Republic of Rwanda

Ministry of Health
P. O. Box 84 Kigali
www.moh.gov.rw

Internal Medicine

Clinical Treatment Guidelines

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Acronyms

ABC	: Airway, Breathing, Circulation
ABG	: Arterial Blood Gases
ACE	: Angiotensin Converting Enzyme
ACT	: Artemisinin Combination Therapy
ACTH	: Adrenocorticotrophic Hormone
ADH	: AntiDiuretic Hormone
AHF	: Acute Heart Failure
AIDS	: Acquired ImmunoDeficiency Syndrome
ALCAPA	: Aberrant Left Coronary Artery
ALAT	: Alanine Transaminase
ANCA	: Anti-Neutrophic Cytroplasmic Antibody
ARA	: Angiotensin Receptor Antagonists
ARDS	: Acute Respiratory Distress Syndrome
ARF	: Acute Rheumatic Fever
ASLO	: Anti-Streptolysin O
AST	: Aspartate AminoTransferase
AVBD	: Adriamycin, Vinblastine, Bleomycin, Dacarbazine
AVSD	: Atrio Ventricular Septal Defect
AVPU	: Alert, Voice, Pain, Unresponsive
BCG	: Bacille Calmette -Guérin
BD, BID	: Twice per day
BP	: Blood Pressure
BBE	: Benzyl Benzoate Emulsion
BE	: Base Excess
BW	: Birth Weight
CAB	: Circulation Airway Breathing
CCF	: Congestive Cardiac Failure
CHD	: Congenital Heart Disease
CK, CPK	: Creatine Phosphokinase MB Isoenzyme
CKMB	: Creatinine (Phospho) Kinase
CKD	: Chronic Kidney Disease
CMV	: CytoMegalo Virus
CNS	: Central Nervous System
COPD	: Chronic Obstructive Pulmonary Disease
CPR	: Cardio Pulmonary Resuscitation
CRP	: C – Reactive Protein

CRC : Corrected Reticulocyte Count
CT : Computerized Tomography
CSF : Cephalo Spinal Fluid
CVD : CardioVascular Disease
CXR : Chest X-Ray
DIC : Disseminated Intravascular Coagulation
DKA : Diabetic Keto-Acidosis
DM : Diabetes Mellitus
DNA : Deoxyribonucleic acid
DVT : Deep Venous Thrombosis
EBV : Epstein-Barr Virus
ECF : Extra-Cellular Fluid
ECG : Electrocardiogram
EEG : Electroencephalography
ENT : Ear Nose and Throat
ESKD : End Stage Kidney Disease
ESR : Erythrocyte Sedimentation Rate
ESRD : End Stage Renal Disease
FBC : Full Blood Count
GFR : Glomerular Filtration Rate
GTCS : Generalized Tonic Clonic Seizures
GIT : Gastro-Intestinal Tract
GORD : Gastro-Oesophageal Reflux Diseases
LV : Left Ventricle
GXM : Group and Cross-Match
HAART : Highly Active Anti-Retroviral Treatment
Hb : Hemoglobin
HDR : High Density Lipoprotein
HSV : Herpes Simplex Virus
HT : Hematocrite
HHS : Hyperosmolar Hyperglycemic State
HIE : Hypoxic Ischemic Encephalopathy
HIV : Human Immunodeficiency Virus
RSV : Respiratory Syncytial Virus
HTN : Hypertension
HZV : Herpes Zoster Virus
HR : Heart Rate
ICF : Intra-Cellular Fluid
ICU : Intensive Care Unit

IM : Intra-muscular
IR : Intrarectal
INH : Isoniazide
INR : International Normalized Ratio
ITP : Idiopathic Thrombocytopenic Purpura
IU : International Units
IV : Intravenous
JVP : Jugular Venous Pressure
KD : Kidney Disease
KOH : Potassium Hydroxide
LBW : Low Birth Weight
LDH : Lactate Dehydrogenase
LE : Lupus Erythematosis
LGS : Lennox-Gastaut syndrome
LFM : Life Style Modification
LFT : Liver Function Tests
LGIB : Lower Gastro-Intestinal Bleeding
LMWH : Low Molecular Weight Heparin
LP : Lumbar Puncture
MAP : Mean Arterial Pressure (=diastolic + 1/3 of pulse pressure)
MCV : Mean Cell Volume
MI : Myocardial Infarction
MRI : Magnetic Resonance Imaging
NHL : Non-Hodgkin's Lymphoma
NGT : Naso Gastric Tube
NPO : Nil Per Os (Nil By Mouth)
NSAID : Non Steroidal Anti Inflammatory Drugs
NVE : Native Valve Endocarditis
OD : Once per Day
ORS : Oral Rehydration Salts
PA : Postero-Anterior
PaO2 : Partial Pressure Oxygen
PCP : Pneumo Cystis Pneumonia
PDA : Patent Ducus Arterousus
PE : Pulmonary Embolus
PEF : Peak Expiratory Flow
PEEP : Positive End Expiratory Pressure
PO : Per Os (Take orally)
PPI : Proton Pump Inhibitor

PRN	: Pro Re Nata (As need Arises)
PT	: Prothrombin Time
PTT	: Partial Thromboplastin Time
QID	: Four times a day
PUD	: Peptic Ulcer Disease
RBC	: Red Blood Cell
RNA	: Ribonucleic Acid
RHD	: Rheumatic Heart Diseases
RR	: Respiratory Rate
RV	: Right Ventricle
RVA	: Rabies Vaccine Absorbed
SBP	: Systolic Blood Pressure
SL	: Sublingual
SLE	: Systemic Lupus Erythematosis
SSSS	: Staphylococcal Scaled skin Syndrome
SMEI	: Severe Myoclonic Epilepsy of Infancy
T4	: Thyroxine
TB	: Tuberculosis
TDS, TID	: Three times per Day
TORCH	: Toxoplasmosis Other Rubella Cytomegalovirus Herpes
TSH	: Thyroid Stimulating Hormone
UGIB	: Upper Gastro-Intestinal Bleeding
UTI	: Urinary Tract Infection
VLBW	: Very Low Birth Weight
VSD	: Ventricular Septal Defect
VZV	: Varicella-Zona Virus
WAS	: Wiskott Aldrich Syndrome
WBC	: White Blood Cell Count
WHO	: World Health Organization

Foreword

The guidelines and protocols presented in this document are designed to provide a useful resource for healthcare professionals involved in clinical case management in Rwanda. They were developed by taking into consideration services provided at different levels within the health system and the resources available, and are intended to standardize care at both the secondary and tertiary levels of service delivery across different socio-economic levels of our society.

The clinical conditions included in this manual were selected based on facility reports of high volume and high risk conditions treated in each specialty area. The guidelines were developed through extensive consultative work sessions, which included health experts and clinicians from different specialties. The working group brought together current evidence-based knowledge in an effort to provide the highest quality of healthcare to the public. It is my strong hope that the use of these guidelines will greatly contribute to improved the diagnosis, management, and treatment of patients across Rwanda. And it is my sincere expectation that service providers will adhere to these guidelines and protocols.

The Ministry of Health is grateful for the efforts of all those who contributed in various ways to the development, review, and validation of the Clinical Treatment Guidelines. We would like to thank our colleagues from District, Referral, and University Teaching Hospitals, and specialized departments within the Ministry of Health, our development partners, and private health practitioners. We also thank the Rwanda Professional Societies in their relevant areas of specialty for their contributions and for their technical review, which enriched the content of this document, as well as the World Health Organization (WHO) and the Belgium Technical Cooperation (BTC) for their support.

We would like to especially thank the United States Agency for International Development (USAID) for both their financial and technical support through the Management Sciences for Health (MSH) Integrated Health System Strengthening Project (IHSSP) and Systems for Improved Access to Pharmaceuticals and Services (SIAPS).

To end with, we wish to express our sincere gratitude to all those who continue to contribute to improving the quality of health care of the Rwanda population.

Dr Agnes Binagwaho
Minister of Health

1. Internal Medicine Emergencies

1.1. Cardio Respiratory Emergencies

1.1.1. Cardio Pulmonary Arrest

Definition: Cardio pulmonary arrest is a sudden cessation of spontaneous effective breathing and circulation, which may lead to death in few minutes.

Causes

- Cardiac conditions
- Severe haemorrhage and fluid loss
- Airway obstruction
- Multiple Injuries
- Anaphylactic shock
- Drugs and toxins

Signs and Symptoms

- Unconsciousness
- Un-responsiveness
- Not breathing/gasping
- No Pulse

Management

- Principles
  - Immediate recognition and activation of the emergency
  - Early cardiopulmonary resuscitation (CPR) with emphasis on chest compression (action must be taken within 4 to 6 minutes) at least 100/min chest compressions.
  - Rapid defibrillation if no response to CPR
  - Effective life support
  - Integrated post-cardiopulmonary arrest care

- CPR procedures in Adults
  ABC changed to CABD (Ref AHA 2010 guidelines)

  - C: Circulation
    - ➔ Shout for help
    - ➔ Start chest compression without delay
    - ➔ 30 chest compression first to precede 2 positive pressure ventilations

- A: Airways
  - Clear airway immediately
  - Aspirate vomitus and secretions if applicable

- B: Breathing
  - Ventilation via mask with 100% O2 saturation delivery and bag ventilation if available or mouth to mouth resuscitation until intubation is possible
  - Ensure chest movement and give 2 rescue breaths followed by 30 chest compressions, keep doing this until a portable defibrillator is available or emergency personnel arrives

- D: Drugs
  - IV line and maintain circulation
  - IV fluid
  - Inotropic support; *Adrenaline* 1mg IV every 2-5min or 3mg in endotracheal tube if no IV line
  - *Atropine* 0.5mg every 3-5min in case of bradycardia (< 40)
  - *Sodium bicarbonate* 1mEq/kg in case of metabolic acidosis, or prolonged CPR (>15min), and hyperkalemia for known cases of renal failure, crash injury
  - In case of Ventricular Tachycardia and Ventricular Fibrillation give *Amiodarone* 300mg IV, if reoccurrence give 150mg IV, alternatively give lidocaine 1.5mg/kg

- Integrated post-cardiopulmonary arrest care
  - Correct the immediate underlying problem with appropriate management

Recommendations

- Refer to ICU to maintain ventilation
- Pacing if indicated
- Any other required management

1.1.2. Pulmonary Oedema

Definition: Pulmonary oedema is an acute medical emergency due to an increase in pulmonary capillary venous pressure leading to fluid in the alveoli.

Causes

- Cardiac origin
    - Myocardial infarction
    - Severe mitral valve disease
    - Arrhythmias

- Non cardiac
    - Acute lung injury and acute respiratory diseases syndrome
    - Aspiration pneumonia
    - Pancreatitis
    - Sepsis
    - Trauma
    - Fluid overload
    - High altitude

Signs and Symptoms

- Dyspnoea/ orthopnoea, tachypnoea
- Tachycardia
- Cyanosis, Hypoxia
- Wheezing, crepitations in the lungs
- Cough with frothy blood- tinged sputum
- Anxiety, sweating
- Oedema
- Chest pain should alert the physician to the possibility of acute myocardial ischemia/infarction.

Complications

- Arrhythmias
- Brain hypoxic damage

Investigations

- Arterial Blood Gasses (ABG)
- FBC, urea, creatinine and serum electrolytes, cardiac enzymes
- Chest X ray
- ECG
- Echocardiogram
- Other tests according to non cardiac causes

Management

- CABD management
- Bed rest (semi –sitting position unless severely hypotensive)
- Administer oxygen (to keep oxygen saturation above 90%)
- Correct arrhythmias and acid base disorders
- Reassure the patient
- Inform the family about the severity of the condition
- If from Cardiac causes
    - *Frusemide IV* 20 -40mg if needed repeat every after 10-15 min
    - *Morphine IV* 3mg start then repeat every 5min when necessary
    - Inotropic support (in case of cardiogenic shock) *Dopamine* 2-20µg/kg/min or *dobutamine*10µg/kg/min
    - Vasodilatator: *Nitroglycirin* 0.5mg sublingual or 0.5-12mg/hr IV (according to the tolerance of the patient)
    - Treat underlying cardiac cause

- If from non cardiac causes
    - Treat the cause
    - Inotropic support if hypotensive (SBP<90mmHg)
    - Monitor vital signs (especially oximetry), fluid input and output (urinary catheter)

Recommendation

- Refer to ICU if:
    - Persistent hypoxia and signs of respiratory fatigue: Need to ventilate with Positive End Expiratory Pressure (PEEP)
    - Fluid overload: Need for Haemodialysis or Ultrafiltration

1.1.3. Acute Pulmonary Embolism

Definition: It is an acute condition resulting from clot embolism into the pulmonary arterial circulation, resulting in reduction of blood flowing in the pulmonary arteries

Classification

- Classification of Pulmonary embolism
  - Small or Moderate: Normal hemodynamics and normal right ventricular function and size
  - Submassive: Hemodynamically stable but with moderate or severe right ventricular dysfunction or enlargement.
  - Massive: Hypotension or poor tissue perfusion or multisystem organ failure + right or left main pulmonary arterial thrombus

Causes/Risk factors

Risk factors: Family history, obesity, recent surgery, trauma or immobility, acute infections, thrombophilia, long haul air travel, malignancy, pregnancy, cigarette smoking, advanced age

- Causes of Thrombophilia
  - Hereditary: Deficiency of protein C and protein S, anti thrombin III deficiency, Factor V Leiden deficiency
  - Acquired: Antiphospholipid syndrome, Hyperhomocysteinemia

Signs and Symptoms

- Sudden onset of dyspnoea, pleuritic chest pain, sometimes cough and haemoptysis
- Cyanosis, Hypoxia
- Tachypnoea and tachycardia, low blood pressure, low grade fever
- Signs of deep venous thrombosis
- Some severe cases may present as syncopal attacks, hypotension or cardiac arrest
- Signs of pulmonary hypertension (palpable P2, tricuspid regurgitation murmur) with chronic cases

Complications

- Disease related: cardiac arrhythmias, pulmonary hypertension, cor pulmonale, right heart failure, cardiac arrest.
- Treatment related: haemorrhage

Investigations

- CXR (exclude other causes of similar symptoms)
- ECG
- Arterial Blood Gases (ABG)
- Cardiac enzymes
- Echocardiography
- Duplex Doppler of lower limbs if suspicion of DVT
- D-Dimer test
- Chest CT scan
- Pulmonary angiography (Gold standard)
- Ventilation-perfusion scanning

Management

General

- Administer oxygen (keep saturation above 90%)
- IV fluid for hypotension, avoid diuretics
- Stabilize the patient and treat according to the classification of pulmonary embolism

Specific

- Small to moderate: Anticoagulation
- Submassive: Anticoagulation, ± Thrombolysis
- Massive PE: Thrombolysis (using *Streptokinase* or *Alteplase* or *Recombinant* TPA), then anticoagulation
  Anticoagulation
  - ➔ Low molecular weight Heparin (*Enoxaparin*): 60 mg two times a day subcutaneous is the most preferred treatment
    Or
  - ➔ *Heparin*: 10,000 IU IV bolus followed by infusion of 1000 IU/hr (Aim at APTT patient being 2 times the control) if LMWH not available
    Maintenance: *Warfarin*: 5 mg once a day (Target: INR between 2.0-3.0) or any other oral anticoagulant (e.g: Sintron)
- Duration of therapy: DVT below the knee 3 months, above the knee 6 months, PE 1 year, recurrent DVT (3 times) anticoagulation indefinite.
- Start *Heparin* and *Warfarin* at the same time and stop Heparin once INR reaches 2.0)
- Monitor INR on daily basis until it reaches 2.5 then weekly and monthly if stable; and if unstable, restart closer monitoring.

- Fibrinolytics
  - Indicated if patient is hemodynamically unstable
  - *Streptokinase*: 250,000 IU IV over 30 minutes followed by 100,000 IU/hour for 24 hours
  - Contra-indications of anticoagulation and fibrinolytics
    - Absolute: Any prior intracranial haemorrhage, known structural cerebrovascular lesion, known intracranial neoplasm, ischaemic stroke within 3 months, suspected aorta dissection, active bleeding or bleeding diathesis (except menstruations), significant closed head or facial trauma within 3 months
    - Relative: Active peptic ulcer, current use of anticoagulant, severe uncontrolled HTN on presentation, pregnancy, recent internal bleeding within 2-4 weeks

- Surgery: (Embolectomy) indicated if contra-indication of thrombolytics

Supportive care

- Compressive stockings for those with proven DVT

Recommendation

- Refer to tertiary level, all cases with
  - Massive PE not responding or/ and complicated PE
  - Inability to initiate or monitor anticoagulation
  - Need for ventilation or surgery

1.1.4. Pneumothorax

Definition: It is a collection of free air in the pleural cavity leading to loss of lung expansion.

Causes

- Traumatic (Falls, traffic accident injuries, iatrogenic etc)
- Spontaneous (emphysema, asthma, COPD, Marfan syndrome, TB, PCP etc)

Signs and Symptoms

- Sudden onset of chest pain and dyspnoea
- Chest asymmetry and tracheal deviation to contra lateral side
- Decreased tactile fremitus on the affected side
- Tympanism on the side of the pneumothorox
- Decreased breath sounds or silent chest on the affected side
- Hypotension if severe pneumothorax
- Surgical Emphysema
- Signs of the causing disease

Complication

- Tension pneumothorax leading to cardiac arrest

Investigations

- CXR in expiration (PA and lateral views)
- Other tests according to the suspected cause

Management

- Administer oxygen at high concentration
- Intercostal drainage tube insertion
- Treat the predisposing cause

1.1.5. Acute Asthma Attack

Definition: It is a deterioration of the baseline asthma control leading to acute wheeze, shortness of breath and dyspnoea.

Causes

- Upper respiratory tract infections (especially viral)
- Shortage of asthma drugs
- Exposure to triggers (cold, dust, Smoke, etc)
- Stress

Signs and Symptoms

- Wheezing
- Dyspnoea
- Mucus secretions
- Cough
- Chest tightness
- Quiet chest and decreased oxygen saturation (severe signs)

Complications

- Pneumothorax
- Status asthmaticus : an intractable asthmatic crisis with severe bronchospasm; It is managed by first evaluating ABC, with 100% oxygen, salbutamol 0.5mg/hr IV, hydrocortisone 200mg IV bolus; if not responding give adrenaline 0.1mg/ IV bolus and magnesium sulphate 2g IV over 20min; if still not responding consider intubation and mechanical ventilation under sedation with ketamine1-2mg/kg IV

Investigations

- FBC
- Blood gases
- CXR
- Spirometry

Management

- Start treatment immediately
- Semi-sitting position
- O_2 to keep saturation above 90%
- Short acting Beta 2 agonist nebulisation (e.g *Salbutamol* 5 mg in 5 ml of normal saline over 10 minutes repeated ½ hour later).
- *Hydrocortisone* 100 mg IV every 6 hrs
- Assess the need of ventilation according to the response to therapy
- Avoidance of the triggering agent if known
- Patient education on medication and other strategies

Note:

- *Do not give sedatives or aminophylline*
- *Give anticholinergic such as ipratropium bromide in case of increased respiratory secretions.*
- *Monitor parameters indicating severity*

Recommendations

- Refer to tertiary level all cases with failure of above therapy of acute asthma, development of status asthmaticus

1.2. Shock

Definition: Shock is a syndrome characterized by decreased perfusion of the tissues in the body which if prolonged leads to irreversible multiple organ failure.

Classification

- Hypovolemic
- Cardiogenic
- Septic
- Anaphylactic

Complications

- Renal Failure
- Hepatic Failure
- Metabolic Acidosis
- Coma, Death

1.2.1. Hypovolemic Shock

Definition: This is due to loss of intravascular fluid volume (blood and/or fluid loss).

Causes

- Excessive haemorrhage (e.g. trauma, internal bleeding, such as in the gastrointestinal tract)
- Excessive fluid loss (e.g. diarrhoea, vomiting, severe burns)
- Intestinal obstruction (mechanical or paralytic ileus)

Symptoms

- Fainting
- Palpitations
- Sweating (cold sweat)
- Restlessness, clouding of consciousness

Signs

- Pallor
- Cold extremities
- Tachycardia
- Hypotension : Systolic BP <90 mmHg
- Temperature is subnormal (less than 35°C)

Investigations

- FBC
- Serum urea , creatinine and electrolytes
- Blood sugar
- Group and cross-match blood
- Blood gas analysis if possible
- Blood cultures

Management

Non-pharmaceutical

- Control obvious bleeding with direct pressure
- Insert one or two large bore IV catheters for rapid IV infusion
- Urinary catheter

Initial volume resuscitation

- Raise drip stand or squeeze bag to increase infusion rate: Give colloids and/or crystalloids e.g. *Sodium Chloride* 0.9%. Aim to give 70 ml/kg body weight
- Monitor blood pressure, pulse and clinical response: Target a mean arterial pressure ≥ 65mmHg and urine output > 30ml/hr
- Most patients will respond to the initial fluid bolus
- If they respond initially and subsequently deteriorate, there may be an ongoing occult haemorrhage
- Consider blood transfusion (if haemorrhage is >25% of total blood volume)
- Fluid should be given quickly and slowed only when BP rises and urine flow is adequate
- Give Oxygen 6 L/min via nasal or facial masks if indicated
- Continue to monitor BP, pulse and urine output

Recommendations

- Refer to ICU if needed
- Refer for surgical intervention if indicated

1.2.2. Cardiogenic Shock

Definition: This is advanced cardiac failure with inadequate peripheral tissue perfusion. Hemodynamic criteria are:

- Sustained hypotension for at least 30min(SBP<90mmHg)
- Low cardiac index(<2.2 l/min/m^2)
- Elevated capillary wedge pressure(>15mmHg)

Causes

- Valvular Heart Disease
- Myocardial Infarction (Right or Left)
- Pericardial Tamponade
- Myocarditis
- Hypertensive Obstructive Cardiomyopathy
- End stage cardiomyopathy
- Myocardial contusion

Signs and Symptoms

- BP less than 90mmHg systolic
- Weak or undetectable pulse
- Cold extremities
- Peripheral cyanosis
- Poor urine output
- Pulmonary signs (Crepitations, Dyspnoea)
- Raised JVP

Investigations

- FBC
- Serum urea, creatinine and electrolytes
- Cardiac Enzymes (LDH, Troponin, Creatinine Kinase)
- CXR
- ECG
- Echocardiography

Management

Non-Pharmaceutical

- Oxygen to keep saturation >90%
- Large bore IV cannula
- IV fluid bolus (if predominant right heart failure)
- Urinary Catheter

Pharmaceutical

- Diuretics if predominant left heart failure and pulmonary congestion (avoid otherwise): *Frusemide* eg 40mg IV stat and monitor response
- Management of underlying cause
  - ➔ Ischaemia: *Aspirin* 100mg po stat, *Morphine* 2-10mg IV/IM for pain, *Glyceryl Trinitrite* (if BP permits, contraindicated in hypotension), Thrombolysis (see Pulmonary Embolus chapter)
  - ➔ For Pericardial Tamponade: pericardiocentesis

Recommendation

- Refer to ICU or a tertiary centre
  - All patients with cardiogenic shock not responding to above measures

1.2.3. Septic Shock

Definition: Sepsis associated hypotension (SBP<90mmHg or a reduction of more than 40mmHg from baseline) and perfusion abnormalities or the requirement for vasoactive drugs despite adequate fluid resuscitation in the absence of other causes for hypotension.

Causes

Any primarly or secondarly generalized infection can lead to septic shock but the most common causative agents of septicaemia in a previously healthy individual:

- E.coli
- Pneumococcus
- Staphylococcus aureus
- Meningococcus
- Group A beta-haemolytic streptococcus

Note: *In-patients with symptoms from the urinary tract, E. coli, Klebsiella species and enterococci are the most common causes of urosepsis.*

Signs and Symptoms

- Low blood pressure but the patient's skin is warm ("warm hypotension")
- General malaise, chills
- Fatigue, weakness, pain

- Nausea and vomiting
- Skin signs (often petechiae, haematoma)
- Confusion
- Unexplained worsening of an underlying illness

Complications

- Myocardial depression
- Acute Respiratory Distress Syndrome: (ARDS)
- Acute Kidney Disease
- Disseminated Intravascular Coagulopathy (DIC)
- Liver failure

Investigations

- FBC
- Urea, creatinine and electrolytes
- Blood sugar
- Blood and body fluid culture
- Liver function tests
- Coagulation tests
- Chest X-ray
- ABG

Management

General management

- Commence resuscitation measures immediately the patient is seen
- Start empirically broad-spectrum antibiotics after obtaining samples for appropriate cultures within 1 hour :
  - *Cefriaxone* 1 g IV once daily OR *Benzyl penicillin* 4 mega units IV every 6 hours
  - PLUS *Gentamycin* 80 mg 12 hourly with adequate fluid replacement and close monitoring of urea, creatinine and electrolytes
  - PLUS *Metronidazole* 500 mg IV 8 hourly
  - PLUS *Hydrocortisone* 100 mg 8 hourly for 24-48 hours: only to septic shock patients after it has been confirmed that their blood pressure is poorly responsive to fluid resuscitation and vasopressor therapy

- Vasopressor: *Dopamine* and *Noradrenaline* are the first line vasopressors. Target a MAP>65mmHg. In case of inadequate cardiac output, consider *Dobutamine* or *Adrenaline* infusions

- Oxygenotherapy and Mechanical ventilation (High PEEP and permissive hyparcapnia in case of ARDS) under sedation/ analgesia
- Start oral medication once the required course of IV antibiotics is completed. Choice of antibiotics depends on the source of infection, and culture and sensitivity results

Note:

- *Always anticipate the onset of disseminated intravascular coagulopathy*
- *Prevention of stress gastric ulcers if critically ill in ICU: Ranitidine or Omeprazole*
- *Prevention of DVT with LMWH (e.g: Enoxaparin 40mg SC OD)*
- *Other supportive therapy accordingly: Hemodialysis*

Recommendation

- Refer if complicated; especially if urinary output starts failing, serum urea, creatinine and potassium start rising, or if there is evidence of any other organ failure despite attention to adequate hydration with prompt attention to electrolyte balance and antimicrobial administration

1.2.4. Anaphylactic Shock

Definition: is a life-threatening serious allergic reaction often involving respiratory difficulties and circulation failure.

Causes

- Foods
  - Nuts (tree nuts and peanuts), fish, seafood, celery, kiwi, egg, milk, avocado, carot and bananas

- Drugs
  - Antibiotics (especially penicillins, sulphonamides, muscle relaxants)
  - Analgesics (opioids, NSAIDs)
  - ACE inhibitors

- Vaccines and serum
- Insect stings
  - Wasp, bee, mosquito, snake bites

- Radiographic contrast media, blood products, allergenic products used in examinations and treatment.
- Natural rubber (Latex allergy)
    - Gloves, catheters, condoms, balloons

- Physical exercise (eating wheat followed by physical exercise as a rare phenomenon), shaking, cold.

Signs and Symptoms

- Erythema
- Angioedema
- Rash
- Urticaria
- Bronchospasm
- Cardiovascular collapse – severe hypotension

Complication

- Circulatory and respiratory arrest

Management

- Check CABD and stop the administration of any potential trigger, particularly IV agents.
- Call for help
- Maintain airway and give O2 100%
- Elevate the legs
- Give *Adrenaline* in 50µg IV increments at a rate of 100µg/min until blood pressure or bronchospasm improves (Alternative: *Adrenaline* 0.5mg-1mg IM to be repeated 10min after if necessary)
- Give IV fluid (Crystalloid)

Subsequent management

- *Chlorpheniramine* 10-20mg slow IV OR *Promethazine* IM, 25 mg 8–12 hourly
- If bronchospasm develops, give nebulised *Salbutamol* 5mg.
- Give 500ml–1 litre of *Sodium Chloride* 0.9% 4 hourly
- *Hydrocortisone*, IV, 100-300 mg IV 12 hourly, to control any late allergic reaction that may occur
- Ensure that the name of the drug or substance that caused the reaction is written prominently on the patient's folder and educate the patient and relatives on future avoidance

1.3. Neurological Emergencies

1.3.1. Coma and Depressed Conscious State

Definition: Altered level of consciousness due to a pathological process.

Classification

Depends on whether the patient has focal signs of a hemiplegia or abnormal brainstem reflexes:

- Diffuse: Depressed conscious state without any focal neurological signs
- Cerebral hemisphere: Depressed conscious state and hemiplegia
- Brainstem: Depressed conscious state and abnormal brainstem reflexes

Causes

- Diffuse
  - Severe hypotension from any cause
  - Drugs (alcohol, opiates, sedatives)
  - Meningitis, encephalitis and cerebral malaria
  - Subarachnoid hemorrhage, acute hydrocephalus
  - Hypothermia
  - Metabolic disturbances
  - Hypoglycemia or hyperglycemia
  - Hypoxia
  - Hypercapnia
  - Hyponatremia or hypernatremia
  - Hepatic Coma

- Cerebral hemisphere
  - Extradural, subdural and intracerebral hemorrhage
  - Tumours
  - Brain abscess
  - Herpes Simplex Encephalitis

- Brainstem
  - Brainstem hemorrhage or infarction

Signs and Symptoms

- Try to get a history from an eyewitness
  - Telephone relatives to get more history of patient and their circumstances

- Then examine patient to determine depth and type of coma

Document the Glasgow Coma Scale (varies from 3 to 15) *to determine* ***depth*** *of coma:*

ACTIONS	RESPONSE	SCORE
Eye opening	Spontaneous	4
	Response to verbal command	3
	Response to pain	2
	No eye opening	1
Best verbal response	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No verbal response	1
Best motor response	Obeys commands	6
	Localizing response to pain	5
	Withdrawal response to pain	4
	Flexion to pain	3
	Extension to pain	2
	No motor response	1

- Classify the type of coma
    - Check the eye movements and papillary, corneal and gag reflexes looking for evidence of a brainstem problem, and look for focal neurological signs by testing withdrawal of each limb to pain. This enables classification into a diffuse, cerebral hemisphere or brainstem problem
        - ➔ Diffuse: All limbs symmetrical, usually normal brainstem reflexes
        - ➔ Cerebral hemisphere: Limbs asymmetrical
        - ➔ Brainstem: Abnormal brainstem reflexes

Investigations

- Urgent blood glucose
- FBC, Electrolytes, Urea and Creatinine, Liver Function Tests, ESR, CRP
- Blood gas (if available)
- Drug screen (if available)

- Other tests depending on the suspected cause including:
  - Blood smear for malaria
  - Lumbar Puncture
  - Blood cultures
  - Thyroid function tests
  - ECG
  - Skull Xrays
  - CT scan Brain

Management

- CABD
  - Circulation – check pulse and blood pressure; treat hypotension with IV fluids and vasopressors.
    - ➔ Hypotension suggests sepsis, internal hemorrhage, drug overdose, severe hypothyroidism or an adrenal crisis as a cause for coma
  - Airway – ensure it is not obstructed; put patient in the recovery position
  - Breathing – check respiratory rate and oxygen saturation - if not adequate the patient needs oxygen and probably endotracheal intubation
  - Drug
    - ➔ Insert IV line
    - ➔ Give 50ml of 50% *Dextrose* IV and 100mg of *Thiamine* IV while waiting for test results
    - ➔ If febrile, give antipyretics, and start treatment for meningitis (*Ceftriaxone* IV 2g/day) and herpes simplex encephalitis (*Acyclovir* 10mg/kg IV tds) and consider treatment for malaria (*Artseunate*) until these diagnoses are excluded
    - ➔ If raised intracranial pressure is suspected give *Mannitol* 1g/kg IV stat and do NOT perform lumbar puncture. Intubation and hyperventilation may also be helpful
    - ➔ If the patient has had a seizure, a therapeutic trial of *Diazepam* 10mg IV is reasonable in case of non-convulsive status epilepsy
    - ➔ Insert urinary catheter and consider NGT, keep patient NPO
    - ➔ Treat any apparent electrolyte disturbance
    - ➔ Definitive therapy depends on the underlying cause

Recommendation

- Intubate patients that are deeply comatose (GCS<8) and do not improve with above measures, and transfer to tertiary centre for further management

1.3.2. Status Epilepsy

Definition: This is a succession of seizures in which the patient does not regain consciousness between attacks.

Causes

- See Seizures and Epilepsy in Neurology Chapter

Signs and Symptoms

- Patient is unconscious
- The patient may appear to be in continuous clonic phase, the short tonic phases being difficult to see
- May be in respiratory failure with cyanosis or may be hypoglycemic

Management

Non-Pharmaceutical

- Place patient by the side (lateral position). Do not attempt to put anything into the patient's mouth to stop biting of the tongue
- Start treating immediately. Do not wait for results of special investigations
- Maintain cardiorespiratory status: check CABD
- Maintain fluid, electrolyte and blood sugar status
- Blood specimen for electrolytes and anticonvulsant levels

Pharmaceutical

- Seizure control should occur as soon as possible to prevent brain damage
- Initial treatment
  - → If IV line
    - *Diazepam*, IV 10–20 mg, not faster than 2 mg/minute
      Or *Clonazepam*, IV 1 mg may be repeated after 5 minutes. Maximum dose: 4 mg
      Or *Lorazepam*, IV 4 mg

- If no IV line
  - Rectal *Diazepam* 10 mg using the contents of an ampoule **Or** *Clonazepam* IM 1 mg **Or** *Midazolam* SL 5–10 mg using the contents of an ampoule

    AND THEN
  - *Phenytoin*, IV, 20 mg/kg diluted in sodium chloride 0.9% (and not dextrose) administered not faster than 50 mg/minute preferably with cardiac monitoring

- If arrhythmias occur, interrupt the infusion temporarily and reintroduce slowly
- If there is no venous access, give same dose orally or via nasogastric tube. Flush the tube
- After administering phenytoin: continue maintenance dose of 100mg tid

- *Phenobarbital* as second line after phenytoin if seizures continue
  - Loading dose 20 mg/kg IV at a rate of 50-75 mg/minute
  - If no response repeat at 5-10 mg/kg
  - Maintenance dose 1-5 mg/kg/day orally
  - Phenobarbital should only be used where respiratory support is available

- Seizures continuing after 30 minutes
  - Intubate and ventilate patient
  - *Thiopental sodium*, IV, 2–4 mg/kg, followed by 50 mg bolus every 2–3 minutes to control seizures
    - Maintenance dose: 1–5 mg/kg/hour
    - Beware of hypotension

  - Once seizures controlled for 24 hours, wean off thiopental sodium by decreasing dose by 1 mg/kg every 12 hours.

- Maintenance therapy once seizures controlled
  - *Phenytoin*, IV, 100 mg 8 hourly or oral, 300 mg daily.. First maintenance dose should be no more than 12 hours after the loading dose
  - Long term maintenance therapy: See Section on Seizures and Epilepsy

1.3.3. Spinal Cord Compression

Definition: A syndrome of pain and loss of neurological function due to compression of the thecal sac within the spinal column.

Causes

- Malignancy, especially prostate, breast and lung cancer
- TB (Pott's Disease)
- Epidural Abscess
- Benign tumours: meningiomas
- Epidural Haematoma

Signs and Symptoms

- Pain is usually the first symptom: a severe local back pain which progressively increases in intensity. Pain is often worse with recumbency
- Symmetric lower extremity weakness with typical pyramidal pattern, preferentially affecting the flexors in the lower extremities and, if above the thoracic spine, the extensors of the upper extremities
- The progression of motor findings typically consists of increasing weakness followed sequentially by loss of gait function and paralysis
- Hyperreflexia below the level of the compression and extensor plantar responses may be seen
- Patients frequently report ascending numbness and paresthesias.
- Gait ataxia

Complications

- Irreversible loss of spinal cord function if not promptly decompressed
- Pressure Sores
- Constipation
- Urinary retention

Investigations

- Plain spinal X-rays
- CT Myelography
- MRI spine
- CXR for TB
- Other tests looking for malignancy

Management

General principles

- Pain Control
  - → *Paracetamol* 1g o qid PLUS opiates if necessary

- Avoidance of Complications
  - → Bowel regimen – Regular aperients to ensure bowel opening at least every 2-3 days
  - → Urinary catheter to avoid urinary retention
  - → Pressure Care and regular turning of the patient
  - → *Heparin* 5000 units SC bd for immobile patients

Specific Therapy *(directed at underlying cause to prevent permanent injury)*

- For malignant cord compression
  - → Administration of glucocorticoids (*Dexamethasone* 16mg po or IV daily OR if *Dexamethasone* not available, prednisolone 100mg po daily)
  - → Urgent referral for neurosurgery, external beam radiation therapy, or stereotactic body radiotherapy
  - → Chemotherapy may be beneficial in patients with chemosensitive tumors
  - → Antituberculosis therapy (see TB chapter) in patients with Xray or CT findings consistent with Pott's disease of the spine
  - → Antibiotic therapy for patients with suspected epidural abscess
    - ▪ *Cloxacillin* PLUS *Metronidazole* PLUS Ceftriaxone
  - → Steroid therapy (as for malignancy) and early referral for neurosurgery in patients with suspected benign tumours

1.4. Toxicology

1.4.1. Stings and Bites

RABIES

Rabies is a viral infection of certain warm-blooded animals and is caused by a virus in the Rhabdoviridae family. It attacks the nervous system and, once symptoms develop, it is 100% fatal in animals, if left untreated.

Animal Type	Evaluation and Disposition of Animal	Post-exposure Prophylaxis Recommendations
Dogs and cats	Healthy and available	Should not begin prophylaxis, 10 days observation, unless animal develops symptoms of rabies
	Rabid or suspected rabid	Immediate vaccination (consider also tetanus toxoids)
	Unknown (escaped)	Consult public health officials

Signs and Symptoms

- Paresthesia
- Headache
- Stiff neck
- Lethargy
- Pulmonary symptoms
- Maniacal behavior
- Muscle spasm of throat with dysphasia
- Convulsion →coma →paralysis →death

Management

- Local care
  - Thorough irrigation
  - Cleansing with soap solution
  - Debridement
- Administration of tetanus toxoid
- Antibiotics
- Rabies Vaccination
  - Rabies vaccine adsorbed (RVA) (*Imovax*)
  - Human diploid cell rabies vaccine (HDCV)
  - Either administered with HRIG (Imogan rabies)
  - Vaccine administered intramuscularly in deltoid

SNAKEBITES AND VENOM

Snakebites are generally only of clinical significance if envenomation occurs.
Adders and cobras produce local necrosis. Mambas produce distal neurotoxic effects.

Signs and Symptoms

- Hypotension
- Weakness
- Nausea/vomiting
- Pain, swelling, tenderness and ecchymosis at site of bite
- Paresthesia and muscle fasciculations
- Defect in blood coagulation
- Pulmonary edema

Complications of snake bites

- Serum sickness due to antivenom
- Anaphylaxis

Management of snake bites

- Clean the wound, transfer patient to hospital
- Pressure immobilisation with a bandage is the best first aid for snakes with neurotoxic venom (eg Mamba)
- Never use application of a tourniquet, incision or suction
- The most important treatment for snake bite is antivenom (*crotalidae polyvalent immune fab*)
    - Only use antivenom in patients with clear signs and symptoms of envenomation
    - The initial doze should be large; at least contents of 20 ml, but the condition of the patient may demand the injection of up to 4 or 5 times as much
    - When given intravenously, the venom serum should be at room temperature, and the injection given very slowly, with the patient recumbent

- IV Fluids if required to replace the decreased extra cellular fluid volume resulting from oedema formation
- *Vit K* may be required to correct bleeding and clotting abnormalities
- Tetanus toxoid and antibiotics recommended to prevent secondary infection.

SPIDER BITES

Signs and Symptoms

- Generalized muscle spasm is the most prominent physical finding
- Severe bite results in necrosis and sloughing of skin with residual ulcer formation
- Fever, nausea, vomiting, headache, weakness, arthralgia, malaise, petechiae
- Hemolysis and thrombocytopenia responsible for death

Management

- Analgesics for pain
- Muscle relaxant (eg *Diazepam* 5-10mg po) for spasm
- *Calcium gluconate* relieves most symptoms

Note: *Most patients recover within 24 hrs*

1.4.2. Poisoning

Definition: Poison is anything that kills or injures through its chemical actions. This includes toxins, drugs, and venoms

Causes

- Deliberate: Suicidal or Criminal
- Accidental: Drugs, radiation, occupational exposure
- Poisoning epidemics (e.g: Aflatoxins in cereals)

Clinical Features and Associated Poisons (Toxidromes)

Clinical Features	Poisons
Odour of Breath	Chloroform, Ethanol, Cyanide, Arsenic, Organophosphates, Phosphorus, Kerosene
Hypertension with Tachycardia	Amphetamines, Cocain, MAO inhibitors, Marijuana, Phencyclidine, Alcohol withdrawal, Nicotine, Antihistamines, Antipsychotic agents, Antidepressants
Hypotension with bradycardia	Antidepressants (severe cases), Barbiturates, Narcotics, Benzodiazepines, Cyanide, Nicotine, Organophosphates
Hypotension with tachycardia	Aluminium phosphide, Antipsychotics, Caffeine, Cyanide, Disulfiram-ethanol interaction, Tricyclic antidepressants
Hyperthermia	Amoxapine, Amphetamines, Antidepressants, Cocaine, Lithium , MAO inhibitors, Phencyclidine, Anticholinergic agents, Salicylates, Antihistamines
Hypothermia	Antidepressants, Ethanol, Benzodiazepine, Narcotics, Barbiturates, Phenothiazines
Tachypnoea	Amphetamines, Atropine, Cocaine, Salicylates,Carbon monoxide, Cyanide, Hepatic Encephalopathy (paracetamol, amatoxin mushrooms), Metabolic acidosis
Bradypnoea	Antidepressants, Antipsychotic agents, Barbiturates, Ethanol, Benzodiazepines, Chlorinated hydrocarbons, Narcotics, Nicotine, Organophosphates, Cobra bites
Altered sensorium	Antidepressants, Antihistamines, Antipsychotics, Atropine, Organophosphates, Barbiturates, Lithium, Cyanide, Benzodiazepines, Ethanol, Narcotics, Carbon monoxide
Seizures	Antidepressants (amoxapine and maprotiline), Antipsychotic, Antihistamines, Chlorinated hydrocarbons, Organophosphates, Cyanide, Lead and other heavy metals, Lithium, Narcotics, Sympathomimetics (amphetamines, cocaine, phencyclidine)
Meiosis	Barbiturates, Phenothiazines, Ethanol, Narcotics, Nicotine, Organophosphates
Mydriasis	Amphetamines, Caffeine, Cocaine, MAO inhibitors, Nicotine, Antidepressants, Antihistamines, Atropine
Cyanosis	Methaemoglobinaemia-inducing agents, Terminal stages of all poisonings

Investigations

Laboratory tests should be based on information revealed in the history and physical exam.

- Full blood count (FBC)
- Urea and electrolytes (U/E)
- Liver function test (LFT) e.g. hepatotoxic drugs
- Prothrombin time / partial thromboplastin time (PT/ PTT) e.g. hepatotoxic drugs
- Arterial blood gas (ABG) e.g. sedative poisoning, salicylates, toxic alcohols
- Electrocardiogram (ECG)
- Chest X-ray (CXR) e.g. inhalation of poisonous gas, paraquat poisoning
- Magnesium, calcium and phosphate levels
- Methaemoglobin e.g. dapsone
- Serum cholinesterase levels e.g. anticholinesterases
- Electroencephalography (EEG) e.g. some centrally-acting drugs
- Serum osmolality for toxic alcohols
- Group and cross-match (GXM) for fresh frozen plasma (FFP) e.g. anticoagulants
- Carboxyhemoglobin in case of CO suspect
- Anion gap metabolic acidosis

Management

The principles of managing a case of poisoning are as follows

- Emergency management
- Decontamination
- Antidotes
- Enhanced elimination
- Follow-up

Emergency management

On arrival of a patient with poisoning, the initial priorities are the maintenance of Circulation, Airway and Breathing (CAB)

- C: Assessment of circulation should include heart rate, blood pressure, peripheral circulation and hydration status of the patient
    - *Dopamine* and *Dobutamine* may be needed to maintain the BP
    - IV fluids (crystalloids, colloids) if necessary
    - CVP monitoring may be necessary
    - patient may require ECG monitoring

- A: Airway should be cleared of vomitus or any other obstruction
- B: Breathing should be assessed by observation and oxymetry and if in doubt by measuring arterial blood gases. Patients with respiratory insufficiency should be incubated and mechanically ventilated.

Note: *After initial resuscitation, all patients with altered sensorium should receive 50% dextrose in case of Hypoglycemia.*

Decontamination

- Topical decontamination
  - Undress and wash with enough water and soap on the affected part
    - *Precaution*: In case of acid contamination do not use water.
- Gastrointestinal Decontamination
  - This is used for poisons which have been ingested.
  - Decontamination can best be achieved by one of the following methods, depending on the agent ingested:
    - Oral adsorbents
    - Dilution

- Management of Gastrointestinal
  Decontamination with Oral adsorbents (Activated charcoal) to decrease the absorption of the poison into the system
  - Oral absorbant
    - Indications
      - Any significant ingestion of a well charcoal-bound drug
    - Contraindications
      - Ileus or intestinal obstruction
      - Corrosive agent ingestion
      - Unprotected airway or impaired consciousness
    - Administration of Charcoal
      - Adults: First dose: 50 - 100 g (orally or via a nasogastric tube) Subsequent doses: 15 - 20 g at 4 - 8 hourly intervals for up to 24 hours
  - Dilution
    - Water is the best diluent. Maximum 250 ml is administered to adults

Note: *Corrosives e.g. cleaning agents can be well managed with dilution.*

- Contraindications: Dilution should not be used under the following circumstances:
  - When the poison ingested is in the solid form e.g. capsules, tablets; as dilution will tend to promote dissolution and absorption of the poison.
  - Unconscious patients
  - Patients without a gag reflex

Specific Therapy (Antidotes)

Common poisonings and their specific antidotes

Antidote	Poison	Administration
Atropine	Cholinesterase inhibitors	Initially, administer 2-4 mg for adults and 0.05 mg/kg for children. Repeat it every 5-15minutes until there is cessation of oral and tracheal secretions. Then lower the dose and give at less frequent intervals to maintain atropinization for 24-48 hrs.
Pralidoxime	Organophosphates	1-2 gm (25-40 mg/kg in children) IV over 10-20 minutes. Repeated every 4-8 hours.
Naloxone	Opiates	
Ethanol	Methanol, Ethylene glycol	Loading dose is 0.75 g/kg which is followed by maintenance dose of 0.1 g/kg/hr.
Desferoxamine	Iron	90 mg/kg (upto 1 gm) i.m. followed by 90 mg/kg (upto 1 gm) every 4-12 hours. If hypotension is present, give intravenously at a rate not more than 15 mg/kg/hour.
Snake antivenom	Snake bites	Dose varies with the species of snake which has bitten and the severity of envenomation.
BAL (Dimercaprol)	Lead, Arsenic, Mercury	300 mg/sq. meter/day in 6 divided doses (3-5 mg/kg every 4 hours) for 2 days, then 2.5-3 mg/kg every 6 hours for 2 more days, and then every 12 hours for 7 more days.

List of antidotes for specific poisons

Poison	Antidote
Acetaminophen	N-acetylcysteine
Anticholinergics	Physostigmine
Benzodiazepines	Flumazenil
Beta blockers (propanolol)	Glucagon
Calcium channel blockers	Calcium, glucagon
Carbamates	Atropine
Carbon monoxide	Oxygen
Cyanide	Sodium nitrite/sodium thiosulfate
Digoxin	Digoxin immune fab
Ethylene glycol	Ethanol, fomepizole
Isoniazid	Pyridoxine
Nitrates/nitrites	Methylene blue
Heparin	Protamine sulfate
Warfarin	Vitamin k

Enhanced elimination of absorbed poison

This is usually resorted to when antidotes are not available:

- Urinary alkalinization: Recommended for significant aspirin, phenobarbitone and sulfonamide overdoses
    - Give 150m Mol of *Sodium Bicarbonate* in 1 litre of 5% dextrose over 4 hours. Contraindicated in renal failure and volume overload
- Dialysis (Hemodialysis and peritoneal)
    - In case of intoxication by: *Phenobarbital, Salicylates, Methanol, Ethanol, Theophylline* and *Lithium*

After-care

- Emotional support through all phases of emergency management and after discharge from the hospital

Recommendation

- Once the patient is stable, a referral to a clinical Psychologist in made in cases of deliberate overdose

1.5. Metabolic and Endocrine Emergencies

1.5.1. Diabetic Keto-Acidosis (DKA)

Definition: DKA is an acute, severe, life-threatening complication of uncontrolled diabetes mellitus that requires emergency treatment with insulin and intravenous fluids. DKA mainly occurs in patients with type 1 diabetes, but it is not uncommon in some patients with type 2 diabetes.

Causes

- Underlying infection and intercurrent illness
- Interruption of insulin treatment
    - Poor compliance with insulin treatment
    - Psychological stress, particularly in adolescents.
    - Inaccessibility to insulin supply
    - Mechanical failure of the insulin infusion pump
- New onset of diabetes
- Medication (eg. corticosteroids)
- Idiopathic (no identifiable cause)

Signs and Symptoms

- Polyuria and polydipsia
- Malaise, generalized weakness, and fatigue
- Nausea, vomiting with diffuse abdominal pain, decreased appetite, and anorexia
- Ill appearance, dry mucous membranes, decreased skin turgor.
- Shallow rapid breathing or air hunger (Kussmaul or sighing respiration)
- Characteristic acetone (ketotic) breath odor.
- Tachycardia, Hypotension
- Altered consciousness or coma

Note: *Body temperature may be within the reference range or low, even in the presence of intercurrent infection.*

Complications

- Cardiovascular: Myocardial infarction, dysarthymia.
- Metabolic and electrolytic: Hypoglycemia, hypokalemia, hypophosphatemia
- Respiratory: Respiratory distress, pulmonary edema.
- Cerebral edema, Coma, Death

Investigations

- Laboratory studies
  - Blood tests for glucose every 1 h until patient is stable, then every 6 hrs
  - Urine Dipstick testing (positive for glucose and ketones)
  - Serum electrolytes every 4-6 h while acutely ill
  - Blood urea (raised in DKA)
  - ABG
  - FBC (WCC increased).
  - Osmolarity (increased to >290 mOsm/L) Calculation = 2 (Na + K) + urea/3 + glucose(mg/dl)/18
  - Anion gap (elevated) Calculation = ([Na + K] - [Cl + HCO3] >13 mEq/L)
  - Urine and Blood Cultures
  - CXR
  - ECG
  - Abdominal Ultrasound

- Others investigations are done according to suspected etiology.

Management

Principles

- Admission in high dependency area of Medical Ward or ICU.
- Correction of fluid loss with intravenous fluids
- Correction of hyperglycemia with insulin
- Correction of electrolyte disturbances, particularly hypokalemia
- Correction of acid-base balance but most of time corrected with above mentioned measures
- Treatment of concurrent infection, if present

Correction of fluid loss

- *Normal Saline* or *Ringer's Lactate*
  - ➔ Administer 1-3 L during the first hour
  - ➔ Administer 1 L during the second hour
  - ➔ Administer 1 L during the following 2 hours
  - ➔ Administer 1 L every 4 hours, depending on the degree of dehydration

Correction of hyperglycemia

- *Insulin* therapy: 0.1 UI/kg/hr
  - Only short-acting insulin is used for correction of hyperglycemia
  - Use subcutaneous or intramuscular route if IV line not accessible
  - Doses and route : Initial insulin dose: Continuous IV insulin infusion using electric syringe at a rate of 0.1 U/kg/h
    - Mix 24 units of regular insulin in 60 mL of isotonic sodium chloride OR
    - If electric syringe is not available mix 60 units of short acting insulin with 500 ml of normal saline solution
    - Infuse at a rate of 15 mL/h (6 U/h) until the blood glucose level drops to less than 180 mg/dL; Adjust (usually decrease) insulin dosing as required to ensure that:
      - The maximum decrease rate of glucose is 100 mg/dL/h
      - Blood glucose should not fall below 200 mg/dl during the first 6 hours
  - If blood glucose stable and urine ketones negative, then stop insulin infusion and start standard insulin regimen

Correction of electrolyte disturbances

- K+ level > 6 mEq/L: don't administer K+.
- K+ level = 4.5-6 mEq/L: administer 10 mEq/h of *Potassium chloride*
- K+ level is 3-4.5 mEq/L: administer 20 mEq/h of *Potassium chloride*
- Monitor serum potassium levels hourly and stop potassium infusion if the K+ level is greater than 5 mEq/L
- The monitoring of serum potassium must continue even after potassium infusion is stopped to detect recurrence of hypokalaemia
- In severe hypokalaemia: don't start insulin therapy unless potassium replacement is under way; this is to avoid potentially serious cardiac arrhythmias that may result from hypokalaemia

Treatment of intercurrent infection

- Start empiric antibiotics on suspicion of infection until culture results are available

1.5.2. Hyperosmolar Hyperglycemic Syndrome (HHS)

Definition: HHS is characterized by hyperglycemia, hyperosmolarity, and dehydration without significant ketoacidosis in patients with uncontrolled diabetes mellitus.

Causes

- Concomitant illness
  - Intercurrent infection: respiratory and urinary tract infections (UTIs) are the most common.
  - Stroke
  - Myocardial infarction
  - Pulmonary Embolism
- Drugs that raise serum glucose levels: Diuretics, Beta-blockers, Atypical antipsychotics (clozapine, olanzapine).
- Alcohol
- Non-compliance with oral hypoglycemics or insulin therapy
- Neglected elders with diabetes mellitus

Signs and Symptoms

- Symptoms
  - History of type 2 diabetes (though HHS may be initial presentation of type 2 diabetes)
  - Onset is progressive over days to weeks
  - Polydipsia, polyuria, weight loss, and weakness
  - Focal and global neurologic changes: Drowsiness and lethargy, Delirium, Coma, Focal or generalized seizures, visual changes or disturbances, hemiparesis, sensory deficits
- Signs
  - Vital signs: Tachycardia (early indicator of dehydration), hypotension (sign of profound dehydration), tachypnoea, high or low temperatures in case of sepsis
  - Decreased skin turgor, sunken eyes, dry mouth
  - Altered conscious state and coma, possible focal neurologic signs

Complication

- Similar to DKA

Investigations

- Blood glucose (often >600 mg/dL)
- HbA1c
- Electrolytes (especially sodium, potassium)
- Osmolarity (elevated - see DKA)
- ABG
- Urea and creatinine: (elevated)
- Urine analysis (mild ketonuria, glucosuria, evidence of infection)
- CPK and isoenzymes
- Urine and blood culture
- CXR

Management

- CABD
- Intravenous access
- Fluid resuscitation
    - Fluid deficits in HHS are large, the fluid deficit of an adult may be 10 L or more
    - Administer 1-2 L of *Normal saline* (0.45% NaCl if hypernatraemia) in the first 2 hours. Slower initial rates may be appropriate in significant cardiac or renal disease
    - Once S*erum glucose* drops to 250 mg/dl, the patient must receive *Dextrose* 2.5% IV solution

- *Insulin* therapy
    - Some patients with HHS may respond to fluid replacement without insulin therapy
    - Insulin used without concomitant vigorous fluid replacement increases risk of shock
    - IV insulin therapy is similar to that used in DKA

- Treatment of intercurrent illness

1.5.3. Hypoglycemia

Definition: Hypoglycemia is a syndrome characterized by a reduction in either plasma glucose concentration (<70mg/dl or 2.75mmol/l) or its tissue utilization

Causes

- Diabetic patients
  - Medication changes or overdoses (essentially insulin and secreatagogues)
  - Infection
  - Diet changes, or activity changes
  - No acute cause may be found

- Non diabetic patients
  - Fasting
  - Insulinoma and other endocrinopathy
    - → Hepatic failure
    - → Alcohol abuse
    - → Idiopathic causes

Signs and Symptoms

- Adrenergic
  - Sweating, shakiness, tachycardia, anxiety and sensation of hunger

- Neuroglycopenic symptoms
  - Weakness, tiredness, or dizziness
  - Inappropriate behavior, difficulty with concentration; confusion; blurred vision
  - In extreme cases: coma

Management

- Check and record Blood glucose
- Treat as soon as blood sample is obtained
- The main therapy for hypoglycemia is concentrated glucose
- Other medications may be administered based on the underlying cause
- The goal is to achieve BG>100mg/dl
  - Patient alert and cooperative: use oral carbohydrates
    - → 15 grams of glucose: one glass of Juice/soda, 3 teaspoons of sugar orally

- ➔ Then long acting carbohydrate: piece of bread, or one fruit

- Non-alert patient
  - ➔ 25 g dextrose IV (1 ampoule of *Dextrose 50%*) or 1mg *Glucagon IM* if no IV access (may be repeated every 15-30min)
  - ➔ Recheck Blood glucose after 10-15min, depending on response

- Severe hypoglycemia (<40-50mg/dl) recurrent, or related to sulfonylurea or long acting insulin
  - ➔ *Dextrose 50%* followed by *Dextrose 5%* or *Dextrose 10%* drip depending on blood glucose titration
  - ➔ Cause should be investigated
  - ➔ Adjust anti hyperglycemic regimen, depending on situation

Note:
- *Corrected Na+=Measured Na + (Glycemia -5.4 in mmol)/3*
- *Water deficit=Weight (kg)X 0.6 X (corr Na+ - 140)/140.*

1.5.4. Adrenal Insufficiency

Definition: Adrenal insufficiency is a condition due to a decreased secretion of adrenal steroids.

Causes

- Primary adrenal insufficiency
  - Tuberculosis, HIV,CMV infection
  - Addison disease
  - Ketoconazole
  - Thrombosis/hemorrhage, Sepsis, Disseminated Intravascular Coagulation
  - Infiltrative diseases, bilateral cancer metastasis, Amyloidosis, hemosiderosis (rare)

- Secondary adrenal insufficiency failure of Hypothalamic-Pituitary Adrenal axis usually due to chronic exogenous glucocorticoid administration and pituitary failure
- Tertiary adrenal insufficiency: due to hypothalamic dysfunction

Signs and Symptoms

- Acute crisis
  - Hypotensive shock, dehydration, weakness, fever, depressed mentation.
  - GI disturbances
  - Hypoglycaemia, hyponatremia, hyperkalaemia, acidosis

- Chronic
  - Hyperpigmentation
  - Weakness and fatigue, loss of weight, postural dizziness
  - GI disturbances
  - Hypotension, hypoglycemia, hyponatremia

- Always consider in a thin, hypotensive, hypoglycemic patient, or during stress e.g. sepsis

Investigations

- Morning plasma cortisol: 550 nmol/L:(excludes the diagnosis), < 100 nmol/L: (highly suggestive of Addison's disease) And 100–550 nmol/L (is indeterminate and may require an ACTH stimulation test) which is done on referral to a centre with the appropriate expertise and access to the investigational agent
- Stimulation of Adrenocortical secretion: (Give ACTH 1mg IM, then blood sample for cortisol after 45min). Post test level should be > 550 nmol/L or double the pre-test level.

Managemenet

Acute crisis

- Exclude sepsis
- Hormonal replacement:
  - *Hydrocortisone*, IV, 100–500 mg 6 hourly as required, gradually taper to maintenance dose according to patient's clinical status
  - Therapy for mineralocorticoid replacement when maintenance doses reached: *Fludrocortisones*: 0.05 mg - 0.2 mg OD

- Maintain adequate intravascular volume
  - *Sodium chloride* 0.9%, IV ± 4litres in the first 24–48 hours
  - Reduce the risk of hypoglycemia: *Dextrose,* IV/oral

Chronic

- Maintenance therapy
    - *Hydrocortisone*, oral 10–20 mg in the morning, 5–10 mg at night
    - Alternative: *prednisone,* oral, 5–7.5 mg daily
    - For patients who remain symptomatically hypotensive: *Fludrocortisone* 0.05–1 mg daily

Recommendations

- Monitor for relief of Symptoms: improvement in fatigue and GI disturbances
- Monitor Blood pressure: normotensive and no postural drop
- Monitor Electrolytes: normal Na+ and K+
- All patients should wear an alert bracelet
- All patients must receive increased doses of glucocorticoid during times of "stress (acute illness, surgery, trauma, etc)
- For severe stress: hydrocortisone, IV, 100 mg 6 hourly
- Refer all suspected cases to tertiary level for full evaluation.

1.5.5. Hyper/Hypokalemia

HYPERKALEMIA

Definition: A condition in which serum potassium is > 5 mEq/L

Causes

- Excess of potassium intake
    - Potassium supplements
    - Potassium contained in some antibiotics (penicillins)
    - Blood transfusion

- Translocation of potassium from ICF to ECF
    - Acidosis, severe catabolism, rhabdomyolysis, tissue necrosis

- Insulin deficiency
- Adrenal insufficiency
- Periodic pseudoparalysis
- Drugs: Digitalis toxicity, Succinylcholine(suxamethonium), aldosterone antagonists, B-blockers,Catecholamine deficiency state
- Hyperosmolarity

- Decreased excretory capacity
  - Renal failure, oliguria
  - Renal tubular disease
  - Drugs: Potassium sparing diuretics, Cyclosporine, ACE inhibitors/ARAII, NSAID

Signs and Symptoms

- Asymptomatic
- Arrhythmias (ventricular, tachycardia/fibrillation)

Complications

- Ventricular Tachycardia, Ventricular Fibrillation, Cardiac arrest

Investigations

- Electrolytes
- Urinary electrolytes
- Urea and creatinine
- Blood sugar
- ABG
- ECG
- Creatinine Kinase

Management

- Treat underlying cause
  - Restrict exogenous potassium
  - Remove offending drugs

- If K> 6 mEq/l:
  - Give *Calcium gluconate* 2gm IV
  - *Dextrose 50%* 1 ampulule+ 10U rapid insulin IV
  - Give molar *Biocarbonate* 1-2 ampules IV over 5-10 min slowly
  - *Kayexalate* 30- 60 gm PO
  - Give *Lasix* IV40-80mg
  - B- agonist inhaled (*Salbutamol*)
  - Dialysis

HYPOKALEMIA

Definition: it is condition in which serum potassium is <3.5 mEq/L

Causes

- Increased loss:
  - Diarrhoea, Vomiting, Biliary loss
  - Small intestine fistulas
  - Laxative abuse

- Distribution defect
  - Insulin
  - Alkalosis
  - Hyperglycemia
  - Periodic paralysis
  - B_{12} therapy

Signs and Symptoms

- Muscle weakness, Paralysis
- Rhabdomyolysis
- Constipation (paralytic ileus)
- Arrhythmia

Complications

- Arrhythmia
- Cardiac arrest

Investigations

- Electrolytes
- Urinary electrolytes
- ABG
- ECG
- Blood glucose
- FBC

Management

- Give *Magnesium Sulphate* 2 gm over 30 min
- Give *Potassium Chloride* 40mEq PO or IV 10-15 mEq/hour
- Find and correct cause

1.5.6. Hyper/Hyponatremia

HYPERNATREMIA

Definition: is a rise in serum sodium concentration to a value exceeding 145 mEq/l (above 158mEq is severe hypernatremia).

Causes

- Normal total body sodium (Euvolemic)
  - Pronounced pure water loss
    - → Extrarenal
      - fever
      - hyperventilation, mechanical ventilation
    - → Renal losses
      - Diabetes insipidus (central or nephrogenic)
      - Hypodipsia
- Low total body sodium (hypovolemic)
  - Renal losses of water and sodium
    - → Osmotic dieresis: mannitol, Glucose, Urea
    - → Loop diuretics (Furosemide, Indapamide)
  - Extrarenal losses
    - → Diarrhoea
    - → Sweating
- High total body sodium (Hypervolemic)
  - Usually iatrogenic
    - → Infusion of hypertonic solutions(3% NaCl, molar bicarbonate)
    - → Na tablets or sodium-containing antibiotics
    - → Hypertonic dialysis
    - → Glucorticoid excess
    - → Hyperaldosteronism

Signs and Symptoms

- Hypotension, tachycardia if hypovolemia
- Nausea and vomiting
- Increased thirst
- Dyspnea
- Altered mental status, lethargy, irritability, restlessness, hyperreflexia, focal deficits, seizures, coma
- Muscle twitching, spasticity

Investigations

- FBC
- Electrolytes and osmolality
- Urine electrolytes and osmolality
- Urea and creatinine
- Blood glucose
- Head CT scan or MRI
- Endocrine tests
- ADH stimulation
- Corticosteroids

Complications

- Subdural haemorrhage
- Intracranial venous sinuses thrombosis
- Subcortical haemorrhages and cerebral infarction
- Seizures
- Permanent central nervous system damage

Management

- Identify and treat underlying cause
- Correct osmolar imbalance by replacing what was lost (water, hypotonic fluids +/- electrolytes)
    - If Hypovolemic: retore the hemodynamics with *Normal Saline*, then change to *Dextrose 5%* or *NaCl* 0.45%
    - Diabetes insipidus: in case of urinary specific gravity <1005, give desmopressin (minirin) 0.2 µg SC or vasopressin 0.1 IU/kg slow IV
    - If hypervolemic: give loop diuretics (*Frusemide* 40 mg IV then replace the losses by *Dextrose 5%*. Dialysis if renal function impaired
    - If euvolemic: give dextrose 5%

Note: *If Na has risen quickly within the last 12 hours, it can be corrected quickly without consequences. Otherwise, decrease Na by not more than 10 mEq/day*

Calculations of the effect of 1L of fluid on Serum Na:
Change in Na for 1L of fluid of choice = (IVF Na-SerumNa)/ (TBW+1)
Total Body Water (TBW):0.6x Weight in kg

HYPONATREMIA

Definition: is an electrolyte disturbance in which the serum sodium concentration is less than 135 mEq/l (Severe if < 125 mEq/l).

Causes

- Sodium and water deficit (hypovolemic)
  - Renal losses
    - → Diuretic excess
    - → Osmotic diuresis (glucose, urea or mannitol)
    - → Mineralocorticoid deficiency
    - → Salt-losing nephritis, bicarbonaturia, renal tubular acidocis, ketonuria
  - Extra-renal losses
    - → Vomiting, Diarrhoea
    - → Burns, pancreatitis, crush injury
- Water excess (Euvolemia)
  - Glucocorticoid deficiency
  - Hypothyroidism
  - Pain
  - Psychiatric disorders
  - Drugs (thiazidic diuretics)
  - Syndrome of inappropriate ADH secreration
- Sodium and water excess (Hypervolemia)
  - Nephritic syndrome, Acute and chronic renal failure
  - Cardiac failure
  - Cirrhosis
  - Beer drinkers potomania
  - Primary polydipsia
- Pseudohyponatremia
  - High plasma osmolality
    - → Hypoglycaemia
    - → Mannitol
  - Normal plasma osmolality
    - → Hyperlipidemia
    - → Hyperproteinemia
    - → Glycine solutions

Signs and Symptoms

- Fatigue, Headache
- Nausea, Vomiting
- Convulsions
- Abnormal mental status, Irritability, Coma

Complication

- Coma, Brain herniation, Death

Investigations

- Electrolytes, osmolality
- Urine electrolytes/ osmolality
- FBC
- TSH
- Albumin

Management

- If hypovolemia
  - Give isotonic saline (*Normal saline 0.9%*)

- If euvolemia
  - Water restriction
  - Stop any suspected drug

- If hypervolemia
  - Water and sodium restriction
  - Give *frusemide*

- Calculation of Sodium deficit = Plasma sodium deficit/L X total body water
  - Total body water = 0.5 X weight in kg
  - Plasma sodium deficit = targeted sodium – current sodium

Note: *correction of plasma sodium concentration should not exceed 0.5 mEq/H*

1.5.7. Hypercalcemia

Definition: Marked elevation of serum calcium, usually more than 14 mg/dL associated with acute clinical signs and symptoms of hypercalcemia.

Causes

- Malignancy
  - Extensive bone destruction
  - Decreased kidney secretion
- Primary hyperparathyroidism
- Granulomatous disorders - TB, sarcoidosis

Signs and Symptoms

- Nausea and vomiting
- Alterations of mental status, Depression
- Abdominal or flank pain (occasionally new kidney stone)
- Constipation
- Lethargy
- Weakness and vague muscle/joint aches
- Polyuria, polydipsia, nocturia
- Headache
- Confusion

Complications

- Joint Involvement
- Renal calculi
- Coma

Investigations

- Corrected serum calcium levels (Adjusted for albumin level)
- Serum PTH (ParaThyroid Hormone)
- Electrolytes and Renal function test
- Depending on the cause: Xrays, tests for malignancy, ultrasound looking for parathyroid mass

Management

Non Pharmaceutical

- Adequate hydration with normal saline
- Increased urinary calcium excretion
- Manage the underlying cause whenever possible

Pharmaceutical

- Hydration with *Normal saline* IV 1L over 4 hours, then adjust to keep urine output >100ml/hr
- Loop diuretics *Furosemide* 80 mg BD
- *Calcitonin* IM or SC 4IU/kg BD
- *Biphosphonate* oral or IV if available

Recommendations

- Refer to tertiary health facility for management
- Avoid excessive saline hydration in cases of renal failure

1.6. Gastrointestinal emergencies

1.6.1. Upper GI bleeding (UGIB)

Definition: Is defined as bleeding derived from a source proximal to the *ligament de Treitz.*

Causes

- Esophageal causes
  - Esophageal varices, Esophagitis, Esophageal cancer, Esophageal ulcers, Mallory-Weiss tear
- Gastric causes
  - Gastric ulcer, Gastric cancer, Gastritis, Gastric varices
- Duodenal causes
  - Duodenal ulcer, Vascular malformation, including aorto-enteric fistulae, Hematobilia

Signs and Symptoms

- Haematemesis
- Melena
- Signs of anaemia and shock if massive hemorrhage

Complications

- Shock and its complications
- Recurrent Bleeding
- Sepsis, Decompensated Ascites and Encephalopathy in cirrhotic patients

Investigations

- Gastroscopy (key test)
- FBC, urea and creatinine, serum electrolytes, Group and cross-match
- Liver function tests
- Coagulation tests
- Abdominal Ultrasound to confirm cirrhosis

Management

- IV line
- Monitor vital signs
- Correct coagulopathy if present
- Start infusion of normal saline
- Respiratory support
- Transfusion if required for shock, anaemia
- Administer Proton Pump Inhibitors (PPIs) IV 80mg IV(e.g *Pantoprazole*) and 8mg/h infusion for 48hours then continue with PPI 20-40mg bid orally per day or H2 receptor inhibitors (e.g *Cimetidine*) if PPI not available
- Treat underlying causes: Interventional gastroscopy to stop bleeding: variceal ligation; sclerotherapy or adrenaline injection
- Surgical hemostasis in cases where above measures fail
- Give laxatives and *Ceftriaxone* 1g/day for 5 days in varices patients
- Avoid oral intake if ongoing bleeding

Recommendation

- All patients with significant ongoing UGI bleeding should be referred to a centre with interventional endoscopy services

1.6.2. Lower GI Bleeding (LGIB)

Definition: LGIB is defined as bleeding from bowel distal to the ligament of Treitz.

Causes

- Colorectal cancer
- Infectious colitis with E- coli, shigella, C. difficile, Campylobacter jejuni
- Inflammatory bowel diseases: Crohn's disease and ulcerative colitis
- Anorectal disease- hemorrhoids, fissures and fistulas.
- Diverticular disease - diverticulosis, diverticulitis
- Post polypectomy bleeding
- HIV related opportunistic infection- CMV colitis, Kaposi sarcoma and lymphoma
- Drug induced bleeding- Aspirin, anticoagulants, steroids and NSAID's
- Vascular- Angiodyplasia, CTDs, Ischemic Colitis
- Small intestinal causes: Intussusception and Meckel's diverticulum

Signs and Symptoms

- Rectal bleeding either bright or dark red
- Signs of anemia

Investigations

- Full blood count (FBC)
- Serum electrolytes
- Renal function tests (blood urea and serum creatinine)
- Coagulation profile (Prothrombin time and INR)
- Colonoscopy
- Angiography
- Upper GI endoscopy and enteroscopy

Management

- Stabilize the patient: Correct anemia and prevent further bleeding
- Correct coagulopathy if present
- Establish and treat the cause
- Therapeutic colonoscopy is preferred if ongoing bleeding
- If colonoscopy not available consider surgical referral for laparotomy

1.6.3. Acute Pancreatitis

Definition: Acute pancreatitis (AP) is an acute inflammatory condition of the pancreas that may extend to local and distant extrapancreatic tissues.

Causes

- Gallstones (45%)
- Alcohol (35%)
- Other (10%):
    - Medications (eg. azathioprine, estrogen, valaproic acid, ARVs)
    - Hypercalcemia
    - Surgery and certain medical procedures,
    - Abnormalities of the pancreas(pancreas divisum) or intestine
    - High fat levels in the blood (hypertriglyceridemia)
- Idiopathic (10%)

Signs and Symptoms

- Sudden onset of epigastric pain radiating to the back
- Anorexia, Nausea, Vomiting
- Fever, Tachycardia, Hypotension
- Epigastric tenderness, with localized guarding and rebound
- Sluggish or absent bowel sounds indicate coexisting ileus

Complications

Pancreatitis can cause serious complications, including:

- Local and regional complications
    - Pancreatic necrosis ±Infection
    - Pancreatic fluid collection (Pseudocyst)
    - Acute tubular necrosis
    - Chronic pancreatitis
    - Pleural effusion
    - Ascites
    - GI hemorrhage

- Systemic complications
    - Acute respiratory distress syndrome (ARDS)
    - Metabolic and electrolytic complications: Diabetes, hypocalcemia, encephalopathy
    - DIC

Investigations

- FBC and CRP
- Serum amylase and lipase levels (in excess of three times the upper limit of normal)
- Blood sugar (hyperglycemia)
- Serum electrolytes (hypocalcemia)
- Liver function tests (hyperbilirubinemia, serum alkaline phosphatase, AST, LDH, Serum albumin)
- Lipid levels in the blood (hypertriglyceridemia)
- Simple plain films of the chest and abdomen (to rule out pleural effusion and acute abdomen)
- Abdominal ultrasound (evaluating the gallbladder)
- Abdominal CT scan (evaluating severe pancreatitis and detecting complications)

Management

- Admit the patient
    - Monitoring in ICU may be required, especially for patients who are at high risk of rapid deterioration such as the elderly, the obese, patients requiring ongoing volume resuscitation, and patients with substantial pancreatic necrosis

- The choice of treatment is based on the severity of the attack.
- IV line and Fluids: Normal saline 6 L within 48 hrs if no contraindications
- Nasogastric (NG) tube for aspiration and no oral alimentation (NPO)
- Analgesics e.g opoids analgesic: *Pethidine* IV 50mg to 100mg x 3per day or *Morphine* until pain is reduced
- *Metoclopromide* 10 mg IV when necessary for vomiting
- Antibiotic prophylaxis is not recommended
- Enteral nutrition through the jejunum is recommended but parenteral nutrition only be used when attempts at enteral nutrition have failed
- Strict glycemic control
- Transfer to Surgery department for cholecystectomy in case of gallstones, complications (e.g enlargement or severe injury of the pancreas, bleeding, pseudocysts, or abscess)
- Close monitoring of the patient

Recommendations

- Stop alcohol consumption
- Eat small frequent meals
- During an attack, avoid solid foods for several days and
- Eat a diet high in carbohydrates and low in fats
- If pancreatitis is due to medications, discontinue medication

1.7. Cardiovascular Diseases

1.7.1. Cardiomyopathies

Definition: It is a disease of heart muscle that results from myriad of insults such as genetic defect, cardiac myocyte injury or infiltration of myocardial tissue.

Classification

- Dilated cardiomyopthy
- Hypertrophic cardiomyopathy
- Restrictive cardiomyopathy
- Arrthymogenic right ventricular cardiomyopathy
- Ischaemic cardiomyopathy
- Hypertensive cardiomyopathy
- Inflammatory cardiomyopathy
- Peri partum
- Metabolic cardiomyopathy
- General systemic diseases cardiomyopathy

Signs and Symptoms

- General symptoms: dyspnoea, fatigue, chest pain, palpitations
- Signs: lower limbs swelling, abdominal discomfort, abdominal distension, others signs according to the patient NYHA Classification; therefore the patient can present heart failure. In this guideline we considered 2 types of cardiomyopthies: dilated and hypertrophic cardiomyopathies

DILATED CARDIOMYOPATHY

The hallmarks of DCM which is the most common cardiomyopathy are enlargement of one or both ventricles and systolic dysfunction.

Causes

- Acquired: infections (e.g.: HIV), alcohol, toxins and drugs (e.g. adriamycin)
- Genetic predisposition

Investigations

- FBC, urea, creatinine, serum electrolytes
- ECG, echocardiography, CXR,
- Cardiac catheterisation
- Others tests according to suspected aetiology

Complications

- Heart failure
- Arrhythmia
- Embolisation
- Sudden cardiac death

Management

The main goal of treatment includes:
- Control signs and symptoms
- Managing and/or stopping aetiology (e.g Cessation of alcohol)
- Preventing progression and complications

Non pharmacological

- Lifestyle modification (LFM)
  - ➔ Weight Reduction
  - ➔ DASH diet
  - ➔ Low salt diet
  - ➔ Avoid alcohol intake
  - ➔ Regular physical activity

Pharmacological

- It will depend on NYHA classification and complications involved

1.7.2. Heart Failure

Definition: AHF is the rapid or gradual onset of signs and symptomes of Heart Failure that results in urgent unplanned hospitalisation or office or emergency department visit.

Etiology/Causes

The most common causes are
- Coronary heart disease
- Valvular heart disease
- Hypertension
- Diabetes

Signs and Symptoms (According to Framingham criteria):

Diagnosis of CHF requires the simultaneous presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria.
- Major criteria
  - Paroxysmal nocturnal dyspnea
  - Neck vein distention
  - Rales
  - Radiographic cardiomegaly (increasing heart size on chest radiography)
  - Acute pulmonary edema
  - S3 gallop
  - Increased central venous pressure (>16 cm H2O at right atrium)
  - Hepatojugular reflux
  - Weight loss >4.5 kg in 5 days in response to treatment

- Minor criteri*a*
  - Bilateral ankle edema
  - Nocturnal cough
  - Dyspnea on ordinary exertion
  - Hepatomegaly
  - Pleural effusion
  - Decrease in vital capacity by one third from maximum recorded
  - Tachycardia (heart rate>120 beats/min.)

Minor criteria are acceptable only if they can not be attributed to another medical condition (such as pulmonary hypertension, chronic lung disease, cirrhosis, ascites, or the nephrotic syndrome)

The Framingham Heart Study criteria are 100% sensitive and 78% specific for identifying persons with definite congestive heart failure

Investigations

- Serum electrolytes; sodium and potassium
- Urea creatinine
- Liver Function Test
- FBC
- BNP (b- type natriuretic peptide)
- Cardiac enzymes
- CXR
- ECG
- Echo cardiography
- Cardiac catheterisation when appropriate

Complications

- Cardiac arrhythmias
- Renal failure
- Electrolyte disturbances

Management

- Goal for treatment
    - Stabilise the patient ± CVP monitoring
    - Establish the diagnosis
    - Identify the aetiology and precipitating factors
    - Oxygen is indicated when SaO2 is < 95%
    - Non invasive ventilatory support

- Indication for hospitalisation
    - Severe decompasated heart failure
    - Worsening renal functioning
    - Altered mentation
    - Dyspnoea at rest
    - Significant hypoxemia
    - Haemodynamicaly significant arrhythmia
    - Acute coronary syndromes
    - Electrolyte imbalance

Pharmacological

- Diuretic eg *Furosemide IV* 20-80mg bolus start, up to 500mg bolus or continous infusion 5-40mg /hr, alternatively you can use *torsemide* 10-40mg bolus up to

200mg bolus or infusion 5-20mg /hr, change to oral as appropriate
- Inotropes*: Dobutamine* infusion most commonly used 1-2µg/kg/min, alternatively give dopamine 3-5µg/kg/min
- Treat the aetiology and precipitating cause and complication accordingly

1.7.3. Cardiac Arrhythmias

Ventricular and supra-ventricular

Definition: An arrhythmia is a problem with the rate or rhythm of the heartbeat. During an arrhythmia, the heart can beat too fast, too slow, or with an irregular rhythm

Ventricular arrhythmias are abnormal rapid heart rhythms (arrhythmias) that originate in the lower chambers of the heart (the ventricles)

- Types
  - ➔ Ventricular tachycardia
  - ➔ Ventricular fibrillation

Supraventricular arrhythmias begin above the ventricles, while the Ventricular arrhythmias begin in the ventricle.

- Types
  - ➔ Atrial fibrillation
  - ➔ Atrial flutter
  - ➔ Atrial tachycardia

Causes

- Cardiovascular (coronary, valvular, artheroscelosis, hypertension
- Non-cardiovascular (Diabetes, thyroid, stress, alcohol, caffeine, smoking)

Signs and Symptoms

- Palpitations
- Feeling tired or light-headed
- Losing consciousness
- Shortness of breath
- chest pain
- dizziness

Complications

- Heart Failure
- Thrombo-embolism
- Sudden Cardiac death

Investigations

- ECG (12 lead standard, Holter, implantable loop recorder)
- Exercise testing (effort tolerance test)
- Upright tilt table testing
- Invasive electrophysiological studies

Management

- Depend on the type of arrhythmia, cause, the patients age, physical condition and drugs e.g. digoxin
- Goals: control of heart rate, restoration sinus rhythm, prevention of recurrent episodes or decrease in their frequency or duration, prevention of thrombo-emboli complications, minimization of adverse effects from therapy

Pharmacological

- Anti-arrhythmic agents (Class IA): *Quinidine Sulphate* PO
  - Indication: Atrial flutter, atrial fibrillation, recurrency of tachycardias
  - Loading dose PO: 600mg – 1g then 300mg – 600mg x 4/day
  - Side effects include Tinnitus, hearing loss, visual disturbance, confusion;
  - Give *Magnesium* IV 2g over 1 – 2 minutes followed by infusion of 3 – 20 mg/minute.

Alternative treatment

- *Procainamide* PO/IV/IM:
  - Indication: Supraventricular and ventricular arrhythmias, Wolff Parkinson White syndrome
  - Dose: PO; 25 – 50mg/minute repeated every 5 minutes until arrhythmias are controlled; IV infusion 2 – 6 mg/minute depending on patient response

  Or
- Class IB: *Lidocaine* IV route is most commonly used
  - Indication: Ventricular arrhythmias
  - Dose**:** Bolus of 1 – 2 mg/kg at a rate of 20 – 50 mg/minute; 2nd injection half the initial doze 20 – 40 minutes later

Or

- Class IC: Especially in non-structural heart disease (*Flecainide PO)*
  - Indications; Supraventricular tachycardia and ventricular tachyarrhythmias and paroxysmal atrial fibrillation, premature ventricular contractility
  - Dose: 100mg/12hours increased in increment of 50 mgx2/day no sooner than every 3 – 4 days depending on patient response

    Or
- Class II: Beta adreno-receptor blockers (*Propranolol* PO):
  - Indications: related to excessive cardiac adrenergic stimulation e.g. arrhythmias associated with toxicosis, pheochromocytoma
  - Dose: Loading dose of 0.25 – 0.5mg, then maintenance of 10 – 200mg/6-8 hours.

- Class III: *Amiodarone* IV
  - Indications: Ventricular tachyarrhymias, supraventricular and ventricular arrhythmias, VT and VF associated with coronary artery disease, and hypertrophic cardiomyopathy
  - Dosage: Loading dose 15mg/minute/10minutes; Maintenance 200mg – 600mg/day depending on patient response
  - Alternative treatment: *Sotalol* PO; 80 – 160 mg/12hrs

- Class IV: Calcium channel blockers *(Verapamil PO):*
  - Indications: Arrhythmias associated with accessory pathway, paroxysmal SVTs
  - Dose: IV Loading dose of 5 – 10 mg/1-2 minutes; maintenance of 80 – 120 mg/6-8 hourly

- Other anti-arrhythmic agents: Adenosine, digoxin; check doses and indications

Electrotherapy treatment

- Direct current electrical cardio-version
  - Indication: Tachycardias that produce hypotension, congestive heart failure, mental status changes, and those not responding to medical management promptly

- Implantable electrical devices
  - ➔ Indication; symptomatic arrhythmias, drug intolerant anddrug hesitance (refer to literature)

Surgical treatment
- Refer to cardiologist

Recommendations

- Patient should be immediately be referred to a cardiac centre after stabilization
- Advice patients to use relaxation techniques to reduce stress, limit intake of caffeine, nicotine, alcohol and stimulant drugs

1.7.4. Valvular Heart Disease

1.7.4.1. AORTIC VALVULAR DISEASE

AORTIC STENOSIS

Definition: Aortic stenosis is abnormal narrowing of the aortic valve. Narrowing may occur above the valve (supra-valvular) or below the valve (discrete sub-valvular stenosis)

Causes/Etiology

- Three principle causes are Congenital, Calcific (degenerative) and Rheumatic
- Other causes include rheumatic arthritis, ochronosis with alkaptonuria

Signs and Symptoms

- Chest pain (angina)
- Fainting (syncope)
- Shortness of breath (due to heart failure)

Clinical presentation

- Palpation of the carotid upstroke
- Systolic murmur
- Splitting of second heart sound
- Signs of heart failure

Investigations

- ECG
- Chest X-ray
- Echocardiography
- Cardiac catheterization and angiography
- Chest computed tomography
- Cardiac magnet resonance

Management

Non-pharmacological

- To avoid vigorous athletic and physical activity
- Prophylaxis against infective endocarditis

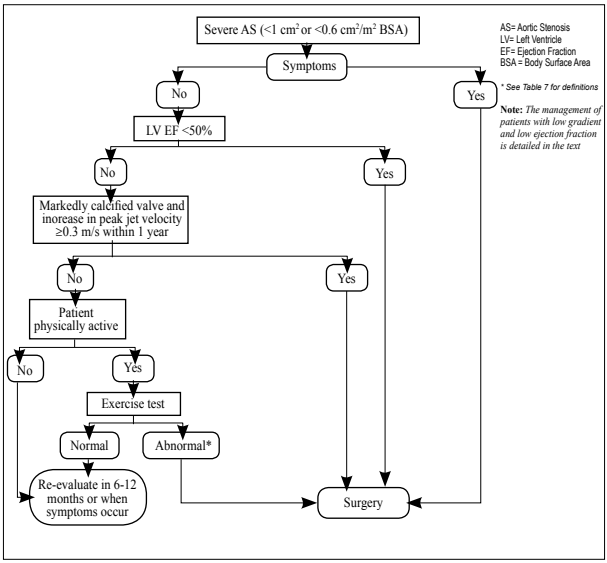
Pharmacological

- ACE inhibitor are beneficial in symptomatic Left Ventricular systolic dysfunction but used with caution
- Symptomatic with severe AS are usually operative candidates because medical therapy has little to offer
- Treatment of arrhythmias

Surgical treatment

- If significant narrowing of the coronary arteries is found, coronary artery bypass graft surgery (CABG) can be performed during aortic valve replacement surgery

ALGORITHM FOR MANAGEMENT OF SEVERE AORTIC STENOSIS



AORTIC REGURGITATION

Definition: Aortic insufficiency is a heart valve disease in which the aortic valve weakens or balloons, preventing the valve from closing tightly. They are of two types, acute and chronic forms

Etiology/Causes

- Congenital
  - Bicuspid valve defect
  - Unicommissural and quadricuspid

- Acquired
  - Rheumatic
  - Infective endocarditis
  - Trauma
  - Large VSD
  - Some connective tissue diseases
  - Infections (e.g. syphilis)

- Aortic dissection
- Drugs (e.g. anorectic)

Signs and Symptoms

- Bounding pulse
- Chest pain, angina type (rare)
- Fainting
- Fatigue, excessive tiredness
- Palpitations
- Shortness of breath with activity or when lying down

Complications

- Left-sided heart failure
- Pulmonary edema
- Infective endocarditis

Investigations

- Echocardiography
- Transesophageal Echocardiography (TEE)
- ECG or chest x-ray may show swelling of the left lower heart chamber
- Left heart catheterization and Aortic angiography
- Routine laboratory tests (FBC, Urea and Creatinine, electrolytes, liver function tests)

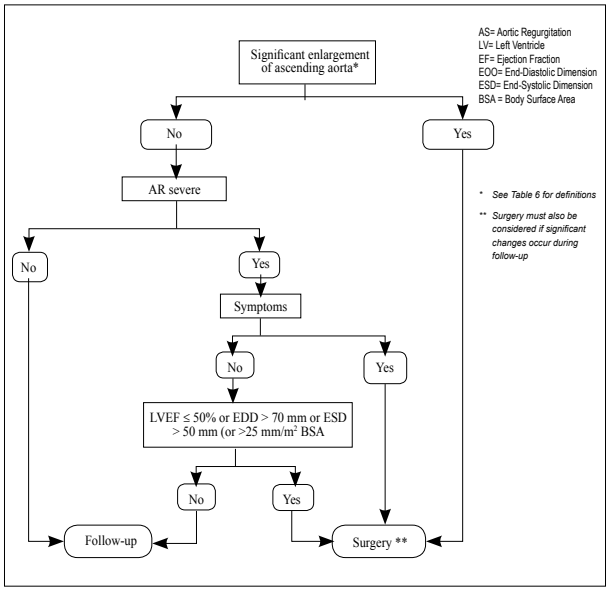
Management

Medical

- Treat hypertension if present with
  - → *Nifedipine* PO: 5-10mg/day, adjusted according to response
  - → *Enalapril* PO: 2.5 – 20mg BID, adjusted according to response
- Vasodilator therapy in patients with evidence of volume overload (after load reduction)

Surgical: When indicated

ALGORITHM FOR MANAGEMENT OF SEVERE CHRONIC AORTIC REGURGITATION:



1.7.4.2. MITRAL VALVE DISEASE

MITRAL STENOSIS

Definition: Is a narrowing of the inlet valve into the left ventrical that prevents proper filling during diastole.

Etiology/Causes

- Congenital, Lutembacher syndrome (rare)
- Acquired
    - Rheumatic
    - Some connective tissue disease
    - Infective endocarditis
    - As a complication of malignant carcinoid disease
    - Drugs (e.g. methysergide)

Signs and Symptoms

- Atrial fibrillations and A.flutter
- Chest discomfort (rare)
- Cough, possibly bloody (hemoptysis)
- Difficulty breathing Fatigue
- Frequent respiratory infections such as bronchitis
- Palpitations
- Swelling of feet or ankles
- Horsiness of the voice
- Mitral facies
- Mid-diastolic thrill and murmur
- Loud fast heart sound
- Signs of heart failure

Complications

- Thrombo-embolism
- Pulmonary hypertension
- Pulmonary haemosiderosis
- Heart failure
- Arrhythmias

Investigations

- Echocardiography
- Transesophageal echocardiography (TEE)
- ECG or chest x-ray may show swelling of the left lower heart chamber
- Left heart catheterization and Aortic angiography
- Routine laboratory tests (FBC, Urea and creatinine, electrolytes, liver function tests)

Management

- Treatment depends on the symptoms and condition of the patient
- Goal is to reduce symptoms, control ventricular rate and prevent thrombo-embolic complications

Pharmacological

- Diuretics in Heart Failure: *Frusemide* PO/IV: 40 – 120mg/day
- Beta blocker: *Atenolol* PO: 12.5 mg – 50mg BID/day
- Anticoagulant therapy in Atrial Fibrillation: *Warfarin* PO: 2.5 – 10mg/day according to international normalization ration (INR), maintain INR 2 -3

Alternative treatment

- Low Molecular Weight *Heparin* SC: 40mg BID if appropriate
- Mitral baloon valvotomy as indicated

Surgical

- Surgical valvotomy
- Mitral valve repair or replacement

MITRAL REGURGITATION

Definition: Mitral regurgitation is when mitral valve doesn't close tightly, which allows blood to flow backward in the heart forcing a constant strain on your cardiac muscle.

Etiologies/Causes

- Congenital
  - Connective tissue disease e.g. mitral valve prolapsed (MVP)
  - Mitral valve clefts or fenestrations
  - Parachute mitral valve abnormalities e.g. endocardial cushion defect

- Acquired
  - Rheumatic
  - Infective endocarditis
  - Annular calcification
  - Cardiomyopathies
  - Ischemic heart disease
  - Others include trauma, tumors, connective tissue disease

Signs and symptoms (Symptoms depend on severity of the disease)

- Shortness of breath, especially during exercise or when you are laying still
- Fatigue, especially during exercise
- Cough, often during the night, when in bed
- Heart palpitations, or fluttering heartbeats, atrial fibrillation
- Swollen feet or swollen ankles
- Pan systolic heart murmur with muffled heartbeat

Complications

- Thrombo-embolism
- Pulmonary hypertension
- Heart failure
- Arrhythmias

Investigations

- Echocardiography and exercise echocardiography
- Transesophageal Echocardiography (TEE)
- ECG or chest x-ray may show swelling of the left lower heart chamber
- Left heart catheterization and Aortic angiography
- Routine laboratory tests (FBC, Urea and creatinine, electrolytes, liver function tests)

Management

- Management depends on acuteness, severity and cause of mitral regurgitation. Acute and severe mitral regurgitation urgent mitral repair or replacement is indicated.

Medical

- After load reduction: ACEI e.g. *Enalapril* PO, 2.5mg – 20mg BID
- Beta blocker: *Atenolol* 12.5mg - 50mg daily or BID (there is accumulating experimental data)
- Anticoagulant therapy in Atrial Fibrillation: *Warfarin* PO: 2.5 – 10mg/day according to international normalization ration (INR), maintain INR 2 -3

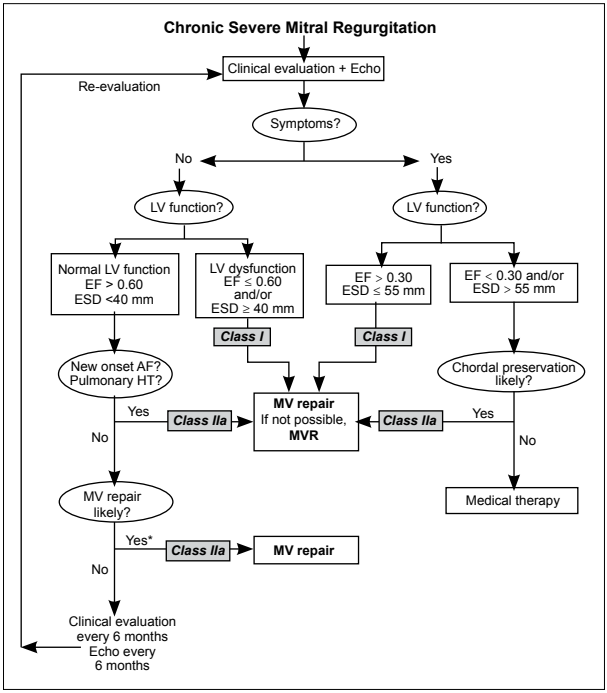
Alternative treatment

- Low Molecular Weight *Heparin* SC: 40mg BID if appropriate

Surgical

- Mitral valve repair or mitral replacement when indicated

ALGORITHM FOR MANAGEMENT OF CHRONIC SEVERE MITRAL REGURGITATION



Recommendation

- Stabilize the patient and refer to the cardiac centre

1.7.5. Acute Coronary Syndrome

Definition: Is plague rupture leading to various degrees of coronary thrombosis and occlusion along with distal micro-embolism. Most often refers to unstable angina and non-ST elevation myocardial infarct (MI) and includes ST segment elevation MI.

Either of the following criteria satisfies the diagnosis of acute evolving or recent MI

- Typical rise and or fall of biochemical markers of myocardial necrosis with at least one of the following
  - Ischemic symptoms
  - Development of pathological Q-waves in the ECG
  - ECG changes indicative of ischemia (ST-segment elevation or depression)
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality

- Pathological findings of acute myocardial infarction

UNSTABLE ANGINA AND NON- ST ELEVATION

Definition: Severe obstruction but not total occlusion of the culprit coronary artery

- Features of Unstable Angina
  - Occurring at rest or minimal exertion and usually lasting more than 20 minutes
  - Being severe and described as flunk pain of new onset i.e. within one month
  - Occurring with crescendo pattern

Etiology/Causes

- Atherosclerosis (most common cause)
- Non-atherosclerotic e.g. Coronary spasm (rare)
- Common risk factors include
  - Diabetes
  - Family history
  - Hypertension
  - High LDL cholesterol
  - Low HDL cholesterol
  - Male gender
  - Sedentary life

- Obesity
- Older age
- Smoking

Signs and Symptoms

- These depend on degree of the unstable angina. Range from being asymptomatic to the following:
  - Typical Chest pain
  - Discomfort that feels like tightness, squeezing, crushing, burning, choking, or aching
  - Discomfort that occurs at rest and does not easily go away when you take medicine
  - Shortness of breath
  - Sweating
  - Pale cool skin
  - Sinus tachycardia
  - A third or fourth heart sound
  - Rarely hypotension

Investigations

- ECG and follow up ECG monitoring
- Echocardiography
- Cardiac enzymes (CK, CKMB and troponins)
- Urea and creatinine
- White blood count
- C-reactive proteins
- B-type Natiuretic Peptide (BNP)
- Stress tests
  - Exercise tolerance test (stress test or treadmill test)
  - Nuclear stress test
  - Stress echocardiogram
- Chest X-ray
- Coronary angiography

Management

- General measures: Admission, bed rest, supplemental oxygen when SO2 < 92%

Pharmacological

- *Nitrates*: sub lingual nitrate, 0.3 - 0.5mg when necessary (PRN)

- Intravenous *Nitroglycerine* is recommended in persistent pain; 5 μg - 10μg/min. every 3 – 5 minutes depending on response
- *Morphine sulphate* IV, 1mg -4 mg (contra-indicated in hypotension or allergy)
- Beta blocker: *Atenolol*, 5 – 10 mg IV bolus followed by 25mg – 100mg PO daily
- Ant-platelets: *Asprin* PO, 75 – 100 mg daily and/or *Clopidogrel* PO, loading dose 300mg, and maintainance doze of 75mg daily
- Others
  - ➔ LMW *Heparin*, 40mg BID subcutaneous
  - ➔ ACEI e.g. *Perindopril* PO, 2mg - 4mg daily
  - ➔ Statin e.g. *Atorva statin* PO, 40mg daily

Surgical

- Coronary angiography and revascularization as indicated

Recommendations

- Urgent referral to the cardiac center immediately after stabilization
- Evaluate and treat causes and risk factors

ST-ELEVATION IN MYOCARDIO INFARCTION

Definition: Severe obstruction but not total occlusion of the culprit coronary artery.

Etiology/Causes

- Arthrosclerosis (most common cause)
- Non atherosclerotic causes
  - Arteritis
  - Trauma to the coronary arteries
  - Metabolic or intimal proliferative diseases
  - Luminal narrowing
  - Emboli to the coronary arteries
  - Congenital coronary artery abnormalities
  - Hematological
  - Myocardial oxygen demand supply mismatch

Signs and Symptoms

- These depend on the condition of the patient ranging from
  - Restlessness
  - Chest pain
  - Cardiogenic shock

Investigations

- ECG and follow up ECG monitoring
- Echocardiography
- Cardiac enzymes (CK, CKMB and troponins)
- Urea and Creatinine
- White blood count
- C-reactive proteins (CRP)
- B-type Natiuretic Peptide (BNP)
- Chest X-ray
- Coronary angiography

Complications

- Hemodynamic disturbances
  - Left ventricular failure
  - Cardiogenic shock
  - Right ventricle infarct

- Mechanical
  - Cardiac muscle rupture
  - Rupture of ventricular free wall
  - Ventricular septal rupture
  - Papillary muscle rupture

- Arrhythmias including complete heart block
- Others
  - Recurrent chest discomfort
  - Left ventricular thrombus and arterial embolism

Management

- Patient stabilization (control pain, BP, fluids, oxygenation)
- Pre-hospital fabrinolysis:
  - *Streptokinase* IV, 1.5million IU in 100mls 5% dextrose water OR 0.9% saline over 30 – 60 minutes, followed by un-fractionated *Heparin infusion* or *LMW heparin* as per protocol

- Alternative
  - *Recombinant human tissue type plasminogen activator* (rt-PA), IV 50mg bolus, then 0.5mg/kg over 60 minutes, followed by un-fractionated Heparin infusion **or** LMW heparin as per protocol

- Others
  - Ant-platelets: *Aspirin* PO 75mg – 325mg daily and/or *Clopedogrel* as per protocol
  - Identify and treat life threatening complications

- Coronary revascularization as indicated

Recommendation

- Stabilize the patient and urgently refer patient to the cardiac center for appropriate management i.e. Coronary revascularization

1.7.6. Pericardial Effusion and Cardiac Temponade

Definition: Pericardial Effusion is the presence of an abnormal amount and/or character of fluid in the pericardial space.

- Cardiac Temponade: Classic Beck triad of pericardial tamponade (hypotension, muffled heart sounds, jugular venous distension)
- Other clinical features (Elevated systemic pressure, Tachycardia, Pulsus paradoxus)

Etiology/Causes

- Infectious
- Systemic autoimmune disease
- Autoimmune process
- Pericardial effusion in disease of surrounding organs
- Metabolic disorder
- Traumatic
- Neoplastic pericardial disease
- Radiation induced
- Congenital

Signs and Symptoms

- Cardiovascular
  - Chest pain relieved by sitting up and leaning forward, intensified by lying supine, pressure, discomfort
  - Light-headedness, syncope, palpitations
  - Pulsus paradoxus: decrease in systolic blood pressure of more than 10 mm Hg with inspiration, signaling falling cardiac output during inspiration
  - Pericardial friction rub: physical sign of acute pericarditis Tachycardia
  - Hepatojugular reflux, increased jugular venous pressure (JVP)
  - Cardiac temponade

- Respiratory: Cough, dyspnea, hoarseness, features of pleural effusion
- Gastrointestinal: Hiccoughs, hepatosplenomegaly
- Neurologic: Anxiety, confusion
- Extremities: Weakened peripheral pulses, edema, cyanosis

Investigations

- ECG
- Laboratory test*s*
  - Cardiac enzymes
  - Electrolytes, urea and creatinine
  - CBC count
  - Thyroid-stimulating hormone : screen for hypothyroidism
  - Rickettsial antibodies - If high index of suspicion of tick-borne disease
  - Rheumatoid factor, immunoglobulin complexes, antinuclear antibody test (ANA) in suspected rheumatologic

- Fluid hematocrit for bloody aspirates
- Viral cultures
- Pericardial fluid analysis: LDH, Total protein
  - Gram stain - Specific but insensitive indicator of bacterial infection
  - Cultures - Signals and identifies infectious etiology

- Tumor markers
- Chest X-ray: “Water-bottle heart”

- Echocardiography
- Peri-cardioscopy and per-cutaneous biopsy

Management

- Treatment will depend on acuteness, severity and cause

Hemodynamic support

- Pericardiocentesis if indicated
- Intravenous fluid resuscitation if indicated

Antibiotics if indicated

- *Ceftriaxone* 1-2 g bid, and *ciprofloxacin* 400 mg/d is mandatory

- Irrigation with urokinase or streptokinase, using large catheters, may liquify the purulent exudate, but open surgical drainage is preferable
- The initial treatment of tuberculous pericarditis: Ceftriaxone TB guidelines
- Antineoplastic therapy (eg, systemic chemotherapy, radiation) in conjunction with pericardiocentesis
- Corticosteroids and NSAIDs are helpful in patients with autoimmune conditions
- Surgery: Should be reserved for patients in whom conservative approaches have failed

1.7.7. Hypertension

Definition: HTN is defined as usual BP of 140/90 mmHg or persistently higher.

Classification

BP Classification	SBP mm Hg	DBP mm Hg
Normal	<120	and <80
Prehypertension	120–139	or 80–89
Stage 1 hypertension	140–159	or 90–99
Stage 2 hypertension	≥160	or ≥100

Causes

- Idiopathic
- Secondary
  - Vascular: coarctation of aorta
  - Endocrine: Pheochromocytoma, Cushing syndrome, primary hyperaldosteronism.
  - Kidney Diseases
  - Renal vascular disease

Signs and Symptoms

- Asymptomatic
- Symptomatic: depend on stage of HTN

Complications

- Hypertensive encephalopathy
- Intracranial haemorrhage
- Unstable angina
- Acute myocardial infarction
- Aortic dissection
- Heart failure ± pulmonary edema
- Eclampsia

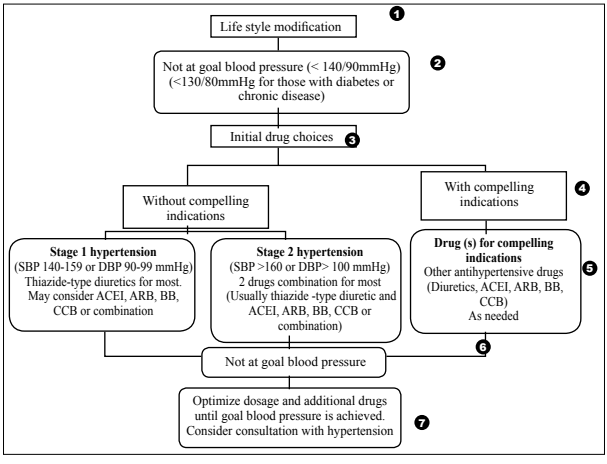
Investigations

- ECG
- Echocardiogram
- CXR
- Urine: sugar

- Urea creatinine, serum electrolytes
- Fundus
- Others investigation s according to suspected aetiology

Management

ALGORITHM FOR TREATMENT OF HYPERTENSION



Non-Pharmaceutical

Lifestyle modification (LFM)

- Weight Reduction
- DASH diet
- Low salt diet
- Avoid alcohol intake
- Regular physical activity

Pharmaceutical

- Thiazides: *Hydrochlorothiazide* 12.5mg or *Bendrofluthiazide* 5mg
- ACEI: *Captopril* 25mg bd; Enalpril 5mg bd; *Lisinopril* 5 mg bd
- B-blocker: Atenolol
- CCB: *Nifedipine* 20mg SR daily; *Diltiazem* 30mg Tds;*Verapamil* 40mg TDS
- ARB: *Losartan* 25mg daily
- Ald antagonist: *Spironolactone* 25mg daily

2. Central and Peripheral Nervous System

2.1. Epilepsy and Seizure Disorders

Definition: A seizure is an episodic disturbance of central neurological function due to excessive and abnormal neuronal electrical activity. Most seizures are brief and self limited.

Epilepsy refers to a clinical syndrome characterized by presence of recurrent seizures.

Repeated or continual seizures without recovery between them is referred to as *status epilepsy* and is a medical emergency

Classification

- The common types are
  - Tonic-Clonic
  - Complex-Partial
  - Absence

Other types include Simple Partial, Myoclonic, Clonic, Tonic, Atonic and Benign Rolandic but are rarer and not covered here

Causes

- Primary
  - Various described epilepsy syndromes which may be idiopathic or familial

- Secondary
  - Metabolic including
    - → Hypoglycemia and hyperglycemia
    - → Hyponatremia
    - → Hypocalcemia
    - → Liver failure
    - → Renal failure

  - Infection such as
    - → Meningitis
    - → Encephalitis
    - → Cysticercosis
    - → Malaria

- Stroke
- Space occupying lesions including tumours
- Post-traumatic
- Drugs such as
  - → Psychotropics
  - → Antibiotics
  - → Anaesthetic agents
  - → Withdrawal of alcohol, benzodiazepines, barbiturates

Signs and Symptoms

- The key to diagnosis is a good history, including history from any eyewitnesses
- Seizures are
  - Episodic
  - Brief in duration (usually 1-3 minutes)
  - Unpredictable as to when they will occur
  - May be preceded by an aura (warning sign)
  - Each episode is usually identical to the previous (unless patient has multiple different seizure types)
  - Have positive phenomena (abnormal taste or smell, movements, sensation, vision, thoughts)
  - May have a post-ictal period of confusion, drowsiness or paralysis
- Most patients will have a normal neurological examination between episodes but if the patient has focal signs refer for urgent neurologist assessment

Investigations

- Electrolytes, glucose, FBC, renal and liver function tests
- EEG (preferably within 24 hours after a seizure; otherwise multiple EEGs may be needed to detect an abnormality)
- CT brain
- Other investigations will depend on suspected cause

Management

- Confirm patient has a seizure
  - This relies mostly on a very detailed history, supported by an early EEG if available
- Define its type
  - Tonic Clonic
    - → May have an aura (unpleasant smell, taste, strange feeling of familiarity)

- Falls to ground without warning, clenched teeth, arms and legs extended (tonic phase)
- Then after <30 seconds, repetitive jerking of arms and legs (clonic phase) usually lasting 1-2 mins
- Tongue biting, urinary and faecal incontinence may occur
- Post ictal state characterized by drowsiness, confusion for up to 30 mins (longer in elderly)

- Complex Partial
  - Aura (same as for Tonic Clonic) precedes episode
  - During episode patient is not aware of what is happening and is unable to respond
  - There may be involuntary movements of mouth or limbs (lasting for seconds to a few minutes)
  - Post ictal state of confusion lasting for several minutes (patient now able to respond but confused)

- Absence seizures
  - No warning prior
  - Brief impaired conscious state during seizure (usually 3-20 seconds) during which patient stares and may blink but is otherwise unresponsive
  - No post-ictal state; patient is normal again immediately after

- Assess frequency and cause
  - Triggers include sleep deprivation, flashing lights, alcohol, menstruation and intercurrent illness
  - Poor compliance with medication is a common cause of seizures in known epileptics
  - If there is no break between seizures this is STATUS EPILEPSY and an emergency

- Advice regarding lifestyle
  - Driving is not recommended for atleast 3 months after a seizure
  - Warn patient not to go swimming, or bathe or walk/sit near fire or water alone (as a seizure may lead to drowning or burns)
  - Pregnancy is a complex area, refer to a neurologist if the patient is already or plans to become pregnant

Pharmacological

- Necessary for patients with more than one seizure or for those with unprovoked seizures who wish to resume driving

- Patients need to take their medication all the time, otherwise they risk seizures
- Aim to use one drug (monotherapy) at the minimum dose required to control the seizures
- Start at low dose and increase slowly
- Monitor the clinical response to treatment
- Tonic-Clonic Seizures
  - *Sodium valproate*, oral, 200–300 mg twice daily, starting dose and Increase as required, every 2 weeks to a maximum daily dose of 1 200 mg twice daily

    Or
  - *Phenytoin*, oral, 5 mg/kg of lean body mass once daily and dose changes over 300 mg should only be done in no more than 50 mg increments at intervals no shorter than 2 weeks

- Complex Partial Seizures
  - *Carbamazepine*, oral, 200 mg twice daily for first 2 weeks, then 300 mg twice daily,increasing at fortnightly intervals to a maximum dose 600 mg twice daily as required

    Or
  - *Phenytoin*, oral, 5 mg/kg of lean body mass once daily
    - Dose changes over 300 mg should only be done in no more than 50 mg increments at intervals no shorter than 2 weeks

- Absence Seizures
  - *Ethosuximide* Initial: 500 mg/day; increase by 250 mg as needed every 4-7 days up to 1.5 g/day in divided doses

    Or
  - *Sodium valproate*, oral, 200–300 mg twice daily, starting dose
    Increase, as required, every 2 weeks to a maximum daily dose of 1 200 mg twice daily

Note: *Phenytoin, phenobarbitone and carbamazepine are potent enzyme inducing agents and should be used with caution with other drugs metabolised by the liver, especially warfarin, ARVs and oral contraceptives.*
Phenobarbital (phenobarbitone) is not a preferred drug for first line therapy but if other drugs are not available it can be started at a dose of 50mg once a day and increased gradually to a maximum dose of 200mg/day.

Recommendation

- Refer to a neurologist
  - All patients with focal neurological signs
  - All patients contemplating pregnancy or who are pregnant
  - If monotherapy does not control the seizures
  - Patients whose history or examination is unclear

2.2. Stroke and Transient Ischemic Attack

Definition: Stroke is a clinical syndrome characterized by the rapid onset of focal neurological signs due to a vascular cause (hemorrhage or ischemia) and persisting for more than 24 hours. Transient ischemic attack (TIA) is the term used to describe symptoms that last for less than 24 hours.

Causes/Risk Factors

- General Cardiovascular Risk Factors
  - Hypertension
  - Diabetes Mellitus
  - Hypercholesterolemia
  - Smoking
  - Advanced Age

- Embolic Stroke
  - Atrial Fibrillation
  - Left Ventricular Thrombus or Aortic Arch Atheroma
  - Valvular Heart Disease and Endocarditis
  - Carotid Artery Stenosis

- Hemorrhage
  - Hypertension (leading to cerebral aneurysm)
  - Head trauma
  - Anticoagulation
  - Vascular malformations

Classifications

Broadly into Ischemic and Hemorrhagic Stroke
- Types of Ischemic Stroke
  - Small Vessel (lacunar) due to hypertension
  - Large Vessel (thromboembolic)

- Types of Hemorrhage
  - Extradural Hematoma
  - Subdural Hematoma
  - Subarachnoid Hemorrhage
  - Intracerebral Hemorrhage

Signs and Symptoms

- Sudden onset of focal neurological signs is the key feature of ischemic stroke
  - Many patients with ischemic stroke may have prior TIAs
  - Ischemic strokes often evolve over the first few hours – some improving and others worsening
  - Need to exclude seizures, syncope, migraine and hypoglycemia which can mimic stroke

- Hemorrhagic stroke may present differently depending on the cause
  - Intracerebral hemorrhage – symptoms are very similar to ischemic stroke but more likely to have early depression of the conscious state, headache and vomiting
  - Extradural hemorrhage – history of severe head trauma, rapid onset of depressed conscious state
  - Subdural hematoma – history of minor head trauma in recent past (days or weeks), gradual onset of confusion and/or weakness
  - Subarachnoid hemorrhage – sudden onset of severe headache, nausea and vomiting with or without depressed conscious state
    - ➔ Blood pressure is often elevated
    - ➔ Patients are likely to have focal upper motor neuron neurological signs on clinical examination, with or without depression of the conscious state
    - ➔ The heart and carotids may have murmurs or bruits
    - ➔ The fundi may have papilloedema and hypertensive changes

Complications

- Dysphagia and Aspiration Pneumonia
- Deep Vein Thrombosis and Pulmonary embolism
- Dehydration
- Malnutrition
- Pressure sores
- Urinary tract infection

- Myocardial Infarction and Heart Failure
- Seizures
- Death

Investigations

- FBC
- Blood Glucose
- Electrolytes, renal and liver function tests
- Clotting Tests
- Cholesterol
- ESR and CRP
- Early non-contrast CT scan of the brain (or MRI) to distinguish hemorrhage from ischemia
- ECG and Echocardiography
- Carotid Ultrasound

Management

It is necessary to make a diagnosis of the type of stroke and the likely cause, as management differs depending on the cause. TIAs should be managed with aggresive treatment of risk factors, like for ischemic stroke.

General Principles

- Manage ABC
- Give supplemental oxygen
- Control fever with paracetamol
- Optimize hydration and nutrition – NGT if patient cannot swallow, IV fluids
- Gentle control of HTN – do NOT give acute therapy unless blood pressure greater than 220/120 in ischemic stroke or greater than 180/130 in hemorrhagic stroke. Aim to only reduce blood pressure slowly and to just below these levels.

Note: *Reducing blood pressure quickly or too far worsens the outcome in stroke – do not do this!*

- Nursing pressure care, urinary catheter if needed
- Physiotherapy and early mobilization, rehabilitation
- *Heparin* 500units SC bd for DVT prevention (in ischemic stroke)
- Prevention, early identification and treatment of risk factors and complications
- Counsel patient and family

Non-pharmacological

- Encourage smoking cessation
- Reduce alcohol
- Regular exercise
- Weight control
- Decrease salt in diet

Pharmacological

- Antiplatelet therapy – *Aspirin* 100-150mg daily.
- Control BP (starting one week post-stroke) with goal of reducing BP to below 140/90 – use ACE inhibitor and other antihypertensives
- Control cholesterol eg *simvastatin* 20-80mg po od.
- Treat diabetes – tight glycemic control
- Anticoagulation with *Warfarin* – for patients with atrial fibrillation or a cardiac source of embolus – target INR 2.0-3.0
- Intracerebral hemorrhage
    - ➔ Stop any anticoagulation the patient is receiving (warfarin, heparin, aspirin) and give an antidote if available (*Vitamin K* for warfarin, protamine for heparin)
    - ➔ Manage hypertension as for ischemic stroke, also starting one week after the stroke unless BP greater than 180/130
    - ➔ Consider *Mannitol* 0.5-1g/kg IV tds for patients with severely depressed conscious state due to raised intracranial pressure
- Extradural, subarachnoid and subdural hematomas
    - ➔ Urgent referral for neurosurgical assessment in a tertiary centre

2.3. Sciatica

Definition: Sciatica is any sort of pain that is caused by irritation or compression of the sciatic nerve or the lumbosacral nerve roots

Causes

- Lumbar disc herniation
- Lumbar spinal stenosis

Signs and Symptoms

- Sciatica is often characterized by one or more of the following symptoms
    - Sciatic pain is typically described as sharp or burning pain radiating down the posterior or lateral aspect of the leg, usually to the foot
    - Sciatic nerve pain is often associated with numbness or tingling
    - Sciatica due to disc herniation usually increases with coughing, sneezing
    - Pain is commonly unilateral
    - Pain is better when patients lie down or are walking, but worsens when standing or sitting
- Sciatica signs and Symptoms vary based on where the compressed nerve root is located:
    - L4 nerve root sciatica symptoms usually affect the thigh. Patients may feel weakness in straightening the leg, and may have a diminished knee-jerk reflex.
    - L5 nerve root sciatica symptoms may extend to the big toe and ankle. Patients may feel pain or numbness on top of the foot, particularly on the "web" of skin between the big toe and second toe

Complication

- Cauda equina syndrome: acute compression characterized by bilateral sciatica with bowel and bladder disturbance

Investigations

- Plain AP and lateral X-ray of the lumbosacral spine to rule out tumor, infection, instability, spondyloarthropathy, and spondylolisthesis
- CT and MRI of lumbosacral spine for detecting infection, cancer, herniated discs and spinal stenosis

Management

Non-Pharmaceutical

- Bed rest has not been shown to be of benefit and should be minimized
- Physical Therapy and Exercise
- Weight reduction should be encouraged in patients with elevated body mass index

Pharmaceutical

- Analgesic medications such as nonsteroidal antiinflammatory drugs e.g. *Ibuprofen* 400mg-600mg po qid, paracetamol 1g po qid
- Epidural Steroid Injections for severe Sciatica, but not recommended during the acute phase

Recommendations

- Referral, usually to a neurosurgeon or orthopedist is indicated when any of the following signs or symptoms are present
  - The cauda equina syndrome: typical features are bowel and bladder dysfunction (urinary retention), saddle anesthesia, and bilateral leg weakness and numbness
  - Suspected spinal cord compression: this may present as acute neurologic deficits in a patient with cancer and risk of spinal metastases

- Referral to a neurologist if any of the following are present:
  - Neuromotor deficit that persists after four to six weeks of conservative therapy
  - Persistent sciatica, sensory deficit, or reflex loss after four to six weeks in a patient with positive straight leg raising sign

2.4. Facial Nerve Palsy

Definition: Weakness of the muscles of facial expression (supplied by the VIIth cranial nerve), often occurring without other neurological signs

Signs and Symptoms

- The most common lesion is a Bell's palsy
  - Lower motor neuron pattern weakness on the same side of the face
  - Often associated with altered taste and hyperacusis (increased hearing) on the same side of the face
  - Symptoms begin rapidly (over hours)

- Clinical signs
  - Sagging eyebrow
  - Inability to close the eye
  - Mouth drawn across to normal side
  - In a lower motor neuron facial nerve palsy, forehead muscles may be involved
  - In an upper motor neuron lesion forehead muscles are spared

Investigations

- HIV test
- EMG (to look for muscle denervation)
- CT of base of skull (looking for other causes eg tumour)
- CT and EMG are not necessary unless the signs and Symptoms are atypical or recovery is slow

Management

Non pharmacological

- Most lesions tend to recover spontaneously, over 1-4 months
- Eye care is vital – use eye ointment and drops or an eye patch to keep the eye moist
- Psychological support and counselling

Pharmacological

- For Bell's palsy, give *Prednisolone* 60mg po OD for 1 week.
- For Ramsay Hunt syndrome, give *Acyclovir* 800mg po five times per day

Recommendation

- Refer patients with facial nerve palsy due to cholesteatoma or ear infection to ENT surgery

2.5. Parkinson's Disease

Definition: Chronic and progressive neurodegenerative disorder characterized by resting tremor, stooped posture, slowness of movement (bradykinesia) and increased muscular tone.

Causes/Risk factors

- Genetic
- Neuroleptic Drugs (antipsychotics)

Signs and Symptoms

- Most patients with genetic Parkinsons are 55yrs and older
- Resting Tremor
- Slowness of movement (Bradykinesia)
- Muscular rigidity
- Postural Instability, Falls
- Muscular weakness and tiredness
- Non motor symptoms: Depression, anxiety, Psychosis and Hallucinations

Complication

- Progressive Disability and Death

Investigation

- Diagnosis is clinical

Management

Non Pharmaceutical

- Patient Education on understanding the disorder
- Emotional and psychological Support
- Exercise with standard physical and occupational therapy components
- Proper Nutrition to avoid weight loss
- Treat depression if present

Pharmaceutical

- Anti parkinson drugs
  - → *Levodopa-carbidopa (Sinemet)* 100mg/25mg TDS, increase to maximum of 8 tabs/day
    Or
  - → *Bromocriptine* start at 1.25mg bd, increase dose weekly by 2.5mg until symptoms controlled – often total dose of 20-40mg per day)
    Or
  - → *Amantadine* 100mg bd
    Or
  - → *Benztropine* 0.5mg to 2mg bd

Recommendation

- Consider referral to a neurologist

3. Endocrine System

3.1. Diabetes Mellitus (Type I and Type II)

Definition: Diabetes mellitus is a chronic metabolic condition in which the pancreas no longer produces enough insulin (impaired insulin secretion) or cells stop responding to the insulin that is produced (insulin resistance) resulting in increased blood glucose.

Classification and etiology of DM

- Four main etiological and clinical classes
  - Type 1 diabetes: Results from Beta cell destruction, usually leading to absolute insulin deficiency
  - Type 2 diabetes*:* Results from a progressive insulin secretory defect following insulin resistance
  - Secondary diabetes*:* e.g. pancreatic diseases, genetic defects in cell function, genetic defects in insulin, chemical and drugs induced diabetes such as ARVs, infections etc
  - Gestational Diabetes

Diagnostic criteria according to WHO/IDF 2006 recommendations

	Fasting plasma glucose	**Venous plasma glucose: 2h after ingestion of 75g oral glucose load**
Diabetes	≥ 7.0 mmol/l (126mg/dl)	≥11.1 mmol/l (200mg/dl) **Or** classic symptoms of hyperglycemia (Polyuria, polydypsia, loss of weight, (signs of hyperglycemic crisis) with a random plasma glucose ≥200 mg/dl (11.1mmol/l).
Impaired Glucose tolerance (IGT)	<7.0 mmol/l (126mg/dl)	≥7.8 and <11.1 mmol/l (140mg/dl and 200mg/dl)
Impaired Fasting Glucose (IFG)	6.1 to 6.9mmol/l (110mg/dl to 125mg/dl)	<7.8mmol/l (140mg/dl)

Investigations

- HbA1c, if results not available within past 2–3 months: quarterly for uncontrolled and twice a year for supposed to be controlled
- If not performed/available within past year:
  - Fasting lipid profile: LDL and HDL cholesterol and triglycerides
  - Liver function tests: prothrombin time, liver enzyms, serum proteins
  - Urine albumin with spot urine albumin-to-creatinine ratio
  - Serum creatinine and calculated GFR
  - Thyroid-stimulating hormone in type 1 diabetes, dyslipidemia, or women over age 50 years
- Fundoscopy, then once annually
- Dental examination, then once a year

Management

Objectives

- Relieve hyperglycemic symptoms
- Prevent and minimize complications
- Obtain and maintain optimal plasma glucose:
  - Fasting bood glucose:70 mg/dl-110mg/dl
  - Random Blood Glucose ≤140mg/dl
  - HbA1c ≤ 7 % and ≤ 8 % in elders or those with cardiovascular disease
- Control of other associated risk factors: obesity, dyslipidemia and hypertension

Pharmacological

- *Insulin* Therapy: Must be initiated in hospital wards.
  - Absolute indications
    - Type 1 Diabetes
    - Type 2 Diabetes which does not respond to maximum dose of oral anti-diabetic agents
    - Secondary diabetes with irreversible beta cells failure
  - Transient insulin therapy may be necessary in case of:
    - Type 2 Diabetes with acute complications
    - Perioperative period, acute infection, pregnancy
- Types of insulin and their characteristics
  - Short acting insulin (SA insulin)

- First choice in combination with IA insulin
- Onset of Action 30 minutes after sub-cutaneous administration
- Duration 4-6 hours but is dose-dependent

→ Intermediate acting insulin (IA insulin) : milky in colour
- First choice in combination with SA insulin
- Long action pick 2-4 hours after injection
- Frequent hypoglycemia corresponding to action picks.
- To prevent hypoglycemic event: suggestion of snacks in action pick time.

→ Long acting insulin analogues
- Second choice to IA insulin
- Long action duration
- Less hypoglycemic event

→ Rapid acting analogues (aspart, lispro, glulisine)
- Second choice to short acting insulin
- Recommended in case of frequent and severe hypoglycemia
- Immediate action after administration: no waiting time for meals, convenient for those with irregular meals and physical activity.
- Good postprandial glycemic control
- Less hypoglycemic event distant to meals

• Inpatient insulin therapy Insulin use in ICU
→ IV insulin infusion
→ Plasma glucose goal: 140-180mg/dl (see DKA and HHS management)
→ Upon transfer from ICU/Transition to conventional insulin regimen:
- Extrapolate the total daily dose from the last 24hours of insulin infusion
- Divide the total into intermediate acting (50%) and short acting (50%)
  - 50% Intermediate acting given BID (max dose first 24hrs: 0.5U/kg) +

- If eating 50% short acting insulin = 3 injections /day: ____U/3=____U/ before meal of rapid acting insulin(max dose first 24hrs :0.1U/kg/meal)

  Or

- 2 injections/day ____U/2=___U before breakfast and before dinner.

- Adjust insulin doses every 2days as following:

Adjustment of basal/prandial (NPH BID + Short acting TID) every 2 days

Day time	**Hyperglycemia(↑PG ± symptoms of hyperglycemia)**	**Hypoglycemia (decreased PG± symptoms of hypoglycemia)**
Middle of night	Increase evening Short acting by 2 units	Decrease evening rapid acting by 2 units
Before breakfast	Increase evening NPH by 2 units	Decrease evening NPH by 2 units
Mid day	Increase morning Short acting by 2 units	Decrease morning Short acting by 2 units
Before dinner	Increase afternoon rapid acting by 2 units	Decrease afternoon short acting by 2 units

Adjustment of NPH/Rapid insulin 2X/day: every 2 days

	Hyperglycemia	Hypoglycemia
Middle of night	Increase evening short acting insulin 2U	Decrease evening short acting insulin 2U
Before breakfast	Increase evening NPH 2U	Decrease evening NPH 2U
Mid day	Increase morning rapid 2U	Decrease morning Rapid 2U
Before dinner	Increase morning NPH 2U	Decrease morning NPH 2U

- Insulin use in Medical or surgical ward
  - If Type 1 DM(Newly diagnosed or known) or insulin treated Type 2 who is Nil Per Oral (NPO):
    - Use home basal (Intermediate) or start with 0.2-0.3 U/kg/day (50% before breakfast- 50% before dinner)
    - Short insulin before every meal (3 times/day) if:
      - <150mg/dl: 0U
      - 150-199mg/dl: 2U
      - 200-249 mg/dl 4U

- 250-299: mg/dl 6U
- 300-349 mg/dl 8U
- ≥350 : mg/dl 10U

→ If type 2 diabetes NOT treated with insulin who is NPO:
  - Discontinue all outpatient anti-hyperglycemic agents and start above short acting regimen:
  - If BG level not controlled:
    - Add intermediate insulin : 0.2-0.3U/kg/day BID and
    - Adjust short insulin by 1-2U/dose every 2days (see adjustment recommendations above)

→ If type 1 DM or insulin-treated type 2DM in medical-surgical ward who is expected to have a Normal Diet:
  - If blood glucose well controlled : Continue outpatient insulin regimen
  - If BG not well controlled :
    - Adjust intermediate insulin and pre-meal short acting insulin according to adjustment recommendation based on insulin regimen.
    - Consider other factors that might be responsible for hyperglycemia: intercurrent disease, diet, physical activity

→ If type 2 DM NOT treated with insulin (on oral agent or diet only) who is expected to have normal diet:
  - If BG well controlled and no contraindication to current therapy: continue his/her current treatment
  - If BG poorly controlled:
    - Discontinue outpatient therapy
    - Start intermediate insulin with 0.2-0.3U/kg/day BID + short acting insulin with 0.05-0.1U/kg/meal).
    - Adjust doses every 2 days and consider other factors that might be responsible for hyperglycemia: intercurrent disease, diet, physical activity

- Outpatients regimens

Breakfast	Lunch	Supper	bedtime	Advantages	Disadvantages
Intermediate +short acting	-	Intermediate +short acting	-	Less injection/ day	Require usual physical activities and same calories /day
Short acting ± intermediate insulin	Short acting insulin	Intermediate +short acting	Intermediate insulin	- Free Life style - No need of snacks Good glycemic control	-Many injections/ day
Oral agent		±oral agent	Intermediate insulin	Less injections	Postprandial BG not well controlled

- Sites of insulin injection
  - ➔ Quickest absorption
    - Subcutaneous tissue of anterior abdomen: advised at breakfast time
    - Exercised limb: best to avoid injecting limb if it will be exercised soon afterward
  - ➔ Slower absorption
    - Thighs, buttocks and deltoid regions (at rest)
    - Use a certain region of the body for certain times of day
    - Within a certain body region, injection sites should be rotated: to prevent lipohypertrophy

Note: *Insulin should be kept in refrigerator between 2-8^{0}C (or at room temperature for max one month)*

- Oral anti-hyperglycemic Therapy
  - ➔ Indication: Type 2 diabetes
  - ➔ Available anti hyperglycemic oral Agents

Table: ORAL Anti-Diabetic Regimens

	Dose/day	Dose interval	Dosage	Side effect	Benefits
Sulfonylureas					
Glibenclamide	1.25-20mg	BID	2.5, 5mg	Weight gain, hypoglycemia Frequent dosing Should be avoided in CKD	Extensive experience, improved microvascular outcome, lower cost
Gliclazide	30-120mg	OD/BID	30mg	Weight gain, hypoglycemia	Single use per day
Glimepiride	1-8mg	OD	1,2,3,4mg	Weight gain, hypoglycemia	Single use per day Variety of dosage May be used in CKD
Biguanides					
Metformin	1000-2550mg/dl	BID-TID	500,850,1000 mg	Nausea, diarrhea, abdominal pain, lactic acidosis	Weight loss or weight neutrality; no hypoglycemia, extensive experience; improved macrovascular outcomes.
Non sulfonylurea secretagogues					
Repaglinide	1.5-16mg	TID-QID/meal	0.5, 1,2mg	Weight gain, hypoglycemia, no long term experience, expensive, frequent dosing (compliance)	Targets postprandial glucose, mimic physiological insulin secretion
Nateglinide	180-380mg	TID/meals based	60, 120mg		

Type 2 DM pharmacological treatment Algorithm

Non-obese patients (BMI ≤ 24kg/m^2)

- Start Sulfonylurea :
  - First choice: *Glibenclamide* 5mg OD, increase the dose at 5 mg bid every 2 weeks if blood glucose not well controlled, max dose 20 mg.
  - Second choice: *Glimepiride* 1mg OD, increasing dose every 2 weeks until blood glucose target is obtained, max dose 6 mg.

- Add *Metformine* 500mg BID, increasing dose (max 2000mg/day) if blood glucose not obtained with maximum dose of sulfonylurea
- *Insulin* is required If BG target not obtained with max doses in combined therapy: insulin should be started in hospital wards after assessment of other risks of BG control failure (see insulin therapy in-patients)

Overweight patients

- Start by *Metformine* increasing doses every 2 weeks
- If Blod glucose targets not achieved with max doses of metformine: add *Sulfonylurea* and *Insulin* as above

Note: Degree of hyperglycemia should be considered in newly diagnosed:

- *BG=100-150mg /dl: Diet/Exercise*
- *BG=151-250mg/dl : 1 oral agent*
- *BG =251-350mg/dl : 2 oral agents*
- *BG>350mg/dl : transient insulin therapy in hospital ward*

3.1.1. Diabetes Complications

HYPERTENSION WITH DM

General recommendations

- Blood pressure should be measured at every routine diabetes visit.
- Repeat systolic blood pressure >130 mmHg or diastolic blood pressure >80 mmHg confirms a diagnosis of hypertension.

Goals

- Systolic blood pressure ≤130 mmHg is appropriate for most patients with diabetes.
- Diastolic blood pressure ≤ 80 mmHg.

Management

- BP 130-139/80-89 mmHg: Life style alone (weight loss, if overweight; reducing sodium and increasing potassium intake; moderation of alcohol intake and increased physical activity.) for a maximum of 3 months and then, if targets are not achieved, add of pharmacological agents.
- BP ≥ 140/90 mmHg: lifestyle + pharmacological therapy
- Pharmaceutical therapy for patients with diabetes and hypertension:
    - 1st choice: ACE inhibitor: *Captopril* 12.5mg BID, increase dose if target not achieved up to 100mg max
    - Alternative if dry cough: ARBs: *Losartan* 50mg OD, optimize dose up to 100mg if target not achived
    - If target not achieved in monotherapy, add thiazide to those with an eGFR ≥30 ml/min/1.73 m2 and a loop diuretic for those with an eGFR ≤30 ml/min/1.73 m2: *Hydrochlorothiazide* 12.5mg OD, optimization up to 25mg
    - If ACE inhibitors, ARBs, or diuretics are used, kidney function and serum potassium levels should be monitored
    - If target not achieved with the 2 classes
        - ➔ Add Calcium channel inhibitors: *Amlodipine* 5mg OD max dose 10mg OD, second choice *Nifedipine* LP 20mg OD, max dose 40mg OD
        - ➔ If lower limb edema due to Calcium blockers replace by Beta blockers: *Atenolol* 50mg OD, max 100mg OD

DIABETIC NEPHROPATHY

General principles

- To reduce the risk or slow the progression of nephropathy:
  - Optimize glucose control
  - Optimize blood pressure control
- Definitions of abnormalities in albumin excretion

Category	Spot collection(µg/mg creatinine)
Normal	< 30
microalbuminuria	30-299
Macro-albuminuria	≥ 300

- Stages of CKD

Stage	Description	GFR (ml/min per 1.73 m2 body surface area)
1	Kidney damage with normal or increased GFR	≥ 90
2	Kidney damage with mildly decreased GFR	60-90
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney failure	<15 or dialysis

Management

- Micro- or macroalbuminuria:
  - ➔ First choice: *Captopril* 6.25mg BID if well tolerated, increase the dose up to 25mg BID

    Alternative
    in case of dry cough or type 2 diabetes, hypertension, macroalbuminuria and renal insufficieny (serum creatinine>1.5mg/dl or moderately decreased GFR):
    Losartan : 50mg OD

- If GFR< 60: assure Vitamine D sufficiency (Vitamine D + calcium)
- Consider referral to a nephrologists in case of:
  - ➔ Kidney disease when there is uncertainty about the

etiology of kidney disease (heavy proteinuria, active urine sediment, absence of retinopathy, rapid decline in GFR),

- ➔ Difficult management issues, or advanced kidney disease.
- ➔ Persistent albuminuria in the range of 30–299 mg/24 h (microalbuminuria)GFR<30

Diabetic Retinopathy

- Refer to an ophthalmologist, for Laser photocoagulation therapy to reduce the risk of vision loss, patients with any level of:
  - Macular edema
  - Severe non Proliferative Diabetic Retinopathy
  - Proliferative Diabetic Retinopathy

Diabetic polyneuropathy

- Screening for peripheral neuropathy should be done every 3 months using turning folk and monofilament.
- Treatment is mainly preventive by a good glycemic controle
- Symptomatic treatment for lower limb paresthesia:
  - *Amytriptylline* : 25mg OD pm increased to 50 mg and add *Tramadol* 50 mg OD pm if pain persists

- Erectile dysfunction:
  - *Tadalafil* (cialis) 50mg OD 1hour before sexual activity
  - Alternative: *Sildenafil:* 25mg maximum 100mg OD ½ hour to 4 hours before sexual activity.

Non Pharmaceutical

- Dietary education
- Physical activity
- Diabetes education
- Smoking cessation

3.2. Pituitary Disorders

3.2.1. Prolactinoma

Definition: Prolactinoma is the most common functioning pituitary tumor, which secretes prolactin.

Clinical manifestation

- Tumor related manifestations: headaches, loss of visual loss
- Galactorhea, loss of libido, amenorrhea, infertility

Investigations

- Blood sample before 9:00 am
  - Serum prolactin
  - LH, FSH
  - ACTH, cortisol
  - TSH, T4
- Imaging: Brain CT/scan, if possible Brain MRI
- Visual field

Note: Other causes of hyperprolactinaemia include:
- *Drugs*
- *Hypothyroidism*
- *Chronic renal failure*
- *Elevated serum prolactin levels up to 200 ng/mL may also be found in other pituitary tumors and hypothalamic-pituitary lesions with stalk compression.*

Management

- 1st choice *Dopamine* agonist therapy:
  - *Bromocriptine*, oral, 1.25 mg at bedtime with food
  - Initial maintenance dose: increase dose to 2.5 mg twice a day with food and check prolactin 4 weeks later. Higher doses may be needed but if total dose of 10 mg does not normalise prolactin, refer

Recommendations

- Refer all following cases to neurosurgeon
  - Compression of optic chiasm
  - Pituitary apoplexy
  - Cases uncontrolled by bromocriptine at maximum dose

3.2.2. Hypopituitarism

Definition: Hypopituitarism is a clinical syndrome of deficiency in pituitary hormone production (ACTH, LH, FSH, Prolactin, GH,TSH)

Causes

- Pituitary adenomas or other intrasellar and parasellar tumors,
- Inflammatory and infectious destruction,
- Surgical removal
- Radiation-induced destruction of pituitary tissue,
- Traumatic brain injury
- Subarachnoid hemorrhage
- Postpartum pituitary necrosis (Sheehan syndrome)
- Empty sella syndrome and infiltrative diseases

Signs and Symptoms

- Varies from asymptomatic to acute collapse
- Depend on the etiology, rapidity of onset, and predominant hormones involved.
- Initially, patient may be asymptomatic.
- Patient with the following deficiencies present with the indicated condition:
    - ACTH deficiency : see “adrenal insufficiency”
    - TSH deficiency : see “hypothyroidism
    - Gonadotropin deficiency : amenorrhea in women, erectile dysfunction and decreased libido in men
    - GH deficiency :Failure to thrive and short stature in children; most adults are asymptomatic, but some may experience fatigue and weakness
    - ADH deficiency : Polyuria and polydipsia with normal or decreased blood glucose

- Other features may be attributable to the underlying cause:
    - A patient with a space-occupying lesion: headaches or visual field deficits
    - A patient with large lesions involving the hypothalamus may present with polydipsia and Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH)

Invetigations

- ACTH (Cortrosyn) stimulation test
- TSH and thyroxin
- FSH, LH, and either estradiol or testosterone (as appropriate for sex)
- Prolactin
- GH stimulation testing
- Brain CTscan or pituitary MRI

Management

- Goal: to restore target hormones to physiologic levels
- Replacement therapies for life
- Requirement of increased doses of glucocorticoids following any form of stress, emotional or physical
- The most common stressor is infection
- Medications vary depending on the specific hormone deficiency that exists:
    - Adrenal insufficiency: *Hydrocortisone* 20mg am 10 mg Pm
      Alternative: *Prednisolone* 5 to 7.25mg OD
    - Hypothyroidism: *Levothyroxine* 100mg to be adapted according to T4 level and clinical features after 6 weeks
    - Diabetes insipidus: *Vasopressin* 5-10 U IM/SC or intranasal BID-QID. Titrate dose based on serum Na, serum osmolarity, fluid balance and urine output
    - Growth hormone replacement: not indicated in adult unless severe fatigue: *Somatotropin* (eg: Genotropin, Omnitrope) 0.04 mg/kg/week SC; titrate every 4-8Weeks, maximum dose: 0.08 mg/kg/week
    - Hypogonadism:
        - ➔ Men: testosterone eg: mesterolone 25mg Bid, then titrate every 2weeks maximum dose 100mg/day
        - ➔ Women: 0.3 mg PO continuous daily regimen or cyclic regimen (25 days on drugs then 5 days off)

- Treatment of the etiology

Recommendation

- Refer to endocrinologist all cases once diagnosed

3.3. Thyroid Diseases

Thyroid disorders include overt and mild/subclinical hypothyroidism, hyperthyroidism, and goiter and thyroid cancer.

3.3.1. Hyperthyroidism/ Thyrotoxicosis

Definition: Hyperthyroidism/ thyrotoxicosis are characterized by elevated thyroid hormones in the blood.

Causes

- Primary hyperthyroidism
  - Graves' Disease, Functioning thyroid adenoma and Thyroiditis.
  - Thyrotoxicosis without hyperthyroidism: Excessive intake of thyroid hormones and Excessive iodine intake.
- Secondary hyperthyroidism: Abnormal secretion of TSH

Signs and Symptoms

- Weight loss with conserved appetite
- Palpitations, tachycardia, sweating
- Muscle weakness, fatigue
- Delirium tremens
- Exophthalmia most of the time bilateral
- Nervousness, Anxiety, Irritability, insomnia
- Abdominal pain, diarrhea or constipation
- Amenorrhea
- Goitre

Investigations

- TSH, if low with these symptoms, thyrotoxicosis is confirmed. If normal, do T4 and T3
- Thyroid ultrasound
- ECG
- FBC

Management

- Symptomatic therapy
  - B –blockers : First choice *Propranolol* 40mg TID, **OR** alternatively: *Atenolol* 100mg OD

- Antithyroid Drugs (ATDs): *Methimazole* tablet 10mg TID maximum dose 60mg DT for 18 months **OR** *Propylthiouracil* (PTU) tablet 50mg TID maximum 300mg for 18 months (better in pregnancy)

- Follow-up: T_4 test every 4-6 weeks until stable then every 3 months

Complications

- Thyrotoxicosis related complication: Angina, Cardiac arrhythmias and Thrombo-embolism, Heart failure
- Treatment related complication: Hypothyroidism, agranulocytosis from ATDs
- Post Thyroidectomy: Hypoparathyroidism, Osteoporosis, Recurrent laryngeal nerve paralysis.

Recommendation

- Refer for Surgery (Thyroidectomy) in case of treatment failure or severe side effects.

3.3.2. Hypothyroidism

Definition: Medical condition due to hyposecretion of thyroid gland**.**

Causes

- Primary hypothyroidism: Hashimoto's disease, thyroiditis, radioactive iodine and post surgery
- Secondary: pituitary origin

Signs and Symptoms

- Tiredness, weakness, fatigue, sleepiness
- Cold intolerance, dry skin, hoarseness
- Constipation, joint pains, muscle clamps
- Mental impairment, depression
- Menstrual disturbance in woman and especially menorrhagia
- Weight gain, myxoedema

Complication

- Myxoedema coma

Investigations

- Blood TSH and T4
- Thyroid ultrasound and FNA (fine needle aspiration) if nodules
- Thyroperoxidase O (TPO) antibodies

Management

Note: *certain drugs e.g cholestylamine, fer sulfate, sucralfate, aluminium hydroxide, antacids, may interfere with Levothyroxine absorption from the gut. Levothyroxime should be spaced at least 4hours apart from these medications. others drugs especially anticonvulsivants (e.g carbamazepine and phyenytoin) and antitubercolosis (e.g rifampicin) may accerelate levothyroxine metabolism, necessitating higher levothyroxine doses.*

- *Levothyroxine* tablet 100µcg -150 µcg OD empty stomach
- Follow up: TSH test every 4-6 weeks then once a year when TSH in normal range.

3.3.3. Thyroiditis

Definition: Thyroiditis is an inflammation of the thyroid gland.

Classification and Causes

- Acute thyroiditis caused by an infection (usually bacterial).
- De Quervain's Thyroiditis (= Sub-acute granulomatous thyroiditis) : Viral or post viral inflammation
- Hashimoto's thyroiditis, Chronic or autoimmune, parasitic thyroiditis (echinococcosis, strongyloidiasis, cysticercosis), traumatic
- Silent thyroditis, mycobacterial infection

Signs and Symptoms

- Signs of Hypo/Hyperthyrodism associated with painful tender goiter.

Complications

- Hyperthyroidism
- Hypothyroidism

Investigations

- Blood T3,T4 and TSH level
- FBC
- ESR, CRP

Management

- Treatment depends on the type of thyroiditis. Analgesics and anti-inflammatory medication (e.g *aspirin* tablet 500mg every 4 to 6 hours) may be prescribed to reduce inflammation and alleviate pain.
- Alternative glucocorticoid (e.g *prednisolone* per oral 40 to 60mg daily, the dose is gradually taped over 6 to 8 weeks) should be given.
- Symptomatic treatment: ß-blocker as indicated in Hyperthyroidism.

4. Hepato-Gastrointestinal Conditions

4.1. Gastro-Oesophageal Reflux Diseases (GORD)

Definition: Gastroesophageal reflux disease (GERD) is a serious form of gastroesophageal reflux (GER), which occurs when the lower esophageal sphincter (LES) opens spontaneously, for varying periods of time, or does not close properly and stomach contents rise up into the esophagus

Causes and risk factors

- Anatomical abnormalities such as a hiatus hernia.
- Other factors
  - Obesity
  - Pregnancy
  - Smoking

- Common foods that can worsen reflux symptoms
  - Citrus fruits, Chocolate, Drinks with caffeine or alcohol, Fatty and fried foods, Garlic and onions, Spicy foods,Tomato-based foods, like spaghetti sauce, salsa, chili, and pizza

Signs and symptoms

- Heartburn
- Regurgitation of sour material into the mouth
- Epigastric or chest pain.
- Extraesophageal manifestations : dry cough, laryngitis, and pharyngitis, asthma symptoms
- Dysphagia
- Odynophagia
- Weight loss
- Anemia

Complications

- Oesophagitis with different grades according to Savery classification
- Barrett's esophagus predisposes to Adenocarcinoma

Investigations if complications

- Endoscopy with biopsy to rule out oesophagitis and Barrett's esophagus
- Barium X-rays for severity of oesophagus stenosis
- FBC look for anemia

Management

The goals of treatment is

- To provide symptom relief
- To heal erosive oesophagitis
- To prevent complications
    - To provide symptom relief
        - ➔ Lifestyle Changes
            - Weight reduction
            - Avoid lying down for 3 hours after a meal
            - Elevation of the bed (Just using extra pillows will not help)
            - Avoid smoking
            - Reduce fatty foods intake and avoid coffee, chocolate, alcohol, orange juice and certain medications (such as anticholinergic drugs, calcium channel blockers, and other smooth-muscle relaxants)
            - Eat small, frequent meals

        - ➔ Medications
            - Antacids e.g. *Aluminium* and *Magnesium hydroxyde* combination
            - Antirefluxant agents e.g *Alginic acid* (*Gaviscon **) after meals.

              Or
            - H2 receptor blocking agents (*Cimetidine* 200 mg bid; *Ranitidine*, 150 mg bid) for one month

              Or
            - Proton pump inhibitors e.g. *Omeprazole* 20 mg od for one month

              Or
            - Prokinetics: help strengthen the LES and make the stomach empty faster : *Metoclopramide* tablet 10mg TDS during symptom period

- Heal erosive esophagitis
  - The PPIs: *Omeprazole* (20-40 mg/d), *Lansoprazole* (30 mg/d), *Pantoprazole* (40 mg/d), *Esomeprazole* (40 mg/d), for 8 weeks
  - The PPI should be taken 30 min before breakfast
  - Refractory patients can double the dose
  - Patients with complicated GERD (Barrett's esophagus, ulceration, bleeding, peptic stricture) may require long-term PPI therapy (6 months to 1 year)
  - The efficacy of prokinetic agents (domperidone and metaclopramide) has not been established
    - Side effects
      - The side effects of PPI therapy are generally minimal.
      - Aggressive acid suppression may cause hypergastrinemia but does not increase the risk for carcinoid tumors or gastrinomas

- To prevent complications
  - *Vitamin B12 and Calcium* absorption may be compromised by the treatment
  - Patients on PPIs for prolonged periods have an increased incidence of hip fractures
  - Patients who have an associated peptic stricture are treated with endoscopic dilation to relieve dysphagia

Recommendation

- Refer to a surgeon for consideration of Nissen fundoplication (surgery where gastric fundus is wrapped around the esophagus) when medicine and lifestyle changes do not help to manage GERD symptom.

4.2. Dyspepsia and Peptic Ulcer Diseases (PUD)

Definition: Dyspepsia is defined as a syndrome (due to peptic ulcer disease or other causes eg gastritis, non-ulcer dyspepsia) characterized by burning epigastric pain of upper gastrointestinal origin, nausea, bloating or disturbed digestion.

A peptic ulcer is defined as a localized lesion of the mucous membrane of the stomach (gastric ulcer) or duodenum (duodenal ulcer), typically extending through the muscularis mucosa.

Causes

- On the basis of gastroscopy findings, the clinical syndrome of dyspepsia can be divided into:
  - Peptic Ulcer Disease (Ulcer seen at gastroscopy)
  - Non-Ulcer Dyspepsia (gastritis, non-erosive GORD etc.)
- Common causes of peptic ulcer disease (PUD) are:
  - Helicobacter pylori infection. (Helicobacter pylori can also be detected in the absence of an ulcer)
  - Use of non-steroid anti-inflammatory drugs (NSAID)

Risk factors

- Chronic H Pylori infection is by far the most important
- Lifestyle factors(eg :Caffeine intake , alcohol,smoking)
- Severe physiologic stress
- Hypersecretory states (uncommon): Gastrinoma (Zollinger-Ellison syndrome) or multiple endocrine neoplasia type I (MEN-I
- Genetic factors

Signs and Symptoms

- Symptoms of dyspepsia and/or uncomplicated ulcer
  - Aching, burning localized pain in epigastrium
  - Nocturnal pain (midnight–3 a.m) or during intervals between meals (pain from hunger)
  - Associated symptoms including nausea and vomiting, bloating, disturbed digestion

Complication

- Gastrointestinal bleeding (melena, hematemesis, positive fecal blood test)

- Obstruction (postprandial vomiting)
- Penetration, perforated ulcer (acute abdominal pain, guarding, rigidity)
- Gastric cancer (weight loss, loss of appetite, obstructive symptoms)

Investigations

- Gastroscopy with targeted biopsy is gold standard for diagnosis
- Other tests
    - Full Blood Count (Blood type and Rh-factor if complicated ulcer)
    - Urease test (performed at endoscopy)
    - ELISA–serology testing for identification of IgG antibodies to H Pylori (it is not recommended as the confirmation test for eradication as it will remain positive for life)

Management

- The management of dyspepsia depends on patients age, and the presence or absence of "alarm" signs and Symptoms suggesting complications
    - Older patients (>40 years) and those with significant weight loss, hematemesis and melena, post prandial vomiting, OR dysphagia should be referred for gastroscopy
    - Patients under 40 years without any of these alarm symptoms can be commenced on a therapeutic trial of antisecretory drugs and non-pharmacuetical measures. If they do not improve, they should also be referred for gastroscopy

Non-pharmaceutical

- Avoid ulcerogenic medications, e.g. NSAIDs
- Stop smoking and drinking alcohol
- Dietary advice by dietician

Pharmaceutical

- Antisecretory drugs
    - ➔ Proton pump inhibitors (PPI) : eg : *Omeprazole* tablet 20 mg bid (in the morning and in the evening before the meal), or H2 blocker: eg : *Ranitidine* tablet 150 mg bid for 7 days and then reduce dose to od for 3-7 weeks. Monitor clinical response and refer if inadequate

- Triple therapy
  - The vast majority of GUs and DUs are associated with H-Pylori infection and eradication therapy is indicated if infection is present. Empiric eradication of H. pylori without testing is not recommended
  - Antibiotics
    - First choice
      - *Omeprazole* tablet 20 mg bid (on empty stomach), ***Or*** : eg : *Ranitidine* tablet150 mg bid for 10-14 days
      - + Amoxicillin 1g bid at the end of the meal for 10-14 days
      - + *Clarithromycin* 500 mg bid at the end of the meal for 10-14 days

  - Alternative
    - *Omeprazole* tablet 20 mg bid (on empty stomach), OR : eg : *Ranitidine* tablet150 mg bid for 10-14 days
    - + *Amoxicillin* 1g bid at the end of the meal for 10-14 days
    - + *Ciprofloxacin* 500 mg bid at the end of the meal for 7 days

      Or
    - *Omeprazole* tablet 20 mg bid (on empty stomach), or eg : *Ranatidine* tablet150 mg bid for 10-14 days
    - + *Tetracycline* 500 mg qid and/or *Clarithromycin* 500mg bd for 10-14 days
    - + *Metronidazole* 500mg bid at the end of the meal for 10-14 days

    (best regime for penicillin intolerant patients)

Ulcers caused by NSAID

- Stop NSAID and/or aspirin (low dose aspirin can be recommenced after 7 days if needed)
- Omeprazole tablet 20 mg bd (on empty stomach), or Ranitidine tablet150 mg bd for 7 days and then od for 3 weeks. Continue od dosing long term if patient needs to stay on low dose aspirin.
- AND if needed Antacid as symptomatic treatment :eg: sucralfate : 1 g tds

Recurrent and refractory ulcer

The most common causes of refractory and recurrent ulcer include

- Ineffective eradication therapy; persistent H Pylori infection
- Unidentified use of NSAID and poor compliance with medications regimens
- Incomplete healing of large ulcers
- Zollinger-Ellison syndrome and malignant neoplasms

Recommendations

- Refer all cases of recurrent and refractory ulcer to the Gastroenterologist/ Surgeon
- Follow up
  - Gastric ulcers : Endoscopy in eight weeks after treatment
  - Complicated duodenum ulcer : Endoscopy in four weeks after treatment
  - Other patients do not need repeat endoscopy if clinically recovered

Note: *Use of serology testing to confirm eradication of HP is not justified, since antibody titer remains elevated even in the absence of HP.*

4.3. Viral Hepatitis

Definition and causes

Viral hepatitis is a systemic infection primarily affecting the liver, usually caused by one of the hepatotropic viruses, hepatitis A, B, C and E. Hepatitis A and E only cause acute hepatitis, whilst B and C cause acute and chronic hepatitis with risk of cirrhosis and hepatocellular carcinoma.

Others viruses less common or rare: Cytomegalovirus, Epstein-Barr virus, Herpes Simplex, Yellow fever.

Transmission

- Hepatitis A and E: Fecal oral route contaminated food, water shellfish.
- Hepatitis B : blood, sexual, perinatal
- Hepatitis C : Blood >sexual

Clinical manifestations

All types of viral hepatitis produce clinically similar illnesses. These range from asymptomatic through symptomatic hepatitis to fulminant and fatal acute infections.

- Acute viral hepatitis occurs after an incubation period that varies according to the responsible agent :
  - Hepatitis A range from 15–45 days (mean, 4 weeks)
  - Hepatitis B and D from 30–180 days (mean, 12–14 weeks)
  - Hepatitis C from 15–160 days (mean, 7 weeks)
  - Hepatitis E from 14–60 days (mean, 5–6 weeks)

- The prodromal symptoms of acute viral hepatitis are:
  - Anorexia, nausea and vomiting, fatigue, malaise, arthralgias, myalgias, headache, onset of jaundice
  - A low-grade fever between 38° and 39°C is more often present in hepatitis A and E than in hepatitis B or C
  - Dark urine and clay-colored stools (from 1–5 days before the onset of clinical jaundice).
  - Hepatomegaly, right upper quadrant pain and discomfort.

Complications

- Acute liver failure
- Cholestatic hepatitis
- Aplastic anaemia
- Chronic liver disease and cirrhosis (Hepatitis B and C)
- Relapsing hepatitis

Investigations

- Liver function tests (LFTs)
  - Increased Serum transaminases
  - The plasma bilirubin reflects the degree of liver damage
  - The alkaline phosphatase rarely exceeds twice the upper limit of normal

- INR - Prolongation of the prothrombin time indicates the severity of the hepatitis
- FBC - The white cell count is usually normal with a relative lymphocytosis.
- Serological Markers of acute viral hepatitis:
  - Anti-HAV-IgM

- If negative, HAV infection is ruled out in immunocompetent patients
- If positive, this is consistent with acute HAV infection. Anti-HAV-IgM may remain detectable for up to 2 years; hence its presence must be correlated with clinical presentation to establish an accurate diagnosis

- HBsAg
  - If negative, HBV infection is ruled out
  - If positive, patient is infected with HBV and is infectious. If positive for longer than 6 months, then the patient has a chronic HBV infection

- Anti-HBc-total (IgM & IgG)
  - If negative, past infection with HBV is ruled out.
  - If positive
    - IgM anti HBc: First antibody to appear; indicates acute infection (window period= HBsAg become negative, anti HBs not yet +)
    - IgG anti HBc: patient has been infected with HBV. Infection may be resolved or ongoing (HBsAg positive). If infection is resolved, the patient is considered naturally immune to HBV Infection (HBsAg negative)
- Anti-HBs
  - If < 10mIU/ml, the patient has no apparent immunity to HBV
  - If ≥10mIU/ml, the patient is considered immune to HBV (either because of resolved infection or as a result of prior vaccination)
- Anti-HCV
  - If negative, chronic HCV infection is ruled out in an immunocompetent patient
  - If positive, the patient has been infected with HCV
  - Active infection can be confirmed by a qualitative test for HCV-RNA

- Other tests to assist in clinical management of HBV and HCV
  - HBeAg (hepatitis B e antigen) is a viral antigen, which is correlated with high infectivity and in chronic carriers correlates with an enhanced risk of progression to cirrhosis

- Anti-HBe (antibody to hepatitis e antigen) in chronic carriers generally denotes a less infectious state and a partial resolution of HBV infection.
- HBV DNA: The presence of HBV DNA in serum or plasma denotes active HBV infection and infectivity.
- HCV-RNA: The presence of HCV-RNA in the serum or plasma denotes active infection and infectivity. HCV RNA can be detected as early as 2 weeks after infection, well before the patient presents with symptoms.
- HCV genotype (1-4) guides duration and predicts response to treatment in hepatitis C (genotype 2, 3>1 ,4)

Management

Non pharmacological management of acute hepatitis

- Most individuals do not need hospital care.
- Bed-rest until acute phase is over.
- Drugs such as sedatives and narcotics, which are metabolised in the liver, should be avoided.
- No specific dietary modifications are needed.
- Alcohol should be avoided during the illness and for several months after clinical recovery.
- Elective surgery should be avoided in cases of acute viral hepatitis as there is a risk of post-operative liver failure.
- For nausea and vomiting: Metoclopramide, IV/oral, 10 mg 8 hourly as required

Chronic Hepatitis B Pharmacological management

- Best performed in a tertiary centre
- Goals: If HBeAg +, HBeAg - and anti-HBeAg +
- Biological indications for therapy
  - HBeAg + DNA HVB > 20000IU /ml and elevated ALT ***Or*** rarely
  - HBeAg - DNA HVB> 2000IU /ml and elevated ALT or liver biopsy demonstrates fibrosis with stage>2

- Treatment Regimen
  - First line: *Lamivudine* 300 mg+ *Tenofovir* 300mg once /day
  - Second line: *Peginterferon alfa -2a*, dose depends on body weight, once a week.

- Prevention: Vaccinate high- risk patients if HBsAg negative (Hep B vaccine at month 0, 1 and 6)

Hepatitis C Pharmacological

- Again, best performed in a tertiary centre.
- *Peginterferon alfa -2*a 180 microgram once a week + *Ribavirin* 200mg twice a day (adjust dose according to the body weight)
  - ➔ Duration: Genotype 1 and 4 : 48 weeks ; Genotype 2 and 3 : 24 weeks

Recommendation

- Refer for treatment at a tertiary centre
  - Acute cases of acute hepatitis with severe jaundice, encephalopathy or coagulopathy
  - Cases of chronic hepatitis B or C meeting the above guidelines

4.4. Liver Cirrhosis

Definition: It is defined histologically as a diffuse hepatic process characterised by fibrosis and conversion of normal liver architecture into structurally abnormal nodules

Causes

- Alcohol
- Chronic viral hepatitis
  - Hepatitis B
  - Hepatitis C

- Others
  - Toxic substances and medicines
  - Autoimmune hepatitis
  - Nonalcoholic steatohepatitis
  - Biliary cirrhosis
  - Cardiac cirrhosis
  - Inherited metabolic liver disease (hemochromatosis, Wilson's disease, antitrypsin deficiency, cystic fibrosis).
  - Cryptogenic cirrhosis

Signs and Symptoms

Patients with cirrhosis may have few or no signs and Symptoms of liver disease.

- Fatigue, Weakness, Loss of appetite, Itch
- Easy bruising

- Ascites, Oedema
- Upper gastrointestinal (GI) hemorrhage
- Digital clubbing
- Jaundice (sclera icterus)
- Spider naevi
- Parotid gland enlargement (with alcoholism)
- Hepatosplenomegaly
- Gynecomastia, Amenorrhea

Investigations

- FBC (anemic, nutritional deficiencies, or hypersplenism related to portal hypertension)
- Liver function test (GGT, Serum bilirubin, Prothrombin time, Albumin, Serum aminotransferases (ALT, AST))
- Serum sodium and potassium levels, urea and Creatinine (correlates with prognosis)
- Anti HCV, HBsAg
- Alpha-foetoprotein
- Liver biopsy can be helpful to confirm a diagnosis
- Abdominal ultrasound
- Ascitic tap and cell count in acites to rule out spontaneous bacterial peritonitis
- Upper endoscopy (EGD) to rule out esophageal varices

Complications

- Portal hypertension and its consequences of variceal hemorrhage, hypersplenism, ascites
- Hepatic encephalopathy
- Spontaneous bacterial peritonitis (SBP)
- Hepatocellular carcinoma
- Hepatorenal syndrome
- Hepatopulmonary syndrome

Management

- Management goals
  - Preventing further damage to the liver
  - Treating the complications of cirrhosis
  - Preventing liver cancer or detecting it early
  - Liver transplantation

- Preventing further damage to the liver
  - Consume a balanced diet and one multivitamin daily

- Patients with Primary Biliary Cirrhosis (PBC) with impaired absorption of fat soluble vitamins may need additional Vitamins D and K
- Avoid drugs (including alcohol) that cause liver damage
- Eradicate hepatitis B and hepatitis C virus by using anti-viral medications

- Remove blood from patients with haemochromatosis to reduce the levels of iron and prevent further damage to the liver
- Suppress the immune system with drugs such as prednisone and azathioprine (Imuran) to decrease inflammation of the liver in autoimmune hepatitis
- Treat patients with PBC with a bile acid preparation, ursodeoxycholic acid (UDCA)

Treating the complications of cirrhosis

- Edema and ascites
  - Bed rest in acute stage
  - The amount of salt in the diet \ is restricted to 2 grams (half tea spoon) per day and fluid to 1.2 litres per day to decrease edema and ascites
  - If salt and fluid restriction is not enough add diuretics: spironolactone (*Aldactone*) and Frusemide:
    - Start treatment with *Spironolactone* tablet: 100mg od. If, after 4 to 5 days with inadequate response, associate with frusemide: *Furosemide* 40 mg od.
    - Increase doses in this ratio as required: Max Doses *Spironolactone* 400mg od, *Frusemide* 80mg bd.
    - Close monitoring of vital signs, serum eletrolytes, urea and creatinine
    - Abdominal paracentesis when the diuretics do not work (in case of refractory ascites)
      - It is common to withdraw large amounts (2-4 liters) of fluid from the abdomen when the ascites is causing painful abdominal distension and/or difficulty breathing. Ideally, for each 2-3 l of ascites fluid removed, give *Albumin* 100 ml 20% (up to 1g/kg/day) otherwise just limit paracentesis volume

- Gastroesophageal varices
  - Medications
    - *Propranolol (Inderal)*, tablet 10-80mg bd or nitrates like isosorbide dinitrate (Isordil)

- *Octreotide (Sandostatin)* also decreases portal vein pressure and has been used to treat variceal bleeding: 25mcg IV bolus followed by infusion 25-50mcg/h

- Procedures
  - Upper endoscopy (EGD) with either sclerotherapy or band ligation
    - Sclerotherapy involves infusing small doses of sclerosing solutions (aethoxisclerol, pure ethanol etc) into the varices
    - Band ligation involves applying rubber bands around the varices to obliterate them

    These treatments are generally used for patients with bleeding, or very large varices

- Hepatic encephalopathy
  - *Lactulose* : initial dosing 30 ml orally once or twice daily; the dose is increased till patient has 2 -4 loose stools/day
  - Dietary protein is restricted (acutely) because it is a source of the toxic compounds that cause hepatic encephalopathy
  - If symptoms of encephalopathy persist, oral antibiotics such as *Neomycin* 250 – 1000 mg po 3 times daily or *Metronidazole (Flagyl)* 500mg TDS, can be added to the treatment regimen

- Hypersplenism
  - Diagnosis criteria
    - Patients with advanced cirrhosis
    - Enlarged spleen
    - Anemia
    - Leukopenia
    - Thrombocytopenia

  - Management
    - Blood transfusion for severe anaemia (Hb<7), platelets only for acute bleeding with platelet count <30
    - Splenectomy should be avoided, because of the risk of excessive bleeding during the operation and the risk of anesthesia in advanced liver disease

- Spontaneous bacterial peritonitis (SBP)
  - Diagnosis
    - ➔ Patients with advanced cirrhosis have immune systems which are weak
    - ➔ Patients suspected of having spontaneous bacterial peritonitis MUST undergo paracentesis.
    - ➔ Presence of elevated numbers of white blood cells (usually predominantly neutrophils) in the ascitic fluid (>250 white cells/cc) is diagnostic – culture positivity is NOT needed

  - Management
    - ➔ Admit and treat with intravenous antibiotics such as *Ceftriaxone* 1-2gr per day for 5 days or *Ciprofloxacin* IV :200mg bd for 5 days, then change to oral therapy for a further 5 days (eg norfloxacin 400mg bd or ciprofloxacin 500mg bd)
    - ➔ *Albumin* 20% 1g/kg TDS up to 5 days

  - Prevention of spontaneous bacterial peritonitis
    - ➔ All patients with a previous episode of spontaneous bacterial peritonitis warrant preventive treatment for the rest of their life: norfloxacin 400mg od ***Or*** Ciprofloxacin 500mg od ***Or*** *Trimethoprim/ Sulfamethoxazole* 160/800mg od
    - ➔ Other patients who may benefit from prophylaxis include:
      - Patients with cirrhosis who are hospitalized for bleeding varices
      - Patients with low protein levels in the ascitic fluid

- Prevention and early detection of liver cancer
  - Alpha fetoprotein and ultrasound examination ideally should be performed annually

- Liver transplantation
  - Cirrhosis is irreversible. Many patients' liver function will gradually worsen despite treatment and complications of cirrhosis will increase and become difficult to treat. Therefore, when cirrhosis is far advanced, liver transplantation often is the only option for treatment

4.5. Liver abscess

Definition: A liver abscess is a focal hepatic infection with cavity formation.

Causes

- Most liver abscesses in Rwanda are due to Entamoeba histolytica. A few may be due to mixed gram negative or anaerobic infections (pyogenic abscess) and the management of these is different.

Risk Factors

- Immunosuppression – HIV, malignancy, malnutrition, extremes of age
- Adult males more commonly effected than females
- Diabetes, liver disease (especially for pyogenic abscess)

Signs and Symptoms

- Fever (often several weeks duration)
- Right upper quadrant pain
- Weight Loss
- Pallor
- Hepatomegaly
- Jaundice, encephalopathy (rare – poorer prognosis)

Complications

- Rupture leading peritonitis, pleural effusion, lung abscess, pericardial abscess
- Jaundice, hepatic failure, encephalopathy
- Severe malnutrition and wasting

Investigations

- FBC – raised white cell count (often >10)
- CRP
- Albumin (often low)
- Liver function tests (raised ALP, sometimes also AST, bilirubin)
- Liver ultrasound (confirms presence of abscess)
- CT scan abdomen (often not necessary)
- Aspiration of liver abscess for microscopy and culture (if in doubt as to diagnosis)
- Entamoeba serology (positive in >90%)

Management

- General
  - Admit the patient
  - Supportive care – antipyretics eg paracetamol, fluid rehydration

- For amoebic liver abscess
  - *Metronidazole* 500-750mg tds for 10 days (amoebic liver abscess)
    Or
  - *Tinidazole* 2g/day for 5 days
  - Monitor clinical response (temperature, white cell count, CRP)
  - If no improvement in 3-5 days, perform ultrasound guided aspiration of the abscess
  - Some patients may need prolonged therapy
  - Ultrasound findings may take 2 months to normalize

- For pyogenic liver abscess
  - ALL should be aspirated
  - Give prolonged therapy with either
    - *Augmentin* 1.2g IV qid
      Or
    - *Ciprofloxacin* 400mg IV bd AND *Metronidazole* 500mg IV tds

  - Monitor clinical response: temperature, white cell count, CRP to decide on therapy duration
  - Most patients may need 1-2 months therapy, with at least the first 2 weeks being IV

4.6. Acute Cholecystitis

Definition: Acute inflammation of the gallbladder wall

Aetiology

- Obstruction of the gallbladder neck or cystic duct by a gallstone.
- Occasionally, obstruction may be by mucus, parasitic worms or a tumour.
- Acalculous cholecystitis can occur in the intensive care setting, critical ill patients

Clinical features

- Right upper quadrant pain radiating to epigastrium, right shoulder tip or interscapular region.
- Fever
- Right hypochondrial tenderness
- Tenderness worse on inspiration (Murphy's sign)
- Jaundice if presence or recent passage of stones in the common bile duct or bile duct oedema (Mirizzi syndrome)
- Dypnea, Right basal consolidation

Investigations

- FBC: (leucocytosis) + CRP
- Ultrasonography detects gallstones and gallbladder thickening, probe tenderness
- Transminases (Minor increases of plasma transaminases)
- Plasma amylase and lipase (to rule out acute pancreatitis as complication of gallstone)
- Plain X-rays of the abdomen and chest may show radio-opaque gallstones (and are important in excluding lower lobe pneumonia and a perforated viscus)

Complications

- Empyema
- Perforation
- Peritonitis

Management

Principles

- Bed rest
- Pain relief
- Antibiotics
- Maintenance of fluid balance

Medical

- Pain relief
  - → Moderate pain : *Diclofenac* 100 mg intrarectal or IM bid,
  - → Severe pain: *Petidine or Tramadol* 100 mg orally TDS.
- Antibiotics
  - → First choice : *Cefotriaxone* IV 2g once day + / - *Metronidazole* 500 mg TDS for 7 days
- Alternative
  - → *Ciprofloxacine* IV 400mg BID + *Metronidazole* 500 mg TDS for 7 days
  - → Fluid balance is maintained by intravenous therapy, and nasogastric aspiration is only needed for persistent vomiting

Surgical

- Indications
  - → Nonresponse to medical therapy
  - → Complications such as empyema or perforation.
  - → Recurrent biliary colic or cholecystitis
  - → After the acute attack has settled, other patients should be referred for cholecystectomy

4.7. Diarrhoeal Diseases

Definition: Frequent passing of an increased volume of loose or watery stools 3 or more times per day.

Classification

- By duration
  - Acute: ≤14 days in duration
  - Persistent diarrhea: More than 14 days in duration
  - Chronic: More than 30 days in duration
- And by type
  - Inflammatory: Presence of blood or leucocytes in stool
  - Non-Inflammatory: No blood or leucocytes in stool

Causes

- Acute Non-Inflammatory
  - Viral causes
  - Bacterial: E Coli, preformed toxins in food (eg Staph)
  - Cholera (very profuse diarrhea)
- Acute Inflammatory
  - Bacterial Dysentry: Salmonella, Shigella, Campylobacter, E Coli
  - Amoebiasis
  - Clostidium Difficile (antibiotic associated diarrhoea)
- Persistent/Chronic
  - Protozoal: Giardia, Cryptosporidium, Cyclospora
  - Bacterial: Shigella, E Coli
  - Viral: HIV associated, CMV etc
  - Non-infectious: Inflammatory bowel disease, malabsorption, thyroid disease etc

Signs and Symptoms

These depend on the aetiology

- Food poisoning
  - Acute vomiting and/or diarrhea
  - May have infectious contacts
- Cholera
  - Sudden explosive watery diarrhea
  - Excessive vomiting and Fever
  - No colic pain
  - Rapid onset of dehydration
  - Asthenia

- Bacterial Dysentery
  - Acute onset
  - Blood and mucus
  - Fever
  - Prominent abdominal cramping pain
- Amoebiasis
  - Foul smelling diarrhea with blood/mucus
  - Usually no fever
  - Abdominal cramps

Complications

- Electrolyte Imbalance
- Dehydration
- Acute Renal Failure
- Bowel perforation or disseminated sepsis with bacterial pathogens
- Malnutrition with chronic causes

Investigations

- Microscopic Stool analysis
- Stool culture and sensitivity
- Full blood count
- CRP, ESR
- Urea and electrolytes

For chronic cases
- Colonoscopy
- Abdominal ultrasound
- Thyroid function tests
- HIV testing

Management

Non-Pharmaceutical
- Asses the patient for dehydration and replace fluids orally (preferably) or IV
- Give: ORS 200-300mls after each loose stool. Encourage more fluid intake to prevent dehydration
- Careful hand washing, barrier nursing, proper disposal of faecal matter
- Health education about food and personal hygiene

Pharmaceutical

Depending on cause

- Acute non-inflammatory
  - → *Loperamide,* oral, 4 mg immediately, followed by 2 mg after each loose stool
    Maximum dose: 16 mg/day.

- Cholera
  - → *Ciprofloxacin,* oral, 1 g immediately as a single dose

- Acute inflammatory
  - → Avoid loperamide
  - → In severe cases use *Ciprofloxacin*, oral, 500 mg 12 hourly for 3–7 days

- Amoebic dysentery
  - → Avoid loperamide
  - → *Metronidazole*, oral, 500-750 mg 8 hourly for 10 days

- Antibiotic associated diarrhea
  - → Withdraw antibiotics
  - → Avoid loperamide
  - → *Metronidazole,* oral, 500-750 mg 8 hourly for 10 days

- Giardiasis
  - → *Metronidazole,* oral, 500 mg 8 hourly for 5 days

5. Selected Infections and Related Conditions

5.1. Sexually transmitted and Opportunistic infections

Definition: Sexual transmitted infections are diseases transmitted via intercourse especially unprotected anal, oral and vaginal sex. STI are spread to children as well during pregnancy and childbirth.

Causes

- Bacterial
  - Gonorrhea
  - Genital chlamydia
  - Syphilis
  - Chancroid
- Viral
  - Genital papilloma virus 30
  - Genital herpes
- Protozoan
  - Trichomoniasis
- Fungal
  - Genital candidiasis

5.1.1. Gonococcal Urethritis

Definition: It is an STI characterized by presence of secretions (pus) from anterior urethral accompanied by burning urethral discomfort when passing urine. Gonorrhea is transmitted through vaginal, anal and oral intercourse or prenatally.

Cause

- Neisseria gonorrhoeae a Gram negative intracellular diplococcus

Signs and Symptoms

- In general: Purulent discharge of the mucous membranes

- In women
  - Asymptomatic in 50% of the time
  - Dysuria
  - Vaginal discharge
  - Bleeding between periods
  - Swelling of the labial folds

Complications

- Urethral strictures
- Pelvic inflammatory disease (PID)
- Chronic pelvic pain
- Infertility
- Ectopic pregnancy
- Gonococcal septicemia
- In men
  - Acute arthritis
  - Dysuria
  - Urethral purulent discharge
  - Prostatis
  - Epididimatis
  - urethral strictures
  - Gonococcal septicemia
  - In neonates
  - Purulent conjunctivitis
- Corneal erosion, perforation and blindness

Investigations

- Gram-stain of urethral/vaginal discharge
- Culture and sensitivity

Management

For adult

- Treatment of uncomplicated anogenital infection
  - ➔ First choice recommended regimens
    - *Ciprofloxacin,* 500mg orally, BID for 7 days (Contraindicated in pregnancy, children)

      Or
    - *Azithromycin,* 2g orally, as a single dose

      Or
    - *Ceftriaxone,* 250mg by intramuscular injection, as a single dose

      Or

- *Cefixime,* 400mg orally, as a single dose

Or

- *Spectinomycin,* 4g (trobicin) by IM injection, as a single dose
- *Doxycycline*, 100mg orally, twice daily for 7 days

- Treatment of complicated infection
  - Recommended regimens
    - *Ceftriaxone*, 1g by IM or IV, once daily for 7 days

OR

- *Spectinomycin*, 2g by IM, twice daily for 7days.
  - For gonococcal meningitis and endocarditis the same dosages apply but the duration of therapy will need to be increased to 4 weeks for endocarditis

Recommendations

- Health education and behaviors change
- Screen /Treat partner for STI

5.1.2. Non gonococcal urethritis

It comprises Vulvo-vaginitis due to Candidiasis (refer to fungal infections), Trichomonas vaginalis and Chlamydia infections

Trichomonas Vaginalis Infection

Definition: STI caused by this protozoan; a common cause of abnormal vaginal discharge

Signs and Symptoms

- In men
  - Asymptomatic
- In female
  - Vaginal pruritis
  - Malodorous yellow green discharge

Complication

- Vulvo-vaginatis

Investigations

- Wet month microscopy
- Culture

Management

- *Metronidazole*, 2g orally, in a single dose
- OR
- *Tinidazole,* 2g orally, in a single dose
- Alternative regimen
    - *Metronidazole*, 500mg orally, twice daily for 7 days
      Or
    - *Tinidazole*, 500mg orally, twice daily for 5 days

Recommendations

- All sexual partners should be notified and treated,
- Patients should be advised against sexual intercourse until both patient and the partner(s) are treated

5.1.3. Chlamydia Infections

Definition: Chlamydia infection is an STI characterized by urethral discharge

Cause

- Infection with *Chlamydia trachomatis*

Signs and Symptoms

- In female
    - Most of the time, asymptomatic
    - Vaginal discharge
    - Dysuria
    - Bleeding after intercourse
    - Abnormal vaginal bleeding

- In men
    - Most of the time, asymptomatic
    - Dysuria
    - Mucopurulent discharge
    - Itching sensation inside the urethra

Complications

- Pelvic inflammatory disease (low abdominal pain)
- Infertility

Investigations

- Culture
- Serology

Management

- First choice
  - *Azithromycin* 1 g orally as one dose
    Or
  - *Doxycycline* 200 mg orally daily for 10 days for ppatients allergic to macrolide (azithromycin)
  - For pregnant women, *Erythromycin* 500mg 4 times per day for 7 days

Recommendations

- All sexual partners should be notified and treated
- Patients should be advised against sexual intercourse until both patient and the partner(s) are treated.

5.1.4. Syphilis

Definition: Syphilis is a systemic disease caused by the spirochete *treponema pallidum* and often referred to as a "great imitator" because it is mimic many diseases

Cause

- Treponema pallidum

Signs and Symptoms

It runs through 3 stages: primary, secondary, tertiary.

- Primary syphilis
  - Single Painless, rubbery ulcer (chancre) with raised and firm edges which typically occurs 21 days after inoculation.
  - Multiple primary lesions may occur in HIV-infected individuals or as "kissing lesions" on opposing skin surfaces
  - Regional lymph node enlargement

- Secondary Syphilis
  - Non-pruritic generalized scaly, papulo-nodular lesions
  - Patchy hair loss, fever, malaise, pharyngitis
  - Lymphadenopathy

- Condyloma lata
- Skin lesions palmo/plantar areas

- Tertiary or Neuro-Syphilis
  - Gummas may be single or multiple
  - Liver and skeleton are commonly affected
  - Fever, jaundice, anemia, and nocturnal bone pains

Complications

- Syphilitic meningitis
- Neurologic disorders
- Congenital syphilis

Investigations

- Non-treponemal test: RPR or VDRL
- Treponemal test: TPHA

Management

Early syphilis (primary, secondary)

- First choice recommended regimen
  - → *Benzathine benzylpenicillin (Extecilline),* 2.4 million IU, by intramuscular injection, at a single session per week for 3 weeks

- Alternative regimen
  - → *Procaine benzylpenicillin (*PPF), 1.2 million IU daily, by intramuscular injection, for 10 consecutive days

- Alternative regimen for penicillin-allergic non-pregnant patients
  - → *Doxycycline,* 100mg orally, twice daily for 15 days **OR** tetracycline, 500mg orally, 4 times daily for 15 days

Neurosyphilis (Tertiary)

- Recommended regimen
  - → *Aqueous benzyl penicillin (Peni G*), 2-4 million IU by IV injection every 4 hours for 14 days

- Alternative regimen
  - → *Procaine benzylpenicillin*, 1.2 million IU, by intramuscular injection, once daily for 10-14 consecutive days and Probenecid 500mg tabs 4 times daily for 10-14 days

- Alternative regimen for penicillin-allergic non-pregnant patients
  - ➔ *Doxycycline,* 100mg orally, twice daily for 30 days or tetracycline, 500mg orally, 4 times daily for 30 days

Syphilis in pregnancy

- Primary and secondary syphilis
  - ➔ *Erythromycin,* 500mg orally, 4 times daily for 15 days

- Tertiary syphilis
  - ➔ *Erythromycin,* 500mg orally, 4 times daily for 30 days

Recommendations

- All patients with syphilis should be encouraged to undergo testing for HIV because of the high frequency of dual infection
- Neurosyphilis should be considered in the differential diagnosis of neurological disease in HIV-infected individuals
- In cases of congenital syphilis, the mother should be encouraged to undergo testing for HIV
- Recommended therapy for early syphilis in HIV-infected patients is no different from that in non-HIV-infected patients

5.2. Genital ulcerations

5.2.1. Chancroid

Definition: Chancroid is a Sexual Transmitted Infection (STI) characterized by painful necrotizing genital ulcers accompanied by usually unilateral adenopathy.

Chancroid is transmitted sexually by direct contact with purulent lesions and by autoinoculation to non sexual sites such eyes and skin

Cause

- Haemophilus ducreyi (gram-negative bacterium)

Risk factors

- Endemic area
- Low economic status
- Prostitution

Signs and Symptoms

- Lesions start as a tender papules that became pistular then erodes to form an extremely painful and deep single or multiple ulcers
- Tender, unilateral lymph node

Complications

- Phimosis
- Urethral stricture
- Urethral fistula
- Superinfection of ulcers with rapid destruction of genitalia known as a phagedenic chancroid

Investigations

- Gram stain of ulcer exudates
- Culture

Management

- First choice
  - *Ciprofloxacin* 500mg twice daily orally for 5 days
    OR
  - *Erythromycin* 500mg orally 6 hourly for 7 days

- Alternative
  - *Sulfamethaxole*(400mg)-trimetoprim (80mg) 2x2/days for15 days

Recommendations

- Follow up strictly medications
- Screen/treat partners
- HIV testing and counsel

5.2.2. Granuloma Inguinale/Donovanosis

Definition: Granuloma inguinale is a chronic bacterial infection that affect the skin and mucus membrane in the genital lesions

Cause

- Gram negative calymatobacterium granulomatis (klebsiella granulomatis)

Signs and Symptoms

- Nodule and papules at the site of inoculation
- Single or multiples ulcerations of genital area
- No adenopathy
- Absence of healing if no treatment

Complications

- Elephantiasis swelling of the external genital area
- Extra genital involvement by auto inoculation or direct extension of lesions

Investigation

- Gram stain of ulcer exudates

Management

- *Sulphametoprim* (400mg)-trimetrprim(80mg), 2x2 /days /10-20 days
  Or
- *Doxycycline* 100 mg, 200mg a day for 10 days (avoided in pregnancy)

5.2.3. LymphoGranuloma Venereum (LGV)

Definition: LymphoGranuloma Venereum is a cutaneous and sometime systemic STI that affects primarily lymphatic tissues of the groin

Cause

- Infection with Chlamydia trachomatis

Signs and Symptoms

- First stage
  - A small painless, papule/ulcers

- Second stage
  - Lymph node involvement resulting in painful buboes.
  - Enlargement of lymph nodes above and below the inguinal ligament result in the classic "groove sign."

- Third stage
  - Rectal fistulas, especially in women, resulting in scarring and chronic lymphatic obstruction

Complications

- Scarring and local tissues destruction with fistula and stricture formation
- Rectal stenosis
- Elephantiasis of genital organs
- Systemic spread

Investigations

- Samples for culture
- Serology

Management

Medical therapy

- First-line treatment is usually with doxycycline 100mg twice-daily for 21 days,
  Or
- Erythromycin 500 mg 4 times daily for 21 days

Surgical therapy

- Buboes may be drained percutaneously to relieve symptoms.
- Surgical excision is best avoided due to the risk of sinus or fistula formation

Recommendation

- The patient should refrain from unprotected sexual intercourse until they and any contacts have completed treatment and follow-up.

5.3. Malaria

Definition: Malaria is a febrile hematozoid parasitic illness due to Plasmodium parasites.

Causes: Plasmodium Falciparum, Plasmodium Ovale, Plasmodium Malariae, Plasmodium vivax.

Signs and Symptoms

- Simple Malaria
  - Moderate fever 37.5 °C or history of fever in the last 24 hours
  - Headache
  - Weakness
  - Chills
  - Loss of appetite
  - Stiffness
  - Joint pain and muscular aches
- Malaria with minor digestive symptoms
  - Signs of simple malaria with vomiting and/or moderate diarrhea
- Severe malaria
  - Vital sign and conscious state alteration
  - positive parasitaemia due to *Plasmodium falciparum*
  - Signs of severity or danger:
    - Inability to drink or suckle
    - Vomiting (leaving nothing in stomach)
    - Convulsions (≥ 2 convulsions in 24 hours)
    - Lethargy and unconsciousness

Complications

- Severe anaemia (haemoglobin < 5 g/dl or hematocrit <15%) ;
- Acute renal failure
- Hypoglycemia
- Pulmonary edema
- DIC

Investigations

- Blood smear or positive malaria rapid tests (RDTs)
- FBC
- Urea Creatinine, plasma glucose, according to severity
- Chest x ray if needed

Management

Simple malaria

- First line treatment
  - *Artemisinin* combination therapy (ACT)
  - *Artemether* 20 mg and Lumefantrine 120 mg, twice a day for 3 days
  - *Paracetamol*: 15mg/ kg TID
    - Contraindications
    - Children weighing less than 5 kg
    - First trimester pregnancy
    - Allergy to one of the two drugs in the combination
    - Severe liver or renal disease

- Alternative:
  - Oral *Quinine sulphate* 10 mg / kg TID for 7 days;

Table: Dosage related weight

Category of body weight of the patient in kg	Type of blister administered	Number of tablets of COARTEM per dose					
		Day 1		Day 2		Day 3	
		First dose	8 hours after first dose	24 hours after first dose	36 hours after first dose	48 hours after first dose	60 hours after first dose
5 kg ≤ weight < 14 kg	6*1 (5-15 kg)	1	1	1	1	1	1
15 kg ≤ weight < 24 kg	6*2 (15-25kg)	2	2	2	2	2	2
25 kg ≤ weight < 34 kg	6*3 (25-35 kg)	3	3	3	3	3	3
≥ 35 kg	6*4 (> 35 kg)	4	4	4	4	4	4

Simple malaria with minor digestive symptoms

- *Artesunate IV*: 2.4 mg/kg (time = 0) then at 12 hour, then daily thereafter
- If no more vomiting, change to oral *Artemether-Lumefantrine* twice a day for three consecutive days

Note/ Preparation: *Artesunate will be diluted in 1 ml 5% sodium bicarbonate (provided in the package), and then further diluted with 5% dextrose or 0.9% normal saline to a total volume of 6 ml, giving a final concentration of 10 mg/ml*

- Alternative
  - In children: *Quinine dihydrochloride* (Salt) intra-rectal: 15mg/kg body weight diluted in 4 ml of distilled water or physiological saline and administered rectally with a 5 ml syringe every eight hours
  - In adult: oral *Quinine sulphate* 10 mg / kg TID for 7 days

- Severe malaria
  - Admit the patient
  - First choice: *Artesunate IV* 2.4 mg/kg IV (time = 0), then at 12h and 24h, then once a day for three days. Then continue with *Artemisinin* combination therapy (ACT): Artemether 20 mg and Lumefantrine 120 mg, twice a day for 3 days
  - Alternative *Quinine* IV
    - Loading dose of 20 mg/kg (do not exceed 1200 mg) diluted in an isotonic solution or 5 or 10% glucose in term of 5 to 10 ml/kg BW to run for 4 hours in IV perfusion
    - Then run IV *Glucose* 5 or 10% for 4 hours as maintenance drip
    - Thereafter, i.e. 8 hours after the beginning of the administration of the loading dose or 4 hours after the beginning of the maintenance drip, administer a maintenance dose of 10 mg/kg body weight of quinine dihydrochloride, to run for 4 hours
    - This maintenance dose of quinine will be repeated every 8 hours until the patient can swallow, at the most within 48 hours
    - After 48 hours, if the patient's state does not permit the patient to take quinine orally, continue the drip of quinine by reducing the doses to 7mg/kg every 8 hours to run for 4 hours
    - Give parenteral antimalarials in the treatment of severe malaria for a minimum of 24h, once started (irrespective of the patient's ability to tolerate oral medication earlier), and, thereafter, complete treatment by giving a complete course of oral Artemether 20 mg and Lumefantrine 120 mg, as recommended for the treatment of simple malaria

  - Supportive treatment
    - If the temperature ≥ 38°C: Tepid sponging, *Paracetamol* 15mg/kg per os or suppository
    - To prevent hypoglycemia : Give 3-5ml/kg body weight of *10% Glucose* bolus or if not available 1 ml/kg of 50% glucose; or administration of water with 10% sugar per os or with nasogastric tube, at a rate of 5 ml/kg.

- In case of convulsions: *Diazepam* 0.5 mg/kg Intra-rectal ; and if convulsions persist, *Phenobarbital* 10-15 mg/kg IM.
- In case of hypovolaemia (severe anemia, rapid breathing, coma or systolic BP < 80 mm Hg), start with *Normal saline* or *Ringer's lactate* infusion in a dose of 20 ml/kg to run for 15 minutes

For the anaemic form of severe malaria, give *Transfusion* if anaemia not tolerated (tachycardia, dyspnea hypoxemia)

5.4. Tuberculosis

Definition: Tuberculosis is a chronic infectious disease caused in the majority of cases by Mycobacterium tuberculosis

Etiology

- Mycobacterium tuberculosis.
- Mycobacterium bovis transmitted by raw infected milk.

Classification of Tuberculosis

- Pulmonary TB
  - sputum smear positive
  - Sputum smear negative
  - Sputum smear not done

- Extra-pulmonary TB
  - Miliary TB
  - Pleural TB (pleural effusion)
  - Peritoneal TB
  - Tuberculosis lymphadenitis
  - Tuberculosis meningitis
  - Pericardial TB
  - Osteo-articular TB
  - Uro-genital TB
  - Cutaneous TB (rare)

Signs and Symptoms

- General features: Prolonged night fever, night sweating, loss of weight, anorexia, asthenia

- According to the localization: chronic cough (> 2 weeks), hemoptysia, dyspnea, chest pain, pleural effusion, ascites, signs of heart failure, pericardial friction, osteoarticular pain and deformities, cervical and axilar adenopathies, hematuria, meningeal syndrome…

Investigations

- Sputum smear microscopy and culture accordingly
- Chest X ray
- According to localization
  - Pleural tap for cytology and biochemistry
  - Abdominal ultrasound and ascites liquid analysis
  - Cardiac ultrasound.

- FNA and Lymph nodes biopsy
  - Urine analysis
  - Lumbar puncture for CSF analysis, staining and biochemistry (Protein and glucose)
  - FBC, HIV test, plasma glucose
  - Liver enzymes, urea and creatinine

Management

- First-treatment (adults from 15 years)
  - *2 RHZE* / 4 RH (total duration: 6 months)
  - Indications: New cases.

Table: First treatment for new cases

Phase	Months / N° dosis	Drug	29-37 kg	38-54 kg	³ 55 kg
Intensive	2 months (56 doses)	($R_{150}H_{75}Z_{400}E_{275}$)	2	3	4 tab
Continuation	4 months (112 doses)	($R_{150}H_{75}$)	2	3	4 tab

- Retreatment
  - *2 S*RHZE / 1 *RHZE* / *5 RHE* (total duration: 8 months)
  - Indications: relapses, failures to first treatment, patients who return to treatment after default, « other» cases previously treated.

Table: Retreatment after first treatment

Phase	Months / N° doses	Drug	29-37 kg	38-54 kg	³ 55 kg
Intensive (1)	2 months (56 doses)	$(R_{150}H_{75}Z_{400}E_{275})$	2	3	4 tab
		S (*)	0.5 g	0.75g	1 gr (**)
Intensive (2)	1 months (28 doses)	$(R_{150}H_{75}Z_{400}E_{275})$	2	3	4 tab
Continuation	5 months (140 doses)	$(R_{150}H_{75}E_{275})$	2	3	4 tab

N:B (*) *Never give Streptomycin to pregnant women.*
N:B (**) Patients > 50 years: 0.5-0.75 g/day maximum.

- First Treatment of Children between 0 - 14 Years of Age: 2 (RHZ)E/ 4 (RH)

Table: First Treatment for children ≤ 14yrs

Phase	Months / doses	Drug	Pediatric tablets			Adult tablets	
			5-7 kg	8-14 kg	15-20kg	21-30 kg	
Intensive	2 months (56 doses)	$(R_{60}H_{30}Z_{150})$	1	2	3	$(R_{150}H_{75}Z_{400}E_{275})$	2
		$(R_{60}H_{60})$	1*	1*	2**	$(R_{60}H_{60})$	2**
		E_{100}	1	2	3		
Continuation	4 months (112 doses)	$(R_{60}H_{30})$	1	2	3	$(R_{150}H_{75})$	2
		$(R_{60}H_{60})$	1*	1*	2**	$(R_{60}H_{60})$	2**

* If $(R_{60}H_{60})$ is not available, replace by 1 tab of $(R_{60}H_{30})$.
** If $(R_{60}H_{60})$ is not available, replace by 2 tab of $(R_{60}H_{30})$ + ½ tab of H_{100}.

- Retreatment: 2 S(RHZ)E / 1 (RHZ)E / 5 (RH)E.
- Tuberculosis Meningitis and Osteo-Articular TB: 2 (RHZE) / 10 (RH)
  - In case of meningitis, give the maximum dosage according to patient's weight:
  - Babies weighting less than 5 kg: Use the dosages below according see dosages below

Table: Treatment of Tuberculosis Meningitis and Osteo-Articular TB

DOSAGES		
Drug	**CHILD**	**ADULTS**
Rifampicin (R)	15 mg/kg (10 à 20 mg/kg), max 600 mg/j	10 mg/kg (8 à 12 mg/kg), max 600 mg/j
INH (H)	10 mg/kg (10 à 15 mg/kg), max 300 mg/j	5 mg/kg (4 à 6 mg/kg), max 300 mg/j
Pyrazinamide (Z)	35 mg/kg (30 à 40 mg/kg)	25 mg/kg (20 à 30 mg/kg)
Ethambutol (E)	20 mg/kg (15 à 25 mg/kg)	15 mg/kg (15 à 20 mg/kg)
Streptomycin (S)	15 mg/kg (15 à 18 mg/kg)	15 mg/kg (15 à 18 mg/kg)

Note: *Supervised daily administration during the whole duration of Treatment*

TUBERCULOSIS AND HIV/AIDS

Management of patients co-infected

- TB treatment: Treatment regimens are the same as for HIV negative patients.
- Antiretroviral treatment
    - All TB patients who are found to be infected with HIV are eligible for ART regardless of their CD4 count (Recommendation WHO 2010)
    - TB treatment is first initiated, followed by ART as soon as possible within 8 weeks following initiation of TB treatment (usually can be begun safely after about 2 weeks)

- Isoniazide prevention treatment (IPT)
    - For close contacts of TB infected cases

MULTIDRUG-RESISTANT TUBERCULOSIS

Definition: Multidrug resistance TB is a resistance to at least Rifampicin and Isoniazid confirmed by drug sensitivity test (DST)

Causes

- Non adherence/poor compliance
- When is MDR to be suspected
    - Every failure of treatment despite a regular, correct and supervised treatment
    - Any TB case diagnosed among the contacts of a know MDR-TB patient
    - Any re-treatment case

Investigations

- Sputum culture with sensitivity test
- Bronchoalveolar lavage

Management

- 6 months of Kanamycin, Pyrazinamide, Levofloxacin, Prothionamid, Cycloserin (Km-Z-Lfx-Pto-Cs) followed 14 months of Km-Z-Lfx-Pto-Cs

Table: Treatment Regimens for Multi-Resistant Tuberculosis.

		31-40 kg	41-50 kg	51-70 kg	> 70 kg
Kanamycin (Km)	*1 gr / ampoule*	500 mg	750 mg	1000 mg	1000 mg
Amikacin (Am)	*0,5 gr / amp*				
Capreomycin (Cm)	*1 gr / amp*				
Ofloxacin (Ofx)	*tab 200, 400 mg*	800 mg	800 mg	800 mg	800 - 1000
Levofloxacin (Lfx)	*tab 250, 500 mg*	750 mg	750 mg	750 mg	750 - 1000
Moxifloxacin (Mfx)	*tab 400 mg*	400 mg	400 mg	400 mg	400 mg
Prothionamid (Pto)	*tab 250 mg*	500 mg	500 mg	750 mg	750 - 1000
Cycloserin (Cs)	*tab 250 mg*	500 mg	500 mg	750 mg	750 - 1000
Pyrazinamide (Z)	*tab 400 mg*	3 cés	4 cés	5 cés	6 cés
	tab 500 mg	2 cés	3 cés	4 cés	5 cés
Pyridoxin (Vit B6)	*tab 50, 100 mg*	100 mg	100 mg	150 mg	150 –200
PASER	*Sachet 4 gr)*	8 gr	8 gr	8 gr	8-12 gr
Clofazimin	*tab 50, 100 mg*	100 mg	200 mg	300 mg	300 mg

5.5. Leprosy

Definition: Leprosy is a chronic bacterial disease of the skin, peripheral nerves and /or the upper airway

Cause

- Mycobacterium leprea

Signs and Symptoms

- Lepromatous leprosy (multibacillary form)
  - Skin : bilaterally symetrical numerous and extensive nodules, papules, and diffuse infiltrations
  - Nasal mucosa
  - Eyes: iritis and keratitis
- Tuberculoid leprosy (paucibacillary form)
  - Skin lesions (single or few and bilaterally asymetrical): Sharply demarcated, hypoesthetic or anasthesic.
  - Peripheral nerve involvement tends to be severe

Investigations

- Lepromin test: intradermal injection of autoclaved M leprea (induration at day 28)
- Skin lesion biopsy

Management

- Lepromatous leprosy (multibacillary form)
  - Monthly dose: day 1 and every 28 days (monthly for 12 months):
    - → *Rifampicin* 600mg + *Clofazimine* 300mg + *Dapsone* 100mg

    AND
  - Daily dose from Day 2 every day (all other days for 12 months):
    - → *Dapsone* 100mg + *Clofazimine* 50mg

- Tuberculoid leprosy (paucibacillary form)
  - Monthly dose: day 1 and every 28 days (monthly for 6 months)
    - → *Rifampicin* 600mg +Dapsone 100mg

    AND

- Daily dose from day 2 every day (all other days for 6 months)
  - → *Dapsone* 100mg

5.6. Meningitis

Definition: Meningitis is inflammation of the meninges that results in the occurrence of meningeal syndrome.

Causes

- Infectious
  - Bacterial
    - → Streptococcus pneumoniae meningitis meningococcal meningitis, or Haemophilus influenzae meningitis, BK
  - Fungal
    - → Cryptococcal meningitis, Histoplasma meningitis
  - Parasitic
    - → Amoebic meningoencephalitis
  - Viral
    - → Enterovirus meningitis, herpes simplex virus [HSV] meningitis
- Non-infectious
  - Carcinomatosis
  - Head injury

Signs and Symptoms

- Fever, headache, neck stiffness, photophobia, nausea and vomiting
- Positive Kernig's and Brudzinski's sign
- Signs of cerebral dysfunction (eg, lethargy, confusion and coma)

Complications

- Hydrocephalus
- Seizures
- Neurological deficit

Investigations

- The cornerstone in the diagnosis of meningitis is examination of the CSF
- Performing a fundoscopy before lumbar puncture is not mandatory but is recommended if possible Patients with a normal conscious state and no focal signs are at low risk for complications from LP
- Lumbar puncture
  - Appreciation of the opening pressure
  - CSF macroscopic aspect
  - CSF analysis: Cell count and differential, chemistry (glucose and protein), and microbiology (Gram-stain, Indian ink stain and cultures)

Note: *Lumbar puncture is best considered after CT scan in case of*

- *Coma with a GCS <11/15*
- *Focal deficit*
- *Ongoing focal or generalized seizures*
- *Presence of any sign of cerebral herniation (unilateral mydriasis, decebration, hemodynamic instability-Cushing syndrome)*

- HIV test may also be ordered depending on clinical suspicion

Table: CSF Picture of Meningitis According to Etiologic Agent

Agent	Opening Pressure (mm H20)	Macroscopic aspect	WBC count per mL	Glucose (mg/dL)	Protein (mg/dL)	Microbiology
Bacterial meningitis	200-300	Cloudy	100-5000; >80% PMNs*	<40	>100	Specific pathogen demonstrated in 60% of Gram stains and 80% of cultures
Cryptococcal meningitis	180-300	Clear or opalescent	10-200; lymphocytes	Reduced	50-200	India ink, cryptococcal antigen, culture
Viral meningitis	90-200	Clear or opalescent	10-300; lymphocytes	Normal, reduced in mumps	Normal but may be slightly elevated	PCR† assays if available
Tuberculous meningitis	180-300	Clear or opalescent	100-500; lymphocytes	Reduced, <40	Elevated, >100	Acid-fast bacillus stain, culture, PCR
Aseptic meningitis	90-200	Clear or opalescent	10-300; lymphocytes	Normal	Normal but may be slightly elevated	Negative findings on workup
Normal values	80-200	Crystal Clear	0-5; lymphocytes	50-75	15-40	Negative findings on workup

- FBC and ESR/CRP
- Blood culture
- Urea and creatinine
- Liver function tests
- Brain CT-scan and MRI imaging of the brain depending on clinical conditions
- Blood glucose (compare with CSF as CSF glucose will be higher if blood glucose high)

Management

Bacterial Meningitis

- The first choice for empiric antiobiotherapy: The third-generation cephalosporins (*Ceftriaxone* 2-4 g/d or *Cefotaxime* 8-12 g/d); Consider using *Penicillin G* 24 million U/d where penicillin-susceptible strains occur and for pneumococcal meningitis
- Give *Dexamethasone* (10mg IV 6hourly for 48-96hrs) in adults as adjunctive treatment for pneumococcal and meningococcal meningitis to reduce sequel of meningitis such as deafness.

Staphylococcus species

- Treat meningitis caused by S aureus with *Nafcillin* (9-12 g/d) or *Oxacillin* (9-12 g/d)
- *Vancomycin* (2-3 g/d, adjusted to serum levels) is the alternative in patients who are allergic to penicillin and is the first-line therapy for methicillin-resistant S Aureus (MRSA) strains

Tuberculous meningitis

- Refer to the TB Section in this chapter for treatment protocol

Viral meningitis

- *Acyclovir* (10 mg/kg IV q8h) indicated for HSV-1 and HSV-2 meningitis

Fungal meningitis

- Treatment of AIDS-related cryptococcal meningitis (ie, C neoformans)
  - ➔ Induction therapy: Administer *Amphotericin B* (0.7-1 mg/kg/d IV) for at least 2 weeks, with or without *Flucytosine* (100 mg/kg PO) in 4 divided doses
  - ➔ Consolidation therapy: Administer *Fluconazole* (400 mg/d for 8 wk). *Itraconazole* is an alternative if fluconazole is not tolerated

- ➔ Maintenance therapy: Long-term antifungal therapy with *Fluconazole* (200 mg/d) is most effective to prevent relapse

- Treatment of cryptococcal meningitis (ie, *C neoformans*) in patients without AIDS
  - ➔ Induction/consolidation: Administer *Amphotericin B* (0.7-1 mg/kg/d) plus *Flucytosine* (100 mg/kg/d) for 2 weeks. Then, administer *Fluconazole* (400 mg/d) for a minimum of 10 weeks.
  - ➔ A lumbar puncture is recommended after 2 weeks to document sterilization of the CSF. If the infection persists, longer therapy is recommended.
  - ➔ Monitor vital signs and assess neurological status
  - ➔ Airway, breathing and circulation management
  - ➔ Provide analgesic for headache
  - ➔ Pressure care
  - ➔ Treat raised intracranial pressure with Mannitol 20% 0.5g/kg, hyperventilation and sedation.

Recommendation

- Refer to neurosurgery for hydrocephalus management if needed

5.7. Typhoid Fever (Enteric Fever)

Definition: Typhoid fever is a systemic disease characterized by fever and abdominal pain and caused by dissemination of *S.* Typhi or *S.* Paratyphi.

Cause

- Bacteria of the genus *Salmonella* (*Salmonella* Typhimurium) serotypes Salmonella typhi and/ or Salmonella Paratyphi

Signs and Symptoms

The incubation period for *S.* Typhi averages 10–14 days but ranges from 3 to 21 days, with the duration likely reflecting the inoculum size and the host's health and immune status.

Symptoms

- The most prominent symptom is prolonged fever (38.8°–40.5°C; 101.8°–104.9°F), which can continue for up to 4 weeks if untreated (fever does not respond to antimalarials)

- Constipation in the early stages
- Abdominal pain and diarrhoea in the second week of illness
- Severe headache
- Psychosis and confusion in 10% of adults

Signs

- High fever with a relatively slow pulse rate (pulse may be fast, especially with complications)
- Abdominal tenderness (non-specific unless intestinal perforation)
- Hepato–splenomegaly
- Mental confusion

Complications

- Intestinal perforation with peritonitis (rapidly fatal, refer urgently to a surgeon) – presents as severe abdominal pain, tenderness, rebound tenderness and guarding
- Acute psychosis (never refer any patient with fever and psychosis to the psychiatric hospital)
- Severe intravascular hemolysis leading to acute renal failure (especially in G6PD deficiency)

Investigations

- FBC, differential (white cell count may be high or low, thrombocytopenia is also common)
- Blood film to exclude malaria
- Blood culture
- Stool culture
- Urine culture
- Widal test

Note:

- ***Diagnosis of typhoid fever is based on a strong clinical suspicion backed by:***
  - *Blood cultures, positive during first 10 days of fever*
  - *Stool cultures, positive after tenth day up to fourth or fifth week*
    Urine cultures, positive during second and third week

The above tests are superior to the Widal test, which is unreliable and rarely useful, in confirming a diagnosis of typhoid fever

- A Widal test with 'O' titres of 1/160 or less seldom suggests typhoid fever in the absence of positive blood and stool cultures
- The Widal test, if done, must be repeated after 10 days
- Positive Widal's test may occur in non–specific febrile illnesses (anamnestic reaction) and autoimmune disease
- Some patients with typhoid fever may have a negative Widal's test

Management

Pharmacological

- *Ciprofloxacin*, oral Adults: 500 mg bid for 14 days
  Or
- *Ciprofloxacin*, IV, 400 mg bid may be given in severely ill patients who cannot take oral medication. Revert to oral medication as soon as clinically indicated.
  Or
- *Ceftriaxone*, IV, Adults: 1–2 g daily for 7 days

Other alternatives

- *Chloramphenicol* 500-750mg qid orally or IV for 14 days
  Or
- *Azithromycin* 1g stat, then 500mg-1g orally OD for 5-7 days

Recommendations

- Refer to a tertiary centre
  - If diagnosis is in doubt
  - Any deteriorating case
  - If patient does not improve after 7 days therapy

- Refer to a surgeon
  - If suspicion of intestinal perforation

5.8. Tetanus

Definition: Tetanus is a nervous system disorder characterized by muscle spasms that is caused by the toxin-producing anaerobe, Clostridium tetani.

Predisposing factors

- A penetrating injury
- Coinfection with other bacteria
- Devitalized tissue
- A foreign body
- Localized ischemia

Signs and Symptoms

- Incubation period
  - Average period from exposure to onset of symptoms : 7 days (from 3 to 21 days)
- Generalized tetanus
  - Muscle spasms appear at onset or when muscular rigidity becomes generalized.
  - Muscular rigidity
    - → Trismus
    - → Risus sardonicus (sardonic smile)
    - → Dysphagia
    - → Opisthotonus
    - → Restriction of respiratory muscles
    - → Guarding
    - → Extension of the lower limbs and flexion of the upper limbs

The severity is related to the incubation period of the illness and the interval from the onset of symptoms to the appearance of spasms. The longer the interval, the milder the clinical features of tetanus.

Management

- General Supportive Management
  - Admit patient in ICU in a quiet room (avoid nose, light and touch)
  - Prevent bedsores
  - Establish IV access for hydration and IV injections.
  - Insert nasogastric tube for hydration and feeding or oral medications

- Gentle aspiration of secretions from nose and oropharynx.
- Provide hydration and nutrition in feeds divided over 24 hours. For newborns, give expressed breast milk every hour

- Halting the toxin production
  - Wound management: Wound debridement to eradicate spores and necrotic tissue
  - Antimicrobial therapy: Duration: 7 to 10 days
    - ➔ First Choice: *Metronidazole* (500 mg IV every 6 to 8 hours)
    - ➔ Second choice: *Penicillin G* (2 to 4 million units IV every 4 to 6 hours)

- Neutralization of the unbound toxin
  - Human tetanus immune globulin (HTIG): 3000 to 6000 units intramuscularly

- Active immunization
- Control of muscle spasms
  - *Diazepam* Adult: 10 to 30 mg IV, up to 30 mg every 4 hours. Newborns 0.1 – 0.5 mg/kg by slow IV injection (over 3 to 5 minutes) or 0.5 mg/kg by rectal route (max 10mg/dose, to be repeated every 1 to 4 hours)
  - Ventilatory assistance is imperative at higher doses of diazepam
  - Alternative: *Magnesium sulphate* 50 mg/kg/day slow IV or infusion or *Baclofen*, intrathecal, either in a bolus of 1000 mcg or by continuous intrathecal infusion

- Supportive care
  - DVT prevention
  - Tracheotomy if prolonged ventilation
  - Stress ulcers prevention by PPI
  - Prevention of bedsores
  - Physiotherapy when appropriate

5.9. Fever of Unknown Origin

Definition: Temperature greater than 38.3°C on several occasions, more than 3 weeks' duration of illness, and failure to reach a diagnosis despite 1 week of inpatient investigations.

Causes

- Infections
  - Bacterial
    - → Typhoid
    - → Rickettsial diseases
    - → Occult Abscesses (CNS, lung, bone)
    - → Endocarditis
  - Protozoan
    - → Amoebic Liver Abscess
    - → Malaria
  - Mycobacterial
    - → TB
    - → Atypical mycobacteria
  - Viral
    - → HIV
    - → CMV. EBV
  - Fungal
    - → PCP
    - → Fungal meningitis, pneumonia
- Malignancy
  - Leukaemia
  - Lymphoma
  - Liver malignancy (primary or secondary)
  - Renal Cell Carcinoma
- Drug Fever: Many drugs implicated
- Autoimmune conditions
  - SLE
  - RA
  - Other vasculitis

- Thyrotoxicosis
  The longer lasting the fever, the more likely it is due to non-infectious causes

Signs and Symptoms

- Fever of more than 101 °F (38.3 °C), either continuous or intermittent, for at least 3 weeks with no known cause, even after extensive diagnostic testing.
- Weight loss
- Night sweats
- Headaches
- Rashes
- Other signs depending on the cause
  - Lymphadenopathy
  - Meningeal signs
  - Focal neurologic signs
  - Organomegaly
  - Cardiac murmurs
  - Arthritis

Investigations

- FBC
- Liver function tests, renal function, ESR, CRP, Thyroid Function Tests
- Repeated Blood cultures
- Lumbar Puncture
- Serology for suspected diagnoses – Rheumatoid Factor, Widal, HIV, etc
- Urinalysis and culture
- CXR
- Abdominal ultrasonography
- CT-scan chest/abdomen/brain
- Bone Marrow Aspiration
- Endoscopic examination – bronchoscopy, gastroscopy, colonoscopy
- Echocardiography
- Biopsy examination of suspected tissues

Management

- Depending on underlying cause
  - *Paracetamol* 1g po QID
  - When drug fever is suspected, discontinue any possibly implicated drug

- For suspected bacterial sepsis cases
  - Direct treatment at any proven infection
  - Empirical therapy can be considered for:
    - ➔ Rickettsial disease (*Doxycycline* 100mg bd for 2 weeks)
    - ➔ Typhoid (*Ciprofloxacin* 200mg IV bd for 10 days)
    - ➔ TB (see protocols)

- For suspected inflammatory conditions
  - *Aspirin* and other NSAIDs.

Note: *Avoided for children and teenagers*

  - Corticosteroids for from one week to several years

Recommendation

- Refer any patient who is deteriorating or who needs testing not available at that care level.

6. Musculoskeletal and Connective Tissues Conditions

6.1. Osteoarthritis

Synonyms: Degenerative Joint Disease; Osteoarthrosis

Definition: Osteoarthritis (OA) is a chronic arthropathy caused by a degenerative process that involves deterioration of the articular cartilage, with an early alteration in its biomechanical properties followed by a progressive loss of thickness

Causes

- Primary OA
  - Idiopathic (most common and likely genetic)
    - → Usually appears in middle-aged or elderly people and gets worse over time
    - → If Primary OA involves multiple joints, it is classified as Primary Generalized OA

- Secondary OA
  - It results from conditions that change the microenvironment of the cartilage. These conditions include
    - → Post-traumatic or mechanical
    - → Post-inflammatory (e.g. Rheumatoid Arthritis, gout) or infections
    - → Heritable skeletal disorders (e.g. scoliosis)
    - → Metabolic disorders (e.g. hemochromatosis, acromegaly)
    - → Neuropathic: atypical joint trauma due to loss of proprioceptive senses (e.g diabetes, syphilis)
    - → Other: e.g. congenital malformation

Risk factors

- Genetic factors
- Constitutional factors (for example, ageing, female sex, obesity, high bone density)
- Biomechanical risk factors (for example, joint injury, occupational/recreational usage, reduced muscle strength, joint laxity, joint misalignment)

Signs and Symptoms

- Over age 40
- Onset is most often gradual, usually beginning with one or a few joints
- Signs and symptoms localized to affected joints (OA is not a systemic disease)
- Insidious pain that typically worsens with weight bearing and activity and improves with rest but can eventually become constant
- Short duration of morning stiffness < 30 minutes or after immobility
- Tenderness on palpation and pain on passive motion are relatively late signs
- Muscle spasm and contracture add to the pain
- Deformity, subluxations and limited motion may occur late
- Periarticular muscle atrophy
- Minimal/no signs of inflammation
- Presence of crepitus on moving and palpating the joint and/or limitation of joint motion or locked joint
- Primary or idiopathic osteoarthritis usually affects two types of joint:
    - Weight-bearing joints: the spine, hips, knees and first metatarsophalangeal joints
    - The hands: first carpometacarpal joint and/or proximal and distal interphalangeal joints ("nodal" osteoarthritis)

Investigations

- Lab results are normal in OA (especially ESR and CRP) but may be required to rule out other disorders (eg, RA) or to diagnose an underlying disorder causing secondary OA
- If OA causes joint effusions, synovial fluid analysis can help differentiate it from inflammatory arthritides; in OA, synovial fluid is usually clear, viscous, and has ≤ 2000 WBC/μL.
- X ray of joint affected show 4 classic findings:
    - Asymmetric Narrowing of the joint space
    - Bony erosions and cysts
    - Subchondral sclerosis (seagull sign)
    - Osteophytes

Management

General principles

- Relieving symptoms
- Maintaining and/or improving function.
- Limiting physical ability
- Avoiding drug toxicity

Non- pharmaceutical

- Educating the patient
  - ➔ Basic understanding of the disease and its treatment
  - ➔ Normal range body weight (Weight reduction)
  - ➔ Walking aids
  - ➔ Appropriate footwear
  - ➔ Appropriate regular physical exercise
- Physical therapy Range-of-motion exercises (Physiotherapy)
  - ➔ Muscle-strengthening exercises
  - ➔ Assistive devices for ambulation
  - ➔ Patellar taping
  - ➔ Appropriate footwear
  - ➔ Lateral-wedged insoles (for genu varum) Bracing
- Occupational therapy
  - ➔ Joint protection and energy conservation
  - ➔ Assistive devices for activities of daily living

Pharmaceutical

- Presently no treatment alters the natural history of OA
- Analgesic agents (e. g. *Paracetamol* in doses of up to 4g/ day),
- NSAIDS (e.g. *Diclofenac, Ibuprofen*), cyclooxygense-2 (COX-2) for secondary inflammation
- Intraarticular corticosteroids occasionally useful for inflammatory component (maximum 3 injections per year) e.g. Methyl prednisolone ; *Hyaluronan* (hyaluronic acid in intraarticular with a series of 3 to 5 weekly injections)
- Use of concomitant gastroprotective therapy with *Misoprostol* or a proton pump inhibitor in patients at increased risk for an upper GI adverse event

Recommendation

- Refer
    - Patients with severe symptomatic OA who have pain or functional limitation that has failed to respond to medical therapy should be referred to an orthopedic surgeon for evaluation and orthopedic surgery (Debridement of the joint /Arthroscopic cleaning/Osteotomy/Partial or total prosthesis)

6.2. Septic Arthritis

Definition: Septic arthritis is defined as an acute monoarticular infection caused by bacteria

Causes/Risk factors

- Advanced age
- Alcoholism
- Arthrocentesis / Previous intra-articular corticosteroid injection or joint surgery
- Diabetes
- Immunosuppressive therapy, including corticosteroids, Hemodialysis
- IV drug abuse
- Rheumatoid arthritis or osteoarthritis, Systemic Lupus Erythematosus (SLE), Sickle cell disease
- Skin infections
- Risk factors for sexually transmitted infections (STIs)

Signs and Symptoms

- The classic clinical presentation is acute onset of painful, warm, and swollen joint, usually monoarticular and affecting large weight-bearing joints (knee, shoulder or hip)

Complications

- Acute nongonococcal bacterial arthritis can destroy articular cartilage, permanently damaging the joint within hours or days
- Osteomyelitis
- Sepsis

Investigations

- Arthrocentesis with synovial fluid examination is the cornerstone of diagnosis (cell count and differential, Gram stain, aerobic and anaerobic culture, and crystals.)
- Blood culture before starting antibiotic treatment.
- FBC and ESR (or C-reactive protein)

Note:

Plain xrays of the involved joint are not diagnostic of acute infection but can exclude other conditions under consideration (eg, fractures)

Management

- Admit the patient to hospital for prompt assessment
- Drainage of pus from infected joints
- NSAIDs can help decrease pain and inflammation.
- IV antibiotics: Initial antibiotic selection is directed at the most likely pathogens. The regimen is adjusted based on the results of culture and susceptibility testing
- Suitable choice for empirical therapy include β-lactamase-stable penicillins, such as cloxacillin 2g IV tid), or the *Cephalosporins* if Gram Negatives are isolated from the aspirated pus (e.g, *Ceftriaxone 2* g IV q 8 h)
- Antibiotic treatment is usually given for up to 6 weeks, with the first 2 weeks administered intravenously followed by a switch to oral treatment if an oral option exists and clinical signs, symptoms, and inflammatory markers are settling
- For N gonorrhoeae a 1-week course of a third-generation cephalosporin is indicated

6.3. Gout

Definition: Gout is a clinical syndrome characterized by joint inflammation due to deposition of monosodium urate crystals in a (usually male) patient with high levels of uric acid in the blood.

Causes/Risk factors

- Primary Gout (overproduction of uric acid): Most patients with idiopathic gout have a genetically reduced renal excretion of urate which can lead to high serum uric acid level
- Secondary Gout (underexcretion of uric acid):
  - Factors that increase serum urate concentration include
    - Diet: meat, fish, alcoholism
    - Obesity/ weight gain
    - Diseases
      - Haematological diseases
      - Chronic renal disease, Hypertension
      - Hypothyroidism or Hyperthyroidism
      - Hyperlipidaemia
    - Drugs such as thiazide diuretics, low-dose aspirin, cytotoxics, pyrazinamide, ethambutol

Signs and Symptoms

- Asymptomatic hyperuricemia
  - Many patients with hyperuricemia do not develop gout, while some patients with repeated gout attacks have normal or low uric acid levels

- Acute gouty arthritis
  - Acute gout is characterized by rapid onset of excruciating pain, swelling associated with redness of the affected joint (most commonly great toe, foot, ankle, knee, wrist, finger, and elbow)
  - Several factors have been recognized as precipitants of acute attacks of gout. These include:
    - Acute illness
    - Trauma
    - Surgery
    - Alcohol (especially beer and wines)
    - Diuretics, Allopurinol

- Intercritical gout
    - After an initial acute attack patients may be free of symptoms for months or years; but some go on to have more frequent attacks and a few eventually develop chronic tophaceaous gout or permanent joint damage, or both, depending on degree of hyperuricaemia

- Chronic tophaceous gout
    - Patients who develop chronic gout usually are those whose hyperuricemia is not controlled
    - Crystal deposits (tophi) may develop around hands, feet, elbows, and ears as well as acutely affected joints

Criteria for the clinical diagnosis of gout (American College of Rheumatology)

- Six or more of these criteria are needed to make a diagnosis
    - More than one attack of acute arthritis
    - Maximum inflammation developed within one day
    - Attack of monoarthritis
    - Redness over joints
    - Painful or swollen first metatarsophalangeal joint
    - Unilateral attack on first metatarsophalangeal joint
    - Unilateral attack on tarsal joint
    - Tophus (proved or suspected)
    - Hyperuricaemia
    - Asymmetric swelling within a joint on radiograph
    - Subcortical cysts without erosions on radiograph
    - Joint fluid culture negative for organisms during attack

Complications

- Recurrent gout
- Tophi in advanced gout
- Kidney stones
- Joint damage
- Psychological effects

Investigations

- Serum urate concentration: Hyperuricemia is defined as a serum or plasma urate concentration greater than 7.0mg/dl (0.42mmol/l) in males or 6.0mg/dl (0.36 mmol/l) in females but may not be evident in acute gout
- FBC (To exclude myeloproliferative disorders; raised white cell count may indicate septic arthritis), ESR

- Renal function tests: urea and creatinine
- Liver function tests
- Fasting lipids, glucose and thyroid function (Hyperlipidaemia, diabetes, hypothyroidism, and possibly hyperthyroidism are associated with gout)
- Urinary urate excretion
- Arthrocentesis and analysis of synovial fluid (SF) or tophus aspirate and identification of monosodium urate (MSU) crystals. The gold standard for making a diagnosis of gouty arthropathy is visualization of negatively birefringent, needle-shaped crystals
- Xrays: may see subcortical cysts without erosions

Management

- Therapeutic objectives
  - To relieve pain immediately
  - To reduce joint inflammation
  - To prevent recurrent attacks and joint damage

Non–Pharmaceutical

- Patient information on gout
- Rest affected joint
- Encourage copious fluid intake
- Identify and manage underlying or predisposing factors
- Weight reduction in obese or over weight individuals
- Dietary modification (refer to dietician)
- Local treatments: application of ice to the affected area

Pharmaceutical

- Management of acute gout
  - → NSAIDs e.g. *Diclofenac* IM 75 mg stat then 50 mg p o every 8 hours or *Ibuprofen* 400 -800 mg /8 hrs for 1-2 weeks. Take into consideration side effects especially renal and gastrointestinal
  - → *Colchicine* 0.5 mg-1 mg hourly till patient improves or GI side effects appear (especially diarrhea), or maximum of 6 mg has been taken
  - → If NSAIDs not tolerated, Corticosteroids IM: e.g *Methylprednisolone* 40mg **Or** *Prednisone* tabs 40-50mg qd
  - → *Allopurinol* should not be commenced during an acute attack but in patients already established on allopurinol, it should be continued and the acute attack should be treated conventionally

- If diuretic drugs are being used to treat hypertension, an alternative antihypertensive agent should be considered, but in patients with heart failure, diuretic therapy should not be discontinued

- Prevention of Recurrent Gout
  - No drug treatment needed for asymptomatic hyperuricemia
  - Advise patient to reduce weight
  - Avoid or decrease alcohol consumption
  - Avoid heavy consumption of foods containing high concentration of purines,e.g. roasted meat, etc
  - *Allopurinol*, oral, 100–300 mg once daily. Start at a low dose (100 mg/day) and increasing by 100 mg every 2 -4 weeks; Reduce dose in renal or hepatic impairment. Do not give Allopurinol in the acute phase. Start only when pain is under control i.e. after approximately 2 weeks

- Management of Chronic tophaceous gout
  - Initiate colchicine prophylaxis 1 mg/day, then treat with allopurinol 300 mg per day
  - Watch out for renal impairment, uric acid nephrolithiasis
  - Treat other comorbidities

Recommendations

- Refer patients to a dietician for dietary modification and weight reducing diet in the obese and overweight
- Refer patient to surgery in case of severe joint damage/ deformations

6.4. Rheumatoid Arthritis

Definition: Rheumatoid arthritis (RA) is an autoimmune disorder of unknown etiology characterized by chronic, additive, symmetrical progressive polyarthritis and multisystem extra - articular manifestations.

Causes /Risk factors

- Smoking
- Genetic susceptibility: Human Leucocyte Antigen (HLA) - DR4
- Environmental factors : diet (Low fruit and vitamin C intake, A high intake of red meat),
- Women
- The presence of Rheumatoid Factor (RF) is not absolutely specific for the disease but is generally highly predictive

Signs and Symptoms

- Articular signs (joints)
    - Symmetrical peripheral polyarthritis mostly of small joints (warm, painful, stiff, swollen)
    - All the joints in the skeleton can be affected with the exception of thoracic and lumbar spine
    - In its initial stages, it has a strong preference for MCPs, PIPs and metatarsophalangeal joints
    - Proximal joints, like elbows, shoulders, knees and hips are usually affected later
    - Stiffness worse in the morning
    - Deformities

- Extra-articular manifestations normally appear in more advanced stages
    - Fever, weight loss, anemia
    - Subcutaneous nodules
    - Splenomegaly, lymphadenopathies, keratoconjuctivitis, pericartitis, pleuritis

Clinical Manifestations

- Subjective
    - Degree of joint pain
    - Duration of morning stiffness
    - Duration of fatigue
    - Limitation of function

- Physical examination
  - Actively inflamed joints (tender and swollen joint counts)
  - Mechanical joint problems: loss of motion, crepitus, instability, misalignment, and/or deformity
  - Extraarticular manifestations

- ACR criteria for classification of RA: Require 4 or more for classification
  - Morning stiffness greater than 1 hr greater than 6 weeks duration
  - Swelling in 3 or more joints for greater than 6 weeks duration
  - Swelling MCP or PIP greater than 6 weeks duration in wrist
  - Symmetrical joint swelling
  - Rheumatoid nodules
  - Serum rheumatoid factor
  - Hand X-ray changes: Erosions or decalcification

Complications

- Sicca syndrome (secondary Sjögren's syndrome): Dryness of the mucosae due to inflammatory infiltration of the exocrine glands
- Rheumatoid nodules preferentially located on the extension surface of the elbows and
- Serositis (pleural and pericardial effusion)
- Pulmonary fibrosis which can lead to respiratory impairements.
- Felty's syndrome: Association of rheumatoid arthritis with splenomegaly and leucopenia
- Secondary amyloidosis
- Rheumatoid vasculitis: Affect small vessels of lower extremities
- Septic arthritis

Investigations

- FBC (moderate nypochromic, microcytic anemia or leucopenia in case of Felty's syndrome)
- Raised acute phase reactants, e.g. ESR, CRP
- Positive rheumatoid factor (false positive rate of approximately 4%, especially at the low titres). Approximately 20% of patients with rheumatoid arthritis have a negative rheumatoid factor and RF is positive in about 5% of normal population
- Antinuclear antibodies (ANA) test: Significant positive result is a titre of 1:160

- X-rays of joints: erosions are often seen first at the MTP joints. Finding of erosions in x-rays of the hands and feet is significant, presence of uniform loss of joint space
- Magnetic resonance imaging (MRI) to detect joint erosions
- Evaluation of serum electrolytes, renal function and liver function should be undertaken
- Other investigations to rule out complications or associated conditions

Management

- Goals of Therapy
    - Control disease activity
    - Alleviate pain
    - Maintain function for essential daily activities
    - Maximize quality of life
    - Slow progression/rate of joint damage
    - Educating patients and their families

Non-Pharmaceutical

- Patient education on disease and its therapy
- Physiotherapy
- Occupational therapy

Pharmacetical

- Symptomatic medication
    - ➔ Simple Analgesics can be taken regularly for long-term pain but are usually insufficient eg *Paracetamol* or *Codeine* analogues. For pain at night *Amitriptyline* in low doses may be helpful
    - ➔ NSAIDs e.g. *Ibuprofen* tabs 400 mg 8 hourly until pain is relieved, *Diclofenac* 50 mg 3 times a day
        - Precautions: The drugs should always be taken with food
        - Potential side effects: GI haemorrhage, renal, acute renal failure
        - For patients at risk of GI upset, associate *Misoprostol* or a PPI (e.g *Omeprazole* 20 mg/day)
    - ➔ Corticosteroids e.g. Daily dose of *Prednisolone* up to 10 mg/day

- *Disease Modifying Anti-Rheumatic Drugs (DMARDs)*
    - ➔ These agents are also called SAARDS (Slow Acting Anti-Rheumatic Drugs)

- DMARDs should be prescribed as soon as a definite diagnosis of rheumatoid arthritis is established
- The first-line choices of a single agent in RA consist of :
  - *Methotrexate* is currently the gold standard DMARD, with doses accelerated to achieve 20 mg/week within 6–8 weeks of commencement (start by 7.5 mg/week po), with folic acid supplementation of 5 mg/week

    Or
  - *Sulfasalazine* in doses of 500 mg twice daily increased to 1 g twice daily in 2 weeks up to a maximum of 3 g
  - *Hydroxychloroquine* 200-400 mg once daily (add to methotrexate)

- Admit the patient for
  - Management of acute exacerbation
  - Bed rest may need to splint the affected joints
  - Intensive physiotherapy
  - Systemic complications

Recommendation

- Refer for orthopaedic review all cases with
  - Severe deformities with limitation of function, ankylosis
  - Compression of nerves

6.5. Lupus Erythematosus (LE)

Definition: Lupus erythematosus (LE) is an acute and chronic auto immune disorders causing inflammation of various connective tissues of the body

Classification

- Cutaneous LE
  - Acute Cutaneous Lupus Erythematosus (ACLE),
  - Subacute Cutaneous Lupus Erythematosus (SCLE)
  - Chronic Cutaneous Lupus Erythematosus (CCLE)

- Systemic LE (SLE)

Signs and Symptoms

- Cutaneous LE

Types of Skin Disease	Signs and Symptoms
Acute cutaneous lupus erythematosus (ACLE)	- Typical malar eruption in a butterfly pattern and/or a more generalized photosensitive dermatitis. - Strong association with systemic diseases
Subacute cutaneous lupus erythematosus(SCLE)	- Non scarring lesions that expend to form plaques with scaling (papulosquamous variant)or polycyclic lesions(annular variant) - Fatigue - Joint pain
Chronic cutaneous lupus erythematosus (CCLE), also called discoid lupus	- Papules or plaques , adherent thickness of lesions, follicular plugging - Resolution of active lesions results in atrophy and scarring - Photosensitivity - Usually do not itch

- Systemic LE(SLE)
  - Multisystemic disease associated with immunologic abnormalities
  - Cutaneous manifestations are frequent & account 4/11 criterions of the American College of Reumatology (ACR) for classification of SLE.

The 1982 revised criteria for the classification of systemic lupus Erythematosus

Criterion	Definition
1. Malar-rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesion
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by physician
5. Arthritis	Nonerosive arthritis involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion
6. Serositis	a) Pleuritis: convincing history of pleuritic pain or rubbing heard by a physician or evidence of pleural effusion. b) Pericarditis: documented by ECG or rub or evidence of pericardial effusion
7. Renal disorder	a) Persistent proteinuria ≥ 0.5 g/ per day. b) Cellular casts may be red cell, hemoglobin, granular, tubular, or mixed
8. Neurologic disorder	a) Seizures in the absence of offending drugs or known metabolic derangements. b) Psychosis: in the absence of offending drugs or known metabolic derangements.
9. Hematologic disorder	a) Hemolytic anemia: with reticulocytosis, or b) Leukopenia: ≤4,000/mm3 on 2 or more occasions, or c) Lymphopenia: less than 1,500/mm3 on 2 or more occasions; or d) Thrombocytopenia less than 100,000/mm3 in the absence of offending drugs.
10. Immunologic disorder	a) Positive LE cell preparation, OR b) Anti-DNA: antibody to native DNA in abnormal titer ,OR c) Anti-Sm: presence of antibody to Sm nuclear antigen ,OR d) False positive serologic test for syphilis known to be positive for at least 6 months.
11. Antinuclear antibody	An abnormal titer ofantinuclear antibody.
For the purpose of identifying patients in clinical studies, a person shall be said to have SLE if any 4 or more of the 11 criteria are present, serially or simultaneously, during any interval of observation.	

Investigations

- Clinical diagnosis
- FBC for cytopenias
- Urea and Creatinine
- Urine test for blood, protein
- Antinuclear antibodies (if available)
- Biopsy of lesions for histopathology

Management

Non-pharmacological

- Sun-protective measures (sunscreens, protective clothing)
- Smoking cessation
- Avoid pregnancy during active disease

Pharmacological

- Local treatment: Control of cutaneous lesions by
  - → Topical steroids (with regard to type of lesions & site of involvment)
    - First choice
      - o *Clobetasol propionate* (*Dermovate)* OR *Betamethasone* dipropionate (Diprosone, Diprolene) OR *Betamethasone valerate (Betneval)* Cream/Ointment 2 applications/ day for 3-4 days. Then 1 application/day for 3 days then 1 application every 2 days/week for 2 weeks

    - Alternative
      - o *Methylprednisolone (Advantan*) Cream/ Ointment 1 application/day/3-4days then every 2 days/week for 1 week

        Or
      - o *Hydrocortisone* Cream/Ointment 2 applications/day for 3-4 days. Then 1 application/day for 3 days then 1 application every 2 days/week for 2 weeks

Systemic treatment

- Antimalarial agents
  - → *Hydroxychloroquine* (*Plaquenil)*200mg tabs: 200-400mg/day for 3 months then evaluate for improvement
  - → *Chloroquine* 100mg tabs, 200mg/day for 3 months then evaluate for improvement
- Other systemic treatment: Systemic steroids:
  - → *Prednisolone* 1-2 mg/kg /day until lesions resolve before tapering off
  - → *Dapsone* 100mg daily for 3 months then evaluation for improvement

Recommendation

- Refer all patients with complex disease or not responding to first line therapy for specialist assessment

7. Malignancies

7.1. Oesophageal Cancer

Definition: Cancer of the esophagus (either squamous cell carcinoma or adenocarcinoma) is an extremely lethal malignancy

Risk Factors

- Age over 50, low socio-economic status
- Excess alcohol consumption, smoking
- Other ingested carcinogens
    - Nitrates (converted to nitrites)
    - Smoked opiates

- Mucosal damage from physical agents
    - Hot tea
    - Radiation-induced strictures
    - Chronic achalasia
    - Chronic gastric reflux
    - Intestinal metaplasia of the epithelium (Barrett's esophagus)

Signs and Symptoms

- Dysphagia
    - Initially with solid foods and gradually progresses to include liquids
    - May be associated with pain on swallowing (odynophagia)

- Rapid Weight Loss
- Regurgitation or early postprandial vomiting, and aspiration pneumonia
- Left supraclavicular lymph nodes (Troisier's sign)
- Signs of metastases in liver, lungs, pleura, and bone

Investigations

- FBC
- Serum electrolytes (Calcium, Sodium, Potassium)
- Upper GIT endoscopy with biopsy
- Barium swallow
- Chest and Abdomen CT scan

Management

- The prognosis for patients with esophageal carcinoma is poor. Curative surgery is difficult and many patients present with advanced incurable tumours
- For the incurable, surgically unresectable patient with esophageal cancer
  - Symptomatic treatment, pain relief
  - Repeated endoscopic dilatation
  - Gastrostomy or jejunostomy for hydration and feeding,
  - Endoscopic placement of an expansive metal stent to bypass the tumor

Recommendation

- Referral
  - To Oncologist for preoperative chemotherapy and radiation therapy if contemplating curative surgery
  - For Palliative Radiotherapy if available

7.2. Gastric Adenocarcinoma

Risk factors

- H. pylori
- Smoking, Alcohol
- Diet rich in salted or pickled foods
- Autoimmune gastritis (pernicious anaemia)
- Adenomatous gastric polyps
- Previous partial gastrectomy (> 20 years)
- Lower Socioeconomic status

Signs and Symptoms

- Early gastric cancer is usually asymptomatic and discovered incidentally during endoscopy for investigation of dyspepsia
- For Advanced cancers
  - Weight loss, Anorexia and nausea
  - Haematemesis, melaena, anaemia from occult bleeding
  - Dysphagia (gastro-oesophageal junction tumor)
  - Palpable epigastric mass
  - Left supraclavicular lymph nodes (Troisier's sign)
  - Signs of liver, lung, peritoneal or bone marrow metastases

Investigations

- Upper gastrointestinal endoscopy with biopsies from the edge and base of a gastric ulcer
- Barium meal is a poor alternative approach
- Abdominal CT scan

Management

Surgical Therapy

- Complete Resection for early stage cancer.
- Palliative surgery for obstruction, perforation, or bleeding.
- No evidence to suggest adjuvant chemotherapy or radiotherapy

7.3. Hepato-Cellular Carcinoma

This is the most common primary liver tumour.

Risk factors

- Chronic hepatitis B and C infection
- Cirrhosis from any cause, but especially viral and alcoholic aetiologies

Clinical features

- Weight loss, anorexia and abdominal pain
- Jaundice
- Ascites
- Hepatomegaly or a right hypochondrial mass
- Many tumours detected through screening programmes are asymptomatic
- Worsening synthetic LFTs and variceal haemorrhage

Investigations

- Serum markers
  - Alpha-fetoprotein (AFP) is produced by 60% of hepatocellular carcinomas
    - ➔ AFP is not therefore a totally reliable screening tool for hepatocellular carcinoma

- Abdominal Ultrasound or Abdominal CT scan
- Liver biopsy: to confirm the diagnosis and exclude an alternate diagnosis eg. metastatic liver tumour

Management

- Prevention: Hepatitis B vaccination
- Hepatic resection: Treatment of choice for non-cirrhotic patients

Recommendation

- Refer small tumours for consideration of
  - Liver transplantation
  - Percutaneous ablation (Best for small tumours)
  - Chemoembolisation (Hepatocellular cancers are not radiosensitive and the response rate to chemotherapy with drugs such as adriamycin is only around 30%)

7.4. Lung Cancer

Definition: Uncontrolled growth of malignant lung tissue with possibility of metastasis.

Classification

- Small Cell Lung Carcinoma (SCLC)
- Non Small Cell Lung Carcinoma (NSCLC: Squamous, Adenocarcinoma, Large Cell, Bronchoalveolar carcinoma etc.)

Risk factors

- The most important is smoking
- Others are genetic predisposition and environmental (eg asbestos exposure)

Signs and Symptoms

- Local tumor growth
  - Weight loss, chest pain, cough, hemoptysis, dyspnoe
  - Recurrent pneumonia
  - Fever, focal skeletal pain, finger clubbing, wheezing, weakness

- Regional spread and metastasis
    - Dysphagia, pleural effusions, pericardial effusion, hoarse voice, superior veina cava syndrome, Horner's syndrome, lymphadenopathy

Complications

- This is a very lethal disease with a 15 % five year survival and complications are many, often depending on the location of metastases

Investigations

- CXR (especially compare to old CXR)
- Sputum cytology
- Flexible Bronchoscopy and histology
- Chest CT Scan
- Mediastinoscopy,Thoracoscopy/FNA and histology
- Tests to diagnose metastases (CT Scan Brain and Abdomen, Bone scan)

Management

- SCLC is treated with chemotherapy (Regimen depends on available drugs - not detailed here)
- NSCLC
    - Stage I and II: Surgery +/- chemotherapy and radiation according to subtype
    - Stage III: Chemotherapy and radiotherapy
    - Stage IV: Palliation with Chemotherapy and Radiotherapy

- The role of early detection and screening is still controversial

Recommendation

- Referring to an oncologist and/or thoracic surgeon is advised as the staging and decision making about the appropriate therapy is very specialized

7.5. Pancreatic Adenocarcinoma

Approximately 90% of pancreatic neoplasms are adenocarcinomas which arise from the pancreatic ducts. This tumour involves local structures and metastases to regional lymph nodes at an early stage.

Risk Factors

- Age >70 years
- Sex: Men are twice affected than women
- Smoking and chronic pancreatitis
- Genetic predisposition (hereditary pancreatitis, Multiple Endocrin Neoplasma (MEN), Hereditary Non-Polyposis Colon Cancer-HNPCC)

Clinical features

- The majority of patients have advanced disease at the time of presentation
  - Weight loss (cachectic.)
  - (Often painless) Obstructive jaundice with severe pruritus
  - Upper abdomen pain may be present later in the disease
  - Anorexia, steatorrhoea and metabolic effects of the tumour
  - Diabetes mellitus, recurrent venous thrombosis, acute pancreatitis
  - An abdominal mass due to the tumour
  - Courvoisier's sign

Investigations

- FBC
- Serum bilirubin , gamma GT, Alkaline Phosphatase
- Serum electrolytes (Calcium, Potassium, Sodium)
- Plasma glucose
- Abdominal ultrasound / CT scan
- ERCP: The main role of ERCP is to insert a stent into the common bile duct to relieve obstructive jaundice in inoperable patients

Management

- Surgical resection is the only method of effecting cure but is rarely possible
  - Adjuvant chemotherapy using 5-*fluorouracil*.
  - For the great majority of patients, therapy is based on palliation of pain and obstructive jaundice

- Pain relief (see protocol for pain management)
- Obstructive jaundice is relieved by choledochojejunostomy in fit patients; percutaneous or endoscopic stenting is used in the elderly or in patients who have very advanced disease
- Duodenal obstruction should be treated surgically
- *Pancreatic enzyme* supplements should be used to maintain weight and increase quality of life (Pancreatin Adults: 25,000 units 3times daily during meal)
- Attention to dietary intake and the use of specific nutritional supplements may improve well being

7.6. Colorectal Cancer

Colorectal adenocarcinoma is the most prevalent malignancy of the lower GI tract

Risk factors

- Both environmental and genetic factors are important in colorectal carcinogenesis:
- Genetic factors
  - Hereditary Non-Polyposis Colon Cancer (HNPCC)
  - Familial Adenomatous Polyposis (FAP)
  - Other family history
  - Suspect especially if cancer before age 40 or a strong family history

Dietary Risk Factors For Colorectal Cancer Development

Risk Factors	Comment
INCREASED RISK	
Red meat	High saturated fat and protein content Carcinogenic amines formed during cooking
Saturated animal fat	High faecal bile acid and fatty acid levels May affect colonic prostaglandin turnover
DECREASED RISK	
Dietary fibre	Effects vary with fibre type; shortened transit time, binding of bile acids and effects on bacterial flora proposed
Fruit and vegetables	Green vegetables contain anticarcinogens, e.g. glucosinolates and flavonoids. Little evidence for protection from vitamins A, C, E
Calcium	Binds and precipitates faecal bile acids
Folic acid	Reverses DNA hypomethylation

NON-DIETARY RISK FACTORS IN COLORECTAL CANCER

Medical conditions	Colorectal adenomas
	Long-standing extensive ulcerative colitis or Crohn's colitis
	Ureterosigmoidostomy
	Acromegaly
	Pelvic radiotherapy
Others	Obesity and sedentary lifestyle-may be related to dietary factors
	Smoking (relative risk 1.5-3.0)
	Alcohol (weak association)
	Regular aspirin use

Clinical manifestations

- Colicky abdominal pain
- Rectal bleeding
- Iron deficiency
- Signs of anaemia
- Large Bowel Obstruction
- Metastases : lymph nodes, liver, lung, peritoneum

Investigations

- Colonoscopy : investigation of choice for diagnosis or screening
  - Can screen starting at age 50
  - Earlier and /or more frequent screening for high risk patients

- Consider CT colonoscopy if colonoscopy cannot be performed.
- Stool occult blood test
- Colonoscopy+ Biopsy
- CT scans of chest and abdomen/pelvis
- Baseline CEA in patients with known CRC to follow response to therapy

Staging

- Follows TNM system but is complex and based on pathologic correlation with observed survival data

Management

- Treatment based on TNM and Modified Dukes Staging of Colorectal cancer

TNM	Dukes	Path criteria	Treatment
I	A	Into submucosa or muscaris	Surgery alone
IIA	B	Into serosa	Sugery, no established the role of adjuvant chemo for colon cancer
IIB	B	Peritoneum	
IIC	B	Direct invasion	
IIIA	C	<6+LNs	Surgery + chemotherapy 5-FU+ leucovorin+ Oxoliplatin (folfox) Add radiotherapy
IIIB-C	C	Varying degrees of +LNs and local invasion	
IV	C	Distant metastasis	- Chemotherapy - Consider resection if complications: perforation, Obstruction or bleeding,

7.7. Leukaemia

Definition: A group of diseases characterised by the proliferation of a single malignantly deranged line in the haemapoietic system. Leukemias are classified according to the cell type involved (broadly lymphoblastic and myeloblastic) and the speed of evolution of the disease (acute or chronic).
Acute leukaemia, if untreated, has a rapidly fatal course. Chronic leukaemia has a more prolonged course.

Classification

- Acute Myeloid Leukaemia
- Chronic Myeloid Leukaemia
- Acute Lymphoblastic Leukaemia
- Chronic Lymphoblastic Leukaemia

Symptoms

- Symptomatic anemia (Fatigue, Palpitations etc)
- Bleeding into skin, nose and mucous membranes
- Fatigue, malaise, weight loss
- Fever
- Bone Pain

The duration of symptoms depends on whether the leukaemia is acute (usually weeks-months of symptoms) or chronic (months-years)

Signs

- Pallor
- Hepatosplenomegaly
- Lymphadenopathy
- Focal neurological signs
- Skin or oral involvement
- Signs of coagulopathy: petechiae, purpura, optic fundal haemorrhages
- Signs of opportunistic infection

Investigations

- FBC may show a raised white cell count or cytopenias (anemia, thrombocytopenia)
- Blood film may reveal the presence of blasts
- Bone Marrow Aspiration is the definitive test to confirm the diagnosis

- Further testing on the bone marrow including immunohistochemistry and cytogenetics is required for exact diagnosis
- Tissue from other sites (CSF, lymph node biopsy etc) may also be diagnostic
- Ultrasound or Xrays of painful or enlarged bones/organs may show infiltration
- In the presence of fever, tests should be performed to exclude infection
- Clotting tests
- Urea and Creatinine, LFTs
- Height and weight (to enable calculation of Body Surface Area (BSA)
    - Mosteller Square Root method
        - ➔ BSA = Square root of [Weight in kg x Height in cm/3600]

Management

- Supportive care of cytopenias: Transfuse for anaemia (Hb<8), platelets for severe thrombocytopenia (Plt<10 or <30 with bleeding
- Treat any intercurrent infection
- For acute leukaemias, urgent referral and transfer to a tertiary centre for assessment and chemotherapy
- For chronic leukaemias, routine outpatient referral can be undertaken unless complications have developed
- Oncological management mostly revolves around combination systemic and intrathecal chemotherapy for acute leukaemias, and less intensive (often oral single agent) chemotherapy for chronic leukaemias

7.8. Lymphoma

Definition: Lymphomas are malignant tumours of the lymphoreticular system and are classified into Hodgkin's disease and Non-Hodgkin's lymphoma (NHL)

7.8.1. Hodgkin's Disease

Symptoms

- Painless lymphadenopathy (often cervical – especially with Hodgkin's)
- "B symptoms" – fever(>38°C), weight loss (>10%), drenching night sweats
- Fatigue, pruritis
- Cough, dyspnoea (if mediastinal mass)

Signs

- Careful examination of all lymph node groups, oro and naso-pharynx, abdomen and skin for involvement with lymphoma

Investigations

- Lymph node biopsy of an affected node is the key investigation
- FBC looking for cytopenias
- ESR, LDH (often raised)
- Urea and Creatinine (renal involvement), LFTs
- Calcium (hypercalcemia)
- HIV and hepatitis B serology
- CXR
- Chest and abdominal CT scanning

Staging (Ann Arbor with Cottswold)

- Stage I: Involvement of a single lymph node region or of a single extralymphatic organ or site
- Stage II: Involvement of two or more lymph node regions on the same side of the diaphragm alone or with involvement of limited, contiguous extralymphatic organ or tissue
- Stage III: Involvement of lymph node regions or lymphoid structures on both sides of the diaphragm
- Stage IV: Diffuse or disseminated foci of involvement of one or more extralymphatic organs or tissues, with or without associated lymphatic involvement

All stages are designated either A (no B symptoms) or B (with B symptoms)

Management

- Early stage disease (Stage I-II): Ideally combination chemotherapy and radiotherapy, alternatively combination chemotherapy alone where radiotherapy is not available
- Advanced stage disease (Stage III-IV): Combination chemotherapy with or without radiotherapy
- Chemotherapy regimens are complex but include ABVD and BEACOPP
- All patients should be seen and treatment planned in a tertiary centre

7.8.2. Non-Hodgkin's Lymphoma

Signs and Symptoms

- Depend on how aggressive the tumour is: This is highly variable
- Aggressive tumours
    - Rapidly growing mass
    - "B symptoms" – fever(>38°C), weight loss (>10%), drenching night sweats
    - Fatigue, pruritis
    - Mediastinal mass: Cough, dyspnoea
    - Rash
    - Ascites, Pleural Effusions
    - GI symptoms: Anorexia, nausea and vomiting, pain, bowel obstruction
    - CNS symptoms: Headache, focal signs, seizures, cord compression

- Indolent NHL
    - Slowly growing lymphadenopathy
    - Hepatosplenomegaly
    - Cytopenias

- Careful examination of all lymph node groups, skin, chest, abdomen for organomegaly or masses, testes and neurological system is vital for NHL

Complications – Oncological Emergencies

- Spinal cord compression
- Pericardial tamponade
- Hypercalcemia
- Superior or inferior vena cava obstruction
- Hyperleukocytosis
- Acute airway obstruction
- Lymphomatous meningitis and/or CNS mass lesions
- Hyperuricemia and tumor lysis syndrome
- Hyperviscosity syndrome
- Intestinal obstruction, intussusceptions
- Ureteral obstruction, unilateral or bilateral hydronephrosis
- Severe hepatic dysfunction
- Venous thromboembolic disease
- Severe autoimmune hemolytic anemia and/or thrombocytopenia
- Seek urgent assistance in a tertiary centre for these complications after stabilising the patient

Investigations

- Lymph node biopsy of an affected node is the key investigation
- ESR, LDH, Beta-2 Microglobulin (often rasied)
- FBC looking for cytopenias
- Urea and Creatinine (renal involvement), LFTs
- Calcium (hypercalcemia)
- Pleural, ascitic or CSF aspiration (lymphocytosis)
- HIV serology (NHL is an AIDS defining illness)
- CXR
- Brain, chest and abdominal CT scanning
- Bone Marrow Aspiration
- Hepatitis B and C serology

Staging

- Is basically the same as for Hodgkin's Disease, using the Ann Arbor classification

Management

- Principles include
    - Distinguish high grade from low grade NHL as management differs
    - Give HAART for HIV positive cases as it improves prognosis

- Chemotherapy with or without radiotherapy for early stage aggressive disease
- Combination chemotherapy for advanced stage aggressive disease
- Radiotherapy for early stage indolent disease
- Various different modalities are used for palliating advanced stage indolent disease

8. Hematological Conditions

8.1. Anaemia

Definition: This is a reduction in the haemoglobin concentration in an individual to below the normal range for that individual's age and sex: i.e below 12 g/dl in male adults, 11 g/dl in Female Adults (non pregnant).
Anaemia is not a diagnosis in itself as there is always an underlying cause, which must be determined.

Causes

- Poor production of normal red blood cells
    - Nutritional deficiency anaemias such as iron, folic acid and vitamin B12 deficiency anaemia, malnutrition, malabsorption
    - Bone marrow failure: Aplastic anaemia, malignant infiltration of bone marrow, leukaemia
    - Viral infections (HIV)
    - Reduced erythropoietin production: Chronic renal failure
    - Chronic illness (e.g. cancer, HIV, TB, leukaemia or other blood cancers)
    - Lead poising

- Increased destruction of the red blood cells (haemolysis)
    - Infections: Viral, bacterial, parasitic (e.g. malaria)
    - Medicines: ARVs (e.g zidovudine), chemotherapy, sulphonamides, methydopa, dapsone, lead poisoning
    - Autoimmune disorders: Antibody-mediated haemolytic disease
    - Inherited red cell or haemoglobin disorders: Sickle cell anaemia, thalassaemia, G-6-PD deficiency, spherocytosis
    - Haemolytic disease of the newborn
    - Other disorders: Disseminated intravascular coagulation, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, hypersplenism

- Increased loss of red blood cells
    - Acute blood loss: Traumatic, surgical, or obstetric haemorrhage

- Chronic blood loss: usually from gastrointestinal, urinary, or reproductive tracts (e.g. parasitic infestations such as hookworm and schistosomiasis, bleeding peptic ulcers, inflammatory disorders, malignancy, and heavy menstrual loss or menorrhagia)

Signs and Symptoms

- Tiredness, weakness
- Dizziness, faintness
- Headache
- Shortness of breath on exertion (exercise intolerance)
- Palpitations
- Visual disturbances
- Confusion, decreased mental acuity
- Pale mucous membranes, palms and nail beds
- Symptoms of decompensation:
  - Rapid heartbeat or palpitations
  - Dyspnoea
- Signs of heart failure in severe anaemia
  - Oedema (if severe case)
  - Low central venous pressure, low blood pressure, low urine output, shock
  - Poor peripheral perfusion
  - hepatosplenomegaly

Complications

- Pulmonary edema
- Congestive heart failure
- Acute renal failure
- Acute respiratory distress syndrome (ARDS)

Investigations

- Full Blood Count and reticulocyte count
- Blood smear for malaria parasites
- Stool examination for intestinal parasites
- Stool for occult blood
- Sickling test, if positive, haemoglobin electrophoresis
- Nutritional deficiencies: Iron studies, serum ferritin, serum vitamin B12, serum folate
- Bone marrow aspiration to assess the decreased production of red cells
- Other investigations will depend on the clinical evaluation of the patient

Management

General principles

- Obtain a detailed history from the patient or caregivers
- Remove or correct the underlying cause
- Always investigate cause of anaemia before initiating treatment
- In an emergency, take all blood samples then treat

Therapeutic objectives

- Treat underlying cause of anaemia and restore haemoglobin levels to normal
- In sickle cell disease patients restore haemoglobin to steady state level
- In iron deficiency replenish iron stores after correction of anaemia

Pharmacological Management

- Iron deficiency
  - → *Ferrous Sulphate* oral: Adults 200 mg 3 times daily after meals until the Hb has reached the normal range. Continue with 200mg daily for 6 months to build up iron stores
  - → Alternative treatment: *Ferrous fumarate*, oral 200 mg 3 times a day after meals until Hb has reached the normal range
  - → In sickle cell disease patients, it may not be necessary to give iron tablets, unless there is evidence of iron deficiency

- Megaloblastic anaemia
  - → *Folic acid,* oral: Adults: 5 mg-10 mg daily for 30 days or for as long as required
  - → *Vitamin B12* (Hydroxycobalamin) injection: Initially 1mg i.v. repeated 5 times at intervals of 2-3 days. Maintenance dose 1mg every 2-3 months. Lifelong may be required

- Severe anaemia
  - → Severe anaemia with signs of cardiac failure will need treatment of the heart failure in addition to blood transfusion with packed cells
  - → Transfuse the patient if Hb < 7 g/dl: 10 ml/kg body weight slowly over 3 hours

8.2. Bleeding disorders

Definition: A bleeding disorder is an acquired or inherited tendency to bleed excessively.

Etiology

- Blood vessels defect
  - Age (e.g easy bruising, senile purpura)
  - Acquired (e.g severe infections, a side effect of medicines such as steroids or NSAIDS)
  - Genetic (e.g. hereditary telangiectasis, connective tissue disorders)

- Platelet defects
  - Decreased platelet number (e.g. from blood cancers, aplastic anaemia, medicines, chemicals, viruses)
  - Increased destruction (e.g. autoimmune disease, heparin, hypersplenism, massive blood transfusion, DIC, TTP, uraemia)

- Coagulation defect
  - Hereditary (e.g. haemophilia A or B, von willebrand's disease)
  - Acquired (e.g anticoagulant treatment, liver disease, alcoholism, DIC)
  - Vitamine K deficiency in the newborns, Vit K defiency drug-induced (e.g. herbal preparations, prednisolone, NSAIDs)

- Infections such as haemorrhagic fevers

Signs and Symptoms

- Bruising of skin, petechiae, ecchymoses, purpura
- Bleeding from mucosal membranes
- Epistaxis (i.e. spontaneous nosebleeds)
- Haemarthrosis (i.e. bleeding into joints)
- Haematomas (i.e bleeding into muscles)
- Bleeding in GIT, melena
- Bleeding into the brain
- Prolonged bleeding after operations, injuries, or cuts

Complications

- Anaemia
- Haemorrhagic shock
- Chronic renal insufficiency

Investigations

- Full blood count, platelet count and peripheral film comment, Blood smear
- Coagulation tests
    - Prothrombin time (PT): Prolonged in factor VII, X, V, II, or I deficiencies, liver disease or warfarin treatment.
    - International normalized ratio (INR): Monitors anticoagulation therapy
    - Partial thromboplastin time (PTT): Prolonged in factor VIII, XII, XI, IX, X, V, and I deficiencies
    - Fibrinogen assay and FTP (longer in fibrinogen deficiencies, heparin, DIC)

- Test for haemorrhagic fevers

Management

Non-pharmacological

- Avoid trauma in haemophiliacs
- Find the root cause of the bleeding disorder and treat accordingly
- Avoid injections and unnecessary surgical procedures.

Pharmacological

- Transfuse with fresh whole blood if patient is severely anaemic or in shock.
- In older children and adults the following measures will help to arrest bleeding depending on cause:
    - ➔ Fresh frozen plasma or if not available fresh whole blood
    - ➔ In cases of liver disease, give phytomenadione (*Vitamin K*), IM, 3–5 mg in children, 10 mg in adults. IV preparation is preferred if available
    - ➔ Stop any drugs thought to be responsible for bleeding or which may aggravate bleeding
- For patients with haemophilia A and Willebrand's disease, use factor VIII concentrate (e.g. *Haemosolvate*)

Recommendation

- Refer patients requiring surgery for expert assessment

8.3. Polycythaemia

Definition: Polycythemia is a condition that results in an increased level of circulating red blood cells in the bloodstream. People with polycythemia have an increase in haematocrit (> 48% in women and >52% in men), haemoglobin (> 16.5g/dL in women or >18.5 g/dL in men), or red blood cell count

Causes

- Primary polycythaemia: Acquired or inherited genetic mutations causing abnormally high levels of red blood cell precursors.
- Secondary polycythaemia:
  - Chronic hypoxia conditions
    - COPD
    - Chronic heart disease (congestive heart failure)
    - Sleep apnea
    - Pulmonary hypertension
    - People living in high altitudes
  - Erythropoietin secreting tumors
    - Hepatocellular carcinoma
    - Renal cell carcinoma
    - Adenocarcinomas
    - Uterine (womb) tumors
  - Benign renal cysts and hydronephrosis

Signs and Symptoms

- General and non-specific symptoms: Weakness, Fatigue, Headache, Itch, Bruising, Joint pain, Dizziness, Abdominal pain
- Other signs and Symptoms related to the cause

Complications

- Thrombus or clot formation leading to stroke, heart attack, pulmonary embolism
- Renal dysfunction, kidneys stones, and gout
- Complications of secondary polycythaemia are related to those of the underlying disease

Investigations

- FBC
- CXR
- ECG
- Echocardiogram.
- Erythropoietin (EPO) blood levels

Management

- The treatment for polycythaemia depend on the cause
- Phlebotomy (drawing blood or blood letting):
  - The most essential part of the treatment
  - Goal: Haematocrit < 45 % in men and < 42 % in women

- *Hydroxyurea (Hydrea)*
  - Recommended for patients with primary polycythemia and higher risk of blood clot formation
  - Start 15-20 mg/kg/24h bid or tid followed by 10 mg/kg/24h

- *Aspirin* 75-100 mg/day may also be beneficial in patients with polycythemia by reducing clotting complications, unless the patient has a history of bleeding problems

8.4. Thrombocytopenia

Definition: Thrombocytopenia is defined as a low blood platelet count (Normal range 150,000 - 450,000/μL)

Causes

- Trapping of platelets in the spleen (Any cause hypersplenism)
- Reduced production of platelets by bone marrow e.g. leukemia, aplastic anaemia, viral infections, including HIV, drugs (thiazides, oestrogen, chemotherapy drugs), alcohol
- Increased breakdown of platelets. Examples include:
  - Idiopathic thrombocytopenic purpura (ITP)
  - Pregnancy (mild)
  - Autoimmune diseases eg. SLE, rheumatoid arthritis
  - Bacteraemia
  - Thrombotic thrombocytopenic purpura (TTP)
  - Hemolytic uremic syndrome
  - Medications, e.g., heparin, quinidine, quinine, sulfa-containing antibiotics, anticonvulsants and gold salts, cephalosporins

Signs and Symptoms

- Easy or excessive bruising
- Skin bleeding: Petechiae usually on the lower limbs
- Prolonged bleeding from cuts
- Spontaneous bleeding: Gum bleeding or epistaxis
- Haematuria, or blood in stools
- Unusually heavy menstrual flows
- Profuse bleeding during surgery or after dental work

Complications

- Internal bleeding if platelet count < 10,000 platelets /µl
- Brain haemorrhage if severe thrombocytopenia

Investigations

- FBC and blood film
- Antiplatelet antibodies
- Abdominal ultrasound
- Other tests to determine the cause of thrombocytopenia

Management

Treating thrombocytopenia may involve several options:

- Treating the underlying cause
- Blood transfusions of packed red blood cells or platelets
- Treatment for idiopathic thrombocytopenic purpura
- Corticosteroids
- If no improvement with corticosteroids, splenectomy

Recommendation

- Refer patients with severe thrombocytopenia or significant bleeding for specialist assessment

8.5. Neutropenia

Definition: Neutropenia is defined in terms of the absolute neutrophil count (ANC) < 1500/μL.

Causes

- Genetic (hereditary)
- Acquired neutropenia
  - Intrinsic bone marrow disease:
    - Aplastic anemia, Hematologic malignancy
    - Ionizing radiation
    - Infiltration, Granulomatous infection, Myelofibrosis
  - Drugs
    - Aminopyrine, Quinidine, Cephalosporins, Penicillins, Sulfonamides, Phenothiazines, Phenylbutazone, Hydralazine
  - Autoimmune diseases
    - Rheumatoid arthritis (with or without Felty syndrome), SLE
    - Crohn's, Chronic autoimmune hepatitis
    - Sjogren syndrome
    - Hodgkin Lymphoma, Thymoma
  - Infections
    - Bacterial sepsis
    - Viral infections (eg, influenza, measles, EBV, CMV, viral hepatitis, HIV)
    - Typhoid
    - Tuberculosis
    - Malaria
    - Toxoplasmosis, Brucellosis, Dengue fever, Rickettsial infection

Clinical features

- Patients with neutropenia often present with infection
  - Low-grade fever
  - Sore mouth, Odynophagia, Gingival pain and swelling, Recurrent sinusitis and otitis
  - Skin abscesses
  - Symptoms of pneumonia (e.g. cough, dyspnoea)
  - Perirectal pain and irritation

- Cervical lymphadenopathy
- Splenomegaly
- Associated petechial bleeding

Investigations

- FBC with Differential white blood cell (WBC) count
- Bone marrow aspiration and biopsy
- Peripheral smear
- Immuno serological test according to the cause:
  - Antinuclear antibody (ANA)
  - Rheumatoid factor (RF)
  - Serum immunoglobulin (Ig) studies
  - Liver function tests (LFTs)
  - Peripheral blood flow cytometry
  - HIV test
  - Blood cultures for anaerobic and aerobic organisms.
  - Urinalysis, urine culture and sensitivity
  - Culture of wound or catheter discharge
  - Sputum Gram stain and culture
  - Stool for Clostridium difficile
  - Skin biopsy

Management

Non-pharmacological

- Removal of any offending drugs or agents if drug exposure; if the identity of the causative agent is not known, stop administration of all drugs until the etiology is established.
- Use careful oral hygiene to prevent infections of the mucosa and teeth; control oral and gingival lesion pain with saline and hydrogen peroxide rinses and local anesthetic gels and gargles
- Avoid rectal temperature measurements and rectal examinations
- Use good skin care for wounds and abrasions

Pharmacological

- Broad-spectrum antibiotics should be started within 1 hour of cultures.
  - ➔ Third-generation *Cephalosporins* (e.g, ceftazidime, cefepime)
  - ➔ *Gentamicin* or another aminoglycoside should be added if the neutropenic patient's condition is unstable or the individual appears septic

- → *Vancomycin* should be added if methicillin-resistant *Staphylococcus aureus* or *Corynebacterium* species is suspected

- Patients with low-risk neutropenia can be treated on an outpatient basis with oral antibiotics
  - → Fluoroquinolones (eg, *Ciprofloxacin, Ofloxacin*), either alone or in combination with amoxicillin-clavulanate or clindamycin

Surgical Treatment

- Splenectomy in individuals with neutropenia and Felty syndrome who have recurrent life-threatening bacterial infections

Recommendation

- Refer to ICU if septic shock

8.6. Eosinophilia

Definition: Eosinophilia is defined as an increase in peripheral blood eosinophilic leukocytes to more than 600 cells/μL of blood.

Causes

- Connective tissue diseases
  - Churg-Strauss vasculitis
  - Rheumatoid arthritis
  - Eosinophilic fasciitis

- Helminthic (ie, worm) parasitic infections
  - Ascariasis
  - schistosomiasis
  - Trichinosis
  - Visceral larva migrans
  - Strongyloidiasis
  - Fascioliasis
  - Paragonimiasis

- Idiopathic hypereosinophilic syndrome (HES)
- Neoplasia
  - Lymphoma (eg, Hodgkin lymphoma, non-Hodgkin lymphoma)

  - Human T-cell lymphotropic virus I (HTLV-I)
  - Adult T-cell leukemia/lymphoma (ATLL)
  - Gastric or lung carcinoma (ie, paraneoplastic eosinophilia)

- Allergic/atopic diseases
  - Asthma
  - Allergic rhinitis

Investigations

- FBC with differential
- Blood chemistries can indicate specific organ involvement (i.e, liver, kidney)
- Spinal fluid examination to assess the cerebrospinal fluid (CSF) eosinophilia due to worm infections (eg, *Angiostrongylus cantonensis*), drug reactions (eg, Dilantin), and coccidioidomycosis fungal meningitis
- Patients with allergic symptoms should have a nasal smear for eosinophilia and Gram stain
- Stool samples should be evaluated for ova and parasites if indicated by history
- CT scans of the lungs, abdomen, pelvis, and brain evaluate for focal defects due to diverse causes of eosinophilia.
- A bone marrow biopsy may be helpful
- Urine examination for the eggs of *S hematobium*

Management

- Most cases of secondary eosinophilia are treated based on their underlying causes
- Allergic and connective tissue disorders may be amenable to corticosteroid treatment
- In patients with primary eosinophilia without organ involvement, no treatment may be necessary

9. Conditions in Pregnancy

9.1. Anemia in Pregnancy

Definition

Hemoglobin levels that fall <10 g/dl in pregnancy
- Mild anemia Hb: 8-10g/dl,
- Moderate Hb: 6-7g/dl,
- Severe anemia: <6g/dl

Causes

- Low intake of iron and folic acid
- Malignancies
- Sickle cell anemia
- Repeated blood loss associated with pregnancy
- Repeated pregnancies
- Infections
- Parasites (Malaria, hookworms)

Signs and Symptoms

- Tiredness, weakness
- Exercise intolerance
- Pale color of skin and mucosa
- Dizziness, faintness, headache
- Intermittent claudication

Complications

- Abortion
- Intrauterine growth retardation
- Intrauterine fetal death
- Premature labor
- Infections

Investigations

- Full blood count and blood cross-match
- Red cell morphology
- Red bloodcell electrophoresis
- Blood smear for malaria
- Stool and Urine analysis

Management

Determine the cause of anemia and treat accordingly

Non-pharmaceutical

- Iron rich diet (Fish, liver,eggs, vegitables etc etc)
- Prevent and early treatment of malaria
- Investigate and treat associated infections

Pharmaceutical management

- HB <7g/dl, *Ferrous sulfate* 300mg tabs PO, TDS for 2weeks.
- Transfuse in case of clinical signs of severe anemia
- HB >7 to 10 g/dl start iron and vitamin supplements to include *Ferrous Sulphate* BD for 2 weeks, folic acid 1 mg/day PO and *Vitamin B12* tabs PO BD and mineral supplementation PO BD for 2 weeks

Recommendations

- Explain to the patient the causes and risk factors of anemia
- Advice on nutrition and balanced diet
- Instruct patient to come back after 2 weeks for follow up
- Childbirth spacing

9.2. Diabetes in Pregnancy

Definition: A type of diabetes that occurs in non-diabetic women during pregnancy, it usually begins in the second half of pregnancy, and goes away after the baby is born.

Risk factors

- Previous pregnancy with diabetes and/or macrosomia.
- Obesity (BMI ≥30)
- A previous birth defect with amniotic fluid having gestational diabetes defect
- A family history of gestational diabetes (ie your mother, grandmother or sister had it)
- A polycystic ovarian syndrome (PCOS).
- Habitual abortion or fetal demise
- Age >40 years

Signs and Symptoms

- Excessive weight gain
- Excessive hunger or thirst
- Excessive urination or recurrent thirst
- Excessive urination or recurrent vaginal infections
- Tiredness

Complications

- Maternal
  - Hypertension
  - Pre-eclampsia
  - Premature labour
  - Hydramnios
  - Urinary tract infection

- New born
  - Congenital malformations
  - Hypoglycemia at birth
  - Hypothermia
  - Hypocalcemia

- Jaundice
- Respiratory distress syndrome
- Stillbirths

Investigations

- Ultrasound (16-22 Weeks) monthly
- Glycemia, FBC
- Glucose tolerance test, taken from week 24 through week 28 of pregnancy
- Fasting blood sugar
- Vaginal swab and urine analysis

Management

- Monitoring glucose levels and, if necessary, daily *Insulin injections*.
  - 0.5-1IU/kg/daily
  - 70% of long-acting Insulin
  - 30% of regular/Actrapid
  - 2/3 in the morning and 1/3 in the evening

- Eating a carefully planned diet and doing required exercise
- Maintaining a healthy pregnancy weight
- Admit if uncontrolled diabetes
- Induce labor between 38-39 weeks of gestation
- Never go beyond the term(40 weeks)
- If macrosomia: deliver by C/Section

Recommendations

- Transfer newborn to neonatology for follow up
- Mother is monitored for blood sugar levels
- If the mother was taking any medication for diabetes and if blood sugar is normal, she is advised to stop these after the baby is born
- The mother is given a blood sugar test at six-week check-up
- Oral antidiabetic drugs should not be given during pregnancy

10. Lower Respiratory Tract Conditions

10.1. Pneumonia-Adults

Definition: Inflammation of the lung parenchyma most often secondary to infections

Causes

- Infectious causes:
  - Bacterial: Streptococcus pneumoniae, haemophilus influenza, Klebsiella
  - Viral: Herpes
  - Fungal: Cryptococcus, aspergillus
  - Parasitic: Pneumostis jerovecci
- Non infectious causes: Aspiration, eosinophilic, etc

Signs and Symptoms

- Fever
- Productive cough of acute onset
- Pleuretic chest pain
- Malaise
- Chills and dyspnoea
- Tachypnoea
- Signs of consolidation on the diseased side or simply crackles
- Confusion or decreased level of consciousness
- Low blood pressure

Complications

- Empyema
- Septic metastasis (meningitis, otitis)
- ARDs

Investigations

- CXR
- FBC
- Urea and creatinine
- Sputum Microscopy, Culture and sensitivity
- Blood Culture

Management

The assessment of severity is important to decide about the right treatment. Following are the severity criteria and with 3 of them, transfer to a facility with ventilation should be considered.

- Clinical features
  - Confusion or decreased level of consciousness
  - Low blood pressure: Systolic BP<90 mm Hg or Diastolic BP <60mmHg OR acute renal failure or oliguria<80ml/4 hours
  - Need for vasopressors >4 hours
  - Respiratory rate >30 breaaths / min OR PaO2 / FiO2 < 250 mmHg
  - Multilobar consolidation OR expansion of Rx features >50% within 48 hours
  - Extrathoracic septic complications.

- Laboratory and radiology parameters
  - Hypoxemia (<60mmHg/)
  - White Blood Cell count (<4or >30x 10- 9 /1)
  - Abnormal renal function (including urea > 7 mmol/1)
  - Abnormal liver function (including albumin<30g/1)
  - Rapidly expanding infiltrates , multilobar consolidation, bronchopneumonia or cavitation

Pharmaceutical

- O2 and rehydration
- Analgesics and antipyretics
- Antibiotics
  - First choice: *Amoxycillin* 1g tds po X 7days
  - Second choice: *Amoxy-clavulinic* acid po or IV1g bid or *Cefuroxime* IV 750 mg bid X 7 days.
  - If staphylococcus suspected: *Cloxacillin* 500mg quid po or IV X 7 days
  - If atypical pneumonia suspected: *Erythromycin* 500 mg qid po for 7 days
  - If general condition is not good, consider IV drugs in first 2-3 days and then change to oral therapy
  - If viral, parasitic, fungal cause suspected treat accordingly

Note: *Allergy to penicillins, the choice should be erythromycin*

Recommendation

- Refer to ICU if needed for care (ventilation, inotropic support)

10.2. Asthma in Adults

Definition: It is a chronic inflammatory obstructive disease of the airway characterized by reversible airway flow (spontaneously or secondary to treatment).

Causes

- Asthma occurs as the result of a combination of genetic susceptibility and triggering factors (allergens, exercise, infections, psychological factors, occupational and environmental factors)

Signs and Symptoms

- Cough and chest tightness
- Expiratory Wheezing
- Intermittent pattern
- Night or cold temperature as the time of symptoms
- Reduced expiratory pick flow
- Limitation of activities

Complications

- Status asthmaticus
- Pulmonary hypertension
- Cor pulmonale

Investigations

- Spirometry to prove reversibility
- CXR

Management

- Goals of treatment
  - Achieve and maintain control of asthma symptoms
  - Maintain normal activity levels, including exercise
  - Maintain pulmonary function as close to normal as possible
  - Prevent asthma exacerbations
  - Avoid adverse effects from asthma medications
  - Prevent asthma mortality

Non-pharmaceutical

- Prevent exposure to known allergens and inhaled irritants
- Oxygen if hypoxic
- Ensure adequate hydration

Pharmaceutical

- ß2-stimulants
  - → *Salbutamol* or *Fenoterol*, MDI, 1–2 mg immediately via larger volume spacer
    (1–2 mg = 1 000–2 000 mcg = 10–20 puffs of 100 mcg)
    If patient responds, follow with 200 mcg 4–6 hourly
    OR
  - → *Salbutamol*, nebulised, 2.5–5 mg, administered undiluted and nebulise over 3 minutes or diluted with sodium chloride 0.9% to a total volume of 4–5 mL and nebulise over 20 minutes
    - Repeat 4–6 hourly
    - Continue with this inhalation until peak flow returns to 80% of predicted, or of personal best.
    - In very severe cases, and in patients not responding to standard dosages, these dosages may be given more frequently, i.e. every 20 minutes for 1 hour or continuously, after which patient should be reassessed clinically, and by peak flow meter and pulse oximetry/oxygen saturation and monitoring of pulse, BP and respiratory rate
    - Consider admission to an intensive care unit in life-threatening asthma, when there is no response to treatment, as intubation and ventilatory support may be required

- Corticosteroids
  - → Patients having an acute attack of asthma, unless the attack is very mild and the response to ß2-stimulants very rapid:
    - *Prednisone*, oral, 40 mg immediately
      OR in patients who cannot use oral therapy:
    - *Hydrocortisone*, IV, 100 mg immediately

  - → Follow with *Prednisone*, oral, 20–40 mg daily for 7–10 days

→ Monitor response closely by measurement and clinical signs. If there is a good response, prednisone can be discontinued abruptly after 7–14 days. If used for longer, dosage must be tapered and then stopped

- Anticholinergics
  - → For the duration of the acute attack, until peak flow returns to 80% of predicted or of personal best:
    - *Ipratropium bromide*, MDI, 40–120 mcg 3–4 times daily via large volume spacer
      OR
    - *Ipratropium bromide, nebulised*, 0.5 mg 4 hourly

Recommendation

- Refer to Specialist/ Pulmonologist if failure to control asthma (see parameters for control asthma)

10.3. Chronic Obstructive Pulmonary Diseases

Definition: COPD is a preventable and treatable disease characterized by airflow limitation that is not fully reversible

Causes

- Genetical predisposition
- Exposure to particles
  - Tobacco smoke
  - Occupational dusts, organic and inorganic
  - Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
  - Outdoor air pollution
  - Lung growth and development
  - Oxidative stress
  - Gender
  - Age
  - Respiratory infections
  - Socioeconomic status
  - Nutrition
  - Comorbidities

Signs and Symptoms

- Onset in mid-life
- Symptoms slowly progressive
- Long smoking history (active or passive)
- Dyspnea during exercise
- Dry or productive Cough
- Largely irreversible airflow limitation
- COPD has significant extrapulmonary (systemic) effects including:
    - Weight loss
    - Nutritional abnormalities
    - Skeletal muscle dysfunction

Complications

- Pneumothorax
- Cor pulmonale and Right heart failure

Investigations

- Spirometry
    - A post-bronchodilator FEV1/FVC < 0.70 confirms the presence of airflow limitation that is not fully reversible
    - CXR
    - Comorbidities are common in COPD and should be actively identified

Management

- Goals of COPD Management
    - Relieve symptoms
    - Prevent disease progression
    - Improve exercise tolerance
    - Improve health status
    - Prevent and treat complications
    - Prevent and treat exacerbations
    - Reduce mortality

- Assessment of severity

Stage I	Mild	FEV1/FVC < 0.70	FEV1 > 80% predicted
Stage II	Moderate	FEV1/FVC < 0.70	50% < FEV1 < 80% predicted
Stage III	Severe	FEV1/FVC < 0.70	30% < FEV1 < 50% predicted
Stage IV	Very Severe	FEV1/FVC < 0.70	FEV1 < 30% predicted or FEV1 < 50% predicted plus chronic respiratory failure

Non-pharmacologial

- Smoking cessation is the single most effective and cost effective intervention
- Reduction of exposure to smoke, occupational dusts and chemicals, and air pollutants

Pharmacological (Goal is to decrease symptoms and/or complications)

- *Bronchodilators* (ß2-agonists, anticholinergics, and methylxanthines) used singly or in combination, with long-acting bronchodilators being more effective and convenient
- The addition of regular treatment with inhaled glucocorticosteroids to bronchodilator treatment for Stage III and IV disease patients
- Avoid long term systemic steroids
- Antibiotics: Only used to treat infectious exacerbations of COPD
- Mucolytic agents, Antitussives, Vasodilators are not recommended in stable COPD
- Home oxygen in the last stages

10.4. Pleural Effusion

Definition: Presence of fluid in the pleural cavities

Causes

- Transudative causes
  - Congestive Heart Failure, Liver Cirrhosis, Pulmonary Embolism, Nephritic Syndrome, Malnutrition, Myxoedema

- Excudatives causes
  - Cancers, Infections, Pulmonary embolism, Connective Tissue Diseases, Asbestos, Uremia, Drugs, Radiotherapy, Hemothorax, Chylothorax

Signs and Symptoms

- Fever
- Dry cough
- Pleuritic chest pain
- Dyspnoea
- Decreased vocal fremitus on palpation
- Dullness on percussion
- Absence of breath sounds on the affected side

Complications

- Mediastinal shift, iatrogenic pneumothorax, infections, pulmonary edema if massive removal of fluid

Investigations

- CXR: Pleural effusion
- Pleural Effusion tap (paracentesis)
  - Macroscopic aspect
    - → Haemorragic: suspected cancer
    - → Pus
    - → Chyle
    - → Strow/yellowish

  - Lab: Chemistry, cytology, staining
    - → It is important to first identify if it is an exudates or transudate (using Light criteria)
    - → Exudates: Local disease
    - → Transudate: Systemic disease

- Pleural biopsy
- Chest CT scan if underlying mass is suspected
- Video assisted thoracoscopy

Management

- If massive effusion, temporary relief by pleural tap or intercostal drain tube
  - Remove intercostal tube quickly once drainage complete
- Treat underlying cause

Recommendation

- Refer to specialist if unable to ascertain the etiology of the pleural effusion

10.5. Bronchiectasis

Definition: It is an abnormal and permanent dilatation of the airways

Causes

- Infections
  - Pulmonary TB
  - Recurrent pneumonia
  - Adenoviruses
- Non infective
  - ά1 antitrypsin deficiency
  - primary ciliary dysfunction,
  - Aspiration pneumonia
  - Cystic fibrosis
  - Immunoglobulin deficiencies

Signs and Symptoms

- Dyspnoea, Productive cough with purulent sputum, Haemoptysis,
- Chronic fatigue, Weight loss
- Recurrent pneumonia,
- Wheeze, Coarse crackles, Finger clubbing
- Cor pulmonale and right ventricular heart failure.

Complication

- Lung abscess, amyloidosis

Investigations

- FBC, ESR
- Sputum MC&S, Blood Culture
- Bronchoscopy
- CXR
- CT Scan Chest
- Pulmonary lung tests (Flow volume loop)
- According to suspected Cause (Sweat test, Ig levels ,etc)

Management

- Antibiotics during exacerbations: especially anti-Pseudomanas e.g *Ceftazidime* 1g IV tids for 14 days
- Bronchodilatator
- Chest physiotherapy for airways secretion clearance
- Surgery (for severe localized bronchiectasis or hemoptysis)
- Treat according to the cause

10.6. Tuberculosis Sequelae

Definition: Clinical condition as a consequence of previous tuberculosis that has been cured in the past.

Types of sequelae

- Bronchiectasis, Emphysema, Aspergilloma, Pleural calcifications
- Haemoptysis (Rupture of Rassmussen aneurysm)
- Cor pulmonale
- Constrictive pericarditis
- Seizures, Sterility, Bone deformity

Sign and Symptom

- Variable and depending on the particular patient and sequelae suffered.

Investigations

- Will be those of the clinically suspected condition, but as a general rule CT chest is recommended as it is the most helpful single investigation for respiratory complications
- Sputum for m/c/s, AFBs, fungi
- ECG, Echocardiogram for cardiac disease
- CXR

Management

- Treat the underlying condition and avoid restarting anti TB or TB resistance regimen unless TB proven

Note: - *Many of the conditions result in cough, shortness of breath or haemoptysis and a progressive pattern that leads doctors to label them as AFB negative pulmonary TB and restart treatment for normal or resistant TB.*
- *Reassurance of the patient if no active TB*

10.7. Interstitial Lung Diseases

Definition: Disease that result from a pathological process that involves the interstitium as opposed to airways, vessels or pleura.

Causes

- Occupational and environmental exposures
- Drugs and poisons
- Connective tissues diseases
- Other systemic diseases
- Idiopathic interstitial pneumonias
- Infections

Signs and Symptoms

- Dyspnoea
- Cough
- Hemoptysis
- Wheezing
- Inspiratory crackles
- Chest pain
- Signs of the specific cause (eg. Finger clubbing)

Complications

- Progressive respiratory failure
- Recurrent pulmonary infection
- Cor pulmonale
- Bronchogenic cancer

Investigations

- FBC, LFT, Urea and creatinine, Electrolytes
- CXR (Reticular, nodular or honeycombing patterns)
- Bronchoscopy with lavage and biopsy
- High Resolution CT chest
- ABG
- Serology directed to the potential cause
- Lung function (Restrictive pattern) and DLCO (Reduced)

Management

- Directed to the cause
- General supportive measures:
    - Smoking cessation
    - Supplemental oxygen therapy in patients with hypoxemia (≤ 88% at room air)
    - Remove from exposure is mandatory (eg. Occupational form, toxic medication etc)
    - Respiratory infections should be treated
    - Corticosteroids: *Prednisolone* 1mg /kg

Recommendation

- Refer all cases with advancing disease for specialist input

11. Urinary Tract and Renal Conditions

11.1. Lower UTI (Acute Uncomplicated Cystitis)

Definition: It is an acute infectious inflammation of the bladder and is the commonest lower urinary infection.

Causes

- The ascending Faecal-Perineal-Urethral route is the primary mode of infection.
- The commonest organisms are E. coli (about 70-80%),
- Enterobeccteriaceae, such as Klebsiella spp, Proteus spp, Staphylococcus saprophyticus and Enterococci.
- The spectrum of aetiological agents is similar in uncomplicated upper and lower UTIs.

Signs and Symptoms

- Dysuria
- Frequent and urgent urination
- Suprapubic pain or tenderness, and possibly hematuria
- Absence of vaginal symptoms (e.g., vaginitis, urethritis)

Investigations

- Mid stream specimen (MSSU) or clean catch urine
  - Urine dipstick testing or microscopy
  - Urine culture and sensitivities: Colony count of ≥ 1000 cfu/mL of uropathogens is diagnostic

- Blood glucose
- Renal Ultrasound (for recurrent cases or males)

Management

Pharmacological

- *Nitrofurantoin* 100 mg bid for 5 days
  OR
- *Ciprofloxacin* 500 mg bid for 5 days
- Change to simple narrow spectrum antibiotic once sensitivities known

Non-pharmacological
- Increase water intake

Recommendation

- Refer patients with frequent recurrent UTIs (≥2 UTIs in 6 months or ≥3 UTIs in 12 months) or those with persistent haematuria for urological investigations

11.2. Upper UTI (Acute Pyelonephritis)

Definition: Acute pyelonephritis is bacterial infection of the kidney and renal pelvis, often bilateral.

Causes

- As for lower UTI

Signs and Symptoms

- Flank pain,
- Nausea and vomiting,
- Fever (> 38°c), shaking and chills
- Costovertebral angle tenderness,
- Can occur in the absence of lower UTI symptoms

Investigations

- Urine dipstick, urine microscopy
- Urine culture (Colony counts > 103 cfu/mL of uropathogens) and sensitivity
- Ultrasound is mandatory to rule out urinary obstruction or renal stone disease
- Additional investigations like CT-Scan as needed

Management

- Mild and moderate cases of acute uncomplicated pyelonephritis
    - First choice: *Ciprofloxacin* 500mg tab BID for 7-10 days
    - Alternative treatment: *Ceftriaxone:* 1g OD until susceptibility testing demonstrates that oral drugs can also be used.

- Severe cases of acute uncomplicated pyelonephritis
  - *Ceftriaxone*: 1g OD IV + *Ciprofloxacin* 500mg tab BID for 7 days or Aminoglycosides (*Amikacin or Gentamycin* in case of normal renal function)
  - IV fluids

Recommendation

- Routine post-treatment urinalysis and urine cultures

11.3. Recurrent (Uncomplicated) UTIs in Women

Definition: Recurrent UTI is defined as recurrences of UTI: ≥2 UTIs in 6 months or ≥3 UTIs in 12 months and are common among young, healthy women.

Investigations

- Recurrent UTIs need to be diagnosed by urine culture.
- Excretory urography, cystography and cystoscopy are not routinely recommended for evaluation of women with recurrent UTIs.

Management of recurrent UTI

- Antimicrobial prophylaxis for prevention of recurrent UTI should be considered only after counselling and behavioural modification has been attempted.
- Before any prophylaxis regimen is initiated, eradication of a previous UTI should be confirmed by a negative urine culture 1–2 weeks after treatment.
- The choice of antibiotic should be based upon the identification and susceptibility pattern of the organism causing the patient's UTI and history of drug allergies.
  - Prophylactic or intermittent antimicrobial therapy (eg. *Nitrofurantoin*)
  - Cranberry juice
  - Postcoital prophylaxis: A single antibiotic dose taken after sexual intercourse: Is an alternative to continuous therapy.

11.4. Complicated UTIs

Definition: A complicated urinary tract infection (UTI) is an infection associated with a condition, such as a structural or functional abnormality of the genitourinary tract, or the presence of an underlying disease that interferes with host defence mechanisms, which increase the risks of acquiring infection or of failing therapy

Factors that suggest a potential complicated UTI

- The presence of an indwelling catheter, stent or splint (urethral, ureteral, renal) or the use of intermittent bladder catheterization
- A post-void residual urine of > 100 mL
- An obstructive uropathy of any aetiology, e.g. bladder outlet obstruction (including neurogenic urinary bladder), stones and tumour
- Vesicoureteric reflux or other functional abnormalities
- Urinary tract modifications, such as an ileal loop or pouch
- Chemical or radiation injuries of the uroepithelium
- Peri- and post-operative UTI
- Renal insufficiency and transplantation, diabetes mellitus and immunodeficiency

Causes

- Enterobacteriaceae are the predominant pathogens, with Escherichia coli being the most common pathogen
- Non-fermenters (e.g. Pseudomonas aeruginosa) and Gram-positive cocci (e.g. staphylococci and enterococci) may also play an important role, depending on the underlying conditions

Signs and Symptoms

- Clinical presentation may vary from severe obstructive acute pyelonephritis with imminent urosepsis to a catheter-associated post-operative UTI, which might disappear spontaneously as soon as the catheter is removed
- Apart from urological abnormalities, concomitant medical conditions, such as diabetes mellitus (10%) and renal failure, which can be related to urological abnormalities, are often present

Investigations

- Urine cultures
- Significant bacteriuria in a complicated UTI is defined by counts of > 10^5 cfu/mL in the MSU of uncatheterized women and > 10^4 cfu/mL in catheterized women and all men
- For an asymptomatic patient, two consecutive urine cultures (at least 24 hours apart) yielding > 10^5 cfu/mL of the same micro-organism are required
- The requirement for pyuria is > 10 WBC per high-power field (x 400) in the resuspended sediment of a centrifuged aliquot of urine or per mm3 in unspun urine
- A dipstick method can also be used for routine assessment, including a leucocyte esterase test, haemoglobin and probably a nitrite reaction

Management

- General principles
  - Treatment strategy depends on the severity of the illness.
  - Appropriate antimicrobial therapy and the management of the urological abnormality are mandatory
  - If needed, supportive care is given
  - Hospitalization is often necessary depending on the severity of the illness

- Choice of antibiotics
  - *Ciprofloxacin* 500mg bd po or IV for 7-14 days depending on response
    OR
  - *Augmentin* (Amoxycillin-clavunic acid) 1.2g IV bd for 7-14 days depending on response

In the case of failure of initial therapy, treatment should be switched to an antibiotic active against *Pseudomonas*, such as *Meropenem* 500mg IV tds

Recommendation

- Prior to and after the completion of the antimicrobial treatment, urine cultures must be obtained for the identification of the micro-organisms and the evaluation of susceptibility testing

11.5. Acute Glomerulonephritis

Definition: A group of diseases of inflammatory or non-inflammatory nature involving renal glomeruli.

Causes

- Primary (idiopathic)
- Secondary
  - Infection which may be bacterial (e.g. post-streptococcal), viral (e.g. HBV, HCV, CMV), parasitic (e.g. Schistosoma mansoni, Malaria)
  - Connective tissue diseases (e.g. SLE, polyarteritis nodosa, rheumatoid arthritis)
  - Drugs (e.g. Penicillamine, Paradione, Aspirin, Heroin)
  - Metabolic disease (e.g. Diabetes mellitus, amyloidosis)
  - Malignancy (e.g. lymphoma)
  - Familial (e.g. Alport syndrome)

Clinical manifestations

- Patient with glomerulonephritis may present with any of the following five syndromes:
  - Nephrotic syndrome:
    - ➔ Nephrotic range proteinuria (more than 3.5 gr/1.73 m^2/24 hs), hypoalbuminaemia, hyperlipidaemia, and oedema, in many cases complicated by predisposition to venous thrombosis and bacterial infection. Serum creatinine is usually normal
  - Acute nephritic syndrome (acute nephritis)
    - ➔ Characterized clinically with rapid onset of oedema (less in severity than in nephrotic)
    - ➔ Urine analysis: red cell casts, proteinuria (less than in nephrotic syndrome), haematuria and leukocyturia.
    - ➔ Increased serum creatinine, normal serum albumin and cholesterol
    - ➔ Recent onset of haematuria and proteinuria, renal impartment, and salt and water retention, causing hypertension
  - Rapidly progressive glomerulonephritis (RPGN)
    - ➔ Progression to renal failure over days to weeks, in most cases in the context of a nephritic presentation, typically associated with the pathological finding of extensive glomerular crescent formation on renal biopsy

- Chronic nephritic syndrome
  - → Persistent proteinuria with or without haematuria and slowly progressive impairment of renal function
- Asymptomatic urinary abnormality
  - → Subnephrotic-range proteinuria, and/or microscopic haematuria, not accompanied by renal impairment, oedema, or hypertension
  - → The prognosis is usually excellent and no treatment is required

Management

- Symptomatic treatment and strategies to delay progression:
  - Regular clinical follow-up
  - Blood pressure control.
  - Use of ACE inhibitor in patients with proteinuria exceeding 1gr/d
  - Mild dietary protein restriction
  - Treatment of Hyperlipidaemia
  - Immunosuppression in selected cases
    - → Oral *Prednisolone*: 0.5-1.0mg/Kg/daily/6 weeks
    - → *Cyclophosphamide,* chlorambucil, azathioprine, cyclosporin
- Renal replacement therapy with dialysis or transplantation if needed

11.6. Acute Renal Failure

Definition: It is defined as an abrupt or rapid decline in renal filtration function with or without oligo-anuria.

Causes

- AKI may be classified into 3 general categories, as follows:
  - Prerenal: As an adaptive response to severe volume depletion and hypotension, with structurally intact nephrons
  - Intrinsic: In response to cytotoxic, ischemic, or inflammatory insults to the kidney, with structural and functional damage
  - Postrenal: From obstruction to the passage of urine

RIFLE classification of the acute kidney injury:

RIFLE Classification System for Acute Kidney Injury Stage	GFR** Criteria	Urine Output Criteria	Probability
Risk	SCreat (serum creatinine) increased × 1.5 or GFR decreased >25%	Urine output(UO) < 0.5 mL/kg/h × 6 h	High sensitivity (Risk >Injury >Failure)
Injury	SCreat increased × 2 or GFR (glomerular filtration rate) decreased >50%	UO < 0.5 mL/kg/h × 12 h	
Failure	SCreat increased × 3 or GFR decreased 75% or SCreat ≥4 mg/dL; acute rise ≥0.5 mg/dL	UO < 0.3 mL/kg/h × 24 h (oliguria) or anuria × 12 h	
Loss	Persistent acute renal failure: complete loss of kidney function >4 wk		High specificity
ESKD (End Stage Kidney Disease)	Complete loss of kidney function >3 mo		
Note: *Patients can be classified by GFR criteria and/or UO criteria. The criteria that support the most severe classification should be used. The superimposition of acute on chronic failure is indicated with the designation RIFLE-FC; failure is present in such cases even if the increase in SCreat is less than 3-fold, provided that the new SCreat is greater than 4.0 mg/dL (350 μmol/L) and results from an acute increase of at least 0.5 mg/dL (44 μmol/L).*			

Signs and Symptoms

- Asthenia
- Nausea and vomiting
- Dyspnea
- Oliguria
- Coma

Investigations

- FBC, bleeding time
- Biochemistry: ABG, electrolytes, AST/ALT, creatinine, BUN
- The calculation of fractional excretion of sodium (FeNa) as follows:
    - FeNa = (urine Na/plasma Na)/(urine creatinine/plasma creatinine)
    - FeNa < 1% suggests prerenal acute renal failure
    - FeNa > 1%, this suggests acute tubular necrosis (ATN)

- ECG and Echocardiography
- Abdominal US: Mandatory to identify an obstructive renal failure
- Chest X-ray
- Renal biopsy

Complications

- Severe electrolytes imbalance: K+, Mg++, Ca++, PO4, Na+
- Severe metabolic acidosis
- Volume overload: Acute pulmonary edema
- Arrythmias, pericardial effusion, tamponade
- Encephalopathy, seizures, coma
- Infection: Pneumonia, UTI
- Coagulation disorders: GI bleeding
- Chronic kidney disease: ESKD

Management

Non-Pharmaceutical

- Dietary modification: Salt and fluid restriction, protein restriction (1g/kg/day)

Pharmaceutical

- Treat the metabolic acidosis: *Sodium bicarbonate*
- Treat hyperkalemia: *Kayexalate* (30-60g/day), *Insuline-Glucose, salbutamol* IV 0.5mg/hr, renal replacement therapy, calcium gluconate
- Treat hypocalcemia: *Calcium gluconate*
- Diuretics: *Furosemide* up to 500mg-1g/24hrs (contraindicated in hypovolemia)
- Treat the underlying caus
    - ➔ Prerenal: Restore the hemodynamic by IV fluids and/ or vasopressors

- Intrinsic: stop the precipitating medications, treat sepsis/ septic shock /HUS, revascularisation in case of renal artery obstruction
- Postrenal: remove the obstacle/mass

- Prevention
  - Fluids management optimization
  - *N-acetylcysteine* 200mg : Po, 1sacket x 3/24hr
  - Tight-controlled glycemia in critically ill patients (Targeted Glycemia:4.4-6.1mmol/L)

Surgical

- Indicated in postrenal acute kidney injury (obstructrive renal failure)
  - Urinary catheter (urethral/suprapubic)
  - Percutaneous nephrostomy
  - Extracorporeal Lithotripsy

Recommendation

- Refer for dialysis if:
  - Volume expansion that cannot be managed with diuretics (pulmonary edema)
  - Hyperkalemia refractory to medical therapy(>6mmol/L)
  - Correction of severe acid-base disturbances that are refractory to medical therapy
  - Severe azotemia (BUN >40mmol/L)
  - Uremic syndrome: coma, pericardial effusion, bleeding.

11.7. Chronic Kidney Disease

Definition: Progressive and irreversible deterioration in glomerular +/- tubular function over months and years

Criteria for CKD

- Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either:
  - Pathological abnormalities
    OR
  - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
    GFR < 60 ml/min/1.73 m^2 for≥3 months, with or without kidney damage
    GFR (Cockcroft Gault) = (140 - age) x lean body weight [kg]
    Cr [mg/dL] x 72

Classification of CKD

Stage and glomerular filtration rate (mL/ minute/1.73m^2)	Description	Actions (Include those for above steps)
Stage 0 or GFR > 90	At increased risk CKD because of CKD or CVD risk factors	Screening CKD risk reduction CVD risk reduction
Stage 1 or GFR > 90	Kidney damage with normal GFR	Diagnose and treat comorbidities Slow progression CVD risk reduction
Stage 2 or GFR 60–89	Kidney damage with mild decrease in GFR	Estimate risk of progression
Stage 3 or GFR 30-59	Moderate decrease in GFR	Evaluate and treat complications
Stage 4 or GFR 15-29	Severe decrease in GFR	Prepare for dialysis
Stage 5 or GFR<15 or On dialysis	End Stage Renal Disease (kidney failure requiring renal replacement therapy)	Renal replacement therapy, i.e. dialysis or transplant if uraemic

Causes

Commonest Underlying Causes of CKD
- Diabetes: Most common cause
- HTN
- Glomerular disease (Glomerulonephritis, HIV, Viral hepatitis, SLE)
- Polycystic Kidney Disease

Signs and Symptoms

- Initial symptoms
  - Unintentional weight loss, nausea, vomiting, general ill feeling, edema, fatigue, headache, frequent hiccups; generalized itching
- Later symptoms
  - Decreased urine output, easy bruising or bleeding, hematochezia, melena, decreased alertness, muscle twitching or cramps, seizure, uremic frost
- Additional symptoms
  - Excessive urination at night, excessive thirst, , unusual breath odor, loss of appetite
- Signs
  - Pallor
  - High blood pressure
  - Polyneuropathy

Investigations

- Serum electrolytes, urea and creatinine
- Calcium, phosphate, uric acid, magnesium and albumin
- Urinalysis, microscopic exam, quantitation of protein in urine (protein: Creatinine ratio)
- Calculation of creatinine clearance and protein losses
- FBC
- Consider complement levels, protein electrophoresis, antinuclear antibodies, ANCA
- Renal biopsy: Particularly in mixed or idiopathic disease
- Renal Ultrasound: Evaluate for obstruction, stones, tumor, kidney size, chronic change
- CT scan to evaluate renal artery stenosis

Management

- Pre-Dialysis Treatment
  - Hypertension should be aggressively treated:
    - ➔ Maintain blood pressure less than 130/80 mm Hg;
    - ➔ Use an ACE Inhibitor or ARB (Caution with use of ACE inhibitors in renal artery stenosis)
    - ➔ More than one drug is usually required and a diuretic should be part of the regimen

  - Treat cardiovascular risk, especially smoking and high LDL cholesterol
  - Maintain normal electrolytes : Potassium, calcium, phosphate are major electrolytes affected in CRF
  - ACE inhibitors may be tolerated even in many patients with creatinine >3.0mg/dL. ACE inhibitors may slow the progression of diabetic and non-diabetic renal disease
  - Reduce or discontinue other renal toxins (including NSAIDS)
  - Diuretics (e.g. furosemide) may help maintain potassium in normal range but must be used carefully to avoid dehydration and worsening renal failure.
  - Renal diet including high calcium and low phosphate
  - Reduce protein intake to <0.7gm/kg body weight
  - Monitor hemoglobin and bone mineral metabolism with treatment as needed
  - Fluid intake maybe restricted, often to an amount equal to the volume of urine produced

- Management options for the patients with ESRD
  - Dialysis: Hemodialysis, Peritoneal dialysis
  - Kidney transplantation

- Indications for Hemodialysis
  - Uremia with symptoms and/or signs
  - Severe Hyperkalemia
  - Volume Overload: Usually with congestive heart failure (pulmonary edema)

11.8. Nephrotic Syndrome

Definition: Nephrotic syndrome is a renal condition characterized by proteinuria (≥3 grams/day or 2 g of protein/ gram of urine creatinine), hypoalbuminemia, and edema

Causes

- Kidney diseases
  - Minimal-change Nephropathy
  - Membranous Nephropathy (may be associated with HIV or viral hepatitis)
  - Focal Glomerulosclerosis

- Systemic diseases
  - Diabetes Mellitus
  - Connective Tissue Diseases (e.g. SLE, Rheumatoid arthritis)
  - Amyloidosis

- Drugs: NSAID, anticancer drugs

Signs and Symptoms

- Generalized edema: Initially develops around the eyes and legs
- Increase in weight
- Ascites, and/or pleural effusions
- Foamy urine
- Features related to the cause of nephrotic syndrome
- Hematuria and hypertension manifest in a minority of patients
- If the kidney function is reduced: hypertension and/or anemia

Complications

- Subnutritional State
- Infections
- Clotting episodes: deep vein thrombosis (DVT), renal vein thrombosis
- Premature atherosclerosis
- Hypovolaemia
- Drug related complications
  - Diuretics (hypovolaemia, hypokalaemia, or hyponatraemia)
  - Corticosteroids (diabetes mellitus, cataract, infections, and bone disease)

- Other Immunosuppressive drugs e.g., cyclophosphamide (haemorrhagic cystitis, alopecia, infection malignancy)

- Acute renal failure
- Anemia

Investigations

- Urinalysis
  - 3+ or 4+ readings on the dipstick corresponds to ≥ 300 mg/dL of urinary protein

- Urine sediment examination: Show cells and/or casts
- 24 hours urine for proteinuria
- Serum albumin
- Serologic studies for infection and immune abnormalities
- Renal ultrasonography
- Renal biopsy indicated
  - For childhood nephrotic syndrome
    - ➔ Congenital nephrotic syndrome
  - Children older than 8 years at onset
    - ➔ Steroid resistance
    - ➔ Frequent relapses or steroid dependency
    - ➔ Significant nephritic manifestations
  - Adult
    - ➔ Nephrotic syndrome of unknown origin

- In children: Genetic testing for the *NPHS1* and *NPHS2* mutations
- Serological tests: Hepatitis B and C, HIV test
- Lipids profiles

Management

Non-pharmacological

- Rest in bed during exacerbation to promote diuresis and early ambulation after to avoid DVT
- Diet: Salt restricted balanced diet supported with vitamins (especially vitamin D and calcium)
- Treatment of the cause in secondary cases
- Treatment of complications

Pharmacological

- Diuretics
  - *Furosemide* 20-60 mg/d, up to 120 mg IV in severe resistant cases.
  - Addition of *Spironolactone* for diuretic resistant cases

- *Albumin infusion* (to improve plasma oncotic pressure) is indicated only if severe oedema resistant to large doses of diuretics and if surgery or invasive procedure (e.g. biopsy)

- Corticosteroid Indications
  - When no response to previous lines of treatment
  - Especially useful for Minimal Change Glomerulonephritis
  - The dose and duration of steroid treatment depends on the type of disease and response
  - In primary (idiopathic) Minimal Change nephritis 40-60 mg daily *Prednisone* are given orally (for children 1-2 mg/kg/d), for 4-6 weeks followed by gradual withdrawal

- Other immunosuppressives (*Cyclophosphamide, Azathioprine*, cyclosporine) in selected cases

Recommendation

- Refer cases not responding to treatment for specialist input

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