Ministry of Health

CLINICAL GUIDELINES FOR MANAGEMENT OF CHRONIC ON-COMMUNICABLE DISEASES (NCDs)

An integrated provider's manual

For

Hypertension & Cardiovascular Diseases, Diabetes, Asthma & COPD, Epilepsy & Sickle Cell Disease and Renal Diseases

Non-communicable Diseases and Mental Health Unit

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ACRONYMS

AMI	Acute Myocardial Infarction
ACS	Acute Coronary Syndrome
CDC	Centre for Disease Control
ARF	Acute Rheumatic Fever
BMI	Body Mass Index
COPD	Chronic Obstructive Pulmonary Disease
CRD	Chronic Lower Respiratory Disease
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
IHD	Ischemic Heart Disease
MOH	Ministry of Health
NCDs	Non Communicable Diseases
PEN	Package of Essential NCD Interventions
RF	Rheumatic Fever
RHD	Rheumatic Heart Disease
WHO	World Health Organization
STEMI-ST	Segment Elevated Myocardial Infarction
FEDOMA	Federation of Disability Organizations of Malawi
TIA	Transient Ischemic Attack

FOREWORD

Non-Communicable Diseases (NCDs) are a worldwide epidemic. Particularly, the most common diseases - Cardiovascular diseases, Chronic Obstructive Pulmonary Diseases (COPD), Chronic Kidney Diseases, Cancer, Diabetes, injuries and disabilities contribute to the morbidity and mortality accounting for over 70% of deaths worldwide with an estimated 78% of these deaths occurring in low- and middle-income countries (LMICs). The disease pattern is also changing from infectious to chronic in Malawi like other developing countries due to the epidemiological transition.

The burden of infectious diseases is still preeminent; but in addition, the problem of NCDs is creating new challenges for our public health system. Malawi MOH plans to continue to prevalent infectious conditions, as well as to reach the next frontier through expansion of access to care for Non-Communicable Diseases (NCDs) which are a recognized and significant cause of morbidity and mortality around the world. It is in the wake of NCDs burden worldwide that all health care stakeholders, individuals and organizations are called upon to play an active role in improving the quality of life in Malawi.

The National Guidelines for prevention and management of NCDs have been developed in accordance with the international standards by a recognized team of experts. The guidelines reported were developed and validated by a Technical Working Group composed by general practitioners and specialists with extensive experience in both urban and rural areas.

Dr Charles Mwansambo

Secretary for Health

ACKNOWLEDGEMENTS

The Ministry of Health would like to acknowledge the efforts of the Individuals and organizations that contributed to the success in finalizing the national NCD Protocols. The Ministry's effort towards improved quality of clinical care for people affected by chronic Non-Communicable Diseases in Malawi, especially through the development of these standardized guidelines, has been made possible by technical and financial support from several institutions and individuals. The evident cooperation among the partners was critical to the success of the document.

Management protocols in this manual are adapted from a rigorous systematic approach, with health specialist's contributions on the practicability of providing the optimum care services for all. Further, has ensured the document provides the reference guide for health workers in Malawi to sustain and build on their professional development. The work is coupled with the growing trend in other chronic NCDs, notably Rheumatic Heart Disease, Sickle Cell Disease to mention a few. This is attributed to the improved clinical investigations among health workers and we believe the protocols have articulated to the management of the chronic conditions.

Special gratitude goes to the Curative and Medical Rehabilitation Services particularly the NCDs and Mental Health Unit for providing leadership in the development of this document. The efforts of coordinating meetings, putting together vital pieces of information, comments, criticisms and suggestions and final compilation of the document have not gone unnoticed.

We are heavily indebted to many other partners and actors in the health sector that made valuable contributions to the development of this policy. Please accept our sincere thanks

Dr George Chithope-Mwale

Director of Curative and Medical Rehabilitation Services

CHAPTER

INTRODUCTION 1

Global burden of non-communicable diseases

Non-communicable diseases (NCDs) – mainly cardiovascular diseases, cancers, chronic respiratory diseases and diabetes – are the major cause of death worldwide. In 2016, NCDs were responsible for 41 million of the world's 57 million deaths (71%). 15 million of those deaths were 'premature', between the ages of 30 and 69 years. 85% of premature NCD deaths occurred in low- and middle-income countries and could have largely been prevented. Cardiovascular diseases account for most NCD deaths, or 17.9 million deaths annually, followed by cancers (9 million), chronic respiratory diseases (3.8 million), and diabetes (1.6 million) [1]. Most NCD deaths are linked to common risk factors, namely tobacco use, unhealthy diet, physical inactivity and harmful use of alcohol.

To strengthen national efforts to address the burden of NCDs, the 66th World Health Assembly endorsed the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020 (resolution WHA66.10). The global action plan offers a paradigm shift by providing a road map and a menu of policy options for Member States, WHO, other UN organizations and intergovernmental organizations, NGOs and the private sector which, when implemented collectively between 2013 and 2020, will attain 9 global targets by 2025, including 10% relative reduction in harmful use of alcohol, 10% relative reduction in prevalence of insufficient physical exercise, 25% relative reduction in the prevalence of raised blood pressure, 30% relative reduction in mean population salt intake, in addition 16 best-buys, 9,000 lives can be saved by 2025, by implementing all of the 16 WHO best buys and 30% relative reduction in current tobacco use[2].

NCDS in Africa

In the WHO African Region, the burden of NCDs and their risk factors are now well documented. Based on data from WHO STEP-wise approach to non-communicable disease risk factor surveillance (STEPS) from 33 countries in the region and global school-based student health surveys (GSHS) from 19 countries, the prevalence of hypertension, or high blood pressure, in the African region is the highest worldwide, affecting an estimated 46% of adults. At least one in three adults was found to be hypertensive in half of the countries, prevalence of daily tobacco use among adults ranged from 5% to 26% (12% across the Region), people who are overweight ranged from 12% in Madagascar to 60% in Seychelles, with a median of 35%, while alcohol consumption the median prevalence is at 31%.

NCDs in Malawi

NCDs are estimated to account for 32% of all deaths in Malawi. Efforts to address NCDs in our country included conducting a second STEPS survey in 2017, in order to determine the magnitude of non-communicable diseases and their risk factors in Malawi. This survey revealed that 16.7% of adults had raised blood pressure (BP) or currently on medication for raised BP. Among those diagnosed only 30% are taking medication. The prevalence of diabetes was estimated to be 1.4%. the survey revealed that 96% of the respondents had never been measured for raised blood glucose and less than 1% (0.4%) of respondents were diagnosed with raised blood sugar in the past 12 months. The 2017 STEPS Survey also revealed 14% of households have someone in the family with Epilepsy.

The guidelines include the protocols required for management of cardiovascular diseases, diabetes, chronic respiratory diseases and cancer. Implementation of the NCD guidelines is key to achieving Sustainable development goal number 3.4 to reduce by one-third pre-mature mortality from non-communicable diseases (NCDs) through prevention and treatment, and promote mental health and wellbeing by 2030 as adopted by the United Nations Member States Assembly in 2015.

The NCD guidelines enable early detection and management of NCDs to prevent life-threatening complications, such as heart attacks, stroke, kidney failure, amputations, and blindness.

These guidelines can be used by healthcare workers working in NCD clinics at tertiary, Secondary and Primary level of care.

CHAPTER

CARDIOLOGY 2

1. HYPERTENSION

- Three measurements ≥ 140 /90 over at least two different days (e.g. two measurements on first day and one confirmatory measurement on second visit)
- No need to repeat if first measurement is normal
- If BP ≥ 180 / 110 (systolic or diastolic) on first reading and again ≥ 180 / 110 on second reading on the same day, hypertension is diagnosed on that day without needing to come for a second day measurement. Treatment is started that same day.

Note: In patients with renal failure and diabetes lower blood pressure thresholds are used

In children, hypertension is defined statistically because BP levels vary with age and outcome. Based data are not available for this population. Hypertension is defined as systolic and /or diastolic pressure levels greater than the 95th percentile for age and gender on at least 3 occasions

- The upper limit for normal systolic Bp in children greater than One year may be calculated as follows:
  - {Age in years x 3} +100
  - Diastolic BP is 2/3 of systolic BP
  - 90% of hypertension in children is caused by renal conditions

The table below shows normative blood pressure levels {systolic/diastolic} in children up to age 5 years. Blood pressures above the 95th percentile indicate hypertension

Age	Mean BP levels	95th Percentile
1-3 days	64/41 {50}	78/52 {62}
1mo -2yr	95/58 {72}	110/71 {86}
2-5yr	101/57 {74}	115/68 {85}

*Child has hypertension if BP > 95th percentile

Treatment of hypertension prevents development of other cardio-vascular diseases (CVDs) and extends life.

A. PATIENT IDENTIFICATION

Hypertension is often silent, and the symptoms are very subtle and non-specific.
All adults (Clients/ patients) should have their blood pressure taken at **every visit** to a health facility.
Special attention should be given to the following higher risk groups:

- Age > 30 years
- overweight (bmi ≥ 25kg/m^2)[1]*
- Weight for height for children
- Waist circumference ≥ 90 cm in women and ≥ 100 cm in men
- Diabetes mellitus
- Family history of diabetes, hypertension or kidney disease
- Family history of premature cardio-vascular death (cvd death at < 65years for female patients and < 55 years for male patients)
- Smokers: current and former
- Excessive or at-risk alcohol use
- Hiv positive patients
- Pregnant women

General principles for blood pressure measurement

- The patient should be seated for at least 5 minutes, relaxed, and not moving or speaking.
- The arm must be supported at the level of the heart. Ensure no tight clothing constricts the arm.
- Place the cuff on neatly with the indicator mark on the cuff over the brachial artery. The bladder should encircle at least 80% of the upper arm (but not more than 100%). Obese adults will need a larger size cuff. Malnourished adults and children will need a smaller cuff.
    - ***If you use a cuff that is too small the reading will be higher***

Measure once. If BP is over the cutoff point, rest for 5 minutes and repeat measurement.

Table 1: Appropriate Size for Blood Pressure Cuff

Indication	Cuff Width (cm)	Cuff length (cm)	Arm Circumference (cm)
Small Adult/Child	10 – 12	18 – 24	< 23
Standard Adult	12 – 33	23 – 35	< 33
Large Adult	12 – 16	35 – 40	< 50

B. BASELINE INVESTIGATIONS IN HYPERTENSION

Background – History and Physical Exam
Basic investigations – Glucose, urine analysis (protein and blood), creatinine HIV, Pregnancy Test
For patients with suspected co-morbidities or to exclude secondary causes – electrolytes, cholesterol, ECG, Cardiac Echo, Chest X-ray, and Doppler USS,

[1]BMI: Body Mass Index = weight in kilograms / (height in metres)^2

Table 2: Classification of Hypertension

Class	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)
Borderline	130 – 139	85 – 89
Mild/ I	140 – 159	90 – 99
Moderate/ II	160 – 179	100 – 109
Severe/ III	≥180	≥110

C. APPROACH TO MANAGEMENT OF HYPERTENSION

I. Determine the risk factors and stratify according to risk added

Table 3: Risk Factors and Complications of hypertension

MAJOR RISK FACTORS	TARGET ORGAN DAMAGE	COMPLICATIONS
Modifiable Factors Body Weight-Waist circumference - abdominal obesity: Men ≥ 100 cm; Women ≥ 90 cm • Smoking • Exercise • Salt intake • Dyslipidaemia: • Total fasting cholesterol > 5.1 mmol /L (197 mg/dl) • OR LDL > 3 mmol/L (116 mg/dl) • OR HDL men < 1 mmol/L (39 mg/dl) and women < 1.2 mmol/L. (46 md/dl) **Non-Modifiable Factors** • Sex • Diabetes mellitus • Men aged <55 years; Women aged <65 years • Family history of early onset of CVD • History of secondary causes of hypertension	• LVH: based on ECG or echo, chest x-ray • Proteinuria. • Slightly elevated creatinine: - Men 115-133 µmol/L (1.3-1.5 mg/dl) - Women 107-124 µmol/L (1.2-1.4 mg/dl)	• Coronary heart disease • Heart failure • Chronic kidney disease: - Proteinuria ≥ 2+ - Creatinine men > 133 µmol/L (1.5 md/dl) or creatinine women >124 µmol/L (1.4 mg/dl) • Stroke or Transient Ischaemic Attack • Peripheral arterial disease • Peripheral vein Disease (DVT) • Advanced retinopathy: - Haemorrhages; exudates Papilloedema

ii. Stratify according to added risk and determine initiation of treatment

We treat at level of blood pressure above which the benefits of investigation and treatment outweighs the harm

Table 4: Risk Stratification and Treatment

	Borderline Hypertension 130/85- 139/89	Class 1 Hypertension 140/90-159/99	Class 2 or Class 3 Hypertension ≥160/100
No diabetes or no complications	Low risk Lifestyle change only	**Low risk** Lifestyle change only	**High risk** Treat with drugs immediately Continue lifestyle changes
		Moderate risk If ≥ 2 risk factors (including smoking, age) Lifestyle change for 3 – 6months Treat with drugs if BP still high	
Diabetes or complications (See Table 3)	**Moderate risk** Lifestyle change for 3 - 6months Treat with drugs if BP still high	**High risk** Treat with drugs immediately Continue lifestyle changes	**High risk** Treat with drugs immediately Continue lifestyle changes

iii. Treating Hypertension

- Always check for treatment adherence at every visit by self-report of number of days of missed drugs.
- General Target for treating hypertension BP <140/90 mmHg for adults and the cut off point for children and neonates:
  - o *Use target BP of 130/80mmHg for diabetic patients and in patients with elevated creatinine or 2+ proteinuria.*
  - o *Use a target BP of 125/75 in diabetic patients who have nephropathy*

- Lifestyle modification should precede and always accompany treatment with medications. For detailed step wise approach treatment of hypertension refer to guidelines below.
- Where possible use once daily drugs.
- There will be reverse referral between all levels of care (Tertiary Secondary , Secondary and Primary).

Table 5: Treatment Steps and Drug Classes for Hypertension in non-diabetic or diabetic without Nephropathy

Hypertension in non-diabetic or diabetic without nephropathy				
Step 1	**Step 2**	**Step 3**	**Step 4**	**Step 5**
Thiazide Diuretic	**Add Calcium Channel Blocker (CCB)**	**Add ACE Inhibitor (ACEI)**	**Add Beta-blockers**	**Add Methyldopa or Hydralazine**
Hydrochlorothiazide 12.5mg-25 mg OD or Bendroflumethiazide 2.5 mg OD Encourage potassium intake, e.g. banana	Amlodipine 5mg OD (max 10mg OD) Nifedipine 20mg BD (max 80mg) slow release Do not use plain (short acting) nifedipine as this can lead to paradoxical increase in BP and may precipitate a vascular event.	Enalapril 5mg OD (max 20 mg OD) or Ramipril 2.5mg OD (max 10mg OD) or Lisinopril 5-10mg OD (max 40mg OD) OR Captopril 12.5mg TDS (max 50mg TDS) Where possible creatinine should be checked prior to treatment and 2-4 weeks after commencing ACE inhibitors A creatinine increase of ≤ 30% is acceptable. An increase of > 30 % requires discontinuation of the ACE-I	Atenolol 25-50mg OD (max 100mg) Carvedilol 12.5-25mg	Methyldopa 250mg BD/TID (max 2g) Hydralazine 25mg-50 mg TID

iv. Treating Hypertension in Children

a. Calcium channel blocker

a. Nifedipine slow release 0.1-0.25mg/kg 6 hourly PO or

b. Amlodipine 0.1mg/kg 4 to 6 hourly PO

b. ACE-Inhibitor

a. Enalapril 0.1mg/kg PO daily or 12 hourly or

b. Lisinopril0.1mg/kg PO daily

c. Beta Blockers

a. Propranolol 0.5-1mg/kg twice daily

Table 6: Treatment for Hypertension in Special Circumstances

Pregnant	Previous Heart Attack	Renal Failure (Target BP 130/80)	Diabetic nephropathy (target BP 125/75)	Heart Failure
Methyldopa 250mg bd/tds (max 3g daily) or Nifedipine SR 20 -40 mg bd ARBs and ACEIs are contraindicated	Step 1 - ACEI and Beta Blocker Step 2 - Add thiazide Step 3 – Add CCB	Step 1 – CCB Step 2 – HCTZ (avoid if creat cl < 30 ml/min) Step 3 – Consider ACEI and recommend monitoring K and creatinine Step 4 – propranolol (not atenolol)	Step 1 - ACEI Step 2 – ACEI and HCTZ or ACEI and CCB	Furosemide, Beta Blocker and ACEI

Table 7: Key Facts about Anti-Hypertensive Drugs

Drug class & Examples	Important facts	Side effects
<u>Thiazide diuretics:</u> Hydrochlorothiazide 12.5-25mg OD Bendroflumethiazide 2.5mg OD	Well tolerated, best taken in the morning Furosemide & Spironolactone are NOT ANTI-HYPERTENSIVES on their own Avoid in advanced renal failure – (creatinine clearance < 30)	Erectile impotence (refer for specialist care) Hypokalaemia, hyponatraemia Mild hyperglycaemia Hyperuricemia and gout
Calcium Channel Blockers (CCBs): Amlodipine 5-10mg OD Nifedipine SR 20-40mg BD	DO NOT USE short acting nifedipine, as it causes rapid swings in BP and reflex tachycardia & can precipitate ischaemic events Efavirenz may theoretically reduce concentration of CCBs	Minor GI disturbances Flushing (usually stops after 2 weeks) Headache (usually stops after 2 weeks) Ankle oedema

Drug class & Examples	Important facts	Side effects
Angiotensin-Converting Enzyme inhibitors (ACEI): Lisinopril 10-40mg OD Enalapril 5-40mg OD Captopril 12.5-50mg TDS Ramipril 2.5-10mg OD	Addition of a diuretic may enhance effect ACEIs are first choice anti-hypertensive in diabetic nephropathy ACEIs are CONTRAINDICATED in pregnancy & Breastfeeding	Dry cough (most common) Severe hypotension (therefore give at bedtime) Renal impairment Angio-oedema
Beta Blockers: Cardio-selective: Atenolol 25-50mg od Non-selective: Propranolol 80-160mg bd Recommended for HF: Bisoprolol 5-20mg od	Reduce dose in renal/hepatic impairment Contraindicated in severe asthma Contraindicated in uncontrolled heart failure Avoid in pregnancy	Fatigue Nightmares Cold feet (PVD) Impotence Bradycardia
Methyldopa: Dose range 250-500mg bd or tds	Centrally acting; Safest antihypertensive in pregnancy;	CNS side effects: drowsiness, depression, parkinsonism; GI disturbances, dry mouth, oedema;

When should aspirin be given?

Aspirin 75 mg od should be given for:

- Primary prevention:
  - o hypertensive diabetic patient aged 45 years or above
  - o any patient with diabetic nephropathy
  - o patients with diabetes in pregnancy- to prevent preeclampsia

- Secondary prevention:
  - o previous ischaemic stroke,
  - o Previous Myocardial infarction (MI)
  - o Peripheral Vascular Disease

v. Cardiovascular risk assessment Score

How do you use the WHO/IHS Cardiovascular Risk Prediction Charts to assess cardiovascular risk?

Step 1 Select the appropriate chart depending on whether the patient has diabetes.
Step 2 Select the male or female table.
Step 3 Select the smoker[A] or non-smoker box.

Step 4 Select the age group box (i.e. if age is 50-59 years, select 50).
Step 5 Within this box select the cell nearest to the patient's systolic blood pressure (mmHg). The color of this cell determines the 10-year cardiovascular risk.

[A] Smokers are defined as current smokers and those who have quit within the last year.

Figure 1: WHO/ISH risk prediction Chart

Figure 4. **WHO/ISH risk prediction chart for AFR E.** 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus.

YELLOW: Risk 10% to <20%	
Patient at *moderate* risk of fatal or non-fatal vascular events.	
Anti-hypertensive drugs	• If BP ≥160/100 mmHg, start antihypertensive medications • If BP ≥140/90 mmHg, counsel on lifestyle changes and re-check BP every 6R12 months
Anti-platelet drugs	• Patient should NOT be treated with aspirin
Monitoring	• Monitor cardiovascular risk profile every 6-12 months

ORANGE: Risk 20% to <30%	
ORANGE: Risk 20% to <30%Patient at *high* risk of fatal or non-fatal vascular events.	
Anti-hypertensive drugs	• If BP >140/90 mmHg, start antihypertensive medications
Anti-platelet drugs	• Patient should NOT be treated with aspirin
Monitoring	• Monitor cardiovascular risk profile every 3-6 months

RED: Risk ≥30%	
Individuals in this category are at very high risk of fatal or non-fatal vascular events.	
Anti-hypertensive drugs	• If BP >130/80 mmHg, start antihypertensive medications
Anti-platelet drugs	• Patient should be treated with low-dose aspirin
Monitoring	• Monitor cardiovascular risk profile every 3-6 months

D. HYPERTENSION COMPLICATIONS

Hypertension increases the risk of ischemic heart disease, strokes, heart and kidney failure. The risk of developing these complications is higher in the presence of other risk factors such as diabetes and high blood cholesterol.

a) Hypertensive urgency - asymptomatic grade III hypertension

- Commence two oral agents. Use calcium channel blockers (eg amlodipine 5 mg daily/slow release nifedipine 20 mg BD) and diuretic (e.g. HCTZ 25 mg)
- Aim to lower the blood pressure slowly over 48-72 hrs. Review after one week and escalate treatment as needed.

b) Hypertensive emergencies in Adults

The main difference is that patients with hypertensive emergencies are symptomatic and have acute target organ damage.

- e.g. progressive retinopathy (hemorrhages, papilledema), deteriorating renal function and microangiopathic hemolytic anaemia.

Examination:

- Check BP in both arms (aortic dissection or coarctation). Check lying and standing blood pressure if possible (to look for patients who have volume depletion)
- Fundoscopy for grade III/IV retinopathy
- Neurological Examination (with focus on Glasgow Coma Scale)
- Urine dip stick for red blood cell and microscopy for RBC casts
- Chest examination (respiratory and cardiac systems)
- ECG for any evidence of ischaemic changes or end organ damage (Left ventricular hypertrophy)
- Oxygen saturation

Usually, the life-threatening situation requires immediate lowering of blood pressure with intravenous anti-hypertensive.

- Admit in HDU/ICU
  - Simultaneously start oral and intravenous agents and aim to lower the blood pressure to at least 160/100 or by 25 % over 24 hours
  - See below for intravenous medication
    - Hydralazine 5-20 mg.

      Give 5mg Hydralazine and repeat BP at 5 and 15 minutes

      Give another 5mg if BP has not improved after 15 minutes, continue to monitor BP

      Give 10mg if BP has not improved over another 15 minutes

      If BP still not improving, start infusion

      In pregnancy 6.25-12.5 mg slow infusion and carefully avoid hypotension
    - Nitroglycerin, (Glyceryl trinitrate) 0.6-12 mg/hr give a bolus of 0.1 mg/isosorbide dinitrate, IV infusion 1-2 mg/hr to maximum dose of 8-10 mg /hr; only when hypertension occurs with myocardial infarction, rapid tolerance occurs therefore add other oral agent quickly.
    - Labetalol IV infusion10-20 mg bolus repeated in 10 minutes then 2mg/minute(50-200mg)
  - Give above intravenous medication simultaneously with oral treatment using a CCB

The complications include:

- Hypertensive encephalopathy (headache, visual disturbances, confusion, seizures and coma)
- Unstable angina/myocardial infarction
- Acute aortic dissection
- Acute left ventricular failure
- Acute renal failure

E. Hypertensive emergencies in Children

Non-Pharmacological Treatment

- Neuroprotective measures
    - o Nurse head at 30 degrees
    - o Treat seizures
    - o Maintain normoglycemia
    - o Give oxygen
    - o Keep temperatures normal

Pharmacological

- Assess and manage Airway, Breathing, Circulation and Disability
- Reduce BP slowly in order to prevent stroke, retinal and spinal cord infarction
    - o One third of the total desired reduction in the first 12 hours
    - o The next one third in 12 to 36 hours
    - o Last one third between 36 and 72 hours
- hypertensive encephalopathy: Give Hydralazine 0.15 mg/kg slow IV
    - o Repeat every 30-90 minutes as required
    - o Maximum dose: 1.7-3.6 mg/kg in 24 hours
    - o long term management of hypertension would depend on the cause hence these patients need to be referred for proper management.
- Labetalol
    - o Loading dose 0.25mg/kg IV
    - o Then continuous infusion of 0.25mg-3mg/kg/hour
- Sodium Nitroprusside 0.5-8mcg/kg/min continuous infusion
- If patient has oedema add frusemide 1-5mg/kg IV/PO 6 to 12 hour

2. ISCHAEMIC HEART DISEASE (IHD)

This is a condition in which there is inadequate blood and oxygen supply to any portion of the myocardium

General measures

- Minimize risk factors by:
    - o Weight reduction (if obese)
    - o Control of hypertension
    - o Control of diabetes
    - o Stop smoking
    - o Address other factors such as:
        - ▪ High blood cholesterol
        - ▪ Stressful lifestyle
        - ▪ Stop use of alcohol

- Encourage regular moderate exercise

A) Stable Angina

Central chest pain (squeezing, heavy discomforts) with radiation to left arm or jaw on exertion or at rest lasting 2-5 minutes, crescendo –decrescendo pattern. Chest pain worsens with exertion and improves with rest. ECG may show ST depression, flat or T wave inversion or normal resting ECG)

Chronic disease management

- Encourage regular exercise, stop smoking, stop alcohol use.
- Aspirin 150mg daily (alternative clopidogrel 75 mg od)
- Statin e.g., Simvastatin 40 mg nocte or atorvastatin 10 mg od and adjust accordingly
- In a step wise fashion for symptom relief:
  - isosorbide dinitrate 5-10mg
  - Atenolol 50mg od
  - Amlodipine 5-10mg daily/nifedipine SR 10-20 mg daily (replace or be cautiously added to atenolol)
- If pain continues despite the above treatment refer to next level of care

Acute relief of angina

- Give glyceryl trinitrate 0.5mg sublingually as required.
  - Maximum 3 tablets per 15 minutes.
  - Deteriorates on storage: keep tablets in original container for no more than 3 months after opening.
- Alternatively use isosorbide dinitrate 5-10mg sublingually as required instead of glyceryl trinitrate.

B) Acute Coronary Syndromes

Unstable Angina/non-ST segment elevation

Central chest pain lasting more than 10 minutes and has a crescendo pattern, usually occurring during rest and associated with raised cardiac markers with ST segment depression or T wave inversion, not relieved by glyceryl trinitrate or isosorbide dinitrate

Management plan

- Aspirin 300mg stat
- Admit to HDU
- Bloods for cardiac markers (Troponin T, Creatinine Kinase-MB: CK ratio-normal should be less than 5%)
- Anticoagulation: unfractionated heparin IV 5000 IU as a bolus over 10 minutes, subsequent dose should be determined by PTT (5000-10,000 IU 4- 6 hourly) usually 30,000-35,000 IU in a day. Aim to keep PTT x2 normal. Alternatively, low molecular heparin e.g. Enoxaparin Sodium subcutaneous at 1 mg/kg 12 hour. Anticoagulate for at least 48 hours

- Pain control: IV Nitrate 0.5 mg tablet. If pain persists, give morphine 5mg as needed
- B blockers (atenolol) if not contraindicated
- If ongoing chest pain refer for coronary angiography

On discharge – chronic disease management, same as for angina

- Review after 4 weeks to assess ongoing angina, echo and clinical assessment for cardiac failure and to ensure good blood pressure control.

ST segment elevation myocardial infarction (classic MI)

Typical angina pain lasting more than 10 minutes, often associated with restlessness, anxiety and pallor. ECG shows hyper acute tall T waves, ST segment elevation. New left bundle branch block may develop and pathological Q waves occur within hours to days of an infarct.

NB: It is very important to consider other causes of chest pain before initiating treatment for acute coronary syndrome; below are the differential diagnoses:

- Cardiovascular:
  - Pulmonary emboli
  - aortic dissection
  - pericarditis
  - myocarditis
- Non-cardiovascular:
  - pneumonia
  - pneumothorax
  - muscular chest wall pain
  - oesophageal reflux
  - oesophageal rupture
  - herpes zoster
  - nerve root pain

Investigations for ischaemic heart disease

ECG* CXR*Glucose*, FBC*, Urea & Electrolytes*, Cardiac Enzymes** {Troponin I or T, CK-MB: CK ratio (cardiac isoenzyme), lipid profile**.Echo-cardiography*percutaneous coronary angiography (external referral)

**should be performed at both secondary or tertiary level facilities*

***should be performed at tertiary level facilities*

Management plan

- Aspirin 300 mg stat
- Admit in ICU

- Oxygen therapy
- Continuous ECG monitoring
- Pain control: IV Nitrate /0.5 mg tablet. If pain persists, morphine 5mg and repeat as needed.
- Beta blocker: e.g. Atenolol 50 mg OD 12 hours later
- ACE inhibitor: e.g. Enalapril 5mg BD (started after the acute event, if systolic pressure > 100 mmHg.)
- Statin, e.g. Simvastatin 80 mg nocte or atorvastatin 10mg OD
- Reperfusion therapy:
    - Thrombolysis is beneficial when given within 6 hours of myocardial infarction, make sure that there are no contraindications.

3. TRANSIENT ISCHEMIC ATTACK (TIA) & STROKE

A) TRANSIENT ISCHEMIC ATTACK

Uncontrolled hypertension is a significant risk factor for TIA and stroke. TIA presents with the following:

- Sudden onset of weakness or sensory loss of one side of the body, or of a limb
- Sudden difficulty of speaking or understanding
- Sudden disturbance of vision
- Sudden severe, unusual headache
- Sudden dizziness or unsteadiness of gait

A TIA is defined as the above symptoms lasting less than 24 hours with no long term neurologic deficits. If the patient has had persistent neurological deficits for >24 hours, diagnosis is stroke. If neurological deficits have disappeared within 24 hours diagnosis is TIA

B) STROKE

This is defined as sudden reduction of blood flow to the brain resulting in a neurological deficit corresponding to that area of the brain's function. There are 2 types of stroke: ischemic/embolic and hemorrhagic. Without brain imaging (not commonly available) you cannot distinguish between the two groups but 85% of the strokes are ischemic. In those rare cases where one needs to decide on either to start thrombolytic in the absence on CT Scan and MRI; some scoring tools like SARIRAJ STROKE SCORING may be used to differentiate hemorrhagic stroke from Ischemic.

Risk factors include hypertension, diabetes, smoking, genetic disorders, atherosclerosis, cardiac disease, atrial fibrillation, HIV and cholesterol.

Look for treatable cause and counsel the patient.

Clinical features

- Facial drooping, slurred speech, dysphasia, dragging a leg, arm/leg weakness on one side, ignoring one side of the body, unsteady gait.
- Conditions that may present similar to stroke include subdural hematoma, brain masses, meningitis and encephalitis. 25% of HIV positive strokes have a CNS opportunistic infection as a cause of stroke (START study).
- Investigations: Glucose, HIV, syphilis, full blood count, urea and creatinine, SCD workup, ECG (to look for atrial fibrillation)

Acute Treatment

- If hypertension is higher than 180/120 mmHg, start Hydrochlorothiazide 25mg once daily orally. Avoid reducing BP by > 25% to reduce the risk of cerebral hypoperfusion.
- If patient has a previous diagnosis of hypertension, continue medication. If not on medication, closely monitor the patients BPs daily for 2 weeks and if the BPs remain high then start the treatment.
- Hemorrhagic stroke proven by CT: reduce BP faster (140/90) and avoid Aspirin
- Assess safety/ability to swallow without aspirating by giving water on a spoon and then from a glass. If concerned about safety in swallowing, insert NG tube
- Give IV fluids to correct any dehydration,
- Treat hyperglycemia
- Treat any fever: look and treat for infections (aspiration pneumonia, urinary tract infection common).
- Give paracetamol 1g every 8 hours orally if febrile
- Prevent pressure sores through regular turning of the patient
- As pulmonary embolus is a common cause of death, prevent DVT by support stockings, regular leg movements and hydration. (Do not give heparin or heparin like medication to treat ischemic strokes)
    - o Start physiotherapy and speech therapy on day one and consider referral to rehabilitation unit
    - o Recurrent stroke when already taking aspirin should be referred to a specialist.

Chronic Treatment

- Rehabilitation
- Treat underlying conditions with reference to their sections, such as: syphilis, HIV, diabetes, hypertension, hyperlipidemia (simvastatin), atrial fibrillation (aspirin or warfarin)
- Give long term aspirin 75mg once daily
- All strokes/TIAs will benefit from statin therapy. Eg simvastatin (40 mg) or atorvastatin (10mg)
- Give long term statin regardless of cholesterol level
- ACE-I and thiazide started regardless of hypertension diagnosis as long as SBP >100mmHg) (Progress study- 25% risk reduction of second stroke)

4. HEART FAILURE

Clinical condition where the cardiac output and blood pressure are inadequate for the body requirements. In hypertension, heart failure can be due to hypertensive heart disease (associated with LV hypertrophy and poor diastolic function, but preserved systolic function) or to cumulative damage to LV due to ischaemic heart disease (which will impair systolic function).

A. ACUTE HEART FAILURE

The cardiac causes of pulmonary oedema include myocardial infarction and malignant hypertension. These patients will present with dyspnoea, pink frothy sputum, distress, increased jugular venous pressure, gallop rhythm, bilateral fine crackles or wheezes

Management

- Admit in ICU/HDU
- Position patient in Semi fowlers and give oxygen therapy
- Intravenous access and put on monitor to assess vital signs whilst doing an ECG to assess rhythm
- Give morphine 2.5 - 5 mg IV slowly
- Give furosemide 40-80 mg IV slowly
- If patient not responding to diuresis, consider non-invasive ventilation (CPAP) or intubation
- If systolic blood pressure is < 90mmHg give inotropic support: Dobutamine 2.5-10mcg/kg/minute as an IV infusion or Dopamine 0.5-1.0 mcg/kg/minute IV infusion(consider this in patients with potentially reversible cardiogenic shock.

B. CHRONIC HEART FAILURE

Heart failure is a syndrome and not a final diagnosis, therefore it is very important to identify and treat the cause. In hypertensive patients with heart failure, echocardiogram is extremely helpful for differentiating hypertensive heart disease with diastolic dysfunction from systolic dysfunction.

Causes of Chronic Heart Failure

- Hypertensive Heart Disease
- Rheumatic Heart Disease
- Cardiomyopathy
- Valvular Heart disease
- Right Ventricular Failure
- Pericardial Disease
- Congenital Heart Disease

Diagnosis

- History
  - Orthopnoea
  - Dyspnoea on exertion
  - Dry Cough
  - Fatigue
- Physical
  - Oedema
  - Bibasilar Crackles
  - Jugular Venous Distention
  - Cardiac Murmur
  - Tachycardia
- Investigations
  - Cardiac Echo
  - EKG
  - Lab Tests: FBC, electrolytes, urinalysis
  - Other if available: Cardiac enzymes, thyroid function tests

Management

- Treat exacerbating factors e.g. anaemia, infections, thyroid disease, and uncontrolled hypertension
- Avoid exacerbating factors e.g. use of NSAIDS, poor compliance to medication
- Lifestyle modifications e.g. stop smoking, reduce salt intake, moderate exercise and avoid excessive intake of fluids.

Congestive Heart Failure Treatment

The NYHA Class helps you understand how sick the patient is. Specifically, it tells you who is stable enough to continue outpatient management and who should be evaluated by a physician in the hospital.

Figure 2: Management of NYHA according to level of care

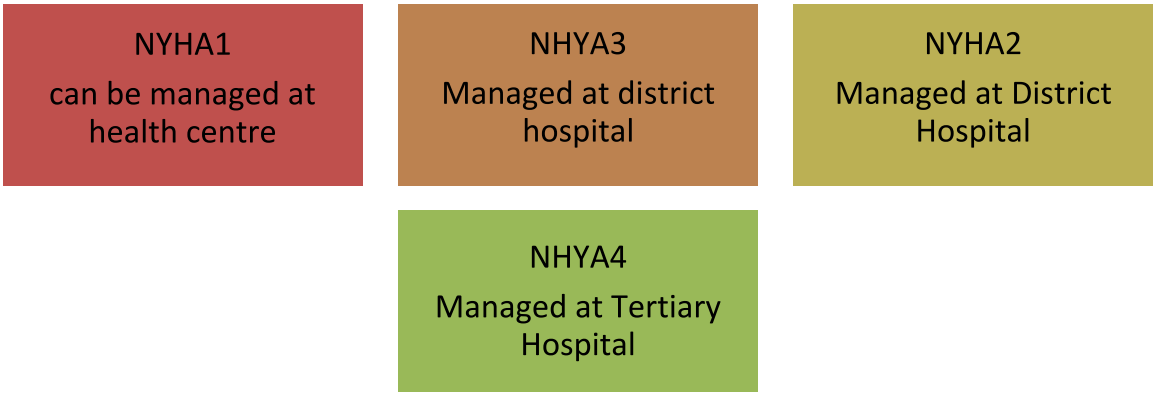


Table 8: Treatment of Heart Failure According to Class

	Medications	Treatment Considerations
NYHA Class I (Symptoms with significant exertion)	ACEi	● Check creatinine and electrolytes before starting ACE-I, if Cr >2 start β-blocker instead ● Check creatinine and electrolytes within 1 month of starting ACE-I
NYHA Class II (Symptoms with ordinary activity)	ACEi +β-blocker	● Do NOT start β-blocker in an acute heart failure exacerbation
NYHA Class III (Symptoms with minimal activity)	ACEi +β-blocker +Furosemide +Spironolactone	● Check creatinine and electrolyes within 1 month of starting Spironolactone
NYHA Class IV (Symptoms at rest)	ACEi +/R-Rblocker +Furosemide +Spironolactone +Digoxin*	● Consider stopping β-blocker as it may worsen symptoms by reducing heart rate and cardiac output ● Check creatinine and electrolytes before starting Digoxin, if Cr >1.2 use an alternative agent ● *Digoxin has significant side effects and is difficult to monitor, ONLY add if patient has poor symptom control OR atrial fibrillation

Ensure that HR>50, systolic BP>90 and diastolic BP>50 before start ACE-I or β-blocker

Medication	Class	Starting Dose	Increase Dose By	Maximum Dose	Contraindications
Enalapril (5m tab, 20 mg tab)	ACE-I	5mg OD	5-10mg	40mg OD	Renal failure Hyperkalemia
Atenolol (50mg tab)	B-blocker	50mg OD	50mg	100mg OD	Bradycardia
Bisoprolol (tab)	B-blocker				Bradycardia
Propranolol (40 mg tab)	B-blocker				Bradycardia
Furosemide (40 mg tab)	Loop diuretic	5-10mg OD	5-20mg	80mg BD	Renal failure
Spironolactone (25mg tab)		25mg OD	25mg	100mg QD	Renal failure Hyperkalemia

Medication	Class	Starting Dose	Increase Dose By	Maximum Dose	Contraindications
Digoxin (250 microgram tab)		0.125mg OD	0.125mg	0.25mg OD	Renal failure Bradycardia Arrhythmia

Additional Considerations

- Diurese for symptom relief using furosemide and spironolactone
- Use B-blockers if tachycardic
- ACE-I and B-blockers should be used if EF < 40% to reduce cardiac remodelling and improve survival.

5. RHEUMATIC HEART DISEASE

Rheumatic Heart Disease develops due to a streptococcal infection (rheumatic fever). If the bacteria enters the blood stream it can spread to the heart valves, most commonly the mitral valve. Repeated infections can cause mitral valve stenosis or regurgitation. Patients can be asymptomatic for many years before developing rheumatic heart disease.

Diagnosis

- History
  - Symptoms of chronic heart failure
  - History of streptococcal infections
- Physical
  - Edema
  - Systolic heart murmur
  - Bibasilar crackles
  - Jugular venous distension
- Cardiac Echo

Rheumatic Heart Disease Treatment

- Penicillin
  - Benzathine Penicillin
    - Children <15 y/o and <20 kg: 600,000 units every 4 weeks
    - Adults: 1.2 million units every 4 weeks

- Penicillin V
  - Children <15 y/o and <20kg: 250mg po bid
  - Adults: 500mg po bid
- Treat symptoms by NYHA classification as above

6. CONGENITAL HEART DISEASE

Congenital heart disease encompasses a series of cardiac abnormalities that are present upon birth.

- Transposition of the great arteries
- Tetrology of Fallot
- Coarctation of the aorta
- Bicuspid aortic valve
- Atrial/septal defect
- Ventricular/septal defect
- Eisenmenger's syndrome
- Patent Ductus Arteriosis

HYPERTENSIVE DISORDERS IN PREGNANCY

A) Pregnancy Induced Hypertension

At Health Centre

- Blood Pressure ≥ 140/90mmHg or an increase of Systolic BP of 20 and Diastolic BP of 15 from pre pregnancy levels.
- Recheck Blood Pressure after resting for 10 - 15 minutes
  - If still raised:
    - Refer to the next higher level if it's severe PIH, Pre-eclampsia and eclampsia with accompaniment of health personnel.
    - In case of eclampsia or eminent eclampsia; give a loading dose of 4g magnesium sulphate 20% solution in 500 ml of normal saline infused over 10 minutes plus 5 g of magnesium sulphate 50 % I each buttock deep IM with 1 ml of 1% lignocaine

At the hospital

- Admit
- Re-assess the patient and exclude severe forms.
- If it's Pregnancy Induced Hypertension (PIH)
- Give Methyldopa 500mg to 1g q8h until BP settles. If no improvement, add Nifedipine SR po to a maximum of 40 mg tds

B) Pre-eclampsia

- Raised BP ≥ 140/90mmHg, proteinuria ≥+ dipstick, ± oedema gestation ≥ 20 weeks

Treatment

- *If signs of pre-eclampsia*
  - Admit, evaluate and take full history,

- Check for signs of imminent eclampsia, check weight, urine dip stick daily, and BP every 4 hours
- Evaluate wellbeing and gestation. Do ultrasound

- *If diastolic BP >90mm Hg and <110mm Hg then give*
  - Methyldopa 500mg to 1g tds and review daily

- *If diastolic >110mm Hg*
  - Do not lower BP abruptly and avoid use of sublingual nifedipine
  - Give Hydralazine 5mg IV slowly over 5 min.
  - Repeat every 20 minutes until diastolic pressure is below 110 mm Hg.

- If *diastolic* BP is still >110
  - Give Hydralazine 40mg IV in 1 litre of Ringer's Lactate over 8 hours to maintain BP at below 110 mmHg.
  - *Alternatively*
    - Give Nifedipine 10mg. Recheck BP in 20 minutes. Repeat nifedipine if diastolic ≥110mmHg, manage as severe preeclampsia.
    - Watch carefully for eclampsia: If this develops *see section for eclampsia*
  - *Consider delivery regardless of gestational age if:*
    - BP is difficult to control
    - Urine output is decreasing Critical signs/symptoms persist (suggesting severe pre-eclampsia)
    - Develops eclampsia

D. Severe Eclampsia

- *Diastolic BP* >110, marked oedema, proteinuria ++/+++, headache, blurred vision, epigastric pain, oliguria, hyper-reflexia

Management

- Admit in labour ward
- Put up an IV line normal saline
- Give 4g of 20% of Magnesium Sulphate solution IV over 5 minute period (20 mls)
- Administer 5g of 50%MagnesiumSulphate (20mls) with 1ml of 1% Lignocaine IM deep in each buttock (total 10 g)
- Catheterize
- Monitor BP every 15 minutes until BP is lowered, then hourly
- In theeventof a convulsion after 15 minutes administer2g of 50% Magnesium Sulphate solution IV over 5minutes (4mls)
- Monitor foetal heart every 30 minutes
- Refer to hospital labour ward and the midwife to escort the woman

Fetal Wellbeing or Maturity

- Check
  - Full blood count, Urea & creatinine in serum
  - Liver function tests
  - Electrolytes: sodium, potassium, and chloride
    - Refer to central hospital if lab results are deranged
- *If >34 weeks gestation*:
  - Stabilize patient
  - Delivery within 24 hours either by induction, if cervix is favourable, or by caesarean section
- *If <34 weeks gestation*:
  - Inform clinician
  - Assess foetal wellbeing using Ultrasound scan or Cardiotocograph
  - Give Dexamethasone 6mg every twelve hours IM for 4 doses
  - *Alternatively*
    - Betamethasone 12mg IM once daily for a total of 2 doses

D. Eclampsia

- Convulsions
- Diastolic BP 90 mm Hg or more after 20 weeks' gestation
- Proteinuria 2+ or more

Note: Convulsions can occur prior to labour, intrapartum or postpartum.
If a pregnant woman convulses start treatment for eclampsia, but rule out other organic causes, including Epilepsy, Meningitis, Cerebral malaria, Encephalitis, Hypoglycemia

Management

- Place the woman on her side to reduce risk of aspiration
- Secure airway, aspirate secretions or vomitus
- Give adequate oxygen supply by nasal prongs or face mask
- Protect the woman from injury
- Put up an IV line normal saline
- Control convulsions with magnesium sulphate (see dose below)
- Give 4g of 20% of Magnesium Sulphate IV over 5minute period (20mls)
- Administer 5g of 50% Magnesium Sulphate(20mls) with 1ml of 2% Lignocaine IM deep in each buttock (total 10 g)
- Catheterize
- Monitor BP every 15 minutes until BP is lowered, then hourly
- In the event of a convulsion after 15minutes administer 2g of 50% Magnesium Sulphate IV over 5 minutes (4mls)
- Monitor foetal heart half hourly

Treatment

- Closely monitor for signs of magnesium sulphate toxicity such as presence of patella reflexes, the respiratory rate (not less than 16), and urinary output should not be less than 25mls an hour.
- Continue magnesium sulphate for 24 hours post-delivery or 24 hours after the last convulsion whichever was the last
- Maintenance dose: Magnesium sulphate 5 g of 50% solution every 4 hours deep IM till 24 hours post-delivery or 24 hours after the last convulsion which ever was the last. Addition of 1.0ml of 2% lidocaine minimizes discomfort

Note: Once magnesium sulphate is administered a decision must be made to deliver the pregnant woman within 12 hours

- *If magnesium sulphate is not available give*
  - Loading dose of Diazepam 10mg IV slowly over 2 minutes
  - Maintenance dose of Diazepam 40mg in 500mls of normal saline or Ringer's Lactate
  - Do not give more than 100mg in 24 hours
  - If not already at hospital, refer the patient to hospital

RED FLAG: In case of magnesium sulphate toxicity administer calcium gluconate 1gm as IV stat dose and stop magnesium sulphate

Mode of delivery

- Carry out an obstetric assessment to decide on appropriate mode
- Only allow assisted vaginal delivery if labour is progressing quickly
- Consider caesarean section if unlikely to deliver in 6-12 hours regardless of gestational age
- Give Oxytocin 10 IU (1mL amp) by IV push in the 3rd stage
- Do not use ergometrine

Monitoring

- Continue careful observation (and treatment if necessary) for at least 48 hours after delivery

CHAPTER

DIABETES MELLITUS 3

WHAT IS DIABETES?

- Diabetes Mellitus is a disorder of metabolism where the body is not able to regulate the glucose levels in the blood. Diabetes Mellitus results from defects in insulin secretion, action or both This usually leads to high glucose levels in the blood, which ultimately leads to damage to the blood vessels and organs of the body.

Where does glucose in the blood come from?

Our diet: Sugary foods and drinks and carbohydrate are digested and absorbed into the blood as glucose

Glucose is also made in the liver by a process of GLUCONEOGENESIS and secreted into the blood.

Glucose is stored in muscle as glycogen. Glycogen can be broken down by a process called GLYCOGENOLYSIS, which releases glucose into the blood.

Figure 3: How Glucose is Normally regulated

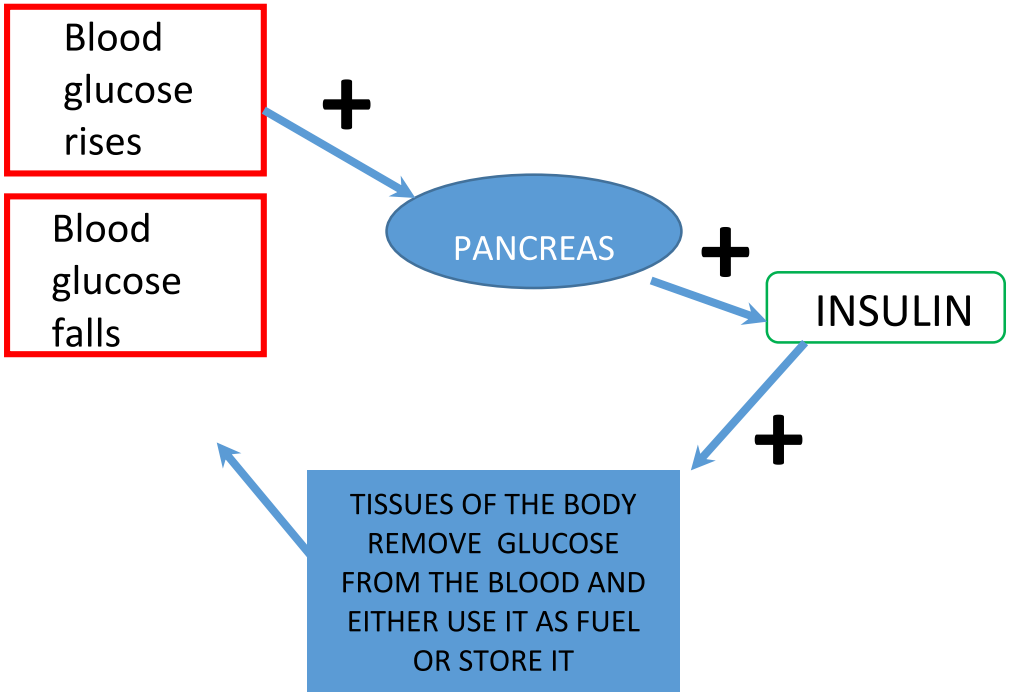
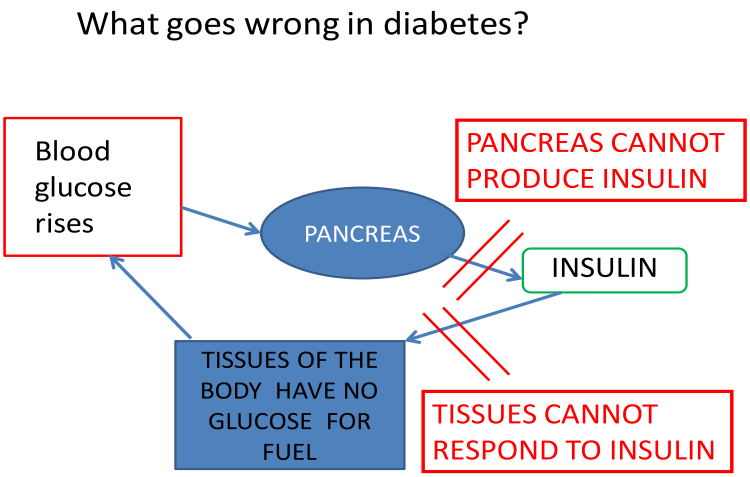


Figure 4: What goes wrong in Diabetes



TYPES OF DIABETES

1. TYPE 1 (INSULIN DEPENDANT)

- Autoimmune disease, causing destruction of pancreatic islet cells
- Usually <30 years, but not always
- Usually, lean weight
- Onset is acute- usually from 6 months of age
- Almost always symptomatic (eg. polyuria, polydipsia, polyphagia and weight loss)
- Prone to ketosis, often ketoacidosis at diagnosis
- Insulin dependent

2. TYPE 2

- Non-autoimmune disease due to decreased insulin sensitivity
- Usually older, but prevalence in children, adolescents and young adults increasing
- Mostly overweight or obese
- Onset is gradual and can be asymptomatic
- Not usually prone to ketosis
- Usually controlled by non-insulin therapies (20% may require insulin)
- Often has comorbidities (hypertension)
- Often has family history of type 2 diabetes

3. GESTATIONAL

- Onset during pregnancy
- May not resolve after pregnancy

4. OTHERS

- Infections e.g. HIV
- Pancreatic diseases e.g. pancreatitis secondary to alcohol use, trauma, pancreatic cancer
- Drugs e.g. corticosteroids, protease inhibitors.

DIAGNOSIS AND SCREENING

Screening for diabetes is based on a selected criterion (Table 9). However, if a person does not meet the criteria but is presenting with signs and symptoms of diabetes they are eligible to get screened.

Table 9: Screening Criteria for Diabetes

ASYMPTOMATIC ADULTS CRITERIA FOR SCREENING FOR TYPE 2 DIABETES	SYMPTOMATIC ADULTS AND CHILDREN ALSO SCREEN FOR DIABETES IF ANY OF THE FOLLOWING
High risk individuals ▪ All adults (any age) with body mass index (BMI) ≥ 25 kg/m2 (overweight or obese), plus one or more additional risk factors: ▪ Physical inactivity ▪ Hypertension [blood pressure (BP) ≥ 140/90 mmHg] ▪ Family history of diabetes ▪ Dyslipidemia ▪ Polycystic ovarian syndrome ▪ High-risk ethnic group e.g. those of South Asian descent ▪ Cardiovascular disease history ▪ Gestational diabetes or baby weighing >4 kg ▪ Previous impaired fasting glucose or impaired glucose tolerance ▪ Other conditions associated with insulin resistance e.g. Cushing's syndrome ▪ HIV **Low risk individuals** ▪ If no risk factors: Age ≥ 45 years	▪ Frequency of urination, penile/vagina thrush, recurrent infections e.g. boils, abscess, unhealed wounds, abnormal sensation of the feet (pins and needles, tingling, burning) ▪ Thirst, progressive visual loss, unexplained weight loss despite good appetite ▪ Presenile cataract, ▪ Retinopathy suggestive of diabetes ▪ Lethargy, weakness, unconsciousness

FREQUENCY OF SCREENING

▪Annually if normal
▪Abnormal with no symptoms, repeat after 1 month

DIAGNOSING DIABETES

1. Diagnosis in symptomatic individuals

- A single abnormal test is sufficient to confirm the diagnosis of diabetes in patients who have the classic symptoms of hyperglycemia (i.e. polyuria, polydipsia and weight loss), diabetic ketoacidosis or hyperglycemia hyperosmolar state (HHS- previously hyperosmolar non-ketotic hyperglycemia (HONK).
- It is very important to rule out stress related hyperglycemia in hospital admitted patients by using FBG/RBG after discharging patient from the hospital.

2. Diagnosis in asymptomatic individuals

If the patient has no symptoms they need two abnormal blood glucose measurements, done on 2 separate occasions. If a patient has 1 normal and 1 raised FBG they should be screened again after 3 months while taking a normal diet

CLINICAL PRESENTATION OF DIABETES

Typical symptoms of high sugar:

- Frequent urination (polyuria)
- Excessive thirst (polydipsia)
- Dizziness
- Weight loss (mostly type 1 diabetes mellitus)
- Tiredness
- Blurred vision
- Numbness and/or burning pain in the legs.
- Recurrent infections
- Complications e.g. visual loss, cataracts or foot numbness/sores
- Asymptomatic

Table 10: Diagnosing Diabetes and Other Hyperglycemic State Using Venous Plasma Glucose

	Plasma venous* glucose Mmol/L (mg/dL)
Diabetes Mellitus fasting and/or 2 hours postprandial/random	≥ 7.0 (126) ≥ 11.1 (200)
Impaired glucose tolerance (IGT) fasting AND 2 hours post glucose	< 7.0 (126) 7.8 – 11.0 (140-199)
Impaired fasting glucose (IFG) fasting AND 2 hours post glucose	5.6 - 6.9 (100 – 125) < 7.8 (140)

NOTE

- Random (casual) plasma glucose cannot be used to diagnose IFG or IGT.
- Capillary blood glucose from a finger prick tends to be higher than venous glucose so if using a capillary sample for diagnosis the corresponding values for the 2-hour measurements are as follows: for diabetes mellitus, 2 hours ≥ 12.2 mmol/L (> 220 md/dL); for IGT, 2 hours ≥ 8.9 mmol/L (≥ 160 md/dL) and < 12.2 mmol/L (< 220 md/dL).
- Blood glucose control for past 3 months in diabetic patients is determined by HBA1C and above 6.5 is considered poorly controlled Diabetes. This is an investigation that should be available for follow up of all Patients with Diabetes to determine whether they are doing well on medications or not.

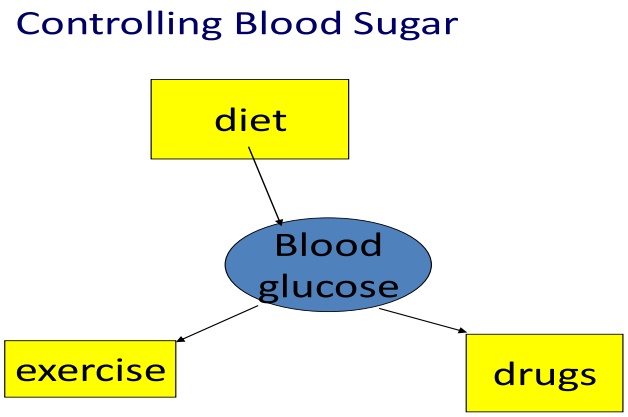
MANAGING DIABETES

Diabetes is best managed by a multidisciplinary team, which includes not only healthcare professionals, nutritionists and psychosocial counselors, but also the patient and their family. Evidence for extending the team beyond the physician comes from studies showing the benefits to patient outcomes of patient education and of interventions by nurses.

Table 11: Treatment Target

Patient type	Fasting Plasma Glucose (FPG) mmol/L (md/dL)	Random Plasma Glucose (2hrs PPG) mmol/L (md/dL)	HbA1c %
Most patients	4.4 - 6.1 (80-110)	4.4-8.0 (80-145)	≤ 6.5
Elderly or poor short term prognosis	7.0 – 9.0 (126-162)	<12.0 (<216)	not indicated
Pregnant Women	< 5.5 (100)	< 7.0 (126)	≤ 6.5

Figure 5: Cornerstone of Controlling Blood Glucose



PATIENT EDUCATION

1. SELF MANAGEMENT EDUCATION

- Basic knowledge of diabetes: try to explain this in simple vernacular language
- Causes of diabetes
- Signs and symptoms
- Treatment
- Importance of compliance to treatment and good glycaemic control
- Signs of impending danger signs and symptoms of acute complications such as hypoglycaemia, HHS and DKA
- Recognition and management of chronic complications
- Foot care
- Insulin injection technic and sites of injection for insulin dependent diabetes mellitus
- Sick day management in insulin dependent diabetes mellitus
- Exercise in insulin dependent diabetes mellitus

- Life style modification: diet, physical exercise, cessation of smoking and alcohol
- Psychosocial counselling and family support

*Refer to NCD Job Aids for Chichewa patient education

2. DIETARY EDUCATION

Diet education is aimed at providing information on the locally available foods that the patient can afford. Emphasis is on eating a balanced meal that consists of the six food groups and **Portion size matters** (Table 12)

Table 12: Examples of Food to be taken

HEALTHY DIET	UNHEALTHY DIET
Avoid sugar and fizzy drinks Eat breakfast, lunch and evening meal- evenly distributed throughout the day, with in between meals snacks e.g. fruits, brown bread sandwich Drink enough safe/clean water, approximately 2 liters per day Use unrefined food/cereals (whole grain) Eat fresh fruits and vegetables every day No need for special diabetes food or nutritional supplement products Be careful with alcohol which can make you very ill because it lowers blood sugar levels (if on insulin or sulphonylurea tablets). Avoid alcohol intake.	Excessive carbohydrates Excessive sugars Excessive fats and oils Excessive animal fats Excessive salt Excessive red meat Ready-made (processed) or street food is unhealthy with a lot of fat and salt, home cooked food is better

1. EDUCATION ON PHYSICAL ACTIVITY

- Engage in regular physical exercise (e.g brisk walking) for 30 minutes per day, on 5 days of the week.
- Advise to eat before physical activity.

DRUG TREATMENT OF DIABETES MELLITUS

Pharmacology of drugs that lower blood glucose

I. SULPHONYLUREAS

Glibenclamide

- Mechanism of action: Stimulates pancreatic β cells

- Elimination: Glibenclamide is renally excreted
- Dose range: 5 mg od to 10 mg bd
- Side effects: weight gain

Main risk of glibenclamide is hypoglycemia
Caution in elderly and those with renal impairment

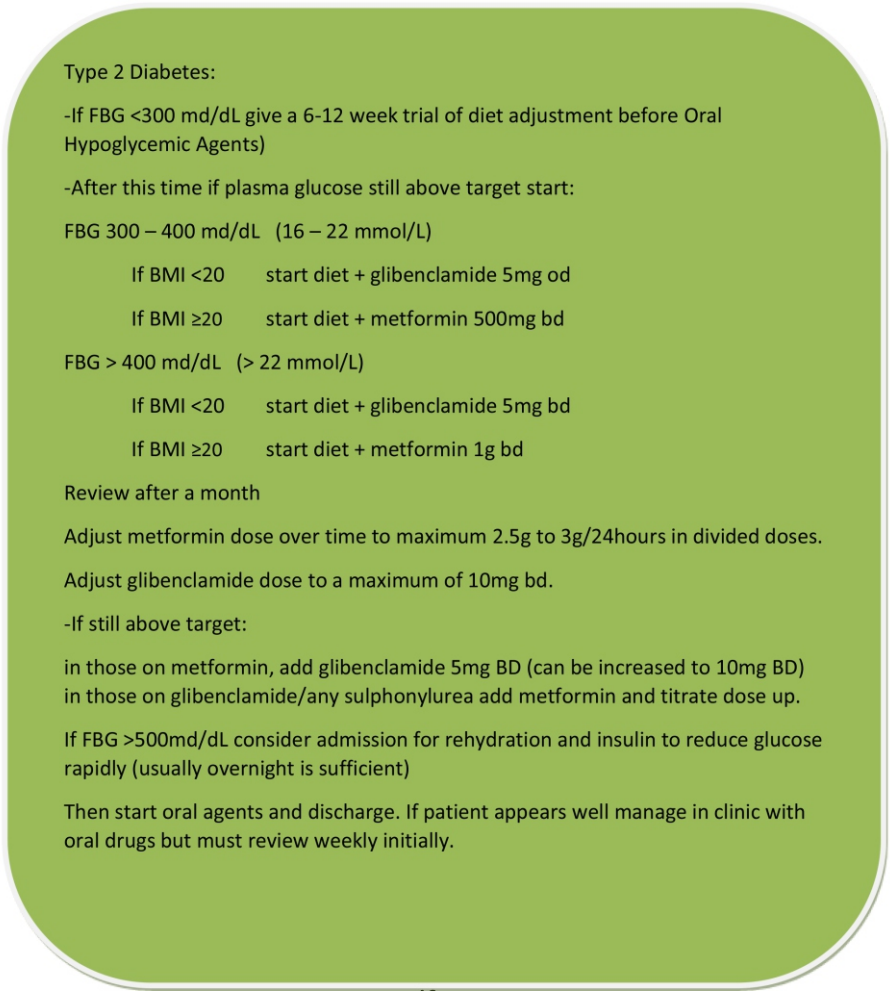
II. BIGUANIDES

Metformin

Mechanism of action: increases peripheral insulin sensitivity, hepatic effects (on glycogenolysis), malabsorption of glucose, promotes weight loss
Elimination: Metformin is renally excreted
Dose range: 500mg od to 1g tds
Side effects: diarrhea, nausea

Most serious risk of metformin is lactic acidosis
Contraindicated in renal impairment (creatinine >1.5 md/dL)
Contraindicated in acute illness, fasting, severe CCF or liver failure

Figure 1: Starting medication for in type 2 Diabetes



NOTE:

- Avoid metformin in congestive cardiac failure and renal failure
- Maximum dose of metformin in patient on DTG is 1gm per day
- If the patient is on maximum oral antidiabetic medication, the diet is OK, adherence is good and the FBG is still >150 md/dL, then patient will need to switch to insulin.
- A patient who is gaining weight and has poor glycemic control is probably not adhering to lifestyle advice. Revise lifestyle before considering insulin.
- At least 20% of type 2 DM need insulin
- If available check HbA1C before considering insulin
- If the patient is obese use insulin PLUS metformin (except in patients with creatinine of >2 md/dL)
- Diabetes education remains the cornerstone in management of all forms of diabetes including Type 1 diabetes mellitus.

III. INSULIN

NPH/cloudy- onset of action is 2-4hrs, peak is 4-10hrs and duration is 10-18hrs
Soluble/clear/actrapid – onset of action is 30-60min, peak is 2-3hrs and duration is 5-8hrs
Most serious side effect is hypoglycemia
Also causes weight gain: therefore in obese diabetics who need insulin, combine insulin+ metformin.

Treatment of Type 1 Diabetes (Insulin Dependent Diabetes)

- ✔ Start with 0.5units/kg/day as total insulin for your patient given subcutaneously.
- ✔ Make sure that 2/3 of total insulin is intermediate acting insulin (NPH) and 1/3 should short acting insulin.
- ✔ Divide intermediate insulin dose into 2/3 in the morning preferably before breakfast and 1/3 in the evening preferably before supper. The principle is to give less evening doses of intermediate insulin to prevent nocturnal hypoglycemia which could be lethal to the patient.
- ✔ The short acting insulin dose should be divided into 3. Thus taking into consideration that we take 3 standard meals per day. Adjustments can can be done if the HCW has an understanding of quantities of meals at breakfast, lunch and supper. Thus giving more when patient eats more.
- ✔ It should be made clear that short acting insulin/ soluble insulin is given 15 to 30 minutes before a meal.
- ✔ If patient eats 3 times a day, inject intermediate insulin (NPH) twice and 3 boluses of soluble insulin
- ✔ If patient eat once, inject intermediate insulin (NPH) twice a day and soluble insulin once at meal time.
- ✔ T1DM Patient should inject Intermediate insulin (NPH) whether there is food or not and short acting insulin will only be given with meals.

- ✔ Insulin will be adjusted accordingly with subsequent visits depending on response with all factors taken into consideration such as diet injection technique, expiry dates of insulin and quality injection sites as well as progression into puberty which also increases insulin demand of the body.
- ✔ In case of available premixed insulin (which usually contain 30% short acting and 70% intermediate acting or 40% to 60% respectively) insulin should be administered twice a day only. Thus if no short acting insulin is available.
- ✔ If short acting/Soluble insulin is also available, give premixed insulin twice (am and pm) and a dose of short acting/soluble insulin at lunch if patient is taking lunch.
- ✔ For school going children make sure they are injecting a dose of short acting/ soluble insulin at lunch only if they are eating a substantial quantity of food. Otherwise they should carry a health snack for lunch with less sugar or carbohydrate which does not require insulin injection.
- ✔ Exercise increases insulin sensitivity, make sure that patients have checked their glucose level before and after exercise and doses can be adjusted depending on level of blood glucose.
- ✔ Sick children with T1DM should NOT ommit/stop insulin. Acute illness causes stress which leads to production of hormones that decrease the effect of insulin in the body.

When should aspirin be given?

Aspirin 75 mg od should be given for:

a) Primary prevention: hypertensive diabetic patient aged 45 years
b) Primary prevention: any patient with diabetic nephropathy
c) Primary prevention: patients with diabetes in pregnancy- to prevent preeclampsia
d) Secondary prevention: In previous ischaemic stroke, Myocardial infarction (MI), Peripheral Vascular Disease

If someone is intolerant to Aspirin, give Clopidogrel (this is not given in pregnancy)

MANAGING DIABETES IN PREGNANCY

Type 2 diabetes is increasingly common in women of childbearing age and can have a devastating impact on the growing baby. All women with the potential to become pregnant need to have good pre-conceptual care to avoid significant risk of fetal malformations and early fetal loss. This includes:

- Pre-conceptual counselling, including complication screening, and where appropriate, contraception advice until targets have been achieved Optimising glycaemic control, preferably with a normal HbA1c
- Folate supplementation (5 mg/day)
- Stopping statins and reviewing antihypertensive medications to avoid those contraindicated in pregnancy especially ACEIs.

- Replacing oral hypoglycaemic agents with insulin therapy wherever possible.
    - Insulin requirements are lower in the first trimester and can drop in the third trimester, so close monitoring and adjustment of insulin therapy is necessary
- During pregnancy, tight glycaemic control and close obstetric monitoring is required, with early intervention where necessary.
- Eyes should be tested for retinopathy and its progression in each trimester.

Table 14: Optimal Management in Pregnancy

ANTENATAL VARIABLE DOSE, BASAL BOLUS REGIME: SOLUBLE INSULIN GIVEN SUBCUTANEOUSLY TIMES:07H30, 11H30,16H30 (TDS)-GIVEN ½ HOUR BEFORE MEALS		
Blood glucose mmol/l	60 KG	60-90 KG
<4.0	0 units	0 units
4.1-6.0	4 units	6 units
6.1-8.0	8 units	12 units
8.1-10	12 units	18 units
10.1-12	16 units	24 units
>12	20 units	32 units
ANTENATAL BASAL BOLUS REGIME: LENTE INSULIN GIVEN SUBCUTANEOUSLY TIME:21H30		
<6.0	0 units	0 units
6.1-8.0	4 units	6 units
8.1-10	8 units	12 units
10.1-12	12 units	18 units
>12	16 units	32 units

POST NATAL VARIABLE DOSE, BASAL BOLUS REGIME: SOLUBLE INSULIN GIVEN SUBCUTANEOUSLY (only in IDDM) X 24 HRS TIMES:07H30,11H3016H30 GIVEN ½ BEFORE MEALS		
Blood glucose mmol/l	60 KG	60-90 KG
<6.0	0 units	0 units
6.1-8.0	4 units	6 units
8.1-10	8 units	12 units
10.1-12	16 units	18 units
>12	24 units	24 units

POSTNATAL BASAL BOLUS REGIME: LENTE INSULIN GIVEN SUBCUTANEOUSLY TIME:21H30		
>6.0	2 units	3 units
6.1-8.0	4 units	6 units
8.1-10	8 units	12 units
10.1-12	16 units	18 units
>12	24 units	24 units

NB: All known Insulin dependent diabetics (KIDD) must have insulin.

DIABETIC EMERGENCIES

a. Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is characterised by uncontrolled hyperglycaemia, metabolic acidosis and increased total body ketones.

Diabetic ketoacidosis management

- ABCCCD: give oxygen to patients with circulatory impairment or shock.
- Fluid replacement
- If in shock give 10 ml/kg 0.9% saline over 1 hour
- Fluid requirement = maintenance (for 48 hours) + deficit
- Deficit (ml) = % dehydration x weight (kg) x 10
- Do not calculate above a 7.5% deficit
- Correct over 48 hours
- Do not include bolus fluids in this calculation unless a total of 20 ml/kg or more has been given
- Insulin therapy
    - o Should be short acting, soluble, 'clear'
    - o Ideally administered via a syringe pump
    - o Start IV at 0.05 units/kg/hour
    - o Once RBS <15 mmol/l change fluid to 0.9% saline and 5% dextrose. Do not reduce the rate of insulin.
- Potassium replacement
- Needed for every child in DKA if they are passing urine
- Add KCL to IV fluids (20 mmol to each 500 ml bag)

Investigations

Blood glucose, urea, electrolytes (calculate anion gap [Na-Cl-CO2]), creatinine, bicarbonate, osmolality (can be calculated from 2X (Na+K) +urea+glucose, all units in mmol/L), (Blood gases), FBC, (blood culture, chest X-ray if infection suspected)

Urine and serum ketones, urine microscopy

Fluid management

Fluid deficit 4-6 litres
Give 0.9 % normal saline, 1 litre stat, 1 litre over 2 hours, 1 litre over 4 hours, 1 litre over 8 hours and 1 litre 12hrly
Use 5 % dextrose if blood glucose <15 mmol/L as it is important to continue to give insulin if the patient is still acidotic

Be cautious with fluid management in patients with heart failure

Note: Child is usually approx. 7.5 to 10 % dehydrated. Deficit is calculated as % body weight loss. Maintenance is calculated as per shown below

Maintenance requirements are as follows:

- o First 10 kg body weight 100mls /kg /day
- o Next 10 kg body weight 50mls/kg/day
- o Each kg thereafter 20mls/kg /day.

For example:

- o Comatose child weighing 20kg on admission in shock in DKA X 10ml/kg bolus needed to correct shock = 2 X 200 = 400mls
- o Maintenance is 1.5L/ day (1000mls +500mls}
- o Deficit= 20kg X 7.5% = 1.5L (one litre weighs1kg}
- o Requirement over 48 hours
- o Maintencance (1.5 +1.5L} +deficit(1.5L} minus bolus (400} 4.1L +/48hours = 85ml/hr

Add KCl to IV fluids when patient urinates and peripheral circulation has improved.

Potassium replacement

Table 16: Potassium Replacement Guide

Potassium level (mmol/L)	Potassium replacement (mmol/L)
<3	40
3-4	30
4.1-5	20
5.1-6	10
>6	Do not give

NB: Monitor potassium 4 hourly

Withhold potassium in first litre and do not give > 20mmol/L of K^+ over 1 hour

Insulin

- Give Insulin Via insulin infusion pump:
  - 1 vial (10 mls) of soluble insulin contains 1000 iu of insulin
  - Mix 50 iu of soluble insulin (0.5 ml) with 50mls of normal saline in a 50cc syringe
  - Start insulin infusion at 0.1iu/kg/hour (e.g. 70 kg patient give 7 iu)

NB: use 5 % dextrose if blood glucose <15mmol/L

2) If no pump give IV bolus insulin hourly (Do not give IM insulin)
Load with 10 iu **soluble** insulin intravenous

Blood glucose md/dL (mmo/L) Checked 2 hourly	Dose of soluble insulin IV	Type of fluid
< 200 (11)	5	5% dextrose
200-299 (11-16.5)	5	NS 0.9%
>300 (16)	10	NS 0.9%

*Important to avoid "stacking" insulin. Do not give 10u every one hour without monitoring blood sugars.

- If no pump, can create insulin drip. Mix 50 units of insulin in a 50cc bag of saline and titrate insulin as needed.

When to switch to scheduled insulin

- Patient is out of DKA evidenced by; no ketones in serum and urine and normal acid base balance (pH and bicarbonate). In our context when there is 2++ or less ketones in the urine and patient is well and eating.

- Use the rule of 2/3 and 1/3 and titrate according to insulin requirements

Note: Patient should continue with their NPH insulin as before whilst still on the iv insulin.

a. Hyperglycaemic Hyperosmolar state

The hyperglycaemic hyperosmolar state (HHS) is characterised by the slow development of marked hyperglycaemia (usually > 50 mmol/L), hyper osmolality and severe dehydration

Hyperglycemic hyperosmolar state management

Rehydrate over 48 hours with 0.9 % normal saline at half rate of fluids given in DKA patients

Wait for 1 hour before giving insulin, usually with small doses e.g. 1 iu/hr if using infusion pump and 10 iu soluble insulin is usually enough.

Table 15: Differences between DKA and HHS

	DKA	HHS
Precipitants	Infection Non-compliance on insulin	Infection Myocardial infarction Cerebrovascular accident
Signs and Symptoms	Usually type 1, younger patients, acute onset Dehydration Hyperventilation Smells of ketones Lethargy Weakness Loss of Consciousness	Usually type 2, older patients, gradual onset Severe dehydration Focal neurological signs may be present Lethargy Weakness Loss of Consciousnees
Serum and urine ketones	Strongly positive	Usually negative/weakly positive
Blood glucose	Raised	Markedly raised
Serum pH	Decreased	Usually normal
Serum bicarbonate	Low	Usually normal

COMPLICATIONS OF DIABETES

A. HYPOGLYCEMIA

Blood glucose of <40mg/dL (2.5 mmol/L)

Causes of hypoglycaemia and response

1) Insulin or sulphonylurea

At the beginning of treatment, the doctor should start with a low dose and gradually increase, adjusting the dose carefully.

2) Decrease, delay or omission of meals

Patients should have a stable amount of food, regular meal times and should decrease drug dosage if they cannot tolerate their usual amount of food.

3) Increase of physical exercise

Extra complex carbohydrates should be eaten before exercising.

4) Excessive alcohol intake, particularly without food

Symptoms tremor, tachycardia, palpitations, sweating, faintness, anxiety, hunger, weakness, headache, disturbed intellect, amnesia, paralysis, seizures, coma

Management

- If patient is alert, start with oral sugar: mix sugar with water or juice/soda
- If patient not alert and awake
  - o If available, use glucagon injection
  - o Otherwise 50 mL of 50 % dextrose repeat until blood glucose is 5-10 mmol/L. Maintain on 5% dextrose for a minimum of 48 hours if a patient is on sulphonylureas because of its duration of action. Once patient is awake feed them with a carbohydrate meal.

B. INJECTION SITE COMPLICATIONS

Lipoatrophy, fibrosis infection are common in patient using poor technique of insulin injection, therefore advise the patient to rotate sites of insulin injection. Inspect injection sites at each clinic visit. Injection site complications lead to poor control.

Sites of insulin injection

- Belly
- Front of thighs
- Back of upper arms
- Upper buttox

C. MACROVASCULAR COMPLICATIONS

Microvascular complications are more likely in those with hypertension, hyperlipidemia and those who smoke. These vascular risk factors should all be addressed as part of general management. Patients who have microvascular complications should be treated with aspirin 75mg od.

I. Ischemic heart disease

Myocardial infarction is common in diabetes and tends to be silent

NB: for management see under cardiac disease section

II. Stroke

Twice as common in diabetes

NB: for management see under cardiac disease section

III. Peripheral Vascular Disease

Occlusive disease of the arteries of the lower limb. Most common cause is atherosclerosis. Others include arteritis, aneurysm + embolism.

Has both acute and chronic presentation

Symptoms

- Intermittent claudication: reproducible pain in calves on exercise which is relieved by rest. Pain can also reproduced by elevating the leg,
- A burning or aching pain in the feet (especially at night)
- Cold skin/feet
- Increased occurrence of infection
- Non-healing ulcers
- Asymptomatic

Remember the 6 Ps; Pain, Pallor, Pulseless, Perishing cold (Poikilothermic), Paresthesia, Paralysis

On examination, feel the pulses, listen for bruits.

Carry out ABPIs (check Appendix 5)

If there is critical stenosis of more than 60, impending acute ischemic limb: rest pain, ischemic ulceration, gangrene

Management

- Risk factors modification: smoking cessation, look for trophic changes and foot sores, rigorous glucose control, BP reduction (See hypertension management), lipid lowering, smoking cessation, exercise (45-60mins 3x weekly)
- Claudication exercise rehabilitation program
- Medical therapy: antiplatelet therapy e.g. aspirin/clopidogrel
- Refer for surgery if poor response to medication (by symptoms).

D. MICROVASCULAR COMPLICATIONS

I. Diabetic Nephropathy

Common cause of end stage kidney disease, therefore it is of paramount importance to screen for early signs of nephropathy. Microalbuminuria (30-300mg albumin) indicates early renal disease, the test can be positive while urine dipstick for protein is negative. Therefore, test regularly at 3-6 month intervals (Use urine dipstick for proteins in our context). All patients with proteinurea/albuminurea on two consecutive occasions should be considered to have diabetic nephropathy and have creatinine checked.

Management:

- Aim for rigorous glucose control
- Start ACE inhibitor regardless of blood pressure reading
- Statin e.g. Simvastatin 20-40 mg once nocte/ Atorvastatin 10-20mg can be taken in the morning
- Consider adding fibrates if uncontrolled hypertriglyceridaemia
- Control hypertension; aim for target BP of 125/75 mmHg

E. Ophthalmic complications

- Arrange for annual check of acuity and fundoscopy.
- Details on grading of diabetic retinopathy and maculopathy are given in Appendix 2

I. Diabetic retinopathy (DR)

Classification

No diabetic retinopathy:
Non-Proliferative (background) diabetic retinopathy:
Proliferative diabetic retinopathy:

Management

Mild-Moderate non-proliferative DR	Review in 6 months
Severe non-proliferative DR:	Review in 3 months
Proliferative DR:	Fast-track referral to tertiary hospital eye service
Maculopathy:	Retinal specialist within 1 week Laser treatment Pan Retinal Photocoagulation Focal Laser

II. Diabetic Maculopathy

- It is a condition of retinal thickening at or within 500 microns of centre of the macula. Hard exudates may be present at or within 500 microns of the centre of the macula.
- Exudates within 1disc diameter (DD) of the centre of the fovea
- Retinal thickening within 1DD of the centre of the fovea
- Any micro-aneurysm or haemorrhage within 1DD of the centre of the fovea

III. Cataract

IV. Rubeosis iridis

New vessel formation on iris, this is usually a late presentation and leads to glaucoma

F. DIABETIC NEUROPATHY

Damaged blood vessels supplying the nerves with reduction in conduction velocity and increased sensory thresholds.

Clinical presentation

1) SENSORY

·Diffuse symmetrical sensory polyneuropathy

- Reduced proprioception, reduced pain perception, burning feet. Stress on bones and joints with increased plantar pressure will lead to callus formation.

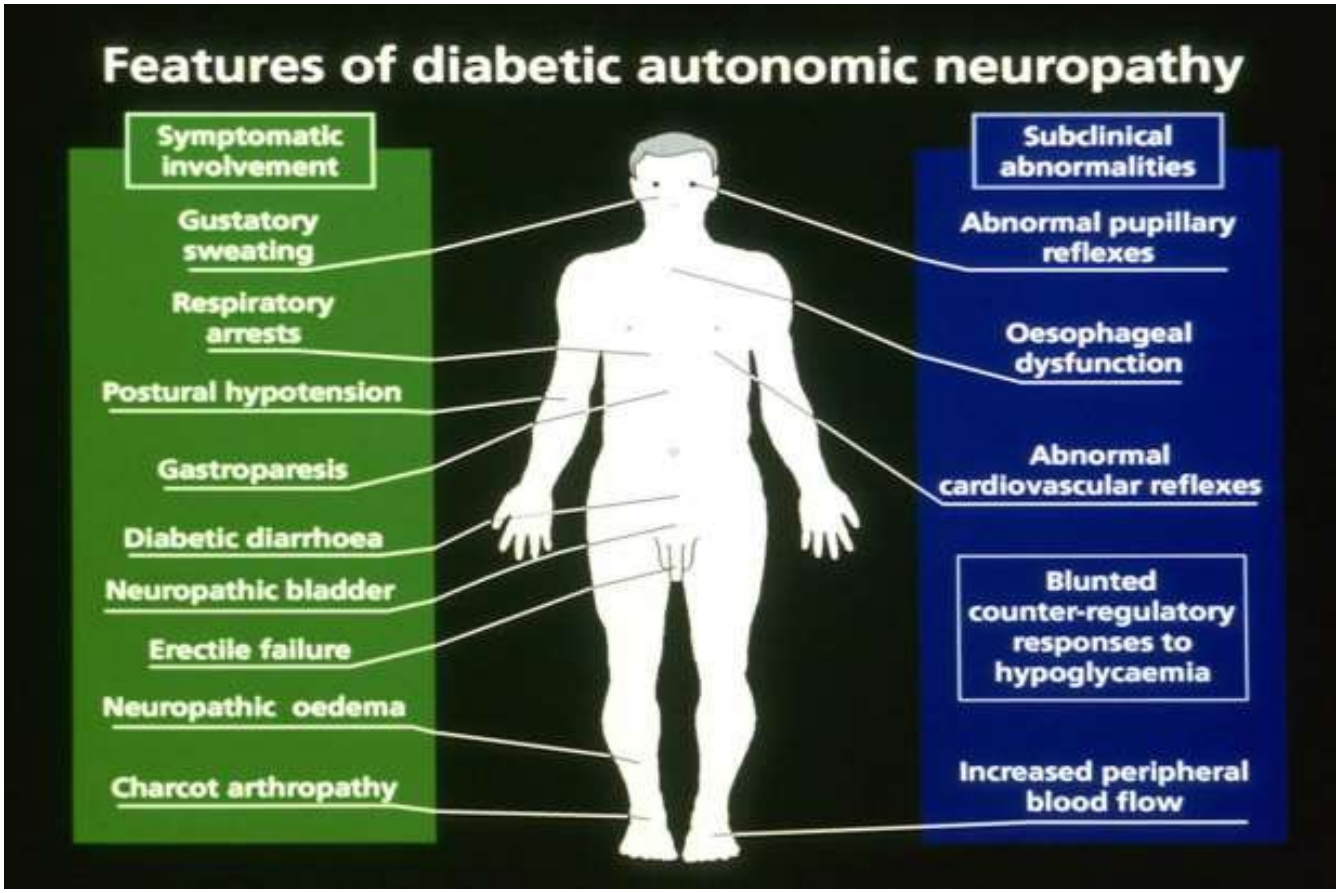
2) AUTONOMIC

- Autonomic neuropathy leads to reduced sweating, dry skin and the development of cracks and fissures. Systemic effects include postural hypotension, impotence, gastroparesis and gustatory sweating.

3) MOTOR

- Diffuse symmetrical motor polyneuropathy
    - o Patient will present with muscle wasting and weakness, postural deviation and this leads to deformities, stress and shear pressure

Picture 1: Features of diabetic autonomic neuropathy



Clinical assessment: Annual review

- Enquire annually for: painful neuropathy, loss of sensation, erectile impotence and other manifestations of autonomic neuropathy as shown in picture above.

Clinical examination

- Evidence of peripheral neuropathy: abnormal light touch, vibration, joint position and pain
- Evidence of autonomic neuropathy; absent sweating, resting tachycardia, postural hypotension (check BP on lying flat and let the patient stand for 2 minutes, check BP whilst standing normal fall is less than 10mmHg while a fall of more than 30mmHg is abnormal)

Management of neuropathy

1) Painful sensory neuropathy

- Analgesics (paracetamol but not NSAIDs), anti-seizure medication for neuropathic pain e.g. carbamazepine, gabapentin, anti-depressants for neuropathic pain e.g. amitriptyline.
- Diabetic amyotrophy is self-limiting, usually after approximately 6 months but many patients benefit from switching to insulin

2) Autonomic neuropathy

i) Erectile /sexual dysfunction

- Lifestyle modification (for example, quitting smoking, exercising more and avoid alcohol.
- Taking drugs to treat ED such e.g. sildenafil (Viagra)

Sildenafil is available as oral tablets at doses of 25 mg, 50 mg, and 100 mg. It should be taken approximately one hour before sexual activity. In some men, the onset of action of the drug may be as early as 11-20 minutes. Sildenafil should be taken on an empty stomach for best results since absorption and effectiveness of sildenafil can be diminished if it is taken shortly after a meal, particularly a meal that is high in fat. Sildenafil has been found to be effective and safe in the treatment of erectile dysfunction in men with stable heart disease due to atherosclerosis of the coronary arteries, provided that they are not on any type of nitrates. Precautions to be taken in patients with liver and kidney failure.

NB: Take Viagra once per 24 hours!

- Psychotherapy

G. DIABETIC FOOT

The diabetic foot may be defined as a group of syndromes in which neuropathy, ischaemia, and infection lead to tissue breakdown resulting in morbidity and possible amputation' (WHO 1995)

Table 17: Distinguishing Features of Neuropathic and Ischemic ulcers

FEATURE	NEUROPATHIC	ISCHAEMIC
Skin colour	Normal or red	Pale/bluish
Skin condition	Dry skin ,fissures, cracks	Thin, dry skin
Callus	Seen in weight bearing areas	Usually not present
Foot deformities	High arched, clawed & Charcot	Not present, amputated
Location of ulcer	Plantar aspect	Tips of toes, heel, lateral aspect of foot
Foot temperature	Warm	Cold
Ankle reflexes	Usually absent	Present
Sensation	Decreased	Normal/pain
Foot pulse	Present	Absent

MANAGEMENT

1) Improve general condition

- Control hypertension, lipids, glucose
- Treat retinopathy, malnutrition, nephropathy, foot infections, and edema

- Regular removal of hard skin at pressure points (callus) which predisposes to neuropathic ulcers. To be done by nurses but never the patient.
- Regular foot cleaning
- Well fitting, closed toed shoes

2) Decrease weight bearing

- Crutches, wheelchair, bed rest
- Therapeutic footwear
- Removable cast walkers

3) Prompt debridement or foot surgery

- Incision and drainage of abscess
- Debridement
- Amputation

4) Combine foot care and diabetic clinic

CHAPTER

OBSTRUCTIVE LUNG DISEASE 4

1. ASTHMA

Asthma is chronic inflammatory airway disease characterized by recurrent reversible airway obstruction, increased responsiveness of bronchial tree to a variety of stimuli resulting into recurrent episodes of wheezing, cough, chest tightness and shortness of breath. May be chronic or acute

PATIENT IDENTIFICATION

Signs and symptoms

- Cough – this can be the only symptom and is often chronic
- Audible wheeze
- Dyspnea
- Chest tightness
- Symptoms are intermittent with periods of normal breathing in between
- Symptoms can be worse at night, in early hours of the morning or during an upper respiratory tract infection
- Symptoms improve or disappear after using inhaler
- Symptoms start during childhood or early adulthood

Risk Factors:

- Family history of asthma
- History of hay fever, eczema, and / or allergies
- Indoor cooking
- Exposure to cigarette smoke or pollution
- Occupational exposures like cement, pesticides, tobacco industry, or other chemicals, etc.

Precipitants – asthma symptoms can be triggered by:

- Exercise
- Exposure to allergens (such as animal fur or dust), wood fire or cigarette smoke
- Weather (cold, wet)

- Upper respiratory tract infections
- Drugs (beta-blockers, aspirin or NSAIDs)

EXAMINATION

Examination should include vital signs and detailed respiratory exam. The first thing is to identify whether the patient is having an acute asthma attack.

Symptoms of acute attacks:

- Wheezing
- Diminished air entry
- Tachypnea

The following are symptoms of severe acute attack and can be life threatening:

- Use of accessory breathing muscles or nasal flaring
- Severe breathlessness: unable to complete sentences in one breath
- Silent chest
- Central cyanosis
- Pulsus paradoxus (systolic BP drops > 10mmHg on inspiration)
- RR > 25 breaths / min
- Sp02 < 97%
- Very late signs can be bradycardia, confusion, exhaustion, and feeble respiratory effort.

INVESTIGATIONS

Chronic, no acute attack	Mild acute attack	Severe acute attack
Consider sputum for chronic cough HIV test Spirometry (tertiary level)	Peak flow If febrile, work up for pneumonia or other infection.	CXR Sputum FBC Urea and creatinine MPS/MRDT if febrile

Table 18: Assessment of Chronic Asthma Severity using Symptoms

	Intermittent	Mild Persistent	Moderate Persistent	Severe Persistent
Day Symptoms	2 days/week	>2 days/week, but not daily	Daily	Multiple times each day
Night Symptoms	2 x/month	3-4x/month >2 days/week	>1x/week, but not nightly	Nightly
Inhaler Use	None	but not daily	Daily	Several times per day
Limitations of Activity	None	Minor limitation	Some limitation	Extremely limited
Hospitalizations for asthma	0-1x/year	2x/year		

MANAGEMENT

Prevention and General Measures

Patient counseling is very important, particularly on identifying and avoiding triggers for individual patients.

- Indoor cooking of solid fuel is a very common risk factor for asthma in Malawi. Patients with asthma, or parents of children with asthma, should be counseled to try to cook outdoors in an area with good ventilation wherever possible.
- Avoid exposure to personal and second-hand tobacco smoke
- Avoid contact with furry animals
- Reduce pollen exposure
- Reduce exposure to house dust mites
- Avoid sensitizers and irritants (dust and fumes) which aggravate or cause asthma especially in the workplace
- In certain patients, they may need to avoid drugs that aggravate asthma such as beta-blockers and aspirin and non-steroidal anti-inflammatory drugs.

PHARMACOTHERAPY

Pharmacotherapy for asthma is shown in Table 19.

In general, salbutamol refers to the inhaled form, and the use of oral salbutamol is not recommended for treating asthma patient.

Table 19: Pharmacotherapy for Asthma

Relievers	Controllers	
To quickly **settle acute symptoms** and be used as needed for attacks	Anti-inflammatory action to **prevent** asthma attacks. Must be taken routinely, even in absence of symptoms.	Sustained broncho-dilator action to **prevent** asthma attacks. Must be taken routinely, even in absence of symptoms.
Short-acting beta-agonists ● Inhaled or nebulized salbutamol ● Terbutaline	Inhaled corticosteroids ● Beclomethasone ● Budesonide ● Fluticasone	Long-acting inhaled beta-agonists ● Salmeterol ● Formoterol
Anti-cholinergics ● Inhaled or nebulized ipratroprium	Oral corticosteroids ● Prednisone ● Prednisolone Leukotriene antagonists ● Montelukast	Sustained release theophylline tablets ● aminophylline

General principles of maintenance therapy

- Start with relievers, adding preventers & controllers as necessary
- If the patient is poorly controlled, assess adherence & inhaler/spacer technique before escalating drug treatment (See Table 20)

Table 20: Drug Escalation for Outpatient Therapy

		Asthma Severity	Inhaled Salbutamol	Inhaled Steroid	Aminophylline	Inhaled ipratroprium	Prednisone / Prednisolone
STEP -UP when poor control on current regimen	*STEP-DOWN when doing well > 3 months*	**Step 5: Severe Uncontrolled**	Yes	High Dose	Consider	Consider	Yes
		Step 4: Severe Persistent	Yes	High Dose	Consider	Consider	
		Step 3: * Moderate Persistent	Yes	Medium Dose			
		Step 2: Mild Persistent	Yes	Low Dose			
		Step 1: Intermittent	Yes				
		Dosing Instructions: **Adults and children >30kg**	**Salbutamol 100mcg** inhaler: 2 puffs every 4 hours as needed for wheezing, cough, or dyspnea; use 10 minutes before known triggers. Before progressing to inhaled steroid, try 2 puffs qid standing.	Beclomethasone **200mcg** inhaler: **Always use a spacer** ***Low dose:*** 1-2 puffs 2x/d ***Medium dose:*** 3-5 puffs 2x/d ***High dose:*** 6-8 puffs 2x/d	Aminophylline: 10-12 mg/kg/d in 3 divided doses (max: 800mg/d) ●Give ½ dose if: >65 years-old or cardiac or liver problems	Inhaled ipratroprium:	Prednisone, short-course for exacerbations: **First, rule-out TB (CXR, sputum AFB x3)** 40mg daily x 5 days

		Asthma Severity	Inhaled Salbutamol	Inhaled Steroid	Aminophylline	Inhaled ipratroprium	Prednisone / Prednisolone
		Children 10-30kg *(Children <10kg CONSULT WITH PEDIATRICIAN)* Very small children should use a mask attached to a spacer	Same as above	Beclomethasone **50mcg** inhaler: **Always use a spacer** ***Low dose***: 1 puff 2x/d ***Medium dose***: 2 puffs 2x/d	Aminophylline: 20 mg/kg/d in 3 divided doses (max: 400mg/d) Avoid if <1 year-old		Same as above

*Long-acting beta-agonists are not currently routinely available in Malawi. If available, recommend adding at Step 3.

*Leukotriene inhibitors are not currently routinely available in Malawi. If available, recommend adding at Step 3, or in patients with significant hay fever or eczema.

MANAGEMENT OF ACUTE ATTACKS

I. Primary Level Care

- Oxygen therapy if saturation <90%
- Insert IV line, infuse Normal Saline
- Administer salbutamol (beta agonist) therapy via
  - Large volume spacer (1-2 litres): 400mcg (4 puffs) every 20 minutes for 1hour then reassess
    - *Large volume spacer can be improvised using a plastic bottle. Cut a small hole in the bottom of the bottle that will fit the inhaler with an airtight seal, and use the mouth of the bottle for the patient to inhale from.*

OR

  - Nebuliser (oxygen driven nebulizer is preferable) 1 or 2 ml of 0.5% salbutamol solution in 3mls of sodium chloride every 20 minutes for 1 hour
- If no immediate response or the episode is severe (unable to talk in sentences, cyanosis, silent chest) administer IV steroids. The patient should complete a 5-day course of steroids in the hospital and when they stabilize enough to go home.
- If the client is already taking oral prednisolone at home, consider increasing the dose or utilizing IV steroids.
- If febrile, consider pneumonia and rule out Malaria. Consider giving an appropriate antibiotic eg amoxicillin or doxycycline
- After one hour assess response to treatment:
  - BETTER OR NO SYMPTOMS
    - If improving/ stable after 1 hour, follow discharge plan below
  - NO CHANGE OR WORSE
    - still cyanosed, exhausted, pulsus paradoxus, unable to talk in sentences, silent chest
- Consider other causes of acute severe breathlessness with careful examination: acute left ventricular failure, pneumothorax, pulmonary embolus, upper airway obstruction, massive pleural effusion, severe pneumonia.
    - Add 2 ml ipratropium bromide solution to salbutamol solution OR Aminophylline 250mg IV slow push over 20 minutes
    - Continue nebulisation every 20 minutes with oxygen in between
    - Reassess every hour and **refer immediately if no response within 3 hours of arrival**

II. Secondary Level Care

Continue treatment as for primary care:

- Add 2 ml ipratropium bromide solution to salbutamol solution OR Aminophylline 250mg-500mg IV infusion in 1L of 5% Dextrose or 0.9% Sodium Chloride over 12hours

*Leukotriene inhibitors are not currently routinely available in Malawi. If available, recommend adding at Step 3, or in patients with significant hay fever or eczema.

- If still not improving after 1 hour add Magnesium Sulphate 1 - 2g IV over 20 minutes
- If still not improving after 1 hour add Adrenaline 0.5-1ml of 1:1000 slowly nebulised or IM
- Continue nebulisation every 20 minutes with oxygen in between

III. Tertiary Level Care

- Provide treatment as for primary and secondary care if not already given
- If no change consider intubation and ventilation.

2. COPD

Chronic Obstructive Lung Disease is marked by persistent shortness of breath and obstructive lung symptoms.

Because of the similarities between COPD and asthma, only the differences to consider in the diagnosis and management of COPD are highlighted

PATIENT IDENTIFICATION

Risk factors are similar to those in asthma. The biggest risk in Malawi for COPD is indoor cooking of solid fuels. Additionally, in much of the world this disease is hallmarked as a result of long term cigarette smoking.

Symptoms are similar, although COPD patients will:

- Long history of daily or frequent cough and sputum production (usually starts long before the onset of shortness of breath)
- Symptoms are persistent rather than only at night or during the early hours of the morning
- Typically have a history of indoor cooking and/or cigarette smoking
- Symptoms typically start in adulthood or later adulthood from exposures during their life
- Symptoms slowly worsen over a long period of time.
- Can often have a lower oxygen saturation even when at rest and stable: COPD patients adjust and can live with oxygen saturation 87-93%
- Symptoms often won't completely reverse with bronchodilators

EXAMINATION & INVESTIGATIONS

- Patients with COPD are more likely to have mild wheezing during lung examination, even when they are not under acute distress.

- CXR can reveal hyper inflated lungs (flattened diaphragms).
- Spirometry is more useful in COPD patients than asthma patients.

MANAGEMENT

The management of COPD is very similar to that of asthma. However, there are some very important considerations in these patients:

Maintenance Therapy

- ***Use of inhaled ipratroprium*** can be initiated for COPD early in the steps, along with inhaled salbutamol.

Treatment of COPD exacerbations

- ***Exacerbations need antibiotics and steroids***
    - COPD exacerbations, in addition to nebulizers of salbutamol and ipratroprium, should be treated with:
        - Prednisone 40mg for 5 days. *If the patient is on chronic steroids, consider a higher dose with a long taper.*
        - Antibiotics. *In the absence of underlying pneumonia, doxycycline 100mg bd for 5 days is a good choice.*
- ***Oxygen saturation and the use of oxygen***
    - COPD patients often present with a lower oxygen saturation than asthma patients, even when they are stable. In asthma, if Sp02 drops below 97%, it is worrisome. However, a COPD patient may be stable as low as 87%.
    - Given the above, avoid the use of high flow oxygen in COPD patients wherever possible.
    - It is recommended to use 2L oxygen as treatment or less, and to target oxygen saturations to 88-92%.
- ***Use of magnesium*** is not used for the treatment of COPD exacerbations.

CHAPTER

SEIZURES AND EPILEPSY 5

1. EPILEPSY

Epilepsy is a chronic neurological condition that manifests with recurrent unprovoked or repeated seizures. Many people will have a single seizure at some time in their lives, but this does not mean that they have epilepsy.

2. SEIZURES

A seizure is a transient disturbance of cerebral function caused by excessive electrical discharge of nerve-cells in the brain. It may be manifested by loss of consciousness, abnormal motor activity, behavioral disturbances, sensory disturbances, or autonomic dysfunction.

Causes of Seizures

- Idiopathic – no cause identified
- Epilepsy
- Metabolic: hypoglycaemia, hypocalcaemia, other electrolyte imbalances
- Infections: meningitis, encephalitis, cerebral malaria, neurosyphillis
- Trauma: birth trauma, head injury later in life
- Anoxia: birth asphyxia, hypoxic ischemic injury
- Toxins: alcohol and alcohol withdrawal, carbon monoxide poisoning
- Space occupying lesions: tumors, neurocysticercosis, tuberculoma, cryptococcoma
- Cerebral oedema: eclampsia, hypertensive encephalopathy
- Congenital: hydrocephalus, microcephaly
- Febrile: febrile illness, usually in childhood

CLASSIFICATION OF SEIZURES

A. Generalized Seizures

Generalized seizures are characterized by complete loss of consciousness.

- Tonic Clonic Seizures: The patient loses consciousness and the body becomes stiff. Their muscles relax and tighten rhythmically making the body jerk and shake (convulse)
- Absence Seizures: Common in children rather than adults, the patient looks blank and and unresponsive for short periods, usually a few seconds
- Tonic Seizures: Sudden sustained muscle contractions fixing the limbs in some strained position
- Clonic Seizures: There is repetitive rhythmic flexing and stretching of limbs without a tonic component
- Atonic Seizures: The muscles suddenly relax and become floppy. Recovers instantly, facial and head injuries are common
- Myoclonic Seizures: Sudden, brief, shock-like muscle contractions, either occurring in one limb, or more widespread and bilateral. May be with atonic or tonic

B. Focal/Partial Seizures

I. Simple Partial Seizures

Consciousness is retained but patient will have localized motor, sensory or autonomic symptoms

II. Complex Partial Seizures

Consciousness is impaired with localized motor, sensory or autonomic symptoms

III.Partial seizure with secondary generalization

A seizure begins as a simple partial seizure or complex partial seizure but evolves to have generalized motor, sensory or autonomic symptoms

IV. Temporal Lobe Epilepsy

Patients characteristically present with auras (eg olfactory, gustatory, a rising epigastric sensation, déjà vu') or altered or abnormal sensation.

KEY FEATURES IN HISTORY OF A SEIZURE

- Preceding medical history, chronic medical illnesses (e.g. Diabetes Mellitus, HIV)
- Headache, fever, trauma, altered behaviour
- Previous seizures and lack of adherence to medication
- Pregnancy (consider eclampsia)
- Drug and alcohol abuse
- Focal or generalized symptoms, loss of consciousness
- Time and place of onset
- Aura symptoms, triggers: lights, sound
- Sensory and autonomic symptoms: numbness, visual distortions, auditory or visual hallucinations, nausea, unusual smells or tastes

- Motor symptoms: limb movements unilateral, bilateral, synchronous, clonic, or irregular and thrashing.
- Physical description from observer: tongue biting, forceful head deviation, mouth open, eyes open, incontinence, response to verbal commands/stimuli
- Duration of seizure
- Behavior in post- ictal state: drowsiness, confusion, cannot recall events during seizure.

Table 21: Differentiating Seizures from Pseudo Seizures

SEIZURE	PSEUDOSEIZURE
Cannot be interrupted with verbal or physical stimuli	Patients with seizures may mimic incontinence, tongue biting and may cause self injury
If all 4 extremities are involved often there will be loss of consciousness (with rare exceptions)	Individuals may exhibit protective behavior (eyes tightly closed, arms outstretched when falling, "arm on face" maneuver)
Tonic-clonic movements do not wax and wane	
Seizures rarely produce "negative phenomena" such as pallor, cold, apnea, bradycardia. Consider syncope, arrhythmia or breath-holding spells	
Directed acts of violence are very rare except in some frontal lobe seizures. Frontal lobe seizures may also be associated with out-of-phase limb movements, pelvic thrusting, kicking, thrashing, side-to-side head movements	
Will often have a postictal state	Will often not have a postictal state

Differential Diagnoses

- Syncope
- Psychogenic attacks (depersonalization/derealization)
- Narcolepsy/cataplexy
- Tics

MANAGEMENT OF SEIZURES AND EPILEPSY

A. During the seizures don't

- Restrain the person
- Put anything in their mouth
- Try to move them unless they are in danger
- Give the person anything to eat or drink until they have fully recovered
- Attempt to wake them up

B. Immediate Management

- Check ABC (Airway, Breathing and Circulation)
- Manage airway and secure IV access
- Check blood sugar - if <4 mmol/L immediately give 50ml of IV dextrose 50%
- Seizures may be associated with hypoxia, give O2

C.Pharmacological Management of Seizures

- Adults: give Diazepam 10mg IV stat over 5 minutes, repeat if seizures continue with no more than 3 doses. If no response to Diazepam manage as status epilepticus below.
    - o Child: give Diazepam 0.2mls/kg/IV
    - o If convulsions continue for another 10 minutes or are repeated more than 3 times without the patient regaining consciousness between seizures, treat as status epilepticus below:
        - **Phenobarbitone:** Give 10mg/kg IV. Dilute with water for injection 1: 10 and give slowly no more than 100mg/minute. OR
        - **Phenytoin:** Give 15mg/kg (600 – 1200mg) IV at 25-50mg/min. Dilute 100mls with 0.9% Normal Saline and give slowly. Do not mix with glucose/5% Dextrose or other drugs as this can cause precipitation of Phenytoin OR
        - **Paraldehyde:** Paraldehyde 5ml deep IM in a buttock, and repeat 5ml IM in opposite buttock. Paraldehyde can also be given through the rectum using a syringe with the needle removed. Paraldehyde dissolves plastic, make sure it is administered promptly.

- If still seizing after 30 minutes seek senior advice, consider intubation, anaesthesia and transfer to HDU/ICU
- Consider giving Thiamine 100mg IV or IM once daily before giving glucose if you suspect alcohol withdrawal seizures

INVESTIGATIONS

- Blood tests
- MRDT/blood film
- Random Blood Glucose
- U&E, Creatinine
- FBC
- VDRL, HIV test
- Pregnancy test
- Urine dipstick if pregnant
- Lumbar Puncture
- CT/MRI scan of brain if available if patient has focal neurological signs/epilepsy not responding to maximum medication
- Consider EEG if available

STARTING ANTI-EPILEPTIC DRUGS

General Guidelines

- Do not start epilepsy medication after a single seizure unless there is a high chance of recurrence eg patient with secondary cause of seizures. If a patient has more than 2 seizures in a year, consider starting anti-epileptic therapy.
- Do not use a trial of medication as a test
- Give appropriate drugs for specific type of seizure
- Use maximum dose of one medicine before adding another. Avoid several anti-epileptic drugs concurrently.
- Always start with small dose, increase dose gradually over weeks or months
- Treatment should not be stopped suddenly, rather taper off over weeks or months to prevent rebound seizures
- Patients on ARTs with epilepsy should avoid DTG and start on regiment 5A or 4P
- ***Only discontinue medication if patient is seizure free for 2 years for idiopathic epilepsy and if seizure free for 3 years for symptomatic epilepsy.***

Goals of Antiepileptic Drug Therapy

- Prevent recurrence of seizures
- Decrease frequency and / or severity
- Avoid side effects from anti-epileptic drugs
- Attain therapeutic drug levels
- Ensure compliance

Table 22: Antiepileptic Drugs Indication And Dosages

Drug	Indications	Starting Dose	Standard maintenance Dose	Maximum recommended Dose	Common Side Effects
Phenobarbitone	Partial and generalised tonic-clonic, myclonic, clonic and tonic seizures. Status epilepticus.	60mg nocte	60 -180mg nocte	300mg	Tiredness, sedation, mental slowing
Carbamazepine	Partial and generalised tonic-clonic seizures	200 mg/day in divided doses (BD)	800mg-1200mg/ day in divided doses (BD-QID)	1600mg/day	Double vision, dizziness, unsteadiness, fatigue, headache

Drug	Indications	Starting Dose	Standard maintenance Dose	Maximum recommended Dose	Common Side Effects
Ethosuximide	Absence seizures	500 mg/day in divided doses (OD-BD)	500mg – 750mg in divided doses	1500mg/day	Nausea, headache, drowsiness
Lamotrigine	Partial seizures and generalised tonic clonic seizures	12.5mg-25mg	100mg – 200mg in divided doses	500mg	Drowsiness, double vision, dizziness and headache
Levetiracetam (Keppra)	Partial, generalized, myoclonic seizures	500mg BD	500mg-1000mg bd	3000mg/day	Drowsiness, fatigue, headache
Phenytoin	Partial and generalised tonic-clonic seizures. Status epilepticus	100 mg	150 – 300 mg/day in divided doses	600mg 3000mg	Drowsiness, unsteadiness, slurred speech
Sodium Valproate	All generalized seizures Partial seizure	500 mg/day in divided doses	500mg – 2000mg/ day in divided doses		Drowsiness, tremor, irritability, weight gain

Table 23: Antiepileptic Drugs Efficacy Spectrum

Seizure Type	Phenobarbitone	Phenytoin	Carbamazepine	Valproate
Simple partial	+	+	+	+
Complex partial	+	+	+	+
Secondary GTC	+	+	+	+
Primary GTC	+	+	-	+
Myoclonic	+	-	-	+
Absence	-	-	-	+

PATIENT EDUCATION ON TREATMENT ADHERENCE

- Counsel the patient and guardians on the diagnosis of epilepsy, adherence to medication and follow up condition and importance of medication.
- Counsel women of childbearing age with epilepsy on family planning

- Avoid stigma with epilepsy and educate the community on reducing stigma
- Safety Precautions for Patients with Epilepsy. Patients with uncontrolled seizures should avoid:
    - o Ascending heights
    - o Working with fire or cooking;
    - o Using power tools (machineries like: drilling machine, grinders);
    - o Taking unsupervised baths and swimming. The patient should preferably take a shower rather than bath in a bathtub filled with water
    - o Driving: A person with controlled epilepsy should not drive any motor vehicle, whether a light vehicle for private use or as a driver for passengers or goods conveyance. A person with controlled epilepsy may drive a motor vehicle if they have had a seizure free period for 1 year

NOTE: Do not underestimate the consequences that the diagnosis of epilepsy may have on patients. For instance, patients with epilepsy may live in fear of experiencing the next seizure, and they may be unable to drive or work at heights.

REFERRAL PRINCIPLES FOR EPILEPTIC CARE IN MALAWI

I. Health Centre

- Patients with controlled epilepsy can be managed at the health centre. If the patient does not respond to first line treatment (i.e. if side effects occur or if maximum tolerated dose does not produce seizure control)
- refer to secondary or tertiary facility

II. District Hospital

- Consider adding second line drugs if required. If still no response, then refer to tertiary

III. Tertiary Hospital

- For specialist review, and investigations (neuro-imaging, EEG if available). Consider and ruling out other diagnoses.

CHAPTER

RENAL FAILURE

6

1. ACUTE RENAL FAILURE

Described as a rapid decline in renal function occurring over hours or days. The most common symptoms are oliguria, edema, weakness, nausea, and confusion, but often acute kidney injury is asymptomatic and is detected by rising urea and creatinine. There are many causes of acute renal failure one of which includes hypertensive emergency.

MANAGEMENT APPROACH

- Rule out other causes, especially
  - prerenal causes – hypovolemia and hypoperfusion
  - postrenal causes – obstruction (renal ultrasound!)
  - Admit patient in HDU/ICU
- Assess and treat volume status (patients may be hypovolaemic even with high blood pressure)
- Stop nephrotoxins (NSAIDs, tenofovir, in AKI stop ACE-inhibitors)
- Control blood pressure. Start with low dose Calcium Channel Blockers eg amlodipine 5 mg. Follow same pathway as per hypertensive urgency. Be cautious of rapid falls in blood pressure. Patient may need IV normal saline if this happens.
- Treat complications
  - Hyperkalemia;
    - ECG changes; tall tented T waves, small or absent T waves, increased PR interval, widening QRS complex, sine wave and asystole
    - Give Calcium gluconate 10mls 10 % via big vein over 2 minutes
    - IV insulin 10 IU in 50 mls of 50% dextrose over 30 minutes
    - salbutamol nebulizer 5mg
    - Potassium Binders if available

      If the patient is acidotic correcting the acidosis with oral sodium bicarbonate (500 – 1000 mg tds) can lead to a drop in the potassium levels
  - Pulmonary edema
    - see management under acute heart failure
    - Furosemide 80 -160 mg given over 1 hour

- Bleeding
  - increased urea may impair hemostasis; therefore, consider giving FFP, platelets if patient is bleeding
  - be very cautious if transfusion is needed, as transfusion is contra indicated in hyperkalaemia

INDICATIONS FOR ACUTE DIALYSIS

- Fluid overload (especially pulmonary edema)
- Refractory hyperkalemia
- Severe metabolic acidosis
- Uremic symptoms (Uremic encephalopathy)
- Uremic pericarditis

2. CHRONIC KIDNEY DISEASE

Chronic kidney failure implies long-standing, more than 3 months, and usually progressive, impairment in kidney function as a result of various causes, one of which includes uncontrolled hypertension.

IDENTIFICATION OF KIDNEY DISEASE

Chronic kidney disease is usually asymptomatic until eGFR falls below 30ml/min. Patients often present late in the course of CKD or high creatinine is discovered incidentally.

Symptoms include:

- malaise, loss of energy, loss of appetite, insomnia, depression, itching , nausea, vomiting, paraesthesia due to polyneuropathy, bone pain due to metabolic bone disease, hypertension, anaemia, and peripheral or pulmonary oedema

INVESTIGATIONS FOR KIDNEY DISEASE

- FBC, electrolytes, creatinine, glucose, calcium, phosphate
- Urine dipstick and, microscopy
- Renal ultra sound - look for small hyperechoic kidneys with loss of cortical-medullary differentiation, rule out hydronephrosis
- Infection screen – HIV, hep B and C, malaria. Consider treating schistosomiasis

MANAGING HYPERTENSION IN KIDNEY DISEASE

- Blood pressure management is the most important aspect of renal disease: both a cause and an effect
- Lifestyle modification should be core to the management
- Treat to target if possible
- Initiate treatment at 140/90 with TARGET 130/80 if no proteinuria
- Initiate treatment at 130/80 with TARGET 125/75 if proteinuria

Drug choice:

- Calcium channel blockers are safe and effective anti hypertensives in CKD
- ACE inhibitors reduce both BP and proteinuria but use with caution
  - Not recommended, if eGFR < 30ml/min
  - Not in AKI
  - Remember the risk of hyperkalemia
- HCT is usually not effective, if eGFR < 30ml/min

FOLLOW UP CARE FOR CHRONIC KIDNEY DISEASE

- Treat hypertension as above
- Stop nephrotoxins (NSAIDs, tenofovir)
- Correct hyperlipidaemia with a statin
- Correct anaemia by giving iv/po iron and if persisting giving erythropoietin. Exclude other causes of anemia.
- Match dietary and fluid intake with excretion, recommend salt restriction, K+ restriction if hyperkalaemia and moderate protein intake
- Chronic kidney disease is associated with an increase of phosphate, therefore minimize intake of foods rich in phosphate, e.g. red meat, cheese, eggs, milk or alternatively consider giving phosphate binders (calcium carbonate together with meals)
- Give Vitamin D, preferable 1-alpha hydroxylated forms.
- Give Sodium bicarbonate 500 – 1000 mg tds for acidosis or hyperkaelemia
- Patients presenting with restless legs consider giving clonazepam 0.5-2mg daily or gabapentin
- Calculate GFR during clinic visits counsel and refer patient for possible dialysis with GFR 20 - 30ml /min with symptoms

CHAPTER

SICKLE CELL DISEASE (SCD) 7

SCD is a group of disorders that cause red blood cell become misshapen and breakdown.

SICKLE CELL DISEASE SUSPECT

- Recurrent transfusions for anemia or hemoglobin less than 10g/dL
- Frequent non-traumatic pain episodes
- Frontal bossing
- History of cerebrovascular accident (CVA) or stroke in children
- Swollen extremities (hand and foot)
- Frequent infections
- Big spleen
- Delayed growth in children
- Recurrent or unexplained jaundice

DIAGNOSING SICKLE CELL DISEASE

- FBC - Usually shows decreased hemoglobin with mildly elevated WBC count and normal or raised platelet count. Platelet count may be decreased with spleen sequestration
- Peripheral blood smear - Will demonstrate sickled cells, increased polychromatic cells and target cells
- Point-of-care immunoassay such as Sickle SCAN
- Sickling test - Note that this test may be positive in patients with AS genotype and should be confirmed by additional tests.
- Chromatography
- Isoelectric focusing such as Gel electrophoresi
- The World Health Organization (WHO) recommends newborn screening for SCD

PRINCIPLES IN THE MANAGEMENT OF SCD ACUTE CRISES

- National Emergency Cards For SCD should be considered for patients presenting with acute crises. The goal of the cards will be to provide simple care instructions to an emergency responder and facilitate timely care for the patient in crisis.
- Acute complications of SCD (crises) include:

- Acute Vaso-occlusive crisis (VOC),
- Splenic sequestration crisis,
- Aplastic crisis
- Hemolytic crisis

- VOC (acute pain crisis, acute sickle crisis) is the hallmark of SCD, and is the most common acute presentation. Long bones are common sites for VOC but any other sight or organ may be involved including the axial skeleton, abdomen (abdominal crisis), chest (acute chest syndrome), kidneys, central nervous system (strokes) and soft tissues (priapism); in children dactylitis may be the first presenting manifestation of SCD typically occurring between the ages of 6 months and 3 years.
- Any drop in oxygen tension or related events can precipitate a sickle crisis. Precipitating factors include :
  - (A, B,C,D,E,F,G,H,I,O) –
    - Acidosis, anesthesia, anxiety, (high) altitude
    - Bouts of infection, bad habits, e.g. smoking, alcohol
    - Cold exposure
    - Dehydration
    - Exercise (vigorous)
    - Folate deficiency (e.g. megaloblastic crisis)
    - General surgery
    - Hypoxia
    - Infection
    - Other – trauma, menstruation.
- Fever frequently accompanies a pain crisis. As the temperature rarely exceeds 38^{o}C, temperatures above this level should be investigated, guided by the clinical findings and further investigations, e.g. Malaria test, chest radiograph, and blood/urine culture. Empiric antibiotics should be administered until culture results are known, and adjusted where necessary.
- Hydration with intravenous fluids (e.g. normal saline or 5% dextrose in saline) is necessary. Check oxygen saturation and administer oxygen if <95%.
- VOC often causes excruciating pain and can lead to despair and panic. This guideline will cover in detail the management of pain below.

MANAGEMENT OF COMMON COMPLICATIONS OF SCD

I. Pain

Pain in Sickle Cell Disease (SCD) is commonly due to vaso-occlusion.

- Pain management should be individualized, as patients have varying thresholds of pain and different levels of tolerance from past exposure to analgesics. Multidisciplinary teams including palliative care specialists should be involved in developing an individualized emergency card for the patient to include prehospital care of pain, indications for hospital care and referral indications.

- Prehospital care: Bed rest, hydration and simple oral analgesia should be instituted by the patient. Failure of self-treatment should mandate prompt referral to hospital (emergency department/casualty /admission ward).
- Upon admission, rapid clinical assessment and reassurance are important.
- Analgesics should be administered as soon as possible, and within 30 minutes to one hour of arrival at the hospital.
- For mild to moderate pain, paracetamol with codeine, non-steroidal anti-inflammatory drugs (NSAIDs) or tramadol may be used as single agents or in combination, bearing in mind the WHO three-step ladder for pain management:
    - Step 1: Mild pain – non-opioid ± adjuvant;
    - Step 2: Moderate pain – weak opioid (or low dose of strong opioid) ± non-opioid ± adjuvant;
    - Step 3: Severe pain – strong opioid ± non-opioid ± adjuvant).
    - In hematology, NSAIDs are generally not commendable because of their antagonistic effects on platelets and for SCD patients who frequently require prolonged and repeated analgesia, prolonged and repeated NSAID therapy introduce other risks such as renal compromise. As such, paracetamol, tramadol and morphine are often the preferred medications for patient with SCD for both home, outpatient and inpatient care.
    - However in children, there have been concerns about tramadol safety and dosing but not necessarily in SCD. Since NSAID can not be entirely avoided, patient follow up should include evaluation for the serious side effects of NSAIDS.
- Opioids are generally required for severe pain. Morphine is the drug of choice, except where contraindicated (e.g. allergy, intracranial disease, liver disease, etc.). Ideally morphine should be administered parenterally at fixed intervals. Table below serves as a general guide to dosing. **Avoid Pethidine.**
    - Close monitoring of vital signs, pain control and sedation is essential at 15 - 20-minute intervals for the first hour, then at 30-minute intervals, and thereafter 2-hourly once pain control has been achieved. After 24 - 48 hours of pain relief, parenteral morphine should be weaned off over the next 2 - 3 days. A non-opioid analgesic, such as paracetamol or an NSAID, may be added as an adjunct. For breakthrough pain, oral morphine solution can be used (e.g. 5 - 10 mL 4 - 6-hourly in adults; or 0.1-0.2ml/kg of weak morphine solution in children). The frequency of and response to pain-relieving medication should be documented with pain charts or scales appropriate to the patient's age and cognitive abilities. Patient-controlled analgesia pumps are particularly useful for frequent, ongoing pain and should be offered where available.
- Routine use of sedatives should be avoided. For extremely anxious and agitated patients, anxiolytics such as haloperidol, benzodiazepines or antihistamines may be used with caution.
- Constipation is a common adverse effect of morphine. Stool softeners should be prescribed. The patient should be assessed daily for stooling and constipation regimen escalated as necessary.
- Hydration: The aim is to have the patient on 100% maintenance (oral + IV fluids). While hydration is very important, overhydration can be detrimental. This can be all orally if tolerated or as IV fluids 0.9% normal saline (may use Ringers Lactate if NS not available), and consider adding 5% dextrose if limited oral intake) if necessary. Encourage oral fluid intake and wean IV fluids as soon as possible

- If localized pain does not improve after 48-72 hours of analgesics and febrile, be concerned for osteomyelitis. Consider imaging of affected limb, however note that x-ray changes associated with osteomyelitis may take 10-14 days to appear, and may be indistinguishable from bone changes due to recurrent bone infarcts.
    - If osteomyelitis or septic arthritis is suspected, obtain a blood culture, and start empirical antibiotics that cover for both Staph, Strep and Salmonella as these bacteria are commonly associated with osteomyelitis in SCD. For example Ceftriaxone, plus Cloxacillin or Clindamycin.
- Blood transfusion is not indicated in the routine management of uncomplicated pain episodes.
    - It is indicated if Hb is =<6g/dL or 2 below baseline the patient's normal baseline Hb (check atleast 3 previous Hb in health passport).
- All patients should be encouraged to mobilize and to do incentive spirometry to prevent the development of Acute Chest Syndrome (ACS). Ensure the head of the bed is elevated at all times. Where possible involve the physiotherapy team in the management of all SCD patients.
- At discharge ensure that the patient receives counseling on avoiding the triggers of vaso-occlusive crisis such as keeping warm, and continuing to have good oral intake so as to ensure good hydration. Additionally, supply the patient with 48 – 72 hours supply of pain medication.

II. Fever in sickle cell disease

Patients with SCD have functional asplenia and are at increased risk of infection with encapsulated bacteria such as Streptococcus, Haemophilus, Salmonella and Klebsiella. They should be properly evaluated if they are febrile. Fever in SCD is concerning if temperature is greater than 38.5.

- Obtain a thorough history and perform a full examination to identify a possible source of the fever
- Obtain a malarial test and if positive manage according to WHO guidelines
- If a source of fever is identified, investigate accordingly e.g. urine for suspected UTI, chest X-ray for coughing and treat infections accordingly
- If no source of fever is identified, obtain a blood culture prior to the first dose of empirical antibiotics. Ceftriaxone (dose in children 50mg/kg once per day; or 2g once per day in adults).
- If blood culture is not available and no source of fever is identified, consider treating empirically with Ceftriaxone and transitioning to oral antibiotics if the patient improves clinically. Recommended options for oral antibiotics include Amoxicillin, Augmentin, Ciprofloxacin or any 3rd to 4th generation oral Cephalosporin.

III. Acute Chest Syndrome

Acute Chest Syndrome (ACS) is a major cause of mortality in patients with SCD. It may be caused by infection (e.g. pneumonia), pulmonary infarcts, vaso-occlusive episodes in the lung vessels, hypoventilation or fat embolism. It is simply defined by presence of new onset hypoxemia or respiratory signs in a patient with SCD. A more detailed diagnostic criteria is listed below:

- A new infiltrate seen on CXR or new respiratory signs on examination **PLUS**

- Fever >38.5
- Chest pain, Tachypnea, cough, wheezing or increased work of breathing; hypoxemia (SaO2 <92% on room air, or less than 3- 5% below the baseline)

II. Management of ACS

- Admit, obtain FBC and start on oxygen therapy
- Treat with empirical antibiotics - Cetriaxone (dose in children 50mg/kg once a day; 2g in adults) and Azithromycin (dose in children 5mg per kg x 5 days or 10mg per kg x 3 days: adults 500mg daily x 3 days)
- If hemoglobin is less than 8 g/dL, give a simple transfusion (10-15ml/kg of packed red cells or 20ml/kg of whole blood in children; 400-450ml of packed cells or 1-2 units of whole blood in adults).
- If a patient's respiratory distress is worsening, REFER TO CENTRAL HOSPITAL for ICU care and exchange blood transfusion.
- Treat pain accordingly if also in a pain crisis. Use morphine cautiously to avoid oversedation which may result in hypoventilation and worsening of ACS.
- Intravenous fluid is not recommended except absolutely necessary, and should not exceed maintenance fluid. Patients with ACS are at higher risk of fluid overload.
- Ensure the patient is taking breathing exercises or participates in incentive spirometry to help expand the lungs and avoid atelectasis.

III. Stroke in SCD

Stroke in SCD is an emergency. It is defined as any new neurological symptom in a patient with SCD. Some of these symptoms include:

- Acute limb weakness
- Slurred speech
- Convulsions
- Severe headaches
- Change in behavior or level of consciousness

1) Management of stroke in SCD

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- Admit, obtain FBC and start on oxygen therapy
- As soon as possible (preferably within 4 hours of onset of symptoms) if hemoglobin is less than or equal to 9 g/dL, give a simple transfusion (10-15ml/kg of packed red cells or 20ml/kg of whole blood in children; 400-450ml of packed cells or 1-2 units of whole blood in adults).
- If hemoglobin is >9 g/dL, an urgent exchange blood transfusion is recommended.
- Intravenous fluid is not recommended except absolutely necessary, and should not exceed maintenance fluid. Patients with stroke are at higher risk of cerebral edema

- If febrile, evaluate further with blood culture and lumbar puncture if stable (to rule out meningitis) and treat infection accordingly with appropriate antibiotics.
- Manage fevers appropriately with antipyretics as this may worsen neuronal injury.
- In adults also evaluate for other causes of stroke e.g hypertension and diabetes
- Obtain CT scan to help identify hemorrhagic stroke which might require neurosurgical intervention
- Remember to institute physiotherapy as soon as possible
- If improved and ready for discharge, recommend increasing the dose of hydroxyurea or initiating monthly chronic blood transfusions.

IV. Splenic sequestration in scd

Splenic sequestration is one of the most common cases of death in SCD children under the age of 2 years old. It results from the rapid sequestration of red blood cells by the spleen and may cause an abrupt drop to half of baseline Hb within a few hours of onset resulting in hypovolemic shock. It is the second most common cause of death in the first decade of children with SCA.

Signs and symptoms

- Pallor, lethargy, signs of hypovolemic shock
- Diffuse abdominal pain
- Abdominal distension with acute splenomegaly, often tender
- +/- Fever
- Sudden drop in Hb of >2g/dL
- hrombocytopenia(Low platelets)

Immediate action

- If a patient is in shock, admit to HIGH DEPENDENCY UNIT if available as this is an EMERGENCY
- Urgent group and cross match, FBC, reticulocyte count (if available)
- Needs minimum of every 30min observations (heart rate, pulse rate, O_2 saturations, Blood Pressure, GCS) until patient stabilizes
- Bolus of 10ml/kg normal saline fluid may be given to restore circulatory volume whilst awaiting blood depending on clinical condition. You can give up to two boluses.

Management

- If febrile, obtain Blood culture and malaria test. Give broad spectrum antibiotics with Ceftriaxone 50mg/kg IV every 24 hours (Refer to Fever section).
- IMMEDIATE blood transfusion with packed red cells 10cc/kg or whole blood 20cc/kg to be given over 3-4 hours to a goal Hb of 8 g/dL.

- CARE must be given not to over-transfuse as subsequent release of pooled blood from spleen to the circulation can lead to hyper viscosity
- Check Hb 4-6 hours after transfusion. Repeat transfusion as appropriate.

- Monitor spleen size for the first 12-24 hours until it is seen to be reducing in size
- Give supportive oxygen therapy if sats <95%
- At discharge ensure that the patient receives counseling.

V. Priapism

Priapism is a prolonged and painful penile erection, often not associated with sexual stimulation. It can also be triggered by sexual activity or a full bladder.

Commonly in male children, especially adolescents, with SCD should be made aware of this and advised to inform parents/doctors as it can lead to impotence if left untreated.

Aims of Treatment

The aim of treatment is threefold:

- Achieve rapid relief from pain and discomfort
- Preserve potency
- Prevent recurrence

Signs and symptoms

- Stuttering
  - Lasts <4 hours and tends to resolve spontaneously
- Major/Fulminant
  - Lasts >4 hours;
  - Requires URGENT urological assessment and management

Assessment

Clinically assess whether the patient has urinary retention and whether or not the glans penis is soft or turgid. This determines treatment.

Management

- Document time of onset of the episode and any precipitating factors e.g. trauma, sexual stimulation, infection, medication.
- If less than two hours from the onset, give fluids à IV NS bolus followed by IV + PO goal of 100% maintenance rate.

- Check Hb. If Hb =<6g/dL or 2 points below baseline (check atleast three Hb readings in health passport) and priapism is persisting beyond 4 hours and/or recurring, then consider simple blood transfusion.
- Analgesia (refer to Pain section) and anxiolytic agents should be prescribed as needed.
    - This can be very painful, so please ensure adequate pain management
- Have the patient take a warm bath and/or apply a warm compresses to the penis.
- Micturition (urination) should be encouraged once priapism starts as this may provide detumescence.
- If no relief/ detumescence after 2 hours from onset:
    - Give tablets of pseudoephedrine. Start with 0.5mg/kg bd for 3 days. If this is successful in achieving detumescence, then it can be stopped. Alternatively, it can be continued at a dose of 0.5mg/kg/day for seven days. A dose of 0.25mg/kg/day for one month can be considered for stuttering priapism.

- **If the priapism persists >4-6 hours from onset:**
    - Fluid intake should be increased à IV NS bolus followed by IV + PO goal of 100% maintenance rate. Consider blood transfusion. (See management above)
- Refer to central hospital for Urology interventions.

POINT-OF-CARE TOOL FOR THE EMERGENCY MANAGEMENT OF SCD

- In case a provider encounters emergency SCD cases pertaining to problems not covered in this guideline one recommended resource is the American College of Emergency point-of-care tool that can be accessed at https://www.acep.org/sickle-cell/ Providers can deploy this evidence-based, clinical content to deliver quality care to patients with SCD in the emergency department. It covers emergency care including and beyond acute pain management. MOH welcomes feedback on the utilization of this tool to facilitate its integration to local settings.

ROUTINE MANAGEMENT OF SICKLE CELL DISEASE (SCD CLINIC)

I. Hydroxyurea

- Indicated for all children, regardless of severity. Indicated for adults if symptomatic.
- Can be started in children older than 12 months
- Start at 20 mg/kg orally (see dosing table) in children or 1gram daily in adults
- In children, re-weigh at each visit to adjust dosage
- Lab tests to order and criteria needed to be met
    - ANC > 1,500/µl
    - Platelets > 100,000/ul
    - ALT < 2x upper limit of normal
    - Creatine: normal
- Check FBC at 1 month, 3 months and every 6 months thereafter

Table 24: Hydroxyurea Dosing

	20mg/kg/dose		
PATIENT WEIGHT (kg)	# HU 500mg capsules per week	1 month supply	3 months supply
4kg - 5kg	1	4	12
6kg - 8kg	2	8	24
9kg - 12kg	3	12	36
13kg - 16kg	4	16	48
17kg - 19kg	5	20	60
20kg - 23kg	6	24	72
24kg - 26kg	7	28	84
27kg - 30kg	8	32	96
31kg - 33kg	9	36	108
34kg - 37kg	10	40	120
38kg - 41kg	11	44	132
42kg - 44kg	12	48	144
45kg - 48kg	13	52	156
49kg - 51kg	14	56	168

- Dose escalation for hydroxyurea is indicated for the patients with the following
  - o Cerebral vascular accident
  - o Acute chest syndrome in the past 24 months
  - o More than one pain crises requiring admission in the past 24 months
- The following should be observed during dose escalation:
  - o Increase hydroxyurea 5mg/kg/day every 8 weeks
  - o Check FBC at 1 month, 3 months and every 6 months after escalation
  - o Max dose of 30mg/kg
- Consider holding or reducing hydroxyurea dose when
  - o HGB < 4.0 g/dL
  - o ANC < 1.0 x 10^9/L
  - o PLT < 80 x 10^9/L
- Recheck counts every two weeks, if recover in two weeks can restart same dose if still elevated in two weeks, try to decrease the dose by 5mg/kg

I. Nutritional Supplementation

- Folic Acid 2.5mg daily
- Avoid iron supplementation unless confirmed severe iron deficiency anemia

II. Infection Prevention

- Penicillin for under 5 children

- Penicillin V
  - < 3 y/o: 125mg po BD
  - > 3 y/o 250mg po BD, OR
- Benzathine Penicillin
  - < 25 kg: 600,000 units every 4 weeks
  - > 25 kg: 1.2 million units every 4 weeks

NOTE: Ask if patient reacts to Penicillin before administration

- SP for Malaria prophylaxis

SP Dosing Table	
Weight (kg)	**No. of tablets/ monthly**
<10kg	0.5
10 - <20	1
20 - <30	1.5
30 - 45	2
> 45	3

- Mosquito net
  - Provide to all new diagnosis

Always verify if they have them and provide if available

- Vaccines: Per Malawi National EPI schedule. Additional vaccines to consider:
  - Pneumococcal
  - Meningococcal
  - Influenza
  - COVID-19

EMERGENCY MANAGEMENT OF HAEMOPHILIA AND VON WILLEBRAND DISEASE IN MALAWI

Treatment First

- Delay in the restoration of haemostasis to the patient with haemophilia or von Willebrand disease may be life or limb-threatening.
- Prompt triage and assessment.
  - Determine the severity of the bleed.
  - Recognize that bleeding in the head, spine, abdomen or pelvis may initially be occult and potentially life-threatening.
- Treat first and investigate later - "treatment first".
  - Avoid invasive procedures such as arterial punctures unless the patient has factor replacement.
  - NO IMinjections andNO Aspirin.

- The patient or guardian may be your most important resource, so do ask about specific treatment protocols
- Provide cleardischarge instructions andarrange a follow-upplanor admitto hospital if necessary.

- Treatment for life or limb threatening bleeds and Patient must receive product urgently
  - Hemophilia A: (all severities)
    - Recombinant factor VIII concentrate 40-50 IU/kg
  - Hemophilia B: (all severities)
    - Recombinant factor IX concentrate 100-120 IU/kg>15yrs Recombinant factor IX concentrate 135-160 IU/kg<15yrs The dosage for recombinant factor IX is substantially higher because of its lower recovery,particularly in children.
  - Von Willebrand Disease:
    - A VW factor concentrate containing factor VIII such as Alphanate 60-80 Ristocetin cofactor units/kg
  - It is critical to raise the factor level to 80-100°/o urgently for all life or limb-threatening bleeds.
- Treatment for moderate/ minor bleeds. Patient must receive product within 30 minutes whenever possible
  - Hemophilia A: (severe/moderate)
    - Recombinant factor VIII concentrate 20-30 units/kg
  - Hemophilia A: (mild)
    - Desmopressin (Octostim/DDAVP) 0.3 meg/kg (max. 20 mcg)-SC/IV
  - Hemophilia B: (severe/moderate/mild)
    - Recombinant factor IX concentrate 35-50 IU/kg>15yrs Recombinant factor IX concentrate 50-70 IU/kg <15yrs
  - Von Willebrand Disease:
    - Type 1 and Type 2A or 2B known to have used desmopressin safely and effectively-(Octostim/DDAVP) 0.3 meg/kg (max. 20 mcg)-SC/IV
    - For patients not responding to desmopressin (such as Type 3 or Type 2B) use a VW factor concentrate containing factorVIII such as Alphanate 60-80 Ristocetin cofactor units/kg
  - For mucosal bleeds inall above add: Tranexamic Acid (Cyklokapron) 25 mg/kg po tid 1-7 days (contrain- dicated if haematuria)

TYPES OF BLEEDS

I. Life or limb-threatening bleeds

- Head (intracranial) and neck; Chest, abdomen, pelvis, spine; iliopsoas muscle and hip; extremity muscle compartments; fractures or dislocations; any deep laceration; any uncontrolled bleeding.

II.Moderate/minor bleeds

- Nose (epistaxis); joints (hemarthroses); menorrhagia; abrasions and superficial lacerations.

CRYOPRECIPITATE AND FFPS

Not standard treatment: Make every effort to obtain the preferred recombinant factor concentrate for patients before resorting to the use of Cryoprecipitate and/or FFPs. Thawing: Thaw between 30 °C and 37 °C in a water bath under continuous agitation or with another system able to ensure a controlled temperature. Thawing takes 20-30 min.

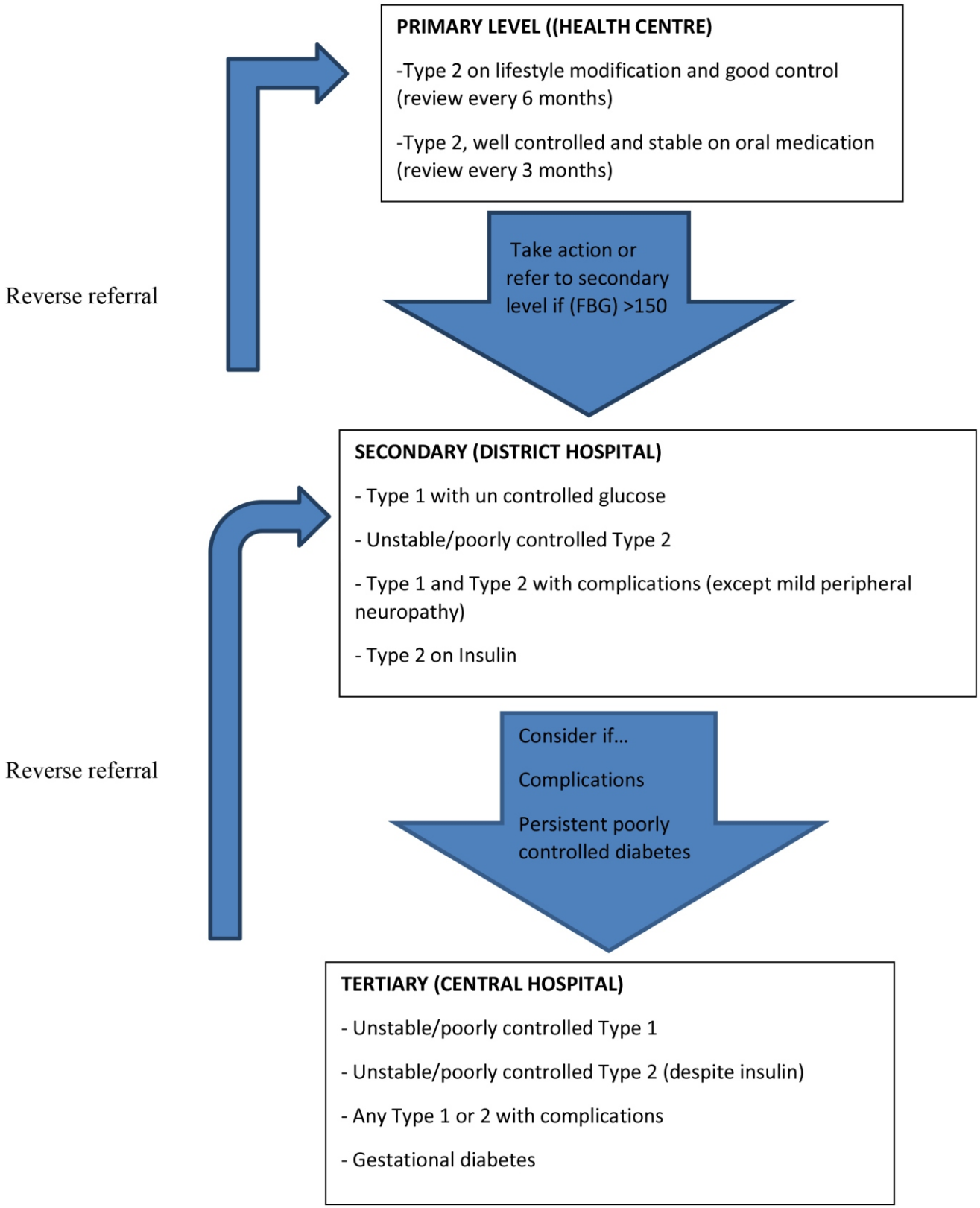
Cryoprecipitate Administration

- ABO compatible preferred but not required
- Infuse within 4 hrs of thaw, pooling
- Dose:
    - 10 pooled units (adult).
    - 1 unit/5 kg (infants/children).
    - Repeat dosing may be required every 8-12 hours for up to 3 days followed by once daily dosing.
        - Rate:
    - Like FFP (200-250 cc/20-30 min)
        - Preferable to FFP for the treatment of hemophilia A, cannot be used for treatment of hemophilia B
        - **FFP Administration**
    - FFP must be transfused as soon as possible after thawing, but in any case within 24 hours, if stored at 4 ± 2 °C
    - ABO (but not Rh) compatible
    - Transfused within 4 hrs after leaving Blood Bank
    - volume 250 ml/unit
    - Dose:10-15 ml/kg body weight
    - Rate:1 unit per 30-60 min (10 cc/min) OR: as fast as possible and tolerated

NOTE: Dosages are patient specific - these are general guidelines only. Round doses up to the nearest vial/unit bag.

APPENDIXES

Appendix 1: Referral Pathway for Patients with Diabetes



Appendix 2: Requirements of Diabetic Clinic

Dedicated, formally trained staff
Adequate space: - For individual consultation - For group education
Protocols covering: - Screening -Management - Regular care, including referrals
Equipment: - Scale - Height measure - Accurate sphygmomanometers, with two cuff sizes - Monofilament - Glucometers in good working order - HbA1c testing equipment (at tertiary level) - Educational material
Regular supply of medication Register with recall system for non-attenders
Annual audits of: - Numbers of patients reaching targets for glycaemia, blood pressure (BP) - Numbers of patients receiving designated processes of care

Appendix 3: History, Examination and special Investigation on Patient with Diabetes

HISTORY	INITIAL VISIT EVERY SCHEDULED VISIT	ANNUAL VISIT	
Symptoms of hyperglycemia, and duration of symptoms	X	X	X
Relevant family history	X		
Other risk factors (e.g. gestational diabetes, high birth weight)	X		X
RELEVANT MEDICAL HISTORY	X		
Co-morbid conditions	X		X
Symptoms of complications: Cardiovascular, neurological, sexual function (i.e. erectile dysfunction), feet, visual, infection	X	X	X
Weight loss			
DRUGS			
Current Side-effects and adherence	X	Side effects and adherence	Side effects and adherence
Allergies	X		X
hypoglycemic symptoms	X	X	X
LIFESTYLE			
Weight history	X		X
Physical activity	X	X	X
Eating pattern	X	X	X
Smoking	X	X	X
Alcohol	X	X	X
Psychosocial			
Occupation	X		X
Family and community support	X	X	X
Depression	X	X	X
Examination			
Weight	X	X	X
Height	X		X
Body mass index (BMI) (kg/m2)	X	X	X
Blood pressure (mmHg)	X	X	X
Feet			
Inspection: Ulcers, soft tissue, deformities, Footwear	X	X	X
Monofilament assessment	X		X

Foot pulses	X		X
Eyes			
Visual acuity	X		X
Direct fundoscopy (dilated pupils), indirect fundoscopy, or fundus photographs	X		X
Cardiovascular system examination	X		X
Injection sites, if appropriate	X	X	X
Special investigations:			
Blood tests:			
Glucose	X	X	X
*HbA1c	- Type 1 every 6 months and in type 2 only in those with poor control and aiming treatment change. (where it is available) - Cholesterol	X	X
Creatinine (and calculate estimated GFR)	X		X
HIV	X		X
Urine:			
Glucose	X	X	X
Ketones	X	X	X
Protein	X		X
ECG: If known ischemic heart disease, older than 45 years and other cardiovascular disease risk factors (In secondary and tertiary care)	X		X
Other important tasks			
Education: Self-management and lifestyle adjustment, including smoking cessation	X	X	X
Setting goals	X	X	X
Preconception counselling and family planning	X		X
Medication revision/adjustment	X	X	X

Note: Interval for retinopathy screening can be increased to once every 2 years if the last 2 examinations were normal; more frequent examinations are required in the presence of abnormalities

Appendix 4: Basic Diet Recommendation For Patients with Diabetes

DIABETIC DIET- USING LOCALLY AVAILABLE FOODS

Sweet foods such as **sugars and soft drinks** should be **avoided** as much as possible.

BREAKFAST OPTIONS

Mgaiwa porridge without sugar (thin 1 ½ cup, thick 1 cup)
Plain tea
Brown bread (3 slices), no margarine if possible
A piece of sweet potato or cassava
Boiled Irish potatoes (6 small or 2 big)
Zitumbuwa not mandasi
Zimimina zanthochi
Green maize (1 cob)
Pumpkin (11/4 small)
Fruits 1 at a time e.g. 1 banana in the morning and 1 orange (medium) in the evening
Tangerine 2 small
Lemon 2 medium
Banana 2 small or 1 big
Peaches 5-7 small
Pawpaw ¾ cup
Mango 1 small
Guava 2 small
Pineapple ¾ cup
Canned fruits ½ cup
Fruit juice ½ cup
Boiled eggs 2 per week
Oats porridge
Soya porridge – from locally made not donated because donated soya or likuni has a certain percentage of sugar in it.
A glass of milk about 250mls daily (recommended from dairy board has less fats in it)
Rice porridge once a weekPorridge with ground nut flour once a week.

NOTE: ***Do Not take all the above mentioned foods at one serving but try to make a balanced meal.***

LUNCH/ SUPPER

- Mgaiwa nsima with any type of relish with little oil added to it.
  Beans (1/2 cup)
  Chambo ½ medium, fresh utaka 2 small dried utaka 3
  Chicken 1 piece
  Meat ½ hand size slice
- Local chickens- avoid skin because it contains fats.
- No soft drinks, no sobo
- No rice, gramil/white nsima because it contains a lot of starch.

NOTE: Recommended methods of cooking include boiling, roasting and grilling.

WHEN TRAVELLING

- Carry mgaiwa.
- Choose a diabetic diet
- Carry sweets (too take when sugar levels go too low)
- Eat before or soon after medication

Things to Avoid

- **Sugar:** for Tea, Porridge.
- **Jam:** For Bread.
- **Soft drinks:** Coke, Fanta, Sobo, Mahewu, Thobwa. Diet coke can be taken
- **Sweet things:** Doughnuts, Freezes, Candy, Milk scone, Biscuit, Cakes, Sugar cane
- **Oiled Starches:** Chips, Samoosa, and Puffs.
- **Avocado: has lots of fats**
- **Groundnuts:**
- **Alcohol:** Beer such as Carlsberg, Chibuku, Napolo, and, Masese, Wine, Gin.
- **Tobacco.**

Non –Nutritive Sweeteners, (Artificial)

- Aspartame,
- Acesulfame K
- Diet Coke.

*These Sweeteners are **considered safe** and are used by people with Diabetes to satisfy their taste for sweets without affecting blood sugar level,*

SAMPLE MENU FOR A DAY

Meals/ snacks	Menu
Break fast	2 slices of bread no margarine, no jam Or 1 cup of thick porridge no nsinjiro, no sugar Tea no sugar
Snack 10:00	1 small mango or fruit in season
Lunch	3 small chipande of nsima Or 3 small cups of rice 1 cup beans (no oil) 1 cup boiled vegetables with 2 tsp of oil
Snack 15:00	2 small bananas or fruit in season
Supper	3 small chipande of nsima ¾ cup usipa no oil or 1/8 chicken (no oil) 2 cups of cabbage salad (no oil)

Appendix 5: Doppler ABPI Methodolody

DOPPLER ABPI METHODOLOGY

Explain the procedure and reassure the patient. Ensure the patient is lying flat and is comfortable, relaxed and rested with no pressure on the proximal vessels.

To measure the brachial systolic BP:

Place an appropriately sized cuff around the upper arm.
Locate the brachial pulse and apply ultrasound contact gel.
Angle the Doppler probe at 45 degrees and move the probe to obtain the best signal.
Inflate the cuff until the signal is abolished then deflate the cuff slowly and record the pressure at which the signal returns, being careful not to move the probe from the line of the artery or to apply too much pressure with the probe.
Repeat the procedure for the other arm.
Use the highest of the two values (Pb) to calculate the ABPI.

Measure the ankle systolic BP:

Place an appropriately sized cuff around the ankle immediately above the malleoli having first protected any ulcer that may be present.
Examine the foot, locating the dorsalis pedis or anterior tibial pulse and apply contact gel.
Continue as for the brachial pressure, recording this pressure in the same way.
Repeat this for the posterior tibial and if required the peroneal arteries.
Use the highest reading obtained (Pa) to calculate the ABPI for that leg.
Repeat for the other leg.

The following broad categories can be defined based on the ABPI:

In a normal individual, the ABPI is between 0.92 and 1.3 with the majority of people having a ratio between 1 and 1.2.
An ABPI above 1.3 is usually indicative of non-compressible blood vessels.
An ABPI <0.9 indicates some arterial disease.
An ABPI >0.5 and <0.9 may be associated with intermittent claudication. Refer to a vascular surgeon if symptoms indicate.
An ABPI <0.5 indicates severe arterial disease and may be associated with rest pain, ischaemic ulceration or gangrene and may warrant urgent referral to a vascular surgeon.

Appendix 6: Grading Criteria for Diabetic Retinopathy

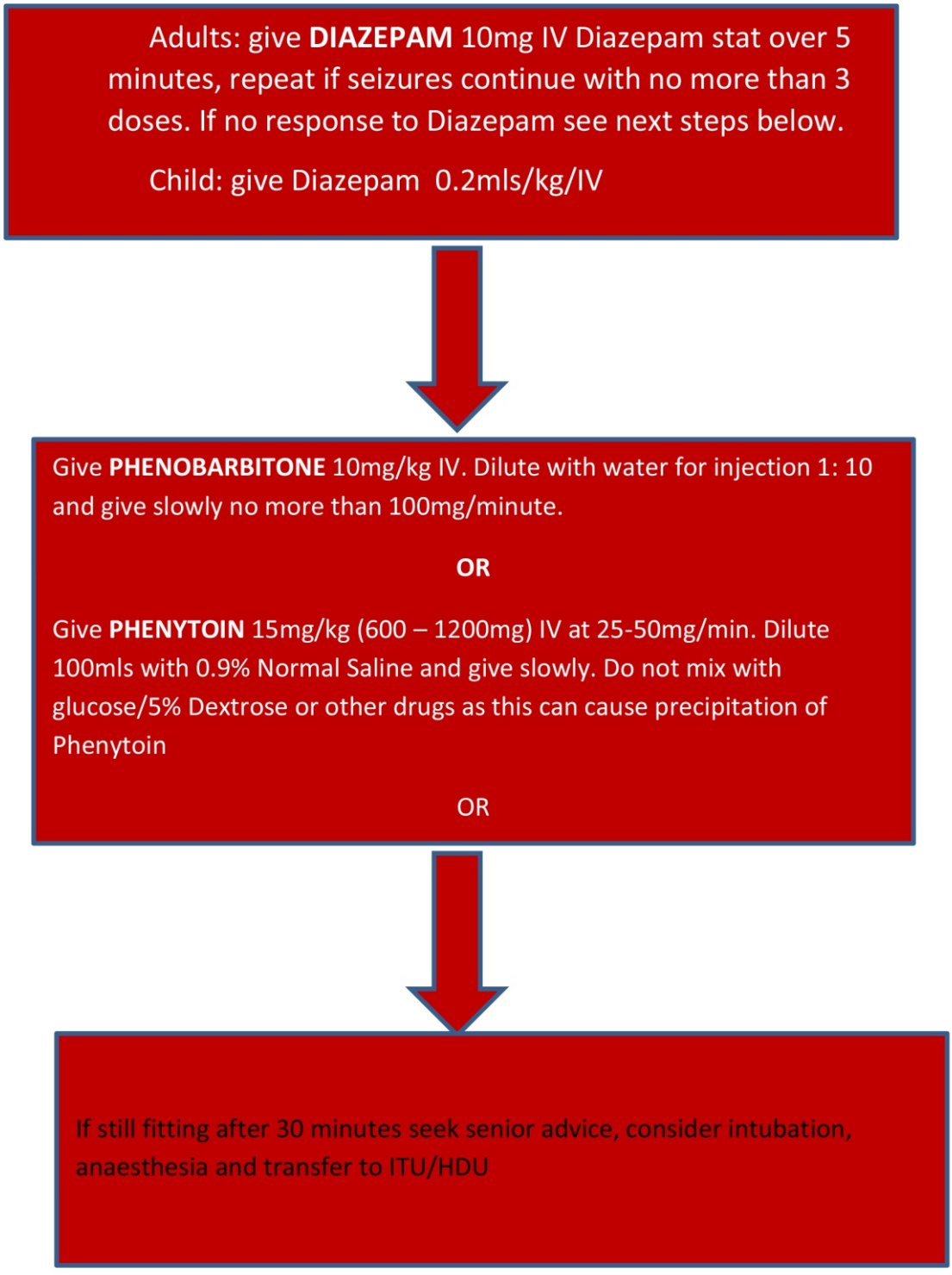
No diabetic retinopathy	**No abnormalities**
Non-Proliferative (background) diabetic retinopathy Mild non-proliferative retinopathy Moderate non-proliferative retinopathy Severe non-proliferative retinopathy	Micro-aneurysms, Mild retinal haemorrhages, hard or soft exudates More retinopathy than mild stage, venous beading, or intra-retinal micro-vascular abnormalities definitely present Soft exudates, venous beading in 2 quadrants, and intra-retinal micro-vascular abnormalities all definitely present in at least 1 quadrant, haemorrhages and micro-aneurysms present in these 4 quadrants
Proliferative diabetic retinopathy: Without high risk characteristics NVE without vitreous haemorrhage or pre retinal haemorrhages	NVD less than one quarter disc area
With high risk characteristics New vessels elsewhere (NVE) Pre-retinal or vitreous haemorrhage Pre-retinal fibrosis ± tractional retinal detachment Neovascular glaucoma, micro-aneurysms	new vessels on disc (NVD)

Appendix 7: Epilepsy Management per level of Care

INITIAL VISIT	**Assessment**- history, seizure description, investigations **Initiate treatment** **Counsel (diagnosis, treatment, psychosocial issues)** **Information/education** (plus leaflet) **Provide seizure diary** **Refer to support group** **Next date of review (monthly visits)**	**Assessment**- history, seizure description, investigations **review/initiate treatment** **Counsel** **Information/education** (plus leaflet) **Provide seizure diary** **Refer to support group** **Next date of review (monthly to 2monthly visits)**	**Assessment**- history, seizure description, investigations, **Review /initiate treatment/ consider switching to/adding 3rd line drug** **Counsel** **Information/education** (plus leaflet) **-Provide seizure diary** **-Refer to support group** **-Next date of review (monthly to 3 monthly visits)**
SUBSEQUENT VISIT	**Assess progress** (from client, witness and seizure diary; - Seizure frequency **Treatment:** compliance, side effects, review treatment **<u>If good progress</u>** Continue treatment/adjust dose prn Counsel/Reassure/psychological support Refer to support group Next date of review (monthly visits) **<u>If poor progress:</u>** **-ask following history:** triggers (fevers, infections, alcohol, drug compliance, side effects, missed drugs **- Investigations where appropriate)** - **Manage identified cause**- triggers (counselling, investigations/treatment); **If poor progress but compliance is good**	**Assess progress** (from client, witness and seizure diary; - Seizure frequency **Treatment:** compliance, side effects, review treatment **<u>If good progress</u>** Continue treatment/adjust dose prn Counsel/Reassure/psychological support Refer to support group Next date of review **<u>If poor progress:</u>** **-ask following history:** Triggers (fevers, infections, alcohol e.t.c. drug compliance, side effects, missed drugs **- Investigations where appropriate)** - **Manage identified cause**- triggers (counselling, investigations/treatment); **If poor progress but compliance is good**	**Assess progress** (from client, witness and seizure diary; - Seizure frequency **Treatment:** compliance, side effects, review treatment **<u>If good progress</u>** Continue treatment/adjust dose prn Counsel/Reassure/psychological support Refer to support group Next date of review **<u>If poor progress:</u>** **-ask following history:** Triggers (fevers, infections, alcohol e.t.c. drug compliance, side effects, missed drugs **- Investigations where appropriate)** - **Manage identified cause**- triggers (counselling, investigations/treatment); **If poor progress but compliance is good**

	-Reassess (review diagnosis/seizure type/syndrome; and history/seizure description and treatment), -emotional factors -Treat as appropriate(adjust dose; revise treatment or refer as appropriate)	-Reassess (review diagnosis/seizure type/syndrome; and history/seizure description and treatment), -emotional factors -Treat as appropriate (adjust dose; revise treatment /consider switching to/adding 2nd line drug -if no response or refer to tertiary facility for possible further investigations i.e. EEG, CT scan, MRI, X-Ray	-Reassess (review diagnosis/seizure type/syndrome; and history/seizure description and treatment), -emotional factors - investigations {prn} EEG, CT scan, MRI, X-Ray -Treat as appropriate(adjust dose; revise treatment/ consider adding 2nd drug/surgery

Appendix 9: Management of Status Epilepticus



HEALTH CENTRE

follow up patients with well controlled epilepsy

Refer to Rural/ District Hospital if:

Epilepsy not controlled on medication within 3 months

Patient < 2 years old

Psychological and/or psychiatric co-morbidity

RURAL/ DISTRICT HOSPITAL

consider adding second line therapy if required

TERTIARY HOSPITAL

specialist review, and investigations (neuro-imaging, EEG if available). Consider other diagnoses.

Refer to Tertiary Hospital if:

epilepsy not controlled with medication within 3 months

epilepsy uncontrolled on two drugs

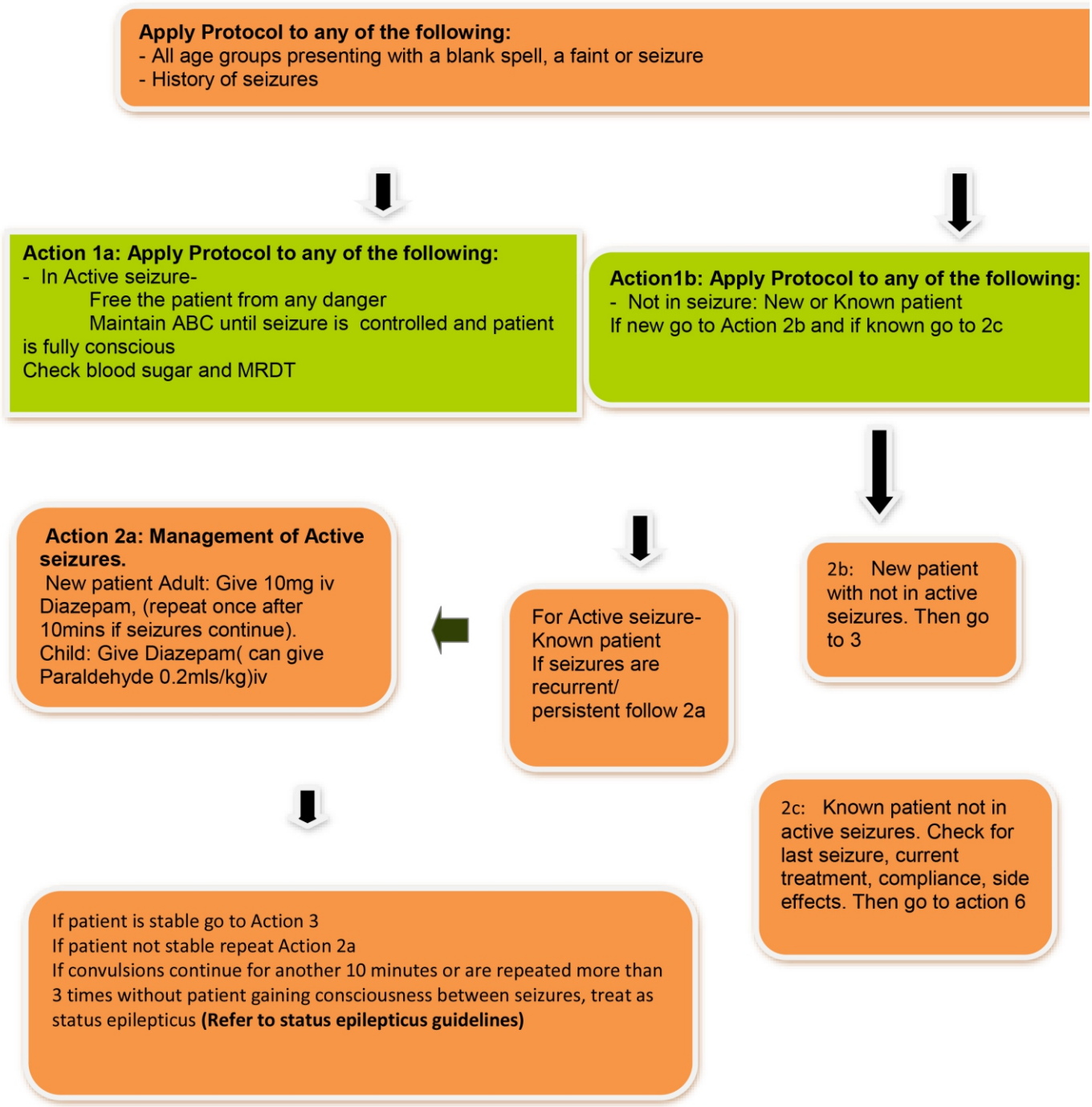
patient has unacceptable side effects from medication

psychological and/or psychiatric co-morbidity

diagnostic doubt as to the

Appendix 10: Management Algorith of Epilepsy

Protocol 4: Integrated Management of EPILEPSY



Action 3: Ask new and stable patients collect the following history at all levels of care :

Seizure History (from client and witness)

Ask, When seizure occurred and seizure description

Ask Known seizure history, onset, year, age at onset and current

Circumstances that triggered the seizure, frequency and duration

Remission (possibly there was improvement or no improvement, or it was spontaneous)

Recurrence of the seizure

Treatment of the Last Seizure

any drugs taken to treat the onset of seizure, any use of traditional medicine

Medical History

Ask past and present medical history

Ask medication history (modern and traditional/alternative medicine)

Ask history of head injury

Ask history of head surgery

Family History

Ask family history of epilepsy, seizures, mental illness and abrupt or episodic behaviour problems

Birth History:

Ask for birth complications, neonatal infections and developmental/growth milestones

Menstrual History

Social History: Ask occupation, education, marital status, hobbies, Alcohol, smoking, pork consumption

Effects of Epilepsy on: occupation, school, marital status, overprotection (basis for counselling)

Action 4: Measure/ Examine/Observation for new patient

After history, examine the following:

Step1 and 2: Primary and Secondary Level Care

Vital Signs- BP, Temperature, RR,PR and Sat O2

Physical and Neurological examination

Check for Blood Glucose, MRDT,HB, CSF

Step 3: for tertiary Level care

CT Scan for acute and MRI Scan

EEG

NO

YES

Action 5: Diagnosis
Epilepsy

Not Epilepsy:
Treat identified Condition e.g.:
Syncope
Febrile seizure
Psychogenic

Refer to Appropriate Clinics

Generalised Epilepsy:	Partial Epilepsy
Tonic Clonic	Simple
Absence	Complex
Myclonic	
Clonic	
Tonic	
Atonic	

Action 6: Treatment - Refer to tables below:

Action 6 a: Child Treatment – below 15yrs

Action 6 b: Adult Treatment Options - Above 15yrs

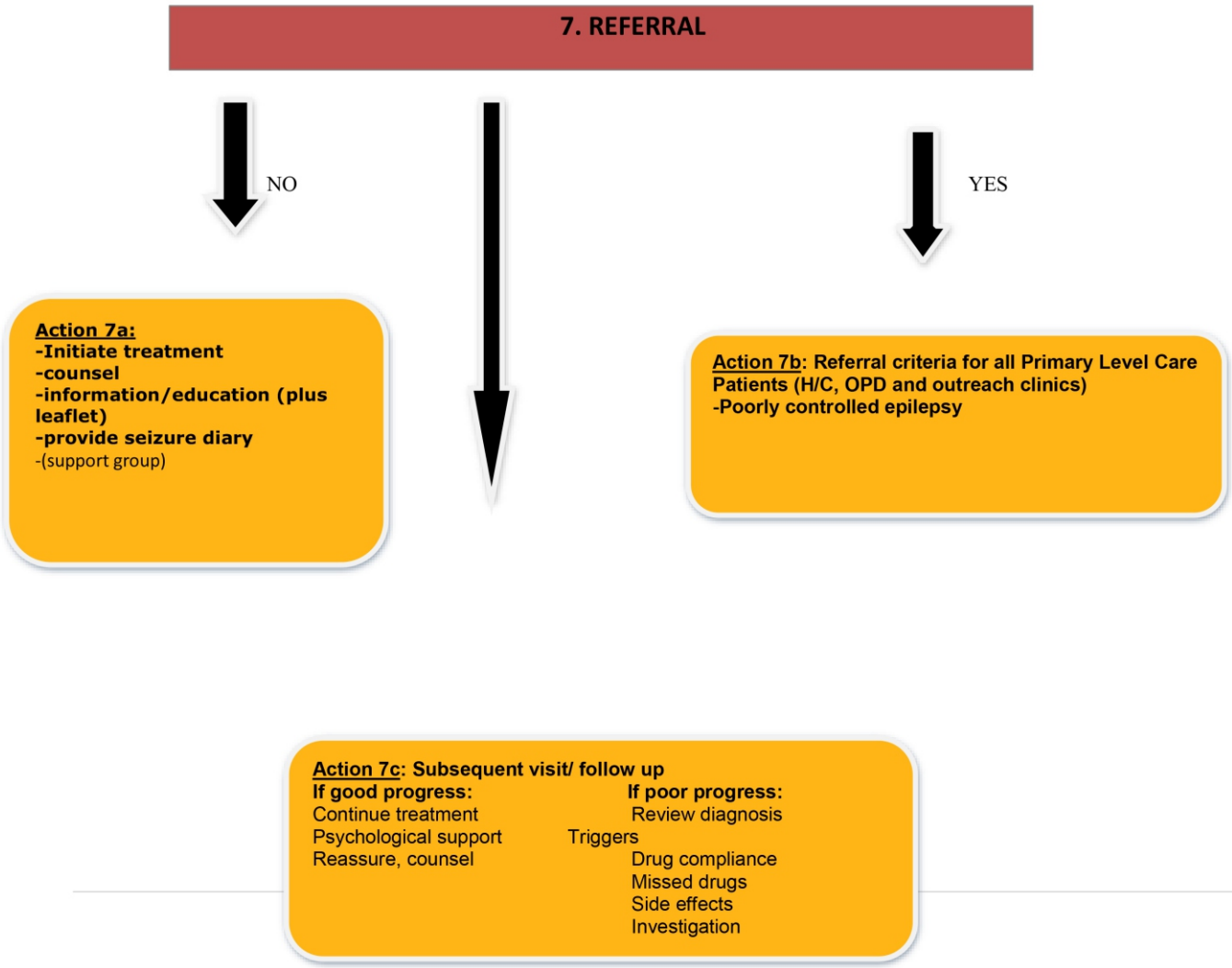
Refer to Table 6a: Child Treatment – below 15yrs

Refer to Table 6b:Adult Treatment - Above 15yrs

Child Treatment below 15yrs			
	First Step	**Second**	**Third**
Generalised			
Tonic-clonic	Sodium valproate 20-40 mg/kg/day in 2 to 3 divided doses	Carbamazepine-5mg/kg/day in 2 divided doses (2.5mg/kg bd),	Phenytoin ethosuximide-15 mg/kg at night as a single dose Phenobarbitone-5-8mg/kg daily.
Myoclonic	Sodium Valproate 20-40 mg/kg/day in 2 to 3 divided doses	Lamotrigine*	Ethosuximide* 15 mg/kg at night as a single dose Clonazepam* Phenobarbitone 5-8mg/kg daily.
Tonic	Sodium valproate 20-40 mg/kg/day in 2 to 3 divided doses	Carbamazepine 5mg/kg/day in 2 divided doses (2.5mg/kg bd), Lamotrigine*, Topiramate*	Clobazam* Phenobarbitone 5-8mg/kg daily.
Atonic	Sodium Valproate 20-40 mg/kg/day in 2 to 3 divided doses	Lamotrigine	Clobazam Carbamazepine5mg/kg/day in 2 divided doses (2.5mg/kg bd),
Absence	Sodium valproate 20-40 mg/kg/day in 2 to 3 divided doses	Lamotrigine	Clobazam acetazolamide
Partial (simple/ complex seizures)	Carbamazepine	Vigabatrin, Gabapentin Lamotrigine Topiramate	Sodium Valproate Clobazam Phenyton
Infantile spasms	Vigabatrin*	Sodium Valproate 20-40 mg/kg/day in 2 to 3 divided doses Nitrazepam* Prednisolone	Lamotrigine* ACTH* Pryridoxine*

Table 6b: Adult treatment above 15 years

Adult treatment above 15 years				
DRUG	**INDICATIONS**	**STARTING DOSE**	**STANDARD MAINTANANCE DOSE**	**DOSAGE FREQUENCY**
CARBAMEZAPINE	Partial and generalised tonic-clonic seizures	200 mg	10 – 25	Bd – qid
ETHOSUXIMIDE	Absence seizures	500 mg	500 – 2000 mg	0d – bid
LAMOTRIGINE	Partial seizures and generalised tonic clonic seizures	25	200 – 400 mg	Bid
PHENOBARBITONE	Partial and generalised tonic-clonic, myclonic, clonic and tonic seizures. Status epilepticus.	60 mg	60 – 240 mg	Od – bid
PHENYTOIN	Partial and generalised tonic-clonic seizures. Status epilepticus	200 mg	100 – 700 mg	Od – bid
SODIUM VALPROATE	All generalized seizures Partial seizure	500 mg	500 – 3000 mg	Od – tid


7. REFERRAL
NO
YES
Action 7a:
-Initiate treatment
-counsel
-information/education (plus leaflet)
-provide seizure diary
-(support group)
Action 7b: Referral criteria for all Primary Level Care Patients (H/C, OPD and outreach clinics)
-Poorly controlled epilepsy
Action 7c: Subsequent visit/ follow up
If good progress:
Continue treatment
Psychological support
Reassure, counsel
If poor progress:
Review diagnosis
Triggers
Drug compliance
Missed drugs
Side effects
Investigation

Appendix 11: Epileptic Drugs

Drug	Pharmacology	Adverse effects
Phenobarbital (Luminal)	Binds GABA-R and prolongs Cl channel open duration, enhancing GABA transmission. Also blocks high voltage activated Ca channels, and glutamate receptors Protein binding: 30-40%, $t_{1/2}$ > 72h Metabolism: 75% hepatic, 25% renal, enzyme inducer • Children are faster metabolizers and require higher dose • Reduces pentobarb metabolism	Idiosyncratic ◦ Skin rash, SJS, hepatitis, bone marrow depression ◦ SLE-like reaction • Dose-related ◦ Sedation, slowing in intellectual processes, fatigue ◦ Paradoxical hyperactive behavior in children, elderly ◦ Depression ◦ Fetal depletion of vitamin K ◦ Vitamin K dependent coagulopathy ◦ Osteopenia ◦ Megaloblastic anemia from folate depletion ◦ Dependence occurs with withdrawal symptoms
Carbamazepine (Tegretol)	Inhibits voltage-gated Na+ channels (binds to inactive form) Protein binding: 75%, t ½ 8-17h Metabolism: 98% hepatic, P450 enzymes (CYP 3A4) • Major active metabolite: CBZ-10,11-epoxide Drug interactions: many, strong p450 enzyme inducer • Induces metabolism of VPA, ethosuximide, PHT, clonazepam, OCPs, coumadin • Enzyme inhibitor (cimetidine, proposyphene, verapamil) increase CBZ levels ***Notes:*** Worsens atonic, absence, myoclonic seizures	Idiosyncratic ◦ Skin rashes (3-5%), Stevens-Johnson, rare alopecia ◦ Aplastic anaemia (1/200,000) or agranulocytosis ◦ Granulomatous hepatitis, cholangitis Dose-related ◦ CNS: dysequilibrium, drowsiness, nystagmus, dizziness, ataxia, headache, diplopia ◦ irritability, hyperactivity, impaired attention, memory ◦ Anorexia, nausea, vomiting, GI discomfort ◦ Leukopenia, thrombocytopenia (rare) ◦ Hepatotoxicity: very rare ◦ Hyponatremia ◦ Osteomalacia ◦ Teratogenicity: increased risk for spina bifida

Drug	Pharmacology	Adverse effects
Valproate (Depakote/ Depakene)	◦ Enhances GABA effects in specific circuits.Blocks voltage-dependent sodium channels, blocks T-type Ca channels ◦ Protein binding: 90% ◦ Metabolism: >95% hepatic, t ½ ~10-12h ◦ Marked fluctuations in plasma levels (10-fold) ◦ Drug interactions: many, P450 inhibitor • Displaces PHT from plasma protein and inhibit metabolism • Increased PB levels (inhibit metabolism) • PB, PHT, CBZ decrease VPA conc. b/c of induction ***Notes*** **o** Useful in Lennox-Gastaut **o** Selenium for hair loss **o** Use carnitine in the young (but no good evidence…) **o** Increased seizure with supratherapeutic levels **o** Follow CBC, LFT's, lipids ammonia **o** Treatment of choice in Absence seizures	◦ Idiosyncratic • Hepatotoxicity: overall fatal 1:50,000 ◦ *Within first 6 months of treatment and most often in kids* • Acute hemorrhagic pancreatitis **o** Dose-related • Mental dulling, sedation: polytherapy, levels 100mcg/ml • Anorexia, nausea, vomiting, GI distress, rare diarrhea • Weight gain • Hair loss • Tremor • Hyperammonemia / encephalopathy • Hepatic dysfunction • Thrombocytopenia and bruising, abnormal platelet function (also can be idiosyncratic) • Polycystic ovarian disease, menstrual irregularities • Teratogenicity: spina bifida in 1% (SUPPLEMENT with Folic Acid)
Phenytoin (Epanutin)	◦ Inhibits sustained repetitive firing effects on Sodium dependent voltage channels	◦ Idiosyncratic • Morbilliform rash ◦ Lymphadenopathy, fever, eosinophilia • Bone marrow depression • hepatitis

Drug	Pharmacology	Adverse effects
	◦ Drug interactions: ◦ Phenytoin decreases the serum levels of: • *Folate, vitamin D, griseofulvin* • *Carbamazepine, clonazepam* • *Contraceptive hormones* • *Vitamin K in newborns* ● Phenytoin sometimes increases the levels • *Phenobarbitone* ● Phenytoin levels may be increased by • *INH, rifampicin and ketoconazole* ***Notes*** **o** Not indicated in: absence – and myoclonic seizures of febrile convulsions **o** Useful in partial seizures with or without secondary generalization **o** Useful in status epilepticus	**o** Dose-related • Nystagmus, ataxia, drowsness, slurred speech • Vomiting, choreiform movements • Gingival hypertrophy • Acne, coarse facies • Re-occurrence of seizures • Cerebellar syndrome