MTRH PROTOCOLS

Medicine

MOI UNIVERSITY

TABLE OF CONTENTS

HIV/AIDS RELATED CONDITIONS

TUBERCULOSIS

Pulmonary TB

Clinical features:

- Chronic cough (longer than 2 weeks), fever, fatigue, weight loss, night sweats, LAD, FTT

Diagnosis:

- AFB sputum – 3 samples must be taken including one early in the morning
- CXR
- W riteria for diagnosis of smear negative PTB:
  - Three negative AFBs (including one early morning)
  - XR consistent with PTB
  - No response to broad spectrum antibiotics (except fluoroquinolones)

Treatment:

- Current National TB guidelines recommend: 2 months RHZE + 4 months RH
- Another potential regimen: 2 months RHZE + 6 months EH
- Dosing of components:
  - **Isoniazid:** 5mg/kg/day (max 300mg/day)
  - **Rifampin:** 10mg/kg/day (max 600mg/day)
  - **Ethambutol:** 15-25mg/kg/day (max 2.5g/day)
  - **Pyrazinamide:** 15-20mg/kg/day (max 2000mg)
  - **Streptomycin:** 15mg/kg/day IM OD
- **NB:** Try to order baseline liver enzymes prior to initiation

NMedication	Formulation	Weight in kg			
		<30	30-37	38-55	>55kg
FDC of Rifampicin 150mg + Isoniazid 75mg + Pyrazinamide 400mg + Ethambutol 275mg (Rifafour/Rihaz-E)	Combo Tab (RHZE)	mg/kg dosing	2	3	4
FDC of Rifampicin 120mg + Isoniazid 50mg + Pyrazinamide 300mg (Rifater/Rihaz)	Combo Tab (RHZ)	mg/kg dosing	2	3	4
FDC of Rifampicin 150mg + Isoniazid 75-100mg	Combo tab (RH)	mg/kg dosing	2	3	4
FDC of Ethambutol 400mg + Isoniazid 150mg (Ethizide)	Combo tab (EH)	mg/kg dosing	1.5	2	2
Streptomycin	IM	15-20 mg/kg	500 mg	750mg	1000mg

FDC=fixed dose combination

- **NB:** Neither Protease Inhibitors nor Nevirapine can be combined with rifampicin. If on Nevirapine, switch to Efavirenz

Dosing of antituberculous medication in renal and hepatic impairment

		CrCl > 50	CrCl 30-50	CrCl 10-29	CrCl < 10	Hepatic Adj.
RIHAZ	30-37 kg	2 tabs daily	q24-36 hrs		q48 hrs	

RIHAZ-E Ethizide	38-54 kg	3 tabs daily	q24-36 hrs	q48 hrs	
	55-70 kg	4 tabs daily	q24-36 hrs	q48 hrs	
	>= 71 kg	5 tabs daily	q24-36 hrs	q48 hrs	
Ethambutol		15 mg/kg daily	q24-36 hrs	q48 hrs	N/A
Isoniazid (INH)		5 mg/kg daily (max 300 mg/day)		2.5 mg/kg daily (max 150 mg)	Reduce dose in severe disease
Pyrazinamide		15-30 mg/kg daily (max 2g/day)	12-20 mg/kg daily or avoid use		N/A
Rifampin		10 mg/kg daily (max 600 mg/day)			No data
Streptomycin		15 mg/kg daily (max 1g/day)	q24 -72 hrs	q72-96 hrs	N/A

- Relapse – Subsequent TB occurrence in a patient who was previously judged to be cured of TB
- Treatment failure - Patient with a positive sputum smear at end of four months (when RH is used in the continuation phase) or five months (when EH is used in the continuation phase) of anti-TB treatment.

Patients on TB treatment should be monitored for clinical and bacteriologic response. ***For smear positive PTB patients a follow up sputum smear should be carried out at the completion of the intensive phase of treatment (two months) and four (RH) or five (EH) months and at the end of treatment.*** Patients who have a positive smear at the end of the intensive phase should have the intensive phase extended for not more than one month and weekly sputum smears until these become negative at which point they should be switched to the continuation phase. Patients who still have a positive smear at month 4 (RH) or month 5 (EH) should be considered to have failed initial treatment and switched to the re-treatment regimen (2SRHZE/1HRZE/5RHE). The medications given and the bacteriologic and clinical response should be recorded in the patient record card and the TB treatment register.

Consult TB department when MDR/XDR is suspected

TB MENINGITIS

Clinical features:

- Generally very difficult to diagnose – usually a diagnosis of exclusion
- Symptoms tend to progress over weeks instead of days
- Slow onset of progressive headache and vomiting with progression to neck stiffness
- Night sweats and weight loss
- Gradual reduction in level of consciousness leading to coma and death if not treated

Investigations

- CSF proteins markedly elevated (usually >100-200 mg/dl); glucose generally <3 mmol/L
- WBC count in CSF usually <500, but mainly lymphocytes
- CSF is normally clear and sometimes xanthochromic
- CSF may form spider webs if allowed to stand
- AFB stain of CSF is rarely positive (<10%) while TB culture improves yield slightly
- Head CT scan may show basal enhancement

Management

- Standard regimen for TB – 2RHZE/6EH or 2RHZE/4RH
- Corticosteroids – Dexamethasone 12mg/day IV/PO (or prednisone 1mg/kg/day PO) for 3 weeks then taper over the next 3 weeks

Monitoring parameters:

- Level of consciousness
- LFTs

General points to consider:

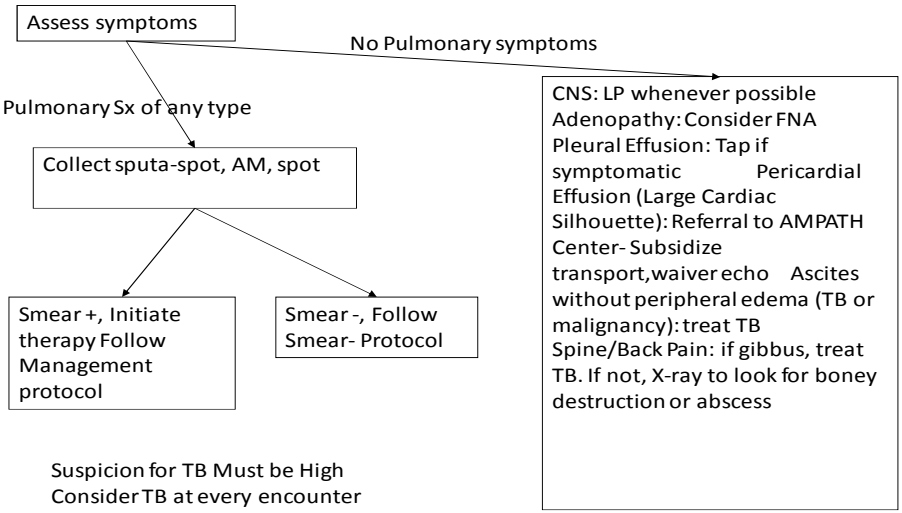
- Keep a high index of suspicion for TBM in HIV+ patients presenting with features of meningitis
- If patient does not improve on treatment for bacterial meningitis within 72 hours, consider TBM
- Repeat LP can be done on patients not improving on bacterial meningitis treatment and if CSF proteins show no change or are increasing, TBM is more likely. (NB: It is still possible that CSF proteins of patients with bacterial meningitis may remain high upto 6-8 weeks after treatment)

Other forms of extrapulmonary TB

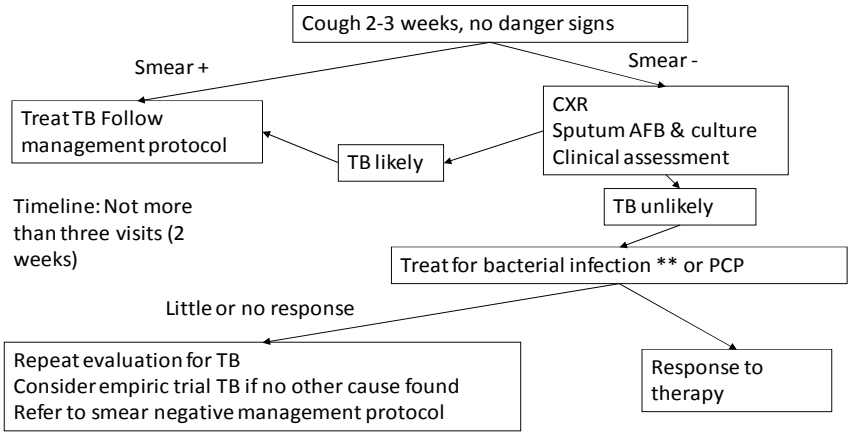
- **Tuberculoma** – Presentation is similar to other space occupying lesions and includes headache, vomiting, focal deficits, seizures and cranial nerve palsies. CT scan may or may not be able to demonstrate the presence of tuberculomas. MRI is more sensitive.
- **Tuberculous effusion and empyema** – Percussion reveals stony dullness; CXR confirms effusion. Pleural fluid aspiration can help distinguish between empyema and effusion
- **Tuberculous pericardial effusion** – Presents with chest pain, SOB, peripheral oedema, fever, cough, tachycardia, hypotension, quiet heart sounds and signs of CHF. CXR shows a large globular heart while echocardiography confirms the diagnosis. Pericardiocentesis may be life-saving if there are signs of cardiac tamponade
- **Miliary TB** – Presents with gradual onset of fever, malaise, night sweats and wasting with very little respiratory symptoms. CXR shows multiple small millet-sized nodular shadows.
- **TB peritonitis** – Presents with progressive vague abdominal pain, abdominal distension in the absence of systemic oedema, vague abdominal mass that may have a doughy feeling, fever and wasting. Often difficult to diagnose.
- **TB adenitis** – Presents with cervical lymphadenopathy. Lymph nodes are large, usually painless and firm. They eventually become matted together and then breakdown with sinus formation and pus discharge.
- **TB adrenalitis** – Destruction of the adrenal glands resulting in Addison's disease

Treatment of extrapulmonary TB is similar to PTB. Steroids are indicated in TBM, tuberculoma and pericardial TB. Use of steroids in TB peritonitis is not studied very well but the decision of whether to use steroids or not lies with the clinician.

Evaluation of the HIV patient suspected to have TB

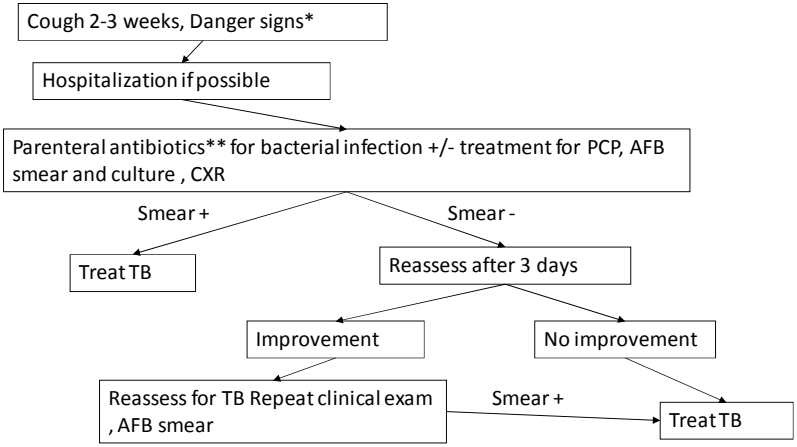


The ambulatory patient with no danger signs*:



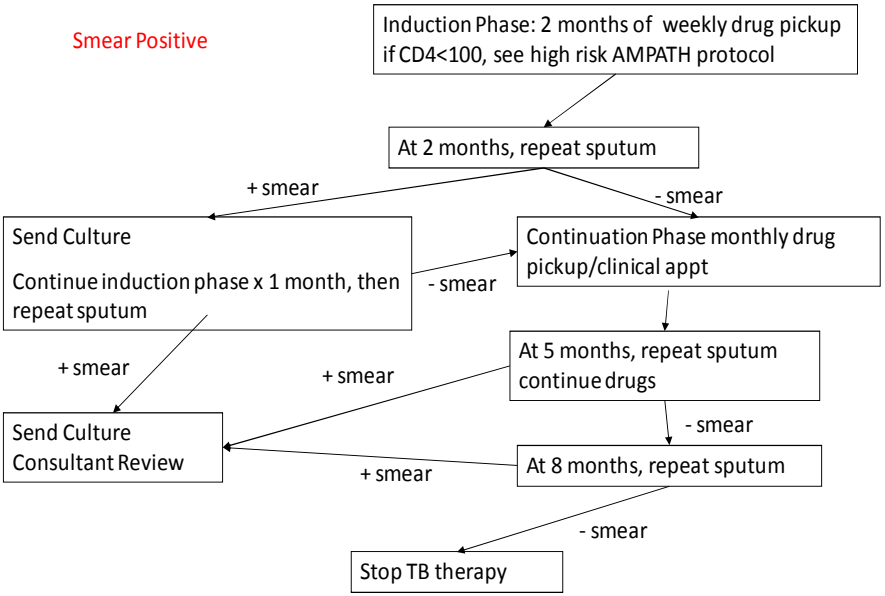
*The danger signs include any one of respiratory rate >30/minute, fever >390 C, pulse rate > 120/mt and unable to walk unaided. **Antibiotics should not include Fluoroquinolones

The Seriously ill patient:



*Danger signs include any one of respiratory rate >30/minute, fever >390 C, pulse rate > 120/mt and unable to walk unaided. **Antibiotics should not include a fluorquinolone.

Pulmonary TB management protocol for the HIV patient



Smear Negative

Induction Phase: 2months weekly drug pickup
if CD4<100, see high risk AMPATH protocol

2 month reassessment

Clinical Response **

No Clinical Response

Change to continuation phase therapy
Complete course of therapy

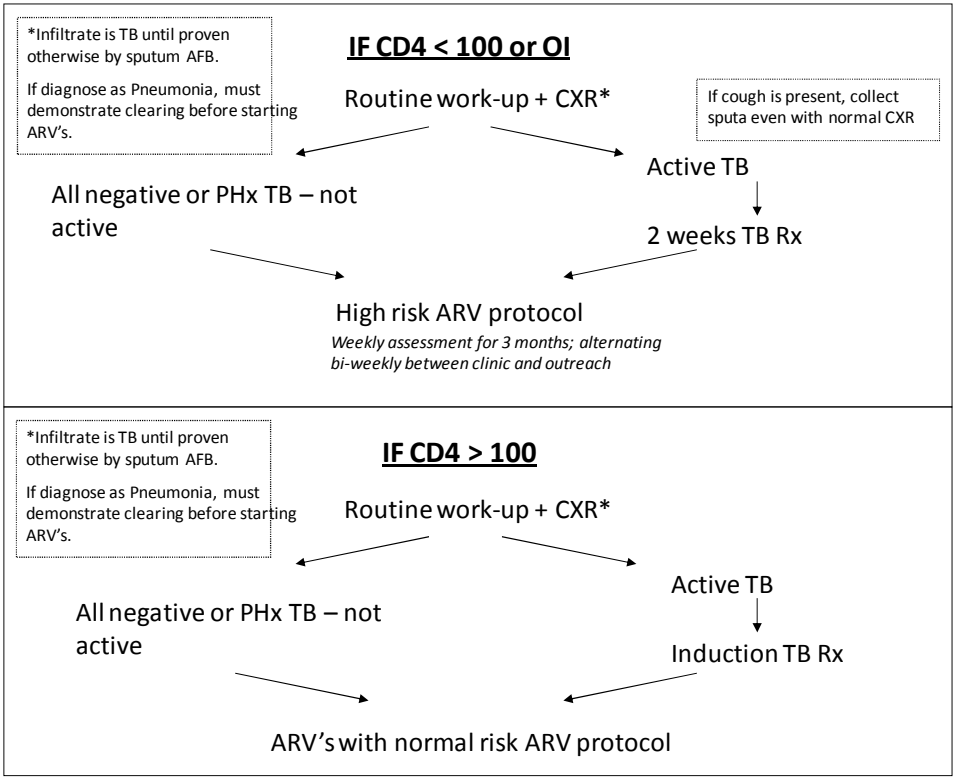
Monthly drug pickup/appt to completion

Change to continuation phase drugs and continue. Consider other diagnoses Consultant Review

**Weight gain, resolution of symptoms (fever, cough, weakness), resolution of the presenting problem (for example, the lymph nodes went away, the effusion disappears, etc)

Repeat sputa at 2,5, 8 months should still be obtained as in the smear + follow-up exams

If CD4 < 100 or OI



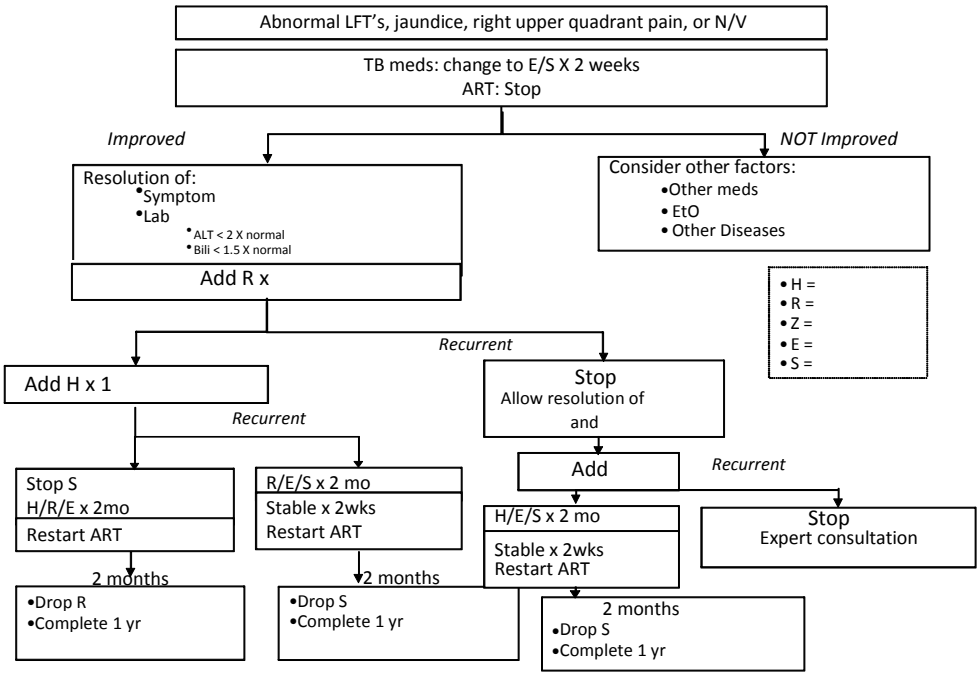
Patients taking rifampicin should not be placed on an ARV regimen containing nevirapine or a protease inhibitor. Patients on nevirapine can be switched to efavirenz. Patients on a second line regimen including a protease inhibitor should consult the TB department or an AMPATH consultant to determine the best treatment strategy.

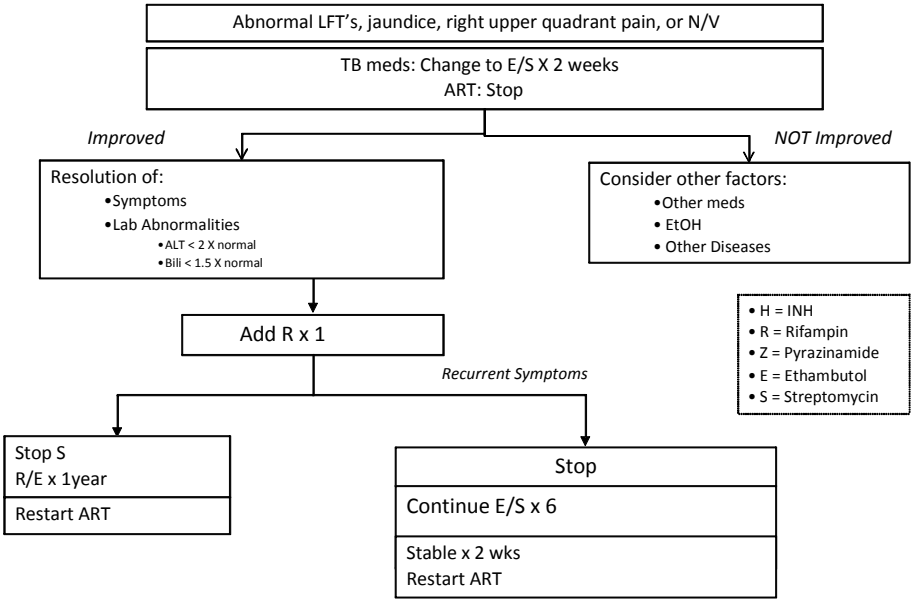
Hepatotoxicity in TB

- Common signs and symptoms include: malaise, fever, nausea, vomiting, anorexia, abdominal pain, hepatomegally and jaundice
- Hepatitis caused by antiTB medication is defined as elevation of AST three or more times the upper limit of normal with the presence of the above symptoms OR elevation of AST five or more times the upper limit of normal in the absence of symptoms
- AntiTBs implicated are rifampicin, isoniazid and pyrazinamide
- Management of a patient with hepatotoxicity:
    - Stop all potentially hepatotoxic drugs i.e. RIF, INH and PZA
    - Keep patient on a holding regimen that includes at least 2 non-hepatotoxic drugs e.g. ethambutol and streptomycin
    - When AST returns to less than twice the upper limit of normal (or to less than twice the baseline levels if baseline was higher than normal), add rifampicin
    - If there is no increase in AST after a week, add isoniazid.
    - Pyrazinamide is not normally added back as it is the most toxic of the three
    - Continue regular monitoring of LFTs all through TB treatment

TB Hepatitis Complication Protocol

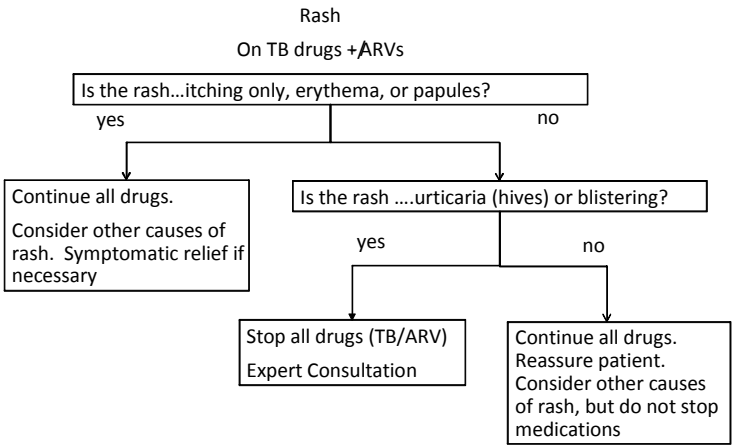
Induction Phase





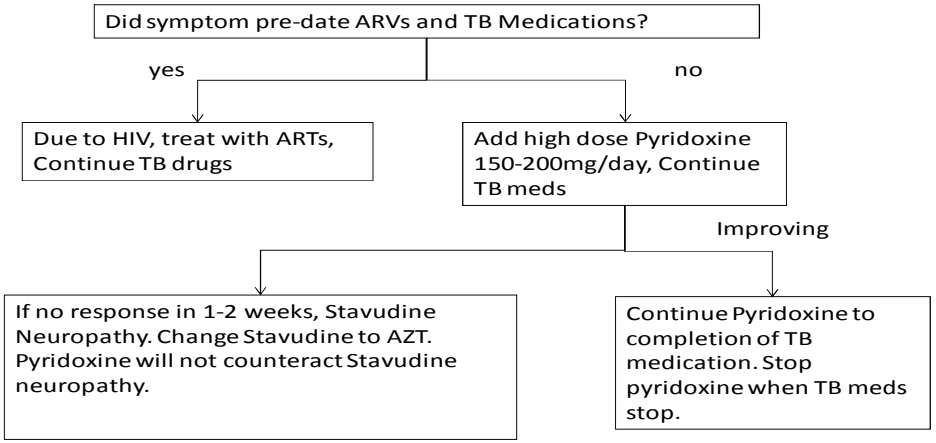
Continuation Phase

Rash with TB/HIV

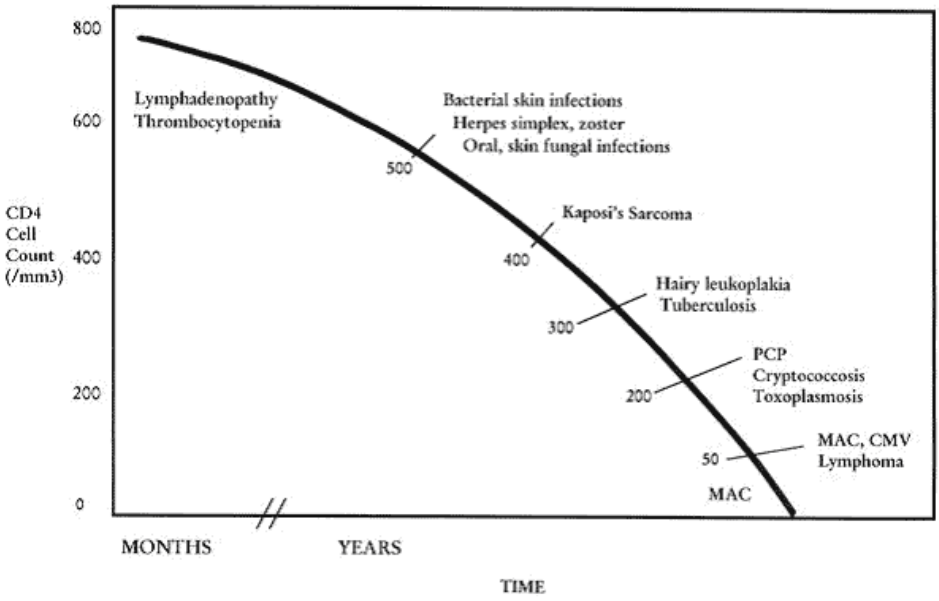


Peripheral neuropathy in TB/HIV

Symptoms: Painful hands/feet, paresthesias hands/feet, numbness in hands/feet



HIV OPPORTUNISTIC INFECTIONS



Pneumocystis Carinii Pneumonia

Clinical Findings:

- Cough, dyspnea, fever
- Tachypnea, tachycardia, diffuse dry rales on exertion

- Hypoxemia (if blood gas is available)
  - Mild-mod: pO2>70; A-a gradient <35
  - Mod-sev: pO2<70; A-a gardient >35
  - In the absence of a blood gas, pulse oximetry is useful with a pulse ox <90% being consistent with PCP
- Lactate dehydrogenase >500 is common
- CXR: Diffuse, bilateral, **symmetrical** interstitial infiltrates **OR** normal CXR
- Cysts and trophozoites on Giemsa stain
  - Collected by bronchoscopy or biopsy
- Most commonly pneumonia but can also infect liver, lymph node, spleen, bone marrow

Treatment:

- Trimethoprim/Sulfamethoxazole 15-20 mg/kg/day based on TMP x 21 days (or 2 DS tabs TID)

If pO2 <70 mmHg or pulse ox <90%, add prednisone 40mg BID x 5d, 40mg QD x 5d, 20mg QD x 11d (begin steroid prior to TMP/SMX)

- Alternatives:
  - Dapsone 100mg/day + Trimethoprim 15mg/kg/day (not to be used for G6PD, only for sulfa allergy)
  - Atovaquone 750mg BID
  - Clindamycin 600mg IV Q8hr (300-450PO Q6hr) + Primaquine
- Secondary Prophylaxis
  - Lifelong until immune system improves
  - Discontinue when CD4 > 200 for ≥ 3 months (Kenyan guidelines suggest indefinite prophylaxis)
- Prophylaxis Options
  - Trimethoprim-sulfamethoxazole one SS or DS daily (one DS daily covers toxoplasmosis adequately as well)
- Alternative prophylaxis options:
  - TMP/SMX 1 DS 3 times/week
  - Dapsone 100 mg po OD
  - Dapsone 50mg QD + pyrimethamine 50mg QW + Leucovorin 25mg QW
  - Aerosolized pentamidine 300 mg via Respirgard (Not commonly available)
  - Atovaquone 1500 mg po QD (Not commonly available)
- **Discontinuation of Primary Prophylaxis**
  - CD4 >200 for ≥ 3 months

Cryptococcal meningitis

- Typically occurs when CD4 < 100

Clinical Features:

- Fever and Headache (most common) [chronic persistent HA is typical]
- Nausea and vomiting
- Meningismus
- Photophobia
- Altered mental status
- Focal neurologic deficits and seizures (<10%)

Diagnosis:

- CSF – usually glucose decreased and protein elevated. However, CSF biochemistry can be normal.
- CSF Antigen titer (CRAG and India Ink, culture are frequently positive)
- Poor prognosis (Mean survival of 5 months)
  - AMS at baseline
  - CSF WBC <20
  - CSF Ag titer >1:1000
  - CSF opening pressure >200mm H20

Treatment:

- First line treatment

- Routine Therapeutic Lumbar Punctures!! (once every three days, significantly reduce mortality)
- Amphotericin B (0.7-1 mg/kg/day) x 2 weeks, then
- Fluconazole 400mg daily x 8 weeks, then
- Fluconazole 200mg daily for life

(When using Amphotericin B, ensure patient receives adequate IV fluid hydration [pre and post 1 Liter normal saline infusion], prophylactic paracetamol and antihistamines [chlorpheniramine] for infusion reactions. Please remember amphotericin B must be mixed in D5W.)

- Second line treatment (used when Ampho B is unavailable)
  - Fluconazole 800mg daily x 2 weeks, then
  - Fluconazole 400mg daily for life
- Fluconazole 800mg daily is often started based on the suspicion of cryptococcal meningitis. This is subsequently switched to ampho upon confirmation of diagnosis based on the LP Crag and India Ink. This is done to minimize unnecessary exposure to amphotericin B for patients without cryptococcal meningitis.

Monitoring parameters:

- Serum creatinine; Amphotericin B causes ATN
- Serum potassium; Amphotericin generally causes hypokalemia but it can also indirectly cause hyperkalemia secondary to acute renal failure

Toxoplasmosis

Symptoms (generally occurs in patients with CD4 <100 but not necessarily):

- Headache
- Confusion
- Fever
- Lethargy
- Seizures
- Poor coordination/gait
- HA/confusion/fever/seizure

Diagnosis:

- Ring enhancing lesions on CT scan (often difficult to differentiate from CNS lymphoma and brain abscesses)

Treatment:

- **Sulfadoxine 500mg-pyrimethamine 25mg** Tabs (Fansidar)
  - 8 tablets on day 1
  - 3-4 tablets OD x 6-8 weeks
- **SMX-TMP** 10mg/kg of trimethoprim component divided 2-3 times daily
  - 2 DS tablets BD
  - 4 SS tablets BD

Cochrane Review from 2008 claims there is no significant difference between these two regimens; however, pyrimethamine has the highest activity against toxoplasmosis.

In resource-rich settings, leucovorin (activated folate) is often given with pyrimethamine based regimens to reduce the risk of bone marrow suppression. This is often too expensive to be routinely done in this setting; however, doses may be acquired for special cases.

Candidiasis

Oropharyngeal candidiasis:

- **Clinical features:**
  - Painless, creamy white plaque like lesions in the mouth
  - Lesions cannot be scraped with a tongue depressor
- **Treatment:**
  - Fluconazole 100-200mg OD x 7 days

Esophageal candidiasis:

- **Clinical features:**
  - Retrosternal burning pain or discomfort and odynophagia.
  - Endoscopic examination reveals whitish plaques similar to those observed with oropharyngeal disease
- **Treatment:**
  - Fluconazole 200mg OD x 14 days

NB: Assume esophageal involvement unless proven otherwise by endoscopy.

Epidemiologic forms of KS:
1. AIDS-related/epidemic KS
2. Endemic/African KS
3. Organ transplant associated
4. Classic KS

Kaposi's sarcoma

Clinical features:
- Most common site of lesions is the skin especially on the legs, hands, sole, face, mouth, genitals. Features of the lesions:
  - Oval in shape
  - Purple/black in colour
  - No pain or pruritis
  - Flat or nodular
  - May ulcerate or bleed
  - May cause periorbital or extremity oedema due to dermal lymphatic invasion
- Can be present in any organ except the brain:
  - Oral cavity – results in pain and difficulty in swallowing. Lesions are usually on the palate but could be present anywhere else including the tongue, gums and pharynx
  - GI tract – results in weight loss, abdominal pain, diarrhea, bleeding
  - Lungs – results in SOB, cough, haemoptysis, chest pain; lung involvement usually signifies a poor prognosis

Diagnosis:
- Definitive diagnosis is biopsy of the lesion
- Bronchoscopy for KS of the lungs
- Can have any CXR finding
- Staging based on extent of tumour lesions (T), patient's immune system (I) and presence of opportunistic infections and B symptoms (S). Lowest risk: $T_0I_0S_0$ whereas highest risk is $T_1I_1S_1$.

Treatment:
- There is no cure. The goal is palliation
- Start ARVs immediately and follow for 3 months
- Chemotherapy should be started immediately if:
  - Life threatening lesions are present
  - Internal organ involvement is suspected
  - There is extensive oedema and skin involvement
  - There are disfiguring facial lesions
- Isolated skin lesions can be treated using:
  - Panretin gel 0.1% - induces apoptosis
  - Vinblastine intralesional injection
  - Radiation
- Chemotherapy regimens include:
  - ABV – Doxorubicin (10-20 mg/m^2), Bleomycin (10-15 units/m^2), Vincristine (1-2 mg). Is the first-line chemotherapy.
  - Single agent etoposide – 50 mg/day for 7 days of an every 2 week cycle
  - Paclitaxel – 135 mg/m^2 every 3 weeks as a 3-hour infusion. Used in patients who have failed first-line.
  - Single agent gemcitabine – still being studied as an alternative to ABV

  NB: Consult with oncologist and specific oncology protocols for doses as these can change

Monitoring parameters:
- CD4 count
- Cardiac function when on doxorubicin. Maximum cumulative dose of doxorubicin is 450 mg/m^2
- Monitor CBC, UEC, LFTs during and after chemotherapy

Immune Reconstitution Inflammatory Syndrome (IRIS)

- Treatment with HAART and increase in CD4 counts may produce inflammatory responses against latent infections
- Important to Distinguish between IRIS and true infection
- **Several OIs associated with IRIS**
  - MAC
  - PCP, NHL, KS, TB
  - CMV
  - Herpes
  - HBV, HCV, cryptococcus,
- **Treatment**
  - Continue HAART
  - Anti-inflammatories
    - 1st line would be to try NSAIDs, if no improvement, consider low dose steroids
  - Antibiotic against OI

RENAL DOSING OF AGENTS USED IN THE MANAGEMENT OF HIV/AIDS IN ADULTS

Calculating Creatinine Clearance:

To convert Creatinine to mg/dl: Lab value obtained / 88.4

To calculate Creatinine Clearance from Creatinine American Units (mg/dL):

(140- Age)(Wt in Kg) x (0.85 for women)
(72)(Serum Creatinine mg/dl)

To calculate Creatinine Clearance from SI units (Kenyan units)

(140- Age)(Wt in Kg) X 1.23 x (0.85 for women)
(Creatinine in µmol/L)

** Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTIs) **

Agent	Dose for normal renal function	Estimated Creatinine Clearance (CrCL) in ml/min			Hepatic Adjustments
		> 50	10 - 50	< 10	
Abacavir/ABC (Zyogen)	300mg po bid	No adjustment recommended			No data
Didanosine/ddI (Videx)	Weight <60kg: 125mg bid	125mg bid	125mg qd	62.5mg qd	Extensive hepatic metabolism*
	Weight > 60kg: 200mg bid	200mg bid	200mg qd	100mg qd	Extensive hepatic metabolism*
Lamivudine/3TC (Epivir)	150mg bid	100%	150mg qd	150mg every other day	No data
Stavudine/d4T (Zerit)	30mg bid	30mg bid	15mg bid or qd	15mg qd	No data
Zidovudine/AZT (Retrovir)	300mg bid	300mg bid	300mg bid	300mg qd	200mg bid

** Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) **

Agent	Dose for normal renal function	Estimated Creatinine Clearance (CrCl) in ml/min			Hepatic Adjustments
		> 50	10 - 50	< 10	
Efavirenz/EFV (Stocrin)	600mg po qd	No adjustment recommended			Extensive hepatic metabolism*
Nevirapine/NVP (Viramune)	200mg qd x 14 days, then 200mg po bid	No adjustment recommended			Extensive hepatic metabolism*

** Protease Inhibitors (PIs) **

Agent	Dose for normal renal function	Estimated Creatinine Clearance (CrCl) in ml/min			Hepatic Adjustments
		> 50	10 - 50	< 10	
Loprinavir/ ritonavir LPV/r (Kaletra)	400/100mg bid	No adjustment recommended			No data
Nelfinavir/NFV (Viracept)	750mg tid or 1250mg bid	No adjustment recommended			Extensive hepatic metabolism*

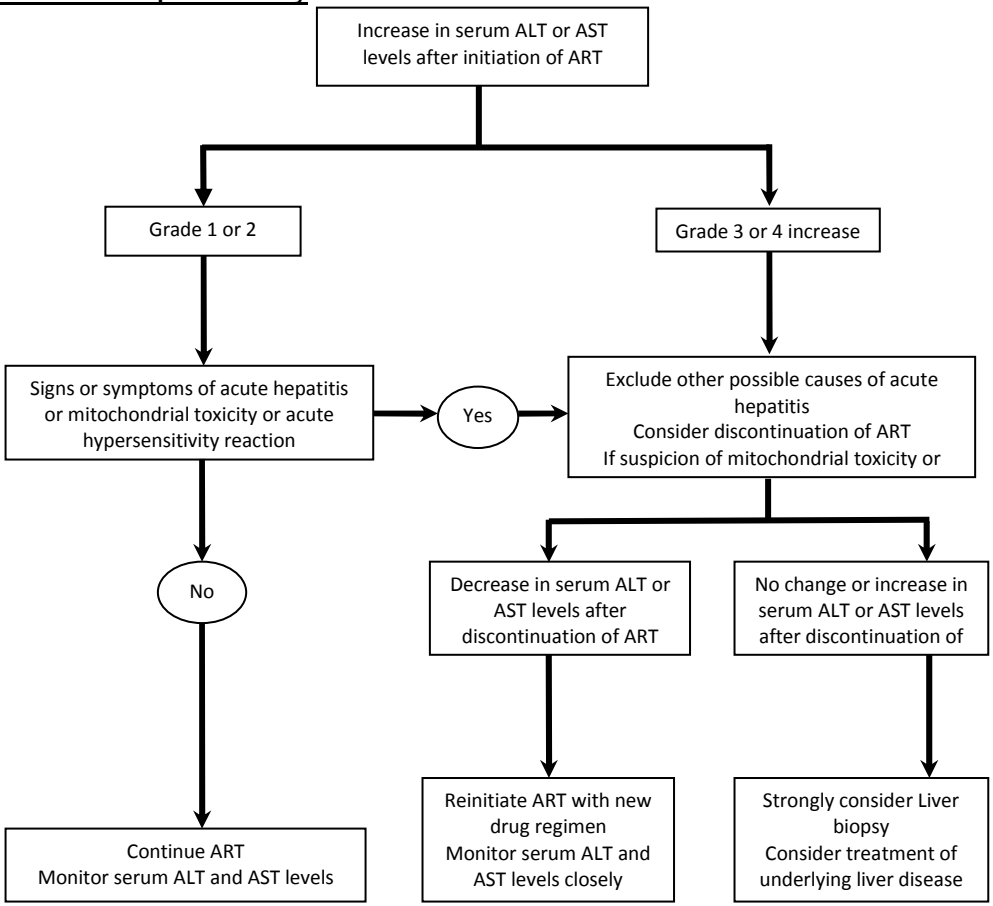
** Combination Products **

Agent	Dose for normal renal function	Estimated Creatinine Clearance (CrCl) in ml/min		
		> 50	10 - 50	< 10
Zidovudine/Lamivudine AZT/3TC (Combivir)	300/150mg bid	300/150mg bid	Use individual drugs at doses listed above	
Nevirapine/Lamivudine/Stavudine NVP/3TC/d4T (Triomune)	200/150/30mg bid	200/150/30mg bid	Use individual drugs at doses listed above	

*No guidelines for extensive hepatic metabolism given, empiric dose reduction suggested

Information compiled from 2003 Medical Management of HIV Infection by John G. Bartlett, M.D. and Joel E. Gallant, M.D., M.P.H.

HAART and hepatotoxicity



NB:
Hepatoxicity is characterized by biochemical liver abnormalities using the upper limit of normal (ULN) or increase above baseline value of serum alanine aminotransfarase (ALT) or aspartate aminotransferase (AST) [1, 2]

Alternatively, hyperbilirubinaemia secondary to HAART induced cholestasis may be used to gauge hepatoxicity[3]. Severe hepatotoxicity is hyperbilirubinaemia of grade 3 or 4.

GRADE	ALT/AST ELEVATIONS		Bilirubin
	Times the ULN	Times the baseline value	Times ULN
0	<1.25	<1.25	<1.1
1	1.25-2.5	1.25-2.5	1.1-1.5
2	2.6-5.0	2.6-3.5	1.6-2.9
3	5.1-10.0	3.6-5.0	3.0-5.0
4	>10	>5	>5

POST EXPOSURE PROPHYLAXIS (PEP)

Post Exposure Procedures for Occupational Exposures

Exposed Individual:

Needle sticks, lacerations or exposure of intact skin:

1) Allow wound to bleed but **do not** squeeze enough to bruise or suck wound
2) Wash the affected area gently with soap and water **do not** scrub strongly or use nail brush

Mucous Membrane Exposure:

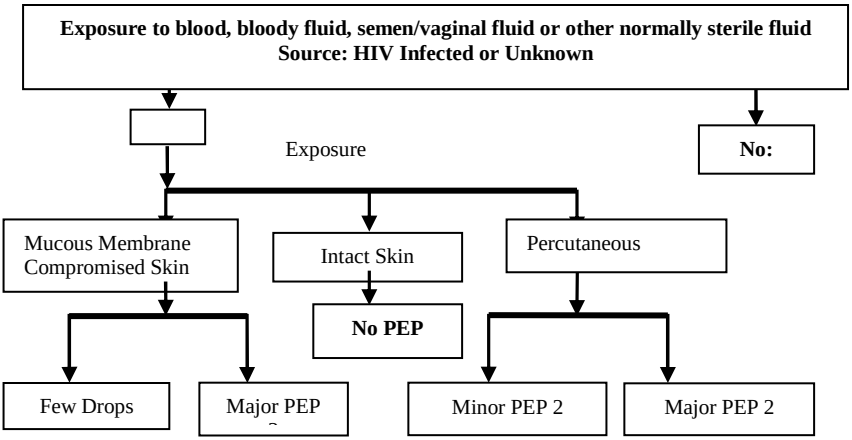
1) Irrigate the affected area (eye, mouth etc) with clean water

General:

1) Inform the senior member of staff in charge
2) Immediately contact the HAART Clinic **2237**; if after hours contact **Dr. Kimaiyo, Dr. Mamlin or Dr. Siika** regarding need for treatment

Clinician Evaluating Patient:

1) Assessment of the exposure using the **Post Exposure Intake Form**
2) If possible obtain rapid HIV test on source (however do not wait for the results to start ARVs – if source is negative can stop ARVs)
3) Check rapid HIV test on exposed individual
4) Determine the need for ARVs if within 72 hours of exposure (Treatment Duration 4 wks):



Adult:
PEP 1: Combivir 1 tab bid
PEP 2: Combivir 1 tab + Lopinavir/r 2 tabs bid*

5) Determine need for Hepatitis B immunization for the exposed individual
6) Check ALT, Creat, Full Hemogram on exposed individual
7) Follow-up in 2 weeks in HAART Clinic for evaluation
8) Follow-up HIV test at 6 wks, 3 months, and 6 months

* If source is on ARVs, regimen may need to be altered

Post Exposure Procedures for Sexual Exposures

1) Medical Officer Review
2) Assess need for ARV prophylaxis: If source in unknown or HIV infected then use **PEP 2** (4 weeks of treatment)
3) Check Rapid HIV Test
4) Take blood for ALT, Creat, and Full Hemogram
5) Check Pregnancy test, UA
6) Counsel about emergency contraception
7) Provide empiric treatment for STIs
   - Benzithine PCN 2.4 mu IM
   - Azithromycin 1 gm orally **or** Doxycycline 100mg bid x 7 days **or** Erythromycin 500 qid x 7 days
   - Ciprofloxacin 500 mg Stat **or** Ofloxacin 400 mg Stat **or** Levofloxacin 250 mg Stat
8) Consider Hepatitis B immunization
9) Provide emotional counseling for the victim
10) Schedule an appointment in the HAART Clinic for 2 weeks
11) HIV Testing at 6 wks, 3 months, and 6 months

ACUTE RHEUMATIC FEVER

Predisposing factors:

- Group A streptococcal tonsillopharyngitis

Clinical features:

- More common in children but can still occur in adults
- Migratory polyarthritis:
  - Affects several joints in quick succession, each for a short time
  - Commonly affected joints are the knees, ankles, elbows and wrists
  - Only one joint may be affected especially if the patient self-medicated with NSAIDs before presentation
- Carditis – Rheumatic fever produces a pancarditis affecting the pericardium, epicardium, myocardium, and endocardium. Cardiac manifestations may be subtle and include a variety of signs or symptoms:
  - Mild to moderate chest discomfort, pleuritic chest pain, or a pericardial friction rub are indications of pericarditis.
  - Physical examination may reveal new or changing murmurs. Mitral regurgitation is the most common finding.
- Sydenham chorea – a neurologic disorder consisting of abrupt, purposeless, nonrhythmic involuntary movements, muscular weakness, and emotional disturbances.
- Subcutaneous nodules:
  - Firm and painless
  - The overlying skin is not inflamed and usually can be moved over the nodules.
  - The diameter varies from a few millimeters to one or two centimeters.
  - The nodules most commonly are located over a bony surface or prominence or near tendons.
  - Nodules are present for one or more weeks, rarely for more than a month.
- Erythema marginatum:
  - An evanescent, non-pruritic rash, pink or faintly red, usually affecting the trunk and sometimes the proximal parts or the limbs, but not the face.
  - The name derives from the observation that the lesion extends centrifugally while the skin in the centre returns to normal.
- Other features include arthralgia and fever.

- Recurrent untreated episodes of rheumatic fever can lead irreversible valvular damage i.e. chronic rheumatic heart disease.

Laboratory investigations:

- Evidence of infection:
  - Throat culture for group A beta-haemolytic streptococcus – is negative in 75% of patients by the time rheumatic fever appears. (Reliability of culture results may be questionable)
  - Elevated or rising antistreptolysin O titre (ASOT)
- ESR
- CXR – cardiomegally is common in carditis
- ECG, Echocardiogram – to confirm carditis and assess the presence and severity of valvular regurgitation or stenosis.

Diagnosis:

- Based on Modified Jones Criteria. Classified into major and minor criteria as follows:

Major Criteria	Minor Criteria
• Carditis • Polyarthritis • Subcutaneous Nodules • Erythema marginatum • Chorea	• Prolonged PR interval on ECG • Arthralgia • Fever • Evidence of preceeding streptococcal infection • Increased Acute phase reactants (incr ESR or incr CRP)

- Presence of two major or one major and two minor criteria is enough for diagnosis of acute rheumatic fever.
- For the diagnosis of recurrent episodes of acute rheumatic fever, the recommendations are as follows:

Table 1 Summary of 2002-3 World Health Organization criteria for diagnosis of rheumatic fever and rheumatic heart disease (based on revised Jones criteria)[2]

Diagnostic categories	Criteria
Primary episode of rheumatic fever	Two major or one major and two minor manifestations plus evidence of a preceding group A streptococcal infection
Recurrent attack of rheumatic fever in patients without established rheumatic heart disease	Two major or one major and two minor manifestations plus evidence of a preceding group A streptococcal infection
Recurrent attack of rheumatic fever in patients with established rheumatic heart disease	Two minor manifestations plus evidence of a preceding group A streptococcal infection
Rheumatic chorea. Insidious onset rheumatic carditis	Other major manifestations or evidence of group A streptococcal infection not required
Chronic valve lesions of rheumatic heart disease (patients presenting for first time with pure mitral stenosis, mixed mitral valve disease, and aortic valve disease)	Do not require any other criteria to be diagnosed as having rheumatic heart disease

Treatment:

- Bed rest until inflammation subsides
- Antiinflammatory therapy:
  - Aspirin – 80-100 mg/kg per day in children and 4-6 g/day in adults in 3-4 divided doses. Used to prevent heart disease.
  - Therapy should be maintained until all symptoms are absent and ESR is normal.
  - In patients with carditis, corticosteroids are often used but a 2003 Cochrane review concluded that there was no significant difference in outcome when corticosteroids and aspirin treatment were compared.
  - Dose of steroids: 2 mg/kg of oral prednisone for the first 1 or 2 weeks, which is then tapered over the next 2 weeks. Once steroids are begun to be tapered, aspirin may be added.
- Patients with heart failure secondary to carditis can be treated with conventional therapy for heart failure including diuretics, ACE inhibitors and beta blockers.
- Antibiotic therapy:
  - Should be initiated regardless of the presence or absence of pharyngitis at the time of diagnosis.
  - Penicillin V 500 mg TID in adults and 250 mg TID in children for 10 days.
  - Alternatively, a single dose of IM benzathine penicillin G can be given; 1,200,000 units in adults and 600,000 units in children.
  - Alternative agents include first generation cephalosporins and erythromycin for 10 days
- Chorea can be treated symptomatically using phenobarbitone or haloperidol

Primary prophylaxis:

- All patients with a sore throat and symptoms suggestive of a streptococcal infection (pharyngeal exudates, enlarged tender cervical lymph nodes and absence of cough and other prominent URTI symptoms) should be treated with oral penicillin for 10 days or with a single IM injection of benzathine penicillin G.

Table 2 Antibiotics used in primary prevention and treatment of group A streptococcal throat infection (World Health Organization guidelines)[2]

Antibiotic	Route of administration and dosage	Dose
Benzathine benzylpenicillin	Intramuscular injection; childen should be kept under observation for 30 minutes	Single dose 1.2 million U; <27 kg, 600 000 U
Phenoxymethylpenicillin (penicillin V)	Oral, 2-4 times daily for 10 days	Children 250 mg twice or three times daily, adolescents or adults 250 mg three or four times daily or 500 mg twice daily
Amoxicillin	Oral, 2-3 times daily for 10 days	25-50 mg/kg/d in three doses; total adult dose 750-1500 mg/d
First generation cephalosporins	Oral, 2-3 times daily for 10 days	Varies with formulation
Erythromycin if allergic to penicillin	Oral, 4 times daily for 10 days	Varies with formulation

Secondary prophylaxis:

- The goal of secondary prophylaxis against group A streptococcal infection is to prevent recurrences of ARF, thereby preventing development of rheumatic heart disease
- Should be started immediately after the resolution of the primary episode of ARF.
- WHO recommendations for the duration of secondary prophylaxis are:
  - Patients without proven carditis – At least five years of antibiotic prophylaxis following diagnosis of ARF or until age 18
  - Patients with mild mitral regurgitation – At least ten years of prophylaxis or until age 25

- Patients with severe valve disease and/or after valve surgery – Life-long prophylaxis
- Agents used are IM benzathine penicillin G, oral penicillin V or erythromycin (for patients allergic to penicillin).

Table 3 Antibiotics used in secondary prevention of rheumatic fever (World Health Organization guidelines)[2]

Antibiotic	Route of administration	Dose
Benzathine benzylpenicillin	Intramuscular injection, every 3-4 weeks	≥30 kg, 1.2 million U; <30 kg, 600 000 U
Phenoxymethyl penicillin (penicillin V)	Oral	250 mg twice daily
Erythromycin if allergic to penicillin	Oral	250 mg twice daily

ALCOHOL WITHDRAWAL SYNDROME

Clinical features:

- Minor withdrawal symptoms – due to CNS hyperactivity and include:
  - Insomnia
  - Tremulousness
  - Mild anxiety
  - GI upset; anorexia
  - Headache
  - Diaphoresis
  - Palpitations

  These symptoms usually present within six hours of cessation of drinking and may develop while patients still have a significant blood alcohol concentration. If withdrawal does not progress, these findings resolve within 24 to 48 hours.
- Withdrawal seizures:
  - Generalized tonic-clonic convulsions that usually occur within 12-48 hoursafter the last drink.
  - Predominantly in patients with a long history of chronic alcoholism
  - Usually singular or occur as a brief flurry over a short period
  - If untreated they progress to delirium tremens in one-third of patients.
- Alcoholic hallucinosis:
  - NOT synonymous to delirium tremens
  - Refers to hallucinations that develop within 12-24 hours of abstinence and resolve within 24-48 hours (which is the earliest point at which delirium tremens typically develops).
  - Not associated with global clouding of sensorium, but with specific hallucinations, and vital signs are usually normal.
- Delirium tremens:
  - Defined by hallucinations, disorientation, tachycardia, hypertension, fever, agitation, and diaphoresis in the setting of acute reduction or abstinence from alcohol.
  - Electrolyte imbalance – hypokalaemia is common due to renal and extrarenal losses, alterations in aldosterone levels, and changes in potassium distribution across the cell membrane.
  - DT typically begins between 48-96 hours after the last drink and lasts one to five days.
  - Symptoms that occur a few hours after the cessation of drinking, even if severe, are not manifestations of DT.
  - Risk factors for the development of DT include:
    - A history of sustained drinking
    - A history of previous DT
    - Age greater than 30
    - The presence of a concurrent illness

        - The presence of significant alcohol withdrawal in the presence of an elevated alcohol level
        - A longer period since the last drink (i.e. patients who present with alcohol withdrawal more than two days after their last drink are more likely to experience DT than those who present within two days).
    - Generally associated with a high mortality
    - Death usually is due to arrhythmia, complicating illnesses such as pneumonia, or failure to identify an underlying problem that led to the cessation of alcohol use, such as pancreatitis, hepatitis or central nervous system injury or infection.
    - Older age, preexisting pulmonary disease, core body temperature greater than 40ºC (104ºF), and coexisting liver disease are associated with a greater risk of mortality.

Diagnosis:

- Based mainly on clinical findings
- Alternative diagnoses should be ruled out. These include: infection (e.g. meningitis), trauma (e.g. intracranial hemorrhage), metabolic derangements, drug overdose, hepatic failure, and gastrointestinal bleeding.

Treatment:

- Supportive management:
    - Adequate fluid and electrolyte replacement
    - Thiamine (100 mg IV) and glucose should be administered in order to prevent or treat Wernicke's encephalopathy.
    - Multivitamin supplements containing folate
    - Nutritional support
- Benzodiazepines:
    - Used to treat the psychomotor agitation most patients experience during withdrawal and to prevent progression from minor withdrawal symptoms to major ones.
    - Longer acting agents are preferred as there is less risk of recurrent withdrawal or seizures.
    - Dosing is based on the patient's risk factors and ability to tolerate DT.
    - Generally use IV diazepam, 5-10 mg every 5 to 10 minutes until the appropriate level of sedation is achieved.
    - In severe withdrawal, patients may require massive doses to achieve initial control (> 500 mg).
    - Once initial control has been achieved, a symptom triggered approach to therapy must be followed, whereby a regular systematic assessment should be made of the patient's status using a validated instrument, such as the Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWAS-Ar), a measure of withdrawal severity (see below).
    - Evaluation intervals as frequent as every 10-15 minutes are appropriate for patients with more severe symptoms. Once severe symptoms are controlled, hourly reassessment of such patients is reasonable. In contrast, an interval of 4 to 6 hours is reasonable for stable patients with mild symptoms receiving oral benzodiazepines.
    - When the score is elevated (> 8), additional diazepam 5-10 mg is given.
- Refractory DT:
    - Is present despite use of high doses of benzodiazepines.
    - Add phenobarbitone 120-240 mg every 15-20 minutes until symptoms are controlled.
    - Another alternative is propofol. However, if propofol is used, endotracheal intubation and mechanical ventilation is necessary.
- **NB:** Antipsychotics such as chlorpromazine and haloperidol should NOT be used because they lower the seizure threshold

- **Criteria for ICU admission (if bed space is available) of patients with alcohol withdrawal:**
    - Age >40
    - Cardiac disease (heart failure, arrhythmia, angina, myocardial ischemia, recent myocardial infarction)

- Hemodynamic instability
- Marked acid-base disturbances
- Severe electrolyte defects (hypokalemia, hypophosphatemia, hypomagnesemia, hypocalcemia)
- Respiratory insufficiency (hypoxemia, hypercapnia, severe hypocapnia, pneumonia, asthma, COPD)
- Potentially serious infections (wounds, pneumonia, trauma, urinary tract infection)
- Signs of gastrointestinal pathology (pancreatitis, GI bleeding, hepatic insufficiency, suspected peritonitis)
- Persistent hyperthermia (temperature >39°C)
- Evidence of rhabdomyolysis
- Renal insufficiency or increased fluid requirements
- History of prior alcohol withdrawal complications (e.g. delirium tremens, alcohol withdrawal seizures)
- Need for frequent or high doses of sedatives or an intravenous infusion to control symptoms
- Withdrawal despite an elevated ethanol concentration

- **Prophylaxis** – Patients with a history of seizures, delirium tremens, or prolonged, heavy alcohol consumption, who are minimally symptomatic or asymptomatic and are admitted to the hospital for other reasons, can be prophylactically treated with oral diazepam.

Monitoring parameters:
- Vital signs
- Pulse oximetry
- Fluid status
- Neurological function

Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA-Ar)

NAUSEA AND VOMITING: Ask "Do you feel sick to your stomach? Have you vomited?" Observation.
No nausea and no vomiting (0 points)
Mild nausea with no vomiting (1 point)
Intermittent nausea with dry heaves (4 points)
Constant nausea, frequent dry heaves and vomiting (7 points)

TREMOR: Arms extended and fingers spread apart. Observation
No tremor (0 points)
Not visible, but can be felt fingertip to fingertip (1 point)
Moderate, with patient's arms extended (4 points)
Severe, even with arms not extended (7 points)

PAROXYSMAL SWEATS: Observation
No sweat visible (0 points)
Barely perceptible sweating, palms moist (1 point)
Beads of sweat obvious on forehead (4 points)
Drenching sweats (7 points)

ANXIETY: Ask "Do you feel nervous?" Observation.
No anxiety, at ease (0 points)
Mildly anxious (1 point)
Moderately anxious, or guarded, so anxiety is inferred (4 points)
Equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions (7 points)

AGITATION: Observation

Normal activity (0 points)
Somewhat more than normal activity (1 point)
Moderately fidgety and restless (4 points)
Paces back and forth during most of the interview, or constantly thrashes about (7 points)

TACTILE DISTURBANCES: Ask "Have you any itching, pins and needles sensations, burning sensations, numbness or do you feel bugs crawling on or under your skin?" Observation.

None (0 points)
Very mild itching, pins and needles, burning or numbness (1 point)
Mild itching, pins and needles, burning or numbness (2 points)
Moderate itching, pins and needles, burning or numbness (3 points)
Moderately severe hallucinations (4 points)
Severe hallucinations (5 points)
Extremely severe hallucinations (6 points)
Continuous hallucinations (7 points)

AUDITORY DISTURBANCES: Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.

Not present (0 points)
Very mild harshness or ability to frighten (1 point)
Mild harshness or ability to frighten (2 points)
Moderate harshness or ability to frighten (3 points)
Moderately severe hallucinations (4 points)
Severe hallucinations (5 points)
Extremely severe hallucinations (6 points)
Continuous hallucinations (7 points)

VISUAL DISTURBANCES: Ask "Does the light appear to be too bright? Is its colour different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.

Not present (0 points)
Very mild sensitivity (1 point)
Mild sensitivity (2 points)
Moderate sensitivity (3 points)
Moderately severe hallucinations (4 points)
Severe hallucinations (5 points)
Extremely severe hallucinations (6 points)
Continuous hallucinations (7 points)

HEADACHE, FULLNESS IN HEAD: Ask "Does your head feel different? Does it feel as if there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.

Not present (0 points)
Very mild (1 point)
Mild (2 points)
Moderate (3 points)
Moderately severe (4 points)
Severe (5 points)
Very severe (6 points)
Extremely severe (7 points)

ORIENTATION AND CLOUDING OF SENSORIUM: Ask "What day is this? Where are you? Who am I? Count forward by 3

Oriented and can do serial additions (0 points)
Cannot do serial additions or is uncertain about date (1 point)
Disoriented for date by no more than 2 calendar days (2 points)
Disoriented for date by more than 2 calendar days (3 points)
Disoriented for place and/or person (4 points)

Score interpretation:

- 0-9 points: very mild withdrawal
- 10-15 points: mild withdrawal
- 16-20 points: modest withdrawal
- 21-67 points: severe withdrawal

Traditional brews in Kenya

Traditional Brews in Kenya	
Busaa	Made from maize flour fermented with yeast. Has a similar content to beer. Approximate alcohol content is 5-10% v/v
Chang'aa	Main ingredient is sugar and yeast. The remaining ingredients depend on the area in which it is brewed. For example around Eldoret, maize and wheat are commonly used, whereas at the Coast, coconut is used. It is much more potent than Busaa having an alcohol content of approximately 50-70% v/v.
Kumi Kumi	Is a type of Chang'aa mainly brewed in the slum areas of Nairobi. It is of special concern because it occasionally gets contaminated with methanol which is highly toxic. Other possible contents include jet fuel, formalin and dead animal remains.
Muratina	A spirit made from sugarcane. Mainly brewed in Central and Eastern provinces. It has an alcohol content of up to 70% v/v.
These are the main traditional brews commonly consumed in Kenya. Others are simply modifications of the major types.	

AMOEBIASIS

Clinical features:

- Asymptomatic (90% of cases)
- Amoebic dysentery (10% of cases) presents with:
  - Bloody diarrhea due to invasion of intestinal mucosa by trophozoites
  - Cramping abdominal pain
  - Weight loss
- Amoebic liver abscess (<1% of cases) presents with:
  - Fever
  - Cough
  - Constant, dull, aching abdominal pain in the right upper quandrant or epigastrium
  - Right-sided pleural pain or referred shoulder pain if the diaphragmatic surface of the liver is involved
  - Gastrointestinal symptoms may or may not be present
  - Hepatomegally with point-tenderness over the liver is a common finding

Diagnosis:

- Stool microscopy for the cysts and trophozoites of *Entamoeba histolytica*
- CBC – may have leukocytosis and anaemia in amoebic liver abscess
- LFTs – normal Alk P but raised ALT
- Abdominal ultrasound/CT – may show lesions in the liver but is not specific for amoebic abcesses
- Biopsy/drainage – to confirm diagnosis

Treatment:

- Non-invasive amoebiasis – paromomycin (aminosidine): 500 mg BD for 5 days or metronidazole 400mg BD for 5 days. Paromomycin is not systemically absorbed and only provides local activity
- Invasive amoebiasis – Metronidazole: 400 mg TDS for 7-10 days. Alternatives include tinidazole, ornidazole, secnidazole etc. Treatment with metrondazole should be followed with paromomycin or diloxanide furoate as the parasites may persist in the intestinal lumen in up to 40-60% of patients. Paromomycin should not be given at the same time as metronidazole, since the diarrhea that is a common side effect of paromomycin may make it difficult to assess the patient's response to therapy. Metronidazole and diloxanide furoate can be given at the same time. Therefore, it is more convenient to use a combination formulation of the two (Entamizole®, Entamaxin®, Orogyl®) given as 2 tablets TDS for 7-10 days.
- Amoebic liver abscess – Metronidazole 800 mg TDS for 14 days but if there is no clinical response to drug therapy within 5-7 days, consider therapeutic drainage of the abscess either surgically or using ultrasound guided catheter drainage.

ASTHMA

Clinical features:

- Breathlessness
- Wheezing
- Increased expiratory phase of respiration
- Chest tightness
- Hyperinflated chest
- Cough
- Cyanosis in severe cases
- Expiratory ronchi/wheezes on examination
- In teenagers/adults, there is usually a PMH suggestive of asthma or other atopic disease

Treatment:

- Acute exacerbation of asthma:
    - Nebulize with salbutamol (albeterol) STAT then every 4 hours until wheezing is reduced. Continue nebulization every 6 hours until respiratory distress (wheezing, tachypnea, retractions etc) resolves.
    - Systemic corticosteroids: Hydrocortisone 200 mg STAT then prednisone – 1 mg/kg OD for 5-7 days
    - Investigate and treat the precipitating factor of the exarcebation e.g. infection with appropriate antibiotics
- Mantenance treatment (prophylaxis of acute exacerbation):
    - Mild asthma – An inhaled short-acting beta-2 agonist e.g. salbutamol with or without an inhaled anticholinergic e.g. ipratropium bromide; 1-2 puffs to be taken PRN (occasionally, salbutamol/albuterol is not available by itself and it is necessary to give the combination agent)
    - If there is recurrence of exacerbations, place the patient on chronic inhaled corticosteroid e.g. fluticasone or budesonide and and inhaled long acting beta-2 agonist e.g. salmeterol or formeterol.
    - If there is continued recurrence while patient is on above, then consider addition of oral sustained release theophylline and/or systemic corticosteroids on a long term basis until there is no recurrence of exacerbations.

  Once control is achieved, treatment may be stepped down.

General points to consider:

- Kenyan guidelines recommend use of IV aminophylline for the treatment of severe acute exacerbations of asthma. However, due to the lack of drug level monitoring and limited evidence to support its use, the use of aminophylline should be discouraged unless absolutely necessary.
- Ensure patients requiring nebulization are actually getting nebulized as prescribed because it is a common misconception that nebulization is supposed to be done just once!!

- When prescribing an inhaler, ensure that the patient knows how to use it before they are discharged.
- The cost of inhalers should also be kept in mind when prescribing. Often, patients may not be able to sustain the use of a chronic inhaled beta-2 agonist/corticosteroid (normally cost approximately Kshs. 1500-2500 for a 200-dose metered dose inhaler). In this case, long term use of a systemic corticosteroid may be considered. Kenyan providers will often resort to Franol tablets which contains aminophylline, catecholamines, such as ephedra, and an assortment of other compounds.
- Peak flow meters to monitor therapy can be obtained from local chemists, but this is not routinely done.

BACTERIAL MENINGITIS

Clinical features:

- Generally acute onset of symptoms
- Fever
- Nuchal rigidity
- Change in mental status
- Severe and generalized headache
- Photophobia
- Neurologic complications – seizures, focal neurologic deficits (including cranial nerve palsies), papilledema, hearing loss

Diagnosis:

- Raised CSF proteins
- Reduced CSF glucose (less than 50% of serum glucose)
- Gram's stain on CSF
- Increased WBC count in CSF with a differential of mainly granulocytes
- Positive CSF culture

Treatment:

- Empiric treatment with ceftriaxone 2 g BD
- Once the causative organism is confirmed, then appropriate antimicrobial therapy, based on sensitivity studies and achievement of adequate concentrations in the CSF, can be initiated.
- Adjunctive dexamethasone may be given at a dose of 0.15 mg/kg every 6 hours for 2-4 days with the first dose administered 10-20 minutes before, or at least concomitant with, the first dose of antimicrobial therapy. There is only limited conflicting evidence for doing this and it is not a required aspect of treatment for baceterial meningitis. The data for introduction of steroids with TB meningitis is more compelling and steroids should be added in those situations
- Treatment duration with antibiotic is 10-14 days
- Alternative treatment options include chloramphenicol 1 g QID IV combined with Benzyl penicillin G (X-Pen) 4,000,000 units QID IV
- In rare circumstances, high dose fluoroquinolones may be considered but there is only limited to support its use

General points to consider:

- In this setting, it is often difficult to obtain WBC counts in CSF and hence difficult to differentiate bacterial meningitis from viral or tuberculous meningitis. Moreover, gram stains and culture rarely show the presence of any bacteria. Hence, patients are treated empirically for bacterial meningitis and if there is no clinical improvement, viral or tuberculous meningitis are considered

BACTERIAL PNEUMONIA

Clinical features:

- SOB
- Cough – with or without sputum

- Fever
- Pleuritic chest pain
- Bronchial breathing
- Reduced chest movements
- Reduced breath sounds
- Tachypnoea
- Crackles
- Dullness on percussion, suggestive of pleural effusion

Diagnosis:

- CXR – can vary depending on type of pneumonia
- Gram's stain and culture to identify the causative organism have little value

Treatment:

- Out-patient treatment:
    - In previously healthy patients: a macrolide such as erythromycin, azithromycin or clarithromycin
    - Presence of comorbidities such as chronic heart, lung, liver or renal disease, diabetes, alcoholism, malignancies, HIV or any other immunosuppressing conditions:
        - A beta lactam plus a macrolide. Beta lactams that can be used include: amoxicillin, amoxiclav and cefuroxime; OR
        - A respiratory fluoroquinolone such as levofloxacin can be considered, but is typically avoided due to the risk of providing fluoroquinolone monotherapy for tuberculosis misdiagnosed as pneumonia
- In-patient treatment:
    - A beta lactam plus a macrolide. Preferred beta lactam agents include: ceftriaxone, amoxiclav and cefuroxime; OR
    - A respiratory fluoroquinolone such as levofloxacin can be considered but is typically avoided due to the risk of providing fluoroquinolone monotherapy for tuberculosis misdiagnosed as pneumonia
    - For *Pseudomonas* infections, use an antipneumococcal antipseudomanal beta lactam (cefepime, imipenem or meropenem) plus EITHER ciprofloxacin or levofloxacin; OR an aminoglycoside and azithromycin; OR an aminoglycoside and an antipneumococcal fluoroquinolone such as levofloxacin
- Patients should be switched from IV to oral therapy when they are haemodynamically stable and improving clinically, are able to ingest medications and a normally functioning GIT.
- Patients should be discharged as soon as they are clinically stable. In-patient observation while receiving oral therapy is not necessary
- Duration of treatment is a minimum of 5 days. A longer duration of therapy may be needed if there is no improvement within 72 hours or if the pneumonia was complicated by extrapulmonary infections.

Dosing of the antibiotics used:

- Erythromycin – 500 mg QID PO
- Azithromycin – 500 mg OD PO
- Clarithromycin – 500 mg OD PO
- Amoxicillin – 500 mg 1 g TDS
- Amoxiclav – 1.2 g BD or TDS IV or 625 mg BD or TDS PO
- Cefuroxime – 750 mg BD IV or 500 mg BD PO
- Levofloxacin – 500 mg OD IV/PO or 750 mg OD IV/PO (for *Pseudomonas*)
- Ciprofloxacin – 500 mg BD PO or 500 mg TDS PO (for *Pseudomonas)* or 400 mg BD IV or 400 mg TDS IV (for *Pseudomonas)*
- Ceftriaxone – 1-2g OD- IV
- Cefepime – 1-2 g BD/TDS IV
- Imipenem – 500 mg QID IV
- Meropenem – 1 g TDS IV

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Clinical features:

- History of indoor air pollution (usually due to cooking with firewood in unventilated kitchens) or tobacco use
- Dyspnoea that is:
    - Progressive
    - Persistent
    - Worse on exercise
    - Worse during respiratory infections
- Chronic cough – usually productive of mucoid sputum that becomes purulent during exacerbations
- Wheezing
- Hyperinflation of the lungs
- Crackles at lung bases on auscultation
- Distant heart sounds

Diagnosis:

- Mainly based on clinical features above.
- CXR – Hyperinflation of the lungs, a flattened diaphragm, a long and narrow cardiac shadow, prominent hilar vascular shadows
- CBC – May show polycythemia
- Low oxygen saturations
- Arterial blood gases – mild to moderate hypoxemia without hypercapnia in patients with mild COPD. As the disease progresses, hypoxemia becomes more severe and hypercapnia develops

Complications:

- Acute respiratory failure
- Pulmonary hypertension leading to right-sided heart failure i.e. cor pulmonale

Treatment:

- Mild COPD – inhaled short acting bronchodilators as and when needed. A combination of a short acting beta agonist and anticholinergic is preferred (e.g. albuterol/ipratropium). However, single agents can be used.
- Moderate COPD – regular use of an inhaled long acting beta agonist (salmeterol formeterol) in addition to a short acting bronchodilator PRN.
- Severe COPD – Inhaled glucocorticoids in addition to regular use of a long acting bronchodilator and a short acting bronchodilator PRN
- Very severe COPD – Long term oxygen therapy in addition to all the above.

General points to consider:

- The most common cause of COPD in Kenya (especially in the areas around Eldoret) is cooking with firewood in unventilated kitchens. As a result, women are mostly affected.
- Majority of patients who present at the MTRH wards already have very severe COPD that has progressed to corpulmonale and there is very little that can be done except for supportive treatment with diuretics, steroids and bronchodilators.
- Patients should be advised to avoid smoke-filled rooms as much as possible.

DEEP VEIN THROMBOSIS

Risk factors:

- Inherited thrombophilia (rarely diagnosed here):
    - Factor V Leiden mutation
    - Prothrombin gene mutation
    - Protein S deficiency
    - Protein C deficiency
    - Antithrombin deficiency

- Dysfibrinogenemia
- Acquired risk factors:
  - History of immobilization or prolonged hospitalization/bed rest
  - Recent surgery especially orthopedic
  - Obesity
  - Prior episodes of DVT
  - Lower extremity trauma
  - Malignancy
  - Use of oral contraceptives or hormone replacement therapy
  - Pregnancy or post-partum status
  - Stroke
  - Presence of a central venous catheter
  - Antiphospsolipid antibody syndrome
  - Myeloproliferative disorders – polycythemia vera, essential thrombocythemia
  - Nephrotic syndrome
  - Sickle cell anemia
  - HIV

Clinical features:

- Pain, swelling and discoloration of the affected extremity
- Physical examination may reveal a palpable cord (reflecting a thrombosed vein), warmth, tenderness and superficial venous dilation

Diagnosis:

- Doppler ultrasonography – confirms presence of a thrombus in the lower limb veins
- Differential diagnoses: cellulitis, muscle strain or tear, lymph obstruction etc.

Treatment:

- Intravenous unfractionated heparin – 80 units bolus then 18 units/kg/hour continuous infusion; monitor aPTT frequently
- Subcutaneous unfractionated heparin – 333 units/kg initially then 250 units/kg every 12 hours; frequent aPTT monitoring is not necessary
- Subcutaneous low molecular weight heparin – Enoxaparin: 1 mg/kg BD or 1.5 mg/kg OD
- Warfarin – start at 5 mg OD then do an INR after 3 days and adjust accordingly. Once INR is therapeutic (2-3), stop heparin and consider discharging the patient.
- Duration of anticoagulation – 3 months if there is a reversible risk factor; 6 months if there is no known risk factor; indefinite if there is continuous presence of one or more risk factors e.g. malignancy, antiphospholipid syndrome etc

General points to consider:

- Low molecular weight is very expensive and therefore unfractionated heparin is used
- Heparin infusions require frequent monitoring of aPTT which is difficult to do in this setting, hence, subcutaneous heparin is preferred. This is often dosed at 10,000 units SC TDS or 17,500 units SC BD
- There is a pharmacist managed anticoagulation clinic at MTRH so contact the clinic immediately if a patient is diagnosed with DVT (before starting warfarin) or inform any pharmacy student. This can also be accomplished by filling out a referral form and submitting to pharmacy personnel. This can be done for patients in either the inpatient or outpatient setting.

DIABETIC KETOACIDOSIS (DKA) AND HYPEROSMOLAR HYPERGLYCEMIC STATE (HHS)

Definitions:

- DKA – Characterised by hyperglycemia, metabolic acidosis and ketonemia
- HHS – Hyperglycemia (much higher than in DKA), little or no ketonemia, and neurologic abnormalities are frequently present (including coma).

Precipitating factors:

- Inadequate insulin treatment or noncompliance
- New onset diabetes
- Acute illness:
    - Infection – pneumonia, UTI, sepsis
    - Stroke
    - Myocardial infarction
    - Acute pancreatitis
- Drugs – glucocorticoids, high dose thiazides, sympathomimetics (e.g. dobutamine, terbutaline), atypical antipsychotics such as clozapine and olanzapine.

Clinical features:

- DKA evolves rapidly, over a 24 hour period, whereas symptoms of HHS develop more insidiously often persisting for several days before hospital admission.
- Earliest symptoms of marked hyperglycemia are polyuria, polydipsia, and weight loss.
- As the degree or duration of hyperglycemia progresses, neurologic symptoms, including lethargy, focal signs, and obtundation, which can progress to coma in later stages, can be seen.
- Neurological symptoms are most common in HHS, while hyperventilation and abdominal pain are primarily limited to patients with DKA.
- The presence of abdominal pain is associated with the severity of metabolic acidosis.
- Volume depletion (severe dehydration) – decreased skin turgor, dry axillae and oral mucosa, low jugular venous pressure, and, if severe, hypotension.
- Patients with DKA may have a fruity odor due to exhaled acetone and deep respirations reflecting the compensatory hyperventilation (called Kussmaul respirations).

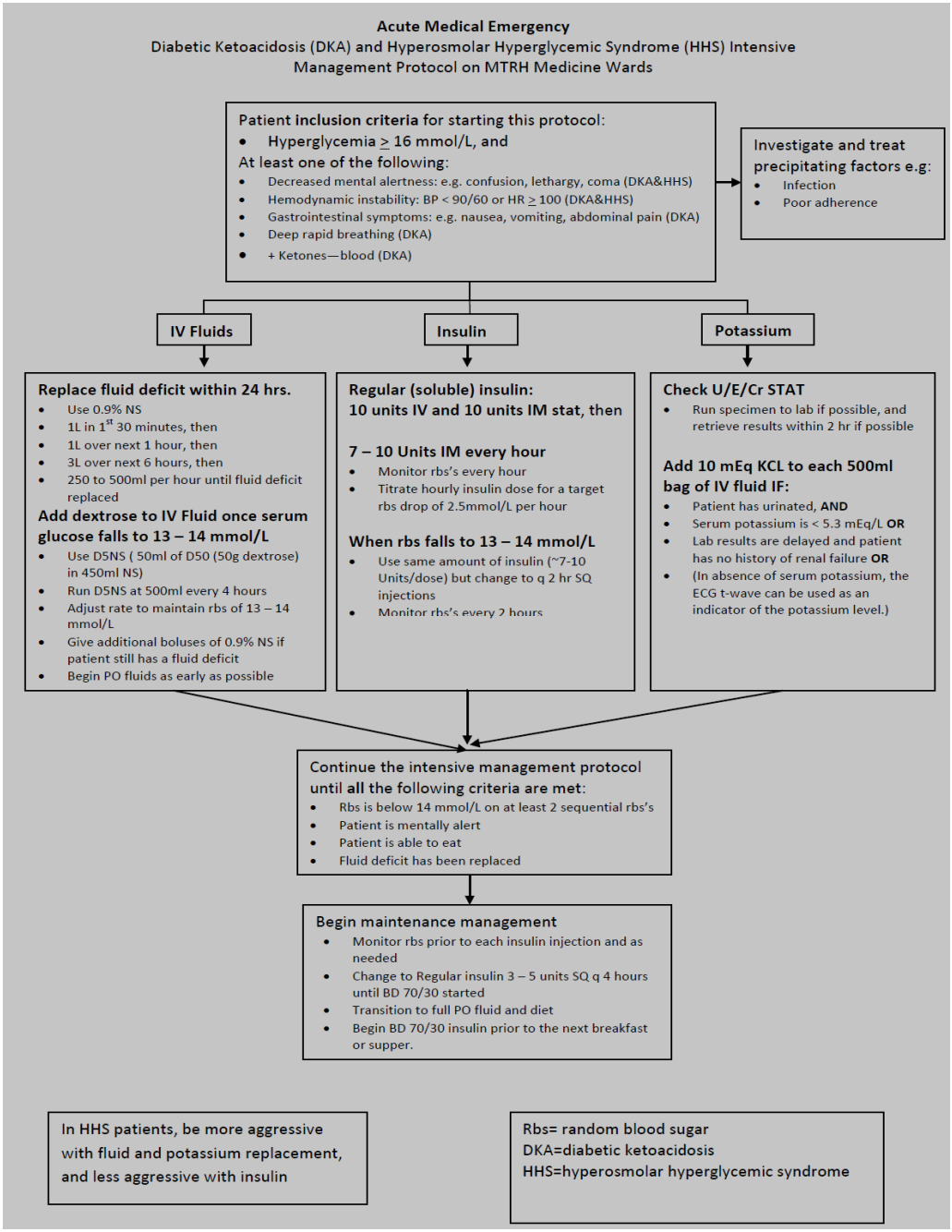
Laboratory findings:

- Hyperglycemia – Normally very high (> 30 mmols/l); glucose is normally higher in HHS than in DKA
- Ketones – present in blood and urine in DKA; normally absent in HHS.
- Serum bicarbonate – low in DKA but normal in HHS; however bicarbonate levels are not routinely done
- Serum potassium – Patients normally have a potassium deficit but this is not reflected on the serum potassium which may be falsely normal or high. This is due to insulin deficiency (insulin normally promotes potassium uptake by the cells) and hyperosmolality (which leads to osmotic water movement out of the cells resulting in parallel movement of potassium into the extracellular fluid).
- Leukocytosis – occurs in majority of patients with DKA and HHS and may be unrelated to infection. This may be due to increased cortisol and catecholamine secretion. However, a white blood cell count greater than 25,000/microlitre indicates a need for further work up.

Treatment:

- Consists of fluid replacement, insulin replacement and potassium supplementation.

Protocol for the management of DKA/HHS at MTRH Medicine Wards



EPILEPSY

Clinical features:

- Partial seizures:
  - Simple partial seizures – Visible manifestations such as jerking one limb as well as subjective experiences such as epigastric discomfort, fear or an unpleasant smell i.e. an 'aura' but NO impaired concsiousness
  - Complex partial seizures – Clouding of consciousness, staring and repetitive motor behaviours e.g. swallowing, chewing or lip smacking. After the seizure, the patient may experience confusion, fatigue and a throbbing headache. Patients normally don't have any recollection of the seizure.
  - Secondarily generalized seizures – A partial seizure that evolves into a generalized tonic-clonic seizure
- Generalized seizures:
  - Grand mal seizures – these are generalized tonic-clonic seizures
  - Petit mal seizures – absence seizures
  - Myoclonic seizures
- Postictal state
  Is the recovery period for the brain. It may last from seconds to minutes to hours depending on what part of the brain was affected, the length of the seizure, whether the patient was on antiepileptic drugs and age. There may also be a postictal paresis which is a transient neurologic deficit that lasts for hours after an epileptic seizure. The deficits include transient aphasia, amaurosis, hemianopsia and sensory loss.
- Status epilepticus
  Defined as two more sequential seizures, without full recovery of consciousness between seizures, or more than 30 minutes of continuous seizure activity.

Treatment:

- Total control of seizures is possible in less than 75% of patients. For the remainder, a balance between partial control and adverse effects may need to be struck
- Generalized tonic-clonic seizures – Drug of choice is valproate. Alternatives include: carbamazepine and phenytoin
- Partial seizures – Carbamazepine
- Absence seizures – Ethosuximide or valproate
- Drug therapy should be initiated slowly and the dose increased gradually to reduce toxicity
- Monotherapy is preferred; if the first drug fails, a second drug should be tried alone.
- The dose of the second drug should be maximized before a combination of two drugs is used.
- When stopping an anti-epileptic drug, it should be tapered by 20% every 5 half-lives and not stopped abruptly.

Dosing:

- Carbamazepine - Starting dose is 200 mg BD with a target maintenance dose of 600-1200 mg/day. A baseline full hemogram should be taken if patients are expected to be in the hospital for a long duration of time with prolonged exposure to carbamazepine.
- Phenobarbital – Loading dose is 15 mg/kg followed by a maintenance dose of 1-5 mg/kg.
- Phenytoin – Oral loading dose: 15-20 mg/kg (can be given every 2-4 hours to minimize GI adverse effects); maintenance dose 300 mg/day or 5-6 mg/kg/day in 3 divided doses
- Valproic acid – Initial 10-15 mg/kg/day; increase by 5-10 mg/kg/day at weekly intervals up to a maximum of 60 mg/kg/day.

Common side effects

- Carbamazepine: Serious (Aplastic anemia and agranulocytosis)* Other: hyponatremia, cardiac conduction disturbances, decreased WBC, hyponatremia, accommodation disorders of the eye (blurred vision), light sensitivity

- Phenobarbital: depression, behavior changes, connective tissue disorders, metabolic bone disease, hyperactivity, cognitive impairment
- Phenytoin: Gingival hyperplasia, coarse facial features, cerebellar syndrome, connective tissue changes, metabolic bone disease, hirsutism, acne, peripheral neuropathy, rash, GI disturbance.
- Valproic acid: Serious (Hepatic Failure)* Other: weight gain, hair loss (transient), decreased platelets (bleeding), tremor, polycystic ovary-like syndrome, ammenorrhoea and irregular periods, hyperammonemia (50%), hyperinsulinemia, Rare: pancreatitis, encephalopathy.

General points to consider:

- Drug levels cannot be measured,therefore, it is important to look out for the side effects of the antiepileptic drugs so that doses can be adjusted before the adverse effects become irreversible.
- Carbamazepine is the cheapest and most readily available agent in this setting, therefore, it is most commonly used.

Status Epilepticus

Most common causes of Status Epilepticus are idiopathic:

Adults (> 16)	**Children (<16)**
Change of AED dose	Change of AED dose
Cerebral vascular event	Febrile event or infection
Metabolic/Anoxic	Metabolic

Treatment:

Treatment goal: Stop seizures ASAP to prevent irreversible brain injury
Within the first 5 minutes: ▪ Confirm diagnosis. Airway (A), Breathing (B), Circulation (C) **A** – Position patient on their side with their head down to prevent aspiration **B** – Ensure proper respiration (give oxygen) **C** – Start IV line and keep open with normal saline ▪ Monitor vital signs (BP, HR, RR, Temp) and start ECG recording (not always available) ▪ Collect blood for CBC, UEC, RBS, LFT, blood gases (not always available). Obtain urine for UA ▪ When lab results return, treat any abnormalities. ▪ Lower body temperature (cerebral metabolic rate increases by 12% for every degree over 37°C
Within the first 30 minutes: ▪ Administer diazepam 0.2 mg/kg at 5 mg/min up to 40 mg ▪ Start second IV line for second drug or fluids ▪ Monitor ECG and vital signs
If seizures don't stop within 10 minutes: ▪ Repeat the diazepam dose up to the maximum dose noted above ▪ Administer phenytoin 20 mg/kg no faster than 50 mg/min. Monitor vitals and ECG (if possible) during the infusion and adjust rate as needed. Decrease the rate in elderly. ▪ If both diazepam and pheytoin fail, give phenobarbital 20 mg/kg at 60 mg/min (watch for additive respiratory depression and sedation)
If status persists for 30-60 minutes: ▪ Administer additional phenytoin 5 mg/kg until a maximum of 30 mg/kg ▪ Valproic acid 10-20 mg/kg (IV not usually available; can give PO via NGT if possible)
If status persists for > 60 minutes: ▪ Admit in ICU and intubate

- Administer anaesthesia with pentobarbital 2-10 mg/kg followed by 0.5-1.0 mg/kg/hr, midazolam 0.2 mg/kg followed by 0.02-0.4 mg/kg/hr or propofol 1-2 mg/kg over 5 minutes followed by 5-10 mg/kg/hr
- Record EEG and follow strict ICU monitoring procedures.
- Add vasopressors or fluid as needed
- Attempt taper after 12 hours

GENITAL HERPES SIMPLEX VIRUS INFECTION

Causes:

- HSV-2 is the main causative agent but HSV-1 is often implicated

Clinical features:

- Primary infection:
  - Refers to infection in a patient without preexisting antibodies to either HSV-1 or HSV-2
  - Can be severe with painful genital ulcers, dysuria, fever, tender local inguinal lymphadenopathy and headache
  - In other patients, the infection may be mild, subclinical or entirely asymptomatic
  - Lesions tend to be multiple, ulcerating and pustular
  - Average incubation period after exposure is 4 days while the mean duration of the lesions is 19 days
- Non-primary infection:
  - Refers to the acquisition of genital HSV-1 in a patient with preexisting antibodies to HSV-2 or the acquisition of genital HSV-2 in a patient with preexisting antibodies to HSV-1.
  - Associated with less lesions and less systemic symptoms than primary infections possibly because antibodies against one HSV type offer some protection against the other
- Recurrent infection:
  - Refers to reactivation of genital HSV in which the HSV type in the lesion is the same type as the antibodies in the serum
  - Typically less severe than primary or nonprimary infections.
  - Mean duration of lesions is 10 days
  - Lesions are small, unilateral and vesicular or ulcerative
  - Frequency of recurrence depends on the severity and duration of the initial episode, the infecting serotype and the host
- Extragenital complications:
  - Occur in a minority of patients who present wi
  - th primary HSV infection
  - Include: aseptic meningitis, urinary bladder retention, distant skin lesions and proctitis
- Immunosuppressed patients:
  - Generally have extensive mucocutaneous involved, variable appearance of the lesions, and the development of chronic and recurrent ulcers.
  - Recurrences are often more frequent, more extensive and of longer duration than in immunocompetent patients.
  - Tend to have more severe and rapidly evolving neurologic complications including aseptic meningitis, sacral radiculopathy and transverse myelitis.

Diagnosis:

- Mainly based on clinical findings as laboratory studies such as viral culture, PCR assays and serologic testing are not available

Treatment:

- Primary infection

- Initiation of oral antiviral therapy with 72 hours of the appearance of the lesions may decrease duration and severity of the illness by days to weeks.
- Antiviral therapy also decreases the risk of complicated infection
- Use acyclovir 400 mg TID for 7-10 days or 200 mg 5 times a day for 7-10 days
- Alternatives include famciclovir or valacyclovir but these are not commonly available

- Recurrent infections – therapeutic options include:
  - Chronic suppressive therapy – involves use of daily antiviral therapy, appropriate for patients very frequent recurrences or for patients who have non-infected sexual partners. Use acyclovir 400 mg BD. Not commonly done in this setting due to cost.
  - Episodic therapy – involves self-administered antiviral therapy for individual outbreaks as they arise. Patients must be counseled to start therapy at the first sign of prodromal symptoms (e.g. tingling, paraesthesias, pruritis), which may occur prior to the onset of discrete lesions. Use acyclovir 800 mg TID for 2 days or 400 mg TID for 3-5 days.
  - No intervention – appropriate for patients with infrequent episodes and/or minimal symptoms.

HEART FAILURE

Acute decompensated heart failure

Clinical features:

- Dyspnoea
- Orthopnoea
- Cough
- Paroxysmal nocturnal dyspnoea
- Peripheral oedema
- Ascites
- Distension of neck veins
- Raised jugular venous pressure
- Tender hepatomegaly

Investigations:

- CXR – Features of pulmonary oedema
- ECG and echocardiography – useful in establishing diastolic versus systolic heart failure and ejection fraction

Treatment:

- Treatment depends on the type of decompensation
- Supplemental oxygen and assisted ventilation if necessary
- Diuresis – usually with a loop diuretic (furosemide) at an initial dose of 40 mg IV if there is normal renal function. In patients who have been using a loop diuretic chronically, the equivalent IV dose should be administered. The same dose can be repeated every 8-12 hours depending on severity of symptoms until resolution of dyspnea. Once the patient is stable, diuretic dose can be reduced and IV can be switched to PO.
- For patients in whom bolus administration of diuretics does not work, a continuous infusion of furosemide may be considered or a thiazide or potassium-sparing diuretic may be added.
- Morphine sulphate may be given to reduce patient anxiety and decrease the work of breathing. Dose of morphine: 2-4 mg IV initially which can then be repeated after 15 minutes if necessary.
- Vasodilators – e.g. nitrogylceryn can reduce filling pressures, improve symptoms and facilitate dieresis.
- Inotropes – may be useful in patients with advanced heart failure and hypotension. Examples include dopamine, dobutamine and milrinone (difficult to obtain). Inotropes are preferably administered in an ICU setting.

Chronic heart failure

New York Heart Association (NYHA) classification (based on symptoms):

Class	Description
I	Symptoms of HF at levels of exertion that would limit even normal individuals
II	Symptoms occur on ordinary exertion
III	Symptoms occur on less-than-ordinary exertion
IV	Symptoms present even at rest

Treatment:

- ACE inhibitors/ARBs and beta blockers:
  - Preferably started after the patient is haemodynamically stable
  - If the patient has been on an ACEI or ARB, then it can be continued. However, the dose may have to be reduced transiently if the patient becomes hypotensive. Enalapril is the cheapest and most readily available ACE-i. Losartan is the cheapest and most readily available ARB.
  - If the patient has been on a beta blocker, it may be continued, the dose may be reduced or it may be withheld depending on the severity of heart failure decompensation and the presence and degree of hypotension.
  - Can we include the cost of these agents in addition to a table with the starting doses, maintenance doses, side effects, cost, carvedilol
- Aldactone
  - Aldactone is the most costly of these agents and is only indicated for stage 3 or 4 heart failure. This should only be added after all other agents are maximized
- Digoxin
  - Has very limited justifiable use in this setting due to the lack of routine creatinine or any form of digoxin level monitoring. Digoxin should only be used for patients requiring additional treatment for atrial fibrillation despite maximized beta blocker therapy or in end stage heart failure to improve quality of life.
  - Digoxin at higher levels will likely increase mortality and side effects.

Commonly used medications in heart failure:

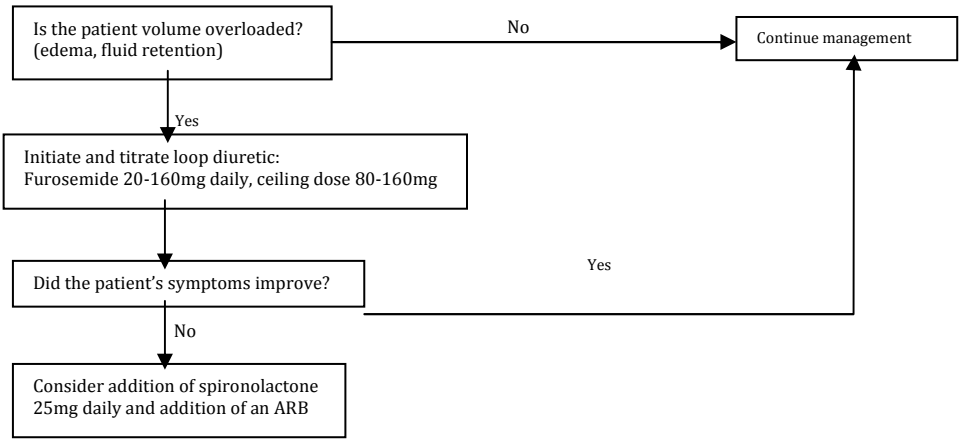
Medication	Starting dose	Maintenance/Target dose	Side effects	Cost
Enalapril	2.5-5 mg BD	10-20 mg BD	• Worsening of renal function in patients with bilateral renal artery stenosis, hypovolemia, ARF • Cough • Angioedema (rare)	Kshs. 5 per 5 mg tablet
Captopril	6.25-12.5 mg TDS	50 mg TDS	• Worsening of renal function in patients with bilateral renal artery stenosis, hypovolemia, ARF • Cough • Angioedema (rare)	Kshs. 5 per 25 mg tablet
Carvedilol	3.125 mg BD	25 mg BD (double the dose every 2 weeks)	• Hypotension • Hyperglycemia • Diarrhoea	Kshs. 5 per 6.25 mg tablet
Losartan	50 mg OD	50-100mg OD	• Angioedema (rare) • Chest pain	Kshs. 10-15

				per 50 mg tablet
Spironolactone	12.5-25 mg OD	25-50 mg OD	• Hyperkalemia • Gynecomastia • Dehydration	Kshs. 10-30 per 25 mg tablet

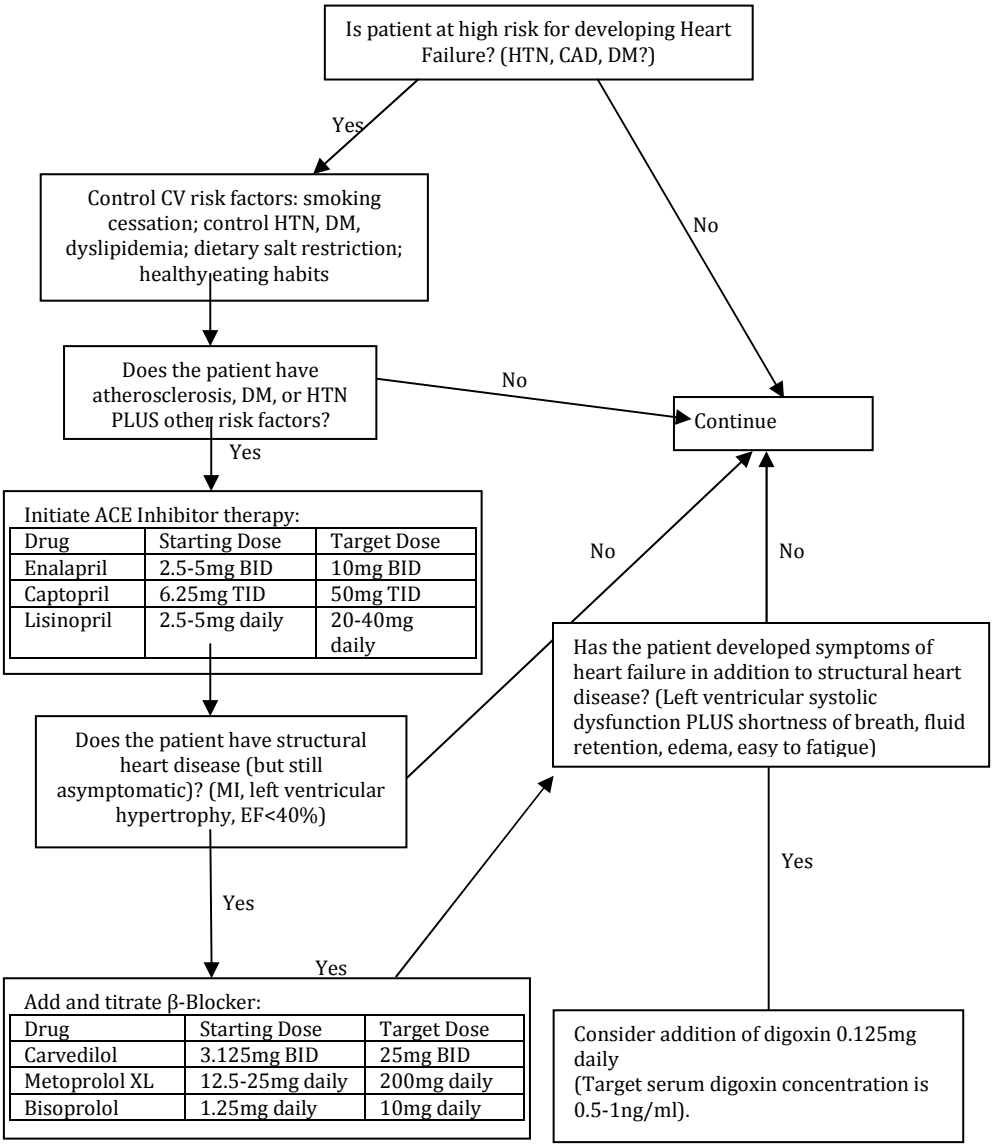
Monitoring parameters:

- Daily vitals especially BP
- Daily weights
- Fluid intake and output
- Signs and symptoms of fluid congestion
- UEC's (ACEi's, ARBs, and Aldactone can cause hyperkalemia especially when initiated together. ACEi's and ARB's can also worsen acute renal failure but can be used in stable chronic renal failure. ACEi's and ARB's can also cause a transient non clinically significant elevation in creatinine upon initiation which resolves with continued use.)

Monitoring for fluid overload



Management protocol for chronic heart failure



HSV-1 (HERPES LABIALIS)

Clinical features:

- Normally causes vesicular lesions on the oral mucosa but can cause disease in a wide variety of anatomic locations including the genitalia, liver, lung, eye and CNS.
- Infections are more severe in immunosuppressed patients
- Clinical manifestations depend upon the anatomic site involved and whether the clinical episode is due to primary infection or reactivation disease.
- Primary infection – Sudden appearance of multiple characteristic painful, vesicular lesions superimposed upon an inflammatory erythemous base usually located at a single anatomical site on the mucosal surface. There may be associated systemic symptoms such as fever and malaise. The lesions last for 10 to 14 days.
- Recurrent infection – Prodromal symptoms such as pain, burning, tingling and pruritus. This is followed by appearance of the vesicles, which tend to recur at the same site.
- Immunocompetent hosts – Recurrent episodes are usually of shorter duration than the primary episode. The median time from onset of prodromal symptoms to healing of the lesion is approximately five days.
- Immunosuppressed hosts:
    - Are at risk for increased frequency and severity of recurrent HSV infections
    - Are at risk for disseminated infection. Visceral dissemination is associated with high mortality
    - Patients with advanced HIV infection (CD4 <200) can have HSV infections anywhere on the skin, often presenting as extensive oral or perianal ulcers. They can also develop oesophagitis, colitis, chorioretinits, acute retinal necrosis, tracheobronchitis and pneumonia.

Diagnosis:

- Mainly based on clinical features
- Serological tests – ELISA radioimmunoassay etc. (Not available in Kenya)

Treatment:

- Primary infection – use of acyclovir within the first three days of onset of lesions in children with primary herpes gingivostomatitis was shown to shorten the duration of all clinical manifestations and the infectivity of affected children.
- Recurrent infections in immunocompetent hosts are not usually treated unless a prodromal stage before the appearance of lesions can be identified. In this case acyclovir cream can be used for duration of four days.
- Immunosuppressed hosts – Acyclovir 400mg PO 5 times daily for 7-10 days has been associated with shorter periods of virus shedding, decreased lesion pain and more rapid lesion healing.

INFECTIVE ENDOCARDITIS

Causative agents:

- *Staphylococcus aureus:*
    - An increasingly common cause of IE possibly due to the increase in invasive procedures performed.
    - The only bacteria that can adhere to normally functioning heart valves
    - Causes higher mortality and morbidity than the other organisms
- *Streptococcus bovis*
- *Streptococcus viridans*
- Coagulase negative *Staphylococcus aureus*
- *Enterococcus spp.*
- Fungi

Predisposing factors:

- Valvular heart disease – e.g. rheumatic heart disease, congenital heart disease, prosthetic valves
- IV drug use
- GI pathology
- Invasive procedures, IV catheters
- Dental work (still a questionable cause of bacteraemia)

Clinical features:

- Generalized non-specific symptoms – fever, malaise, night sweats, myalgias and weight loss
- New or changing heart murmurs on examination
- Signs and symptoms of embolization:
    - Splinter haemorrhages under nail beds
    - Focal neurologic signs
    - Petechiae on skin or mucous membranes such as the palate or conjunctiva
    - Janeway lesions – macular, blanching, nonpainful, erythematous lesions on the palms and soles
    - Osler's nodes – painful, violaceous nodules found in the pulp of fingers and toes
    - Roth spots – exudative, oedematous, haemorrhagic lesions on the retina
    - Splenomegaly
- Complications:
    - Stroke
    - Mycotic aneurysm
    - Renal failure
    - Blindness
    - Intestinal infarction
    - Heart block
    - Valve ring abscess
    - Myocardial infarction
    - Pericarditis

Differential diagnosis:

- Non-acute:
    - TB/histoplasmosis/HIV
    - Lymphoma
    - Rheumatoid arthritis
    - Chronic renal disease
    - Anemia
    - Heart failure
- Acute:
    - Pneumonia
    - Meningitis
    - Malaria
    - Typhoid fever
    - Stroke
    - Heart failure
    - Septic arthritis

Investigations:

- CBC, ESR
- UEC
- Urinalysis
- Blood cultures:
    - Should be obtained prior to antibiotic therapy
    - A minimum of three blood cultures should be obtained over a time period based upon the severity of the illness.
    - If the illness is subacute and the patient is not critically ill, it is preferable to delay therapy for 1-3 days while awaiting results of blood cultures and other diagnostic tests.

- However, if the patient is acutely ill, three blood cultures should be obtained (one every hour) before beginning empiric therapy.
- Each set of cultures should be obtained from separate venipuncture sites.
- Blood cultures can be taken at any time; they do not need to be obtained with the appearance of chills or fever since patients with IE typically have a continuous bacteraemia.

- Echocardiography – to visualize vegetations on the valves

Diagnosis:

- Based on Duke's criteria – consists of major and minor criteria.
- Diagnosis requires a combination of two majors or one major and three minor criteria
- Major criteria:
  - Vegetations detected by echo
  - Persistent bacteraemia
  - Evidence of endocardial damage:
    - New regurgitant murmur
    - Paravalvular abscess
    - Confirmed endocarditis at surgery
- Minor criteria:
  - Predisposing heart condition or intravenous drug use
  - Temperature > 38.0° C
  - Vascular phenomena: arterial emboli, pulmonary infarcts, mycotic aneurysms, intracranial bleed, conjunctival hemorrhages, Janeway lesions
  - Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor
  - Microbiologic evidence short of persistent bacteraemia

Treatment:

- Based on results of blood cultures
- *Streptococcus bovis/viridans* **susceptible** to penicillin:
  - Crystalline penicillin G (X-Pen) – 12-18 MU/day IV in 4-6 divided doses for 4-6 weeks; OR
  - Ceftriaxone 2 g OD IV for 4-6 weeks; OR
  - Vancomycin 30 mg/kg/day IV in 2 divided doses (not to exceed 2 g/day) for 4-6 weeks
  - NB: Treatment duration is normally 4 weeks for native valve endocarditis and 6 weeks for prosthetic valve endocarditis
- *Streptococcus bovis/viridans* **relatively resistant** to penicillin:
  - Either X-Pen or Ceftriaxone above for 4-6 weeks PLUS gentamicin 3 mg/kg/day IV/IM in 1 dose or in 2-3 divided doses for 2 weeks; OR
  - Vancomycin (same dose as above) for 4-6 weeks
- *Staphylococcus aureus:*
  - X-Pen (if susceptible) for 6 weeks with or without gentamicin for 3-5 days; OR
  - Cefazolin 2 g TID IV for 6 weeks with or without gentamicin for 3-5 days; OR
  - Vancomycin for 6 weeks
- Indications for surgery (removal of vegetations and valve repair):
  - Heart failure
  - Valve ring abscess
  - Failure of medical therapy or resistant organism
  - Persistent emboli

Monitoring parameters:

- UEC's for patients on gentamicin and vancomycin must be done at least every 2-3 days.
- Blood cultures – should be repeated every 24-48 hours until they turn negative
- Signs and symptoms of embolic events. Regular neurologic examinations should be performed.
- Fluid input/output for patients with CHF

General points to consider:

- Obtaining blood cultures is generally a problem because of the erratic availability of blood culture bottles and the reliability of results even after having obtained blood cultures. Because of the lack of adequate blood cultures, it may not be possible to rely on Duke's criteria for the diagnosis of IE. Therefore, a lot of patients get empiric treatment based on clinical presentation.
- The organisms that commonly cause IE in this setting are not known because there is very little, if any, local epidemiological data available on IE.
- Because blood cultures are sometimes not available, patients end up getting treated empirically with broad spectrum antibiotics (usually ceftriaxone).
- Aminoglycosides and vancomycin should be used with care because they are nephrotoxic and it is not possible to monitor drug levels in patients taking these drugs. For gentamicin, OD dosing is preferred over TDS dosing as it is considered to cause less nephrotoxicity when administered OD.
- Surgery is not routinely done and therefore, medical therapy is the only option in this setting.

LEISHMANIASIS

Classification:
- Visceral leishmaniasis – most common form found in Kenya. Affects internal organs
- Cutaneous leishmaniasis – affects the skin.
- Mucocutaneous leishmaniasis – affects the skin and mucous membranes

Visceral leishmaniasis (Kala azar)

Causative agents:
- *Leishmania donovani* (Kenya, India)
- *Leishmania infantum* (Southern Europe, North Africa)
- *Leishmania tropica*
- *Leishmania chagasi*
- *Leishmania amazonensis*

Life cycle:
- Transmitted by the sandfly (*Phlebotomus spp.*)
- Certain mammals such as rodents and canines serve as reservoirs for the parasite
- Leishmania exist in nature as two morphologic states: as intracellular pathogens within the macrophages of mammalian hosts and as extracellular promastigotes within the gut of the sandfly.
- During the bite of a sandfly, flagellated metacyclic promastigote forms of the parasite are injected into the skin.
- They are taken up by local tissue macrophages, within which the parasites transform into intracellular amastigotes, which then multiply within the phagolysosomes of the macrophages.
- Infected macrophages either remain in the skin and cause cutaneous disease or disseminate throughout the reticuloendothelial system producing disseminated (visceral) disease.
- If an uninfected sandfly bites an infected host, it takes up amastigotes residing within the macrophages.
- These then transform back into promastigotes within the gut of the sandfly over a period of 4-14 days.
- They then migrate to the proboscis (mouth part) of the insect, thereby completing the life cycle.

Clinical and laboratory features:
- Incubation period is 2-6 months
- Infection may remain asymptomatic or subclinical in many cases, or can follow an acute, subacute or chronic course.
- Characteristic features include fever and weight loss
- Massive splenomegaly and moderate hepatomegaly with lymphadenopathy in some patients.

- Pancytopenia – anaemia, thrombocytopenia and leucopenia with neutropenia, eosinopenia and a relative lymphocytosis and monocytosis.
- Thrombocytopenia results in petechiae, eccymoses and gingival bleeding.
- Diffuse nodular skin lesions may also be present. Mucosal lesions involving the oral or nasal cavities may accompany the systemic illness
- As the disease progresses, gastrointestinal involvement develops resulting in diarrhea, malabsorption, hypoalbuminaemia, peripheral oedema, cachexia and debilitation.
- Secondary bacterial infections may develop late in the disease course. These include *Pseudomonas aeruginosa*, *Staphylococcus aureus* and other common pathogens. These infections are normally the cause of death in advanced disease.
- Co-infection with HIV:
    - Visceral leishmaniasis is emerging as an important opportunistic infection in people with HIV.
    - Clinical features are similar to classic disease but can also have involvement of other organs and can present with unusual features.
    - Extensive GI involvement with parasites in the rectal, jejunal, duodenal, gastric and oesophageal mucosa can occur, leading to symptoms such as dysphagia, odynophagia, severe watery diarrhea, intestinal haemorrhage and rectal pain.
    - Splenomegaly may be absent.
    - Patients may also develop diffuse papular skin lesions, and involvement of the central nervous system, larynx and lungs. Pulmonary involvement may lead to pleural effusions and pulmonary nodules.
    - Aplastic anemia has also been described.
- Post kala-azar dermal leishmaniasis:
    - A syndrome that can develop after treatment of generalized visceral disease due to *L. donovani*.
    - A transient crop of papules appears over the face and arms in up to 50 percent of individuals, probably related to an immune response secondary to parasites in the skin.
    - These lesions resolve over a few months and do not necessitate any further therapy.

Diagnosis:

- Bone marrow aspirate – is 60-80% sensitive
- Splenic aspirate – 96-98% sensitive but is not commonly done due to the risk of splenic rupture and haemorrhage.
- Serologic tests – including ELISA, indirect immunoflorescence (IFA) and direct agglutination tests (DAT) are not commonly available. However, these tests may be available in endemic areas where some organizations such as MSF (Medecins Sans Frontiers) have centers for the diagnosis and treatment of leishmaniasis. These tests are more than 90% sensitive.
- Differential diagnoses: hyperimmune malaria syndrome (formerly tropical splenomegaly syndrome), schistosomiasis, cirrhosis with portal hypertension, African trypanosomiasis, military TB, malnutrition, lymphoma, leukaemia.

Treatment:

- Sodium stibogluconate – 20 mg/kg/day IV or IM for 28 days
- Alternatively, amphotericin B – 0.5-1 mg/kg IV daily or every second day for up to 8 weeks
- Pentamidine isethionate – Used only in patients intolerant or unresponsive to antimonial compounds or amphotericin B

Monitoring parameters:

- Platelet count and signs and symptoms of bleeding
- Baseline and follow up ECGs must be done when using stibobluconate as it causes ECG changes including T wave flattening, nonspecific ST segment changes, prolongation of the QT interval, and ventricular arrhythmias.
- Other adverse effects of stibogluconate include: renal insufficiency, proteinuria and elevation of hepatic and pancreatic enzymes.
- Amphotericin B:
    - UECs (hypokalemia and renal failure are common) – should be done at least every 2 days

- Signs and symptoms of infusion reactions such as chills, rigors, thrombophlebitis
- Resolution of fever and general well being is normally an indicator of successful therapy
- Splenomegaly normally resolves within weeks or months
- Freedom from clinical relapse for at least six months is the best indicator for cure.

General points to consider:

- Amphotericin B has been found to be equally or more effective than sodium stibogluconate and therefore, either of the two can be used, depending on availability
- The National guidelines no longer recommend the use of stibogluconate as first-line therapy for leishmaniasis and hence it is rarely available. Amphotericin B is usually readily available.
- Liposomal amphotericin B is associated with lower risk of nephrotoxicity but is not available due to cost.
- Aren't there specific treatment centers where we typically send patients? May want to comment on those areas.

LIVER DISEASE

ACUTE HEPATIC FAILURE

Definition:

- Acute hepatic disease + coagulopathy + encephalopathy
- Fulminant hepatic failure – liver failure that develops within 8 weeks
- Subfulminant – develops between 8 weeks and 6 months

Causes:

- Viral – hepatitis A, B, C, HSV, EBV, CMV, adenovirus etc
- Drugs/toxins – paracetamol, phenytoin, isoniazid, pyrazinamide, rifampicin, aflatoxinetc
- Vascular – ischemic hepatitis, malignant infiltration
- Autoimmune
- Idiopathic

Clinical features:

- Jaundice
- Neurologic:
  - Asterixis – "liver flap"
  - Encephalopathy:
    - Stage I – AMS
    - Stage II – lethargy, confusion
    - Stage III – stupor
    - Stage IV – coma
  - Cerebral oedema – Cushing's reflex (hypertension + bradycardia), pupillary dilatation, decerebrate posturing, apnea
- Cardiovascular – hypotension with low systemic vascular resistance
- Pulmonary – respiratory alkalosis, impaired peripheral oxygen uptake, ARDS
- Gastrointestinal – GI bleed, pancreatitis
- Renal – ATN, hepatorenal syndrome, hyponatremia, hypokalemia, hypophosphatemia
- Hematologic – coagulopathy (due to reduced synthesis of clotting factors +/- DIC)
- Infection – with gram positive organisms and fungi; SBP in some patients (fever and leukocytosis may be absent)
- Endocrine – hypoglycaemia

Investigations:

- LFTs – transaminases are usually elevated > 10 times the upper limit of normal while albumin is usually normal. Bilirubin is markedly elevated
- UEC, CBC, INR
- Viral serologies
- Imaging – abdominal ultrasound or CT (if available)

- Liver biopsy – if there is no coagulopathy
- Toxicology screen (not available)

Treatment:
- Treat underlying cause i.e. N-acetyl cysteine for paracetamol induced liver failure, corticosteroids for autoimmune hepatitis etc
- Supportive management:
    - 10% dextrose drip if hypoglycaemic
    - Lactulose – promotes excretion of ammonia (increased levels of ammonia are thought to be responsible for hepatic encephalopathy). Titrate lactulose dose to target 3-4 bowel movements a day.
    - Monitoring and treating ICP
    - Vitamin K – if INR is high or if there is evidence of bleeding
    - Aggressive monitoring for and treatment of infection
- Liver transplant (not available)

LIVER CIRRHOSIS

Definition:
- Fibrosis and nodular regeneration resulting from hepatocellular injury

Causes:
- Alcohol
- Viral hepatitis (chronic HBV, HCV or HDV infection)
- Autoimmune hepatitis
- Metabolic diseases – hemochromatosis, Wilson's disease
- Biliary tract diseases – primary biliary cirrhosis, secondary biliary cirrhosis (calculus, neoplasm, stricture, biliary atresia), primary sclerosing cholangitis
- Vascular diseases – right sided heart failure, constrictive pericarditis

Clinical features:
- May be subclinical or may present as progressive liver dysfunction (jaundice, coagulopathy, encephalopathy) and/or portal hypertension (ascites, varices)
- Physical exam:
    - Liver – enlarged, palpable, firm, nodular; can also be shrunken and nodular
    - Signs of liver failure – jaundice, spider angiomata, palmar erythema, Dupuytren's contractures, white nail lines (Muehrcke's lines) and proximal nail beds (Terry's nails), increased parotid and lacrimal glands, gynecomastia, testicular atrophy, asterixis, encephalopathy, fetor hepaticus
    - Signs of portal hypertension – splenomegaly, ascites, dilated superficial abdominal veins, epigastric venous hum

Investigations:
- LFTs – Bilirubin levels are usually raised while albumin is low. Transaminases and alkaline phosphatise may be increased or normal
- CBC – anemia may be present secondary to bone marrow suppression, hypersplenism and iron and/or folate deficiencies. Hypersplenism may also cause neutropenia and thrombocytopenia
- Abdominal ultrasound – to assess liver size, presence of ascites and to rule out HCC
- Viral serologies
- Alpha fetoprotein – to rule out HCC

Complications and treatment:
- Portal hypertension
    - Ascites – with or without SBP
    - Gastroesophageal varices – can lead to upper GI bleed. Non-selective beta blockers (propranolol) can be used for pripmary prevention of bleeding. For secondary

prevention, use beta blocker with a nitrate. Beta blocker should be titrated to a 25% reduction in HR.

- Hepatic encephalopathy – restrict dietary protein intake modestly, lactulose, gut decontamination with metronidazole
- Hepatorenal syndrome – progressive azotemia, oliguria, no response to volume challenge, exclusion of other causes of renal failure. Treatment: octreotide, midodrine (none are readily available)
- Liver failure
- Infections
- Hepatocellular carcinoma – consider if there is increase in liver size, increasing ascites, abdominal pain, worsening encephalopathy, weight loss, increasing AFP levels or hepatic mass on ultrasound.

MALARIA

Clinical features:

- Fever, chills, sweats
- Myalgias, arthralgias
- N/V/D
- Malaise, fatigue
- Severe malaria:
  - Cerebral malaria – seizures, AMS, coma
  - Acute renal failure
  - Acute respiratory distress syndrome
  - Severe anemia
  - Hypoglycemia

Diagnosis:

- Blood smear (B/S, MPS) – ring forms
- CBC – anemia

Treatment:

- Combination therapy (regardless of agents) has been consistently shown to produce better outcomes.
- **Artemether-Lumefantrine (Coartem):** Typically 4 tabs every 12 hours for 3 days (see detailed dosing below)

Weight (kg)	Age	# of Tablets
5-14 kg	<3	1
15-24 kg	4-8	2
25-34 kg	9-14	3
>34 kg	>14	4

- **Artemether-Amodiaquine (Coarsucam):** 2 tabs OD for 3 days
- **Artesunate-Piperaquine (Duo-cotexcin):** 3 tabs OD for 2 days then 2 tabs OD for 1 day
- **Artemether/Artesunate/Larither:** 160 mg IM day 1, then 80mg IM OD until can take PO med or x 7days total.
- **Fansidar**: Sulfadoxine-pyramethamine. Fairly high resistance in western Kenya.

Doxycycline: Another option to combine with quinine. 3,g/kg/d PO OD (Max 200mg/day) x 7days. (avoid in <18YO).

Severe Malaria

IV quinine is preferred per the guidelines

	Pediatrics	Adults
Loading dose	15 mg (salt)/kg	20 mg/kg
Maintenance dose	10 mg/kg q12h	10 mg/kg q8h
Oral dose	10 mg/kg q8h	10 mg/kg q8h (max 600 mg)
Total duration	7 days	7 days

Treatment Failure vs. New Infection

- If symptoms recur 14 days after treatment, it should be considered a new infection
  - Treat with first line agents
- If symptoms occur between 3-14 days after treatment, it should be considered a treatment failure
  - Second line treatment is Quinine tablets (10mg/kg q8h) usually in combo with tetracycline or clindamycin

Hyper-reactive Malarial Splenomegaly (HMS)

Clinical features:

- Common presenting symptoms – abdominal swelling and pain and a dragging sensation in the abdomen
- Intermittent fever though fever may be absent altogether
- Massive splenomegaly; most patients also have associated hepatomegaly
- Malnutrition and jaundice may be present
- Anemia (normocytic normochromic) is common and is associated with pancytopenia (hypersplenism)
- Susceptibility to bacterial infections
- Generally associated with a high mortality rate (more than 50%; up to 85% in some centres)

Diagnosis:

- Often difficult to distinguish from malignant lymphoproliferative disorders
- Blood smear for malaria parasites is usually negative
- Recommended diagnostic criteria:
  - Patient comes from an area with a high prevalence of malaria
  - Chronic splenomegaly, often massive (at least 10 cm below the costal margin), usually unexplained by other conditions
  - Serum IgM elevated to more than 2 SD above the local reference mean (not done at MTRH)
  - High malarial antibody titres (not done at MTRH)
  - Hepatic sinusoidal lymphocytosis (not done at MTRH)
  - A sustasined response to malarial prophylaxis with a reduction in the size of the spleen of at least 40%

Treatment:

- Prolonged use of antimalarial medication is the mainstay of management (long term antimalarial prophylaxis)
- The recommended agents for long term prophylaxis are proguanil and chloroquine. However, chloroquine is not used in this setting due to the high level of resistance of malaria to chloroquine.
- Dose: Proguanil - 200 mg OD
- Response to therapy is guided by splenic size and symptomatic improvement
- Splenectomy is not recommended but may be performed in patients in whom there is severe hypersplenism and no response to long term antimalarials

POISONING

COMMON CAUSES OF POISONING IN KENYA, CLINICAL MANIFESTATIONS AND TREATMENT

TYPE OF POISON	COMMONLY FOUND EXAMPLES	ROUTE OF POISONING	CLINICAL MANIFESTATIONS	TREATMENT
Organo-phosphate pesticides	Diazinon, Delnav, Azinfos, Malathion, Parathion, Supona, Stelladone	Ingestion or inhalation	They irreversibly block the cholinesterase enzyme resulting in excessive muscarinic and nicotinic activity including miosis, salivation, bradycardia, bronchospasms, bronchorrhoea, skeletal muscle twitching and convulsions	Atropine, Pralidoxime (to reactivate cholinesterase but mu0st be given within 72 hours of ingestion)
Acaricides (used to kill ticks in domestic animals)	Amitraz (Triatix)	Ingestion	Similar to organophosphate poisoning but atropine has no role as an antidote	Supportive and symptomatic
Herbicides	Paraquat, Diquat	Eyes, skin, ingestion or inhalation	Local irritation, mucosal sloughing, acute renal failure, tremors, convulsions, pulmonary oedema subsequent to inhalation leading to lung fibrosis and death within four days	Has poor prognosis if untreated within 5-6 hours. Use activated charcoal, induce vomitting, lavage and symptomatic treatment
Rodenticides	Warfarin - used in stored grains	Ingestion	Haemorrhage	Vitamin K, blood transfusion, FFP
Rodenticides	Zinc phosphide - Rat & Rat, Rat Kill, Red Cat	Ingestion	Metabolic acidosis, hypocalcaemic tetany, ataxia	Supportive and symptomatic

Aflatoxins - from *Aspergillus flavos*	-	Ingestion of contaminated grains	Acute liver damage leading to hepatocellular carcinoma	Supportive and symptomatic
Methanol	Methylated spirit, "Kumi-kumi"	Ingestion	Retinal oedema leading to blindness, respiratory acidosis, delirium, headache. Commonly leads to death	1. Treat acidosis with IV bicarbonate 2. Antidote - ethanol to produce a blood concentration of 100-200% (approx 2 doubles of whiskey) 3. Dialysis in severe cases

Management of organophosphate poisoning

- Check airway, breathing, and circulation. Place patient in the left lateral position, preferably with head lower than the feet, to reduce risk of aspiration of stomach contents. Provide high flow oxygen, if available. Intubate the patient if their airway or breathing is compromised
- Obtain intravenous access and give 1–3 mg of atropine as a bolus, depending on severity. Set up an infusion of 0.9% normal saline; aim to keep the systolic blood pressure above 80 mm Hg and urine output above 0.5 mL/kg/h
- Record pulse rate, blood pressure, pupil size, presence of sweat, and auscultatory findings at time of first atropine dose
- Give pralidoxime chloride 2 g intravenously over 20–30 min into a second cannula; follow with an infusion of pralidoxime 0.5–1 g/h in 0.9% normal saline
- Five min after giving atropine check pulse, blood pressure, pupil size, sweat, and chest sounds. If no improvement has taken place, give double the original dose of atropine
- Continue to review every 5 min; give doubling doses of atropine if response is still absent. Once parameters have begun to improve, cease dose doubling. Similar or smaller doses can be used.
- Give atropine boluses until the heart rate is more than 80 beats per minute, the systolic blood pressure is more than 80 mm Hg, and the chest is clear (appreciating that atropine will not clear focal areas of aspiration). Sweating stops in most cases.
- Tachycardia is not a contraindication to atropine since it can be caused by overstimulation of nicotinic acetylcholine receptors in the sympathetic system.
- The pupils will commonly dilate; however, this sign is not a useful endpoint for initial atropine treatment because a delay exists before maximum effect. However, very dilated pupils are an indicator of atropine toxicity
- Clinical judgment is needed about additional doses of atropine if the heart rate and blood pressure are slightly below their targets but the chest is clear. More atropine at this point might not be needed.
- Once the patient is stable, start an infusion of atropine giving every hour about 10–20% of the total dose needed to stabilise the patient.
- Check the patient often to see if too much or too little atropine is being given. If too little is given, cholinergic features will re-emerge after some time. If too much is given, patients will become agitated and pyrexial, and develop absent bowel sounds and urinary retention. If this happens, stop the infusion and wait 30–60 min for these features to settle before starting again at a lower infusion rate.
- Continue the pralidoxime infusion until atropine has not been needed for 12–24 h and the patient has been extubated
- Continue to review respiratory function. Intubate and ventilate patients if tidal volume is below 5 mL/kg or vital capacity is below 15 mL/kg, or if they have apnoeic spells or PaO2 is less than 8 kPa (60 mm Hg) on FIO2 of more than 60%.

- Assess flexor neck strength regularly in conscious patients by asking them to lift their head off the bed and hold it in that position while pressure is applied to their forehead. Any sign of weakness is a sign that the patient is at risk of developing peripheral respiratory failure (intermediate syndrome). Tidal volume should be checked every 4 h in such patients. Values less than 5 mL/kg suggest a need for intubation and ventilation
- Treat agitation by reviewing the dose of atropine being given and provide adequate sedation with benzodiazepines. Physical restraint of agitated patients in warm conditions risks severe hyperthermia, which is exacerbated greatly by atropine because it inhibits normal thermoregulatory responses, including sweating. Adequate sedation is therefore important.
- Monitor frequently for recurring cholinergic crises due to release of fat soluble organophosphates from fat stores. Such crises can occur for several days to weeks after ingestion of some organophosphates. Patients with recurring cholinergic features will need retreatment with atropine and pralidoxime.

RENAL FAILURE

Acute Renal Failure (ARF)

Definition:

- Acute deterioration in renal function manifested by an increase in serum creatinine by 45 mmol/L or an increase in serum creatinine by 20% if baseline creatinine is greater than 220 mmol/L
- Oliguria: Urine output = 100-400 ml/24 hours
- Anuria: Urine output < 100 ml/24 hours.

Causes:

- Prerenal:
  - Hypovolemia
  - Reduced cardiac output
  - Systemic vasodilatation
  - Renal vasoconstriction secondary to: ACEIs, ARBs, NSAIDs, contrast dye, cirrhosis (hepatorenal syndrome)
  - Bilateral renal artery stenosis
- Intrinsic:
  - Acute Tubular Necrosis (ATN):
    - Ischemia – progression of prerenal disease
    - Toxins – aminoglycosides, amphotericin B, cisplatin, contrast dye
  - Acute Interstitial Nephritis (AIN):
    - Allergic – Beta lactams, sulfa-based drugs, NSAIDs
    - Infection – pyelonephritis
    - Infiltrative – sarcoid, lymphoma, leukemia
  - Renovascular (small vessel) – TTP, DIC, preeclampsia, cholesterol emboli, endocarditis, hypertensive crisis, scleroderma renal crisis
  - Glomerulonephritis – nephritic or nephrotic syndrome
- Postrenal:
  - Bladder neck – BPH, prostate cancer, neurogenic bladder, anticholinergic drugs
  - Ureteral – Malignancy, lymphadenopathy, retroperitoneal fibrosis, nephrolithiasis (bilateral)
  - Tubular – Precipitation of crystals

Complications:

- Volume overload
- Hyperkalemia, hyperphosphatemia
- Metabolic acidosis
- Uremia (nausea, vomiting, encephalopathy, pericarditis)

Treatment:

- Treat underlying disorder; avoid nephrotoxic drugs
- Review dosing of renally cleared drugs
- Indications for urgent dialysis:
    - **A**cid-base imbalance: acidemia
    - **E**lectrolyte disorder: hyperkalemia
    - **I**ntoxication: methanol, ethylene glycol
    - **O**verload of volume
    - **U**remia: pericarditis, encephalopathy, bleeding

General points to consider:

- The following investigations must be done to prepare the patient for dialysis: CBC, UEC, HIV Long ELISA, Hepatitis B and C screen and renal ultrasound.
- Before dialysis, the patient's family members must be sent to the renal unit for counselling. This is because the cost of dialysis is very high.

Chronic kidney disease (CKD)

Definition:

- Greater than 3 months of reduced GFR (<60 ml/min/1.73 m^2) and/or kidney damage

Causes:

- Diabetes mellitus
- Hypertension
- Polycystic kidney disease
- Glomerulonephritis
- Drug-induced
- Myeloma
- Progression of ARF

Estimation of Glomerular Filtration Rate (GFR):

$$\text{eGFR (Creatinine clearance) (ml/min)} = \frac{(140 - \text{Age}) \times \text{Weight (Kg)}}{72 \times \text{Serum Cr (mg/dl)}} \times 0.85 \text{ (for females)}$$

NB: To convert units of serum creatinine from micromol/l to mg/dl, divide by 88.4

Stages of CKD:

Stage	GFR	Goals
1 (normal)	> 90	Dx/Rx of underlying condition and comorbidities, slow progression, cardiovascular risk reduction
2 (mild)	60-89	Estimate progression
3 (moderate)	30-59	Evaluate and treat complications
4 (severe)	15-29	Prepare for renal replacement therapy (RRT)
5 (kidney failure)	< 15 or dialysis	Dialysis if uremic

Signs and symptoms of uremia:

System	Manifestations
General	Nausea, anorexia, malaise, fetor uremicus, metallic taste, pruritis, uremic frost (white crystals in and on skin), susceptibility to drug overdose
Neurologic	Encephalopathy (AMS, decreased attention and memory), seizures, myoclonus, neuropathy
Cardiovascular	Pericarditis, accelerated atherosclerosis, hypertension,

	hyperlipidemia, volume overload, CHF, cardiomyopathy
Hematologic	Anemia, bleeding (due to platelet dysfunction)
Metabolic	Hyperkalemia, hyperphosphatemia, acidosis, hypocalcemia, 2° hyperparathyroidism, osteodystrophy

Treatment:

- Dietary restrictions – sodium (if hypertensive), potassium (usually if oliguric), phosphate, magnesium
- ACE inhibitors and ARBs – slow progression of diabetic and non-diabetic nephropathy. However potassium levels must be followed very closely
- Hematologic:
  - Erythropoietin – start at 80-120 units/kg SC, divided 3 times/week.
  - Iron supplementation
- Metabolic:
  - Hyperkalemia – kayexalate is not available and all other means of lowering potassium are transient i.e. calcium gluconate, insulin, bicarbonate, beta-2 agonists. If there are ECG changes, IV calcium gluconate should be given and urgent hemodialysis should be considered.
  - Metabolic acidosis – sodium bicarbonate. However, bicarbonate levels are rarely available
  - Vitamin D deficiency – supplement vitamin D
  - Hyperphosphatemia – phosphate binders (not commonly available)
- Dialysis – both peritoneal and hemodialysis are available. (See work up for dialysis under ARF above)

General points to consider:

- Patients who require chronic dialysis often cannot afford to sustain it. However, the Kenyan national insurance programme (NHIF) is able to cover some of the costs of dialysis and patients should be encouraged to get registered.
- Renal transplant is rarely done. This is mainly due the cost both of the transplant as well as of the immunosuppressant drugs used after the transplant. Moreover, it is not possible to monitor serum levels of immunosuppressant drugs such as cyclosporine thereby increasing risk of toxicity secondary to these medications

RHEUMATIC HEART DISEASE

Clinical features (patients normally develop one of these lesions but there may be mixed lesions):

- Mitral stenosis:
  - Is the most common complication of carditis caused by acute rheumatic fever
  - Patients may be asymptomatic in mild to moderate MS.
  - Heart failure symptoms may be precipitated by exercise, emotional upset, fever, pregnancy or atrial fibrillation.
  - Symptoms include: dyspnoea, haemoptysis (due to increased pulmonary pressures and vascular congestion) and chest pain.
  - Patients are susceptible to the development of atrial fibrillation (AF) because of left atrial dilatation in response to valve obstruction, and because of the inflammatory and fibrotic changes caused by the rheumatic process.
  - AF with rapid ventricular response leads to loss of atrial contraction that ultimately results in decreased cardiac output and heart failure. In addition, the loss of atrial contraction leads to stasis of blood in the LA eventually resulting in the formation of thromboemboli. This increases the risk of developing cardioembolic stroke.
  - Severe mitral stenosis is usually defined by a mitral valve area of ≤ 1.0 cm^2 and is associated with a high risk of development of a left atrial thrombus
  - The late stages of uncorrected, severe mitral stenosis may be complicated by the development of pulmonary hypertension, and by failure of the right side of the heart, with oedema and ascites. Secondary tricuspid regurgitation commonly co-

exists at this stage; AF is invariably present and the risk of venous thromboembolic disease is greatly increased.

- Mitral regurgitation:
  - Is well tolerated compared to MS
  - Patients can develop AF and left ventricular systolic dysfunction and are more prone to infective endocarditis
- Aortic stenosis:
  - Has the worst prognosis of all the valvular lesions in rhematic heart disease if left untreated
  - Without valve replacement surgery, the average survival after the onset of symptoms is only two to three years with a high risk of sudden death.
  - Symptoms include: angina, syncope and heart failure
- Aortic regurgitation:
  - Patients tend to remain asymptomatic for a very long time
  - Symptoms include heart failure secondary to left ventricular dysfunction and angina
  - Patients may develop AF
- Multivalvular heart disease:
  - In many patients with chronic RHD, both the mitral and aortic valves may be involved.
  - These patients usually have heart failure and AF

Investigations:

- Echocardiography – to confirm the exact lesion
- ECG
- CXR

Treatment:

- There is no medical therapy available to reverse rheumatic fever induced valvular changes.
- Surgical intervention is the only curative means of managing RHD.
- Where patients cannot undergo surgery either due to cost implications or to contraindications to surgery, symptomatic management is the only option.
- Heart failure is treated with diuretics, beta blockers, ACE inhibitors and aldosterone antagonists.
- ACE inhibitors should be used with care as there is risk of haemodynamic worsening in patients with severe MS and AS.
- Digoxin should NOT be used if the patient is in sinus rhythm.
- As the disease progresses, patients may need to be on chronic or intermittent diuretic therapy to treat symptoms of pulmonary or systemic venous congestion
- Atrial fibrillation:
  - Rate control is preferred over rhythm control.
  - Can use beta blockers or digoxin. Digoxin should only be used if beta blockers are contraindicated (e.g. if the patient is at risk of developing hypotension)
  - Lifetime anticoagulation with warfarin to target an INR range of 2.0-3.0.
  - If embolization occurs despite such treatment an INR of 2.5-3.5 and/or the addition of low dose aspirin is recommended.

Monitoring parameters:

- BP, pulse and pulse deficit (for patients with AF)
- Fluid input-output, daily weights
- Potassium levels for patients on high dose diuretics, ACE inhibitors and aldosterone antagonists.
- Creatinine clearance especially for patients on digoxin because impairment in kidney function leads to accumulation of digoxin.
- Signs and symptoms of digoxin toxicity including: fatigue, blurring of vision, confusion, anorexia, nausea, vomiting, diarrhoea, abdominal pain, headache, bradycardia, ECG changes (PVCs, high degree AV block, ventricular arrhythmias).

General points to consider:

- Valve replacement surgery is not available at MTRH and patients who need surgery have to get it done in Nairobi, which is very expensive. Most patients cannot afford surgery and hence, can only be managed symptomatically.
- Patients requiring anticoagulation should be referred to the pharmacist managed anticoagulation clinic as soon as possible for INR monitoring.

SCHISTOSOMIASIS

Causative agents:

- *Schistosoma mansoni* – causes intestinal and hepatic complications
- *Schistosoma haematobium* – predominantly leads to renal and bladder sequelae, although occasionally, it results in liver disease.
  These are the 2 main species found in Sub-Saharan Africa. Other species include: *S. japonicum, S. intercalatum and S. mekongi*.

Life cycle:

- Humans acquire schistosomiasis via contact with freshwater containing infectious, free-living, cercarial larvae.
- Cercariae penetrate the intact skin of humans and, in the process, shed their forked tail to become schistosomulae.
- Schistosomulae migrate from the skin into the blood and lymph vessels and are carried to the heart and lungs. They then migrate through the pulmonary capillaries into the left side of the heart and, from there, into the arterial circulation.
- They are carried to the mesenteric arteries, splanchnic arteries, and portal veins, subsequently reaching the liver where they mature into adults over a period of one to four weeks.
- Different species have a propensity to affect different organs. The adult worms migrate against portal blood flow to varying destinations:
  - The mesenteric venules of the small intestine – *S. japonicum* and *S. mekongi*
  - The mesenteric venules of the colon – *S. mansoni* and *S. intercalatum*
  - The vesical venous plexus – *S. haematobium*
- The adults remain in these blood vessels for life, residing in permanent copulation and adhering to the wall of the blood vessels with suckers. These worms usually survive for five to seven years but can persist for up to 30 years.
- After one to three months, the female worm begins to produce eggs, which can travel haematogenously to other sites or can traverse from the vascular space through host tissues to the lumen of the intestine or urinary bladder.
- The eggs are then variably excreted in the faeces (*S. mansoni, S. japonicum, S. haematobium, S. intercalatum,* and *S. mekongi*) or the urine (*S. haematobium*).
- Excreted eggs each contain one male or female miracidium, which is an immature larval form.
- When eggs contact freshwater, the osmotic stress ruptures the shell, and the miracidia hatch and swim through water in search of a susceptible snail host.
- The miracidia then penetrate appropriate snail species and undergo asexual reproduction over a period of three to five weeks, developing into sporocysts, and then cercariae.
- Snails release thousands of cercariae into fresh water, each of which can penetrate skin if they come in contact with humans, thereby completing the life cycle. Cercariae can survive up to 48 hours in water but are most infectious to humans for the first few hours after release from the snail.
- Infection cannot be acquired by direct contact with excreta from an infected person, since parasite development in a snail is required. The different schistosomal species have different species of snails that serve as their intermediate hosts:
  - *S. mansoni – Biomphalaria species*
  - *S. haematobium – Bulinus species*
  - *S. japonicum – Oncomelania species*
  - *S. mekongi – Tricula species*
  - *S. intercalatum – Bulinus species*

Clinical features:

- Most patients infected with schistosomes of all species are asymptomatic.
- Acute symptoms tend to be more common in nonimmune individuals, such as travellers, due to a more intense immune response to exposure, while chronic complications require a higher burden of infection and, thus, are mainly seen in individuals from endemic areas.
- Acute infection – may present as "Swimmer's itch" or Katayama fever
    - Swimmer's itch:
        - A localized dermatitis that can result in a pruritic papular or urticarial rash at the site of larval entry, which is typically on the lower legs or feet.
        - Usually seen within one day of exposure. Immediate tingling and itching at the site of entry may develop, followed by an intensely pruritic papular eruption 12 to 24 hours later, which can last more than a week.
        - Prior sensitization to cercariae results in more rapid immune response and more severe symptoms.
        - This manifestation is most common with *S. japonicum* and occurs rarely with *S. haematobium*.
    - Katayama fever:
        - A systemic hypersensitivity reaction against the migrating parasites, which occurs between two to eight weeks after exposure.
        - Seen more frequently with *S. mansoni* or *S. japonicum* infections.
        - Symptoms include sudden onset of fever, chills, myalgias, arthralgias, dry cough, diarrhoea and headache
        - Some patients also develop persistent and more serious disease such as weight loss, dyspnoea, and chronic diarrhoea
- Intestinal schistosomiasis:
    - Most common symptoms include chronic or intermittent abdominal pain, poor appetite and diarrhoea
    - Stools may be grossly bloody and chronic ulcerations may lead to secondary iron deficiency anaemia.
    - Intestinal polyps can arise due to granulomatous inflammation surrounding eggs that are deposited in the bowel wall.
    - Bowel ulcers and strictures can also develop. Rarely, an inflammatory mass can lead to obstruction.
- Hepatic schistosomiasis can lead to two distinct syndromes:
    - Inflammatory hepatic schistosomiasis – causes hepatomegaly and severe splenomegaly in children and adolescents. Severity depends on intensity of egg infestation.
    - Chronic hepatic schistosomiasis - develops years later in young and middle aged adults with a long duration of intense infection. Diffuse deposits in the periportal spaces leads to periportal fibrosis resulting in splenomegaly and portal hypertension. However, hepatocellular function remains normal. Leading causes of morbidity and mortality include the formation of ascites and oesophageal bleeding from varices.
- Urinary schistosomiasis:
    - May be asymptomatic or may cause microscopic or macroscopic haematuria, dysuria, and urinary frequency.
    - Symptoms related to secondary anaemia may be present.
    - Blood is usually seen at the end of voiding (terminal haematuria), but in severe cases can be present throughout.
    - With progressive involvement, fibrosis and calcification of the bladder and ureters can occur resulting in hydroureter and hydronephrosis. Obstruction leading to kidney damage and secondary bacterial infections may also ensue.
    - In addition, chronic inflammation may lead to an increased risk of developing some forms of squamous cell carcinoma of the bladder.
    - In addition to the direct invasion of the urinary system, infection with any schistosomal species can be associated with immune complex deposition in the kidneys, leading to proteinuria and the nephrotic syndrome.
- Neurologic complications:

- Spinal cord neuroschistosomiasis – results in transverse myelitis
- Localized cerebral or cerebellar neuroschistosomiasis – leads to focal CNS impairment, seizures and increased intracranial pressure.

- Pulmonary complications – pulmonary hypertension and cor pulmonale due embolization of eggs into pulmonary circulation secondary to portal hypertension. Pulmonary changes represent end stage alterations and are often irreversible.

Diagnosis:

- CBC – may show eosinophilia; anaemia from chronic blood loss may also be revealed. There may be thrombocytopaenia secondary to splenic sequestration
- LFTs – are normal because fibrosis occurs with the blood vessels and not within the liver parenchyma itself.
- Urinalysis – haematuria is detected in *S. haematobium* infection.
- Microscopy – eggs may be present in urine or stool; depending on the morphology of the eggs the schistosomal species can be identified. Eggs may also be detected from tissue biopsy specimens of rectal, intestinal, liver or bladder biopsies.
- Serology – not routinely used
- Radiology:
  - Abdominal ultrasound may be used to visualize periportal fibrosis, splenomegally and the presence of collateral vessels.
  - CT scans can show characteristic patterns in livers with established hepatic schistosomiasis. CT may also be utilized in patients with suspected central nervous system or spinal cord involvement.
  - Renal and pelvic ultrasounds may show irregularities in the bladder wall due to granulomas caused by *S. haematobium*. Hydronephrosis, bladder polyps and tumours can also be detected.
  - Calcification of the bladder wall may be demonstrated on plain x-ray; the characteristic appearance is often referred to as "fetal head" calcification.
  - Ureteric strictures may also be detected by intravenous pyelogram (IVP).

Treatment:

- Drug of choice is praziquantel 40 mg/kg PO STAT
- Praziquantel acts mainly on the adult worms and has no effect on immature worms and eggs and hence it is ineffective in early infection.
- Glucocorticoids can be used for symptomatic treatment of Katayama fever as well as in neuroschistosomiasis. Use prednisone 40 mg OD for 5 days.
- Patients with severe portal hypertension and oesophageal varices can be treated with propranolol 20 mg BD. They may also benefit from sclerotherapy or shunt procedures

Monitoring parameters:

- Eosinophil count in patients with eosinophilia
- Urine and stool examination for the presence of eggs should be repeated six post treatment to assess cure.

STROKE

Classification and causes:

- Intracerebral haemorrhage – the bleeding is directly into the brain. Most common causes are: hypertension, trauma, bleeding diathesis, amyloid angiopathy and vascular malformations. Less frequent causes include bleeding into tumours, aneurysmal rupture, and vasculitis.
- Subarachnoid haemorrhage – Major cause is the rupture of arterial aneurysm which releases blood directly into the CSF.
- Ischemia – There are three main subtypes of brain ischemia:
  - Thrombotic stroke – occurs due to the formation of a thrombus in large (both intra and extracranial) or small (intracranial) arteries secondary to atherosclerosis. The thrombus causes reduced blood flow distally resulting in ischemia.

- Embolic stroke – Embolism refers to particles of debris originating elsewhere that block arterial access to a particular brain region. Causes of embolic stroke include:
  - Left atrial or ventricular thrombus
  - Atrial fibrillation
  - Sustained atrial flutter
  - Recent myocardial infarction
  - Rheumatic mitral or aortic valve disease
  - Prosthetic heart valves
  - Symptomatic heart failure with LVEF < 30%
  - Dilated cardiomyopathy
  - Bacterial endocarditis
- Systemic hypoperfusion – due to a more general circulatory problem. It can be secondary to cardiac pump failure caused by cardiac arrest or arrhythmia, or to reduced cardiac output related to acute myocardial ischemia, pulmonary embolism, pericardial effusion, or bleeding.

Clinical features:

- Headache – more common in haemorrhagic stroke. In subarachnoid haemorrhage, the headache is of sudden onset and is very severe, often described by patients as "the worst headache of my life"
- Vomiting – also common in ICH and SAH
- Seizures
- Focal neurologic deficits
- Change in mental status
- Impaired consciousness

Diagnosis:

- Head CT scan – to differentiate between haemorrhagic and ischemic stroke and establish the extent of the brain damage caused.
- Investigations to determine the underlying cause of the stroke including ECG, echo, blood cultures, lipid profile, etc.

Management:

- Blood pressure:
  - Is usually elevated in acute ischemic stroke. This elevated blood pressure is necessary to maintain brain perfusion. **Treatment of raised BP is not recommended unless the hypertension is extreme** (systolic blood pressure >220 mmHg or diastolic blood pressure >120 mmHg) or the patient has active ischemic coronary disease, heart failure, aortic dissection, hypertensive encephalopathy, acute renal failure, or pre-eclampsia/eclampsia. In these cases the BP should be lowered very cautiously.
  - In patients with ICH, the blood pressure may be treated more aggressively than in patients with ischemic stroke. Parenteral antihypertensive agents are recommended but these are rarely available, and hence oral agents must be used.
  - In patients with SAH, blood pressure reduction is recommended as this reduces the intracranial pressure thereby improving cerebral perfusion. The recommended drug is nimodipine 60 mg every 4 hours PO. However, it is not commonly available and hence other agents are used including nifedipine, beta blockers and ACE inhibitors.
- Thrombolysis in patients with thrombotic stroke – not routinely done here
- Prevention of seizures – usually in ICH and SAH
- In patients with confirmed ischemic stroke:
  - Aspirin should be started as soon as possible. Dose: 300 mg STAT then 150-300 mg daily
  - Statins should be initiated in patients with thrombotic stroke regardless of the levels of serum lipids
  - Anticoagulation should be considered in patients with embolic stroke secondary to atrial fibrillation and rheumatic heart disease
- ICU admission is recommended for patients with haemorrhagic stroke
- Prevention of medical complications including:

- Myocardial infarction
- Heart failure
- Dysphagia
- Aspiration pneumonia
- Urinary tract infection
- Deep vein thrombosis
- Pulmonary embolism
- Dehydration
- Malnutrition
- Pressure sores
- Orthopaedic complications and contractures

SYSTEMIC LUPUS ERYTHEMATOSUS

Clinical features:

- Constitutional symptoms – fatigue, fever, weight loss, myalgia, photosensitivity
- Arthritis – occurs in over 90% of patients
- Mucocutaneous manifestations:
  - Malar butterfly rash – erythema over the cheeks and nose which appears after sun exposure
  - Discoid rash.
  - Hair loss
  - Oral and nasal ulcers
- Raynaud phenomenon – cold or emotion-induced colour changes of the digits of the hands and feet.
- Renal involvement – patients develop glomerulonephritis secondary to deposition of immune complexes in the nephrons
- Pulmonary manifestations - Pleurisy, pleural effusion, pneumonitis, interstitial lung disease, pulmonary hypertension, and alveolar haemorrhage can all occur in SLE.
- Cardiovascular – pericarditis is common. Patients are also at risk of coronary artery disease.
- Neurologic complications:
  - Cognitive defects, organic brain syndromes, delirium, psychosis, seizures, headache, and/or peripheral neuropathies.
  - Stroke – due to arterial thromboembolism
- Opthalmologic manifestations – most commonly keratoconjunctivitis sicca caused by the reduction in the aqueous component of tears. Patients complain of a 'gritty' or 'sandy' feeling in their eyes.
- Haematologic effects:
  - Leukopenia – not usually symptomatic unless very severe
  - Anaemia – usually due to chronic disease; haemolytic anaemia is rare but can be severe
  - Thrombocytopenia – also common. However bleeding is only seen in platelet counts below 25,000/mm^3
  - Thrombophilia – there is an increased risk of thromboembolic disease especially in patients with antiphospholipid antibodies. This may manifest as venous thromboembolism or arterial disease
  - Lymphadenopathy and splenomegaly

Precipitating factors (of the first symptoms of SLE or a relapse):

- Exposure to the sun or other sources of ultraviolet light
- Infections
- Stress
- Surgery
- Pregnancy

Investigations:

- CBC + ESR

- UEC
- Serum albumin
- Urinalysis
- Autoantibody testing:
    - Antinuclear antibodies (ANA)
    - Antiphospholipid antibodies – not available
    - Antibodies to double stranded DNA – not available
    - Anti-Smith (Sm) antibodies – not available
- Imaging:
    - CXR
    - Echo – for suspected pericardial involvement or to assess for a source of emboli
    - Renal ultrasound – to assess kidney size rule out urinary tract obstruction when there is evidence of renal failure.
    - Head CT scan – for focal neurologic deficits
- Biopsy of an involved organ (e.g. skin or kidney) – not routinely done
- LE cell test – looks for evidence of phagocytosis of nuclear material in blood smear. This test has been replaced by autoantibody testing but can still be done since most autoantibody tests are not available.

Diagnosis:

- Based on diagnostic criteria developed by the American Rheumatism Association(ARA).
- A diagnosis of SLE is made if four or more of the manifestations are present, either serially or simultaneously.
- Patients can be classified as follows:
    - Classical SLE — many criteria
    - Definite SLE — 4 or more criteria
    - Probable SLE — 3 criteria
    - Possible SLE — 2 criteria

ARA criteria for the diagnosis of SLE

Criterion	Definition
Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
Discoid rash	Erythematosus raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
Arthritis	Nonerosive arthritis involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion
Serositis	Pleuritis - convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion **OR**
	Pericarditis - documented by EKG, rub or evidence of pericardial effusion
Renal disorder	Persistent proteinuria greater than 0.5 grams per day or greater than 3+ if quantitation not performed **OR**
	Cellular casts - may be red cell, hemoglobin, granular, tubular, or mixed
Neurologic disorder	Seizures OR psychosis - in the absence of offending drugs or known metabolic derangements (uremia, ketoacidosis, or electrolyte imbalance)
Hematologic disorder	Hemolytic anemia - with reticulocytosis **OR**
	Leukopenia - less than 4,000/mm3 total on two or more occasions **OR**

	Lymphopenia - less than 1,500/mm3 on two or more occasions **OR**
	Thrombocytopenia - less than 100,000/mm3 in the absence of offending drugs
Immunologic disorders	Positive antiphospholipid antibody **OR**
	Anti-DNA - antibody to native DNA in abnormal titer **OR**
	Anti-Sm - presence of antibody to Sm nuclear antigen **OR**
	False positive serologic test for syphilis known to be positive for at least six months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test
Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome

Treatment:

- Sun protection - Avoid exposure to direct or reflected sunlight and other sources of ultraviolet light (e.g. fluorescent and halogen lights). Use sun screens, preferably those that block both UV-A and UV-B, with a minimum skin protection factor (SPF) of 30.
- Topical steroids – useful for local problems
- NSAIDs - generally effective for musculoskeletal complaints and mild serositis
- Hydroxychloroquine – most useful for skin manifestations and for musculoskeletal complaints that do not adequately respond to NSAIDs. It may also prevent major damage to the kidneys and CNS as well as reduce disease flares. Dose: 200 mg BD; can be increased to 400 mg BD.
- Systemic glucocorticoids – are generally reserved for patients with significant organ involvement, particularly renal and CNS disease. They can be combined with immunosuppressive agents. Dose: Prednisone 1-2 mg/kg/day.
- Immunosuppressive agents – are reserved for patients who have had an inadequate response to steroids. They include methotrexate, cyclophosphamide, azathioprine, mycophenolate etc.

Monitoring parameters:

- Because patients with SLE tend to be on medication for a long time, it is important to look out for adverse reactions.
- For patients on long-term hydroxychloroquine:
    - CBC should be monitored regularly as it can cause agranulocytosis and other blood dyscrasias.
    - Regular eye checkups to detect any ocular effects
    - Signs and symptoms of CNS toxicity; regular neurologic and mental state examinations should be done
    - Signs and symptoms of dermotologic effects including Stevens-Johnson syndrome, alopecia, exfolliative dermatitis, etc.
    - Regular CVS examinations
- For patients on long-term glucocorticoid therapy:
    - Regular eye checkups to look out for cataract formation and glaucoma
    - Regular CVS examinations and blood pressure monitoring
    - Lipid profile
    - Signs and symptoms of gastritis, ulcer formation and GI bleeding
    - UEC
    - Signs and symptoms of osteoporosis
    - RBS – glucocorticoids can cause diabetes
    - Signs and symptoms of opportunistic infections

TYPHOID FEVER

Causative agents:

- *Salmonella typhi*
- *Salmonella paratyphi* A, B or C

Clinical features:

- Usually presents non-specifically with abdominal pain, fever, chills, and constitutional symptoms
- The classic presentation in untreated individuals is described in the following stages:
    - First week of illness – rising (stepwise) fever and bacteraemia
    - Second week – abdominal pain and rash (rose spots, which are faint salmon coloured macules on the trunk and abdomen)
    - Third week – hepatosplenomegaly, intestinal bleeding and perforation, related to ileocecal lymphatic hyperplasia of the Peyer's patches, may occur with secondary bacteraemia and peritonitis.
- Other features include: diarrhoea or constipation, abdominal tenderness, cough, athralgias, myalgias, septic shock and altered level of consciousness.

Diagnosis:

- Blood, urine and stool cultures
- Rising Widal titres.

NB: A single Widal test has limited utility because a positive result may represent previous infection. Therefore, repeated Widal tests showing rising titres of the antigens signify the presence of an active typhoid infection.

Treatment:

- Drugs of choice include:
    - Ciprofloxacin 500 mg BD PO or IV for 7-10 days
    - Ceftriaxone 2 g OD IV for 7-14 days
- Alternative agents include:
    - Azithromycin 1 g STAT then 500 mg OD for 5-7 days or 1 g OD for 5 days
    - Chloramphenicol 2 to 3 g per day orally in four divided doses for 14 days.

URINARY TRACT INFECTION

Causative agents:

- *Escherichia coli* – the most common cause
- *Enterococcus spp*
- *Klebsiella spp*
- *Pseudomonas aeruginosa*
- *Citrobacter spp*

Clinical features:

- Dysuria
- Frequency
- Suprapubic pain
- Fever
- Chills

Diagnosis:

- Urinalysis:
    - Pus cells
    - Leukocytes
    - Granular casts
- Urine culture – to isolate the causative agent

Treatment:

- For uncomplicated UTI, a three day course of antibiotics is adequate; complicated infections require at least 5-7 days treatment with antibiotics. Any UTI diagnosed within the inpatient setting should automatically be treated as a complicated UTI.
- Common agents used include:
  - Norfloxacin 400 mg BD
  - Ciprofloxacin 500 mg BD
  - Co-amoxiclav 375 mg TID or 625 mg BD
  - Trimethoprim-Sulfamethoxazole (Septrin) 2 SS tabs or 1 DS tab BD
- NB: Fluoroquinolones should be avoided if there is any concurrent suspicion of TB.

VIRAL ENCEPHALITIS

Causes:

- HSV-1 or 2
- Other herpes viruses – VZV, CMV, EBV, HHV-6
- Adenoviruses
- Influenza A
- Enteroviruses, poliovirus
- Measles, mumps and rubella viruses
- Rabies, etc.

Clinical features:

- Progressive symptoms of fever, headache, altered level of consciousness
- Signs and symptoms of cerebral dysfunction including:
  - Cognitive dysfunction – acute memory disturbances
  - Behavioral changes – disorientation, hallucinations, psychosis, personality changes, agitation
  - Focal neurological abnormalities – dysphasia, hemiparesis, hemianopia etc
  - Seizures

Diagnosis:

- CBC – Lymphocytosis is common in viral infections
- Neuroimaging:
  - CT scan – may be normal in Herpes Simplex Encephalitis (HSE), especially early in the illness, but characteristically shows reduced attenuation in one or both temporal lobes or areas of hyperintensity
  - MRI – is preferred but is rarely done due to cost. Typical features in HSE are areas of focal oedema in the temporal lobes and orbital surface of the frontal lobes as well as the insular cortex and angular gyrus.
- Lumbar puncture:
  - Should only be delayed only in the presence of strict contraindications
  - CSF may be xanthochromic with RBCs; glucose is usually normal; proteins are raised
  - Lymphocyte count: 10-200/mm^3
  - PCR analysis – is highly recommended for the diagnosis of HSV, VZV and CMV but is not available
- Brain biopsy – highly sensitive but not routinely done
- Differential diagnoses:
  - Brain abscess
  - Tuberculous meningitis
  - CNS vasculitis
  - Cryptococcal meningoencephalitis
  - Toxoplasma encephalitis
  - Acute disseminated encephomyelitis (ADEM)

Treatment:

- Acyclovir – 10 mg/kg IV every 8 hours for 10-14 days if there is high suspicion for HSV. Adequate hydration must be provided on this regimen.
- Supportive therapy – anticonvulsants for seizures (IV phenytoin); maintenance of respiration, cardiac rhythm and fluid balance; prevention of DVT and aspiration pneumonia; medical management of raised intracranial pressure and secondary bacterial infections.

Monitoring parameters:

- Renal function – acyclovir may cause acute renal failure due to the precipitation of crystals in the renal tubules. This risk may be minimized by prior hydration and slow drug infusion over 1-2 hours.
- Because more than 80% of acyclovir is excreted unchanged in urine, renal impairment can rapidly precipitate acyclovir toxicity and doses should be adjusted based on renal clearance.

General points to consider:

- HSV encephalitis is generally associated with high mortality – more than 70% if untreated and 28% mortality at 18 months with appropriate treatment.
- Empiric treatment with IV acyclovir is recommended if viral encephalitis is suspected. However, this is rarely possible in this setting because IV acyclovir is very expensive (approximately Kshs. 200,000 for a 10 day course!).
- Even when the diagnosis of HSV encephalitis is confirmed, patients rarely get treated due to the high cost of acyclovir. Hence, the prognosis of viral encephalitis in this setting is even worse. It is unclear if there is any benefit from high dose oral acyclovir as the oral bioavailability is very low and has not previously been studied. However, many patients will often receive oral acyclovir since that is the only option available.

WERNICKE'S ENCEPHALOPATHY

Definition:

- Wernicke's encephalopathy refers to the neurologic complication of thiamine deficiency commonly seen in chronic alcoholism.
- Thiamine deficiency in alcohol abusers results from a combination of inadequate dietary intake, reduced gastrointestinal absorption, decreased hepatic storage, and impaired utilization.
- Other conditions associated with WE include: Anorexia nervosa, hyperemesis of pregnancy, prolonged fasting or starvation, especially with refeeding, gastrointestinal surgery (including bariatric surgery), systemic malignancy etc

Clinical features:

- The classic triad of Wernicke's encephalopathy includes: encephalopathy, oculomotor dysfunction and gait ataxia. However, very few patients will present with the classic triad.
- Encephalopathy – characterised by profound disorientation, indifference, and inattentiveness. If untreated, this progresses through stupor and coma to death.
- Oculomotor dysfunction – nystagmus, lateral rectus palsy and conjugate gaze palsies
- Gait ataxia – involves stance and walking
- Other signs:
    - Vestibular dysfunction without hearing loss
    - Peripheral neuropathy
    - Hypothermia
    - Cardiovascular signs and symptoms: tachycardia, exertional dyspnoea, elevated cardiac output and ECG abnormalities.
- Korsakoff's syndrome – a late, neuropsychiatric manifestation of Wernicke's encephalopathy (WE) in which there is a striking disorder of selective anterograde and retrograde amnesia, apathy, an intact sensorium and relative preservation of long-term and other cognitive skills. Patient's with Korsakoff's syndrome rarely recover and require some form of supervision and social support.

Diagnosis:

- Is primarily based on history and clinical findings
- It is important to have a high index of suspicion if there is a history of alcoholism and any one of the clinical manifestations.
- Institution of treatment takes priority over diagnosis and response to treatment may be diagnostic.

Treatment:

- Thiamine 100 mg OD IV/IM for 5 days followed by oral thiamine in the form of a multivitamin supplement until patient is considered no longer at risk.
- Parenteral thiamine is found in the following formulations: Pabrinex I/II, Vitamin B complex injection, Neurubine (Neurobion) injection.
- Administration of glucose without thiamine can precipitate or worsen WE, thus thiamine should be administered before glucose.
- For practical purposes, all patients with undiagnosed altered mental status, oculomotor disorders, or ataxia should receive parenteral thiamine.

APPENDIX

COMMON LABORATORY PARAMETERS AND REFERENCE RANGES

Parameter	Kenyan Reference Range	American Reference Range
Hemoglobin	6.7-11.1 g/dL	12.0-16.0 g/dL
Platelets	120-411 x 10^9/L	150-350 x 10^9/L
WBC	2.8-8.2 x 1,000	4.5-11.0 x 1,000
MCV	68.8-97.2 fL	80.0-100.0 fL
Neutrophils (absolute)	0.9-4.7 x 10^9/L	NA
Neutophils (%)	20-60	40-70
Lymphocytes (absolute)	1.1-3.5 x 10^9/L	NA
Lymphocytes (%)	20-60	40-70
Sodium	141-152 mmol/L	136-145 mmol/L
Potassium	3.9-5.8 mmol/L	3.5-5.0 mmol/L
Chloride	100-112 mmol/L	98-106 mmol/L
Urea	1.4-4.6 mmol/L	10-20 mg/dL
Creatinine	< 102 µmol/L	< 1.5 mg/dL
Calcium	2.2-2.6 mmol/L	9.0-10.5 mg/dL
Phosphorus, inorganic	1.0-1.4 mmol/L	3-4.5 mg/dL
Glucose	3.1-5.7 mmol/L	75-115 mg/dL
ALT	9.6-52.0 U/L	0-35 U/L
AST	13.8-42.3 U/L	0-35 U/L
AlkP	35-135 U/L	30-120 U/L
Albumin	35.8-48.1 g/L	3.5-5.5 g/dL
Total Bilirubin	< 17.0 µmol/L	< 1.0 mg/dL
Direct Bilirubin	1.1-8.8 µmol/L	0.1-0.3 mg/dL
CSF glucose	2.2-5.0 mmol/L	39.6-90 mg/dL
CSF Proteins	15-45 g/dL	1.5-4.5 g/L

COSTS TO THE PATIENT

Investigation	Cost (Kshs)	Comments
Abdominal CT	6000	
Abdominal ultrasound	1300	
Abdomino-pelvic ultrasound	1300	
ANA	1000	
ASOT	200	
Blood culture	800	
Blood smear for malaria parasites	100	
Cardiac enzymes	900	
Chest CT	6000	
Chest X-Ray	400	
CSF Biochemistry	400	
CSF CrAg	600	
CSF Microscopy, Culture and Sensitivity	600	

Doppler ultrasound (both limbs)	3000	
Doppler ultrasound (one limb)	2000	
ECG	400	
Echo	1000	
Erect abdominal X-ray	500	
FHG	300	
Head CT	4000	
Hepatitis screen (B,C)	1000	
LFT	1300	
Lipid profile	200	
MRI (with contrast)		
MRI (without contrast)		
Pelvic ultrasound	1300	
Rheumatoid factor	200	
Serum amylase	400	
Spinal CT	5000	
Stool culture	400	
Stool for occult blood	200	
Stool for ova/cyst	150	
Thyroid function	1800	
UA	100	
UEC	850	
Urine culture	400	
VDRL	200	

FREQUENTLY ASKED QUESTIONS

Out of stock medication?

1. Go to the pharmacy and check if it really is out of stock. If it's not talk to the nurse and make sure the patient gets it.
2. If it is, ask the pharmacy to confirm if it is available at Main Pharmacy or at any other pharmacy within the hospital. If it is available, ask if they could get it anytime soon.
3. If it is not available within the hospital, contact one the pharmacists (Manji, Mercy or Sonak) to suggest an alternative.
4. If no alternative is available, a prescription of the required medication should be written and given to pharmacy staff so that the medication can be bought from the local pharmacies in town. This could take a few hours. In rare instances, the medication may not be available in Eldoret and may need to be sourced from Nairobi in which case it would take 2-3 days to get the medication. Interns and pharmacists usually carry MTRH prescription pads.

Oncology drug O/S?

You can get these from the AMPATH oncology clinic, located in the basement of the AMPATH building. Go to the pharmacy (ask someone to direct you there) and give the pharmacy technician the patient's name and AMPATH or MTRH number. Although it is an AMPATH clinic, they will provide meds to any patient who needs it. Once you get the drug, go talk to the intern/registrar in charge to see how he/she wants to administer it (they might want to give it stat).

Morphine O/S?

Morphine PO is not commonly stocked at the ward pharmacy. If you find a patient to be severely in pain go with the treatment sheet to the AMPATH oncology clinic pharmacy to get some. The pharmacy technician will give it to you in a bottle (if it is in liquid form) or will give you tablets. The bottle/tablets are then typically stored in the nurse station Dangerous Drugs Cabinet (do not take it to the pharmacy). Then when you write for morphine, inform the primary nurse for the cube where they can find morphine PO.

*****Checking what PO and IV antibiotics are in stock with the pharmacy every morning will also be very helpful. The pharmacy might give you an availability list but availability may change from one day to the other.**

ISS +ve patient?

Newly diagnosed (on admission)
When patients are newly diagnosed with HIV on admission they are supposed to be automatically enrolled in AMPATH. However it is good to make sure that they are actually enrolled. To do this, go to the ground floor of the AMPATH building, find the registration room and ask the person in charge to look up the patients name on their new registration list. If they are enrolled, ask for their AMPATH number and record it in the patient's file. If they are not yet enrolled, ask the primary care nurse for that cube to ensure that the patient is enrolled.
(It is also good to make sure that these patients did get counseling upon diagnosis. This is supposed to happen but does not always)

Known ISS +ve patient?
Find out if they are from AMPATH. If so, you should be able to find their AMPATH number on the sheet at the back of their file, usually in the form of '1234MU-5'.

AMPATH Summary Sheet?
If you have the AMPATH number, look for an AMPATH summary sheet in their file. If it's not there, make sure you print it since it may contain important information about past treatment as well as most recent CD4 counts etc. To print these, you can go to the Diabetes Room (no. 48) or to room labeled 'Module 2' on the ground floor of the AMPATH building.
Put the summary sheet in the patient's file.

ARV refill?
With patients on ARVs, try to check if they need refills. If they do, you can personally get it for them at the AMPATH pharmacy. Ask for the refill forms to fill out for them and bring it to their bedside. Try and talk to the patient to ensure compliance with the ARVs while the patient is in the ward.

Changing a patient's ARVs?
You may need to make switches to patient's ARVs due to drug interactions (usually when antiTB drugs are initiated; rifampicin interacts with nevirapine) or ADRs. To do so, take away patients previous ARVs and exchange them at the AMPATH pharmacy using the ARV forms.

Enrolling patients in the Diabetes Clinic?

Check on all your Diabetic patients in the ward if they are already enrolled in the clinic by giving their names to one of the Diabetes Clinic personnel at the Diabetes Room in AMPATH. If they aren't the DM team will enroll them.

How to get A1C levels?
To get the A1C levels for your patients, the patient has to physically go to the DM clinic to get it checked. Ask for help from one of the staff in the DM clinic and you can wheel the patient to the clinic, have the staff get their A1C and make sure you record the outcome in the patients file. (just write 'date- A1C#-by DM team' on the 'continuation sheet of the file.)

Enrolling patients in the Anticoagulation Clinic?

Patients diagnosed with an indication for warfarin therapy (DVT, AF with RHD, stroke secondary to AF/RHD, etc) should be enrolled in the anticoagulation clinic. For patients with DVT, it is preferable to confirm the presence of DVT using Doppler ultrasound prior to starting warfarin. To enroll use the referral sheet which you can obtain from the Anticoagulation Clinic (room 48 AMPATH). It's easier just to carry a few blank sheets with you on rounds. Fill these out for the patient, get the registrar to sign (or sign it yourself if the registrar okays it) then hand it in to the anticoagulation team. The anticoagulation team will start the patient on warfarin after doing a baseline INR. Avoid starting warfarin before getting the patient enrolled in the clinic because the brand of warfarin available in the ward pharmacy is different from the brand provided by the anticoagulation and this makes the INRs less predictable.

Getting an INR?
If you need INR on the same day, inform one of the anticoagulation staff. Record the outcome in the patient's file.

Inpatient Discharge?

Inpatient discharge (aka 'Discharge-in') is when a patient is discharged but stays in the hospital due to inability to pay the hospital fees. They may stay there for a couple of weeks but the team will usually 'skip' them on rounds because they are discharged. However, make sure to update their t-sheets and check if they are still getting their treatment like (although discharged, they should still be getting treatment. If t-sheets aren't renewed, the nurses won't administer their meds!). Also, check on their nutritional status, or if they need psych counseling (especially for those that are discharged in for a long time). Keep in mind that some of them are there due to lack of social support, depression etc. Therefore get them counseling (AMPATH if ISS +ve) if they need it. These patients may also tend to fall sick again if neglected by the team and therefore, need to be reviewed on a regular basis.

Malnourished patients

There are nutritionists around. You can talk to the one on your team to see if they have some nutritional supplements/shakes to give the patient.

SOME IMPORTANT CONTACTS

Imran Manji – 0722 967480
Mercy Nabwire – 0728 823344
Sonak Pastakia – 0729 027569
Anticoagulation Clinic – 0710 185988 or Ext # 3532
Diabetes clinic – 0713 551414 or Ext # 3532
Oncology pharmacy – Ext # 3527 (Ask for Tony or Julius)
Matt Strother (for Oncology queries) – 0724