI of the nasopharynx, skull base, and neck
- Nasopharyngoscopy
- Endoscopic guided biopsy of the primary tumor for histology
- PET CT
- Immunohistochemistry to further confirm the diagnosis

**Staging:** TNM staging system

#### **Management**

Due to deep location of nasopharynx, and anatomic proximity to critical structures, radical surgery is typically not used. Role of surgery is initially for biopsy for histological confirmation. It may also be used for management of the neck for persistently enlarged lymph node.

Nasopharyngeal cancer is mainly treated by radiotherapy either alone or in combination with chemotherapy.

**Table 22.9 Management of Nasopharyngeal cancer by Stage**

Stage	Management
Stage I	Radiotherapy alone to primary disease and neck
Stage II–IVB	Concurrent chemotherapy and radiation to the primary disease and neck
Stage IVC	palliative care (which may include chemotherapy and radiotherapy)
Induction chemotherapy can be considered for stage III–IVB	If delays are anticipated in initiation of concurrent chemotherapy and radiation.
Local recurrence	Chemotherapy, surgery or re-irradiation

### **22.5.2 Laryngeal Cancer**

Laryngeal cancer is one of the most common cancers of head and neck. It is predominantly found in men and mostly in those with history of tobacco smoking and alcohol intake. It is divided into three major anatomic regions; supraglottis, glottis and subglottic.

#### **Diagnostic Criteria**

- Hoarseness, stridor, difficulty in breathing, neck mass, odynophagia, cough.

#### **Investigations:**

- FBC, RFT and LFT
- CXR
- CT scan and/or MRI of the Head and Neck
- Laryngoscopy
- Pathology: Definitive diagnosis is confirmed by laryngoscopy-guided biopsy of the primary tumor

**Staging:** TNM Staging system

**Table: 22.10 Management of Laryngeal Cancer by Stage**

Stage	Management
Stage I and II	Primary site: Partial or Total laryngectomy OR Radiotherapy alone.
Stage III–IVB	Concurrent Chemoradiation or Total Laryngectomy and neck dissection followed by Adjuvant Radiotherapy or Chemo radiotherapy
Stage IVC	Palliative care

### **22.5.3 Hypopharyngeal Cancers:**

Hypopharyngeal cancer includes tumors arising from the pyriform sinus, posterior pharyngeal wall, postcricoid region. It is associated with tobacco use, alcohol consumption, and Plummer–Vinson syndrome.

#### **Diagnostic Criteria:**

- Dysphagia, odynophagia, change in speech (dysarthria), neck mass, referred otalgia, throat pain, weight loss, sensation of mass in throat and hoarseness of voice.

#### **Investigations**

- FBC, RFT and LFT
- Hypopharyngoscopy and biopsy for histopathology
- CXR
- CT scan and/or MRI of the Head and Neck

**Staging:** TNM staging system.

#### **Management**

Radiation therapy is the mainstay of first-line local treatment for early stage hypopharyngeal carcinoma. For more advanced disease, concurrent chemoradiation reduces the rate of distant metastasis, and improves local control.

## **22.5.4 Salivary Gland Cancer**

Salivary gland cancers arise from major or minor salivary glands in the head and neck region. The most common malignant salivary gland tumors are mucoepidermoid carcinoma and adenocarcinoma.

**Presentation:** Depends on primary site involved.

- Mass, pain, nerve palsies, neck mass

**Investigations:**

- FBC, LFT, and RFT
- CXR
- CT scan and/or MRI of Head and Neck
- Biopsy of the primary tumor for histology.

**Staging:** TNM staging system:

**Treatment:**

- Complete surgical resection with adjuvant radiotherapy if adverse features are present
- If disease is not resectable, definitive radiotherapy or concurrent chemoradiotherapy is indicated
- Neck dissection is indicated for high-grade tumors or clinically positive neck disease

## **22.5.5 Nasal Cavity and Paranasal Sinus Cancer**

These are tumors arising from nasal cavity and the four paired paranasal sinuses (frontal, ethmoid, maxillary, and sphenoid).

**Diagnostic Criteria:**

Nasal obstruction, epistaxis, proptosis, double vision, cheek mass, loss of sensation of the cheek and loosening or pain of the teeth

**Investigations:**

- FBC, RFT and LFT
- CXR
- Abdominal Ultrasound
- CT scan and/or MRI of the Para nasal sinuses and neck
- Direct fibre-optic endoscopy
- Endoscopic guided biopsy of the primary tumor for histopathology

**Staging:** TNM Staging system

**Treatment:**

- Treatment is by surgery and or radiotherapy with or without chemotherapy.
- Surgical resection of the primary tumor and neck dissection followed by radiotherapy can be done in early disease stages. It may also be used for management persistently enlarged lymph nodes, persistent or recurrent disease after radiotherapy.
- Stage I–IINO: Complete surgical resection followed by radiotherapy alternatively definitive radiotherapy.
- Radiotherapy can be given as an alternative definitive treatment, either alone or in combination with chemotherapy. It is used in palliative care for advanced diseases
- Chemotherapy is used in induction, concurrent or adjuvant therapy.

## **22.5.6 Oral Cavity Cancer**

Oral cavity consists of the upper and lower lips, gingivobuccal sulcus, buccal mucosa, upper and lower gingiva, retromolar trigone, hard palate, floor of mouth, and anterior two-third of the tongue. Risk factors include smoking, excessive consumption of alcohol, poor oral hygiene, prolonged focal denture irritation, betel nut chewing, and syphilis.

**Diagnostic Criteria:**

- Non-healing ulcer, speech difficulty, hypersalivation, neck mass, dysphagia and otalgia

**Investigations:**

- FBC, LFT, RFT and HIV
- CXR
- CT Scan and/or MRI of the Head and Neck
- Mirror and fibre-optic endoscopic examination
- Biopsy for histologic confirmation

**Management:**

Surgery is the mainstay treatment modality for cancer of the oral cavity. Single modality treatment with surgery or radiation therapy is preferred for early-stage oral cavity cancer.

Definitive radiation with concurrent chemotherapy is the current standard for unresectable locally advanced disease. Radiotherapy can be given as palliative treatment to primary or metastatic area. Chemotherapy may also be given as palliative care in a very advanced disease.

**22.5.7 Oropharyngeal Cancer**

Oropharynx is located between the soft palate superiorly and the hyoid bone inferiorly. The oropharynx has four walls; soft palate, tonsillar region, base of tongue, and pharyngeal wall. It is associated with tobacco use and alcohol consumption and HPV. Tonsillar and pharyngeal tongue tumors frequently are initially recognized by nodal metastases.

**Clinical Presentation**

- Sore throat, non-healing oropharyngeal ulcers, dysphagia, referred otalgia, hoarseness (with larynx invasion), odynophagia, hot potato voice and impaired tongue movement, including protrusion.

**Investigations:**

- FBC, LFT, RFT and HIV
- CXR
- CT Scan and/or MRI of the Head and Neck
- Mirror and fibre-optic endoscopic examination
- Biopsy for histologic confirmation

**Management:**

Oropharyngeal cancers are mainly treated by Radiotherapy in combination with chemotherapy. Surgery can be used in selected cases.

**Table 22.11 Recommended Radiotherapy and Chemotherapy treatment for Head and Neck tumours**

Curative radiotherapy	Radiotherapy dose for head and neck cancers is 66–70Gy given at conventional fraction of 1.8–2Gy/fractions.
Concurrent Chemotherapy	<b>S:</b> cisplatin (IV) 40mg/m <sup>2</sup> 1hour infusion weekly during Radiotherapy <b>OR</b> <b>S:</b> cisplatin (IV) 75mg/m <sup>2</sup> 1 hour infusion day 1 repeat every 21 days during radiotherapy.
Induction Chemotherapy	For patients with Advanced Head and Neck Cancers - PF or TPF (taxane, platinum and 5 FU) for 3 – 6 cycles. <b>S:</b> carboplatin (IV) AUC 5 1hour infusion day 1 AND 5-flourouracil (IV) 400mg/m <sup>2</sup> bolus day 1 AND paclitaxel (IV) 175mg/m <sup>2</sup> 3 hour infusion day 1 repeat every 21 days for 3-6 cycles.
Adjuvant Chemotherapy:	In curative intent concurrent chemoradiotherapy is indicated with cisplatin/5FU (IV) If induction chemotherapy was not given then adjuvant chemotherapy is recommended. Alone or in combination with cetuximab. <b>S:</b> carboplatin (IV) AUC 5 1hour infusion day 1AND 5-flourouracil (IV) 400mg/m <sup>2</sup> bolus day 1 AND Cetuximab (IV) 400mg/m <sup>2</sup> 2 hours infusion day 1 (to be administered 1 hour before cisplatin/5-Fu) (IV) every 21 days for 3-6 cycles.
Treatment of Recurrent or Metastatic disease	Combination therapy cisplatin or carboplatin/docetaxel or paclitaxel. paclitaxel/ cisplatin/ 5-FU cisplatin/ gemcitabine, gemcitabine/ vinorelbine, carboplatin, cetuximab (IV). Single agents cisplatin, carboplatin, paclitaxel, docetaxel, 5-FU, methotrexate, gemcitabine and capecitabine (IV)

**Note**

- Head and neck tumour patients must be referred to cancer specialized centers for evaluation and definitive management. Follow up visits: 1st visit at 4–6 weeks then after each 3–4 months in the 1<sup>st</sup> year, 6 monthly in the 2<sup>nd</sup> year thereafter yearly.

### 22.5.8 Thyroid Carcinoma

Thyroid cancer is a commonest endocrine malignancy in Tanzania. It accounts approximately 0.8–1% of all malignancies seen at Ocean Road cancer institute annually. Histological types are medullary, anaplastic and well differentiated thyroid cancer.

Majority of these cases are differentiated thyroid cancer, the commonest being follicular subtype followed by papillary subtype and rare ones being Hurthle cell, follicular variant of papillary thyroid carcinoma, tall cell, columnar, solid and clear cell. Female are mostly affected, the male to female ratio being 3:1

#### Diagnostic Criteria

- Thyroid mass (Anterior neck mass), Obstructive symptoms (Stridor, hoarseness), laryngeal nerve palsy, dysphagia
- Metastatic symptoms such as weight loss, difficulty in breathing, bone pain/pathological fractures

#### Investigations:

- Thyroid function tests (T3, T4, TSH), FBC, LFTs, Urea & Creatinine, Serum calcitonin, Serum thyroglobulin levels
- Thyroid Scan
- CXR
- Isotope bone scan
- CT Scan of the neck
- Biopsy or Fine needle aspiration cytology (FNAC) of a thyroid lesion

**Staging:** TNM Staging system

#### Treatment:

Surgery is the mainstay of treatment; lobectomy, total or near total thyroidectomy. Radiotherapy is indicated in all cases of anaplastic carcinoma.

#### Pharmacological Treatment

- Radioactive iodine I-131 sodium or potassium iodide ablation is indicated in all patients with well differentiated thyroid cancer after surgery.
- Post ablation: Thyroid-stimulating hormone (TSH) suppression therapy (levothyroxine) is indicated in all patients post ablation and post-lobectomy. Aim is to keep TSH <0.1 mU/L.
- Tumor recurrence or metastasis: Local recurrence should be managed surgically. Local recurrence or distant metastases not suitable for surgery that are iodine avid are treated with I-131.
- Palliative chemotherapy is indicated for patients with visceral metastatic diseases not responding to I-131. Recommended regimen is:

**S:** paclitaxel (IV) 175mg/m<sup>2</sup> 3 hours infusion day 1 AND doxorubicin (IV) 60mg/m<sup>2</sup> bolus day 1 every 3 weeks up to 6 cycles.

- Radiotherapy is indicated for Adjuvant treatment to the thyroid bed post surgery with macro/microscopic residual disease, in unresectable and local recurrence that does not take up I-131 and palliation of bone and brain metastasis. Palliative dose: 30Gy in 10 Fractions.
- For anaplastic carcinoma radiation is indicated and dose recommended 50–60Gy in 20–30 Fractions.
- Medullary Thyroid Tumor (MTC) is primarily managed by surgery, Radiotherapy
- Anaplastic Thyroid Cancer (ATC) is aggressive disease. A Total thyroidectomy followed by adjuvant radiotherapy is indicated to resectable disease. If unresectable ATC palliative radiotherapy and combination chemotherapy is indicated. The recommended chemotherapy regimen is as above in metastatic disease.

**Note:** All patients must be referred to a cancer specialized center for proper management.

## 22.6 Gastrointestinal Malignancies

### 22.6.1 Esophageal Cancer

Histologically there are two types; SCC and adenocarcinoma. Tobacco and alcohol abuse are major risk factors for SCC whereas obesity, gastroesophageal reflux disease (GERD) and Barrett's esophagus are the major risk factors for adenocarcinoma.

#### Diagnostic Criteria

- Difficult in swallowing (dysphagia) is the commonest symptom which is associated with weight loss and poor performance status.

#### Investigation

- FBC, LFT, Urea, Creatinine
- Barium swallow and meal
- Chest and Abdominal CT scan
- Abdominal USS
- Rigid oesophagoscopy or oesophagoduodenoscopy (OGD) and biopsy for histology

**Staging:** TNM Staging system

**Management: Surgery and radiotherapy**

Surgery is a major component of treatment for resectable disease. Surgery and or radiotherapy may be curative in early diseases. However, most patients present in late stages, hence the goal of treatment is to prolong survival and relieve symptoms. Radiation (alone or in combination with chemotherapy) is given as a definitive, preoperative, postoperative therapy or palliative setting.

#### Chemotherapy

**Table 22.12 Recommended chemotherapy regimens for neo-adjuvant, adjuvant or palliative for Esophageal cancer**

Neoadjuvant Chemotherapy	<p><b>S:</b> paclitaxel (IV) 175 mg/m<sup>2</sup> 3hours' infusion day 1 AND cisplatin (IV) 75 mg/m<sup>2</sup> 1-hour infusion day 1 OR carboplatin (IV) AUC 5 1-hour infusion day 1 given every 21 days for 6 cycles <b>OR</b> <b>S:</b> docetaxel (IV) 75mg/m<sup>2</sup> 3hours' infusion day 1 AND cisplatin (IV) 75mg/m<sup>2</sup> 1-hour infusion day 1 every 3 21 days for 6 cycles</p>
Adjuvant Chemotherapy	<p><b>S:</b> 5-FU (IV) 1000 mg/m<sup>2</sup> (IV) bolus day 1-day 5 AND cisplatin (IV) 75 mg/m<sup>2</sup> 1 hour infusion day1 given every 21 days for 6 cycles</p>
Palliative Chemotherapy	<p><b>S:</b> capecitabine (PO) 1000mg/m<sup>2</sup> 12 hourly on day 1–14, cycled every 21 days for 6 cycles or until disease progression or intolerable toxicity</p>

#### Note

- All patients should be referred to cancer specialized centers for proper management  
Stenting, gastrostomy tube and parenteral nutrition are employed to provide feeding when there is total dysphagia.

### 22.6.2 Gastric Cancer

Gastric cancer is often diagnosed at an advanced stage. Among the risk factors include age, gender, genetic factors, smoking, smoke or salt preserved food, diet less of fruits and vegetables, infection with H. Pylori and Epstein Barr Virus. About 90–95% of the tumors are adenocarcinoma.

#### Diagnostic Criteria:

- Epigastric pain worsened by food intake, early satiety
- Distal tumours may present with obstructive symptoms
- Occult or manifest bleeding may be a feature
- Other symptoms include epigastric mass, pallor, weight loss, supraclavicular nodes, hepatomegaly, periumbilical nodes

**Investigations:**

- FBC, LFT, RFT
- Stool for occult blood
- Carcinoembryonic antigen (CEA) –
- IHC – Her 2 Status
- CXR
- Barium meal (double contrast)
- Abdomen and pelvis CT scan or USS
- Endoscopy and biopsy for histology

**Staging:** TNM staging system**Management:**

Surgery is the primary treatment for early stage gastric cancer. Total or partial gastrectomy is performed together with lymph node dissection. By pass surgery is done to relieve obstructive symptoms. Surgery is usually preceded by Chemotherapy (Perioperative) or adjuvant chemoradiotherapy.

**Pharmacological Treatment****Table 22.13 Recommended chemotherapy regimens for Gastric cancer**

Perioperative chemotherapy	<p><b>S:</b> 5-fluorouracil (IV) 500mg/m<sup>2</sup> bolus day 1 AND epirubicin (IV) 50mg/m<sup>2</sup> 30 minutes' infusion day 1 AND cisplatin (IV) 60mg/m<sup>2</sup> 1-hour infusion day 1, cycled every 21 days for 6 cycles.</p> <p><b>OR</b></p> <p><b>S:</b> capecitabine (PO) 625mg/m<sup>2</sup> 12 hourly daily for 21 days AND epirubicin (IV) 50mg/m<sup>2</sup> 30 minutes' infusion day 1 AND cisplatin (IV) 60mg/m<sup>2</sup> 1-hour infusion day 1, cycled every 21 days for 6 cycles.</p> <p><b>OR</b></p> <p><b>S:</b> 5-fluorouracil (IV) 200mg/m<sup>2</sup>/day Continuous infusion day 1-4 AND epirubicin (IV) 50mg/m<sup>2</sup> 30 minutes' infusion day 1 AND cisplatin (IV) 60mg/m<sup>2</sup> 1-hour infusion day 1, cycled every 21 days for 6 cycles.</p>
locally advanced and metastatic gastric adenocarcinoma.	<p><b>S:</b> paclitaxel (IV) 175mg/m<sup>2</sup><sup>3</sup> hours' infusion AND carboplatin (IV) AUC 5 1-hour infusion on day 1, cycled every 21 days for 6 cycles AND/OR trastuzumab (IV) 6mg/m<sup>2</sup> 2hours loading dose day1, and then 4mg/m<sup>2</sup> every 14 days (For Her 2 + Patients).</p> <p><b>OR</b></p> <p><b>S:</b> docetaxel (IV) 60mg/m<sup>2</sup> 2 hours' infusion day 1 AND cisplatin (IV) 60mg/m<sup>2</sup><sup>1</sup> 1 hour/day1 + 5-FU (IV) 750mg/m<sup>2</sup> continuous infusion over 24 hours on day1-4, cycled every 21 days for 6 cycles AND/OR trastuzumab (IV) 6mg/m<sup>2</sup> 2hours' infusion loading dose day1, and then 4mg/m<sup>2</sup> every 14 days (For Her 2 + Patients).</p>
Palliative setting	<b>S:</b> capecitabine (PO) 1000mg/m <sup>2</sup> 12 hourly on day 1–14, cycled every 3 weeks, 6 cycles or until disease progression or intolerable toxicity.

**Note**

- Concurrent Chemo radiotherapy with 3DCRT may be used as adjuvant post surgery.
- Radiotherapy can also be used in palliative setting to control bleeding and pain.
- Gastric (MALT) lymphoma are associated with Chronic *H. pylori* inflammation. They are managed by *H. pylori* eradication and Chemoradiotherapy (see details in Lymphoma section).
- Patients with CD 117 positive gastro intestinal stromal tumor (GIST) respond well to imatinib.

**22.6.3 Hepatocellular Carcinoma**

Associated with chronic Hepatitis B/C infection

**Diagnostic criteria**

- An arterial bruit and ascites may be present
- Right upper abdominal swelling and pain often associated with weight loss, fever, jaundice

## Investigation

- FBC, LFT, RFT, Biochemistry, Serum alpha feto protein, HBsAg, HBcore antibody, partial thromboplastin time (PTT)
- CXR
- Abdomen and Pelvis USS
- 3 Phase Liver Protocol CT/MRI Scan with IV Contrast
- PET/CT
- Biopsy or FNAC of the liver

**Staging:** TNM staging system

**Table 22.14 Child Pugh Score**

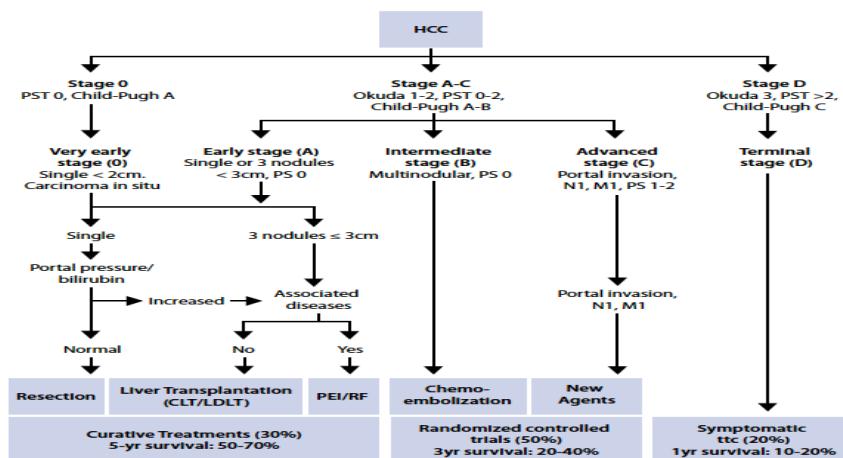
Parameter	Points for increasing abnormality		
	I	II	III
Encephalopathy (grade)	None	1-2	3-4
Ascites	None	Slight	Moderate
Albumin	>3.5	2.8-3.5	<2.8
Prothrombin time (s)	1-4	4-6	>6
Bilirubin (mg/dl) For primary biliary cirrhosis	1-2 1-4	2-3 4-10	>3 >10

## Management

**Table 22.15 Treatment Recommendations**

Presentation	Recommended treatment
Resectable	Partial hepatectomy
Unresectable, medically operable	Liver transplant
Unresectable, medically inoperable	Conformal Radiotherapy +/- Chemotherapy Systemic therapy alone Supportive care
Palliative	Radiotherapy for Bone and Brain metastases

**Flow Chart 22.1 Management of Hepatocellular cancer by Stage and Child Pugh Score**



## Pharmacological Treatment

Recommended systemic regimen used for palliation

**S:** doxorubicin (IV) 60 mg/m<sup>2</sup> over 30 minutes day 1 given every 3 weeks for 4–6 cycles.

**S:** sorafenib (PO) 400mg daily until disease progression or unacceptable toxicity.

## 22.6.4 Rectal Cancer

Risk factors include: inherited genetic syndromes, diet high in red and processed meat, smoking and alcohol abuse, having inflammatory bowel disease, type II diabetes and obesity. Histology; commonest is adenocarcinoma 95%.

### Diagnostic Criteria:

- Change in bowel habit eg constipation or diarrhea, sense of incomplete bowel emptying.
- Rectal bleeding or blood in stool.
- Abdominal mass with or without obstructive symptoms
- Unexplained weight loss and other symptoms of advanced disease.

### Investigations:

- FBC, RFT, LFT, CEA
- Stool for occult blood
- CXR
- Barium enema (double contrast)
- Abdomen and Pelvis USS
- Digital rectal examination
- Sigmoidoscopy or Colonoscopy with Biopsy of the lesion
- Abdomen and Pelvis CT Scan

### Staging: TNM staging system

### Management

Surgery is the primary treatment for early disease. Hemicolectomy with lymphnode dissection is commonly performed in colon cancer. Give preoperative chemotherapy for locally advanced disease to shrink the tumor. Radiotherapy plays a role in rectal tumor as neo-adjuvant, adjuvant or palliative.

### Pharmacological management:

Management of locally advanced and metastatic colorectal cancer involves various active chemotherapy drugs, either in combination or as single agents: 5-FU, leucovorin, capecitabine, oxaliplatin, irinotecan and bevacizumab are available for various combination regimens and schedules.

**Table 22.16 Recommended Chemotherapy regimens for Rectal cancer**

Neo-adjuvant chemo radiotherapy	<p><b>S:</b> 5-FU (IV) 350 mg/m<sup>2</sup> over 30 minutes AND leucovorin (IV) 20 mg/m<sup>2</sup> infusion over 30 minutes' day 1–day 5 given on 1<sup>st</sup> and 5<sup>th</sup> weeks of RT, concurrent with RT: 45 Gy/25#/5weeks followed by surgery in 4–10 weeks.</p> <p>3–10 weeks after surgery continue with chemo as below:</p> <p><b>S:</b> 5-FU (IV) 50 mg/m<sup>2</sup> over 30 min day 1–day 5 PLUS leucovorin (IV) 20 mg/m<sup>2</sup> 30 minutes infusion day1–day5 every 21 days for 4 cycles</p>
Adjuvant chemo Radiotherapy	<p>3–10 weeks after surgery</p> <p><b>S:</b> 5-FU (IV) 500 mg/m<sup>2</sup> over 30 minutes' day 1–5 &amp; day 29–33, concurrent with RT:45 Gy/25#/5 weeks.</p> <p>Four weeks after completion of chemo radiation; continue with chemo: 5-FU (IV) 450 mg/m<sup>2</sup> bolus day 1–day 5, Every 4 weeks for 2 cycles</p> <p style="text-align: center;"><b>OR</b></p> <p>S: capecitabine (PO) 825mg/m<sup>2</sup> 12 hourly during Radiotherapy.</p>

### Management of Metastatic disease

As colon

## 22.6.5 Colon Cancer

### Investigations

- FBC, RFT, LFT, CEA
- Stool for occult blood
- CXR
- Barium enema (double contrast)
- Abdomen and Pelvis USS.
- Digital rectal examination
- Sigmoidoscopy or Colonoscopy with Biopsy of the lesion
- Abdomen and Pelvis CT Scan

**Staging:** TNM staging system

### Management

- **Management of Non-metastatic disease:** Surgery then Adjuvant Post Op Chemotherapy.
- **Management of Metastatic disease:** Single or Combination Chemotherapy.

**Table 22.17 Recommended Chemotherapy regimens for Colon cancer**

Adjuvant Chemotherapy	<p><b>S:</b> oxaliplatin (IV) 85mg/m<sup>2</sup> 2 hours' infusion day 1 AND leucovorin(IV) 400mg/m<sup>2</sup> over 20 minutes day1 AND 5-fluorouracil (IV) 400mg/m<sup>2</sup> bolus day1, then 1200mg/m<sup>2</sup>/day X 2 days (IV) Continous infusion (USE INFUSION PUMP) repeat after every 14 days for 6-12 cycles.</p> <p style="text-align: center;"><b>OR</b></p> <p><b>S:</b> oxaliplatin (IV) 130mg/m<sup>2</sup> 2hours' infusion AND capecitabine (PO) 1000mg/m<sup>2</sup> 12 hourly for 14 days, 21 days' cycles for 4-8 cycles.</p> <p style="text-align: center;"><b>OR</b></p> <p><b>S:</b> capecitabine (PO) 1000mg/m<sup>2</sup> 12 hourly daily for 14 days, 21 days cycle for 6 cycles.</p>
Metastatic disease	<p><b>S:</b> oxaliplatin (IV) 85mg/m<sup>2</sup> 2 hours infusion day 1 <b>AND</b> leucovorin (IV) 400mg/m<sup>2</sup> infusion over 20 minutes day1 <b>AND</b> 5- fluorouracil (IV) 400mg/m<sup>2</sup> bolus day1, then 1200mg/m<sup>2</sup>/day X 2 days (IV) Continous infusion (USE INFUSION PUMP) repeat after every 14 days for 6-12 cycles. With/without bevacizumab (IV) 5mg/kg 1 hour infusion day 1 or cetuximab (IV) 500mg/m<sup>2</sup> infusion over 2 hours day 1</p> <p style="text-align: center;"><b>OR</b></p> <p><b>S:</b> oxaliplatin (IV) 130mg/m<sup>2</sup> 2hours' infusion AND capecitabine (PO) 1000mg/m<sup>2</sup> 12 hourly daily for 14 days, 21 days' cycles for 4-8 cycles. With/without bevacizumab (IV) 5mg/kg 1-hourinfusion day 1</p> <p style="text-align: center;"><b>OR</b></p> <p><b>S:</b> capecitabine (PO) 1000mg/m<sup>2</sup> 12 hourly daily for 14 days, 21 days cycle for 6 cycles.</p>

### Note

- Colorectal cancers are usually asymptomatic until advanced stage hence regular
- Screening with annual digital rectal examination, stool for occult blood + colonoscopy and is recommended starting at 50 years of age.

## 22.6.6 Anal Cancer

### Investigations

- FBC, RFT, LFT, HIV/CD4
- CXR
- Abdomen and Pelvis USS.
- Digital rectal examination
- Sigmoidoscopy or Colonoscopy with Biopsy of the lesion
- Abdomen and Pelvis CT scan

**Staging:** TNM Staging system

## **Management**

- For resectable Good Performance status: Surgery (APR) then Adjuvant Chemoradiotherapy (45Gy-50Gy)
- For Unresectable Good Performance status: Neoadjuvant Chemoradiotherapy (45Gy-50Gy) then Surgery (APR)
- For Inoperable and Poor Performance status: Palliative Radiotherapy

## **Pharmacological Management**

Concurrent Chemoradiotherapy:

**S:** mitomycin C (IV) 10mg/m<sup>2</sup> bolus day 1 and 29 AND 5-flourouracil (IV) 1000mg/m<sup>2</sup> Continuous infusion day 1-4 and 29-32. (USE INFUSION PUMP).

**OR**

**S:** capecitabine (PO) 825mg/m<sup>2</sup> 12 hourly a day during radiotherapy (5 days a week) AND 5- fluorouracil (IV) 1000mg/m<sup>2</sup> Continuous infusion day 1-4 and 29-32. (USE INFUSION PUMP).

## **Metastatic disease**

As Rectum

## **22.7 Lung Cancer**

Worldwide lung cancer is the leading cause of cancer-related death. Approximately 85 %–90% of lung cancer cases are caused by cigarette smoking. There are 2 main types of lung cancer; Non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). These 2 types have different prognosis and management approach.

### **22.7.1 Non-small cell lung Cancer**

Accounts for approximately 85% of all lung cancer cases

#### **Diagnostic Criteria**

- Chronic chest symptoms in a smoker
- Haemoptysis
- May present with superior vena cava obstruction (SVCO) syndrome
- Cough in patient exposed to asbestos
- Findings of chest symptoms, weight loss, poor Karnofsky performance scale (KPS)

#### **Investigations:**

- FBC, LFT, Urea, Creatinine
- CXR PA & lateral views
- CT Scan of Thorax and Abdomen
- Abdominal USS
- Bronchoscopy and Biopsy for histopathology
- Cytology of sputum or bronchial aspirate examination

#### **Staging:** TNM staging system

**Management:** Surgery (pneumonectomy or lobectomy) is curative for stage I and some stage II disease.

#### **Pharmacological Treatment:**

Recommended Chemotherapy regimens for adjuvant, unresectable or recurrent and metastatic disease are;

**S:** carboplatin (IV) AUC 1-hour infusion 6 day1 AND paclitaxel (IV) 175 mg/m<sup>2</sup> 3 hours' infusion day 1 every 21 days for 6 cycles

#### **Radiotherapy**

With advanced radiotherapy machine and treatment technic, RT may be given for neo-adjuvant or adjuvant to surgery. Palliative Radiotherapy is frequently used in metastatic disease to bone, spinal cord compression, brain, liver and in case of superior vena cava obstruction (SVCO), atelectasis, obstructive pneumonitis and fungating masses. Dose of 30GY/10 Fractions/2weeks gives good symptom relief.

## **22.7.2 Small cell lung cancer**

SCLC is characterized by early development of widespread metastases. It is highly sensitive to initial chemotherapy and radiotherapy; however, most patients eventually die of recurrent disease.

**Diagnostic criteria and investigations:** As in non – small cell lung cancer (NSCLC) however brain scan and bone marrow aspirate are necessary

**Staging:** Limited disease versus extensive disease

### **Pharmacological Treatment**

Aim is for local control and palliation. Cure rate is low

Platinum + Etoposide are the major drugs for which the tumor is sensitive.

**S:** cisplatin (IV) 60 mg/m<sup>2</sup> 1-hour infusion Day 1 AND etoposide (IV) 100 mg/m<sup>2</sup> over 30 minutes Day1–3, Every 21 days for 4–6 cycles

**OR**

**S:** carboplatin (IV) AUC 5 1-hour infusion Day 1 AND etoposide 100 mg/m<sup>2</sup> 30 minutes (IV) infusion Day1–3, every 21 days for 4–6 cycles

Other recommended chemotherapeutic drugs are irinotecan and gemcitabine

### **Radiotherapy:**

Consolidation to primary site and mediastinum: 50Gy/25Fractions/5weeks

- Prophylactic brain irradiation in complete responders
- Palliative treatment for symptoms relief in respiratory, bone or CNS symptoms: 30Gy/10Fractions/2wks

## **22.8 Genitourinary Malignancies**

### **22.8.1 Carcinoma of the Prostate**

The most common type of prostate cancer is adenocarcinoma (95 %). Tumours are stratified by T stage, Gleason score (GS), and PSA into three prognostic groups of low, intermediate and high risk.

- Low risk: T1–T2a and PSA < 10 ng/ml and GS ≤ 6
- Intermediate risk: T2b or PSA 10 – 20 ng/ml or GS 7
- High risk: T2c–T4 or PSA > 20ng/ml or GS 8–10

Patient can be offered appropriate treatment options according to stage of disease, prognostic risk group and estimated survival taking into account performance status and comorbidity.

#### **Diagnostic Criteria**

- May be asymptomatic in early stages of the disease
- May present incidentally following examination for benign prostatic hypertrophy or elevated serum prostatic specific antigen (PSA)
- Prostatic symptoms are associated with advanced stages of the disease, which include: reduced potency, urinary frequency and nocturnal, poor stream, hesitancy and terminal dribbling
- Very often patients may present with bone pain including backache or pathological fracture
- Digital Rectal Examination (DRE) typically reveals a hard, irregular prostate. TURP is carried out to both confirm the diagnosis and also as part of the treatment (to relieve obstruction).

#### **Screening for prostate cancer**

Routine screening not recommended, but when done should begin with PSA and digital rectal examination at age 50 if life expectancy is >10 years. It is recommended that screening of high risk group should take place starting at age 45 .

#### **Investigations**

- FBC, LFT, Urea, Creatinine, Serum PSA, ALP, Testosterone
- X-rays of the painful bone or spine
- CXR

- Abdomen and Pelvis USS and or CT Scan
- Pelvic MRI in early-stage disease
- PET/CT
- Bone scan
- Biopsy for histopathology

### **Staging:** TNM staging system

### **Treatment:**

Treatment depends on disease profile (Risk stratification) and patient factors as noted above.

Options include:

- Watchful waiting
- Active surveillance
- Surgery (curative or palliative)
- Radiotherapy (curative or palliative)
- Hormonal therapy (chemical vs surgical castration)
- Chemotherapy

### **Surgery**

Early stages (Low and Intermediate risk groups) can be treated with either radical prostatectomy or radical Radiotherapy with cure intent. However, surgery may cause postoperative impotence and impaired urinary control. TURP is carried out to both confirm the diagnosis and also as part of relieving obstruction.

### **Radiotherapy**

Radical Radiotherapy for Adjuvant and definitive, EBRT up to 74 Gy/37 Fractions can be given using 3DCRT or IMRT Techniques. Palliative radiotherapy is valuable to bone metastases, massive hematuria, spinal cord compression and brain mets,

### **Hormonal Therapy**

Hormonal manipulation is by surgical or medical castration. It is carried out in patients with locally advanced or metastatic disease. Bilateral orchectomy is a surgical hormonal manipulation and should not be regarded curative surgery.

### **Pharmacological Treatment:**

**S:** goserelin (SC) 3.6 mg every 4 weeks or 10.8mg every 12 weeks with/ without oral bicalutamide (PO) 50mg once daily

#### **Note**

- Goserelin is not required after orchectomy but patient may receive Bicalutamide.
- Treatment with goserelin and bicalutamide may be given up to 2 years depending on patient condition and Prostate Specific Antigen (PSA) levels

### **Chemotherapy**

Recommended chemotherapy regimens for hormonal refractory prostate cancer are:

**S:** docetaxel (IV) 75mg/m<sup>2</sup> 2 hours' infusion day 1 given every 21 days for 6 cycles. It is mainly reserved in hormonal refractory prostate cancer.

For Bone metastases/osteolytic/tumour induced hypercalcemia are:

**S:** zolendronic acid (IV) 4mg over 15min given 4 Weekly

### **Metastatic disease**

Life long ADT ± palliative RT ± bisphosphonates for hormone refractory disease. docetaxel and prednisone for androgen independent disease can add Carboplatin if docetaxel not working to Castrate resistant prostate cancer patients.

Evaluation every 3 months (Check PSA level) Castrate resistant patients with rising PSA zoledronic acid should be given monthly. These are given together with Ca2+ and Vitamin D supplements.

**In Castrate resistant patients** which did not respond to Docetaxel plus carboplatin and prednisolone, patients Abberaterone acetate with prednisolone is an option (500mg OD taken with food is highly recommended)

- S:** abberaterone acetate (PO) 500mg one a day (Taken with food)  
**OR**  
**S:** enzalutamide (PO) 160mg daily

## 22.8.2 Urinary Bladder Cancer

Urinary bladder cancers are malignant tumors that commonly arise from the inner lining of the bladder or its connective tissue. Common pathologies include transition cell carcinoma, squamous cell carcinoma, adenocarcinoma, sarcomas and secondary deposits.

Risk factors for bladder cancer include chronic irritation (schistosomiasis, irradiation, and catheterization), chemicals (aromatic amines, aniline dyes, tobacco, analgesics) and genetic predisposition. Symptoms include blood in the urine, dysuria, Lower urinary tract symptoms (LUTS), and low back pain.

### Diagnostic Criteria

- Symptoms include blood in the urine, pain with urination, and low back pain.

### Investigations

- FBC, RFT, LFT, Alkaline phosphatase
- Urinalysis, Urine culture and sensitivity, Urine for cytology
- CXR and /or CT chest
- Bone scan
- Abdomen and Pelvis USS or CT scan
- PET/CT
- Cystoscopy with bladder mapping & Biopsy
- EUA
- Bimanual examination
- TURBT with random biopsies of normal appearing mucosa to exclude CIS. (If trigone involved, biopsy prostatic urethra)

### Staging: TNM staging system

### Management

Treatment of Urinary bladder cancer depends on how deeply the tumor invades into the bladder wall.

**Surgery:** Several modalities that may extend from bladder preserving surgery-TURB; to radical cystectomy with urine diversion depending bladder muscle invasion. Post operation patient may receive adjuvant chemo and/or radiotherapy

**Chemotherapy:** chemotherapy in bladder cancer may be offered before surgery or after surgery. It may also be given concurrent with radiotherapy or as palliative in inoperable tumor.

Recommended chemotherapy regimens for locally advanced and metastatic disease are;

- S:** gemcitabine (IV) 1000mg/m<sup>2</sup> infusion over 30minutes day 1, 8 & 15 AND cisplatin (IV) 70mg/m<sup>2</sup> infusion AND over 30mins day 2 given every 28 days for 6 cycles  
**OR**

### MVAC regimen

- S:** methotrexate (IV) 30mg/m<sup>2</sup> over 5 minutes day1, 15 & 22  
**AND**  
**S:** vinblastine (IV) 3mg/m<sup>2</sup> over 10 minutes day2, 15 & 22  
**AND**  
**S:** doxorubicin (IV) 30mg/m<sup>2</sup> over 15 minutes day2  
**AND**  
**S:** cisplatin (IV) 70mg/m<sup>2</sup> over 30mins day2

## **Radiotherapy**

Radiotherapy may be given after bladder preserving surgery or alone in small lesions with a dose up to 66Gy/33Fractions concurrent with cisplatin. It is also commonly used as palliative therapy to control bleeding and or pain locally advanced and metastatic disease. Palliative dose 30Gy/10Fractions or 20Gy/5Fractions

## **22.9 Haematological Malignancies**

### **22.9.1 Lymphomas**

World Health Organization broadly classifies lymphomas into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL).

#### **22.9.1.1 Non-Hodgkin's lymphoma**

NHLs are a heterogeneous group of diseases which are mainly linked by their origin within the lymphoid system and its different cellular components. They are sub classified based on the stage of maturation (immature vs. mature) and cell of origin [B cell, T cell, or natural killer cell (NK) cell].

##### **Diagnostic Criteria**

- Peripheral Lymph node enlargement (commonest site-neck)
- Hepatomegally and/or splenomegally in advanced stages
- B-symptoms: Unexplained weight loss, fever, drenching night sweats
- Coughing, trouble breathing, or chest pain in case of Superior vena cava obstruction (SVCO)

##### **Investigations:**

- CXR
- Chest and abdominopelvic CT Scan
- PET/CT
- FBC, differential and film
- Bone marrow aspirate and trephine
- Immunohistochemistry (IHC)
- LDH, Urea and Electrolyte, Creatinine, Albumin, Aspartate transaminase (AST), Bilirubin, Alkaline phosphatase, Serum calcium, Uric acid
- Pregnancy test in females of child-bearing age
- Hepatitis B and C
- HIV status
- Tissue Biopsy for histopathology
- MUGA scan/ ECHO

Note: Lumbar puncture and CSF cytology if there is CNS involvement of in NHL associated with a high risk of CNS relapse eg. Testicular, paranasal sinuses, extradural/paraspinal mass.

**Staging:** Ann Arbor classification.

##### **Management:**

NHL diseases are sensitive to both chemotherapy and radiotherapy

##### **Indolent lymphoma**

They include Indolent B-cell lymphomas such as Follicular lymphoma, MALT lymphoma, nodal marginal zone lymphoma, splenic marginal zone lymphoma and small lymphocytic lymphoma, and Indolent T-cell lymphomas such as mycosis fungoides.

##### **Treatment**

Stage 1 and 2 can be treated with involved node radiotherapy or R\_CHOP / R-CVP followed by radiotherapy.

##### **R-CHOP regimen:**

**S:** rituximab (IV) 375 mg/m<sup>2</sup> 3 hours' infusion day 1 AND cyclophosphamide day1 750 mg/m<sup>2</sup> 1-hour infusion AND doxorubicin (IV) 50 mg/m<sup>2</sup> 15 minutes'infusion day 1 AND vincristine (IV) 1.4 mg/m<sup>2</sup> over 10 minutes (maximum 2mg) day1 AND prednisolone (PO) 100mg once a day, day 1–5, every 21 days for 6–8 cycles.

## **Aggressive lymphoma with CD 20 positive**

These include Diffuse Large B-cell lymphoma (DLBCL), primary CNS lymphoma, adult Burkitt lymphoma, mantle cell lymphoma and aggressive T-cell lymphomas.

### **Treatment: R-CHOP**

**S:** rituximab (IV) 375 mg/m<sup>2</sup> 3 hours' infusion day1 AND cyclophosphamide (IV) day1 750 mg/m<sup>2</sup> 1-hour infusion AND doxorubicin (IV) 50 mg/m<sup>2</sup> 15 minutes' infusion day 1 AND vincristine (IV) 1.4 mg/m<sup>2</sup> over 10 minutes (maximum 2mg) day1 AND prednisolone (PO) 100mg once a day, day 1–5, every 21 days for 6–8 cycles.

### **Radiotherapy**

- Radiotherapy is directed to genuinely stage IA and IIA Disease
- Mantle or inverted Y: 40Gy/20 Fractions/4weeks with shielding of the critical organs.
- Involved field RT (IFRT): 46Gy/23 Fractions/4.5weeks

### **Primary CNS Lymphoma**

Standard chemotherapy regimens like CHOP are not effective possibly due to poor penetration of the blood-brain-barrier (BBB).

**S:** methotrexate (IV) 8mg/m<sup>2</sup>/day twice a week until remission is achieved

### **Burkitt Lymphoma (BL)**

Recommended chemotherapy regimens are:

**S:** CODOX-M AND IVAC (Magrath regimen- cyclophosphamide, vincristine, doxorubicin, methotrexate/ifosfamide, etoposide, cytarabine) (IV)

**OR**

**S:** CALGB 9251 (cyclophosphamide, prednisolone, ifosfamide, mesna, methotrexate, leucovorin, vincristine, cytarabine, etoposide, dexamethasone and doxorubicin) (IV)

**OR**

**S:** Hyper CVAD (cyclophosphamide, vincristine, doxorubicin and dexamethasone, methotrexate, cytarabine, leucovorin, methylprednisolone and 6-mercaptopurine) (IV)

**OR**

**S:** Dose-adjusted CHOP+Etoposide (IV)

### **Aggressive T-cell lymphomas**

Rare and more aggressive than DLBCL. First line therapy is usually

**S:** CHOP with Etoposide (CHEOP) (IV)

**OR**

**S:** cyclophosphamide (IV) day1 750 mg/m<sup>2</sup> 1-hour infusion AND doxorubicin (IV) 50 mg/m<sup>2</sup> 15 minutes' infusion day 1 AND vincristine (IV) 1.4 mg/m<sup>2</sup> over 10 minutes (maximum 2mg) day1 AND prednisolone (PO) 100mg once a day, day 1–5 AND etoposide 100mg/m<sup>2</sup> (IV) day 1-day 3; repeat every 21 days for 6–8 cycles.

#### **Note**

- For MALT lymphoma, eradication of Helicobacter pylori is essential. Splenectomy is recommended in splenic marginal zone lymphoma.
- Topical corticosteroids are indicated for localized or generalized skin involvement in mycosis fungoides. Systemic therapy indicated for non responders and Sezary syndrome.

These include **S:** retinoids, interferons and low dose methotrexate.

**S:** fludarabine AND Cyclophosphamide (FC) regimen is used as a second-line therapy for indolent B-cell lymphoma.

### **Hodgkin's disease (HD)**

Hodgkin Lymphoma comprises about 30% of all lymphomas. The disease is characterized by scattered large multinucleated Reed-Sternberg or mononuclear Hodgkin's cells in an inflammatory background of a lymph node biopsy section.

Classified into two main types:

- Nodular lymphocyte predominant Hodgkin lymphoma–NLPHL
- Classical Hodgkin lymphoma–CHL, which is sub-divided into:
  - Nodular sclerosis classical Hodgkin lymphoma–NSHL
  - Mixed cellularity classical Hodgkin lymphoma–MCHL
  - Lymphocyte-rich classical Hodgkin lymphoma–LRCHL
  - Lymphocyte-depleted classical Hodgkin lymphoma–LDHL

#### **Diagnostic Criteria**

- Enlarged painless lymph nodes in the neck or elsewhere
- B symptoms (weight loss, night sweats, and fever), pruritus, alcohol induced pain, general condition, throat, lymph nodes (site, number, size, consistency, mobility, matting), respiratory system, abdomen (liver, spleen, other masses), bone tenderness

#### **Investigations:**

- CXR
- CT Scan of neck, chest, abdomen and pelvis
- PET/CT
- FBC, LFT, RFT, ESR, LDH, HIV Test
- Bone marrow aspirate and biopsy (Not required in Stage I or II A)
- Biopsy for histological diagnosis
- MUGA scan / ECHO

#### **Management:**

As it is for NHL, HL diseases are sensitive to both chemotherapy and radiotherapy.

#### **Pharmacological Treatment**

Chemotherapy aims at cure for any stage of the disease. It is indicated in Stages II–IV.

Recommended chemotherapy regimen is ABVD which include combination of the following drugs:

**S:** doxorubicin (IV) 25 mg/m<sup>2</sup> over 30 minutes **AND** bleomycin (IV) 10 IU/m<sup>2</sup> over 10 minutes **AND** vinblastine (IV) 6 mg/m<sup>2</sup> over 10 minutes **AND** dacarbazine (IV) 375 mg/m<sup>2</sup> infusion over 30 minutes all given on day 1 & 15, every 28 days for 4–8 cycles.

**Other recommended chemotherapy regimens** that can be used as salvage regimens are DHAP, DHAC, IGEC, ICE and MINE-ESHAP.

**Radiotherapy:** can either be; involved field RT or mantle or inverted Y depending on site of disease: 1.8–2Gy/Fraction for 30–40Gy total dose.

### **22.9.2 Leukemia**

The symptoms and signs are caused by: (i) bone marrow failure (e.g. anaemia, neutropenia, thrombocytopenia); and (ii) infiltration of organs (e.g. liver, spleen, lymph nodes, meninges, brain, skin or testes).

#### **Investigations:**

- FBC, LFT, RFT, Coagulation indices
- Peripheral blood film
- Bone marrow aspiration and trephine biopsy
- Flow cytometry analysis, immunophenotyping, cytogenetic and molecular evaluation.
- ECHO/ECG for Cardiac function evaluation.

### 22.9.2.1 Acute Myeloid Leukemia (AML)

**Classification:** WHO classification

**Table 22.18 Treatment recommendations for AML**

Induction phase	7+3 (cytarabine + daunorubicin) regimen;  <b>S:</b> cytarabine (IV) 100mg/m <sup>2</sup> 24 hourly for 7days AND daunorubicin (IV) 60mg/m <sup>2</sup> 24hourly for 3 days
Consolidation phase	If in remission ie blast cells < 2% in bone marrow,  <b>S:</b> high dose cytarabine (HiDAC) (IV) regimen is used.
Transplant	<b>S:</b> Allogeneic hSCT is considered in some patients (high risk patients)
Relapsed AML	(FLAG-IDA) regimen is used in relapsed cases. This is followed by allogeneic hSCT if remission is achieved.  <b>S:</b> fludarabine (IV) 30mg/m <sup>2</sup> for 4 days, ANDhigh dose cytarabine (IV) 2g/m <sup>2</sup> for 4 days AND Filgastrim (SC) 300mcg/m <sup>2</sup> for 5days, AND idarubicin (IV) 10mg/m <sup>2</sup> for 3 days.
Palliative single-dose regimen	<b>S:</b> Low- dose cytarabine (SC) 20mg 12 hourly for 10 days. <b>OR</b> azacitidine (SC) 75mg/m <sup>2</sup> /day for 7 days. Repeat after every 4-6 weeks.

### Management of acute promyelocytic leukemia (APL)

It is a medical emergency. Treatment should be initiated as soon as diagnosis is suspected based on cytologic criteria, before definitive genetic, cytogenetic or immunostaining confirmation is made.

All -trans - retinoic acid (ATRA) is added in all three phases of APL treatment. There is a high risk of developing DIC and differentiation syndrome. Differentiation syndrome is treated with;

**S:** dexamethasone (IV) 10mg twice a day for 3 days or until symptoms resolve. Consider cessation of ATRA if symptoms are severe.

**Table 22.19 Treatment recommendations for APL**

Induction phase	<b>S:</b> ATRA (IV) 45mg/m <sup>2</sup> /day AND Arsenic trioxide (ATO) (IV) 0.15mg/kg/day daily until bone marrow remission. <b>OR</b> ATRA (IV) 45mg/m <sup>2</sup> /day AND daunorubicin (IV) 50mg/ m <sup>2</sup> for 4days PLUS/MINUS cytarabine (IV) 200mg/ m <sup>2</sup> for 7days cytarabine (IV) is added in patients with high risk of relapse.
Consolidation phase	<b>S:</b> ATRA AND ATO, <b>OR</b> ATRA AND daunorubicin <b>OR</b> ATO AND daunorubicin <b>OR</b> daunorubicin AND cytarabine
Maintanance phase	ATRA alone OR ATRA (IV) 45mg/m <sup>2</sup> /day orally for 15 days after every 3months PLUS 6-mecaptopurine (IV) 60mg/ m <sup>2</sup> orally once a day PLUS methotrexate (IV) 20mg/ m <sup>2</sup> orally once weekly. All given for 2 years.

### 22.9.2.2 Acute Lymphoblastic Leukemia (ALL)

**Treatment:** The treatment of ALL is complex. The recommended regimens are;

**S:** HYPER-CVAD/MTX-ARA-C Regimen (cyclophosphamide/mesna/vincristine/doxorubicin/dexamethasone/methotrexate/cytarabine/leucovorin) (IV)

### 22.9.2.3 Chronic Myeloid Leukemia (CML)

**Investigations:** similar to other leukemia, plus BCR-ABL1 analysis by PCR or FISH for Ph chromosome analysis

### Treatment

For BCR-ABL1 positive, first line treatment is Tyrosine kinase inhibitors (TKI)

**Chronic phase:** Characterized by blast cells < 10%.

**S:** imatinib (PO) 400mg once a day every day.

**Accelerated phase:** blasts 10 – 19%.

**S:** imatinib (PO) 600-800mg/day in 2 divided doses until chronic phase is reached. Thereafter continue with 400mg once a day daily.

**Blast crisis:** Blast cells > 20%. If the patient was not on TKIs, treat as in accelerated phase. If patient was on TKIs, treat as acute leukemia.

**S:** Second line TKIs include nilotinib, dasatinib, bosutinib and ponatinib (PO)

If BCR-ABL1 negative

**S:** hydroxyurea (PO) 40mg/kg daily. The dose ranges between 1mg and 3mg based on the WBC count.

### Note

- Adequate hydration should be maintained. Blood transfusion is indicated based on the degree of anaemia

**D:** allopurinol (PO) 300mg 24hourly daily to prevent hyperuricemia.

### 22.9.2.4 Chronic Lymphoid Leukemia (CLL)

**Staging:** Rai and Binet staging systems.

#### Treatment

**S:** chlorambucil (PO) 0.1mg/kg 24hourly for 2 weeks, then rest for 2 weeks, repeat until remission is achieved.

**OR**

**S:** Combination of Fludarabine, Cyclophosphamide and Rituximab (FCR) regimen (IV)

**B:** prednisolone (PO) 1mg/kg 24 once a day for 2 weeks is added if there is evidence of autoimmunity (autoimmune hemolytic anaemia or autoimmune thrombocytopenia)

### 22.9.3 Multiple myeloma

**Clinical features – CRAB:** Features of hypercalcemia, renal impairment, features of anaemia, bone pain, recurrent infections due to impaired antibody production, and bleeding tendencies and hyperviscosity syndrome in rare cases.

#### Investigations:

- FBC, RFT, LFT, Serum electrolytes
- Peripheral smear
- Bone marrow aspiration and trephine biopsy
- Serum protein electrophoresis, urine for Bence Jones protein
- Skeletal survey by X-ray, CT Scan or MRI
- Serum  $\beta_2$  microglobulin

**Staging:** Revised International Staging System (RISS) Adopted by the International Myeloma Working Group

**Treatment:** Radiotherapy is used for pain control of lytic lesions that are refractory to systemic therapy, treatment of spinal cord compression from plasmacytoma and primary treatment of solitary plasmacytoma. Supportive treatment with blood transfusion, antibiotic, hydration and analgesia when indicated.

## **Bisphosphonate therapy**

**S:** zoledronic acid (IV) 4mg once monthly for 2 years

Recommended chemotherapy regimens include the following drugs in various combinations:  
Melphalan, Thalidomide, Lenalidomide, Bortezomib, Cyclophosphamide, Prednisolone and Dexamethasone.

**S:** thalidomide (PO) 200mg 24hourly for 28days

**OR**

**S:** lenalidomide (PO) 25mg 24hourly for 21days,  
AND

**S:** dexamethasone (PO) 40mg 24hourly on day 1, 8, 15, 22, repeats after every 4 weeks.  
**OR**

**S:** bortezomib (IV) 1.3mg/m<sup>2</sup> 24hourly AND dexamethasone (PO) 40mg 24 hourly  
WITH/WITHOUT cyclophosphamide (PO) 300mg/m<sup>2</sup> all on day 1,8,15,22. Repeat every 4 weeks

## **22.10 Central Nervous System Malignancies**

### **22.10.1 Meningiomas**

Meningiomas are the second commonest tumors of the brain and constitute 20% of all intracranial tumors. Commonest sites are cerebral convexity, parasagittal and sphenoid ridge.

#### **Clinical presentation**

- Chronic headache
- Adult onset seizures
- Loss of vision
- Focal neurological deficits

#### **Investigations**

- FBP
- Serum electrolytes
- CT / Brain
- CT/MR angiography
- Histopathology studies

#### **Pharmacological management**

- Seizures: Give anticonvulsants.
- Brain edema: Give Dexamethasone

#### **Non-pharmacological management**

##### **Surgical management**

- Intracranial meningiomas are best managed with total excision following the principle of maximum safe excision (Refer to Simpson grading for intracranial meningiomas)
- Subtotal resection is associated with inferior outcome and higher regrowth rates.

##### **Radiotherapy**

- Radiotherapy is indicated in unresectable tumors, postoperative incomplete resection for WHO grade 1, and all grade 2/3 tumors.
- Meticulous attention to operative notes is required, as well as to postoperative CT/MRI.

##### **Follow up**

- Follow up CT Scan/ MRI every 6 months for 1 year, then annually.
- In older patients and small tumors managed conservatively, consider CT/MRI scan yearly.

## **22.10.2 Pituitary Tumors**

Pituitary tumors constitute 10% of intracranial tumors. Morbidity is often due to mass effect and endocrine consequences including hyper or hyposecretion of pituitary hormones.

### **Clinical presentation**

- Chronic headache
- Loss of vision
- Focal neurological deficits

### **Investigations**

- FBP, Serum electrolytes,
- Anterior pituitary hormones
- CT / MRI Brain
- CT/MR angiography
- Visual fields assessment
- Histopathology studies

### **Pharmacological management of functional tumors**

#### **Prolactinomas**

These should be treated initially with dopamine receptor agonist:

Give:

**D:** bromocriptine (PO) 2.5mg 8 hourly

**OR**

**S:** cabergoline (PO) 0.25mg once/twice a week (Titrate with prolactin levels checked 2 weekly, aim is to maintain PRL < 30ng/ml)

#### **Cushing's disease**

Surgical management is recommended. Consider medicines that inhibit adrenocortical function only when surgery is not possible: **S:** metyrapone 250mg once a day (can be escalated based on response)

#### **Acromegaly**

Somatostatin analogues may be used to treat acromegaly. Give **S:** octreotide SR

Efficacy is measured using clinical response defined as basal GH levels < 2.5 ng/ml, glucose-suppressed levels <1.5 ng/ml and normalization of serum IGF-1 levels.

### **Surgical management of pituitary tumors**

- This is the primary treatment for most pituitary tumors, except for prolactinomas which may be managed medically.
- Trans-sphenoidal approach (endoscopic or microsurgical) is preferred as it is safer and better tolerated.
- Frequently subtotal especially in large tumors or tumors invading into cavernous sinuses. Hypopituitarism occurs post-operative in about 12% of patients.

### **Radiotherapy**

Indicated post subtotal tumor resection, recurrent tumors, persistently elevated circulating hormone levels, and inoperable patients.

Follow up MRI 3 months after surgery to assess residual tumor.

Radiotherapy is very effective for control of growth of pituitary tumors (>95%), but less effective for decreasing circulating hormone levels in functional tumors.

### **Common complications**

**Diabetes Insipidus:** is characterized by excessive urine output due to lack of ADH, usually immediate post-operative. Consider

**D:** desmopressin (PO) 0.05mg 12 hourly daily (titrate based on response).

**SIADH** is characterized by decreased urine output and hyponatremia due to excessive ADH secretion, usually immediate post-operative. Manage hyponatremia and consider

**B:** furosemide (PO) 40mg

**CSW:** characterized by excessive urine sodium secretion and hyponatremia, usually immediate post-operative. Manage hyponatremia with Hypertonic 3% saline. Consider

**D:** fludrocortisone (PO) 0.05-0.1mg 12hourly daily.

#### Follow up

- There is significant risk of pituitary hypofunction after surgery or irradiation and this risk may occur up to 15 years later – the patients should be warned of the symptoms and be tested regularly.
- Patients treated with standard radiotherapy are unlikely to show an early response and would therefore be assessed at 12 monthly intervals in terms of hormone levels and pituitary function.

### 22.10.3 Gliomas

Gliomas constitute the most common tumors of the brain affecting all age groups, with predilection to the adult population.

#### 22.10.3.1 Low grade Gliomas (LGGs)

##### Clinical presentation

- Seizures are common
- progressive neurologic symptoms depending on site of tumor

##### Imaging

- CT or MRI should be done in diagnosis of Gliomas.
- MR spectroscopy
- Diffusion tensor tractography (DTI)

##### Pharmacological management

##### Seizures:

##### Surgical management

Long term survival approaches 100% with complete removal. After partial resection, survival rates range from 80-90% at 5 years to 70-80% at 10 years and 50-60 % at 20 years.

Repeat the scans at 6, 12, 24 months to check for growth. If this is surgically resectable then repeat surgery should be attempted.

##### Radiotherapy

- Dose for low grade gliomas: 1.8 Gy X 28 Fractions = 50.4 Gy (5 times per week). Concurrent and adjuvant use of Temozolomide is indicated if available,
- **S:** temozolomide (PO) 75mg/m<sup>2</sup> daily during RT and 150-200mg/m<sup>2</sup> day 1-5 Monthly for 6 months.
- If the hypothalamus /pituitary are in the RT field, then endocrine function should also be evaluated annually by T4 & TSH, testosterone or FSH/LH.

#### Follow up

- CT scan immediate postoperative to assess resection.
- MRI recommended at 3months and then annually unless other clinical indications emergency.

#### 22.10.3.2 High Grade Gliomas (HGGs)

##### Anaplastic Astrocytoma (AA) and Glioblastoma Multiforme (GBM)

##### Clinical presentation

seizures, progressive neurologic symptoms depending on site of tumor features of mass effect, or focal signs depending on location.

## **Investigations**

- FBP, Serum electrolytes,
- Histopathology studies
- Immunohistochemistry studies: IDH, 1p/19q codeletion, ATRX mutations.

## **Imaging**

- CT brain scan
- MRI preferred investigation
- MR spectroscopy
- CT/MR angiography
- Functional MRI (fMRI)

## **Pharmacological management**

**Seizures:** Treat as per guidelines

## **Surgical management**

- Complete excision of the tumor is essential for improved survival. Preoperative and intraoperative techniques to improve extent of resection in a safe manner (maximum safe resection) including brain mapping, use of intraoperative fluorescein guidance to expand resection margins and neuromonitoring techniques are advocated.
- Extent of resection is best assessed on post-op CT/MRI scans.

## **Radiotherapy**

- Patients should be CT-planned, with contrast administration. 3mm to 5mm slices cuts from Vertex to Base of skull. Large volume PTV = should completely encompass enhancing lesion seen on pre-op T2/FLAIR scan, plus small (2cm) margin.
- Dose to LARGE VOLUME = 2.00 Gy X 23 Fractions = 46.00 Gy (5 times per week).
- Small volume PTV (PTV2) is based on Gd-enhanced T1 weighted image= enhancing lesion on pre-op scans +1- 2 cm margin.
- Dose to SMALL VOLUME = 2.00 Gy X 7 Fractions = 14.00 Gy
- Total dose 60Gy in 30 fractions.
- Other alternative radiotherapy fractionations can be used in elderly, more than 65 years of age are Hypo fractionation; 40Gy/ 15 Fractions and 5Gy X 5 Fractions

### **Note**

- Imaging techniques such as MR Spectroscopy may be indicated during follow up to distinguish tumor recurrence from post RT changes.

## **Chemotherapy**

Concurrent chemotherapy + RT:

**S:** temozolomide (PO) 75 mg/m<sup>2</sup> daily during RT, Then 150-200mg/m<sup>2</sup> given D1-D5 of a 28 day cycle for 6 cycles after RT

Oral steroid/ Ondansetron should be taken half an hour prior to chemotherapy tablet on each day. Tablets must be taken 1st thing in the morning on an empty stomach.

Prophylaxis for PCP pneumonia with co-trimoxazole (one tablet twice daily) should be given during daily temozolomide treatment.

## **Recurrent disease**

- Surgery plays an important role in selected patients- relieves symptoms, improves PS and QOL and reduces steroid requirement.
- Repeat radiotherapy can be considered, depending on size of lesion and previous dose.
- Palliation Chemotherapy may be only modality available- active regimens are BCNU, PCV, Temozolomide and more recently, Irinotecan and Bevacizumab.

## **Follow up**

- A baseline scan should be done at 4 months' post RT as a reference.
- Thereafter scans are usually done at 6 months and annually, or if clinically indicated.
- High index of suspicion and testing if indicated for pituitary function.

## 22.11 Oncological Emergencies

Important oncological emergencies include Hypercalcemia, Superior venous cava obstruction, Spinal cord compression and Neutropenic sepsis.

### 22.11.1 Superior Vena Cava Syndrome (SVCS)

Superior vena cava syndrome (SVCS) is the clinical expression for obstruction of blood flow through the SVC. Malignancy (90%) is the most frequent cause of SVC obstruction. SVC obstruction is a strong predictor of poor prognosis in patients with non-small cell lung cancer. SVC obstruction in cancer patients can result from

- Extrinsic compression of SVC
  - Lung Cancer (65%)
  - Lymphomas (15%)
  - Other cancers (10%)
- Intrinsic compression

#### Diagnostic Criteria

Common symptoms and physical findings of SVCS are:

- Dyspnea
- Headache
- Oedema and change in colour in the areas drained by SVC (examples—face and upper limb)
- Venous distension of neck, upper chest and arms
- Cough
- Pemberton's sign (development of facial flushing, distended neck and head superficial veins, inspiratory stridor and elevation of the jugular venous pressure (JVP) upon raising both of the patient's arms above his/her head simultaneously, as high as possible (Pemberton's maneuver))

#### Investigations:

- CXR
- CT scan Chest Abdomen and Pelvis
- PET/CT
- Tissue diagnosis for appropriate treatment modality
- Bronchoscopy
- Needle aspiration of a peripheral lymph node, or mediastinoscopy
- Sputum cytology
- Thoracentesis.

**Non-pharmacological treatment:** Treatment of SVC syndrome is divided into supportive and definitive therapy

#### Supportive measures

- Head elevation—To decrease the hydrostatic pressure and thereby the edema. There are no data documenting the effectiveness of this manoeuvre, but it is simple and without risk.
- Glucocorticoid therapy (dexamethasone, 4 mg every 6 hours) to relieve inflammation and oedema (to be avoided before biopsy if lymphoma is suspected as steroid induced tissue necrosis might obscure the diagnosis)
- Loop diuretics (furosemide) are also commonly used, but it is unclear whether venous pressure distal to the obstruction is affected by small changes in right atrial pressure.

#### Definitive Therapy

- Radiation treatment to the malignant mass.
- Chemotherapy—in chemo sensitive cancers like lymphoma, germ cell tumours or small cell lung cancer
- SVC Stent—can be useful in cases of thrombosis and for patients not responding to cancer treatment
- Removal of central venous device.

#### Note

- It is advisable to avoid placement of intravenous lines in the arms so that fluid is not injected into the already compressed SVC.

## 22.11.2 Hypercalcaemia

Hypercalcaemia refers to elevated calcium level in blood (normal range 2.2–2.6 mmol/L) that occurs in 10–20% patients with advanced cancers (most commonly in cancer of the breast, kidney, lung, prostate, head and neck and multiple myeloma)

### Diagnostic Criteria

- Symptoms of hypercalcaemia include nausea, vomiting, constipation, polyuria and disorientation
- Psychiatric overtones (depression 30–40%, anxiety, cognitive dysfunction, insomnia, coma)
- Clinical evidence of volume contraction secondary to progressive dehydration may be apparent. Severe hypercalcaemia (above 3.75–4.0 mmol/L) is a medical emergency and a poor prognostic sign

### Investigations include

- Specific biochemistry like PTH,
- ECG to detect arrhythmias and
- Imaging with Bone Scan or PET–CT scan to identify metastatic bone disease.

### Pharmacological Treatment

Treat the hypercalcaemia first and the cause later:

- Hydration & diuresis: 1–2 litres of isotonic saline (NS) over 2 hours with 30–40 mg of furosemide expands intravascular volume and enhances calcium excretion.
  - In elderly and cardiac patients, rate of hydration needs to be slower.
- Bisphosphonates—via a complex mechanism inhibit osteoclast and in turn both normal and pathological bone resorption. Commonly used bisphosphonates are:
  - S: zoledronic acid (IV) infused as 4mg (IV) in 100 mls of NS over 15 mins. Normalisation of serum calcium occurs in 4–10 days and lasts 4–6 weeks. Therefore, if re-treatment is required, dose is repeated after 7 days

**OR**

**S:** ibandronate (IV) 6 mg over 2 hours infusion

### Note

- Bisphosphonates and denosumab cause increasing risk of osteonecrosis of jaw following extraction of teeth or oral surgical procedures. Therefore, a dental review may be necessary to make sure the necessary dental procedures are completed prior to commencing therapy
- Calcitonin – a thyroid hormone given 4–8 IU/kg IM or SC every 6–8 hours can bring about a rapid decline in calcium levels, however tachyphylaxis limits its utility.

## 22.11.3 Spinal-cord Compression

Spinal cord compression threatens mobility, independence and longevity in patients with metastatic cancer and may be the first presentation of curable malignancy in others. It most commonly occurs due to an enlarging vertebral metastasis encroaching on the epidural space or due to pathologic fracture of a vertebra infiltrated by malignancy.

### Management

- Immobilising the patient and obtaining urgent MRI/CT whole spine should be priorities.
  - Corticosteroids should be initiated on suspicion of cord compression.
- B:** dexamethasone (IV) 16 mg immediately followed by 16 mg daily in divided doses.
- Bladder catheterisation is appropriate.
  - Once spinal cord compression is confirmed, urgent neurosurgical opinion should be sought. There are potential improvements in outcomes for patients treated with surgery upfront, though appropriateness for this will depend upon spinal stability, patient and malignancy related factors.
  - Radiotherapy: for patients who are not candidates for upfront surgery.
  - Palliative dose: 8Gy Single fraction or 20Gy/5Fractions or 30Gy/10 Fractions.

**Note**

- All patients suspicious for spinal cord compression should be referred to neurosurgeon and radiation oncologist as soon as possible.

### 22.11.4 Tumor Lysis Syndrome

The syndrome is mostly observed in cancers with a rapid proliferation index such as Burkitt's lymphoma, acute lymphocytic leukemia, acute non-lymphocytic leukemia, and less frequently, solid tumors of small-cell type, breast cancer, and medulloblastoma.

#### Clinical Presentation

Clinically, the syndrome is characterized metabolically by the presence of hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia and acute renal failure.

- Work Up
- FBP, RFT, LFT, LDH
- Serum electrolytes phosphates and calcium
- Urine pH and output
- ECG.
- CXR
- CT-Scan.
- Abdomen and Pelvis USS

#### Treatment

- Frequent monitoring of electrolytes such as blood-urea-nitrogen (BUN), creatinine, uric acid, potassium, sodium, phosphate, calcium levels and Lactate dehydrogenase (LDH) at least three times per day
- Also Alkalization of urine by Sodium bicarbonate added to IV fluids at 100 mEq/L this should continue for 48-72 hours after start of chemotherapy.
- Hydration in high risk patients must start 12-48 hours' prior the start of chemotherapy and continue 48- 72 hours post chemotherapy; continuous infusion should exceed 3 L/m<sup>2</sup> daily, resulting in urine volumes of at least 3L/Day.
- IV Allopurinol 300 mg/day daily
- Patients with high potassium levels must be evaluated and monitored constantly for cardiac rhythm disorders, do administer calcium and exchange resins, those with continuously low levels calcium a calcitriol must be given.
- Empiric antibiotics can be administered for opportunistic infections, consider also parenteral nutrition (TPN) and GCF (neupogen) if indicated.

### 20.11.5 Febrile Neutropenia

Applied only to the management of patients with:

- Fever and neutropenia as a result of a known or suspected malignancy or the use of chemotherapy
- Fever and neutropenia as a result of a bone marrow failure syndrome.
- Fever (or evidence of infection) who are receiving chemotherapy or who have completed cancer therapy within 6 months even though they are not neutropenic.

#### Work up

- FBP, LFT, RFT
- Malaria screen
- Urine analysis Urine / blood / stool culture Serum Electrolytes Throat Swab

#### Treatment

- Antibiotic administration
- Anti pyretics and analgesics

Initial (first-line) and subsequent (second-line – deteriorating patients) empiric antibiotic selection.

Patients with no significant betalactam reactions:

**D:** piperacillin+tazobactam (FDC) (IV) 4 g piperacillin / 0.5 g tazobactam given every IV 6 hourly PLUS Gentamicin 3-6mg/kg once daily. Deteriorating patients on first line treatment with no history of anaphylaxis to Beta Lactams (i.e. if history of rash only, can still use meropenem

**OR**

**D:** meropenem (IV) 500mg 8 hourly **AND** amikacin (IV) 15mg/kg/dose in 2-3 divided dose (or ciprofloxacin 200– 400 mg IV 12 hourly) **AND** vancomycin 15 - 20mg/kg/dose 8 - 12 hourly

Patients with history of definite anaphylaxis to Beta Lactams

**D:** ciprofloxacin (IV) as above **AND** metronidazole (IV) 500mg – 750mg dose 8 hourly **AND** amikacin dose as above **AND** vancomycin dose as above

Culture Negative Patients

First 48 hours

- Patient had a single spike of fever (i.e. patient's temperature returns to normal within 4 hours of the initial fever), antibiotics may be discontinued.
- Patient had more than a single spike of fever, antibiotics must be continued for a minimum of 7 afebrile days. Also consider the following.
  - If patient develops oral herpes or severe mucositis, commence IV Aciclovir.
  - Obvious fungal infection – suspect candida – add fluconazole IV; suspect other fungal infection – add Amphotericin B IV.
  - Diarrhoea and vomiting – culture stool and commence ciprofloxacin and metronidazole
  - Signs of skin infection – add vancomycin
  - No clinical focus but deteriorating rapidly or extremely unwell – consider adding vancomycin

If by day 5-7 patient remains febrile, neutropenic, consider performing a fungal work-up, prior to commencing empiric appropriate antifungal treatment.

# **CHAPTER TWENTY-THREE**

## **MENTAL HEALTH CONDITIONS**

### **23.1. Patients with Aggressive and Disruptive Behaviours**

These are agitated and acutely disturbed patients, who may or may not have a mental disorder. Many acute medical conditions, trauma, toxicological conditions and substance related disorders (especially substance induced disorders) can also present with agitation.

#### **Clinical Presentation**

- Agitation
- Aggressive behaviours

#### **Non-Pharmacological Treatment**

- Ensure the safety of the patient and those caring for them.
- Caution is needed with elderly and frail patients as they are vulnerable to falls and further injury if sedated.
- The use of physical restraint should only be employed when there is a need to protect the patient and surrounding people in an acute setting and it should be for as short time as possible with a constant monitoring of patients' safety
- Assess for signs of delirium.

#### **De-escalation Techniques should be attempted first:**

- Calm the patient
- Manage in a safe environment
- Ensure the safety of all staff members

#### **Pharmacological Treatments**

##### **For cooperative patients**

**A:** promethazine (PO) 25-50mg **stat**

**OR**

**C:** diazepam (PO) 10 mg **stat**

**OR**

**C:** lorazepam PO) 4 mg **stat**

##### **Uncooperative and severely agitated patients**

If oral treatment fails after 30–60 minutes, OR If there is significant risk to the patient and others, give

##### **Parenteral treatment as follows:**

**B:** haloperidol (IM) 2.5-5mg stat, repeat in 30-60minutes, if required. (Maximum dose: 20mg, within 24hours)

**AND**

**A:** diazepam (IV/IM) 10mg stat. Repeat after 30–60minutes if needed. (maximum dose: 60mg per 24hours)

**OR**

**A:** promethazine (deep IM) 25–50mg Repeat after 30–60minutes if needed

**OR**

**C:** lorazepam (IM) 1-4mg stat. Repeat after 30–60minutes if needed to a maximum dose of 12mg in 24hours

**OR**

**D:** midazolam (IV/IM) 2-10mg stat

If haloperidol is unavailable,

**A:** chlorpromazine (deep IM) 25–50mg may be repeated as necessary 4 times in 24hours (Maximum dose: 2000mg per 24hours).

If patient is known to suffer from schizophrenia and is not neuroleptic naïve give:

**S:** zuclopentixol acetate (IM) 50–150 mg (Repeat after 2–3 days, if necessary). Give a maximum of 3 repeat injections and should not be used for longer than 2 weeks. The maximum administered dose should not exceed 400mg.

If patient develops acute dystonia give:

**A:** promethazine (deep IM) 25–50 mg. In the elderly 25 mg.

**OR**

**A:** atropine (IM) 0.5 -2 mg when required

**Note**

- Repeated doses of high potency antipsychotics may lead to the development of the life-threatening neuroleptic malignant syndrome. If suspected, stop antipsychotic, and institute supportive care.
- Elderly patients are at increased risk of respiratory depression and delirium from benzodiazepines, so they should be avoided as far as possible.
- Always monitor vital signs of sedated patients

## 23.2. Delirium

Delirium or acute confusion state is a condition characterized by altered level of consciousness, disorientation to time, place and sometimes to person.

### Clinical presentation

- Reduced awareness of the environment
  - Inability to stay focused on a topic or to switch topics
  - Getting stuck on an idea rather than responding to questions or conversation
  - Being easily distracted by unimportant things
  - Being withdrawn, with little or no activity or little response to the environment
- Poor thinking skills (cognitive impairment)
  - Poor memory, particularly of recent events
  - Disorientation — for example, not knowing where you are or who you are
  - Difficulty speaking or recalling words
  - Rambling or nonsense speech
  - Trouble understanding speech
  - Difficulty reading or writing
- Behavioral changes
  - Seeing things that don't exist (hallucinations)
  - Restlessness, agitation or combative behavior
  - Calling out, moaning or making other sounds
  - Being quiet and withdrawn — especially in older adults
  - Slowed movement or lethargy
  - Disturbed sleep habits
  - Reversal of night-day sleep-wake cycle
- Emotional disturbances
  - Anxiety, fear or paranoia
  - Depression
  - Irritability or anger
  - A sense of feeling elated (euphoria)
  - Apathy
  - Rapid and unpredictable mood shifts
  - Personality changes

### Non-Pharmacological Treatment

- Control the acute disturbance.
- Perform proper physical assessment as well as investigations in order to rule out or ascertain the underlying medical condition and treat accordingly

### Pharmacological Treatment

Treat the underlying medical condition, if present. And any other presentations, symptomatically

### Acute Management

**B:** haloperidol (IM) 5mg stat repeated in 30-60 minutes when required (Maximum dose: 20mg within 24 hours)

- Monitor vital signs and beware of acute dystonia and neuroleptic malignant syndrome
- Dosing may vary according to clinical circumstances

**AND/OR**

**A:** diazepam (IV) 10mg.

**OR**

**C:** lorazepam (IM) 1-4mg.

Switch to oral route once containment is achieved.

**Note**

- Benzodiazepines, especially diazepam IV, can cause respiratory depression. Monitor patients closely
- In the frail and elderly patient or where respiratory depression is a concern, reduce the dose by half
- The safest route of administration is oral followed by IM with the IV route having the highest risk of respiratory depression and arrest. Use the safest route wherever possible.
- Monitor vital signs closely during and after administration
- Use haloperidol instead of benzodiazepines in patients with respiratory insufficiency
- To avoid benzodiazepines toxicity, allow at least 15-30 minutes before repeating the IM dose

### 23. 3. Dementia

It is a condition which involves progressive and cognitive deficits. Dementia usually affects memory first, with subsequent progression to cause dysphasia, agnosia, apraxia, diminished ability with executive function and eventually personality disintegration.

**DSM-5 diagnostic criteria**

To diagnose Dementia, the following criteria need to be met:

- There must be significant cognitive decline from a previous level of performance in one or more of the following cognitive domains - attention, executive function, learning and memory, language, perceptual motor and social cognition.
- These deficits affect independence in performing everyday activities.

**Non-pharmacological Treatment**

- Psychoeducation about the disorder, to the patient and family
- Mini Mental Status Examination, functional and behavioural assessment should be performed every 6 months.

**Pharmacological Treatment**

**Mild to moderate:**

**S:** donepezil (PO) 5mg initially, may increase to 10mg/24hours after 4-6weeks

**Moderate to severe:**

**S:** donepezil (PO) 5mg initially, may increase to 10mg /24hours after 4-6weeks; may further increase to 23 mg/day after 3 months

### 23.4. Schizophrenia

It is a chronic mental disorder, characterized by disturbances in thought, emotions, drive, behaviour and withdrawal from reality. Symptoms vary from patient to patient and from time to time.

**DSM-5 Diagnostic Criteria**

To diagnose Schizophrenia, the following criteria need to be met:

- Presence of 2 or more of the following symptoms over a 1-month period:
  - a. Delusions
  - b. Hallucinations
  - c. Disorganized speech
  - d. Disorganized behavior
  - e. Negative symptoms

(at least 1 of which must be a, b or c)

- Individual's premorbid level of functioning is affected in several major domains of life.

- There must be continuous impairment over a period of at least 6 months, during which the individual might experience either active or residual symptoms.
- These symptoms must not be due to the effects of substance usage or an underlying medical condition

### **Non-Pharmacological Treatment**

- Family counselling and psycho-education
- Cognitive Behavioural Therapy (CBT) for stabilized patients
- Supportive group therapy for patients with schizophrenia
- Rehabilitation may be enhanced by assertive community programs, work assessment, occupational therapy and bridging programs prior return to the community

### **Pharmacological Treatment**

#### **In acute attacks:**

Treat like under section: patients with aggressive and disruptive behaviours.

#### **For maintenance:**

**B:** haloperidol (PO) 3-4.5mg 12hourly,

**OR**

**A:** chlorpromazine (PO) 100–600mg 24hourly in divided doses

**OR**

**S:** olanzapine (PO) 5–10mg titrate to maximum dose 20mg/24hours

**OR**

**S:** risperidone (PO) 1mg 12hourly then increase by 1mg every 2–3 days to 2–3mg 12 hourly. Maximum dose 16mg/day

#### **Note:**

- Titrate to maximum dose while monitoring dose-response to target symptoms against adverse effect
- The above medicines should not be given in combination
- The atypical antipsychotics have been shown to be comparatively more effective in treatment of negative symptoms

#### **For patients who have poor compliance to oral medications and patient preference, give depot antipsychotics**

**C:** fluphenazine decanoate (IM) 6.25-50mg 2-4weekly, and monitor dose-response to target symptomsagainst adverse effect, if necessary, dose may be tapered

**OR**

**S:** zuclopentixol decanoate (IM) 100-600mg 2-4weekly, and monitor dose-response to target symptomsagainst adverse effect, if necessary, dose may be tapered

**OR**

**S:** flupenthixol decanoate (IM) 20–40 mg every 4weeks, and monitor dose-response to target symptomsagainst adverse effect, if necessary, dose may be tapered

#### **Note**

- Give a test dose first. This is in view of the fact that depots are known to be long acting
- Giving a test dose helps to determine whether the patient is sensitive to the medication (either via development of EPSE or any adverse reactions to the oil base)
- Commence treatment with the lowest therapeutic dose
- Administer the depot at the longest possible duration
- adjustment of dosages should be conducted after an adequate period of assessment

### **Adjunct Treatment**

Antiparkinsonian medicines should only be used if extrapyramidal side effects(except tardive dyskinesia) occur, or at higher doses of antipsychotics likely to cause extrapyramidal side effects. Any of the following can be used:

**A:** promethazine (PO) 25-50mg 24hourly, until symptoms/signs subside

**OR**

**A:** benzhexol (PO) 5mg 24hourly to12hourly, last dose before 1400 hourstoavoidinsomnia

## **Referral**

Refer to the next level in the following situations:

- First psychotic episode
- High suicidal risk or risk of harm to others
- Children and adolescents
- Elders
- Pregnant and lactating women
- No response to treatment
- Intolerance to medications
- Concurrent medical conditions or other mental disorders

## **23.5. Catatonia**

**Causes of catatonia:** schizophrenia, severe depressive disorder, bipolar disorder, organic disorders e.g. CNS infections, CNS tumour, cerebrovascular accident, severe intoxication of recreational drugs and lethal catatonia.

**Clinical features:** Ambitendency, automatic obedience, waxy flexibility / catalepsy, negativism, stereotypy, mannerism, echolalia and echopraxia.

**Investigations:** FBP, RFT, LFT, TFT, blood glucose, CK, urine drug screen, ECG, CT, MRI, EEG, urine and blood culture, syphilis screen, HIV, heavy metal screen, auto-antibody screen and lumbar puncture.

### **Non-pharmacological treatment**

Hydration, early mobilization, close monitoring, transferal to ICU if patient deteriorates.

### **Pharmacological treatment**

**A:** diazepam (IV/IM) 10-20mg 24hourly

**OR**

**C:** lorazepam (IM) 1-4mg 24hourly

#### **Note**

- If benzodiazepine does not work and symptoms are severe, ECT is an option

## **23.6. Schizoaffective Disorder**

### **DSM-5 Diagnostic criteria**

For an individual to fulfill the diagnostic criteria, there must be the presence of solely hallucinations or delusions for at least 2 weeks in the absence of an affective episode, throughout the whole duration of the psychiatric illness. There must also have an uninterrupted period where there are prominent affective symptoms concurrent with symptoms of schizophrenia. Individuals should have symptoms fulfilling the diagnosis of an affective disorder for most of the duration of the illness.

DSM-5 has specified 2 subtypes of schizoaffective disorder, which are:

- Bipolar type - Whereby a manic episode is part of the entire course of the illness
- Depressive type - Whereby a major depressive episode is part of the entire course of the illness

### **Non-Pharmacological Treatment**

- Family counselling and psycho-education
- Cognitive Behavioural Therapy (CBT) for stabilized patients
- Supportive group therapy for patients
- Rehabilitation may be enhanced by assertive community programs, work assessment, occupational therapy and bridging programmes prior return to the community

### **Pharmacological Treatment**

#### **For Psychotic symptoms:**

**A:** chlorpromazine (PO) 100-1000mg in divided doses\*, per day (max. dose 1000mg, per 24hours)

**OR**

**B:** haloperidol, (PO) 1.5-6mg in divided doses\*, per day (max. dose 20mg)

**For Manic subtype:**

A: carbamazepine (PO) 200-1000mg 24hourly, in divided dose\*

OR

C: sodium Valproate (PO) 500-1000mg 24hourly, in divided dose\*

**For Depressive subtype:**

A: amitriptyline (PO) 12.5-75 mg nocte

OR

S: fluoxetine (PO) 10-20 mg nocte

**Note**

- Symptoms should be monitored and medication can be tapered\* divided doses: **in acute phase** 8hourly or 12hourly while **in maintenance phase** titrate to 12hourly or preferably 24hourly

## 23.7. Brief or Acute/Transient Psychotic Disorder

**DSM-5 Diagnostic criteria**

For an individual to fulfill this diagnosis;

- He/she must have, for a duration of between 1 day to 1 month the following symptoms:
  - Delusions
  - Hallucinations
  - Disorganized speech
  - Grossly disorganized or catatonic behaviour
- Exclude differentials like major depression or bipolar depression with psychotic features, schizophrenia and exclude the possibility of the symptoms being due to underlying substance use or medical conditions.

**Non-pharmacological Treatment**

Manage as Schizophrenia

**Pharmacological Treatment**

Manage as Schizophrenia

## 23.8. Bipolar Mood Disorders

These are lifelong mental disorders, which may have an episodic, variable courses. The presenting episodes may be manic, hypo manic, depressive or mixed. By definition, a diagnosis of bipolar disorders requires either a current or previous episode of mania or hypomania.

**Bipolar I Disorder Diagnostic Criteria**

DSM-5 specified that an individual need to have at least 1 manic episode in order to fulfill the diagnostic criteria of Bipolar I disorder.

**Manic Episode**

A manic episode is characterized by a period of time, of at least 1 week, during which the individual has persistent elevated (extreme happiness) or irritable mood and present for most of the days.

In addition, the individual needs to have at least 3 (4 if mood is only irritable) of the following symptoms:

- Increased self-confidence(Grandiose and/or religious delusions)
- Reduction in the need for sleep
- Chattier than usual, with increased pressure to talk
- Racing thoughts
- Easily distractible
- Increase in number of activities engaged
- Involvement in activities that might have a potential for serious consequences

There must be marked impairments in terms of functioning with the onset of the above symptomatology.

## **Non-Pharmacological Treatment**

- Hospitalization may be required during acute mania
- Psychotherapy, usually after the manic episode has been controlled with medication
- Family therapy and psycho-education of patient and family to increase compliance and knowledge of the condition
- In severe cases, electroconvulsive therapy may be required.

## **Pharmacological Treatment**

### **For Manic or Mixed Episodes**

For agitated and acutely disturbed patient: See section on patients with aggressive and disruptive behaviours.

### **Maintenance therapy**

**A:** carbamazepine (PO) 600mg 24hourly in 2-3 divided doses, increase by 200mg at three-day interval up to a maximum of 2000mg

**OR**

**C:** sodium valproate (PO) 20 mg/kg/day in 2–3 divided doses (maximum of 2000 mg, per day)

**OR**

**S:** lamotrigine (PO) 600mg once a day, increase by 200mg at three-day interval up to a maximum of 2000mg

### **Note**

- The option of combining two mood stabilizers at S: level should be allowed i.e. sodium valproate and Lithium carbonate

## **Treatment for Severe Depressive Episodes in Bipolar Patients**

Give antidepressant in combination with mood stabilizer and antipsychotic if there is psychosis:

**A:** amitriptyline (PO) 12.5 to 50mg nocte

**OR**

**S:** fluoxetine (PO) 10-20mg nocte,

**AND**

**A:** carbamazepine (PO) 200-400mg 12hourly, maximum 2000mg/per day

**OR**

**C:** sodium valproate (PO) 500-2000mg 24hourly

**AND**

**A:** chlorpromazine (PO) 100-1000mg 24hourly in divided doses, (max. dose 1000mg, per day)

**OR**

**B:** haloperidol (PO) 1.5mg –10mg 12hourly (if there is psychosis) and symptoms should be monitored, and medication to be tapered

### **Note**

Do not use monotherapy antidepressants in bipolar patients.

## **Referral**

Refer to the next level in the following situations:

- Mixed or rapid cycling bipolar disorder
- Depressive episodes in bipolar patients not responding to treatment
- Manic episodes not responding to treatment

## **23.9. Major Depressive Disorder**

It is a mood disorder characterized by at least 2 weeks of depressed mood and/or diminished interest and pleasure in activities. It is associated with impairment in level of functioning in different areas including social and occupational.

### **Diagnostic Criteria**

#### **Psychological symptoms**

- Depressed mood
- Feeling of worthlessness

- Guilt
- Diminished concentration
- Thoughts of death and suicide

### **Somatic symptoms**

- Change in appetite
- Sleep disturbances
- Agitation
- Retardation
- Loss of energy

### **Non-Pharmacological Treatment**

Effective psychotherapies include:

- Cognitive Behavioural Therapy
- Interpersonal psychotherapy
- Stress management / coping skills
- Marital and family issues
- Sleep hygiene advice

### **Pharmacological Treatment**

**A:** amitriptyline (PO) 12.5–75mg 24hourly at night, increase gradually to a maximum of 150mg 24hourly. {Elderly: Initially 12.5–50 mg. Max. 75mg)

**OR**

**D:** citalopram (PO) 10-60mg 24hourly

**OR**

**S:** fluoxetine (PO) 20-60mg 24hourly (morning)

#### **Note**

- Efficacy of the treatment is gauged by amelioration of symptoms and the dose should be titrated according to clinical response.
- Monitor all patients recently started on antidepressants closely for increased agitation and suicidal behaviour, especially young patients (younger than 25 years).
- Some symptoms, such as sleep and appetite, may improve more quickly.
- If partial response or non-response, increase the dose or switch to another antidepressant. The first line is an alternative SSRI. The second line is an antidepressant from a different class.

### **Referral**

Refer to the next level in the following situations:

- Suicidal ideation
- Major depression with psychotic features
- Failure to respond to available antidepressants
- Patients with concomitant medical illness, e.g. heart disease, epilepsy
- Poor social support systems
- Pregnancy and lactation

### **23.10. Suicide**

Suicide is the act of intentionally causing one's own death. Mental disorders—including depression, bipolar disorder, autism spectrum disorders, schizophrenia, personality disorders, anxiety disorders, physical disorders such as chronic fatigue syndrome, and substance abuse—including alcoholism and the use of and withdrawal from benzodiazepines—are risk factors. Some suicides are impulsive acts due to stress (such as from financial or academic difficulties), relationship problems (such as breakups or deaths of close ones), or harassment/bullying. Those who have previously attempted suicide are at a higher risk for future attempts.

Effective suicide prevention efforts include;

- Limiting access to methods of suicide—such as hanging, firearms, drugs, and poisons
- Treating mental disorders and substance misuse
- Careful media reporting about suicide
- Improving economic conditions.

### **23.11. Generalized Anxiety Disorder**

Generalized anxiety disorder is characterized by excessive, exaggerated anxiety and worry about everyday life events with no obvious reasons for worry.

## **Diagnostic Criteria**

Symptoms include

- Persistent worry
- Disturbances in sleep
- Poor concentration
- Mood disturbances
- Muscle tension
- Tremors

## **Non-pharmacological Treatment**

- Psychotherapy
- Most patients can be treated as outpatients

## **Pharmacological Treatment**

Indicated where symptoms are interfering with normal functions of daily living. Where there is concomitant drug/alcohol dependence or co-morbid major depressive episode, an antidepressant may be more appropriate.

### **Acute management**

For an acute episode or intense prolonged anxiety:

**A:** diazepam (PO) 2–5 mg stat repeat 12hourly when required

- Duration of therapy: up to 2weeks, taper off to zero within 6weeks

### **Maintenance Therapy**

**A:** amitriptyline (PO) 25–75mg nocte (Medication should be titrated according to symptoms resolution)

**OR**

**D:** citalopram (PO) 10–40mg 24hourly (Medication should be titrated according to symptoms resolution)

**OR**

**D:** clonazepam (PO) 0.5 – 4 mg 24hourly (Medication should be titrated according to symptoms resolution)

**OR**

**S:** fluoxetine (PO) 20–40mg 24hourly (Medication should be titrated according to symptoms resolution)

### **Note:**

- Prolonged treatment with benzodiazepines often leads to tolerance and withdrawal symptoms if the medicine is discontinued abruptly
- Avoid combining more than one benzodiazepine.

## **Referral**

Refer to the next level if there is lack of improvement with treatment.

## **23.12. Panic Disorder**

Panic disorder is an anxiety disorder characterized by recurrent unexpected panic attacks. A panic attack is characterized by an acute onset of intense anxiety accompanied by a sense of dread/impending threat, usually for no apparent reason.

## **Diagnostic Criteria**

The patient will experience significant fear and emotional discomfort, typically peaking within 10 minutes and resolving within 30 minutes. There will usually be accompanying physical symptoms including:

- Rapid pulse/palpitations
- Shortness of breath
- Dizziness
- Sweating

## **Non-Pharmacological Management**

- Psycho-education and reassurance
- Psychotherapy, e.g. cognitive-behaviour therapy
- Exclude an underlying medical condition, e.g. thyrotoxicosis

## **Pharmacological Treatment**

### **Panic attack**

#### **Acute management**

The initial aim is to control the panic symptoms and exclude an underlying medical cause.

**A:** diazepam (PO) 5-10mg 12hourly (Medication should be titrated according to symptoms resolution)

**OR**

**C:** lorazepam (PO) 2-4mg 12hourly (Medication should be titrated according to symptoms resolution)

**OR**

**D:** clonazepam (PO) 0.5-3mg 12hourly (Medication should be titrated according to symptoms resolution)

### **Panic disorder**

**A:** amitriptyline 25–75mg (PO) nocte (Medication should be titrated according to symptoms resolution)

**OR**

**D:** citalopram 10–40mg (PO) 24hourly (Medication should be titrated according to symptoms resolution)

**OR**

**S:** fluoxetine 20–40mg (PO) 24hourly (Medication should be titrated according to symptoms resolution)

#### **Note**

- Initiate at low dose and gradually titrate to therapeutic dosages according to tolerability.
- Duration of therapy: variable, initially 6 months–1 year.
- Long term medicine treatment may be necessary.
- Relapses may occur when treatment is discontinued.
- Consider short term co-administration of a benzodiazepine, due to the slow onset of action and the potential for increased anxiety during the initial phase of treatment with antidepressants.

### **Referral**

Refer to the next level in the following situations; Treatment resistance or need for benzodiazepine treatment beyond 6 weeks

## **23.13. Obsessive-Compulsive Disorder**

This condition is characterized by the presence of persistent intrusive thoughts or concerns, and is usually associated with compulsions, which are mental acts or behaviours which an individual engages in to attempt to get rid of the obsessions and/or decrease his or her distress i.e. excessive hand washing. Obsessive thoughts and compulsions may interfere with daily functioning. The features are usually distressing to the patient.

### **Diagnostic Criteria**

- A pattern of repetitive behaviours
- Anxiety symptoms

### **Non-pharmacological Treatment**

- Psycho-education
- Psychotherapy
- Behaviour therapy

## **Pharmacological Treatment**

**D:** citalopram, Initial dose: (PO) 20mg. If there is no or partial response after 4-8weeks, increase to 40mg, if well tolerated.

**OR**

**S:** fluoxetine, Initial dose: (PO) 20mg. If there is no or partial response after 4-8weeks, increase to 40mg, if well tolerated.

### **Referral**

Refer to the next level in the following situations: Inadequate response to treatment

## **23.14. Acute Stress Disorder and Post-Traumatic Stress Disorder**

Acute stress and post-traumatic stress disorder arise in response to stressful events. The patient should have experienced the event as life threatening or as a physical threat to themselves or others, at which time they felt fear and helplessness.

### **Diagnostic Criteria**

Symptoms associated with both of these conditions include:

- Re-experiencing of the event, e.g. flashbacks, dreams
- Avoidance of situations associated with the event
- Features of anxiety or increased arousal, e.g. hyper vigilance, heightened startle response and insomnia

The conditions are symptomatically similar but differ with regard to the duration and time of onset of symptoms. The symptoms of acute stress disorder arise within 4 weeks of the event and last up to 4 weeks, whereas the symptoms post-traumatic stress disorder last longer than 4 weeks, and may arise more than 4 weeks after the traumatic incident.

### **Non-pharmacological Treatment**

- Reassurance and support of patient and family
- Psychotherapy, supportive/cognitive-behavioural therapy

### **Pharmacological Treatment**

#### **Acute stress disorder:**

For acute anxiety or agitation give:

**D:** clonazepam (PO) 0.5–2 mg 24hourly to 12hourly for 2weeks

Not for longer than 2 weeks and taper to a stop in the course of 26 weeks. The maintenance treatment needs antidepressants

#### **Note**

- Prolonged use of benzodiazepines > 1 week may be detrimental to adaptation, leading to higher rates of post-traumatic stress disorder

#### **Post-traumatic stress-disorder:**

**A:** amitriptyline (PO) 50–150mg nocte Elderly: 25- 75mg. (PO) for 4-8weeks

**OR**

**D:** citalopram 20-40mg (PO) 24hourly for 4–8weeks

**OR**

**S:** fluoxetine (PO) 20-40 mg 24hourly morning for 4–8weeks

#### **Note**

An adequate antidepressant trial of treatment is 8–12 weeks, before an alternative treatment should be considered.

#### **Referral**

Refer to the next level in the following situations:

- Inadequate response to treatment
- Co-morbid conditions

## **23.15. Substance Related Disorder**

### **23.15. 1. Substance Use Disorder**

#### **23.15.1.1. Alcohol Use Disorder**

##### **DSM-5 diagnostic criteria**

There must be a problematic usage of alcohol that has led to significant impairments occurring over a total of 12 months' duration. The problematic usage of alcohol is manifested by at least 2 of the following:

- Increasing usage of alcohol, or over a longer period than originally intended
- Repeated unsuccessful efforts to cut down or control usage, despite the desire to do so.

- Large amount of time is spent on activities to obtain alcohol, use alcohol, or recover from the effects of alcohol.
- Presence of a strong desire or urge to use alcohol
- Repeated alcohol usage resulting in a significant failure to fulfill major roles
- Persistent usage of alcohol despite having recurrent social or interpersonal problems due to the usage of alcohol.
- Important activities are given up due to the usage of alcohol
- Repeated usage despite significant impairments in physical health
- Continued use despite knowing that there have been physical or psychological problems arising from the usage of alcohol
- Tolerance as defined by either (1) Need for increasing amounts of alcohol to achieve the same or desired effects or (2)
- Reduced effects with continued use of the same amount of alcohol
- Withdrawal as defined by either (1) Characteristic withdrawal symptoms or (2) Alcohol is being used to prevent or avoid withdrawal symptoms

#### **Non-pharmacological Treatment**

- Cognitive Psychotherapy – Involves assessment of the patient's readiness for behavioural change using the stage of change model and also make use of motivation interviewing to enable patients to be empowered to change
- Alcoholic Anonymous groups
- A self-help group, with the sole purpose of enabling patients to quit their drinking habits. Their program is based on 12 core principles.

#### **23.15.1.2. Opioid Use Disorder**

##### **DSM-5 diagnostic criteria**

It states that there must be problematic usage of opioid that has led to significant impairments in terms of functioning over a 12-month period. The rest of the criteria are similar to that of alcohol use disorder

#### **Non-pharmacological Treatment**

- Motivational interviewing
- Therapeutic group therapy in a structured environment is helpful for helping individuals with their addiction.
- Psycho-education with regards to their possibility of HIV transmission when using shared needles would be helpful

#### **Pharmacological Treatment**

##### **Opioid substitutes**

**C:** methadone (PO) 10-30mg stat based on clinical assessment and UDS test then increase by 5-10mg every 3-5days to achieve optimal dose when opioid withdrawal features are well controlled. Once stability is reached, the client should be planned to remain on treatment for a minimum of two years. **For more detail refer to national guidelines for comprehensive management of opioid use disorder**

##### **OR**

**S:** buprenorphine 8-32mg (PO) 8hourly (Medication should be titrated according to symptoms resolution)

#### **23.15.1.3. Nicotine Use Disorder**

For an individual with nicotine use disorder, abstinence from nicotine usually leads to withdrawal symptoms. Nicotine detoxification requires the use of medication to prevent the symptoms which could become severe and potentially lead to mortality.

## **Diagnostic Criteria**

Withdrawal symptoms include:

- Restlessness
- Tremors
- Difficult in getting/maintaining sleep
- Anxiety
- Loss of appetite

## **Non-Pharmacological Treatment**

- Support group that encourage abstinence
- Inpatient rehabilitation programme where necessary

## **23.15.2 Substance Induced Disorder**

### **23.15.2.1. Substance Intoxication**

#### **Alcohol Intoxication**

##### **DSM-5 diagnostic criteria**

It specifies that there must be recent usage of alcohol and that clinically significant behavioral or psychological changes have arisen during or shortly after the usage.

This is characterized by at least one of the following signs or symptoms:

- Slurred speech
- Incoordination
- Unsteady gait
- Nystagmus
- Impairments in attention or memory
- Stupor or coma

#### **Treatment**

Symptomatically, depending on how patient presents

#### **Opioid Intoxication**

##### **DSM-5 Diagnostic criteria**

- It states that there must be recent usage of opioid, with the presence of pupillary constriction (or pupillary dilation due to anoxia from severe overdose) and at least 1 of the following signs and symptoms:
  - Feeling drowsy or losing consciousness
  - Slurring of speech
  - Impairments in attention or memory

There must also be significant problematic behavioral or psychological changes that have arisen during or shortly after the usage.

#### **Pharmacological Treatment**

**B:** naloxone (IM/IV) 0.04-15mg mg; if there is no response, the dose should be increased every 2 minutes

#### **Stimulant Intoxication**

##### **DSM-5 diagnostic criteria**

It specifies that there must be recent usage of amphetamine-type substance, cocaine or other stimulant that has led to significant impairments in functioning, shortly after usage. This is manifested by at least 2 of the following signs and symptoms:

- Increase or decrease in heart rate
- Pupillary dilation
- Elevated or lowered blood pressure
- Perspiration or chills
- Nausea or vomiting
- Evidence of weight lost
- Psychomotor agitation or retardation
- Muscular weakness, respiratory depression, chest pain or cardiac arrhythmias
- Confusion, seizures and coma

### **Pharmacological treatment of cocaine intoxication:**

If patient presents with agitation, refer to treatment of patient with aggressive and disruptive behaviors

If patient presents with psychosis, give

**A:** chlorpromazine (PO) 100-1000mg in divided doses, per day (max. dose 1000mg, per day)

**OR**

**B:** haloperidol (PO) 1.5-6mg in divided doses, per day (max. dose 20mg)

**Note**

Treatment rendered largely targets the symptoms that individuals are experiencing

### **Pharmacological treatment of Amphetamines intoxication:**

If patient presents with agitation, refer to treatment of patient with aggressive and disruptive behaviors

If patient presents with depressive symptoms after detoxification, refer to pharmacological treatment with depressive symptoms

### **Pharmacological treatment of Cannabis intoxication:**

**A:** chlorpromazine (PO) 100-1000mg in divided doses, per day (max. dose 1000mg, per day)

**OR**

**A:** haloperidol (PO) 1.5-6mg in divided doses, per day (max. dose 20mg)

## **23.15.2.2. Substance Withdrawal**

### **Alcohol Withdrawal**

For an individual with alcohol use disorder, abstinence from alcohol usually leads to withdrawal symptoms. Alcohol detoxification requires the use of medication to prevent the symptoms which could become severe and potentially lead to mortality.

### **Diagnosis features**

Withdrawal symptoms include:

- Insomnia
- Tremors
- Chills
- Anxiety

### **Non-Pharmacological Treatment**

- Support group that encourages abstinence
- Inpatient rehabilitation program where necessary

### **Pharmacological Treatment**

**C:** thiamine (IM) 300mg 24 hourly

### **For the CNS symptoms**

**C:** diazepam (PO) 10 mg every 4–6 hours on the first 24 and reduce by 20% over 5 days (only in inpatient care)

**OR**

**C:** Lorazepam (PO)

### **Relapse prevention following detoxification**

**S:** naltrexone (PO) 50mg 24hourly, and should be titrated, according to response

### **Alcohol Withdrawal Delirium (Delirium Tremens)**

It is an acute episode of delirium that is usually caused by withdrawal from alcohol. Although the typical delirium occurs 2–3 days following cessation of prolonged alcohol intake, reaching a peak at around 5 days, some withdrawal symptoms such as tremor may start within 12 hours.

## **Diagnosis Criteria**

- Visual hallucinations
- Disorientation
- Fluctuating level of consciousness
- Agitation
- Tachycardia
- Hypertension
- A low-grade fever may be present
- Withdrawal tonic-clonic seizures may occur between 24 and 48 hours following cessation of alcohol intake

### **Note**

It is important to consider alternative causes, when making the diagnosis. This is especially true for cases with an atypical presentation.

## **Emergency Care**

- Secure airway
- Ensure breathing
- Circulation
- Give IV fluid (Dextrose Normal Saline) to prevent hypoglycaemia and hypotension
- Monitor for respiratory depression

## **Pharmacological Treatment**

**A:** diazepam (IV)10mg for immediate sedative or hypnotic action. If no response gives a second dose.

**OR**

**C:** lorazepam (IM/IV) 2mg for immediate sedative or hypnotic action. If no response gives a second dose.

**OR**

**S:** chlordiazepoxide (IV) 20–60mg taper over one month

**AND**

**C:** thiamine (IM) 100-300mg 24hourly

**OR**

**A:** vitamin B Complex (IV) 1ampoule in 500ml 5% Dextrose

### **Note:**

- Do not administer at a rate over 5 mg/minute
- Switch to oral once containment is achieved

## **Heroin Withdrawal**

Heroin addiction, is a chronic, relapsing brain disease that is characterized by compulsive substance seeking and use, despite harmful consequences. When your body has become dependent on heroin, a number of unpleasant withdrawal symptoms will arise when the drug hasn't been used for a certain amount of time.

### **Diagnostic features include:**

Myalgia, gooseflesh, diarrhea, rhinorrhea, lacrimation, agitation, anxiety, Insomnia, sweating, yawning, abdominal cramping, dilated pupils, nausea and vomiting

## **Pharmacological Treatment**

To prevent repeating using of the heroin, give;

**S:** methadone (PO) 30-120mg 24hourly for a minimum of 1 year

**OR**

**S:** buprenorphine (PO) 2-8mg 24hourly for a minimum of 1 year

**OR**

**S:** naltrexone (PO) 25-50mg 24hourly for 6 months.

## **Symptomatic Treatment**

For difficult to get sleep, give:

**A:** diazepam (PO) 5–20 mg 24hourly to a minimum of 7days

**OR**

**A:** promethazine (PO) 50mg 24hourly at bed time (medication should be titrated according resolution)

**OR**

**A:** Chlorpromazine (PO) 50–100mg 24hourly at bed time (medication should be titrated according resolution)

For abdominal cramps, give:

**A:** hyoscine butyl bromide (PO) 20mg 8-24 hourly (medication should be titrated according resolution)

**OR**

**A:** diclofenac (PO) 50mg 8hourly (medication should be titrated according resolution)

For diarrhoea give

**B:** loperamide 4 mg (PO) stat, then 2mg after each loose stool (medication should be titrated according resolution)

### Cocaine Withdrawal

#### Non-Pharmacological Treatment

These patients usually do not require admission, however beware of depression and assess suicide risk

#### Pharmacological Treatment

No substitute drug available for detoxification

**C:** diazepam (PO) 5–10mg 8hourlyfor 5–7 days (medication should be titrated according resolution)

#### Referral

Refer patients to specialized clinic

### 23.16. Psychiatric Disorders Associated with Epilepsy

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the biologic, cognitive, psychological, and social consequences of this condition. This association may reflect the anatomical and neurobiological source of both epileptic seizures and the behavioral manifestations.

Antiepileptic drugs (AEDs) can play a role in the genesis of psychiatric symptoms; on the other hand, some psychotropic medications can lower the seizure threshold and provoke epileptic seizures.

The following are common psychiatric disorders in patients with epilepsy;

- Major depressive disorder
- Bipolar mood disorder
- Anxiety disorder
- Psychoses
- Suicidality

#### Treatment of Psychotic Disorders in patients with epilepsy;

#### Non-pharmacological Treatment

- Psychoeducation to the patient and the family
- Family therapy
- Supportive group therapy
- Occupational therapy

#### Pharmacological Treatment

**A:** carbamazepine (PO) 200-1000mg, in divided doses, per day (symptoms should be monitored and medication titrated accordingly)

**OR**

**A:** phenobarbitone (PO) 30-200mg, in divided doses, per day (symptoms should be monitored and medication titrated accordingly)

**OR**

**C:** sodium valproate (PO) 500-2000mg in divided doses, per day (symptoms should be monitored and medication titrated accordingly)

If psychosis persists, give

**B:** haloperidol (PO) 0.75-4.5mg 12hourly. Maximum dose 20mg/day

**OR**

**S:** olanzapine (PO) 5-10mg in divided doses, per day. Maximum dose 20mg/day (symptoms should be monitored and medication titrated accordingly)

**OR**

**S:** risperidone (PO) 0.5mg 12hourly then increase by 1mg every 2-3days to 2-3mg 12hourly. Maximum dose 16mg/day

#### Note

- Postictal psychosis remits spontaneously even without treatment but that the use of effective neuroleptics may shorten the duration.
- Interictal psychosis is treated with antipsychotic drugs. Medications that lower the seizure threshold should be avoided.
- Atypical antipsychotic medications may have better profiles than typical antipsychotic medications.
- Medications that lower the seizure threshold should be avoided.
- The doses should be as minimal as possible

### Treatment of Depressive symptoms/signs in patients with epilepsy;

#### Non-pharmacological Treatment

- Psychoeducation to the patient and the family
- Family therapy
- Supportive group therapy
- Occupational therapy

#### Pharmacological treatment

**A:** carbamazepine (PO) 200-1000mg, in divided doses, per day (symptoms should be monitored and medication titrated accordingly)

**OR**

**A:** phenobarbitone (PO) 30-200mg, in divided doses, per day (symptoms should be monitored and medication titrated accordingly)

**OR**

**C:** sodium valproate (PO) 500-2000mg in divided doses, per day (symptoms should be monitored and medication titrated accordingly)

**AND**

**A:** amitriptyline 12.5-75mg (PO), nocte (symptoms should be monitored and medication titrated accordingly)

**OR**

**S:** fluoxetine 1 (PO) 0-20mg in divided doses, per day (symptoms should be monitored and medication titrated accordingly)

#### Note

- In the treatment of epilepsy-related depression, priority should be given to optimizing seizure control, since improved psychosocial functioning tends to accompany seizure remission
- Some anticonvulsant therapies, including sodium valproate, gabapentin, carbamazepine, and lamotrigine, also have antidepressant effects and may prove effective in treating depression in patients with epilepsy.

Phenobarbital is known to produce depression.

## **Treatment of Mania/hypomania in patients with epilepsy; Non-Pharmacological Treatment**

- Psychoeducation to the patient and the family
- Family therapy
- Supportive group therapy
- Occupational therapy

## **Pharmacological Treatment**

**A:** carbamazepine (PO) 200-1000mg, in divided doses, per day

**OR**

**A:** phenobarbitone (PO) 30-200mg, in divided doses, per day

**OR**

**A:** sodium valproate (PO) 500-2000mg in divided doses, per day

### **Note**

Symptoms should be monitored and medication titrated accordingly

## **23.17. Psychiatric Disorders in Pregnancy**

In some women, pregnancy and motherhood increase their vulnerability to psychiatric conditions such as depression, anxiety disorders, eating disorders, panic disorder, bipolar illness, and psychoses. These conditions are often underdiagnosed because they are attributed to pregnancy-related changes in maternal temperament or physiology. In addition, such conditions are often undertreated because of concerns about potential harmful effects of medication.

### **23.17.1 Depression**

Several risk factors and psychosocial correlates have been identified as contributing to depression during pregnancy, like;

- Previous history of depression, discontinuation of medication(s) by a woman who has a history of depression, a previous history of postpartum depression, and a family history of depression

Several key psychosocial correlates may also contribute to depression during pregnancy: a negative attitude toward the pregnancy, a lack of social support, maternal stress associated with negative life events, and a partner or family member who is unhappy about the pregnancy. The relationship between maternal depression and early childhood problems may be part of a sequence that starts with depressive symptoms during pregnancy.

### **Non-pharmacological Treatment**

- Psychotherapies
  - Cognitive behavioral therapy
  - Interpersonal psychotherapy
  - Education and support are also important, particularly as pregnancy is a unique experience for women, some of whom may not know what to expect.

## **Pharmacological Treatment**

**A:** amitriptyline (PO) 12.5–75 mg 24hourly at night, increase gradually to a maximum of 150 mg daily. {Elderly: Initially 12.5–50 mg. Max. 75mg)

**OR**

**D:** citalopram 10-60mg (PO) 24hourly morning or evening and symptoms should be monitored, and medication to be tapered

**OR**

**S:** fluoxetine 20-60mg (PO) 24hourly (morning)

### **Note**

- Full disclosure of both the risk and benefits of various antidepressant medications should be made to the patient and, if possible, her partner prior to starting any pharmacological treatment.
- Low doses of antidepressants should be considered when initiating medication.

## **12.17.2 Panic Disorder**

Some women may experience first-onset panic disorder during pregnancy. Women presenting with panic attacks for the first time should be screened for thyroid disorder. The correlation between plasma levels of cortisol in the mother and in the fetus may have implications for the developing fetal brain.

### **Non-pharmacological Treatment**

- Cognitive behavioral therapy
- Supportive psychotherapy
- Relaxation techniques
- Sleep hygiene
- Dietary counseling

### **Pharmacological Treatment**

Refer panic disorders

#### **Note**

- Full disclosure of both the risk and benefits of various antidepressant medications should be made to the patient and, if possible, her partner prior to starting any pharmacological treatment.
- Low doses of antidepressants should be considered when initiating medication

## **12.17.3 Obsessive-Compulsive Disorder**

Obsessive-compulsive disorder (OCD) is characterized by thoughts that cannot be controlled (obsessions) and repetitive behaviors or rituals that cannot be controlled (compulsions) in response to these thoughts.

### **Non-pharmacological Treatment**

- Cognitive behavioral therapy
- Supportive psychotherapy
- Relaxation techniques
- Sleep hygiene
- Dietary counseling

### **Pharmacological Treatment**

Refer to the specific section above

#### **Note**

Treatments for GAD in pregnancy are the same as those in non-pregnant adults.

## **12.17.4 Bipolar Mood Disorder**

### **Non-pharmacological Treatment**

- Cognitive behavioral therapy
- Supportive psychotherapy
- Relaxation techniques
- Sleep hygiene
- Dietary counseling

### **Pharmacological Treatment**

Refer to the specific section above

#### **Note**

- Decision whether to use mood stabilizers must be made following an assessment of risks and benefits.
- Low doses of mood stabilizers should be as low as possible
- Factors to consider include number and severity of previous episodes, level of insight, family supports, and the wishes of the woman
- Careful monitoring of psychological symptoms throughout the pregnancy is of paramount importance

## **12.17.5 Schizophrenia**

### **Non-pharmacological Treatment**

- Cognitive behavioral therapy
- Supportive psychotherapy
- Relaxation techniques
- Sleep hygiene
- Dietary counseling

### **Pharmacological Treatment**

Treat as in the treatment of schizophrenia in non-pregnant woman

#### **Note**

- Women with a history of psychosis require close monitoring during pregnancy
- Psychosis during pregnancy can have devastating consequences for both the mother and her fetus, including failure to obtain proper prenatal care, negative pregnancy outcomes such as low birth weight and prematurity, and neonaticide or suicide
- Treatment of acute psychosis in pregnancy is mandatory and includes mobilization of supports, pharmacotherapy, and hospitalization
- Electroconvulsive therapy may be used for psychotic depression

## **23.18. Autism Spectrum Disorder**

### **DSM-5 Diagnostic criteria**

It states that an individual diagnosed with Autism spectrum disorder would have marked difficulties in terms of communication and engagement with others across multiple social situations. These difficulties include:

- Difficulties with demonstrating appropriate behaviours in social contexts
- Difficulties associated with non-verbal communications used for social interactions
- Difficulties associated with failure to initiate or adapt to social interactions

In addition, the DSM-5 also requires the individuals to have characteristic repetitive behavioural patterns, such as

- Repeated stereotypical movements or
- Highly ritualized behavioural patterns. DSM-5 criteria specified that these behaviours must have started since the early developmental period and has resulted in marked impairments in terms of functioning.

### **Non-pharmacological Treatment**

#### **For children**

- Every pre-school child diagnosed with autism should have an individualised intervention plan that sets out the goals, type(s), frequency and intensity of intervention, in order to address particular developmental and educational needs
- An individualised intervention plan should consist of a variety of quality programs and activities. This includes attendance in comprehensive early intervention programmes, programmes targeting specific needs and also positive engagement with parents and/or caregivers
- Alternative-augmentative communication systems may be recommended for pre-school children with autism because the expanded (spoken or written) communication may stimulate speech acquisition in non-verbal children and enhance expression in verbal children.
- Visual strategies are useful interventions for children with autism because they offer visual support to communication, increase spontaneous imitation and socially communicative behaviour.
- Social skills programmes depend on the functioning level of the preschool child with autism and may include:
  - Assessment and teaching of social skills interaction in natural settings.
  - Provision of structure, visual cues and predictability.
  - Making abstract concepts more “concrete”.
  - Activities that enable purposeful and appropriate interaction with typically developing peers.
  - Goals focusing on fostering self-appreciation and self-esteem.

### **For the parents**

- Parents and caregivers should be encouraged to discuss the need for practical emotional support. This enables information to be provided, referrals made and support services made available
- Parents and caregivers are recommended to consult appropriate professionals when considering educational placement for their child with autism

### **Pharmacological Treatment**

A: haloperidol (PO) 1.5-3mg 24hourly (medications should be titrated according to symptoms resolution)

**OR**

A: methylphenidate (PO) 18- 54 mg 24hourly(medications should be titrated according to symptoms resolution)

### **23.19. Attention Deficit / Hyperactivity Disorder (ADHD)**

#### **DSM-5 Diagnostic criteria**

It states that an individual diagnosed with attention-deficit and hyperactivity disorder would have difficulties in terms of functioning, mainly due to (a) inattention and/or (b) hyperactivity and impulsivity.

The DSM-5 states that these inattentive and/or hyperactivity and impulsivity symptoms must be present before the age of 12 years old. In addition, these symptoms must have resulted in impaired functioning in at least 2 different social situations.

The DSM-5 requires the individual to fulfill at least 6 of the following signs and symptoms of inattention:

- Failing to pay close attention to details
- Concentration difficulties
- Difficulties with sustaining attention at tasks
- Daydreaming and does not seem to be able to follow normal conversations
- Difficulties with organization of tasks
- Reluctance to participate in tasks that involve much attention
- Frequently loses important objects
- Easily distractible
- Forgetfulness about daily activities.

The DSM-5 also specified that only 5 of the above signs and symptoms of inattention need to be fulfilled if individuals are 17 years of age and above.

DSM-5 also requires the individual to fulfil at least 6 of the following signs and symptoms of hyperactivity and impulsivity:

- Moving about and unable to sit still
- Leaves seat even when required to remain seated
- Climbs or runs about in inappropriate situations
- Always having excessive energy and always on the move
- Chats excessively
- Impulsive and gives answers even before being asked to
- Having difficulties waiting for his/her turn
- Unable to carry out normal conversation due to frequent interruptions

### **Non-pharmacological Treatment**

#### a) Parent-training/ education programmes

Refer parents to educational programmes to learn about ADHD, its management and coping strategy.

- For parents, the programme should include individual or group-based parent-training/education programmes.
- For children and youth with ADHD, the programme should include CBT or social skill training.
- Offer training to the teachers on behavioural interventions in the classroom to help the child to cope with ADHD

#### b) Behaviour therapy

- Positive reinforcement of positive behaviour including reward system and praises. The parents can consider using

- a star chart to promote positive behaviour at home.
- Environmental modifications aim at improving attention e.g. placing the child in the front row of class, minimising distractions etc.
- Combination of behaviour therapy and medication is better than medication alone.

## 23.20. Enuresis

### DSM-5 Diagnostic criteria

- Repeated voiding of urine into bed or clothes (whether involuntary or intentional)
- Behavior must be clinically significant as manifested by either a frequency of twice a week for at least three consecutive months or the presence of clinically significant distress or impairment in social, academic (occupational), or other important areas of functioning.
- Chronological age is at least 5 years of age (or equivalent developmental level).
- The behavior is not due exclusively to the direct physiological effect of a substance (such as a diuretic) or a general medical condition (such as diabetes, spina bifida, a seizure disorder, etc.).

### Non-pharmacological Treatment

- Fluid restriction at night especially 1 hour before the desmopressin dose until the next morning, or at least 8 hours after the dose. If child wakes up during the night, limit the amount that he or she drinks.
- Star chart: effective in one-third of cases
- Alarm: Child must wake up and urinate.

### Pharmacological Treatment

**A:** amitriptyline (PO) 25mg nocte (medications should be titrated according to symptoms resolution)

**OR**

**C:** imipramine (PO) 100mg nocte (medications should be titrated according to symptoms resolution)

## 23.21. Neuroleptic Malignant Syndrome (NMS)

Mostly is caused by the use of high dose of antipsychotics; potent antipsychotics (e.g. haloperidol) and antipsychotics that are given via the intravenous or intramuscular routes.

### Diagnostic Signs and symptoms

- Muscle rigidity
- Fever
- Altered consciousness
- Mutism
- Dysphagia
- Diaphoresis
- Tachycardia
- Labile blood pressure
- Tremor
- Incontinence
- Leukocytosis
- Laboratory evidence of muscle injury: increase in creatinine kinase levels.

### Pharmacological Treatment

**A:** diazepam 10 mg (IV)

**OR**

**C:** lorazepam (IM/IV) 2 mg for immediate sedative or hypnotic action. If no response gives a second dose

**OR**

**C:** bromocriptine (PO) 2.5 mg 8hourly

### Note

- NMS is a clinical emergency, It needs ICU care
- It is important to stop the antipsychotics immediately
- Supportive measures such as bed rest and controlling the hyperthermia by rapid cooling with the help of tepid water spray and via direct fluid replacement should be started immediately
- Consideration of ventilator support or intubation would be necessary if the patient has severe breathing difficulties

## **23.22. Somatic Symptom Disorder**

### **DSM-5 diagnostic criteria**

- One or more somatic symptoms that are distressing or result in significant disruption of daily life.
- Excessive thoughts, feelings, or behaviors related to the somatic symptoms or associated health concerns as manifested by at least one of the following:
  - Disproportionate and persistent thoughts about the seriousness of one's symptoms.
  - Persistently high level of anxiety about health or symptoms.
  - Excessive time and energy devoted to these symptoms or health concerns

DSM-5 specified time duration of at least 6 months of the presentations.

### **Non-pharmacological Treatment**

- Regular appointments: Patients diagnosed with somatic symptom disorder should have a fixed, regular physician whom they can seek help from and be seen on a regular basis.
- Avoid unnecessary investigation but physical examination should be performed if new complaints arise.
- Offer empathy to the sufferings experienced by the patient.
- Psychotherapy:
  - Self-help techniques
  - Supportive psychotherapy
  - Cognitive behaviour therapy (e.g. challenge cognitive distortions, activity scheduling to enhance physical activities).
- Increase in social and occupational functioning

### **Pharmacological Treatment**

**A:** amitriptyline (PO) 25-50mg 24hourly (medications should be titrated according to symptoms resolution)

**OR**

**C:** imipramine (PO) 100mg 24hourly (medications should be titrated according to symptoms resolution)

**OR**

**S:** fluoxetine (PO) 10-20mg 24hourly (medications should be titrated according to symptoms resolution)

## **23.24. Conversion Disorder**

### **DSM-5 Diagnostic criteria**

- One or more symptoms of altered voluntary motor or sensory function.
- Clinical findings provide evidence of incompatibility between the symptom and recognized neurological or medical conditions.
- The symptom or deficit is not better explained by another medical or mental disorder.
- The symptom or deficit causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation

### **Non-pharmacological Treatment**

- Psycho-education
- Cognitive-psychotherapy

### **Pharmacological Treatment**

**A:** amitriptyline (PO) 25-50mg 24hourly (medications should be titrated according to symptoms resolution)

**OR**

**C:** imipramine100mg (PO) once a day (medications should be titrated according to symptoms resolution)

**OR**

**S:** fluoxetine (PO)10-20mg 24hourly (medications should be titrated according to symptoms resolution).

# CHAPTER TWENTY-FOUR

## NUTRITION DISORDERS

Nutrition disorders can be caused by an insufficient intake of food or certain nutrients, or by inability of the body to absorb and use nutrients, or by over consumption of certain foods.

### **24.1 Iodine Deficiency Disorders (IDD)**

#### **Clinical presentation**

- Goitre enlarged thyroid gland from over activity.
- Hypothyroidism - dry skin, weight gain, puffy face, frequent constipation, and lethargy from under-active thyroid
- Hyperthyroidism - exophthalmia, rapid pulse, and weight loss from over-active thyroid
- Cretinism

**Table 24.1: Criteria for Assessing Iodine Deficiency Using Urinary Iodine Concentration.**

Micronutrient indicators	Urinary iodine concentration for determining iodine status in the population	
Median urinary iodine ( $\mu\text{g/l}$ )	Iodine intake	Iodine status
<b>Pregnant women</b>		
< 150	Insufficient	Severe iodine deficiency
150 – 249	Adequate	Adequate iodine nutrition
250 – 499	Above requirements	May pose slight risk of more than adequate iodine intake
> 500	Excessive	Risk of adverse health consequences
<b>Lactating women and children &lt; 2 years</b>		
< 100	Insufficient	Severe iodine deficiency
> 100	Adequate	Adequate iodine nutrition
<b>School age children (6 years or older)<sup>c</sup></b>		
<20	Insufficient	Severe iodine deficiency
20 – 49	Insufficient	Moderate iodine deficiency
50 – 99	Insufficient	Mild iodine deficiency
100 – 199	Adequate	Adequate iodine nutrition
200 – 299	Above requirement	May pose slight risk of more than adequate iodine intake
> 300	Excessive	Risk of adverse health consequences

**Table 24.2: Epidemiologic criteria for assessing iodine nutrition based on median urinary iodine concentrations in different target groups**

	MUIC ( $\mu\text{g/L}$ )		
Population group	Insufficient	Adequate	Above requirement and excessive
School aged children	<100	100-299 <sup>a</sup>	> 300 <sup>a</sup>
Adults (women reproductive age)	<100	100-299 <sup>a</sup>	> 300 <sup>a</sup>
Pregnant women	<150	150-249	> 250
Lactating women	<100	> 100	
Children < 2 years	<100	> 100	

<sup>a</sup> adjusted based on best available scientific evidence to date

#### **Non Pharmacological Treatment**

- Use of iodated salt (strategy for control of iodine deficiency worldwide)
- Use of iodine rich foods like: drinking water (reflecting amount of  $\text{I}_2$  present in the soil), Fish, Sea weeds (Sea weeds are rich in iodine but are a rare component of the diet).

## **Pharmacological Treatment**

**A:** iodized oil (PO) 400mg repeated after one to two years

**AND**

**B:** potassium iodide solution (PO) 21mg stat

## **24.2 Vitamin A Deficiency (VAD)**

### **Clinical presentation**

- Night blindness or inability to see in the dark
- White foamy patches on the eye (Bitot's spot) or conjunctival and corneal dryness
- Keratomalacia or wrinkling and cloudiness of cornea
- Corneal ulceration or the cornea becomes soft and bulges

### **Diagnosis**

Common indicators of VAD used for population surveys/assessments

- Clinical eye signs (Exophthalmia)
- Serum Retinol Concentration

**Table 24.3 Serum Retinol Concentration**

Public Health Importance	Serum or plasma retinol: <0.70 µmol/l in preschool-age children or pregnant women
Mild	> 2% - < 10%
Moderate	> 10% - < 20%
Severe	> 20%

### **Non-pharmacological Measures**

Dietary consumption of vitamin-A rich foods

## **Pharmacological Treatment**

### **Prophylaxis**

**A:** vitamin A (retinol)(PO) 4-6monthly up to the age of 5years.

**Table 24. 4: Administration of Vitamin A**

Age range	Dose units	Frequency	Route of Administration
Infants 6–11 months (including HIV +ve)	100,000 IU (30 mg RE) vitamin A <sup>3</sup>	Stat	Oral liquid, oil-based preparation of retinol palmitate or retinol acetate
Children 12 months–59months (including HIV +ve)	200,000 IU (60 mg RE) vitamin A	4-6 monthly	

### **Treatment**

For children 6- 59months and children refer to **table 24.4**

For adults (except women of reproductive age)

**A:** vitamin A (retinol) (PO) 200,000 IU stat.

### **In case of Exophthalmia and Measles:**

For infants < 6 months' give

**A:** vitamin A (retinol)(PO) 50,000IU immediately on diagnosis repeat next day and on day 14

For infants 6-11months

**A:** vitamin A (retinol)(PO) 100,000IU immediately on diagnosis repeat next day and on day 14

For children 12-59 months

**A:** vitamin A (retinol)(PO) 200,000IU immediately on diagnosis repeat next day and on day 14

For all adults except women of reproductive age

**A:** vitamin A (retinol)(PO) 200,000IU immediately on diagnosis repeat next day and on day 14

For exophthalmia or Bitot's sport for women of reproductive age

**A:** vitamin A (retinol)(PO) 10,000IU 24hourly for 4weeks

**Note**

Children who received a prophylactic dose within the previous month should not receive the treatment dose of vitamin A.

**Referral:** All complicated cases

## 24.3 Vitamin B Deficiencies

### 24.3.1 Vitamin B<sub>1</sub>/Thiamine Deficiency (Wernicke Encephalopathy and Beriberi)

**Clinical features**

- confusion
- short term memory loss
- confusion
- paralysis of one or more of the ocular muscles or ophthalmoplegia
- nystagmus
- ataxia
- peripheral neuropathy
- cardiac failure

**Non-pharmacological Treatment**

- Lifestyle adjustment including discouraging of alcohol abuse.
- Increase intake of thiamine rich foods

**Pharmacological Treatment**

For Peripheral neuropathy and cardiac failure

**C:** thiamine (PO) 100mg 24hourly

### 24.3.2 Vitamin B<sub>3</sub>/Nicotinic Acid Deficiency (Pellagra)

Pellagra is a condition associated with nicotinic acid deficiency. It is usually accompanied by other vitamin deficiencies.

**Clinical features**

- diarrhea
- dementia
- dermatitis with darkening of sun-exposed skin

**Non-pharmacological Measures**

- Lifestyle adjustment including discouraging of alcohol abuse.
- Increase intake of vitamin nicotinic acid rich foods

**Pharmacological Treatment****For severe deficiency**

Children:

**C:** nicotinamide (PO) 50mg 8hourly for 7days

Adults

**C:** nicotinamide (PO) 100mg 8hourly for 7days

**For mild deficiency**

Children

**C:** nicotinamide (PO) 50mg 24hourly for 7days

Adults

**C:** nicotinamide (PO) 100mg 24hourly for 7days.

**Referral:** On failure to respond on above treatment.

### 24.3.3 Vitamin B<sub>6</sub>/Pyridoxine Deficiency

Pyridoxine deficiency is related to malnutrition and alcoholism.

**Clinical features**

- tingling sensation
- burning pain or numbness of the feet
  - Isoniazid or combination TB therapy

### **Non-pharmacological measures**

- Increase intake of pyridoxine rich foods.
- Minimize alcohol consumptions

### **Pharmacological Treatment**

#### **For deficiency**

Children:

**B:** pyridoxine (PO) 12.5mg 24hourly for 3weeks.

Adults:

**B:** pyridoxine (PO) 25 mg 24hourly for 3weeks.

#### **For medicine-induced neuropathy**

Children

**B:** pyridoxine (PO) 50mg 24hourly for 3weeks.

Adults

**B:** pyridoxine (PO) 200mg 24hourly for 3weeks.

Then followed by:

**B:** pyridoxine (PO) 25mg daily as maintenance dose (for patients on TB therapy/isoniazid)

### **Referral**

- Failure to respond.
- Children.

### **24.3.4 Vitamin B<sub>12</sub> (Cobalamin) Deficiency**

Refer Haematological Disease Conditions chapter

### **24.4 Malnutrition**

Classes of malnutrition are moderate acute malnutrition (MAM) and severe acute malnutrition (SAM)

MAM is identified by moderate wasting WfH<-2 z-score for children 0–59 months (or for children 6 - 59months MUAC <125mm and ≥115mm)

SAM is defined by severe wasting WfH<-3 z-score for children 0–59 months (or for children 6-59months, MUAC<155mm) or the presence of bilateral pitting oedema.

#### **Clinical Features**

<b>Marasmus</b>	<b>Kwashiorkor</b>
<ul style="list-style-type: none"> <li>• Severe weight loss and wasting</li> <li>• Ribs prominent</li> <li>• Limbs very thin</li> <li>• Muscle wasting old man's appearance</li> <li>• Extremely emaciated</li> <li>• Frequent infection with minimal signs</li> <li>• Electrolyte imbalance</li> <li>• Alert and irritable</li> </ul>	<ul style="list-style-type: none"> <li>• Bilateral pitting oedema, beginning in the lower legs and feet; can become more generalized (trunk, face "moon", hands, arms).</li> <li>• Reduced fat and muscle tissue which may be masked by oedema.</li> <li>• Skin cracked and peeling off.</li> <li>• Fragile skin prone to ulceration and infection.</li> <li>• Pale appearance.</li> <li>• Hair changes: blond (yellow, red, sparse, dry, thin). Can be pulled out easily and without pain (atrophy of the hair roots). Bald patches.</li> <li>• Frequent infections, e.g. URT, otitis media, URI</li> <li>• Frequent association with dehydration which may be masked by oedema</li> <li>• Generally apathetic lethargic and miserable when left alone. Irritable when handled.</li> <li>• High risk of death</li> </ul>

#### **Diagnostic criteria**

##### **Infants less than 6 months**

- Weight for Length less than <-3SD
- Bilateral pitting oedema of feet

- Infant is too weak to suck effectively
- The infant does not gain weight or lose more than 10% of the initial weight.

**Table 24.5 Summary of medical complications and danger signs**

<b>Appetite</b>	No appetite or unable to eat
<b>Vomiting</b>	Persistent/severe
<b>Temperature</b>	Hypothermia (Axillary Temperature <35.5°C, Rectal Temperature <36.5 °C) High fever ( $\geq 38.5$ °C)
<b>Respiratory symptoms and signs</b>	Cough and fast breathing (as per IMCI guidelines) Lower chest in-drawing
<b>Anaemia</b>	Severe palmar pallor and jaundice
<b>Dehydration</b>	Severe dehydration based on recent history of fluid loss (watery diarrhoea/vomiting) with weight loss
<b>Alertness</b>	Extremely weak and lethargic, unconscious, fitting/convulsions
<b>Infections</b>	Open skin lesions, extensive infection

**Note**

- All children with complicated SAM are at risk of complications or death.
- Stabilize before referral.
- Refer urgently.

#### **24.4.1 Management of Severe Acute Malnutrition (SAM)**

##### **General guidelines for management of SAM:**

Refer to **IMAM guidelines**

##### **Non Pharmacological Treatment**

The therapeutic diet for malnourished children consists of two formulas,

**A:** F-75 initial phase of treatment

**THEN**

**A:** F-100

**OR**

**A:** Ready to use Therapeutic Food (RUTF).

**Note**

- F-100 and Ready Therapeutic food is used when appetite has returned
- For children 6–59 months start with 2hourly feeds (12feeds per day), and gradually decrease the frequency of feeding and increase the volume of each feed until the patient is getting 3hourly feeds (8feeds per day)

##### **If the child is conscious and has hypoglycaemia give:**

<b>Medicine</b>	<b>Child Dose</b>	<b>Frequency</b>	<b>Duration</b>
C: 10% glucose solution OR C: 10% sucrose solution	50ml bolus	stat	
THEN F-75	3ml/kg/Feed	Every 3minutes	2hours
	11ml/kg/Feed	2hourly	2days

Treatment of dehydration in Severe Malnourished Children: Refer to **IMCI guidelines**

## Pharmacological Treatment

**Table 24.5 vitamin and mineral therapy supplementation in severe acutemalnutrition:**

Medicine	Paed age	Dose	Frequency	Duration
A: vitamin A (PO)	<6mnths	50,000iu	24hourly	2days
	6–12mths	100,000iu		
	1-5yr	200,000iu		
AND A: ferrous sulphate (PO)	4-<6kg	6mg Fe	24hourly	14days
	6 - <10kg	12mg		
	1-3yrs	18mg		
	3-5yrs	24mg		
AND A: folic acid (PO)	<6kg	2.5mg	24hourly	14days
	>6kg	5mg		
AND A: albendazole (PO)	≥2 years	400 mg	stat	On discharge from SC/ direct admission to OTP

Children with SAM and signs of shock or severe dehydration, and who cannot be rehydrated orally or by nasogastric tube should be treated with intravenous fluids, either:

**A:** compound sodium lactate

**OR**

**A:** 0.45% saline

**AND**

**A:** Dextrose 5%

**Table 24.6 Inpatient Therapeutic Feeding Recommendations Phase 1**

Phase 1 (Stabilization care)		Phase 2 (Transition and Rehabilitation)
Age Group	Product and Prescription	
Children Months <6	<ul style="list-style-type: none"> <li>Give Diluted F-100 at 130ml/kg of body weight per day.</li> <li>Breastfed children should always be offered breast milk before the therapeutic milk, and always on demand</li> </ul>	<ul style="list-style-type: none"> <li>Give twice the volume offered during phase I</li> </ul>
Children Months 6-59	<ul style="list-style-type: none"> <li>Give F-75 at 130ml/kg of body weight per day until the patient regains appetite.</li> <li>Start with 2hourly feeds (12 feeds per day), and gradually decrease the frequency of feeding and increase the volume of each feed until the patient is getting 3hourly feeds (8 feeds per day)</li> </ul>	<ul style="list-style-type: none"> <li>Replace F75 with F-100 at 150ml/kg of body weight per day.</li> <li>Gradually introduce RUTF in small amounts until the child can consume <math>\frac{1}{2}</math> Sachet per day</li> <li>When accepted, provide RUTF at 130kcal per kg of body weight per day</li> </ul>

### Note

#### If the child is able to swallow:

- If breastfed: ask the mother to breastfeed the child, or give expressed breastmilk.
- If not breastfed: give a breastmilk substitute (F-75). Give 30–50mL before the child is referred.
- If no breastmilk substitute, and IVs available, give 30–50mL of sugar water.

#### If the child is not able to swallow:

- Insert a nasogastric tube and check the position of the tube.
- Give 50mL of milk or sugar water by nasogastric tube (as above).

#### If blood sugar <3mmol/L treat with 10% Glucose:

- Nasogastric tube: 10mL/kg.
- Intravenous line: 2mL/kg.

**Table 24.7 Time frame for the inpatient management of severe acute malnutrition in children**

	Stabilization/Transition*		Rehabilitation
	Day 1-2	Day 3-7	Week 2-6
1. Treat/prevent hypoglycaemia			
2. Treat/prevent hypothermia			
3. Treat/prevent dehydration			
4. Correct electrolyte imbalance			
5. Treat/prevent infection			
6. Correct micronutrient deficiencies	No iron	No iron	Give iron
7. Start cautious feeding	F-75	F-100	RUTF
8. Achieve catch-up growth			
9. Provide sensory stimulation and emotional support			
10. Prepare for discharge and follow-up after recovery			

**Note**

- In case of shock with lethargy or unconsciousness, intravenous rehydration should begin immediately, using 15mL/kg/h of one of the recommended fluids.
- Blood transfusion should be done if a child with severe acute malnutrition presenting with shock does not improve after 1h of intravenous therapy, a blood transfusion (10mL/kg slowly over at least 3h) or presents with severe anaemia, i.e. Hb <4g/dL or <6g/dL if with signs of respiratory distress;
- It is important that the child is carefully monitored every 5–10min for signs of over hydration and signs of congestive heart failure.
- Treat other medical conditions as per Integrated Management of Acute Malnutrition (IMAM) guideline 2018
- All cases require careful assessment for possible TB or HIV

**24.5 Growth Faltering/Failure to Thrive**

Children and infants who have either:

- Unsatisfactory weight gain (growth curve flattening or weight loss) on the Road to Health chart/ booklet.
- OR**
- Low weight for age, i.e. WHZ < -2 but > -3

**Note**

- Babies who were premature and are growing parallel to or better than the Z-score line, should not be classified as having failure to thrive or not growing well.

**Table 24.8 Feeding recommendations for all children**

Age (month)	Frequency (Per day)	Amount of food per serving (in addition to breast milk)	Texture (thickness/consistency)	Variety
At months	6	start complementary foods 2 to 3 meals plus frequent breastfeeds	2 to 3 tablespoons Start with 'tastes'	Thick porridge/pap
From 6 up to months	9	2 to 3 meals plus frequent breastfeeds 1 to 2 snacks may be offered	2 to 3 table spoonful per feed Increase gradually to half (½) 250 ml cup/bowl	Thick porridge/pap Mashed/pureed family foods
From 9 up		Half (½) 250 ml	Finely chopped	

to 12 months	breastfeeds 1 to 2 snacks may be offered	cup/bowl	family foods Finger foods Sliced foods	
From 12 up to 24 months	3 to 4 meals plus breastfeeds 1 to 2 snacks may be offered	Three-quarters ( $\frac{3}{4}$ ) to 1 250 ml cup/ bowl	Sliced foods, Family foods	
From 24- 59 Months	Give 3 family meals a day. Give snacks in between meals.			Staples (local examples) Animal foods (local examples) Legumes (local examples) Fruits (local examples) Vegetables (local examples)
<b>Note:</b> If a baby is not breastfed	Add 1-2 extra times food and snacks	Same as above according to age group	Same as above according to age group	Same as above, plus 1 to 2 cups of milk per day + 2 to 3 cups of extra fluid especially in hot climates
Responsive /Active feeding		Be patient and actively encourage the baby to eat		
Hygiene		<ul style="list-style-type: none"> <li>Feed the baby using clean cup and spoon, DO NOT use a bottle as this is difficult to clean and may cause the baby to get diarrhoea</li> <li>Wash hands with soap and water before preparing food, before eating and before feeding young children.</li> </ul>		

## 24.6 Obesity and Overweight

### Management of Obesity and Overweight

Aim of nutritional management is to:

- Achieve and maintain ideal body weight by bringing about gradual weight loss
- Correct fault food habits

#### Management

- Control total energy intake based on individual assessment by limiting energy intake from total fat and simple sugars.
- Put the client on a weight reduction diet regime of 30-25kcal/kg /day.
- High fiber, restricted fat diets based on individual assessment is recommended
- Offer nutrition education and counseling to the clients with emphasis on weight management, fat diets and other unhealthy practices in weight control
- Recommend suitable exercise program and encourage physical activity for gradual weight loss
- Recommend support systems for the clients who need behavior modification.

#### Note

- A maximum reduction of 1000kcal daily is required to lose about 1kg a week and a reduction. Drastic reduction of calorie intake is however not advisable.
- Diet adjustments should be gradual as such people experience excessive appetite. Use of appetite suppressants is not recommended

### Dietary considerations in the management of obesity and overweight

#### Proteins

Give slightly higher than normal as it gives a feeling of satiety and helps to maintain a good nutritional status yet excess is deaminated. Provide approximately 20% of total energy from proteins. This should include good quality proteins, lean and whole pulses.

#### Fats

Provide 20% or less of total energy from fats. Emphasize on the use of unsaturated fats to reduce the risk of heart problems. Restrict or avoid fried foods

#### Carbohydrates

Provide the rest of energy 60% from carbohydrates which should be mainly in complex form; starches and dietary fiber. Limit simple forms like sugars

### Minerals and Vitamins

Provide adequate amount of essential nutrients like minerals and vitamins to maintain a good nutrition status

Generally, increase intake of the following food:

- Vegetables such as broccoli, mushroom, zucchini, cabbage, lettuce, cucumber
- Fruits such as pineapple, cherimoya, peach, grapefruit
- Tubers such as sweet potatoes
- Low fat milk
- Diuretic foods such as celery, apples, watermelon (diuretic drugs are not recommended)

### 24.7 Nutritional Management in TB, HIV and AIDS

- Maintain and improve nutrition status of a person living with HIV/ AIDS thus delay the progression from HIV to AIDS related diseases.
- Ensure adequate intake of all nutrients thus preventing development of nutritional deficiencies.
- Preservation of lean body mass.
- Maintain body weight and fitness.
- Improve performance of immune system.
- Replenishment of nutrient losses incurred during infection.
- Minimizing symptoms of malabsorption.
- Regeneration of glycogen stores.
- Maintain laboratory values within normal limits.

#### Note

Control side effects due to medication and monitor drug – nutrient interaction

**Table 24.9: Side Effects related to TB drugs and food intake recommendations to minimize them.**

Drug name	Food recommendation	Avoid	Possible side effects
Rifampicin	To be taken 1 hour before or 2 after food. 1 hour before antacids	Alcohol	Nausea, vomiting, appetite loss
Isoniazid	Taken 1 hour before or 2 hours after food. Give 10mg B6 daily	Alcohol	Interferes with
Ethambutol	May be taken with food	Avoid alcohol	
Streptomycin	Increase fluid intake		Taste changes, taste of food, nausea
Pyrazinamide	May be taken with food		
Ethionamide	Take with or after meals(Supplement with Vit B6)	Alcohol	Abdominal discomforts, nausea
Ofloxacin	Take 2hours before or after food	Antacids, milk products	
Kanamycin	Can be taken without regard to food		
Capreomycin	Increase fluid and foods intake rich in potassium(bananas, avocados)		
Para-aminosalicylic acid(PAS)	Take with or immediately after food. Increase fluid intake	Alcohol	
Cycloserine	Supplement with vitamin B6	Alcohol	

## **24.7.1 Nutrient Requirements and Dietary Management in TB, HIV and AIDS Patients**

### **Energy**

Most patients with chronic tuberculosis, HIV and AIDS are malnourished, energy needs are increased in order to minimize weight loss and achieve a desirable weight. An additional 300- 500 kcal (35 -40 kcal per ideal body weight) is recommended. This will help in protein sparing.

### **Protein**

An intake of 1.2- 1.5 g of protein per kg body weight is required to generate serum albumin levels per day, due to tissue wasting and repair of worn out tissues.

### **Fats/ oils**

These should provide 25-30% or less of the total energy requirements of an individual.

### **Vitamins and minerals**

The body should be provided with liberal amounts of vitamins and minerals. In TB conversion of beta carotene to retinol is affected in the intestinal mucosa. The client should be supplemented with vitamin A (as per the National Vitamin A supplementation schedule) and encouraged to eat vitamin A rich food. Patients on isoniazid should ideally be supplemented with 10mg of pyridoxine B6 daily since the drug inhibits its absorption. Additional amounts of vitamin C is recommended in the diet to facilitate healing of lesions. Other antioxidants (Vit A, C, and E, folic acid, zinc and selenium) neutralize free radicals and prevent the production of peroxides from lipids.

### **Water**

At least 8 glasses or more of safe drinking water per day

## **24.8 Dumping Syndrome.**

It is a rapid gastric emptying occurs when food especially sugar moves from stomach into small bowel too quickly.

### **Nutritional implications**

- Loss of nutrients
- Weight loss

### **Aims of nutrition management**

- Provide adequate calories and nutrients to support tissue healing
- Prevent weight loss
- Correct hypoglycaemia in the short term

### **Dietary Management**

After surgery the following should be done:

- All fluids and foods by mouth should be withheld for 3 to 5 days and the patient fed by nasogastric tube
- Ice chips should be held in mouth or small, infrequent sips of water should be given. Some people tolerate warm water better than ice chips or cold water
- Low carbohydrates, clear liquids such as soups, or diluted unsweetened fruit juices should be given and limited to ½ to 1 cup servings, however, at least 6 cups of fluids should be consumed daily to replace losses resulting from diarrhoea. Carbonated beverages and milk are not recommended in the initial stages of the diet
- The post-gastrectomy diet then begins with gradual progression to a general diet as tolerated. Bland foods should be started first, but a more important priority is offering the patient foods he/she likes and can tolerate. By the 5th to 7th day most patients can tolerate solid foods
- For persons near desirable body weight about 1.5g to 2g protein should be given (35Kcal to 45Kcal/kg)

- Pectin, a dietary fibre found in fruits and vegetables maybe helpful in treating dumping syndrome. Pectin delays gastric emptying, slow carbohydrate absorption and reduces glycemic response, though small dry meals are of more benefit
- Vitamin and mineral supplementation maybe necessary depending on the extent of surgery and whether the symptoms of dumping syndrome persist
- Generally, liquids are served between meals rather than with meals to slow the passage of the food mass. Limit simple carbohydrates
- Lie down immediately after eating to help slow the transit of food to the intestines. Clients who experience reflux should not lie down after eating. Beware that lactose intolerance may develop and produce discomfort in relation to milk and milk products.

## **24.9 Dietary Management in Diabetes Mellitus**

There are two main types of diabetes mellitus; Type I and Type II

### **Type I**

Usually under 30 years but can present at any age, present acutely, with weight loss and ketonuria: treated with diet and insulin.

### **Type II**

Usually over 30 years, insidious onset, frequently obese: treated with diet and oral anti-diabetic agents. 40% will eventually require insulin treatment.

Dietary control and weight loss plays an important part in the management of diabetes mellitus. Many **Type II** diabetics are overweight. Reducing body weight through careful control of energy intake and physical activity like walking helps to control the symptoms.

### **General eating guidance when on Insulin:**

- In **Type I** diabetes, when initiating treatment, the starting dose of insulin is **0.5-1.0units /kg/day**. Doses should be given about 30 minutes before meals.
- Ideally a “**basal/bolus**” **regimen** should be used where basal (intermediate acting) insulin is taken at bedtime and 6-8u of soluble insulin (bolus) taken 3 times a day before meals. This regimen allows more flexibility with meals as the soluble insulin dose can be varied according to what is to be eaten and can be given at different times.
- Self-monitoring of blood glucose is recommended (range 5-7mmol/litre), and the patient can be taught to adjust doses appropriately based on results.
- Insulin treatment often leads to weight gain; hence patients need to follow a healthy diet and it is recommended that patients should not change dietary and medicine regimens simultaneously.
- Select an insulin schedule best suited to the individual patient's eating pattern, physical activity and general lifestyle.

### **Diabetic Diet**

Dietician should calculate dietary requirements for individual patients in order to reduce the blood sugar to normal and to maintain a constant blood sugar level.

- 45-50% of energy intake should be in the form of complex carbohydrates than simple sugars with adequate intake of fibers.
- Carbohydrates and calories should be taken in equal portions through the day with addition of snacks between meals.
- Alcohol is NOT RECOMMENDED in Diabetics as it can induce low blood sugars.
- Avoid intake of sugar and sugar-containing food/drinks with the exception of patient feels faint or is ill and cannot eat normally.
- Encouraged exercise and a snack should be taken before and after playing sport.
- Encourage take of other balanced group of foods at right proportion as per individual patients' dosage regimen.
- Encourage change of life style and regular general body check-up such eyes and oral dental care

## 24.10 Nutrition Care and Support in the Intensive Care

The goal of nutrition management is to preserve lean body mass

### Oral Nutrition Supplement

Oral nutritional supplements (ONS) should be used whenever possible to meet patient's needs, when dietary counseling and food fortification are not sufficient to increase dietary intake and reach nutritional goals.

### Enteral and Parenteral Nutrition

Where nutritional requirements cannot be met orally or, expected to be impossible >3 days or expected to be below half of energy requirements for >1 week, enteral nutrition (EN) should be administered.

This should be assessed on a case-by-case basis and the long-term impact of nutrition deficit considered.

### Parenteral nutrition (PN)

Parenteral nutrition (PN) should be considered when EN is not indicated or unable to reach targets over 3-7 days despite use of appropriate management strategies, and calorie and protein delivery is consistently <50% of prescribed targets.

Supplemental PN should be considered after other measures to improve EN have been attempted or insertion of a post-pyloric enteral feeding tube is deemed unsafe and calorie and protein intake remain significantly less than prescribed targets (i.e. <50% over a 3-7day period)

**Table 24.10 Oral Nutrition Supplements**

Drinks					
Name	Amount	Calorie s	Protein	Indication	Contraindications
Fresubin drink 2kcal	200mls	400kcal	20g	<ul style="list-style-type: none"><li>Inadequate intake of meals</li><li>Chronic wasting</li><li>Liver disease</li></ul>	<ul style="list-style-type: none"><li>Not suitable for children &lt;3yrs</li><li>Use with caution in children &lt; 6yrs</li><li>Not suitable in patients with galactosemia</li></ul>
Supportan drink	200mls	300kcal	20g	<ul style="list-style-type: none"><li>Oncology</li><li>Cachexia</li><li>Acute or chronic respiratory conditions</li><li>Immuno compromised</li></ul>	<ul style="list-style-type: none"><li>Not suitable for children &lt;3yrs</li><li>Use with caution in children &lt; 6yrs</li><li>Not suitable in patients with galactosemia</li></ul>
Diben drink	200mls	300kcal	20g	For diabetic patients <ul style="list-style-type: none"><li>-Hyperglycemia</li><li>- insulin resistance</li><li>- Impaired glucose tolerance</li></ul>	<ul style="list-style-type: none"><li>Not suitable for children &lt;3yrs</li><li>Use with caution in children &lt; 6yrs</li></ul> <p>Not suitable in patients with galactosemia</p>
Powder formulae					
Lifegain nutrition supplement (sachet)	30g	120	15g	For building and regaining strength  Note: To be used with caution to diabetic patients	<ul style="list-style-type: none"><li>Not suitable for children &lt;12yrs</li><li>Not suitable for patients with soy or milk protein allergy</li></ul>
Maxvida	30g	122	4	Adults	<ul style="list-style-type: none"><li></li></ul>

Groviva	30g			Children 2yrs and above	•
Vidavance	30g			Diabetic	•

**Table 24.11 Enteral feeds**

Type of enteral feeds	Calories / 100mls	Protein / 100mls	Indications	Contraindications
Supportan	150 kcal	10g	<ul style="list-style-type: none"> <li>• Cancer</li> <li>• Cachexia</li> <li>• Chronic wasting diseases</li> <li>• Immuno-compromised</li> <li>• Ventilated patients</li> <li>• Electrolyte abnormalities</li> <li>• Fluid restrictions</li> </ul>	<ul style="list-style-type: none"> <li>• Not suitable for children &lt; 1yrs</li> <li>• Use with caution in children &lt; 6yrs</li> <li>• Not suitable in patients with galactosemia</li> </ul>
Survimed OPD HN	133 kcal	6.7g	<ul style="list-style-type: none"> <li>• Malabsorption,</li> <li>• Pre-operative preparation of patients who are undernourished,</li> <li>• Patients with proven inflammatory bowel disease,</li> <li>• Following total gastrectomy,</li> <li>• Haemodialysis,</li> <li>• Disease related malnutrition.</li> <li>• After long term parenteral nutrition</li> </ul>	<ul style="list-style-type: none"> <li>• Not suitable for children &lt;3yrs</li> <li>• Use with caution in children &lt; 6yrs</li> <li>• Not suitable in patients with galactosemia</li> </ul>
Diben	105 kcal	4.5g	<ul style="list-style-type: none"> <li>• Impaired glucose tolerance</li> <li>• Insulin resistance</li> <li>• Diabetes mellitus</li> <li>• Hyperglycaemia</li> </ul>	<ul style="list-style-type: none"> <li>• Not suitable for children &lt;3yrs</li> <li>• Use with caution in children &lt; 6yrs</li> <li>• Not suitable in patients with galactosemia</li> </ul>
Fresubin Original	100kcal	3.8g	<ul style="list-style-type: none"> <li>• Anorexia</li> <li>• Convalescence</li> <li>• Low residue tube feed</li> <li>• Jejunostomy</li> </ul>	<ul style="list-style-type: none"> <li>• Not suitable for children &lt;3yrs</li> <li>• Use with caution in children &lt; 6yrs</li> <li>• Not suitable in patients with galactosemia</li> </ul>
Fresubin Original Fibre	100 kcal	3.8g	<ul style="list-style-type: none"> <li>• Long term tube feeding</li> <li>• Anorexia</li> <li>• Convalescence</li> </ul>	<ul style="list-style-type: none"> <li>• Not suitable for children &lt;3yrs</li> <li>• Use with caution in children &lt; 6yrs</li> <li>• Not suitable in patients with galactosemia</li> </ul>

# CHAPTER TWENTY-FIVE

## POISONING

Poison is any substance (liquid, solid, gas), that is harmful to the body, when ingested, inhaled, injected or absorbed through the skin. There is a variability of the clinical presentation and poisonings vary by nature of poison, victims' age group, intention, geographic region, and level of economic development. Poisons can be classified according to whether the chemical is metallic versus nonmetallic, organic versus inorganic, or acidic versus alkaline.

### 25.1 Common Poisons

The common poisoning in our setting are:

- Household agents:
  - Organophosphate e.g malathion (insecticide)
  - Pesticides - nuvan top, rat poison, hydrocarbons e.g kerosene
  - Disinfectants and bleach
- Medicines – Acetylsalicylic Acid, Paracetamol, Anticonvulsants (carbamazepine), Hematinic (Iron and Vitamins),
- Major tranquilizers and herbal products
- Foods-eg Mushroom, infected foods

### 25.2 General Principles of Management of Poisoning

In managing a patient who has been exposed to toxins holistic approach should be considered. These include.

#### Resuscitation and stabilization

- Airway, breathing and circulation should be reassessed and treated accordingly as a priority. Refer Approach to patient with Emergency conditions chapter.

#### Note

- A low respiratory rate with decreased oxygen saturations may indicate *hypoventilation*. A normal saturation does not exclude *hypercarbia* or indeed *hypoxia* in carbon monoxide poisoning. If in any doubt, arterial blood gases should be measured. *Tachypnoea* can be seen with metabolic acidosis (e.g. tricyclics, methanol), *anxiety*, and *stimulant drug overdose* and as an early feature of salicylate poisoning (respiratory alkalosis).
- Supplementary oxygen via facemask should be given to all patients initially, taking account of *pulse oximetry* (noting the limitations described above).
- Many drugs exhibit *cardiovascular toxicity hypotension* and or *cardiac arrhythmias* in overdose (e.g. tricyclics, b-blockers, digoxin, lithium). ECG should be recorded, intravenous access established and initial fluid resuscitation given as appropriate
- General examination may give corroborating evidence of significant ingestions or clues in unknown overdoses (SSRIs, tricyclics, phenothiazines) have *serotonergic* or *anticholinergic* effects with pupil dilatation, and extrapyramidal movements, whilst opioid type drugs will cause sedation and pin point pupils.
- Temperature, blood glucose (low in b-blocker, ethanol poisoning)
- Weight is important in identifying a toxic dose against the weight and may guide treatment, for example in paracetamol overdose.
- Examination for injury (intentional or un-intentional self-harm) suggest appropriate methods for treatment, or the presence of other substances such as alcohol.
- If clinical condition allows, an assessment of the patient's mental state should be made.

Use the tabulated Toxidromes to identify toxins and apply the antidotes

**Table 25.1 Common Toxidromes to help identification of toxins.**

Toxidrome s	Mental status	Pupils	Vitals	Other manifest ations	Examples of toxic agents
Sympathomimetic	Hyper alert, agitation, hallucination, paranoia, Anxiety / Delirium	Mydriasis	Hyperthermia, tachycardia, hypertension, widened pulse pressure	Diaphoresis, tremors, hyperreflexia, seizures, Hyperpyrexia	Cocaine, amphetamines, ephedrine, theophylline, caffeine, phencyclidine (PCP), Lysergic acid (LSD) Withdrawal from narcotics, benzodiazepine, alcohol, long term beta-blocker therapy
Cholinergic	Confusion, drowsiness, Comma, Headache, Insomnia, Giddiness,	Miosis,	Bradycardia, Hypotension tachypnea, hypotension, bradypnea Hypothemia,	Salivation Urinary incontinence Defaecation Gastric cramping, hypermotility Emesis, Diaphoresis, lacrimation, GI cramps, bronchospasm, muscle fasciculations and weakness , seizures	Organophosphate and carbamate insecticides, nerve agents, nicotine, physostigmine, edrophonium
Anticholinergic	Agitation, hallucinations, delirium, coma	Mydriasis	Hyperthermia, tachycardia, hypertension, tachypnea	Dry flush skin, dry mucous membranes, decreased bowel sounds, urinary retention, myoclonus	Antihistamines, TCA, antiparkinsonism agents, atropine, antispasmodics
Hallucinogenic	Hallucinations, perceptual distortions, depersonalization, agitation	Mydriasis (usually)	Hyperthermia, tachycardia, hypertension, tachypnea	Nystagmus	Phencyclidine, MDMA, MDEA
Opioid	CNS depression, coma	Miosis	Bradypnea, apnea	Hyporeflexia, pulmonary edema, needle marks	Heroin, morphine, methadone, diphenoxylate

Sedative-hypnotic	CNS depression, confusion, stupor, coma	Variable	Often normal; hypothermia, bradycardia, hypotension, bradypnea, apnea	Hyporeflexia	Benzodiazepines, barbiturates, alcohols, zolpidem
Serotonin syndrome	Confusion, agitation, coma	Mydriasis	Hyperthermia, tachycardia, hypertension, tachypnea	Tremors, myoclonus, hyperreflexia, clonus, diaphoresis, flushing, trismus, rigidity, diarrhea	MAOIs, SSRIs, meperidine, dextromethorphan, TCA

**Note:**PCP, Phencyclidine; LSD Lysergic acid; TCA, tricyclic antidepressant; MDMA, 3,4-methylenedioxymethamphetamine; MDEA, methylenedioxymethamphetamine; CNS, central nervous system; GI, gastrointestinal; MAOI, monoamine oxidase inhibitor; SSRI, selective serotonin reuptake inhibitor,

**Table 25.2 Toxins causing Dysrhythmias**

Heart rate	Narrow QRS	Wide QRS
Tachycardia	Amphetamines	Antihistamines
	Anticholinergic agents	Cocaine
	Theophylline	Propoxyphene, Sodium channel blockers and Tricyclic antidepressants
Bradycardia	α-Adrenergic lytic agents	β-Adrenergic blocking agents
	β-Adrenergic blocking agents, Calcium channel antagonists, Cardiac glycosides, Class Ia antiarrhythmics And Sodium channel blockers	Calcium channel antagonists

**Note**

- For patients presenting with cardiac problems, consider reading ECG and use the table below to interpret possible causes;

## 25.2.1 Management Protocol of a poison (specific and non-specific antidotes)

### Investigations

The toxicomes are created to assist diagnosis. History may be inaccurate and hence the following laboratory tests should usually be obtained for guidance:

- Complete blood count
- Liver function test
- Serum lactate
- Arterial blood gas
- Electrocardiogram
- Urine pregnancy test in all women of childbearing age
- Basic serum electrolytes, blood urea nitrogen (BUN), and creatinine

**Sympathomimetics investigations** - RBG-bedside, ECG, Serum electrolytes and Renal function test, Liver function test, Creatinine kinase, Clotting screen: PT/PTT/INR, Full Blood Count, Arterial blood gas, Serum osmolality and osmolality gap.

Abdominal X-ray may be useful in diagnosing.

**Cholinergic investigations** - Glucose, BUN, Electrolytes, Prothrombin time, Liver function test, Cholinesterase measurements

Measurement of drug or toxin concentrations in body fluids is not required in most poisonings, but in some exposures, it does influence management. The list of drug concentrations that may assist patient assessment and management are shown here;

**Table 25.3: List of drugs or toxins requiring measurement of drug concentrations.**

Paracetamol	Methanol
Carbamazepine	Methotrexate
Carbon monoxide	Organophosphorus
Digoxin	Paraquat
Ethanol	Phenobarbital
Ethylene glycol	Phenytoin
Iron	Salicylate
Lithium	Theophylline
Methemoglobin	Valproic acid

**Table 25.4: Supportive Care**

Toxic Feature	Methods to reach Diagnosis	Immediate Stabilization	Definitive Management
Signs of COPD	H&P, CXR	O2, NIPPV	Bronchodilators, steroids
Pulmonary edema	H&P, CXR, pro-BNP	O2, NIPPV	Nitrates, diuretics
Pulmonary embolism	H&P, d-dimer, chest CT	O2	Anticoagulation, thrombolysis (massive PE only)
Acute respiratory distress syndrome	H&P, CXR	O2, NIPPV	Ventilatory support
Myocardial infarction	H&P, ECG	O2, nitrates, aspirin, anticoagulation	Revascularization (thrombolysis or PCI)
Metabolic acidosis	H&P, metabolic panel, blood gas	O2	Directed at underlying cause

### Psychosocial Intervention

- The investigations depend on the poison ingested:
- If the toxin cannot be identified, then toxicodrome (signs and symptoms) can be used

## 25.2.2 Management of Ingested Poisons

Ingested toxins are suspected in any patient with signs and symptoms irrespective of reported dose ingested

### Clinical Presentations

- General clinical features: Nausea, vomiting, drowsiness, blurred vision, and dizziness
- Central Nervous System toxicity: Altered level of consciousness, convulsions, acute confusion and coma,
- Renal Toxicity: Acute kidney injury/failure and papillary necrosis
- Metabolic derangement: Metabolic acidosis, respiratory acidosis, hypoglycemia.
- Allergic reactions: Urticaria, angioedema, anaphylaxis
- Haematological toxicity: Aplastic anaemia, agranulocytosis

### Non-pharmacological Treatment

Gastric decontamination - practice of functionally removing an ingested toxin from the gastrointestinal (GI) tract in order to decrease its absorption it includes gastric evacuation (forced emesis or gastric lavage), intra-gastric binding (most commonly by single or multidose activated charcoal), or speeding transit of toxins to decrease total absorption time (whole bowel irrigation or cathartics). GI decontamination is most likely to benefit patients who present for care soon after ingestion (usually within one to two hours).

- Gastric Lavage
- General care: Keep the patient under observation 4–24 hours depending on the poison swallowed.

### Contraindications to Gastric Lavage:

- An unprotected airway in an unconscious patient
- Ingestion of corrosives or petroleum products e.g. kerosene
- Bowel obstruction

- Bowel perforation
- GI bleeding
- Identify the specific agent and remove or adsorb it as soon as possible.

#### Note

- Treatment is most effective if given as quickly as possible after the poisoning event, ideally within 1 hour.
- If the patient has swallowed kerosene, petrol, or petrol-based products (note that most pesticides are in petrol-based solvents) or if the patient's mouth and throat have been burned (for example with bleach, toilet cleaner or battery acid) do not vomit the patient but give water orally? Never use salt as an emetic as this can be fatal.

#### Pharmacological Treatment

**A:** activated charcoal (PO) single dose (if available) within one hour of ingestion and do not induce vomiting; given by mouth or NG tube according to the dosage below:

Dose:  
Children below one year: 1g/kg  
Children 1-12 years of age: 25–50g  
Adolescents and adults: 25–100g

**A:** compound sodium lactate or 0.9% sodium chloride (IV) 30ml/kg 2liters for 24hours if Shock is present

#### Note

Toxins for which multiple doses of activated charcoal are indicated includes Carbamazepine, Dapsone, Digoxin, Paraquat, Phenobarbitone, Quinine, Slow-release preparations such as theophylline, Amanita phalloides fungus, Multiple doses may also be considered in life threatening overdose of other drugs (e.g. tricyclic antidepressants).

Content mixing:

- Mix the charcoal in 8–10 times the amount of water, e.g. 5g in 40 ml of water.
- If possible, give the whole amount at once; if the child has difficulty in tolerating it, the charcoal dose can be divided.
- If charcoal is not available, then induce vomiting but only if the patient is conscious by rubbing the back of the patient throat with a spatula or spoon handle;

**Referral:** Consider transferring patient to next referral level hospital, where this can be done safely, if the patient is:

- |  |                 |
|--|-----------------|
| • Unconscious or deteriorating conscious level | • Cyanosed      |
| • Burns to mouth and throat                    | • Heart failure |
| • Severe respiratory distress                  |                 |

### 25.2.3 Food Poisoning

Food poisoning, also called foodborne illness, is illness caused by eating contaminated food. Infectious organisms — including bacteria, viruses, and parasites — or their toxins are the most common causes of food poisoning as listed in the table. Large intestine and small intestine have an intermediate incubation from about 1 to 3 days.

#### Large intestine

Infections of the large intestine or colon can cause bloody, mucousy diarrhea associated with crampy abdominal pain.

- *Campylobacter spp.* is the common one cause of food-borne disease
- *Shigella spp.* contaminate food and water and cause dysentery (severe diarrhea often containing mucus and blood).
- *Salmonella spp.* infections often occur because of poorly or undercooked cooked and/or poor handling of the chicken and eggs. In individuals with weakened immune systems, including the elderly, the infection can enter the bloodstream and cause potentially life-threatening infections.
- *Vibrio parahaemolyticus* can contaminate saltwater shellfish and cause a watery diarrhea.

## **Small Intestine Infection**

Diarrhea due to small bowel infection tends not to be bloody, but infections may affect both the small and large intestine at the same time.

- *E. coli* (enterotoxigenic) is the most common cause of traveler's diarrhea. It lacks symptoms such as fever or bloody diarrhea.
- *Vibrio cholerae*, often from contaminated drinking water produces a voluminous watery diarrhea resembling rice-water.
- Viruses such as Norwalk, rotavirus and adenovirus tend to have other symptoms associated with an infection including fever, chills, headache, and vomiting.
- Botulism is caused by *Clostridium botulinum* toxin and may present with fever, vomiting, mild diarrhea, numbness, and weakness leading to paralysis.

## **Pharmacological Treatment**

Adult:

**A:** 0.9% sodium chloride 30mL every 30minutes; not to exceed 8-10doses  
**AND**

**C:** loratadine 10mg (PO) 24hourly

Children 2 to 5 years:

**A:** 0.9% sodium chloride 7.5-15mL every 30minutes; not to exceed 8-10doses  
**AND**

**C:** loratadine 5mg (PO) 24hourly  
**AND**

*Antibiotics based on the infection suspected.*

### **25.2.4 Herbal Poisoning**

#### **Investigations**

- Basic blood count, renal function, liver function, and electrocardiogram
- Heavy metal screening if suspected or if symptoms are non-specific
- Analysis methods exist for some herbal toxins only—Colchicines (HPLC, GCMS), tropane alkaloids (GCMS, oxalate (GCMS), vinca alkaloids (HPLC), cardioactive steroids (immunoassay)—check with local laboratory

**Table 25.5 Organ Toxicities and Toxidromes, and Common Dietary Supplements or Herbal Medicines that can cause them**

Clinical features	Xenobiotics
Cardiac	Sodium channel effects— <i>Aconitum</i> species (widen QRS, shock)
	Digoxin-like effects— <i>Digitalis</i> species, bufo toads
Central nervous system	Seizures—strychnine, thujone, essential oils (camphor, eucalyptus)
	Sedation— <i>Valeriana</i> species, kava kava
Dermatological	Blistering—cantharidin (Chinese blister beetle)
Hematological	Coagulopathies—G-herbs (ginger, garlic, gingko)
	Agranulocytosis—anti-mitotic agents (colchicine, podophyllotoxin)
Hepatotoxic	Hepatitis—multiple agents, germander commonly reported
	Veno-occlusive disease—pyrrolizidine alkaloids (comfrey, <i>Senecio</i> species, <i>Heliotropium</i> species)
Nephrotoxic	Renal failure— <i>Aristolochia</i> species
	Hypertension, hyperkalemia—licorice
Anticholinergic	<i>Datura metel</i> commonly used in TCM
	Hexing herbs ( <i>Atropa</i> species, <i>Hyoscyamus</i> species, <i>Mandrago officinarum</i> ) common in Western herbal practice
Sympathomimetic	<i>Ephedra</i> species, <i>Citrus aurantium</i> (bitter orange)
Salicylate poisoning	Willow bark, checkerberry

## **Non-Pharmacological Treatment**

- Ask specifically regarding the use of such products and a matched clinical feature using the above Toxicodrome
- Secure sample for identification
  - Actual herbs or product used
  - Prescription or packaging
- Good resuscitative, symptomatic, and supportive care
- Instruct patients and family to stop using the product
- Consider outpatient monitoring of renal function, liver function, and blood counts
- Report case to regulating authority
- Report unusual cases to National Poison Control Center

## **Pharmacological Treatment**

Use antidote if appropriate, activated charcoal can be given in an acute overdose of toxic dietary supplements and herbal medicines if there is adequate airway protection. Give:

**A:** compound sodium lactate or 0.9% sodium chloride (IV) 30ml/kg 2liters for 24hours if shock is present

### **25.2.5 Management of Skin Contamination**

- Remove all clothing and personal effects and thoroughly flush all exposed areas with copious amounts of running water running for:
  - 5-minutes for non-irritants or mild irritants
  - 15-20 minutes for moderate to severe irritants and chemicals that cause acute toxicity if absorbed through the skin
  - 30 minutes for most corrosives
  - 60 minutes for strong alkalis (e.g., sodium, potassium or calcium hydroxide)
- Use non-abrasive soapand water for oily substances
- Attending staff should take care to protect themselves from secondary contamination by wearing gloves and apron
- Removed clothing and personal effects should be stored safely in a see-through plastic bag that can be sealed, for later cleansing or disposal.

### **25.2.6 Management of Eye Contamination**

Rinse the eye for with clean running water for 15-20 minutes, taking care that the run-off does not enter the other eye.

- tetracaine hydrochloride 1-2drops into affected eye will assist irrigation. Evert the eyelids and ensure that all surfaces are rinsed.
- In the case of an acid or alkali irrigate for 30 minutes and review for possible next 30 minutes
- Where possible, the eye should be thoroughly examined under fluorescein staining for signs of corneal damage.
- If there is significant conjunctival or corneal damage, the patient should be seen urgently by an ophthalmologist.
- Refer when further eye evaluation cannot be performed.

### **25.2.7 Management of Inhaled Poisoning**

- Move the patient to the fresh air immediately. Victims to stay away from all toxic fumes and gases.
- Thoroughly ventilate the involved area

Administer supplemental oxygen if cyanosis or difficulty in breathing

- Mild distress/ hypoxia gives 24–40% oxygen at a flow rate of 2–6 L/min (LPM), (nasal canula)
- Moderate distress/ hypoxia gives 24–50% oxygen at a variable flow of 6 -10 L/min (Face mask / Venture mask)
- Severe distress/ hypoxia gives 50–90% oxygen at 10-15L/min (Non-rebreather Mask / face mask with reservoir bag)
- Apnea give nearly 100% oxygen at 10-15L/min (Bag valve Mask “BVM” device)

Oxygen flow should be moderated to achieve oxygen saturation levels, based on pulse oximetry (with a target level of 94–96% in most, or 88–92% in people with COPD)

Apply Cardiopulmonary resuscitation (CPR) if there are signs of cardiac arrest

Inhalation of irritant gases may cause swelling and upper airway obstruction, bronchospasm and delayed pneumonitis.

Intubation and provision of for bronchodilators;

**A:** salbutamol 4mg (PO) 6-8hourly

**OR**

**A:** adrenaline **B:** ephedrine (SC/MI) 25-50mg or (IV) 5-25mg slowly, repeated in 5-10 minutes, if necessary

**OR**

**C:** salmeterol (inhalation)

**AND**

12 ≥ years old give,

**S:** ipratropium bromide (inhalation) 250-500micrograms 6-8hourly daily maximum dose of 2mg.

6 to 12 years give,

**S:** ipratropium bromide (inhalation) 250micrograms 6-8hourly, maximum daily dose of 1mg

0-5 years give,

**S:** ipratropium bromide (inhalation) 125-250micrograms 6-8hourly, maximum daily dose 1mg

## 25.3 Specific poisons

### 25.3.1 Corrosive Compounds Poisoning

Examples — Sodium hydroxide (Soaps-drain/oven cleaners), potassium hydroxide, acids, bleaches or disinfectants.

#### Non-Pharmacological Treatment

- Give 1Litre of water as soon as possible, beneficial within 30minutes.
- Give oxygen therapy at concentrations of 2–6litres per minute (LPM), 40–70% oxygen (face mask with reservoir bag)

#### Surgical review

- Arrange for surgical review to check for:
  - Esophageal damage/rupture, if severe.
  - Perforation, mediastinitis and peritonitis if suspected

#### Note

Do not induce vomiting or use activated charcoal

### 25.3.2 Petroleum Compounds Poisoning

Examples—Kerosene, Turpentine substitutes and petrol

#### Clinical Presentation:

- GIT-abdominal pain, bloody stool, vomiting
- RS-Throat swelling, pneumonitis and/or pulmonary oedema-cough, tachypnea, cyanosis, crepitation and rhonchi
- CNS-Headache, dizziness, euphoria, restlessness, ataxia, convulsion, encephalopathy and coma

#### Non-pharmacological Treatment

- Remove the patient from source
- Remove contaminated cloth and thoroughly wash the skin with soap and water
- Give supplemental oxygen 2–6litres per minute (LPM), delivering a concentration of 24–40% oxygen (nasal cannula) or 28–50% oxygen (face mask) 40–70% oxygen (face mask with reservoir bag)
- Oxygen flow should be moderated to achieve oxygen saturation levels, based on pulse oximetry (with a target level of 94–96% in most, or 88–92% in people with COPD)
- If large amount of petroleum compound has been ingested less than an hour earlier lavage may be considered and the patient should be intubated

#### Note

Do not induce vomiting or use activated charcoal

## **Kerosene (Paraffin) Poisoning**

There is a higher risk of kerosene poisoning among children. The respiratory system is the main target organ affected. Pneumonia is in most cases interstitial and bilateral. Vomiting after hydrocarbon ingestion is related to the rate of development of pneumonia; Symptoms of CNS impairment correlated with hypoxemia, pneumonia, and fever.

### **Non-pharmacological Treatment**

- Immediately remove the child from the source of the poisoning and ensure the airway is open (this is always the first priority).
- Remove contaminated clothing and thoroughly wash the skin with soap and water.
- If possible, perform pulse oximetry and give supplemental oxygen if indicated. Intubation and mechanical ventilation may be needed in a patient with severe hypoxia, respiratory distress or decreased consciousness.
- Avoid gastric lavage because of the risk of inhalation and hence pneumonitis. If very large amounts of kerosene have been ingested less than an hour earlier then lavage may be considered if the airway can be protected by expert intubation.

### **Pharmacological Treatment,**

**A:** compound sodium Lactate **OR** 0.9% sodium chloride (IV) 30ml/kg 2liters for 24hours if Shock is present

#### **Note**

There is no evidence that corticosteroids are helpful in kerosene poisoning

## **25.3.3 Organophosphorus and Carbamate Compounds Poisoning**

Organophosphates and carbamates are common insecticides that inhibit cholinesterase activity, causing acute muscarinic manifestations (e.g., salivation, lacrimation, urination, diarrhea, emesis, bronchorrhea, bronchospasm, bradycardia, miosis) and some nicotinic symptoms, including muscle fasciculation and weakness.

These can be absorbed through the skin, ingested or inhaled. Examples:

- Organophosphorus – Malathion, Parathion, Tetraethyl Pyrophosphate (TEPP), mevinphos and
- Carbamates – methiocarb and carbaryl.

### **Clinical presentations**

- Vomiting, diarrhoea, blurred vision or weakness.
- Signs of excess parasympathetic activation: salivation, sweating, lacrimation, slow pulse, small pupils, convulsions, muscle weakness/twitching, then paralysis and loss of bladder control, pulmonary oedema, and respiratory depression.

### **Non-pharmacological Treatment**

- Remove poison by irrigating eye or washing skin (if in eye or on skin)
- Give activated charcoal if ingested and within 1 hour of the ingestion.
- Do not induce vomiting because most pesticides are in petrol-based solvents.
- In a serious ingestion where activated charcoal cannot be given, consider careful aspiration of stomach contents by NG tube (the airway should be protected).
- Auscultate the chest for signs of respiratory secretions and monitor respiratory rate, heart rate and coma score (if appropriate)
- Give oxygen saturation is less than 90%

### **Pharmacological Treatment**

If there are signs of excess parasympathetic activation (see above) give:

**A:** atropine (IV) boluses of 5mg

- Repeat every 10minutes until satisfactory atropinization (i.e. no chest signs of secretions, HR>80b/min, Systolic BP >80mmHg, pupils no longer pinpoint, Dry axillae)
- Paediatric patient can start at 0.05mg/kg, then double the dose every five minutes, stop doubling the dose when parameters have improved.

If muscle weakness gives:

**S:** pralidoxime (IV) (cholinesterase reactivator) 50mg/kg diluted with 15ml water by infusion over 30 minutes

- Repeated once to twice.
- Followed by 10–20 mg/kg/hour, as necessary.

If other organophosphates are identified, the following table can be used:

**Table 25.6 List of common Pesticides and Chemical Poisons with their antidotes**

Group	Poisons	Antidote
Agricultural pesticides	Organophosphates	
	Malathion, Acephate, Dichlorvos, Dimethoate, Fenitrothion, Monocrotophos, Phorate,	atropine sulfate <b>A:</b> 2mg (IM) mid-lateral outer thigh
	Quinalphos	pralidoxime <b>S:</b> 1-2g IV infusion (10-20 mg/mL) over 15-30min, repeat in 1hr if necessary and repeat 12hourly thereafter PRN; administer 30 mg/kg IV (IM, SC if no IV access) over 20 min; follow by 4-8 mg/kg/hour maintenance IV infusion
	Carbamates; propoxur, Aldicarb, Carbaryl, Carbofuran, Methomyl	pralidoxime <b>S:</b> 1-2g (IV) infusion (10-20 mg/mL) over 15-30min, repeat in 1 hour if necessary and repeat q12hr thereafter PRN; administer 30 mg/kg (IV) (IM, SC if no IV access) over 20 min; follow by 4-8 mg/kg/hour maintenance (IV) infusion
Industrial chemicals	Organochlorines; Endosulfan, Gamma benzene hexachloride, Heptachlor, Chlordane Rodenticides	cholestyramine <b>S:</b> 4g (PO) 12-24hourly; increase gradually over ≥1month intervals Maintenance: 8-16 g/day (PO) divided 12hourly; not to exceed 24g/day
	Cholestyramine bromadiolone	vitamin K <b>Adults</b> <b>A:</b> Vitamin K (PO/SC) 2.5-10mg; may be increased PRN to 25 mg or, rarely, to 50 mg; may be repeated in 12-48 hours <b>Newborn</b> <b>A:</b> Vitamin K (IM) 0.5-1mg within 1hour of birth
	Arsenic	D-Penicillamine <b>B:</b> Give D-penicillamine (PO) 30-40mg/kg/day 1-6months, 2hours before or three hours after dimercaprol <b>D:</b> dimercaprol (IM) 3mg/kg deep 4hourly for 48hours followed by 3mg/kg 12hourly for 10days
	Methyl alcohol	<ul style="list-style-type: none"> <li>• Ethanol</li> <li>• Loading dose 600 mg/kg (IV) (i.e., 7.6mL/kg of 10% EtOH solution) 600-700mg/kg oral/nasogastric (NG) using a 95% solution diluted to 20% or less with water or juice.</li> <li>• Oral maintenance of 0.15 mL/kg/hour (IV = 1.4 mL/kg/hour)</li> <li>• 10% ethanol.</li> </ul>
	Ethylene glycol	folic acid/ folinic acid <b>S:</b> folinic acid 60mg (IM) over 12-24 hours stat, then 15mg (PO) 8hourly for 48 to 72 hours Ethanol <ul style="list-style-type: none"> <li>• Loading dose 600 mg/kg intravenous (IV) (i.e., 7.6 mL/kg of 10% EtOH solution)</li> <li>• 600-700 mg/kg oral/nasogastric (NG) using a 95% solution diluted to 20% or less with water or juice Oral maintenance of 0.15 mL/kg/hour (IV = 1.4</li> </ul>

		mL/kg/hour) 10% ethanol
		pyridoxine hydrochloride <b>B:</b> 10-25 mg (PO) 8 hourly then observe in 6 hours
		folinic acid • <b>S:</b> Loading dose 600 mg/kg intravenous (IV) (i.e., 7.6 mL/kg of 10% EtOH solution) • 600-700 mg/kg oral/nasogastric (NG) using a 95% solution diluted to 20% or less with water or juice <b>S:</b> Oral maintenance of 0.15 mL/kg/hour (IV = 1.4 mL/kg/hour) 10% ethanol
		thiamine <b>C:</b> 100 mg IV; then 50-100 mg/day IM or IV; then IM: 5-30 mg three times daily (if critically ill); then 5-30 mg three times daily for 1 month
	Cyanide	
		hydroxocobalamin <b>C:</b> 70 mg/kg (usually 5 g) (IV) infusion over 15 minutes; additional 5 g (IV) may be given depending on severity of poisoning and clinical response
	Methemoglobinemia producing agents (nitrites, nitrates, dapsone, copper, aniline, chlorates, naphthalene)	methylene blue <b>C:</b> 1 mg/kg (IV) over 5-30 minutes If Methemoglobin level remains >30% or if clinical symptoms persist, repeat dose up to 1 mg/kg 1hour after the first dose
Drugs	Acetaminophen	N-Acetylcysteine <b>C:</b> 140 mg/kg of <i>N</i> -acetyl cysteine at first, followed by 70mg/kg every 4 hours for 3days or until acetaminophen is no longer detected in the blood
	Iron	deferoxamine <b>D:</b> 1g (IM) initially and then 500mg 8hourly for 48hours
	Benzodiazepines	flumazenil <b>A:</b> 0.2 mg (IV) for 15seconds then 0.1mg for 60second intervals, till consciousness is restored. Maintain 0.3 and 0.6 mg depending on the patient's characteristics and the benzodiazepine used
	Opioids	naloxone <b>B:</b> 0.4 mg to 2mg (PO) depending on amount of opioid taken, then repeat in 2 to 3minutes
	Isoniazid	pyridoxine <b>B:</b> 10-25 mg (PO) 8hourly for 48hours
	Digoxin	digoxin-specific antibodies <b>S:</b> Each vial of DigiFab (40 mg of Fab) binds 0.5mg digoxin. Equimolar dose to ingested digoxin (76/80 mg FAB = 1 mg digoxin)
Environmental toxins	Datura	physostigmine <b>S:</b> 0.5-2mg slow IVP (not to exceed 1 mg/min); keep atropine nearby for immediate use If no response, repeat after 20min PRN If initial dose effective, may give additional 1-4mg q30-60min PRN
	Snake bites	Anti-snake venom <b>A:</b> Anti-snake venom (ASV)- Polyvalent For Mild Degree of envenomation give 5 vials (50 ml) For Moderate Degree of envenomation give 5-10 vials (50-100 ml)

		For Severe Degree of envenomation give 10–20 vials (100–200 ml)
Dog bite		Anti-rabies Immunoglobulins <b>A:</b> Anti-rabies human immunoglobulin 20 IU/kg half the dose given parenterally and the other half injected into and around the wound for victims suspected to be infected
Botulism		Botulinum antitoxin <b>S:</b> Administer slowly by (IV) infusion via volumetric infusion pump; minimize allergic reactions by starting at 0.5mL/min for initial 30minutes

### 25.3.4 Paracetamol Poisoning

It is the commonest taken drug overdose. The toxic dose is highly variable. In general, the recommended maximum daily dose for healthy adults is 4 grams.

Chronic excessive alcohol consumption and Isoniazid can induce CYP2E1, antiepileptics including carbamazepine, phenytoin, and barbiturates induces CYP enzymes thus increasing the potential toxicity of Paracetamol.

#### Clinical Presentation

- Phase-1: 0.5–24 hours after ingestion: asymptomatic, to nonspecific symptoms (anorexia, nausea, vomiting and malaise). Pallor, diaphoresis
- Phase-2: 18–72 hours after ingestion: Right upper quadrant abdominal pain, anorexia, nausea and vomiting, Tender right upper quadrant, tachycardia, hypotension and oliguria.
- Phase-3: 72–96 hours after ingestion: all of the above and jaundice, coagulopathy, hypoglycemia and hepatic encephalopathy, Acute Renal failure.
- Phase-4: 4<sup>th</sup> day to 3weeks after ingestion: patient who survive critical illness in phase 3, have complete recovery.

#### Investigation

- Liver Function Test - Liver transaminases ALT, AST, ALP, Prothrombin Time (PT) with INR (International Normalization Ratio)
- Serum Glucose
- Renal Function Test: Electrolytes, BUN, Creatinine
- ABG-Arterial Blood Gas

#### Non-pharmacological Treatment

- Resuscitation
- In adults, the initial treatment for paracetamol overdose is gastrointestinal decontamination.
- Usually there is no immediate threat to the airway, breathing and circulation with paracetamol poisoning
- Correct hypoglycaemia (Give glucose or sugar or honey)
- If within 1 hour of ingestion of 150mg/kg or more paracetamol give activated charcoal, if available, or induce vomiting.

#### Pharmacological Treatment

**A:** Activated charcoal (PO) (1gm/kg, up to 50gm) if less than 2hours.

If more than 8hours after ingestion, or the patient cannot take oral treatment, give:

**AND**

**C:** n-acetylcysteine (IV) 150mg/kg in 200mls of 5% Dextrose over 20 minutes, then 50mg/kg in 500mls of 5% dextrose over 4 hours, then 100mg/kg in 1 liter of 5% dextrose over 16 hours.

In severe poisoning a further 100mg/kg may be given over the next 24 hours

Children <20kg

**C:** n-acetylcysteine (IV)150mg/kg in 3ml/kg of 5% glucose, over 15 minutes, followed by 50 mg/kg in 7 ml/kg of 5% glucose over 4 hours, then 100 mg/kg IV in 14 ml/kg of 5% glucose over 16 hours.

For conscious and not vomiting or when there is severe reaction to N-acetylcysteine give:

**S:** methionine (IV) (<6 years: 1 gram every 4 hours - 4 doses; 6 years and above: 2.5 grams every 4 hours for 4 doses).

**Note**

- Syrup of ipecac is contraindicated in inducing vomiting to control paracetamol overdose because the vomiting it induces delays the effective administration of activated charcoal and oral acetylcysteine

### 25.3.5 Acetylsalicylic Acid and other Salicylates Poisoning.

**Clinical Presentation**

- Initial signs and symptoms
  - Tinnitus and impaired hearing, rapid breathing (acidotic-like breathing), vomiting, dehydration, fever, double vision and feeling faint
- Late signs
  - Drowsiness, bizarre behavior
  - Unsteady walking and coma

**Investigations**

- Blood gases
- pH and bicarbonates
- Serum electrolytes (Calcium and Magnesium)
- An ECG to evaluate for dysrhythmias
- ABG,
- LFTs,
- Full Blood Picture (Leukocytosis and thrombocytopenia)
- Coagulation studies (PT and PTT)

**Non-pharmacological Treatment**

- Give activated charcoal within one hour of ingestion if available. If charcoal is not available and a severely toxic dose has been given, then perform gastric lavage or induce vomiting as above
- Monitor blood glucose every 6 hours and correct as necessary
- Monitor urine pH hourly.

**Pharmacological Treatment**

**C:** Fluid resuscitation: If hypokalemia, give

**A:** compound sodium lactate (IV) 1 litre for 24hr if CNS hypoglycemia is seen give bolus of 20 mL 50% Dextrose then 5% Dextrose 1 litre for 24hours

**AND**

**C:** sodium bicarbonate (IV) 1mmol/kg over 4hours to correct acidosis and to raise the pH of the urine to above 7.5 so that salicylate excretion is increased.

**AND**

**C:** potassium chloride (IV) 8.4mEq/ml, maintain fluids until urine output is 2-3 mL/kg per hour

Replace fluid losses (Plasma potassium concentration should be corrected before giving sodium bicarbonate as hypokalaemia may complicate alkalinization of urine) Give;

**A:** 0.9% sodium chloride (IV) as maintenance requirements

**OR**

Hemodialysis is required if the concentration exceeds 700mg/liter or in presence of severe metabolic acidosis

### 25.3.6 Iron Poisoning

Symptoms appear at doses greater than 20mg/kg. Iron levels above 350–500 $\mu$ g/dL are considered toxic, and levels over 1000 $\mu$ g/dL indicate severe iron poisoning. Iron pills can look like candy to children. Intentional overdose can occur among adults, but is rare.

**Clinical Presentations**

- Nausea, vomiting, abdominal pain and diarrhoea.
- The vomitus and stools are often grey or black.
- In severe poisoning there may be gastrointestinal haemorrhage, hypotension, drowsiness, convulsions and metabolic acidosis.
- In a child, bloody vomit or stool gastrointestinal features usually appear in the first 6 hours and a patient who has remained asymptomatic for this time probably does not require antidote treatment.

### **Non-pharmacological Treatment**

- Gastric lavage if potentially toxic amounts of iron were taken.

### **Pharmacological Treatment**

Give antidote

**D:** deferoxamine (IM) 50mg/kg up to a maximum of 1g by repeated every 12hours; if very ill, give (IV) infusion 15mg/kg/hour to a maximum of 80mg/kg in 24hours.

### **25.3.7 Carbon-monoxide Poisoning**

Carbon monoxide is a byproduct of burning organic compounds, and may of its exposure occur in private residences. So its toxicity is usually due to improper use of gasoline portable generators and indoor use of charcoal for cooking and heating.

#### **Clinical Presentations**

- Common presentations includes "flu-like" and commonly include headache, dizziness, weakness, vomiting, chest pain,
- Dizziness, nausea or vomiting
- Shortness of breath, blurred vision, loss of consciousness

Large exposures can result in loss of consciousness, arrhythmias, seizures, or death

#### **Investigations**

- Blood gases and serum electrolytes

#### **Non-pharmacological Treatment**

- Give 100% oxygen at 10-15L/min (BVM device) to accelerate removal of 50% carbon monoxide (note patient can look pink but still be hypoxic) until signs of hypoxia disappear.
- Those who are unconscious may require CPR on site.

**Table 24.7 Time to remove 50% carboxyhemoglobin.**

Oxygen pressure O <sub>2</sub>	Time
21% oxygen at normal atmospheric pressure (fresh air)	5 hours 20 min
100% oxygen at normal atmospheric pressure (non-rebreather oxygen mask)	1 hours 20 min
100% hyperbaric oxygen (3 atmospheres absolute)	23 in

### **25.3.8 Opioid Poisoning**

Physical and mental symptoms that occur after taking too many opioids, a substance found in certain prescription pain medication and illegal drugs like heroin. It is caused by complications of substance abuse, unintentional overdose, Intentional overdose, and Therapeutic drug error any time from birth (Delivery/ maternal opioid usage) to terminal care. Drugs involved in substance abuse includes: Codeine, Diamorphine, Di Hydrocodeine, Fentanyl, Heroin, Loperamide, Methadone, Morphine, opium, Tramadol (etc.) alone or in combination.

#### **Risk factors for Toxicity**

- Drug users
- Social disadvantaged
- People who had used the drug earlier for treatment
- Those using alcohol and other sedatives

#### **Clinical Presentation**

- Acute toxicity: drowsiness, nausea and vomiting
- Chronic toxicity: constipation, loss of appetite± nausea and vomiting
- Respiratory depression, tachycardia, hypotension and pin point pupils

#### **Laboratory Investigations**

- Full Blood Picture
- Liver Function Test (ALAT and ASAT)
- Renal Function Test (Serum Creatinine and Blood Urea Nitrogen, BUN)
- Creatinine kinase level
- Arterial blood gas determinations

- An ECG is recommended in all patients with suspected opioid

overdose.

### **Non-pharmacological Treatment**

- Check the airway
- Intubate the patient who cannot protect their airway
- Give oxygen as described above.

### **Pharmacological Treatment**

Antidote: Hypoventilating patient with spontaneous ventilation Naloxone

Adults & children> 20kg:

- **B:** naloxone (IV) Initial dose 0.5mg titrated upward until Respiratory Rate is  $\geq 12$

Children (<20kg): 0.01mg/kg (IV) (Maximum 2mg/dose), increase till hypoventilation resolves

#### **Note**

- The starting dose of naloxone is between 0.4 to 1 mg in adults and 0.1 mg/kg in children. In suspected chronic opiate abusers
- Naloxone must be administered slowly at doses of 0.1 to 0.4 mg IV every 1 to 3 minutes to ensure a more controlled reversal of the opiate effects. If the naloxone is administered rapidly in these patients, the patient may also start to feel the pain which was being suppressed by the opiate.
- If the respiration is shallow, administer 100% oxygen or assisted with bag-valve ventilation until patient becomes more alert and cooperative.
- The onset of action of naloxone is immediate with a peak response observed within 3 to 8 minutes.
- A repeat dose may be indicated if the patient still shows signs of opiate toxicity

Patients with apnoea:

- Newborn with apnoea secondary to maternal opioid: 0.01mg/kg (IV/IM) (Maximum 0.4mg/kg/dose)
- Children: <20kg 0.1mg/kg (Maximum 2mg/dose) start then repeat doses with continuous infusion as required.
- Adults and children>20kg Higher dose of naloxone (0.2-1mg and titrate to clinical response

For life threatening Opioid toxicity

- Pediatrics (< 20kg) dosing: 0.1mg/kg/IV (Maximum 2mg/dose). Repeat dose/continuous infusion as required
- Adults and children (More than 20kg): 2mg IV.
  - The dose should be repeated every 3 min until improvement of Respiratory Distress Syndrome
  - If maximal cumulative dose of 10mg is reached and the respiratory insufficiency has not improvement, consider other pathology

#### **Note**

Withdrawal reaction might be life threatening in neonatal period, hence low doses should be given.

Further management of Psychiatric Management of Opioid Toxicity refer Mental Disorders Chapter

### **25.3.9 Heavy Metal Poisoning**

#### **Lead Poisoning**

Lead is a heavy metal, ubiquitous in our environment (Lead-based paint and its dust, in older buildings) that has no physiologic role in biological systems. Lead poisoning occurs when lead builds up in the body, often over months or years. Lead toxicity is a particularly insidious hazard with the potential of causing irreversible health effects associated with chronic toxicity.

#### **Clinical Presentation**

The clinical presentation varies widely, depending upon the age at exposure, the amount of exposure, and the duration of exposure

- New born: Be born prematurely, have lower birth weight, slowed growth,

- Children: Developmental delay, Learning difficulties, Irritability, Loss of appetite, Weight loss, Sluggishness and fatigue, Abdominal pain, Vomiting, Constipation, Hearing loss, Seizures, Eating things, such as paint chips, that aren't food (pica), lower IQ , anxiety, depression and ADHD Like symptoms
- Adults: High blood pressure, joint and muscle pain, difficulties with memory or concentration, headache, abdominal pain, mood disorders, reduced sperm count and abnormal sperm, miscarriage, stillbirth or premature birth in pregnant women, anaemia, Fanconi's syndrome, wrist drop

### **Laboratory Investigations**

- Lead blood levels > 10 µg/dL
- Free erythrocyte protoporphyrin (FEP) level
- Erythrocyte protoporphyrin (EP) > 35µg/dL
- FBC
- Liver Function Test (ALAT and ASAT)
- Renal Function Test (Serum Creatinine and Blood Urea Nitrogen, BUN)
- Imaging studies according to presentation, -chest, bones, abdomen etc are ordered as appropriate.

### **Non-pharmacological Treatment**

- Remove the source of lead exposure in the community
- Closely monitor cardiovascular and mental status
- Maintain an adequate urine output.
- Assess renal and hepatic functions.

### **Pharmacological Treatment**

Blood Lead levels are 25–40 µg/dL

**D:** d-penicillamine (PO) 30-40mg/kg/day 1-6months, 2hours before or three hours after meals

**OR**

Blood Lead levels are 45–70 µg/dL Chelate the patient using,

**D:** 2,3-dimercapto-succinic acid (IM) 10mg/kg by deep 8 hourly for 5 days, followed by 10mg/kg 12hourly for 14 days.

Blood Lead levels of > 70 µg/dL and/or encephalopathy

**D:** dimercaprol 3mg/kg deep (IM) 4hourly for 48 hours followed by 3mg/kg 12 hourly for 10 days

**AND**

**D:** ethylene diamine tetra-acetic acid (CaNa<sub>2</sub> EDTA) 10mg/kg (IV) 8hourly for 5 days (calcium chelate of the disodium salt of ethylene-diamine-tetraacetic acid (EDTA))

### **Mercury Toxicity**

Mercury in any form is poisonous. Poisoning can result from mercury vapour inhalation, mercury injection and absorption of mercury through the skin. Methylmercury (organic mercury) poisoning is largely linked to eating seafood, mercury-containing fish.

### **Clinical Presentation**

- Inorganic Mercury:
  - Ash-gray mucous membrane, haematochesia, severe abdominal pain, foul breath, hypovolaemic shock, Metallic taste, stomatitis, gingival irritation loosening of teeth and Renal tubular necrosis.
- Organic Mercury:
  - Visual disturbances, - Eg, scotomata, visual field constriction, ataxia, paresthesias (early signs), hearing loss, dysarthria, mental deterioration, muscle tremor, movement disorders, paralysis, and death (with severe exposure).

### **Laboratory Investigations:**

- Blood and Urine Mercury levels
- FBC
- RFT
- Hair, Toenail, and CSF mercury level for chronic exposure
- Plain X-ray of the abdomen

### **Non-pharmacological Treatment:**

- Remove from the exposure,
- Airway Breathing and Circulation (ABC)
- Give oxygen
- Copious irrigation of the skin if skin involvement
- Do gastric lavage if ingested mercury and observed in the abdominal radiographs
- Do Hemodialysis when renal function has declined.

### **Pharmacological Treatment**

Chelation therapy for acute inorganic mercury poisoning can be done with DMSA or Dimercaprol. Occasionally 2,3-dimercapto-1-propanesulfonic acid (DMPS), D-penicillamine (DPCN).

**A:** activated charcoal (PO) as in ingested poisons

**OR**

**D:** 2,3-dimercapto succinic acid (PO) (DMSA or succimer) 10 mg/kg 8 hourly for 5 days; follow by 10 mg/kg/dose 12 hourly for 14 days; not to exceed 500 mg/dose

In acute inorganic mercury poisoning:

**D:** Dimercaprol:

- Day 1: 5mg/kg deep (IM) stat
- Day 2–11: 2.5mg deep (IM) 12 hourly for 10 days

**Surgical intervention:** To remove mercury that has been logged in the intestine or colon

### **25.4 Prevention of Poisoning**

Educate the patient on Dos and Don'ts of poisoning prevention.

#### **Do's**

- Keep medicines and poison in proper containers and out of reach of children.
- Use containers with child resistant caps
- Keep all products in their original container
- Read medicine labels carefully to avoid mistake

#### **Don'ts**

- Leave container open
- Transfer products from their origin
- Remove labels from the medicine products
- Put tablets into another container such as purse or envelope
- Medicine/tablets as sweet
- Take your medicine in front of children as they often copy

### **25.5 Alcohol Intoxication**

Management of alcohol intoxication see mental health conditions chapter.

### **25.6 Bites and Stings**

The insect that is responsible for the majority of serious sting related reactions belong to the order hymenoptera. This includes bees, wasps, spiders, scorpions, ants and centipedes.

#### **Diagnostic Criteria**

- Pain, swelling, redness, and itching to the affected area

### **Non-pharmacological Treatment**

- Clean the area with soap and water to remove contaminated particles left behind by some insects
- Refrain from scratching because this may cause the skin to break down and results to an infection

### **Pharmacological Treatment**

**A:** ibuprofen

Adults: 400–800mg (PO) 8hourly for 3days

Children: 10mg/kg 8hourly maximum 400mg per day for 3days

**AND**

**A:** prednisolone, 2mg/kg/day (PO) in single daily not to exceed 80mg/day for 5days

Where there is an anaphylactic reaction treat according to guideline.

**AND**

**A:** chlorpheniramine and be ready if allergic reaction occurs. Dosage as below

- Children under 6years: 4mg 8hourly needed
- 6–12 years: 8mg (PO) 12hours as needed
- >12 years and older 12mg 12hourly needed

**OR**

**C:** loratadine (PO) 10mg 24hourly

Usual Pediatric Dose:

2-5years:      loratadine                (PO)                5mg                24hourly                (syrup)  
6years or older: Loratadine (PO) 10 mg24hourly (tablets, capsule, and disintegrating tablets)

## **25.6.1 Management of Specific Bites/Stings**

### **25.6.1.1 Bee and Wasps Sting**

Bee Venom contains many toxins including: Haemolytic enzyme, a neurotoxic factor, histamine and lytic peptide. Wasp Venom contains Hyaluronidase and 5-hydroxytryptamine.

#### **Prevention of Complications after Bites / Sting**

- Move victims to a safe area to avoid more bites or stings.
- If needed, remove the stinger.
- Wash the area with soap and water.
- Apply a cool compression using a cloth dampened with cold water or filled with ice
- Apply 0.5 or 1 percent hydrocortisone cream, calamine lotion or a baking soda paste to the bite or sting several times daily until your symptoms are alleviated.

#### **Clinical Presentations**

- Locally: Itching, pain, erythema, and swelling, cellulites
- Systemic: Oedema, fatigue, nausea, vomiting, fever, unconsciousness, Anaphylaxis, diarrhea or stool incontinence, dizziness, hypotension, haemolysis, rhabdomyosid, haemoglobinuria and myoglobinuria

#### **Non-pharmacological Treatment:**

- Airway and breathing
- Remove stingers by forceps or scrap with care
- Elevation of the affected limb
- Clean wound

#### **Pharmacological Treatment**

**A:** adrenaline 0.5mg (IV) (0.1MI) of 1:1000 solution diluted in 10ml of 0.9% sodium chloride slowly over 30minutes

**AND**

**A:** chlorpheniramine (PO) 4mg 4-6 hourly; not to exceed 24 mg/day; 8mg orally 8-12hourly or 12mg every 12hourly; not to exceed 24mg/day

- Children under 2 years: Safety and efficacy not established
- Children 2-6 years: 1 mg (PO) 4-6hourly; not to exceed 6mg/day
- Children 6-12 years: 2mg (PO) 4-6hourly; not to exceed 12mg/day or sustained release at bedtime.
- Children over 12 years: 8 mg (PO) 8-12hourly or 12 mg 12hourly; not to exceed 24 mg/day

**OR**

**A:** promethazine (PO/Rectal) 6.25 to 12.5 mg orally or rectally before meals and at bedtime, if necessary,

**OR**

**A:** promethazine 25mg orally or rectally 24hourly at bedtime

**OR**

**A:** promethazine 25mg (IM or IV) stat, and may be repeated within 2hours if necessary

**OR**

**C:** loratadine (PO) 10mg24hourly

**Pediatric Dose:**

2-5years: loratadine (PO) 5mg 24hourly (syrup)

6 years or older: loratadine (PO) 10mg 24hourly (tablets, capsule, and disintegrating tablets)

**AND**

**A:** 0.9% sodium chloride 10–20mls/kg as a bolus

**AND**

**A:** paracetamol (PO) 1g for adult or 15mg/kg for children 8hourly for 48hours

**OR**

**D:** methylprednisolone (IV) 125mg stat inpatient with respiratory and cardiovascular compromised.

**Note**

Patient with multiple stings: observe for 24hours

- Healthy adults >50stings,
- Children 1 sting

**25.6.1.2 Scorpion Sting (Envenoming)**

Scorpion stings can be very painful for days. Systemic effects of venom are much more common in children than adults.

**Clinical Presentations**

- Local pain and/or paresthesia at the site of envenomation,
- Pain and/or paresthesia remote from the site of sting,
- Autonomic disturbances such as tachy/bradycardia, hyper/hypotension, hypersalivation and lacrimation, urinary and faecal incontinence and pulmonary oedema.
- Blurred vision, roving eye movement, tongue fasculation, dysphagia, dysphonia, restless,
- Severe involuntary shaking or jerking extremities
- Cardiogenic shock

Deaths from scorpion stings are usually due to cardiogenic shock and pulmonary oedema.

**Grading of Envenomation**

- Grade I involves local pain and paresthesias at the sting site. The puncture wound may not be noticeable in this grade.
- Grade II involves local pain and paresthesias existing at the sting site as well as proximal to the sting site.
- Grade III includes grade 2 classification factors with added cranial nerve (increased oral secretions, blurry vision, rapid tongue movement, nystagmus), or skeletal neuromuscular dysfunction (flailing of the extremities and tetanus-like arching of the back) and can also be accompanied by autonomic dysfunction.
- Grade IV includes both 3 and hyperthermia, up to 104 °F, rhabdomyolysis, pulmonary edema, and multiple organ failures.

**Non-pharmacological Treatment**

- Provide adequate airway, ventilation and perfusion
- Calm the patient to lower the heart rate and blood pressure, thus limiting the spread of the venom
- Give oxygen as above
- Monitor vitals: oxygen saturation, heart rate respiratory rate and blood pressure

**Pharmacological Treatment**

**A:** Cleaning of the sting area with Normal saline

**AND**

**A:** compound sodium lactate (IV) 2L for 24hours

**AND**

**A:** adrenalin (IM) dose of 1:1000 (Repeat after 5 min if no improvement)

Children > 12 years and Adults 500 µg (0.5ml)

Children 6-12 years 300 µg (0.3ml)

Children < 6 years 150 µg IM (0.15ml)

Intubation equipment should be made available before the administration of the antivenom in case of anaphylactic shock

**OR**

**S:** equine antivenom (Centruroides Scorpion) for (Grade III or IV envenomations) - intravenous scorpion-specific F(ab')2 equine antivenom at a maximum of three vials in 20 to 50 mL of normal saline and infused over 30 minutes.

Initial dose: infuse 1vial of the 3vials over 10minutes, observe for 60minutes If symptoms persist you may repeat the remaining 2 vials, one vial at a 30minutes interval.

**AND**

**A:** paracetamol (PO) or IV 1g for adult or 15mg/kg for children (PO) 8hourly for 48hours

**OR**

**A:** ibuprofen

Adults: 400–800mg (PO) 8hourly for 3days

Children: 10mg/kg 8hourly maximum 400mg per day for 8hourly a day

**OR**

**C:** morphine (PO) or (IM) according to severity

If very severe, infiltrate site with

**A:** 1% lignocaine.

#### **25.6.1.3 Snake Bite**

A snake bite can be life-threatening if the snake is venomous. Less than 10% of 3500 snake species are poisonous and they include cobras and mamba'sblack mamba, king cobra, banded krait, saw-scaled viper and rattlesnake. (Elapidac), sea snakes (hydrophidac) and the boom slang and vine snakes (columbidac). Clinical condition depends on the type of snake bite and amount of poison (venom) injected.

Hence envenomation (poisoning) are:

- Neurotoxin in cobra, mambas and sea snakes
- Haemotoxic in vipers and boom slang.

Snake bites should be considered in any severe pain or swelling of a limb or in any unexplained illness presenting with bleeding or abnormal neurological signs. Some cobras spit venom into the eyes of victims causing pain and inflammation.

**Table: 25.8 Various snakebites, their fatal dose, quantity of venom injected, and time to fatality**

Snake	LD50 in mice	Fatal dose for humans	Average delivered dose per bite	Average fatal period
Indian cobra ( <i>Naja naja</i> )	0.28 mg/kg	12 mg	60 mg	8 h
Common krait ( <i>Bungarus caeruleus</i> )	0.09 mg/kg	6 mg	20 mg	18 h
Russell's viper ( <i>Daboia russelii</i> )	0.1 mg/kg	15 mg	63 mg	3 days
Saw-scaled viper ( <i>Echis carinatus</i> )	6.65 mg/kg	8 mg	13–40 mg	41 days

#### **Clinical Presentations**

- General signs include pain in the affected area, skin redness, swelling, bleeding, bruise,
- fast heart rate, nausea, or sweating vomiting and headache
- Shock
- Bite for local necrosis, bleeding or tender local lymph node enlargement

- Specific signs and level of envenomation are shown in the table below depending on the venom and its effects.

**Table 25.9: Assessment of severity of Snake envenomation**

Level of Intoxication	Presentation
No envenomation	Absence of local or systemic reactions; fang marks (+/-)
Mild envenomation	Fang marks (+), moderate pain, minimal local edema (0–15 cm), erythema (+), ecchymosis (+/-), no systemic reactions
Moderate envenomation	Fang marks (+), severe pain, moderate local edema (15–30 cm), erythema and ecchymosis (+), systemic weakness, sweating, syncope, nausea, vomiting, anemia, or thrombocytopenia
Severe envenomation	Fang marks (+), severe pain, severe local edema (>30 cm), erythema and ecchymosis (+), hypotension, paresthesia, coma, pulmonary edema, respiratory failure

Additionally, the patient may present with

- These include:
  - Shock
  - Local swelling that may gradually extend up the bitten limb
  - Bleeding: external from gums, wounds or sores; internal especially intracranial
  - Signs of neurotoxicity: respiratory arrest or paralysis, ptosis, bulbar palsy (difficulty swallowing and talking), limb weakness
  - Signs of muscle breakdown: muscle pains and black urine

#### Note

- Avoid picking up the snake or try to wrap it up or kill it, as this will increase your chances of getting bitten again.
- Avoid applying a tourniquet.
- Avoid cutting into the wound at all.
- Avoid trying to suck out the venom.
- Avoid applying ice or use water to submerge the wound.
- Avoid drinking alcohol.
- Avoid drinking beverages with caffeine.
- Avoid taking any pain-relieving medication, such as ibuprofen

#### Investigations

##### Specific investigations

No specific investigations, history is more useful.

- The 20-min whole blood clotting test (20 WBCT)
- Enzyme linked immunosorbent assay (ELISA)

##### Supportive investigations may include

- Hemogram: Presence of neutrophilic leucocytosis signifies systemic absorption of venom. Thrombocytopenia may be a feature of viper envenomation.
- Serum creatinine: This is necessary to rule out renal failure after viper and sea snake bite.
- Serum amylase and creatinine phosphokinase (CPK): Elevated levels of these markers suggests muscle damage (caution for renal damage).
- Prothrombin time (PT) and activated partial thromboplastin time (aPTT): Prolongation may be present in viper bite.
- Fibrinogen and fibrin degradation products (FDPs): Low fibrinogen with elevated FDP is present when venom interferes with the clotting mechanism.
- Arterial blood gas and electrolyte determinations: These tests are necessary for patients with systemic symptoms.
- Urine examination: Can reveal hematuria, proteinuria, hemoglobinuria, or myoglobinuria

- Electrocardiogram (ECG): Nonspecific ECG changes such as bradycardia and atrioventricular block with ST-T changes may be seen.
- Electroencephalogram (EEG): Recently, EEG changes have been noted in up to 96% of patients bitten by snakes.

### **Non-pharmacological Treatment:**

- Reassure the patient;
- Splint the limb to reduce movement and absorption of venom.
- If the bite was likely to have come from a snake with neurotoxin venom,
  - Clean the site with clean water to remove any poison and remove any fangs;
- If any of the above signs, transport to hospital which has antivenom as soon as possible.
- Paralysis of respiratory muscles can last for days and requires intubation and mechanical ventilation or manual ventilation (with a mask or endotracheal tube and bag) by relays of staff and/or relatives until respiratory function returns.
- Do endotracheal intubation +/- elective tracheotomy.
- Elevate limb if swollen
- Monitor very closely immediately after admission, then hourly for at least 24 hours as envenoming can develop rapidly.

### **Pharmacological Treatment**

Give

**A: Anti-Tetanus prophylaxis**

Treat shock, if present.

**A: 0.9% sodium chloride (IV) 10–20mls/kg bolus, repeat after 30min if still in shock**

Give fluids orally or by NG tube according to daily requirements. Keep a close record of fluid intake and output fluid daily requirements to be inserted

If there are systemic signs or severe local signs (swelling of more than half of the limb or severe necrosis), give

**A: Anti-snake venom (IV) (ASV)** are polyvalent immunoglobulins prepared to control venom of poisonous snakes) using indications shown below. Follow the directions given on the antivenom preparation.

- Dilute antivenom in 2–3 volumes of 0.9% Normal saline and give intravenously over 1 hour
- Give more slowly initially and monitor closely for anaphylaxis or other serious adverse reactions.

For mild degree of envenomation give 5 vials (50 ml)

For moderate degree of envenomation give 5–10 vials (50–100 ml)

For severe degree of envenomation gives 10–20 vials (100–200 ml)

**Table 25.10: Indications for Anti-Snake Venom**

System	Clinical features
Cardiovascular	Spontaneous systemic bleeding
	Whole blood clotting time >20 min
	Thrombocytopenia (platelets <100,000/mm <sup>3</sup> )
	Shock
	Arrhythmia
	Abnormal electrocardiogram
Neurological	Ptosis and paralysis
Renal	Acute renal failure
	Generalized rhabdomyolysis and muscular pains
	Hyperkalemia
	Local swelling involving more than half of the bitten limb
	Rapid extension of swelling
	Development of an enlarged lymph node draining the bitten limb

**A:** adrenaline (IM) dose of 1:1000 (Repeat after 5minutes if no improvement)

- Children > 12 years and Adults 500 µg (0.5ml)
- Children 6-12 years 300 µg (0.3ml)
- Children < 6 years 150 µg IM (0.15ml)

**AND**

**A:** chlorpheniramine and be ready if allergic reaction occurs. Dosage as below

- Children under 6years: 4mg 8hourly needed
- 6–12 years: 8mg (PO) 12hours as needed.
- >12 years and older 12mg 12hourly needed

**Note**

- If itching/urticarial rash, restlessness, fever, cough or difficult breathing develop, then stop antivenom and give
 

**A:** adrenalin 0.01 ml/kg of 1/1000 or 0.1 ml/kg of 1/10,000 solution subcutaneously and IM or IV/SC Chlorpheniramine 250 micrograms/kg.
- When the patient is stable, re-start antivenom infusion slowly.
- More antivenom should be given after 6 hours if there is recurrence of blood in-coagulability or after 1–2hour if the patient is continuing to bleed briskly or has deteriorating neurotoxin or cardiovascular signs.
- Blood transfusion should not be required if antivenom is given.
- Response of abnormal neurological signs to antivenom is more variable and depends on type of venom.

**Surgical Intervention**

- Excision of dead tissue from wound
- Incision of facial membranes to relieve pressure in limb compartments, if necessary
- Skin grafting, if extensive necrosis
- Tracheotomy if paralysis of muscles involved in swallowing occurs

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12	Dr. Gisenga Lija (Dermatovenereologist) - Kibaha College of Health and Allied Sciences	Sexually Transmitted Infections
13	Dr. Julia Wang'ari (Dermatologists) - Bombo Regional Referral Hospital	Skin Disease and Allergic Reactions
14	Dr. Bernadetha Shilio (Ophthalmologist) - Directorate of Curative Services, MoHCDGEC	Eye Disease Conditions
15	Dr. Baraka Nzobo (Dental surgeon) - Morogoro Regional Referral Hospital	Oral and Dental Conditions
16	Dr. Martin Elimath (ENT Specialist) - Muhimbili National Hospital	Ear, Nose and Throat Diseases
17	Dr. Bryceson Kiwelu (Orthopedic Surgeon) - Tumbi Regional Referral Hospital	Musculoskeletal Disorders
18	Dr. Deogratius Banuba (Orthopedic Surgeon) - Singida Regional Referral Hospital	Trauma and Injuries
19	Prof. Andrew Swai (Endocrinologist) - Tanzania Diabetes Association	Metabolic and Endocrine Disease Conditions
20	Dr. Engerasiya Kifai (Cardiologist) - Jakaya Kikwete Heart Institute	Cardiovascular Disease Conditions
21	Dr. Kajiru Kilonzo (Nephrologist) - Kilimanjaro Christian Medical Centre	Kidney and Urological Disorders
22	Dr. Jerry Ndumbalo (Oncologist) - Ocean Road Cancer Institute	Malignant Disease Conditions
23	Dr. Enock Changarawe (Psychiatrist) - Mirembe Psychiatric Hospital	Mental Health Conditions
24	Mrs. Elizabeth Lyimo (Nutritionist) - Tanzania Food and Nutrition Centre	Nutrition Disorders
25	Dr. Benard Mbwele (Epidermiologist) - UDSM Mbeya collage of Health and Allied Sciences	Poisoning
26	Prof. Jeremiah Seni (Microbiologist) - Catholic University of Health and Allied Sciences	UTI (Section)

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