Médecins Sans Frontières' HIV Guide for Primary Health Care intends to assist nurses and doctors at primary care level in the management of patients living with HIV.

It is designed as a quick reference guide to be used in the consultation room whilst seeing patients. It has intentionally been kept simple to allow ease of use by different categories of health staff and in different settings in Southern Africa.

MEDECINS SANS FRONTIERES

Management of HIV-related Conditions and Antiretroviral Therapy in Adults and Children
HIV Guide for Primary Health Care

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Dedicated to the memory of Dr. Sarah Ann Christianson (MacIntyre)

May your energy and dedication shine through the pages of this book

Foreword

This guide is designed to assist primary health care workers with decision-making in clinical management of HIV-related conditions in adults and children. This includes antiretroviral therapy and tuberculosis. The first edition was developed for use in primary health care level HIV clinics opened by Médecins Sans Frontières (MSF) in the township of Khayelitsha, Cape Town, South Africa. It successfully became a practical reference tool for nurses and doctors. This edition has been adapted to be used in clinics supported by MSF and we hope it will be useful in other resource limited settings as well.

As larger numbers of patients were started on ARVs, it became increasingly clear that HIV/TB care had to be nurse-based and decentralized to the primary care level.

We tried to keep the guide as simple and as accurate as possible. Although we consulted published literature during its compilation, there is certainly personal bias reflecting the authors' views as well. By no means should this guide replace more detailed textbooks, national guidelines or clinical discussions. It is hoped that this edition will continue to help nurses and other clinicians to prevent many unnecessary deaths from HIV and TB.

The guide is a work-in-progress. Our current management strategies for HIV-related conditions will be confirmed or rejected by observational research in the future. We hope the reader will acknowledge this, and we would be grateful for any comments to make the next edition even better. Have a good read!

Contents

Abbreviations

3TC	Lamivudine
ABC	Abacavir
ADA	Adenosine deaminase (a test done on pleural fluid to detect TB)
AFASS	Affordable, feasible, accessible, safe and sustainable
AFB	Acid-fast bacilli (the tuberculosis germ)
AIDS	Acquired Immunodeficiency Syndrome
ALT/ALAT	Alanine aminotransferase (a “liver blood test”)
ART	Antiretroviral therapy
ARVs	Antiretrovirals
ASAP	As soon as possible!
ATV	Atazanavir
AZT	Zidovudine (occasionally also written as ‘ZDV’)
BCG	Bacillus Calmette-Guérin
BD	Twice daily
BMI	Body mass index (used to classify adults as overweight or underweight)
BSA	Body surface area (sometimes used to calculate ARV dosages in children)
CCM	Cryptococcal meningitis
CrCl	Creatinine Clearance (a measure of kidney function)
CLAT/CRAG	A test for detection cryptococcal meningitis CMV Cytomegalovirus
CNS	Central Nervous System
CRP	C-reactive protein (a blood test that measures inflammation)
CSF	Cerebrospinal fluid
CTX	Cotrimoxazole (Bactrim®, Cotrim®, Purbac® or Cozole®)
CXR	Chest X-ray
D4T	Stavudine
DDI	Didanosine
DR TB	Drug resistant TB (used in this guide to mean at least rifampicin resistance)
EFV	Efavirenz
EPTB	Extra-pulmonary tuberculosis (TB outside of the lungs)
FBC	Full Blood Count
FNAB	fine needle aspiration biopsy

FTC	Emtricitabine
HAART	Highly Active Antiretroviral Therapy
Hb	Haemoglobin
HBsAg	Hepatitis B surface Antigen
HBV	Hepatitis B Virus
HCW	Health care worker
HPV	Human papilloma virus
HIV	Human Immunodeficiency Virus
HSR	Hypersensitivity reaction
HSV	Herpes Simplex Virus
IC	Infection control
IM	Intramuscular
IMCI	Integrated Management of Childhood Illnesses
INH	Isoniazid (one of the TB drugs)
IRIS	Immune Reconstitution Inflammatory Syndrome
IV	Intravenous (same as “drip”)
KS	Kaposi Sarcoma (a cancer)
LFT	Liver Function Test
LIP	Lymphoid interstitial pneumonitis
LP	Lumbar puncture (to diagnose meningitis)
LPV/r	Lopinavir/ritonavir (Kaletra® or Aluvia®)
MAC	Mycobacterium Avium Complex
MDR TB	Multi-drug resistant tuberculosis
MER	More efficacious regimen
MSF	Médecins Sans Frontières (French for ‘doctors without borders’)
MTCT	Maternal to child transmission
NB	“Note Bene” in Latin, meaning note well or, pay special attention to the following
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor (“Non-nukes”)
NRTI	Nucleoside Reverse Transcriptase Inhibitor (“Nukes”)
NTM	Non-tuberculous Mycobacteria
NVP	Nevirapine
OD	Once daily

OI	Opportunistic Infection
ORS	Oral Rehydration Solution
PAP smear	Test for detection of cervical cancer
PCP	Pneumocystis jiroveci Pneumonia (a life-threatening OI)
PEP	Post-exposure Prophylaxis
PCR	Polymerase Chain Reaction (a laboratory test)
PI	Protease Inhibitor
PID	Pelvic Inflammatory Disease
PLWHA	Person living with HIV/AIDS
PML	Progressive multifocal leucencephalopathy
PMTCT	Prevention of Mother-to-Child Transmission (of HIV)
PN	Peripheral neuropathy
PPD	Purified protein derivative (used in TB skin testing)
PPE	Papular pruriginous eruption (a common itchy rash)
PRN	As required
Pt.	Patient
PTB	Pulmonary Tuberculosis (TB of the lungs)
QID	Four times a day
RPR	A test for syphilis
RTV	Ritonavir
SCC	Smear and culture control
SSRI	Selective serotonine re-uptake inhibitor
STI	Sexually Transmitted Infection
TB	Tuberculosis
TBM	Tuberculous Meningitis
TDF	Tenofovir
TDS	Three times a day
TST	TB skin testing
URTI	Upper respiratory tract infection
UTI	Urinary Tract Infection
VDRL	A test for syphilis
WHO	World Health Organization
XDR TB	Extensively drug-resistant tuberculosis

Introduction

1. We are living in the age of HIV. Within a few decades, this virus has caused an enormous amount of morbidity and mortality around the world. Countries in southern Africa have been particularly hard hit.
2. Unfortunately, there is still an enormous amount of fear and stigma surrounding HIV, AIDS, and TB. This is made worse by a general lack of knowledge about these diseases, even among health care professionals.
3. Following infection, HIV slowly makes a person's immune system weak over many **years**. This progressive 'immunodeficiency' roughly correlates with a gradual drop in the CD4 cell count (test), a type of white blood cell. As the CD4 count drops, certain infections and other illnesses are more likely to appear (see Table 1 on **page 3**).
4. As their immune systems weaken and they suffer from more frequent and severe infections (and cancers), we classify adults and children into different **Clinical Stages** of HIV infection. The WHO Classifications (see Appendices 1 & 2) are valuable tools in our clinics; all health care professionals (and patients) should be knowledgeable about the different stages of HIV!
5. Without comprehensive medical care, HIV-positive adults and children ultimately die from serious infections (or cancers). Fortunately, certain medical interventions now widely available can prevent many of these deaths (see **pages 4 and 5**). The medical interventions required for those in the final stages of HIV infection (suffering from recurrent life-threatening infections) are intense, while those in the initial stages of HIV infection need mainly psychological support and counselling.
6. Good nutrition is important at every stage of HIV infection. A healthy balanced diet together with supplementation of certain micronutrients (vitamins and minerals) help to delay disease progression from stage 1 to 4 (AIDS). It is important to note that nutrition alone in the final stages of HIV infection is not enough to prevent death!
7. Early recognition and treatment of Opportunistic Infections (OIs) is vital. People do not die from HIV; they die from infections (and sometimes cancers). If we diagnose these conditions early, and give proper medical treatment, we can avert many deaths. EARLY recognition of tuberculosis (TB) is especially important.
8. Proper medical care in the later stages also includes **prevention** of serious infections (also known as prophylaxis). Never forget to give regular preventive

doses of the antibiotic cotrimoxazole to adults or children in the later stages of HIV infection (see Table 2 on **page 21**). Some individuals may also benefit from isoniazid prophylaxis to help prevent TB. In addition after an episode of cryptococcal meningitis it is essential to continue fluconazole prophylaxis.

9. When an HIV-positive person's immune system has become too weak, we use antiretrovirals (ARVs) to 'stop HIV from growing', which in turn allows the immune system to recover. This is how ARVs prevent unnecessary death in patients with advanced HIV infection. Note that only those adults and older children in the later stages of HIV infection need ARVs. For HIV positive infants, early treatment regardless of clinical or immunological stage has proved to be beneficial (with a 75% reduction in mortality in a South African study-known as CHER study).
10. ARVs are not perfect. Just like all other medications, they have possible side effects. We must monitor people on ARVs closely in order to detect serious side effects and treatment failure early, and then make necessary changes.
11. Good adherence to ARVs is essential to make sure the virus does not become resistant to the medications.

Table 1: Risk of Opportunistic Infections (OIs) and other HIV-related Conditions by CD4 cell count

CD4 count	Condition
Any CD4 count	Persistent generalised lymphadenopathy (PGL)
	Parotid gland enlargement
	Herpes Zoster (Shingles)
	Tuberculosis
	Bacterial pneumonia
	Cervical intraepithelial neoplasia (CIN)
	Vulvo-vaginal candidiasis
	Chronic anaemia
	HIV-related thrombocytopenia
	Lymphocytic Interstitial Pneumonitis (LIP, commonly seen in children)
< 200 cells/µL (when severe OIs begin to appear)	Oral candidiasis (I.e. thrush)
	Oesophageal candidiasis
	Oral hairy leukoplakia (OHL)
	Pneumocystis jiroveci Pneumonia (PCP)
	Cryptosporidiosis
	Lymphoma (non-CNS)
	Kaposi Sarcoma (KS)
	HIV-associated Dementia
< 100 cells/µL	Toxoplasmosis
	Cryptococcal meningitis (CCM)
	Cytomegalovirus infection (Eye)
	Wasting Syndrome
< 50 cells/µL	Non-tuberculosis mycobacterial (NTM) infection
	Lymphoma (CNS)
	Progressive multifocal leukoencephalopathy (PML)
	Cytomegalovirus infection (brain or disseminated)

Summary of Treatment Interventions used to Prevent Death from HIV/AIDS

1. **Early VCT** in order to know one's HIV status early so that treatment interventions can take place early!
2. **Counselling** in order to allow a person to accept being HIV-positive.
3. **Education** about the HIV life-cycle, the different clinical stages of HIV infection, and CD4 counts. Counselling about possible OIs and sexual health.
4. Good **nutrition**, first a healthy diet, but if possible also includes supplementation with micronutrients (vitamins and minerals).
5. Early **diagnosis** and prompt **treatment** of opportunistic infections (OIs), especially TB.
6. **Prevention** of OIs with cotrimoxazole (and other medications) and prevention of TB with INH prophylaxis.
7. **Antiretrovirals (ARVs)** to lower the HIV viral load and allow a person's immune system to recover.
8. **Monitoring** for any side effects of ARVs in the short-term and the long-term.
9. **Prevention** of transmission of HIV, including transmission from mother to child (with PMTCT).
10. **Ongoing adherence counselling** and support, including **support groups**.
11. **Monitoring for resistance** that HIV can develop against ARVs.

Figure 1: Patient Handout describing medical treatment to prevent unnecessary death of people living with HIV and AIDS

Stage	Typical Symptoms	Treatment
1	None Person feels well	Good nutrition, exercise, accept your status, check CD4 regularly (make sure your health care worker gives you a date to recheck CD4)
2	Minor infections - rashes - shingles	Good nutrition, cotrimoxazole, education on TB & HIV and Antiretrovirals (ARVs)
Stage 3 and 4	More serious infections - TB in the lungs - frequent diarrhoea Weight Loss Life-threatening infections - severe pneumonias - TB outside of the lungs - meningitis Cancers	Good nutrition, cotrimoxazole, education on TB & HIV and starting of Antiretrovirals (ARVs)
Get an HIV test done if you don't know your status! If you are HIV-positive, then visit your clinic to get a blood test to find out your CD4 count! If your CD4 count is less than 350, then your immune system is weak. You will need ARVs to prevent life-threatening infection.		

Epidemiology, Life Cycle and Prevention of HIV

Epidemiology of HIV

Countries in sub-saharan Africa have been hardest hit by the global HIV epidemic.

The majority of people acquire HIV:

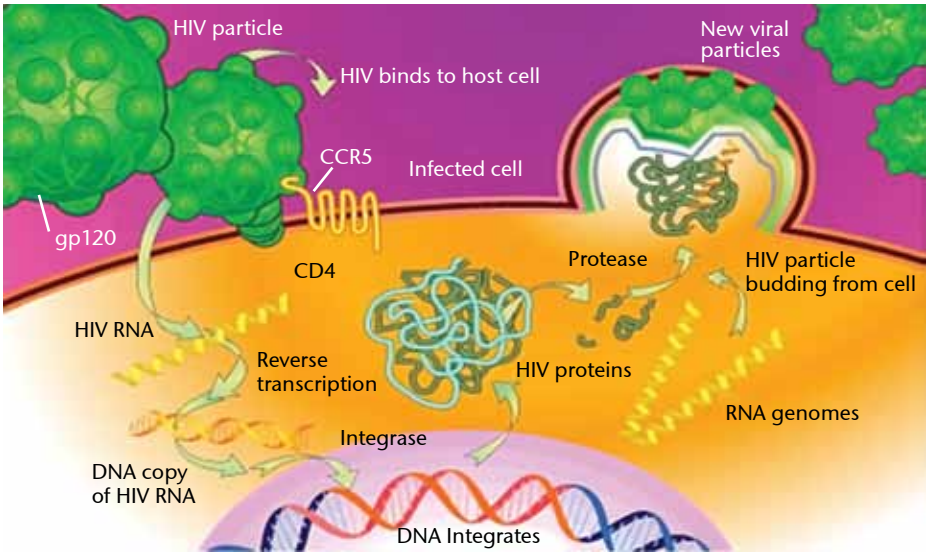
- Through sexual contact
- Before birth or during delivery
- Through breastfeeding
- Through using contaminated needles
- Through blood or blood products (rare when donor blood is carefully screened)

HIV life cycle

There are at least 6 important phases that HIV must go through before new HIV can be produced. These are:

1. Attachment: HIV attaches to the CD4 (and CCR5/CXCR4) receptors of the cell
2. Fusion: HIV fuses with the cell-wall and enters the cell
3. Reverse transcription: Viral RNA is transformed into viral DNA by an enzyme called reverse transcriptase (The drug classes known as NRTI's and NNRTI's act at this level by preventing this process).
4. Integration: Inside the nucleus of the CD4 cell, viral DNA is integrated into the cell's genome, and then new material to form individual HIV's is made.

Figure 2: Life Cycle of HIV



Source: http://www.lifewins.co.za

5. Protein production and protease function: Large proteins are broken into smaller proteins to become functional; Protease Inhibitors act at this stage.
6. Maturation: The final process during which new HIV viruses are released.

Prevention of HIV

Primary prevention

Effective practices to reduce transmission of HIV are:

- Barrier methods: condoms!
- Safer sexual practices: delay sexual debut, reduce concurrent partners...
- Treating STIs
- Male circumcision
- Prevention of mother to child transmission (PMTCT), including infant ARV prophylaxis throughout the breastfeeding period.
- Provision of safe formula feeding
- Needle and syringes exchange programs
- Screening blood donors and testing blood products
- Post exposure prophylaxis (PEP) for health care workers and rape victims

Secondary prevention

Secondary prevention refers to practices that can help an HIV positive person stay well for as long as possible. These include:

- Going for regular clinic check-ups
- Eating a balanced diet and exercising regularly
- Taking preventive drugs such as cotrimoxazole or INH
- Starting ARVs early

Accidental exposure of health care workers and Post-Exposure Prophylaxis (PEP)

Ways in which exposure occurs

Health care workers are at risk of accidental exposure to blood or other body fluids through:

- Percutaneous injury with a needle or another sharp instrument.
- Exposure to blood or body fluids via mucous membranes (eye, mouth) or non-intact skin (wound, dermatitis, abrasion)

What to do in case of occupational exposure

If an occupational exposure happens to you or to one of your colleagues, treat this as an **emergency:**

- **Immediately** let the wound bleed (without scrubbing), wash both the wound and surrounding skin with water and soap (without scrubbing) and then rinse;
- Disinfect the wound and surrounding skin with chlorhexidine gluconate if available.
- If you received an exposure involving the eyes or mucous membranes: rinse the exposed area immediately with as isotonic saline solution for 10 minutes. Antiseptic eye drops can also be used for eye exposure. If none of these solutions are available, use clean water.
- Offer an HIV test to exclude pre-existing HIV infection.
- Start Post-exposure prophylaxis (PEP) **as soon as possible** (ideally within 1 or 2 hours, not later than 72 hours after exposure). **Give Tenofovir (TDF) + Lamivudine (3TC) + Lopinavir/ritonavir (LPV/r).** A good alternative regimen is Zidovudine (AZT/3TC) + LPV/r. These regimens will be taken for 1 month.
- Follow full monitoring guideline to screen for Hep B, C, HIV and side effects.
- **Notify** your supervisor and/or a medical doctor.
- **HIV test to be repeated at month 1, 3 and 6.**

Timetable	In people taking PEP	In people not taking PEP
To be done within eight days of the AEB	HIV, HBV, HCV	HIV, HBV, HCV
Day 15	Hb ALAT Cr	
Month 1	Hb ALAT Cr HIV	HIV
Month 3	HIV, HBV, HCV ALAT Cr	HIV, HBV, HCV ALAT
Month 6	HIV, HBV, HCV ALAT Cr	HIV, HBV, HCV ALAT

Note:

Take Hb only if on AZT

Take Cr only if on TDF

Test yourself

- Name 4 ways HIV can be transmitted

- List the six main stages of HIV's life cycle

- What regimen should be given for PEP and when?

- When should HIV tests be repeated after an accidental exposure to blood?

Notes

Assessment and Follow-Up

First consultation

History

- Chief Complaint ("the main problem today")
- History of the Present Illness
- Past History
  - **Tuberculosis (TB) past history and/or recent TB contacts**
  - Ask about any possible stage 2, 3 or 4 opportunistic infections including any weight loss (the new patient intake form will guide you through this)
  - Other conditions, e.g. diabetes, hypertension, rheumatoid arthritis
  - Psychiatric history
  - **Prior exposure to any ARVs (including PMTCT)**
  - Allergies (e.g. to cotrimoxazole)
- Family History: Children? Partner? All tested? Any on treatment?
- Social History:
  - Employment status and source of income
  - Psychological support
  - Disclosure of HIV status and outcome of the disclosure
  - Alcohol / drug history
- Review of Systems:
  - **Refer to Appendix 4 (or 15)**
  - Identify **any recent weight loss**
  - Screen for symptoms of STIs
  - **Screen for symptoms of TB**

Physical examination

- Does this person look stable or unstable? (If unstable, you will have to spend more time with this person +/- refer to hospital.)
- Vital signs (heart rate, respiratory rate, blood pressure, temperature).
- Check weight and height at first visit and calculate Body Mass Index (BMI = W/H^2, where Weight is in kg and Height is in meters)
- A thorough systems examination to exclude OIs

REMEMBER

Common signs on examination to help your staging decision

- Signs of wasting or weight loss (Stage2, 3, or 4)
- Rashes (PPE, current or old herpes zoster - both stage 2)
- Lymphadenopathy
- Oral examination: thrush, oral hairy leukoplakia, gingivitis, (all stage 3) or Kaposi's sarcoma (stage 4).

Investigations

- Take blood for CD4 and creatinine (FBC instead of creatinine if < 12 years) at first visit or next specimen collection day.
- If clinically anaemic take Hb
- If symptom/signs of hepatitis or hepatomegaly take ALT

Diagnosis

- List any OIs which are present

Clinical staging

- Stage the patient following the WHO staging system (see Appendices 1 and 2)
- Staging gives an idea of how sick a PLWHA has ever been. The stage can increase with new, more serious HIV-related conditions, but cannot decrease, even with improved health after ART initiation.

Treatment

Once in stage 4, a person remains in stage 4 for life!

- Treat any opportunistic infections (OIs)
- Refer to a doctor if severely ill or in doubt
- Treat any STIs
- Prescribe cotrimoxazole for **prevention** of OIs if Stage 2, 3 or 4 or CD4<350 (adults). See Table 2 for criteria to start and stop CTX for children and adults.
- Ensure adequate nutrition (advice on diet and supplementation with vitamins) and, provide nutritional supplements according to national nutritional guidelines.

Counselling

- Reassure that infection with HIV is a treatable condition (not a "death sentence"!)
- Importance of regular follow-up and benefit of prophylaxis and treatment
- Counselling on family planning and condom use (male and female)

- Encourage the client to have just one partner and encourage the partner to get tested for HIV
- If client will start ARV's: Explain that unsafe sex on ARVs can still transmit HIV which can lead to treatment failure.

Second consultation

Review of symptoms

- Follow up on OIs and/or TB Symptoms. Educate client to return early if symptoms develop.

Physical examination

- Does this person look stable or unstable? (If unstable, you will have to spend more time with this person +/- refer to hospital.)
- Vital signs if necessary
- Check weight (at every visit)
- Thorough examination to exclude new OIs and TB
- If the CD4 count is < 100 cells/µL, perform a retinal examination through dilated pupils (to look for signs of TB, Toxo, CMV, etc)

Baseline blood tests

- Hb (or FBC if available)
- CD4 count if not done at first consultation
- Consider screening for syphilis (VDRL or RPR testing)
- Creatinine for TDF, FBC + differential for AZT, ALT for NVP
- Consider checking for HBsAg if baseline ALT > 40 IU/ml **(since important to be aware of Hepatitis B status in case TDF and/or 3TC will be stopped any time in the future)**

Treatment

- If taking CTX and/or INH, check adherence and tolerance
- Treat any opportunistic infection

Counselling

- The patient is encouraged to ask questions.
- Counselling on the use of condoms is provided again.
- Depending on Stage and CD4 result commence pre ART preparation counselling.

Further follow-up consultations

Clinical follow up

- See above
- Remember to check weight at every visit
- Screen for pregnancy
- Perform or refer women for a PAP smear if available, if one was not done during the last year; PAP smears should then should be repeated according to national guidelines.
- If the patient is on TB therapy, sputum should be sent off at 2 and 5 months (3 and 7 months in TB retreatment cases).
- Screen household contacts of PTB patients looking for:
  - Symptomatic **or**
  - < 5 years **or**
  - HIV positive

Treatment and counselling

- Laboratory results are discussed.
- Prevent OIs with cotrimoxazole if not already started (see Table 2, **page 21**, for indications).
- Prevent TB by means of INH prophylaxis, if clinically indicated (Follow national guidelines on INH prophylaxis).
- If the adult (Appendix 3) or child (Appendix 4) is eligible for ART, refer for counseling about ARVs.
- Note that certain patients should be 'fast-tracked' to initiate ART within 2 weeks.

Require fast track (i.e. ART initiation within 2 weeks of being eligible)
• Pregnant women eligible for lifelong ART OR • Patients with very low CD4 (< 100 cells/μL) OR • Stage 4, CD4 count not yet available OR • MDR/XDR TB • Children younger than 1 year

- The patient is advised to bring a person they can trust (treatment assistant) so that both can receive any necessary counselling (and education about ARVs if eligible).
- If the patient is on TB therapy, check the TB card to ensure that the person is adhering to treatment, that follow-up sputa have been taken and that culture and sensitivity results are available if taken.

- Do not interrupt ARVs if TB is diagnosed. Refer to doctor if any complication develops after starting TB treatment.
- Smoking worsens TB treatment outcomes. Urge client to stop.
- Discuss plans for future pregnancies. Efavirenz may cause birth defects if taken in the 1st trimester (but is considered safe in the 2nd and 3rd trimesters). All women of childbearing age should be offered reliable contraception especially if taking efavirenz.
- Recent changes, including changes in residence, telephone numbers, surnames, new sexual partners and disclosure(s) need to be explored.

REMEMBER **The weight should be checked at every visit!**

Frequency of follow-up visits

The frequency of follow-up visits depends on the clinical stage and CD4 count:

- If patient is eligible for ART, refer for counseling about ARVs.
- **If not eligible for ART, the person still requires regular follow-up, including advice on HIV prevention. CD4 testing should be repeated at least every 6 months.**
- Even if not yet eligible for ART, every person must know to seek medical advice if they get sick in the interim.
- Frequency of CD4 testing:
  - If the patient is not yet eligible for ARVs: repeat 6 monthly
  - On ARVs: At month 6, month 12, then 6 monthly
  - On ARVs: If available viral load can be checked at month 3 (or 6 according to local protocol) and then yearly.

REMEMBER **Check CD4 at 6 months , 12 months and then every 6 months.**

A CD4 lower than baseline, < 100 or 30% lower than the highest ever CD4 whilst on ART requires an urgent clinical assessment.

0.I. Preventive therapy (also known as Prophylaxis)

Prevention (or prophylaxis) refers to medication given to **prevent** an infection from happening in the first place. We give cotrimoxazole to many HIV-infected people when they first come to our clinics as **primary** prevention against *Pneumocystis* pneumonia (PCP), cerebral toxoplasmosis and other infections (see Table 2 on **page 21** and Table 17 on **page 158**).

Note that primary prevention is different from secondary prevention. **Secondary** prevention means preventive measures given **after** a person has already suffered from a certain infection, in order to prevent that same infection from coming back again.

Medication used for primary prophylaxis

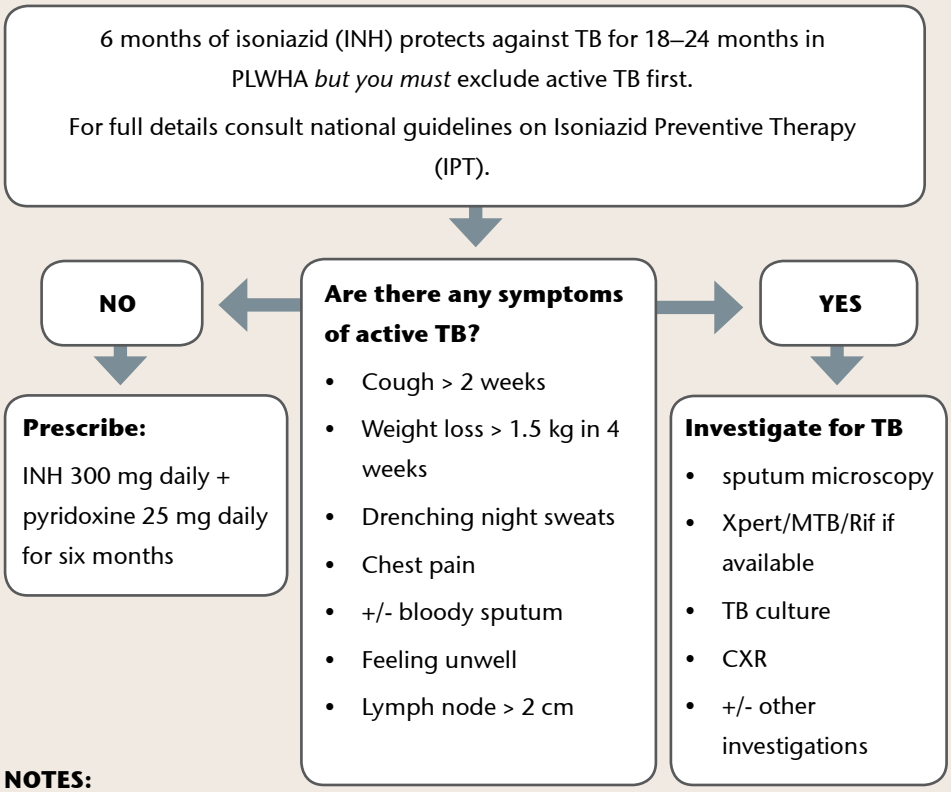
- Cotrimoxazole to prevent PCP or Toxoplasmosis for the first time
- INH to prevent TB for the first time (see Figure 3 on **next page**)

Medication used for secondary prophylaxis

- Cotrimoxazole to prevent recurrence of PCP or Toxoplasmosis
- Fluconazole to prevent recurrence of Cryptococcal disease
- INH to prevent recurrence of TB (see Figure 3 on **next page**)

Both primary and secondary prophylaxis can be discontinued in a person on ARVs when the immune system has sufficiently recovered. See Table 2 on **page 21** and sections on PCP, Cryptococcal meningitis, and Cerebral Toxoplasmosis for when to stop primary and secondary CTX prophylaxis.

Figure 3: INH Prophylaxis (Adults)



NOTES:

- TB skin testing is performed in some settings and INH given only to those adults having a positive result
- Pregnancy is not a contra-indication to INH prophylaxis
- Interrupt INH prophylaxis if adherence is a concern and in case of severe PN or hepatitis (ALT > 5 times the upper limit of normality)
- See **page 96** for INH prophylaxis in children

How to do a TB skin test (TST)?

- Keep PPD refrigerated (discard if open >8 hours or expired)
- Ensure client can return 48–72 hours after test for reading. If not, reschedule test.
- Use 2 units of PPD-RT23 or 5 units of PPD-S.
- Locate area for injection (palm surface of left arm 4–8 cm below the elbow).
- Clean the area with an alcohol swab.
- Pull the skin taut. Using a tuberculin syringe, inject PPD into the layers to see a weal developing.
- Measure swelling/induration after 48–72 hours
- If induration ≥ 5 mm in an HIV-positive person, TST is considered positive.

Table 2: Cotrimoxazole prophylaxis (also see Appendix 16 for desensitization schedule)

Recommended dose/ Protection against	Indications to start	Indications to discontinue	If allergy or intolerance to cotrimoxazole
Recommended dose Adults: CTX 960mg od Infants and children: dosage according to body weight (see Table 17 on **page 158**) **If taken regularly, CTX protects against** • Pneumonia, especially PCP • Brain infections (toxoplasmosis) • Certain types of diarrhea • Other bacterial infections, such as UTI • Malaria CTX is a combination of two antibiotics: Trimethoprim (TMP) and Sulfamethoxazole (SMX) There are several trade names for CTX: Bactrim, Septrim, etc.	**HIV-infected adults** CD4 < 350 cells/µL or clinical stages 2, 3 or 4	**HIV-infected adults** On ARVs and CD4 > 200 cells/ µL on 2 consecutive occasions 3–6 months apart.	**Non-severe side effects (grade 1 and 2):** • Desensitize adults (see Appendix 16) • Desensitization should not be done in children **Grade 3 toxicity to CTX or desensitization not successful:** • Dapsone 100 mg daily (protects against PCP, but limited protection against toxoplasmosis) • Therefore, add Pyrimethamine 50 mg + Folinic acid** 25 mg weekly to protect against Toxoplasmosis if available In case of severe reactions to CTX (grade 4 skin, liver, kidney or bone marrow toxicity), Dapsone should not be used, as there may be cross-reactivity Dapsone is safe in pregnancy Dapsone (2mg/kg/day) can be given to infants and children unable to tolerate CTX **** Note that Folinic acid is not the same as Folic acid!**
	All HIV-exposed infants Starting at 6 weeks of age	**HIV-exposed infant** Negative PCR or rapid HIV test at least 6 weeks after complete breastfeeding cessation and absence of clinical signs of HIV infection.	
	HIV-infected children • Under 5 years: All • > 5 years: treat as adults = stage II,III and IV or CD4 <350cells/ ul	**HIV-infected children without previous PCP or toxoplasmosis*:** • Age 0–5 : Do not stop cotrimoxazole • Age >5 : On ARVs and CD4 >200 cells/ul on 2 consecutive occasions 3-6 months apart **HIV-infected children with previous PCP or toxoplasmosis*:** • < 5 years: Do not stop • > 5 years: On ARVs and CD4 > 200 cells/ul on 2 consecutive occasions 3-6 months apart * Children at risk of malaria should be maintained on CTX until that risk subsides	

Test yourself

- Name 2 conditions that are stage 2, 3 and 4 (i.e 2 conditions for each stage)

- Which HIV positive adults should start cotrimoxazole prophylaxis?

- Which children should be given cotrimoxazole prophylaxis?

- Why is it important to treat all opportunistic infections before starting ART?

Notes

Symptom Management

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Introduction

Patients do not present complaining of a diagnosis (such as TB meningitis). Rather, they come to us with **symptoms** (such as headache or confusion). We must take a good history of the presenting symptoms, perform a proper physical examination, and come up with the diagnosis (with the help of investigations). Only then can we make a treatment plan that will make this patient better. See Appendix 15 for key points for clinical review of symptoms and signs.

REMEMBER

Summary of a Thorough Clinical Assessment (Also see 'First Consultation' on page 14):

It is very important to be thorough when dealing with HIV patients:

1. Take a good **history**.
2. Perform a good **physical examination**.
3. Do any necessary **investigations**.
4. Come up with a **diagnosis**, including the Clinical Stage of HIV Infection.
5. Arrange a **treatment plan** that will make the patient better.
6. Don't forget to prescribe **prevention** treatment (cotrimoxazole or other).

The following **serious symptoms** can be caused by OIs that commonly occur in HIV-positive patients. They require a thorough clinical assessment in order to arrive at the correct diagnosis (and subsequent treatment plan).

Rash

See the algorithm on **page 40** and the text in the following pages for a practical approach to the most common causes of skin rash and their management. Rash is very common in patients with HIV. Patients presenting with rash should always be advised to test for HIV. Of particular importance is to recognize life-threatening skin rashes such as Kaposi sarcoma and severe drug eruptions (Stevens Johnson's syndrome).

Difficulty swallowing

An approach to difficulty swallowing can be found on **page 60**. In patients with low CD4 counts, oesophageal candidiasis is the most common cause of difficulty swallowing. This is a stage 4 defining illness and an indication for urgent treatment and urgent ART. Alternative diagnoses include herpes simplex, aphthous ulcers and CMV ulcers. In early HIV, gastro-oesophageal reflux disease (GERD) is a common cause.

Diarrhoea

See **page 68** for diagnosis and management. Diarrhoea can cause severe loss of weight and be very debilitating. It is important to distinguish between acute and chronic diarrhoea. Whilst acute diarrhoea can occur at any stage of HIV, chronic diarrhoea is a sign of advanced disease and an indication to start ART.

Abdominal pain

See **page 74–75** for algorithm and management. Some differential diagnoses not to be missed are: abdominal TB, acute hepatitis (viral or drug related), gastric ulcers, pelvic inflammatory disease, appendicitis, and pancreatitis.

Cough

See **page 80** for an approach to cough and the most common respiratory diseases. Remember that TB is the first cause of death among patients with HIV. A screening for TB should happen at every consultation.

Fever

High temperature (also known as pyrexia or fever) is common in HIV-positive patients. HIV itself can cause high temperature, as can numerous infections. It is very important to rule out infection first as the cause of the high temperature, before blaming the fever on HIV, since there is a risk of death from many infections if they go undiagnosed (HIV-positive patients die mainly from infections, not from HIV itself!).

Causes

Causes of high temperature include:

- All types of infections: Those related to HIV (opportunistic infections) and those not necessarily related to HIV
- Some cancers (especially Non-Hodgkin's Lymphoma)
- Life-threatening infections (rule these out first)
    - Tuberculosis
    - Other lung infections
    - Acute diarrhoea causing dehydration
    - Sepsis
    - Meningitis

- Other infections such as STIs (PID)
- Certain medications can cause a fever (this is called a 'drug fever'). However, 'drug fever' is a diagnosis of exclusion (meaning that infections must be ruled out first).

Clinical history (see also Appendix 15)

A thorough clinical history is essential to help identify any fever due to infection. Some important symptoms to ask about include:

- Sore throat (suggests pharyngitis or throat infection)
- Facial pain with post-nasal drip (suggests sinusitis)
- Headache (need to rule out meningitis)
- Dysuria or painful urination (check for UTI)
- Diarrhoea (see **pages 68–73**)
- Abdominal pain (see Algorithm 6 on **page 74**)
- Pelvic mass (perform urine pregnancy test)
- Cough (check for pneumonia and investigate for TB)
- Night sweats and loss of weight (check for TB without delay)
- Dyspnoea (check for PCP or other chest infection and **refer to doctor**)
- Enlarged nodes (if not responding to antibiotics, it's probably TB, but also consider lymphoma)
- Seizures (**refer to doctor**)

Clinical examination (see also Appendix 15)

A thorough clinical examination to help identify the cause of the fever must include:

- Weight
- Vital signs (I.e. BP, pulse, temp, and respiratory rate)
- Signs of dehydration +/- shock
- Assessment of vision, including retinal examination
- Examine ears, mouth, throat and sinuses
- Check for neck stiffness
- Listen to chest to check for crackles, wheezing, pleuritic rub
- Listen for a heart murmur
- Look for enlarged lymph nodes in neck, armpits and groin
- Abdominal tenderness, mass, or loss of bowel sounds
- Liver and/or spleen enlargement

- Examine skin for any infected rashes (or oozing sores)
- Examine for focal signs (such as new-onset weakness of an arm and/or leg)

Investigations

Perform investigations as necessary:

- Urinalysis for blood, protein, and leukocytes
- Urine test for pregnancy
- Chest X-ray
- If TB suspected, sputum examination for AFB +/- TB culture
- FBC + differential cell count
- Referral for LP (if meningitis suspected)

Management

Specific treatment depends on the results of the history, examination, and investigations.

- **Always treat the underlying cause of the fever!**
- Ensure adequate fluid intake.
- Unless a virus (such as the 'flu') is suspected as the cause of the high temperature, the patient will usually need treatment with an antibiotic, even when waiting for test results (for example, Amoxicillin for chest infection while waiting for TB 'smear' results).
- **Refer to the doctor** if the patient is very sick or if in doubt about the cause of the fever.
- The following medications can help lower a high temperature and provide some relief, but they do not treat the infection:
  - Paracetamol 500–1000 mg four times daily as required for adults
  - Ibuprofen 200–400 mg four times daily as required for adults
  - Paracetamol syrup four times daily as required for **children**, depending on weight (see Table 18 on **page 188**)

Make sure that patients understand they must return for reassessment if there is no improvement, or they are getting worse.

Weight loss

Weight loss is very common in HIV-infected people. It can be due to HIV itself known as 'HIV wasting syndrome', which is an AIDS-defining condition (I.e. clinical stage 4) requiring ART. 'HIV wasting syndrome' is defined as unexplained weight loss (> 10% of baseline body weight) with obvious wasting or BMI < 18.5, plus unexplained diarrhea and/or fever for > one month. However, wasting is a **diagnosis of exclusion**. More commonly, it is due to infections that cause loss of appetite (E.g. TB) or decreased absorption of nutrients (chronic diarrhoea). After initiation of ARVs, weight loss can also represent a side effect of ARVs (for example, high lactate levels due to D4T). Documented weight loss of > 1.5 kg over 4 weeks should be regarded as significant and must be investigated. If the client is not yet on ARVs and presents with HIV wasting syndrome, "fast-track" for ART initiation regardless of CD4 count.

REMEMBER **Patients should be weighed at every single visit! If weight loss is occurring, it could represent a serious problem, so it should not be ignored! Check thoroughly for TB before blaming the weight loss on 'HIV wasting syndrome'!**

Clinical management

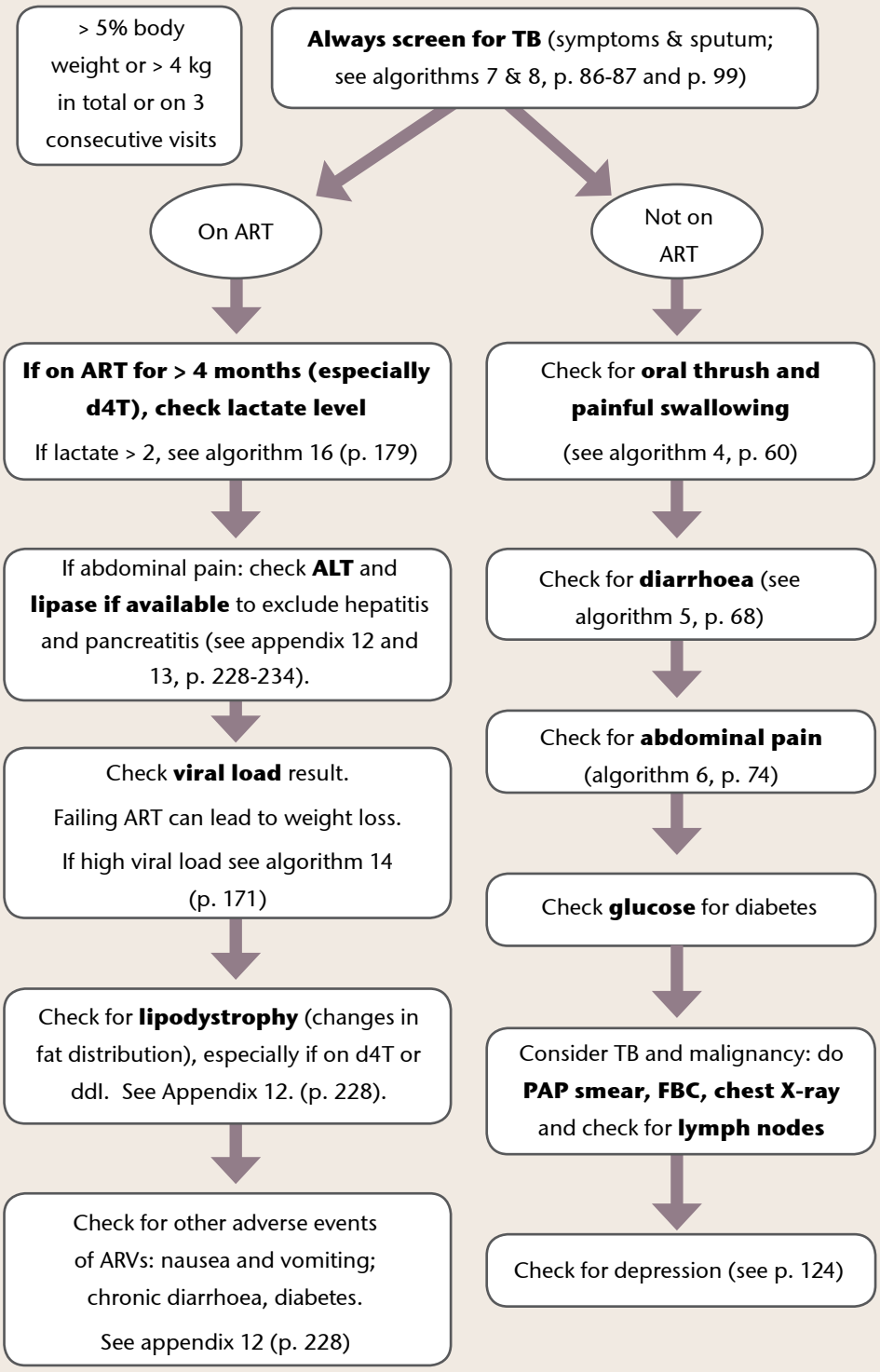
- Weigh the patient at every visit. Also ask about weight loss at the first consultation.
- Estimate the percentage of weight lost; loss of > 10% of previous body weight is considered serious and the cause must be identified ASAP.
- Record a child's height regularly.
- Complete a thorough clinical examination to identify any:
  - Oral problems affecting food intake: aphthous ulcers or dental problems causing pain; oral and/or oesophageal thrush causing difficulty swallowing.
  - Chronic diarrhoea and/or vomiting.
  - Loss of appetite induced by an opportunistic infection (TB is by far the most common cause).
  - High lactate (an uncommon, but serious side effect of ARVs) can initially present as weight loss. If you notice weight loss in a person taking ARVs (especially D4T), then do not ignore it. It is serious and must be investigated.

- **Improving nutrition alone will not necessarily improve the weight of patients in the final stage of HIV infection (Stage 4 = AIDS).**
  - **Any underlying infection must be identified and treated (especially TB).**
  - **If no infections are identified and HIV itself is the underlying cause of the weight loss ('HIV wasting syndrome') then it requires treatment with nutrition plus ARVs in order to prevent death!**
- Try to make sure that the patient has access to quality food. Refer to a nutritionist for fortified food supplements if available. Also refer to a social worker if the patient cannot afford food.
- Energy-rich and protein-rich food should be given together with adequate micronutrients (vitamins and minerals).
- If possible, physical exercise helps to increase appetite.
- Clients who are losing weight should be monitored until the cause is found or the weight loss reverses.

REMEMBER

Tuberculosis (TB) is the most common cause of death in our patients. TB is more difficult to diagnose in HIV-positive people and may occur outside the lungs (EPTB). Weight loss is one of several non-specific signs that an HIV-positive person may suffer from as a result of active TB. Arrange for further investigations (Gene Xpert, TB culture, etc) if you suspect TB, even if the sputum smears are negative!

Algorithm 1: Investigation of Weight Loss



Headache

There are many possible causes of headache, most of which are not life-threatening. However, one must not miss those relatively few patients who are presenting with a life-threatening cause for the headache! An HIV-infected person having headache and one or more of the warning symptoms/signs in Algorithm 2 on **page 33** might have meningitis.

Causes

Common causes are:

- Migraine
- Sinusitis
- Muscle strain (neck)
- Eye strain
- Tension headache or stress
- Any infection causing high temperature
- Hypertension
- Dehydration
- Dental infections
- AZT associated headache

Clinical management

When to refer

You should **refer the patient to the doctor** if one of the following applies:

- The patient's CD4 count is < 100 cells/µL.
- The headache is very severe.
- The headache is associated with fever, neurological symptoms, change in behaviour, confusion, neck stiffness, vomiting, or difficulty with vision.

N.B. The lower the CD4 count, the more you should suspect meningitis! If in doubt, REFER for lumbar puncture (LP) irrespective of the duration or severity of the headache.

Examination

A complete and careful clinical examination is required to look for:

- Signs of meningitis: neck stiffness, Brudzinski's sign, Kernig's sign
- Hypertension (high blood pressure)

- Signs of disorientation or confusion
- Localising signs (such as one-sided weakness or hemiplegia)
- Signs of raised intracranial pressure: papilloedema on retinal examination
- Signs of generalized infection: fever (temperature ≥ 38° C), hepatomegaly, splenomegaly, rash.
- Visual changes (e.g. double vision, photophobia)
- Associated seizure

REFER

Signs and symptoms including one or more of the above may represent *meningitis*. Treat with: *Ceftriaxone* 2 g IM/IV (If none available, give penicillin G 5MU IV stat). Arrange same day referral to hospital.

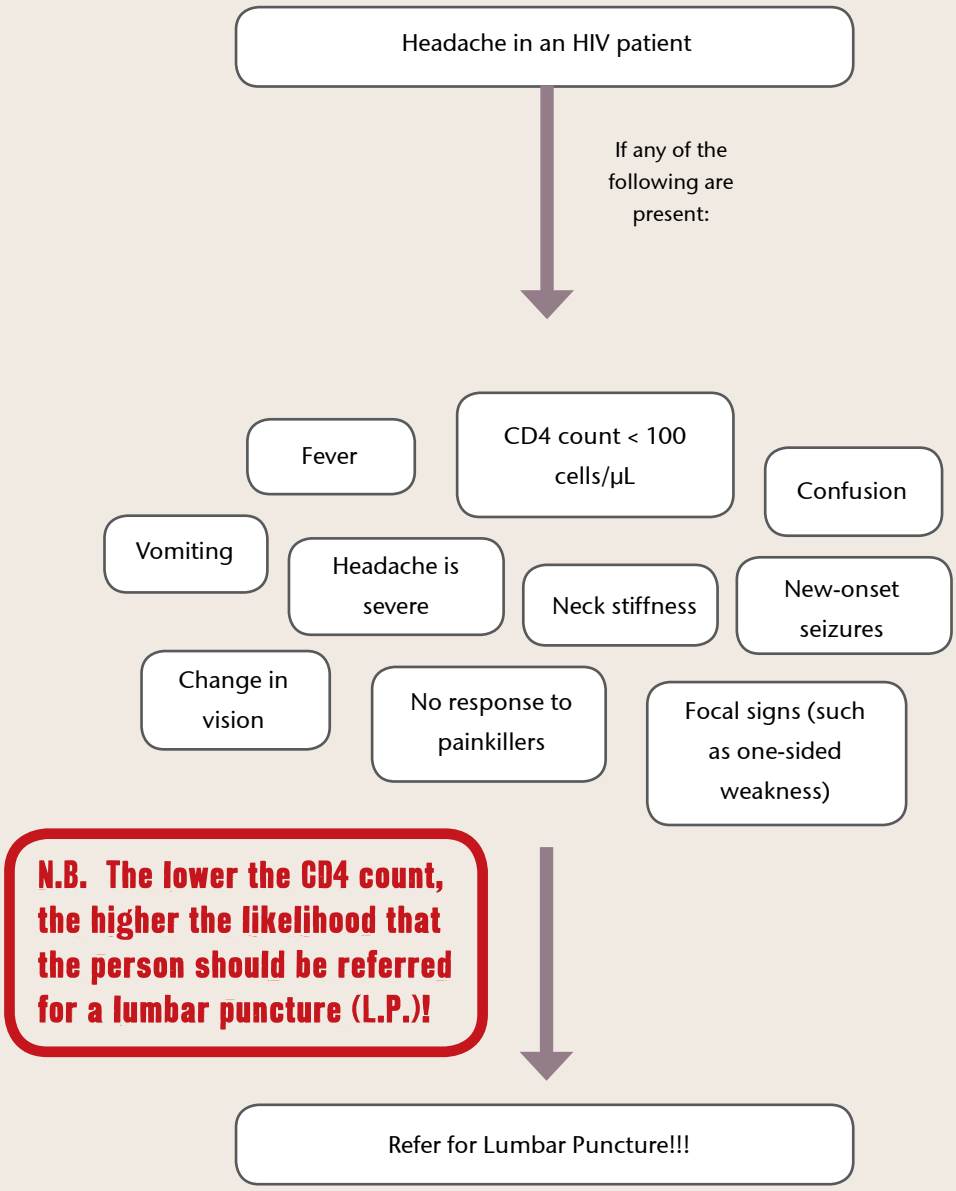
Lumbar puncture

When indicated, a lumbar puncture must be performed urgently to rule out possible serious causes (listed in order of likelihood):

- Bacterial meningitis
- TB meningitis (TBM)
- Cryptococcal meningitis (CCM)
- Viral meningitis (e.g. HSV)
- Neurosyphilis

CSF investigations should include the following: cell count, bacterial culture, CLAT/CRAG, VDRL, AFB, and TB culture.

Algorithm 2: Investigation of a Headache in an HIV patient



Confusion

Confusion is common in the late stages of HIV infection.

Causes

Possible causes are:

- Any severe infection
- Meningitis
- HIV-related encephalopathy
- Cytomegalovirus infection of the brain (perform retinal examination through dilated pupils for CMV retinitis)
- Progressive multifocal leukoencephalopathy (PML)

Diagnosis

All patients presenting with new-onset confusion (and/or new onset seizures) need to be referred for **lumbar puncture** (LP) in order to exclude meningitis (cryptococcal or other types) and/or other treatable severe infections (syphilis, toxoplasmosis, etc).

Management

If a lumbar puncture does not reveal any reversible abnormality and any acute OI is being treated, all HIV-infected patients with disorientation and confusion of unknown cause should be started on ARVs if feasible (if family or other supports are available). The patient's condition often improves after ARVs are started.

Otherwise treatment is palliative. The following nursing care is vital:

- Prevention of bedsores
- Assistance with personal hygiene
- Support for the patient and the family (home based care)
- Appropriate pain management if needed (see **page 186**)

Admission to a **hospice** is invaluable for many of these patients, both to provide nursing care, and to initiate ARVs in a supervised setting. Once the patient improves on ARVs, the patient and family can be counselled about the need for adherence, and then discharged home with good support (home-based care).

Lymphadenopathy

Lymphadenopathy (enlarged lymph nodes) is often a result of infection but can also be caused by cancer (e.g. lymphoma or Kaposi sarcoma). The lymphadenopathy can be generalised or localised. Do not confuse enlarged lymph nodes with swollen parotid glands (in the cheeks) or other swollen salivary glands (Diffuse Infiltrative Lymphocytosis Syndrome or DILS).

Causes of lymphadenopathy

Causes of generalized lymphadenopathy

- HIV itself (but often < 2 cm in size) most commonly during acute seroconversion
- Secondary Syphilis

Causes of localised lymphadenopathy:

- Tuberculosis
- Bacterial infection
- STIs (groin)
- Kaposi Sarcoma (KS)
- Lymphoma
- Cervical carcinoma (groin)

REMEMBER **Think of TB when a person presents with any enlarged lymph node that is chronic!**

Clinical presentation

- Swollen lymph nodes
- Sometimes tender
- Located in neck, axillae, or groin

Clinical examination

- Body temperature
- Assess for weight loss
- **Measure** and note size of lymph nodes (fine needle biopsy indicated if > 2 cm, see Appendix 30)
- Check all other lymph node areas (neck, axillae, groin)
- Check for liver or spleen enlargement

Management

- Correct management depends on the specific diagnosis, so it is important to make an accurate diagnosis.
- A trial of antibiotic therapy is reasonable for localised enlarged lymph nodes, especially while waiting for needle biopsy results: cloxacillin 250-500 mg four times daily x 5 days (depending on weight of adult).
- If the node is > 2 cm in adults, needle aspiration should be performed by a trained clinician as follows:
  - If the node is fluctuant, aspiration is easy and can be performed by the nurse or doctor; liquid aspirate should be sent in a sputum jar for TB testing (AFB +/- culture).
  - If the node is not fluctuant, a **fine needle aspiration biopsy (FNAB)** should be performed by a trained clinician and the material sent on slides for AFB examination and cytology to rule out other possible causes (lymphoma, KS, etc).
  - **See Appendix 30 for detailed information on how to perform a FNAB**
- Needle biopsy material should be sent for:
  - TB smear (AFB)
  - Cytology (to identify any lymphoma)

Test yourself

- Name two possible causes of weight loss for an HIV positive patient on ART and two causes for an HIV positive patient not on ART

- List 4 indications to perform a lumbar puncture for an HIV positive patient presenting with headache

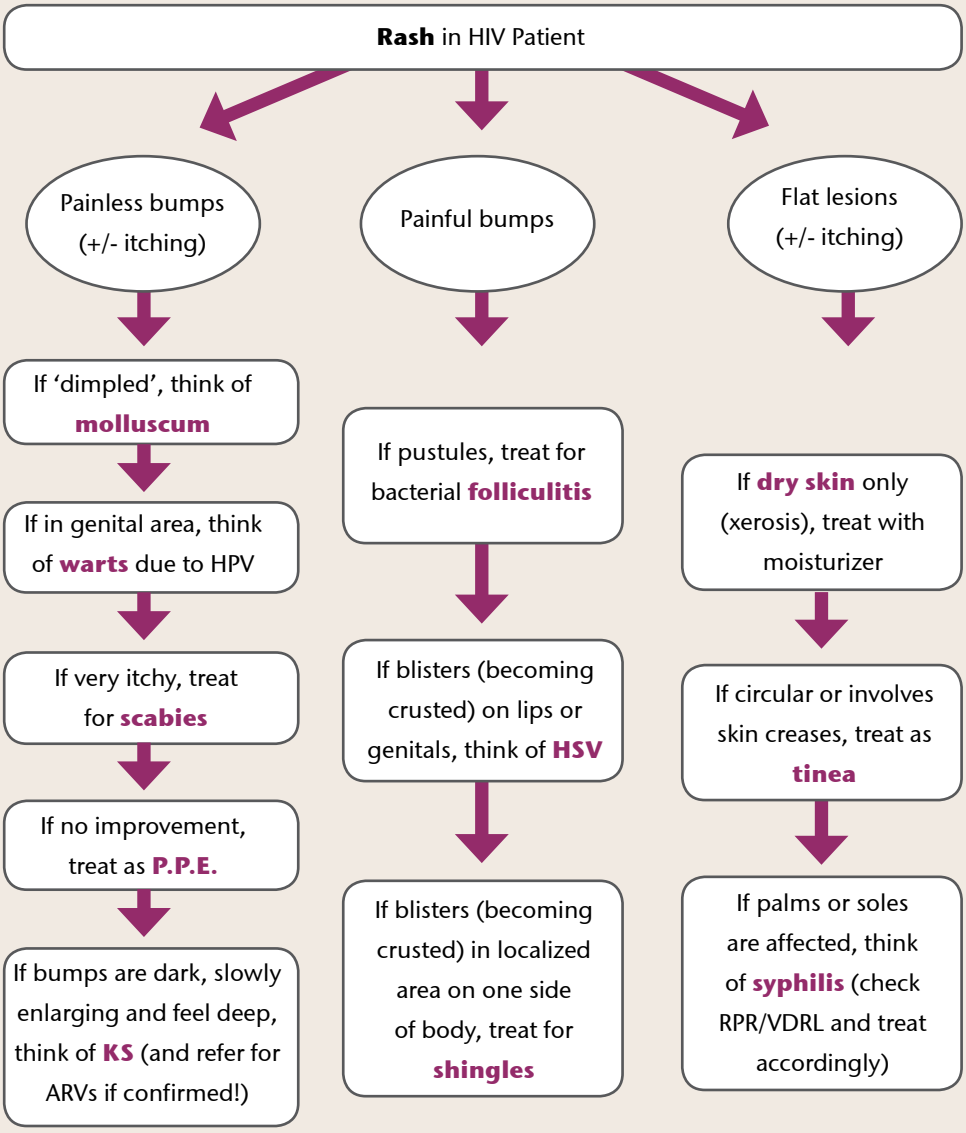
- List three possible causes of meningitis seen in an HIV positive patient

Notes

Notes

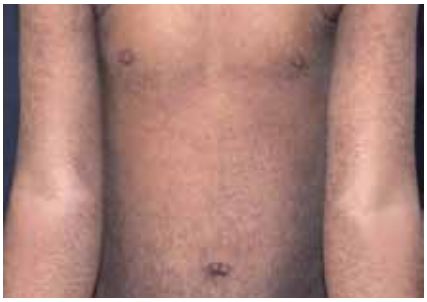
Skin Conditions

Algorithm 3: Diagnosis of a Rash in an HIV-positive patient



Refer to hospital on the same day and stop all drugs, if the patient recently started cotrimoxazole, TB drugs, or ARVs, and presents with skin rash plus one or more of the following:

- Temperature ≥ 38° C
- Systemic symptoms (generally unwell, vomiting, abdominal pain, headache)
- Rash affecting lips, mouth, eyes, genital and/or anal area.
- Blistering or 'raw' areas
- Diffuse purple discoloration of the skin affecting the whole body



Xerosis (Ichthyosis)

Definition

Xerosis means dryness of the skin.

Clinical presentation

Xerosis is common (> 20%) in HIV infection and is characterised by:

- Dry skin with slight to pronounced scaling
- Itching (sometimes severe)
- Watch for bacterial super-infection (which causes a yellow crust +/- weeping in addition to the xerosis)

Treatment

Topical:

- Emulsifying ointment to moisturize (in adequate amounts = at least 500 g per month)
- Use aqueous cream as soap
- If very itchy, add hydrocortisone 1% or betamethasone 0.1% ointment (Lenovate®) twice daily for 7 days
- Limit the use of steroid to short-term as they may cause skin atrophy or a paradoxical reaction. Try to avoid using steroid preparations on the face.

Systemic:

- Promethazine 25 mg or Chlorpheniramine 4 mg at night as required will reduce itching at night, but prescribe this only if the itching is severe.

Children

- Limit the use of promethazine to 3–5 days max, if itching is severe

Age	Promethazine dose	Chlorpheniramine dose
< 1 year	Not recommended	Not recommended
1–2 years	Not recommended	1mg bd
2–5 years	5–15 mg/day	1mg 4 x a day
5–10years	10–25 mg/day	2mg 4 x a day

Papular pruriginous eruption (PPE)

Follicular papules and nodules disseminated over the body

Clinical presentation

- Painless but itchy
- Often with infected crusts
- Can temporarily worsen after starting ARVs.

Management

- Always treat for **Scabies** first (see below); if no response, treat for PPE.

Topical:

- Hydrocortisone 1% or betamethasone 0.1% ointment twice daily for 10 days, alternated with emollients (emulsifying ointment, Vaseline®, or HEB simplex) twice daily for 10 days.
- Zinc oxide compound, applied twice daily for 2 weeks

Systemic:

- Promethazine 25 mg or chlorpheniramine 4 mg at night as required for severe itching.
- If **bacterial infection** (presence of pus or yellow crusts):
  - Apply Savlon® or povidone-iodine solution topically twice daily
  - If severe, add cloxacillin 250-500 mg four times daily for 5 days (actual dose depends on body weight and severity of super-infection).
- PPE is a stage 2 diagnosis. Client needs **cotrimoxazole prophylaxis.**

Children

Topical:

- Hydrocortisone ointment 0.5-1% twice daily for 7 days followed by emollients twice daily for 7 days.
- Use steroids starting with low strength usually hydrocortisone 0.5–1%, then increase strength until the problem is controlled (note that betamethasone 0.1% is stronger than hydrocortisone 1%).
- Apply to all areas affected.

Systemic

- If severe itching: promethazine, 0.1mg/kg PO 6 hourly (limit use to a few days and use only in children > 2 years). See Table on **page 41**.

Scabies

Scabies is a frequent contagious skin infection caused by mites. It is transmitted by close contact (including handshakes and sexual contact).

Clinical presentation

- Extremely itchy
- Papular lesions with linear burrows sometimes seen
- Predominantly on hands (in finger web spaces), wrists, armpits, abdomen and genitals; in infants, also on palms and soles
- Common in children
- Often a history of "itching" contact
- Sometimes a severe form of scabies is seen: Norwegian (crusted) Scabies: presents as thick, greyish crusts, often on elbows or wrists. Such cases are highly contagious with thousands of mites, so isolate this person!

Management

- This should include the patient and all household contacts (whether symptomatic or not).

Topical:

- 25% benzyl benzoate lotion applied to the entire body except the face, eyes, and mucous membranes. Wash off after 24 hours and repeat 72 hours later.
- Wash clothes and bed sheets on the same day (very important to prevent re-infection)
- Chlorpheniramine 4 mg or promethazine 25 mg to be taken as needed at night for itch
- Alternative: Gamma benzene hexachloride 1% lotion, apply once and wash off after 24 hours

Systemic:

- If scabies is severe or resistant to Benzyl Benzoate, add: Ivermectin tablets 200 micrograms/kg once (STAT dose on empty stomach).
- This should be combined with topical therapy (see above).

Children

- Ascabiol (topical benzoate benzyl 25%) - apply to whole body from neck down (including between fingers, along the nail edges, palms/sole and the genitalia). Leave on for 12–24 hours, and then wash off. Repeat the following day, and again in 1 week. (Dilute 1:1- with an equal amount of water - for children between 6 months and 5 years).
- For infants less than six months age use 5% sulphur ointment as above.
- Don't forget to treat all household members at the same time and wash bed sheets and clothes.
- In severe cases, treat with ivermectin in children over 15 kg (15–25 kg: 1 tab of 3 mg; 25–45 kg: 2 tabs of 3 mg).

Tinea pedis (Athlete's foot)

Fungal infection caused by *Trichophyton rubrum*.

Clinical presentation

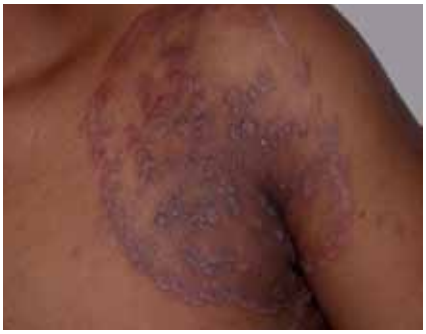
- Peeling, cracking and scaling skin between the toes (giving a "cooked appearance")
- Occasional redness and blisters on the soles and sides of the feet.
- Associated with burning and/or itching.

Management

- Keep the toes and web spaces dry. Advise use of sandals if possible. Change socks as often as possible (and/or avoid sports shoes). Encourage open shoes/ sandals.
- Talcum powder can be used to help the skin dry up and can also be sprinkled into the socks to absorb sweat.
- Miconazole 2% or clotrimazole 1% cream applied twice daily for 2 weeks or until resolved.
- If fingernails involved, consider use of griseofulvin (treatment may be needed for up to 12 months).
- Give advice about dual protection contraception because of the drug interaction between oral contraceptives and Griseofulvin.
- Refer if no response to treatment.
- Fungal nail infection is a stage 2 diagnosis, so need to give cotrimoxazole prophylaxis.

Tinea corporis (also known as "Ringworm") or Tinea capitis

Fungal infection of the skin caused by different types of fungus. Note that this infection has nothing to do with worms!



Clinical presentation

- Circular lesion with a raised, red, active edge (sometimes looks worm-like on the edges!) with scaling and papules on the inside.

Management

Topical:

- Miconazole 1%, clotrimazole 2%, or Whitfield's ointment applied twice daily for several weeks, until lesions are cleared.
- Advise client not to share towels/clothes (very infectious).
- For tinea capitis (scalp lesions): Selenium sulphide (Selsun®) shampoo can be used. Leave on for 30 minutes daily for a week; then use 2–3 times a week until tinea is cleared.

Systemic:

- In case of topical treatment failure, extensive scalp lesions, and/or disseminated infection, oral therapy may be required.
  - Fluconazole 200 mg daily for 1 month (adults) or griseofulvin 500 mg to 1 g per day in one or two doses for 4 weeks for skin infections, 8 weeks for scalp, and 3 to 6 months for nail infections. Griseofulvin needs to be taken after food or milk and should not be given in pregnancy.
- If added bacterial infection:
  - Savlon® may be used for local cleaning plus
  - Cloxacillin 250–500 mg orally 4 times a day for 5 days, or
  - If penicillin allergic, erythromycin 500 mg 4 times a day for 5 days.
- Once the infection has cleared, proceed to antifungal topical cream.

Children

- For tinea corporis: Whitfield's ointment is effective in non extensive lesions.
- Use oral griseofulvin (20 mg/kg/day in 2 doses) for at least 6 weeks if non-responsive or extensive. Griseofulvin should be crushed and taken with food or milk.

- Other alternatives are imidazole cream or fluconazole orally depending on severity.
- For tinea capitis: Griseofulvin 20 mg/kg/day in two doses for 6 weeks; add Betadine or Savlon® shampoo for antibacterial and additive antifungal effects. If scaly, use salicylic acid 2% or aqueous cream over night.

Seborrheic dermatitis

Chronic skin condition occurring most commonly on the scalp and face in clearly defined areas ("seborrheic areas"). Seborrheic dermatitis is often mistaken for fungal infections of the skin (tinea).

Clinical presentation

- "On and off" red patches, often itchy or burning
- Sometimes scaling with a yellowish appearance
- Involving seborrheic areas (naso-labial folds, sternum, head, outer ear, inguinal area and armpits).

Management:

- Mild steroid cream (such as Hydrocortisone cream 1%) twice daily on the skin.
- Imidazole cream twice daily.
- Selenium sulphide (Selsun®) shampoo (or tar shampoo if available) 2–3 times weekly if the scalp is involved. Application is easier if hair is cut short.
- If bacterial super-infection, treat with cloxacillin 250 mg 4 times a day for 5 days. If penicillin allergic give erythromycin 500 mg 4 times a day for 5 days.
- If poor response to treatment, refer to doctor.

Children

- Aqueous cream as soap
- Face and flexures: 1% hydrocortisone cream once or twice daily
- If more severe use Lenovate® (betamethasone valerate) 1:10 in aqueous cream

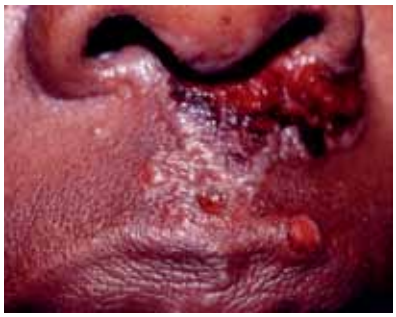
Nappy Rash

Infant rash caused by irritation from persistent moisture and irregular cleaning and drying of napkin area.

Management

- Ensure nappy is changed frequently
- If very mild, a barrier cream with each nappy change should be sufficient e.g. zinc ointment or castor oil
- If more inflamed, apply 1% hydrocortisone cream BD under the barrier cream
- If signs of infection with Candida, use clotrimazole cream. Suspect Candida if skin folds are involved or there is no improvement with above treatment after 3 days.

Herpes Simplex (HSV)



Very common infection caused by Herpes simplex virus, type 1 or 2 (HSV-1 or HSV-2). Genital HSV infection is one of the main triggers of HIV transmission, so treating genital HSV (in addition to condom use) will help to prevent new HIV infections in the general population!

Clinical presentation

- Lips: HSV of the lip is sometimes called a 'cold sore'. It starts as a group of tiny blisters involving the edge of the lip (or occasionally the area under one nostril) which can form small ulcers, then heal by forming crusts.
- Mouth ulcers can be caused by HSV (see algorithm 4, **page 60**)
- Genital area: Genital HSV occurs in women more than men; often multiple deep ulcers occur in the genital area or around the anus. Genital HSV is very painful, and sometimes causes urinary retention!

N.B. Need to adjust dose of Acyclovir if CrCl < 50 mL/min.

Management

- Lips: Keep the lesions dry! Gentian violet may be applied twice daily. Give aciclovir 400mg three times a day for 10 days.
- Genital herpes:
  - Acyclovir 400 mg three times daily for 10 days. In very severe cases, acyclovir 800 mg three times daily can be given. If chronic ulcers: continue treatment until ulcers have healed.
  - Chronic HSV infection (> one month's duration) = clinical stage 4, so "fast-track" for ART.
- **Do not forget painkillers!**

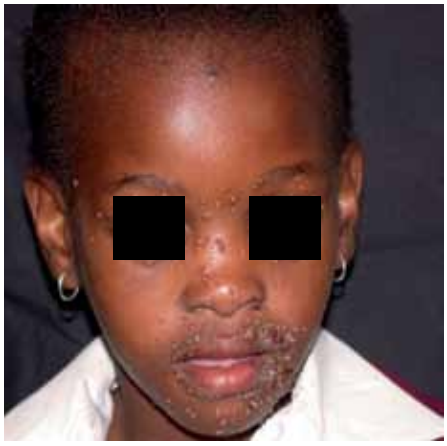
- Pain control:
  - Ibuprofen 400 mg, three times daily or paracetamol + codeine, 500 mg three times daily.
  - +/- carbamazepine, oral, 100 mg twice daily, increased every 12 hours until pain is relieved (maximum 1.2 g/day).
  - If the patient is on ARVs, it is preferable to use amitriptyline, 25 mg at night instead of carbamazepine.
- Admit to hospital if problems urinating.

Children

- Often seen on tongue, lips, all mucosal surfaces, around mouth and nose
- May be recurrent or chronic
- May have secondary bacterial infection
- Treatment with oral acyclovir
  - Under 2 years: 200 mg 8 hourly for 5 days
  - 2 years and over: 400 mg 8 hourly for 5 days
  - A repeat course may be required
- Pain relief (see **page 186**)

Molluscum contagiosum

A skin rash caused by a poxvirus; especially common in **children**.



Clinical presentation

- Skin-coloured papular lesions, **umbilicated** (dimpled) in the centre
- Often on the face, also common on trunk and genitalia, but may occur anywhere on the body; single or in clusters.
- May be extensive in HIV.

Management

- Reassure (usually resolves quickly with ARVs but may get worse first before getting better).
- The lesions can be squeezed out or removed with a large sterile needle or scalpel, followed by disinfection with Savlon® or povidone-iodine or paint with tincture of iodine. This is essential as the white material contains poxvirus and

new lesions will appear if not properly disinfected. If available, cryotherapy ("freezing") works very well.

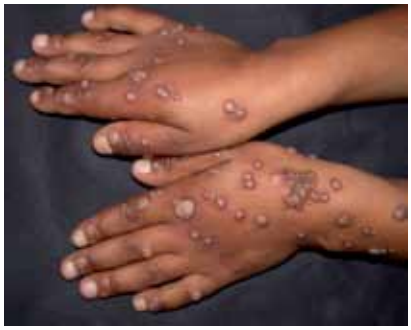
- Refer if no improvement on ARVs.
- If accompanied by chronic headache: refer for lumbar puncture to rule out cryptococcal meningitis.

Children

- No treatment required unless troublesome. Likely to disappear as immune status improves.
- Discuss with doctor about possible treatment with Cantharidin paint (Wart paint), liquid nitrogen, pricking with injection needle, or curettage.

Warts

A skin condition caused by a virus (Human Papilloma Virus). Different sub-types of the virus cause genital and non-genital warts.



Clinical presentation

- Multiple papules; may be raised or flat
- Commonly on hands, face, feet and genitals.

Management

- See **page 137** for the management of genital warts.
- For non-genital warts, reassure that they generally disappear on their own or with improved immune status. For children with extensive flat warts, this may however take time, even after ARVs have been started.
- Various methods of treatment may be used for individual lesions (salicylic paint, cryotherapy, podophyllin or chloroacetic acid). Be careful not to burn surrounding health skin, as warts may then appear on the damaged skin.

Bacterial Folliculitis

Folliculitis is the infection of one or many hair follicles. It is caused by bacteria (*Staphylococcus* species).

Clinical presentation

- Painful yellow pustules (blisters filled with pus) with a red halo.
- Note that fungal infections, especially of the scalp and beard, may be mistaken for bacterial folliculitis.

Management

Topical

- Savlon® fluid or povidone-iodine (mixed 1:10 with water) applied twice daily.

Systemic:

- Widespread or severe: cloxacillin 250-500 mg four times daily x 7 days. Cloxacillin has to be taken at least 30 minutes before food.
- If allergic to penicillin use erythromycin 500 mg 4 times a day for 7 days.

Children

- Cloxacillin 12-25 mg/kg/dose (max 500 mg/dose) 4 times daily for 7 days:
  - < 5 kg: 62.5 mg
  - 5–10 kg: 125 mg
  - 10–20 kg: 250 mg

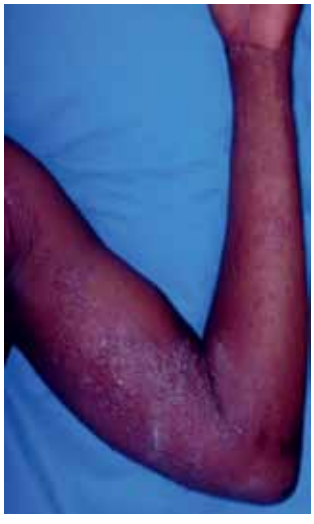
Impetigo

Crusting superficial sores usually seen around mouth or nose. Deeper lesions can be seen on the legs. Caused by bacteria: *Staphylococcus aureus* or *Streptococcus pyogenes*.

Children

- Wash off the crust
- If very localized, topical agents are usually enough e.g. Betadine or Flamazine
- If more extensive, then oral erythromycin 10 mg/kg/dose four times daily, or
- Oral cloxacillin four times daily for 7 days (dosage as for folliculitis)
- Keep fingernails clean and short

Herpes Zoster (Shingles)



Herpes zoster is caused by a reactivation of Varicella-Zoster virus infection. This is the same virus that causes chickenpox during childhood. After the chickenpox heals, the virus lies dormant in our bodies, but 'reactivates' (as Shingles) if our immune system becomes weak (due to stress, old age, or HIV).

Clinical presentation

Herpes zoster is characterised by:

- An eruption of blisters on one side of the body, usually involving one 'dermatome' (one area of skin supplied by a spinal nerve).

- The blisters crust over after 1–2 weeks (with or without treatment) and then heal, but often leave a scar.
- The blistering is usually accompanied by burning pain that often precedes the skin lesions and may continue even after healing of the rash has taken place.
- Pain **after** healing of the rash is called post-herpetic neuralgia.

Management of shingles

Acute topical treatment

- Keep area warm (reduces likelihood of post-herpetic neuralgia).
- Topical treatment with povidone iodine cream or silver sulphadiazine cream.

Acute systemic treatment

- Give aciclovir 400mg three times a day for 10 days.
- Consider Acyclovir 800 mg five times daily for 7 days if the rash has been present for <72 hours.
- Pain control: Amitriptyline 25mg nocte plus Ibuprofen 200 mg 1–2 tablets 3 times daily, as required and/or paracetamol 500mg + codeine phosphate 8 mg, 1-2 tablets four times daily as required (maximum 8 tablets daily).
- A stage 2 diagnosis. Client needs cotrimoxazole prophylaxis.

Treatment for chronic pain (after healing of rash)

If **Chronic pain (post-herpetic neuralgia)** develops:

- Amitriptyline 25 mg daily at night, to be increased as required up to 100 mg daily.

REFER

If shingles involves the eye: give acyclovir tablets as above, plus chloramphenicol or tetracycline eye ointment as a lubricant. Refer to an eye doctor if available!

Children

- Common in all HIV infected children regardless of CD4% or count.
- Can also present as Immune Reconstitution Inflammatory Syndrome (IRIS)

- Oral acyclovir for 7 days if within 72 hours of rash or eye involvement:
  - Under 2 years: 200 mg 4 times daily
  - 2–5 years: 400 mg 4 times daily
  - Over 6 years: 800 mg 4 times daily
- Pain control:
  - Ibuprofen, orally 5–10 mg/kg/dose every 6-8 hours, as required (Max 40 mg/kg/day): 3–6 months (weight over 5 kg) 50 mg 3–4 times daily; 1–3 years 100 mg 3 times daily; 4–6 years 150 mg 3 times daily; 7–9 years 200 mg 3 times daily; 10–12 years 300 mg 3 times daily.
  - Paracetamol 500 mg + codeine 8 mg: 6–12 years, ½–1 tablet 3–4 times daily (maximum 4 tablets daily). For smaller children, see Tables 18 and 19 **page 188**.

Varicella (chickenpox)

Clinical presentation

- Prodromal symptoms (fever, headache, feeling 'unwell') for 2 days prior to the onset of rash
- Presents with vesicles, which start as papules and eventually become crusted, distributed over face, trunk and limbs. Vesicles appear in crops over several days. Mucosal surfaces may also be involved.
- The child with immune suppression may have large and extensive vesicles and is more likely to have complications.

Management of chickenpox

- Isolate the child if possible, since contagious from day 2 before the rash appears until lesions have completely crusted over
- Treat with acyclovir 80 mg/kg per day orally given 4 times a day for 7–14 days (see dose given for Herpes Zoster)
- Provide pain relief
- If secondary bacterial infection develops, add amoxicillin 10–25 mg/kg/dose three times a day and cloxacillin 12–25 mg/kg/dose four times a day.
- Prevention and PEP: **Varicella immunoglobulin (VZIG)** is recommended for children who have been exposed to chickenpox (must be given ASAP and within 96 hours for maximum efficiency). The **varicella vaccine** can be used both as prevention and post-exposure prophylaxis if given within 3 days of exposure.

- Refer to hospital if:
  - Appropriate medication is not available
  - Disseminated infection is suspected (pneumonia, jaundice, abnormal neurological findings)
  - The child is unable to ingest fluids or the child is dehydrated

Kaposi sarcoma (KS)

KS is caused by Human Herpes Virus, type 8 (HHV-8). Kaposi sarcoma is a cancer originating from the inner lining of blood vessels. It affects mainly the skin and mucous membranes, but also any organs inside the body (for example, the lungs). KS lesions signify that a person is in stage 4.

Clinical presentation

- Dark, purple papules on the skin or palate, starting as single lesions which progressively grow, multiply, and disseminate to other parts of the body.
- Lesions range from small bumps to big tumours.
- The nose, palate, legs, and genitals are most often affected.
- KS is sometimes associated with swelling of the affected leg (lymphoedema).

REMEMBER **Patients with KS must be enrolled for antiretrovirals (ARVs) as soon as possible regardless of their CD4 count! Refer the same week for ARVs, as well as to a specialist for chemotherapy and/or radiation.**

Management

- Assess for signs suggesting inner organ involvement (pleural effusion, blood in stools, chronic cough, and/or ascites). **Every patient with KS should have a chest x-ray and a thorough examination of the mouth.**
- **Initiate ARVS** as soon as possible.
- **Refer to doctor the same week to assess need for chemo- or radiotherapy.**

- Ideally, patients with large lesions should be referred to a specialist for chemotherapy and stabilisation of KS before starting ARVS. This helps to limit KS immune reconstitution inflammatory syndrome (IRIS).
- Patients with CD4 counts below 50 should be started on ARVs as soon as possible, regardless of how aggressive the KS lesions are.
- Always make a note of KS lesion(s) on each visit to assess growth or regression; you may need to measure lesion(s) for an accurate assessment.

REMEMBER **Don't forget that KS can occur in children of any age (although not as common as in adults).**

Always examine the child completely undressed to look carefully at the entire skin. Always examine the mouth.

Drug rash

All drugs have the potential to cause side effects. One such possible side effect is a skin rash, sometimes referred to as a 'drug eruption' or 'drug rash'. Common causes of drug rashes include cotrimoxazole, TB drugs, and some ARVs (especially nevirapine; but also efavirenz). The rash caused by nevirapine usually presents within the first three weeks of treatment (often just after increasing the dose to 200 mg twice daily).

Taking a good history is one of the main ways of making a diagnosis of drug rash. Whenever assessing a person with a new rash, always ask about any new medications.

Common manifestations

- Coin-like lesions, well demarcated, often hyperpigmented (dark) and painless.
- Reddish, flat or raised lesions, usually widespread, often itchy or painful.
- **Less commonly, a severe rash can develop (called Stevens-Johnson syndrome) and involve the mouth, eyes and/or genitalia (always look). If this occurs the patient needs to be referred immediately to a doctor or hospital. The offending drug must be stopped immediately.**

Management

Severe rashes

- Usually involves stopping the drug in question. See specific sections regarding management of drug eruptions due to different drugs.

REFER

Refer to hospital and stop all drugs if the patient recently started cotrimoxazole, TB drugs, or ARVs, and presents with skin rash plus one or more of the following:

- Temperature ≥ 38° C
- Systemic symptoms (generally unwell, vomiting, abdominal pain, headache)
- Rash affecting lips, mouth, eyes, genital and/or anal area.
- Blistering or 'raw' areas
- Discoloration of the skin affecting the whole body

Non-severe rashes

- Do not stop drugs.
- Send blood for ALT. Review within a week. (See Appendix 18 for interpretation.)
- Advise client to return urgently if any serious symptoms/signs develop such as blistering of the skin or ulcers/blisters in the mouth.
- Provide symptomatic relief with emulsifying ointment. There is no role for topical steroids in drug rash.

Psoriasis (if severe should be managed by dermatologist then referred down to clinic)

A skin (and joint) condition that may present shortly after infection with HIV. Psoriasis is more common in HIV-infected people. There may be a genetic predisposition.

Clinical presentation

- Scaling, reddish plaques involving scalp, knees, elbows, abdomen, palms and soles.
- Rash may be atypical in HIV-infected people (groin, armpits, etc.)
- Involvement of nails ("pits") and/or joints ("psoriatic arthritis"), especially the foot and ankle.

Management

- Always refer to dermatologist
- Counsel regarding chronic course of psoriasis and encourage sun exposure as tolerated.
- Adults: salicylic acid 2–10% in white soft paraffin, topical, applied 3 times daily until scale is removed. An alternative is Coal tar 5–10% ointment at night. Then: betamethasone 0.1% ointment or modified Adamson's ointment twice daily to plaques.

Children:

- Hydrocortisone 1%, topical, applied 1–2 times daily
- In severe cases: prednisone, orally, 1–2 mg/kg once daily for 7 days

Test yourself

- 25 year old female complains of a burning painful rash on the right side of her body for 2 days. During examination a vesicular rash is noted on the right side of her body.
  - What is the likely diagnosis for this lady?

.....

  - What is your management of the client?

.....

  - What is the clinical stage of the client?

.....

- A 44 year old male comes for a general check up at your clinic. He is HIV+, clinically well and with a last CD4 count of 400. During examination you notice dark purple papules on the client's skin and similar lesions on the palate.
  - From the description what is your likely diagnosis of the lesions?

.....

  - What clinical stage is the client?

.....

  - What is the management of the client?

.....

- What is the treatment of PPE?

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Notes

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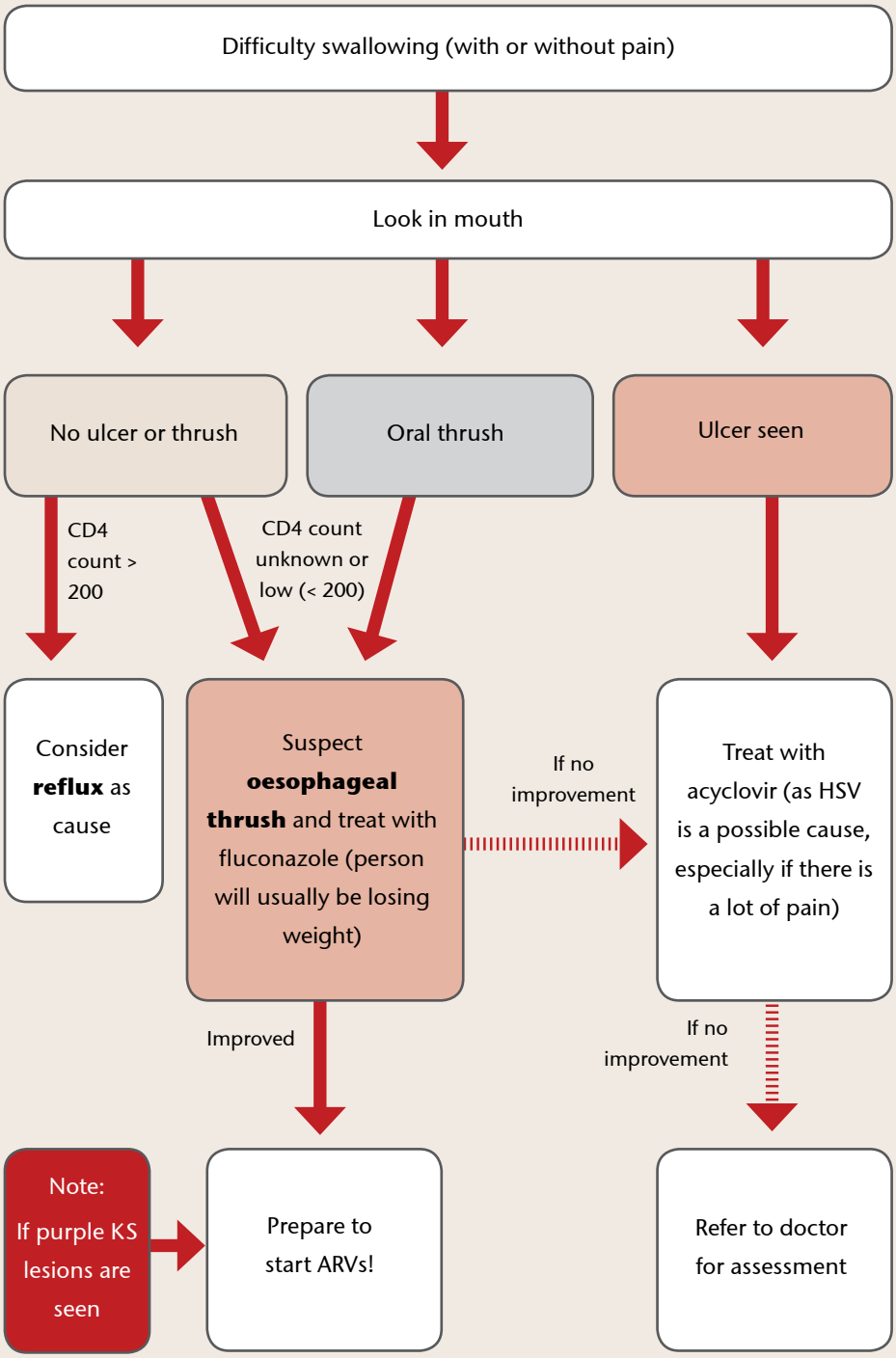
Notes

Mouth Lesions

Algorithm 4: Clinical Management of 'Difficulty Swallowing'



Oral health

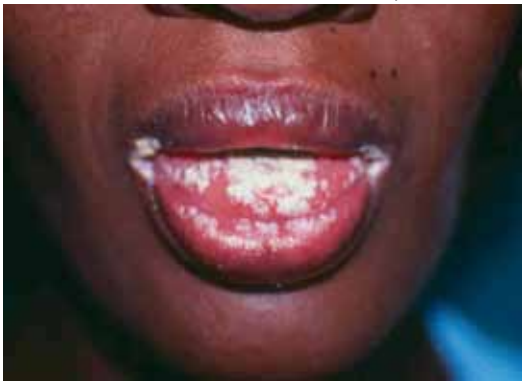
Basic oral health is important to prevent infections of the oral cavity, as these occur with increased frequency in HIV-positive people. This includes:

- Regular brushing and flossing of teeth.
- Do not share a toothbrush!
- Advise a visit to the dentist if gum disease or dental cavities are present.

Oral candidiasis (oral thrush)

Oral candidiasis is caused by yeast called *Candida*. It occurs in newborns, the elderly and those who have very weak immune systems. Remember: "the very young, the very old, and the very sick". **It is a serious symptom in HIV-infected patients indicating advanced immunodeficiency!** It places an adult and a child in stage 3 of HIV infection (see Appendices 1 and 2).

Clinical presentation



- Oral candidiasis has two presentations:
  - Pseudomembranous presentation ("thrush"): white patches (which can be removed with a tongue depressor) surrounded by a reddish border; these involve mostly the inner mucosa of the mouth, the pharynx and the inner lips.
  - Thrush may present as a reddish discoloration and burning of the hard palate ("atrophic thrush"). This may be difficult to diagnose.
  - Patients often complain of having "no taste".
- Ask about 'painful swallowing' and 'difficulty swallowing', which suggests co-existing oesophageal candidiasis (see **page 64**).

Management

- Nystatin oral suspension 2–5 ml to be swished around the mouth for as long as possible five times daily.
- If it still persists then use: nystatin tablets 500.000 IU 1 sucked 4 times a day for 5 days.
- Refer for fluconazole 200mg once daily if the thrush is severe or recurrent.

Children:

- In infants, it is sometimes accompanied by a candidal napkin rash.
- If persistent despite adequate treatment, it is strongly suggestive of HIV infection.
- Nystatin drops 1 ml 5 times daily for 7 days +/- 30 minutes after feed for 7days. Continue for 48 hours after cure.
- If no response / poor response add miconazole (Daktarin®) gel 4–6 hourly for 7–14 days.

REMEMBER

All patients with oral thrush should be assessed for ARVs!

- Treat refractory candidiasis with fluconazole 3 mg/kg/day for up to 21 days.

Angular stomatitis (cheilitis)

Angular stomatitis is also caused by *Candida*.

Clinical presentation

- Involvement of the corners of the mouth, presenting as a fissure (or 'crack')
- Can be painful

Management

- Keep dry and avoid mechanical irritation.
- Nystatin/clotrimazole cream or oral gel twice daily for 10 days is very effective.

Aphthous ulcers ("Canker sores")

Clinical presentation

- One or more ulcers on the mucosa of the mouth, the inner lips, and sometimes the tongue.
- Very persistent and very painful (10 days).
- Cannot be differentiated from herpetic ulcers (caused by HSV).
- Do not forget syphilis as a cause (but these are less painful).

Management

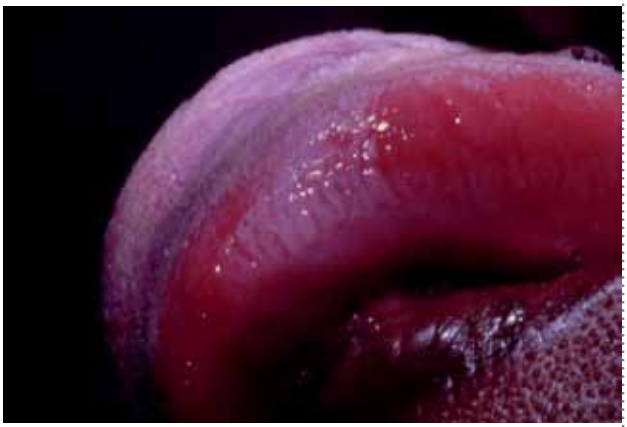
- Avoid acidic foods.
- Prescribe painkillers (see Pain Chapter **page 185**)
- Give acyclovir 400 mg three times daily for 10 days in case of HSV.
- If severe add prednisolone 20–40 mg OD for 7 days.

Oral hairy leukoplakia

Oral hairy leukoplakia is caused by Epstein-Barr Virus. It is specific to HIV infection, and indicates immunosupression. It places a client in stage 3 of HIV infection. Occurs mostly in adults. However, it is worthwhile to look for it in children because if found, the child is stage 3 and therefore eligible for ARVs.

Clinical presentation

- Very typical appearance: white raised vertical lines ("Adidas stripes") on the edges of the tongue.



Management

- No treatment necessary. Often disappears after ARVs are initiated.

Oesophageal candidiasis (oesophageal thrush)

Since the oesophagus (the muscular tube carrying food from the mouth to the stomach) cannot be seen, a diagnosis of oesophageal thrush is not easy to make. Usually, the nurse or doctor has to rely on a good history to make such a diagnosis.

Clinical presentation

- Oesophageal thrush must be suspected when someone with a low CD4 count complains of difficulty swallowing, or pain on swallowing, especially if oral candidiasis is present.
- In immunocompromised patients, it is often associated with a critical decrease in food intake, and consequent weight loss.
- Possible causes of painful and difficult swallowing include:
  - Gastro-oesophageal reflux disease (GERD)
  - Infection of the oesophagus with cytomegalovirus (CMV)
  - An oesophageal aphtous ulcer not related to HSV
  - Kaposi sarcoma (KS)

Management

- **Patient must be enrolled for ARVs as soon as possible!**
- Fluconazole 200–400 mg daily for 10–14 days, then check the response to treatment after 7 days. If there is a good response, then oesophageal candidiasis is the likely diagnosis and the patient is then considered to be in stage 4. Continue the fluconazole for 10 days to 2 weeks.
- If fluconazole is not effective after one week, consider HSV as the possible cause of the painful swallowing and prescribe acyclovir 400 mg three times daily for 10 days.
- If acyclovir is not effective, then **refer to the doctor** for further assessment.

REMEMBER

If someone with a high CD4 count is complaining of retrosternal pain but is not sick (and not losing weight), that person does not have oesophageal thrush (and is therefore not in stage 4!). The diagnosis in this case is more likely to be 'reflux' requiring antacids (not fluconazole).

Children

- Difficult to diagnose in infants. Suspect if infant has oral candidiasis associated with crying and/or refusal to feed.
- Treat with fluconazole 3 mg/kg/day for 21 days.
- If there is no improvement after 7 days, and HSV is suspected, prescribe acyclovir 20 mg/kg/dose three times daily for 10 days.
- Child needs admission to hospital if he/she does not tolerate food and has signs of dehydration.

Kaposi's sarcoma

Clinical presentation

- Fleshy dwelling on roof of mouth or gums.
- May often bleed.

Management

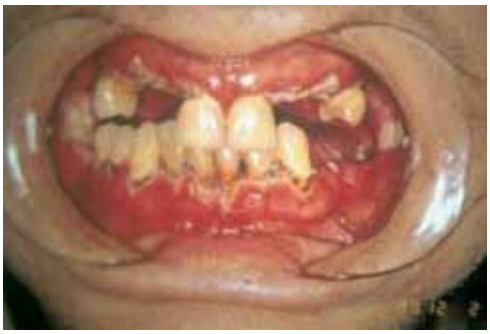
- Patient should be referred for antiretroviral treament immediately
- Patient should be referred for eligibility for chemotherapy or radiotherapy

Necrotising gingivitis

Clinical presentation

- This is an inflammation of the gingiva.
- It may lead to tooth loss, severe pain and foul smelling breath.

Management



- Oral hygiene.
- Antiseptic mouthwashes.
- Antibiotics: Metronidazole 400 mg TDS for 7 days or Clindamycine 600 mg TDS for 7 days.
- Pain management.
- This is a stage 3 condition, so the patient should be referred for antiretroviral treatment

Test yourself

- A 27 year old male complains of having white patches on his tongue. He tried to brush hard with a toothbrush but it wouldn't go away. The client has been HIV + since 2007 and last CD4 count was 380. During examination you find white patches in the mouth and on the tongue.
- What is your most likely diagnosis?

- What is your management of the client?

- What is the clinical stage of the client?

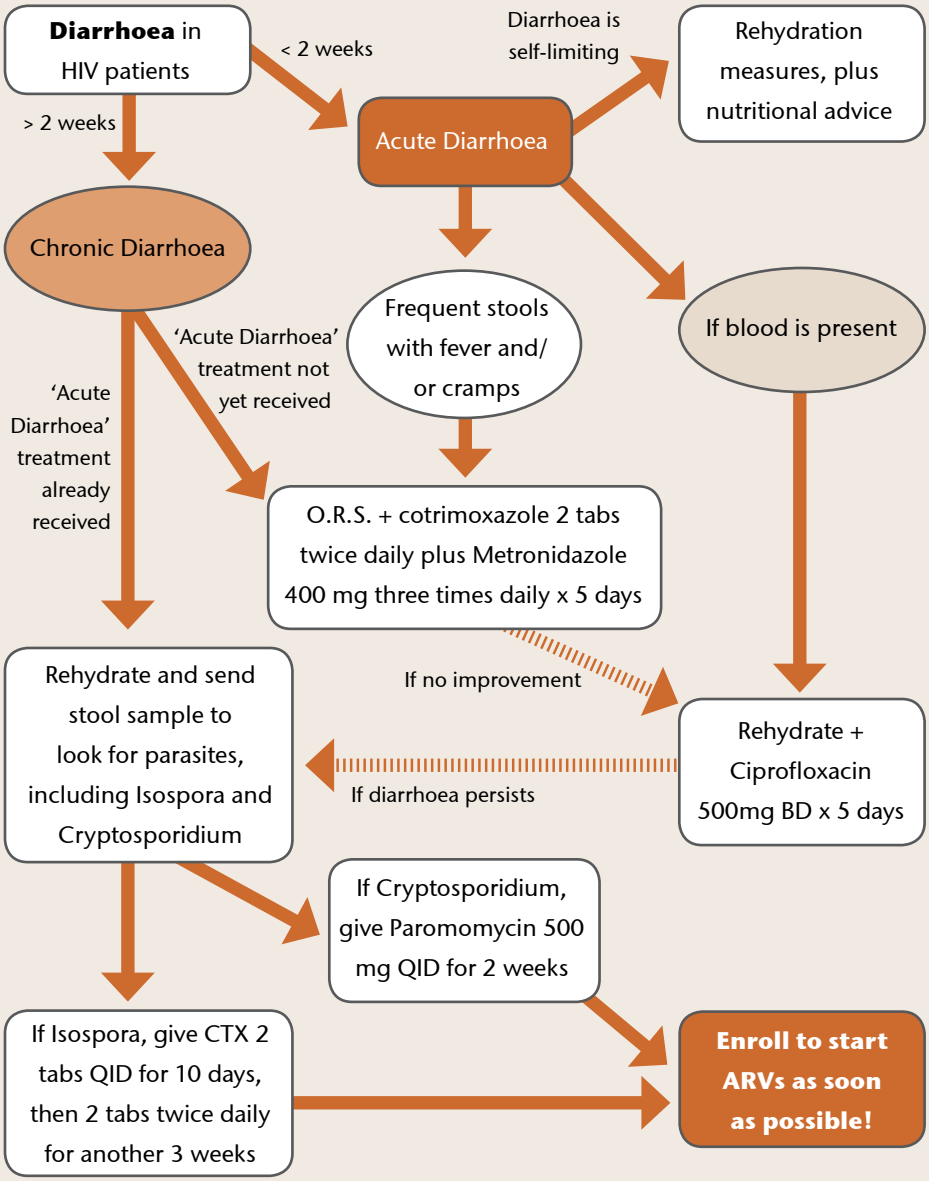
- A 30 year old male known HIV+ , tested 2 years ago and never went for follow up care. CD4 count is unknown. When you examine his tongue he has characteristic stripes along the side when scraped with a tongue depressor
    - What is the likely diagnosis?

    - What is the clinical stage of client?

Notes

Gastro-intestinal Conditions

Algorithm 5: Management of Diarrhoea



Note: CTX = cotrimoxazole. Always ensure good hydration; use IV fluids if necessary!

Refer to hospital if:

- Bloody diarrhoea AND temperature above 38 degrees Celsius
- Or, signs of severe dehydration: poor urine output, confusion or drowsiness, hypotension

Diarrhoea is VERY common in HIV-infected adults and children. For management purposes, it is very important that the nurse or doctor makes a **distinction between acute and chronic diarrhoea**.

Acute diarrhoea

Clinical presentation

Acute diarrhoea is characterised by:

- More than 3 loose stools/day
- A duration of less than 2 weeks
- Without significant weight loss
- Disappearing spontaneously or with appropriate treatment

Two syndromes are to be noted:

1. Gastroenteritic syndrome: simple diarrhoea caused by viruses, bacteria (*E. coli*), food poisoning (*Staphylococcus*), or *Salmonella*.
2. Dysenteric syndrome: painful, diarrhoea with **mucous and/or blood**, with rectal symptoms, caused by *Shigella, Amoeba enterolytica, Campylobacter* and some *E. coli* strains.

Clinically check for fever and signs of **dehydration** (especially in children):

IMCI Classification of dehydration

Signs	Severe dehydration (2 of the following signs)	Some dehydration (2 of the following signs)	No visible dehydration
Level of consciousness	Lethargic or unconscious	Restless and irritable	Alert
Sunken eyes	Sunken	Sunken	Not sunken
Ability to drink	Poor or unable	Eager, thirstily	Normal, not thirstily
Skin pinch (turgor)	Very slow return > 2 seconds	Returns slowly < 2 seconds	Returns immediately

Management

Rehydration

This is crucial! Tell patient to drink as much as possible, and as often as possible. **Oral rehydration salts (ORS)** are best, but any fluid will do. **Sugar Salt Solution (SSS)** can be prepared according to the recipe below. If the person is unable to drink and/or severe vomiting is present, arrange for intravenous fluid.

ORS is prepared by dissolving the contents of one sachet into 1 litre of clean or boiled water.

SSS can be prepared according to the following recipe: One litre of clean boiled water + half a teaspoon of salt + 8 teaspoons of sugar. It is also recommended to add some potassium if possible (for example, by adding some orange or grapefruit juice).

Then give ¼ litre (1 full cup) every 15 minutes

Make a new batch of ORS or SSS every day, and keep the ORS or SSS clean and cool.

Nutritional advice

Continue offering food, which is important especially for children (do not starve the patient!). No special diet is needed, but very spicy food or very oily food should be avoided. Try rice, potatoes, maize porridge, and bananas.

Antibiotic therapy

If the diarrhoea **improves on its own within 1 week**, then only rehydration and nutritional advice are necessary.

If acute diarrhoea **doesn't improve within 1 week**, then **empiric antibiotic therapy** is needed as follows (empiric means that no lab studies, microbiology, or cultures are performed):

If the person has frequent stools (> 6 per day), together with a high temperature and/or bad cramps, then give:

- Cotrimoxazole 480 mg 2 tablets twice daily x 5 days, AND
- Metronidazole 400 mg three times daily x 5 days

If there is **blood** in the stools together with the above symptoms, or the diarrhoea is not improved with the above treatment, then give: ciprofloxacin 500 mg twice daily x 5 days

Symptomatic treatment

Loperamide 2 mg after each episode of diarrhoea up to 6 times per day can be given if there is no bloody diarrhoea and no high fever.

Children

- Look for signs of dehydration and assess gravity as per IMCI guidelines
- Severe dehydration: 20 mg/kg Ringer´s lactate or Normal Saline rapidly. Refer urgently to hospital.

- Some dehydration: Give oral ORS 40 ml/kg over 4 hours. Increase the amount if the child wants more, and encourage the mother to continue breastfeeding where applicable, or to give any other fluids.
- For prevention of dehydration, caregiver needs to give 10 ml/kg of fluids after each loose stool:
  - Child age up to 2 years: 50-100 ml; Child age > 2 years: 100-200 ml
  - Use Sugar salt solution, or if the child has been rehydrated for 'severe dehydration' or 'some dehydration', use ORS
- Zinc supplements (lessen the period of diarrhoea and stool frequency)
  - Age < 6 months: 10 mg daily for 14 days; Age > 6 months: 20 mg daily
- If blood in stool: Ciprofloxacin 15 mg/kg/dose twice daily for 3 days.
- If not on exclusive breast milk offer food-based fluids, e.g. soft porridge, yoghurt, Sugar salt solution or ORS.
- Be cautious with rehydration in severely malnourished children.

REFER

Children with the following symptoms need URGENT referral:

- **Lethargic/unconscious**
- **Eyes sunken**
- **Drink poorly/unable to drink**
- **Decrease in skin turgor**

Chronic diarrhoea

HIV itself can directly cause chronic diarrhoea, but other causes need to be excluded first before blaming the diarrhoea on the HIV. TB can also cause diarrhea and at low CD4s < 50 the stage 4 conditions of mycobacterium avium intracellulare (MAC) or crytosporidium should be considered. On ARVs: didanosine (ddI), lopinavir/ritonavir (Aluvia® and Kaletra®) and ritonavir can cause loose stools, which are ongoing.

Clinical presentation

- Chronic diarrhoea is characterised by diarrhoea for **more than 2 weeks** and is often associated with significant **weight loss**.

Management

Non specific treatment:

- Rehydration as described above.
- Adults with unexplained chronic diarrhoea > one month are in no less than clinical stage 3. Start cotrimoxazole prophylaxis.

- **Chronic diarrhea is a stage III condition, so patient should be started on ARV's regardless of CD4**
- Nutritional advice as described above.
- If on ARV's with ongoing diarrhoea and weight loss, refer for further investigation

Specific Treatment:

1. If the patient has **not** been treated at all for diarrhoea:
   - Empiric antibiotic treatment with high-dose cotrimoxazole and metronidazole as above (or ciprofloxacin as described)
   - Check response to treatment after 3 days.
2. If the diarrhoea persists: **send two stool samples for microscopy, looking for coccidian parasites** (especially Isospora and Cryptosporidium).
3. Treat any infection that shows up in the stool investigation report:
   - Isosporiasis: give cotrimoxazole 480 mg 2 tablets four times daily for 10 days, then 2 tablets twice daily for at least 3 weeks.
   - Cryptosporidiosis: rehydration therapy and nutritional advice as above; can try paromomycin if available (but expensive)
   - Since both represent clinical stage 4, **start counselling about ARVs!**
4. If the chronic diarrhoea has still not improved and the patient is severely immunosuppressed:
   - **Start ARVs as soon as possible!**
   - In the meantime consider:
     - Microsporidiosis or Strongyloides stercoralis: try albendazole 400 mg daily for 2 weeks (if available).
     - CMV colitis or atypical mycobacterium infection, both of which can only be diagnosed at a referral hospital.

Special note about anti-diarrhoeal drugs

Anti-diarrhoeal drugs must be used cautiously as they slow the motility of the intestinal tract which may result in harmful bacteria being retained (or 'kept inside'). The syndromic management of diarrhoea must be completed before considering such anti-diarrhoeal drugs. In the event of a poor response to syndromic management, the following anti-diarrhoeal drugs can be used (while enrolling the patient for ARVs). But prescribing the following drugs requires more frequent patient follow-up (every 2–3 days):

- Loperamide 2 mg tablet after each episode of diarrhoea, up to 6 tablets a day, or
- Codeine Phosphate 30-60mg up to four times a day

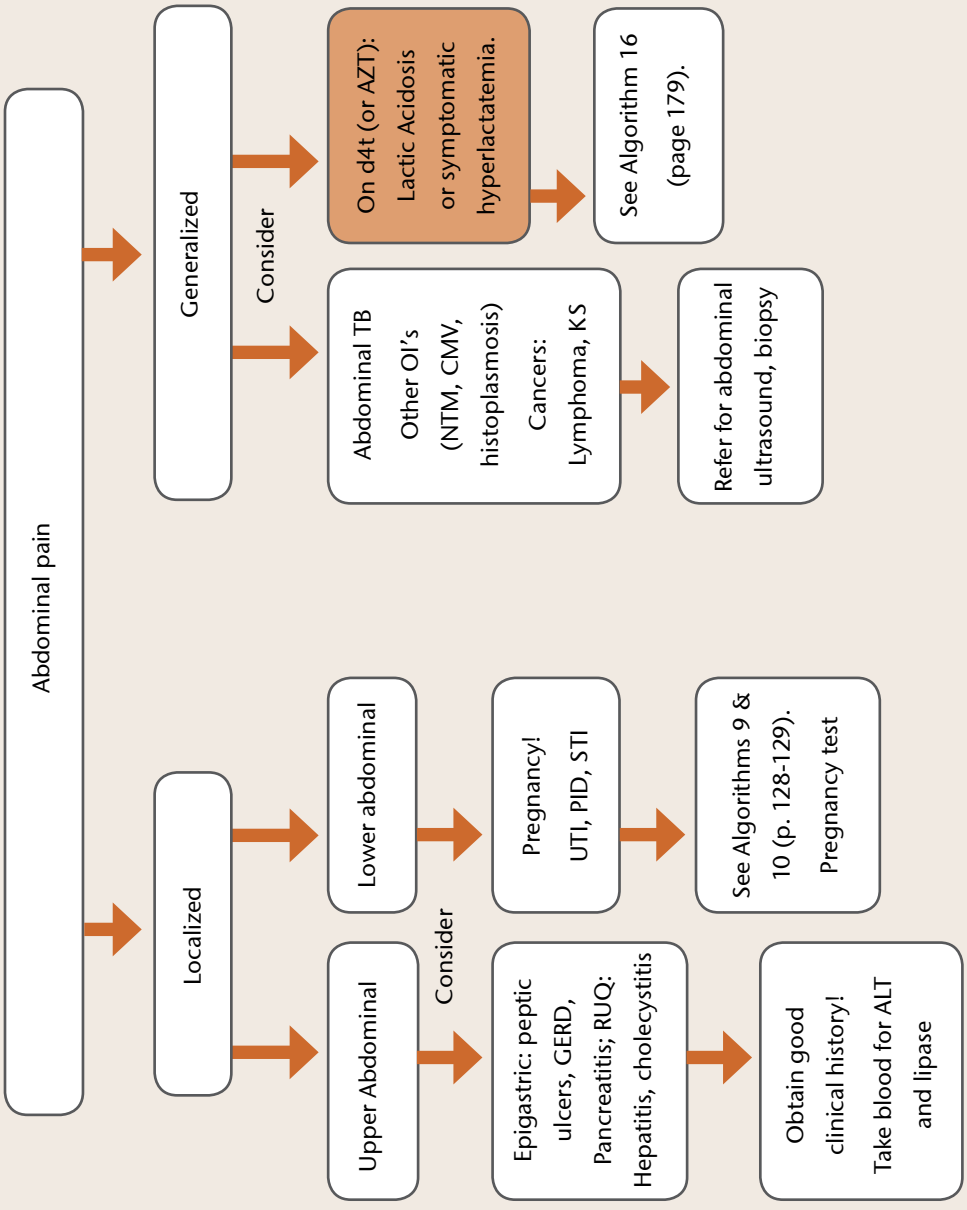
5. In a patient who has recently started a LPV/r based regimen, diarrhea (especially if not severe) might be drug-induced (LPV and Ritonavir): in this case, reassure the patient and treat symptomatically (most of the time, it improves without changing treatment). If it does not, refer to doctor (changing LPV to ATV can be considered).

Children

- Management as above.
- No pathogen identified: CTX 40+8 mg/kg/dose three times daily + metronidazole 10 mg/kg/dose three times daily for 5–7 days.
- Children with unexplained persistent diarrhoea for 14 days or more are in no less than clinical stage 3. Start cotrimoxazole prophylaxis and assess eligibility for ART.

REMEMBER **Always assess children with acute or chronic diarrhea for other infections: UTIs, ear infections, pneumonia and sepsis can be associated with diarrhea.**

Algorithm 6: Approach to Abdominal pain



Note: Also remember that conditions other than GI conditions, such as pneumonia may be felt as abdominal pain, especially in the young child!

Abdominal pain (No diarrhoea)

See Algorithm 6 on previous page for an approach to abdominal pain.

REFER

Recognise the severely ill client:
HIV with abdominal pain and one or more of the following signs:

- **Peritonitis (guarding or rigidity on abdominal examination)**
- **Jaundice**
- **If on ARVs, any sign of lactic acidosis: See algorithm 16 (page 179).**
- **Temperature ≥ 38° C.**

Refer same day to hospital

REMEMBER **Always examine the lungs of a young child who complains of abdominal pain!**
A child with pneumonia often complains of belly pain.

Hepatitis B co-infection

Hepatitis B infection is a serious disease caused by a virus called hepatitis B virus (HBV). HBV infects the liver causing acute +/- chronic liver problems. For the HIV positive co-infected person, it can also complicate management with ARV's. Many National Departments of Health have now added Hepatitis B vaccination to their routine Vaccination Program for children.

Diagnosis

A positive Hepatitis B surface antigen test (HBsAg+) means that a client has active hepatitis B disease. Where the usual first line regimen includes TDF, routine testing is no longer necessary for clients who initiate ARVs, since the usual first line regimen now includes TDF /3TC (or FTC), which are indicated for all HBsAg+ individuals. HBsAg testing should be considered for clients with a baseline ALT > 40, anyone with jaundice or right upper quadrant abdominal pain and for any individual who is being considered for stopping or not starting TDF.

There is a difference between the antibody test and the antigen test. A positive hepatitis B antibody test could mean that: a) the individual has been infected with

hepatitis B at some time in the past, or b) he/she was vaccinated against hepatitis B. Having antibodies for hepatitis B does not mean that the person has chronic hepatitis B disease.

If the HBsAg test comes back as weakly positive, the test should be repeated.

Management

- Patients who need ARVs or are on ARVs and have a positive HBsAg need to be treated with tenofovir (TDF) and lamivudine (3TC).
- TDF can occasionally affect the kidneys. It is contra-indicated if the creatinine clearance (CrCl) < 50 ml/min.
- Serum creatinine is not a good marker of the kidney function. Instead the CrCl should be calculated with the equation of Cockcroft-Gault:

$$\frac{(140\text{-}age) \times Weight\ (kg)}{serum\ creatinine\ (\mu mol/L)} \times c$$

c: in men x 1.23, in woman x 1.04

- TDF is not recommended for use in children less than 12 years due to its effect on bone mineral density.
- Clients to be started on TDF need:
  - A baseline serum creatinine and the calculation of CrCl (If < 50 ml/min, specialist advice is required).
  - CrCl follow up will depend on the local availability of creatinine testing. TDF can still be used if creatinine monitoring is not available. If available 6 monthly monitoring is adequate.
- When switching patients with hepatitis B infection to second-line regimens, **they need to remain on TDF and 3TC!** Stopping TDF could cause a severe flare of the hepatitis. Close monitoring for worsening of hepatitis B status should be done.

REMEMBER

- Always check the creatinine clearance before starting TDF. Only looking at the serum creatinine result is not enough (especially for clients aged > 50 years, those who weigh < 50 kg, or those with serum creatinine > 100.)
- Patients with chronic hepatitis B need to stay on TDF and 3TC, even if they are switched to another regimen.

Test yourself

- A 17 year old female who is known to be HIV+ attends your clinic, accompanied by her mother. She complains of diarrhoea for 40 days. On examination the client is dehydrated. The client was rehydrated at the clinic and samples of stools were sent to the laboratory. The stool MC&S reports presence of cryptosporidium.
  - What is your management of the client?

  - What clinical stage is the client?

  - Does the client require fast-tracking?

- A patient who is HIV positive presents with a one week history of bloody diarrhea associated with mild abdominal pain.
  - How are you going to manage this patient?

Notes

Notes

Pulmonary Conditions

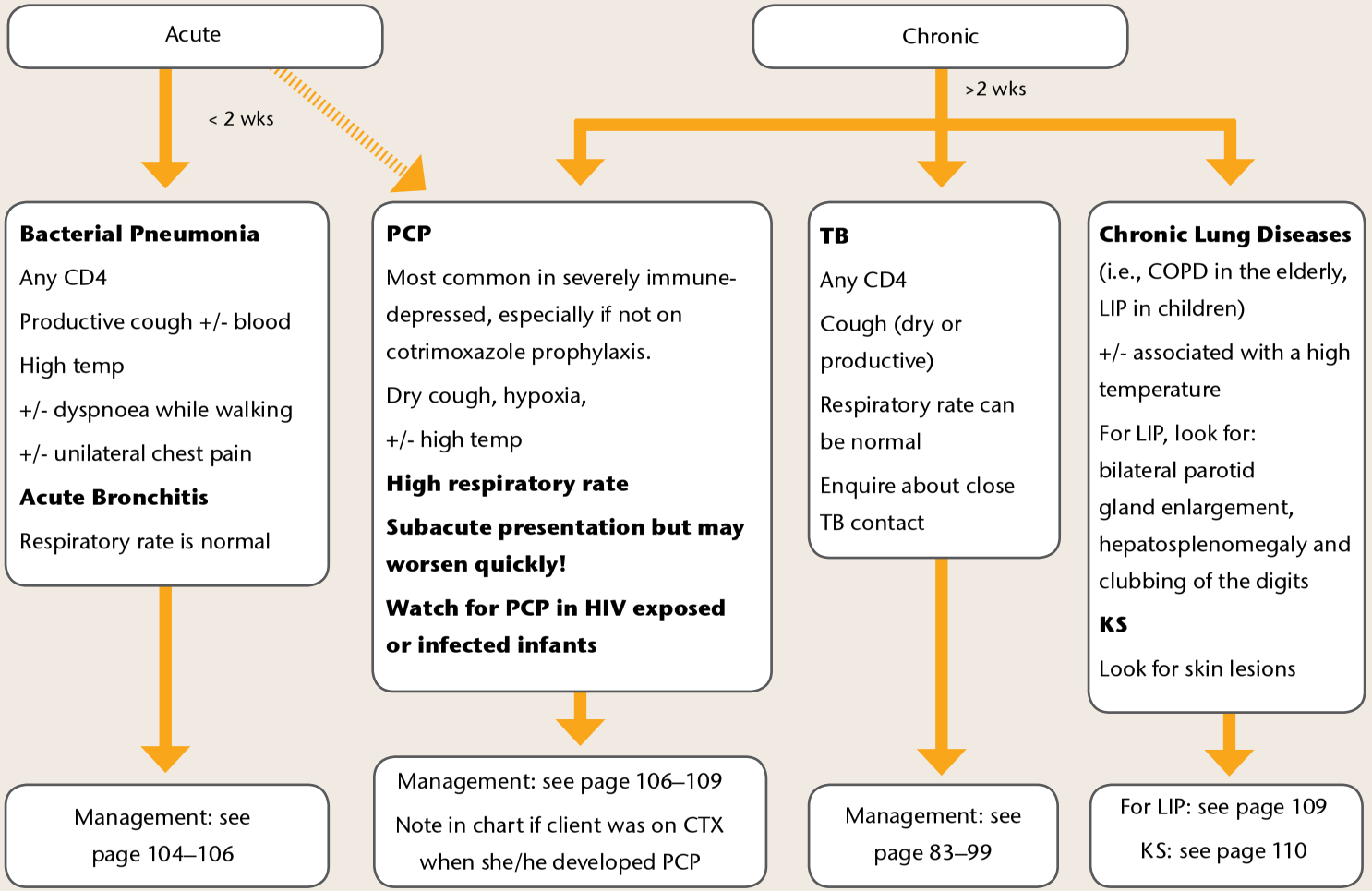


Figure 4: Pulmonary conditions not to miss!

Introduction to Pulmonary Conditions:

Common pulmonary diagnoses

The three most common pulmonary diagnoses in HIV-positive people are:

- Pulmonary Tuberculosis (PTB)
- Lower Respiratory Tract Infections (LRTIs)
  - Acute bronchitis
  - Bacterial pneumonia
- Pneumocystis jiroveci pneumonia (PCP)

Clinical presentation

But of course, people don't come in and tell us their diagnosis. They come to us with **symptoms**. As always, it is important to take a good history, especially when a person is sick. If someone comes in with respiratory symptoms, make sure to identify all of the following worrisome respiratory symptoms and signs (Also see Appendix 15):

- Cough (productive or dry)
- Haemoptysis- blood in sputum
- Dyspnoea (shortness of breath)
- Tachypnoea (fast breathing determined by examination)
- High temperature

Likely **diagnoses** according to presentation (always ask **how long** symptoms have been going on):

- Acute onset (< 2 weeks):
  - Acute bronchitis
  - Bacterial pneumonia
  - Pneumocystis jiroveci pneumonia (PCP), which has a subacute onset, but eventual rapid deterioration.
- Chronic onset (> 2 weeks):
  - Pulmonary TB
  - Pulmonary Kaposi sarcoma
  - Chronic Obstructive Pulmonary Disease (COPD)

It is important to recognize the severely ill client. Look out for the TB suspect with one or more of the following signs:

- Respiratory rate ≥30 breaths/minute

- Breathlessness at rest or while talking
- Prominent use of the breathing muscles
- Agitated or confused
- Unable to walk unaided

Management

If the client is severely ill, he/she will need rapid treatment:

- Give oxygen (40% face-mask oxygen or at least 4 L/min via nasal prongs).
- Ceftriaxone 1g IM/IV (If unavailable, amoxicillin 1g orally. If penicillin allergic give erythromycin 500mg orally).
- Take first sputum for AFB's and arrange follow up.
- Refer same day to hospital.

REMEMBER **TB and HIV together = "Double-Trouble"!**

The clinical presentation and the diagnostic approach are different in HIV-positive patients who have active TB.

As an HIV-positive person's immune system weakens, active TB presents differently.

- TB is more often located outside the lungs in HIV-positive people. This is known as extra-pulmonary TB (or EPTB).
- Active TB is more difficult to diagnose in HIV-positive people. The nurse or doctor has to frequently order investigations other than sputum smears to prove the diagnosis of TB.
- Sputum smears are more likely to be negative in HIV-positive clients with active TB!!! Since their immune systems are weaker, there is less cavity-formation in the lungs. As a result, HIV-positive people tend to cough up fewer TB germs, so their smears are often reported as negative.

Therefore, never tell HIV-positive clients with symptoms of TB (but "negative" smear results) that they do not have TB! Despite the negative smear results, these clients almost certainly still have TB. We just have to do other tests to prove it!!!

Once diagnosed, the treatment of TB is the same whether a person is HIV-positive or negative.

REMEMBER

TB and HIV services should be INTEGRATED in settings where HIV and TB are common

Approximately ten percent of HIV-positive people get TB **every year**! And up to 70% of those receiving treatment for TB are HIV-positive (whether they know it or not) in these settings. Integration of HIV and TB services would help reduce the number of TB deaths in HIV patients by reducing diagnostic delay of TB. Integration would also reduce the number of TB patients dying from other HIV-related infections, by encouraging HIV testing in TB patients and allowing earlier comprehensive HIV treatment of those who are HIV-positive.

All people receiving TB treatment should get an HIV test!

All HIV positive people with TB should get a CD4 count!

All HIV-positive people with pulmonary, extrapulmonary or MDR/XDR TB are eligible for ARVs.

Pulmonary Tuberculosis (TB of the lungs = PTB)

When someone has a chronic cough, PTB is the first diagnosis to think of and always needs to be ruled out! TB is caused by the organism *Mycobacterium tuberculosis*. In HIV-positive patients, a diagnosis of **pulmonary** TB means that the adult or child is in stage 3 of HIV infection (see Appendices 1 and 2). Pulmonary symptoms of TB together with pleural effusion or miliary pattern on chest x-ray are actually considered to be extra-pulmonary TB (EPTB). PTB with pleural effusion or miliary TB means the person is in Clinical stage 4.

Clinical presentation

Typical presentation

The following symptoms usually occur in HIV-positive patients with **mild** immunodeficiency (high CD4 counts). They are similar to the TB symptoms experienced by HIV-negative patients with PTB:

- Chronic cough ≥ 2–3 weeks, not fully responding to antibiotics
- Recent unintentional weight loss (≥ 1.5kg within 4 weeks)
- Drenching night sweats
- Fever ≥ 2 weeks
- Chest pain > 14 days
- Loss of appetite and weight loss
- General weakness and tiredness

- Sometimes haemoptysis (flecks of blood in the sputum when coughing)
- Known TB contact

Atypical presentation

With more **advanced** immunodeficiency (low CD4 counts), the HIV-positive patient may present with different symptoms:

- General malaise and weakness
- "Looks really sick"
- Significant weight loss (> 10% of previous body weight)
- Less coughing, which tends to be a dry cough
- Shortness of breath
- Severe anaemia
- Disseminated TB and extra-pulmonary TB (meaning involvement of any organ outside of the lungs); adults and children with EPTB are in stage 4 of HIV infection (see Appendix 1 and 2). The exception is isolated lymph node TB which is only a stage 3 condition for a child.

Clinical Examination

Always perform a good physical examination to check for **pleural effusion** or **enlarged lymph nodes** (> 2 cm), which are both strongly suggestive of active TB. **If you see a patient with a large or chronically infected lymph node in the neck, armpits, or groin, which does not respond to antibiotics, this is probably TB!** A fine needle aspiration biopsy (FNAB) should be performed without delay (see Appendix 29).

Diagnosis of an HIV-infected person with symptoms of PTB

1. Send 2 sputum samples for TB diagnosis with Xpert MTB /Rif where available or smear. Make sure the patient provides sputum from the lungs, and not saliva from the mouth! Early morning sputum is best but if possible diagnosis should be made on the same day of presentation (see Appendix 20).
2. While waiting for the smear results, prescribe an antibiotic to cover for any bacterial cause of the chronic cough (Amoxicillin 500-1000 mg 3 times daily or erythromycin 500 mg 4 times daily if penicillin allergic). Note the patient's score on the Karnofsky performance scale (Appendix 16).
3. If the smear/ Xpert MTB Rif result is positive, start TB treatment.
4. If the smear/Xpert/ MTB Rif result is negative and the person still has symptoms of TB (despite the antibiotic), follow the **"Smear-negative or Xpert/MTB Rif algorithm"** (see **page 86**). Possible further investigations may include:
    - Chest x-ray

- One more sputum sample for TB culture. This results could take up to 6-10 weeks before coming back.
- A baseline haemoglobin can also be done. Patients with TB are often anaemic.
- Consider a needle biopsy of any enlarged lymph nodes.
- Consider a 'pleural tap' if a pleural effusion is present in order to exclude empyema.

5. If the chest x-ray and clinical picture are consistent with active TB, then the patient needs to be started on TB medication, and monitored.
6. Don't forget to start all TB patients on cotrimoxazole prophylaxis (Bactrim) to prevent other OIs!

GeneXpert MTB/RIF:

GeneXpert MTB/RIF is a new molecular diagnostic technique that detects the DNA of the Mycobacterium Tuberculosis bacteria in sputum samples. It has some advantages compared to smear:

- it is fully automated
- it has a higher sensitivity than smear: it will detect TB in smear negative samples. This reduces the need for CXR.
- it can detect Rifampicin resistance in less than 2 hours. For culture and drug sensitivity testing this can take up to 8 weeks.

Monitoring

While empiric TB treatment is being given, the patient must be monitored every 1–2 weeks for improvement.

Response to treatment is measured by the following:

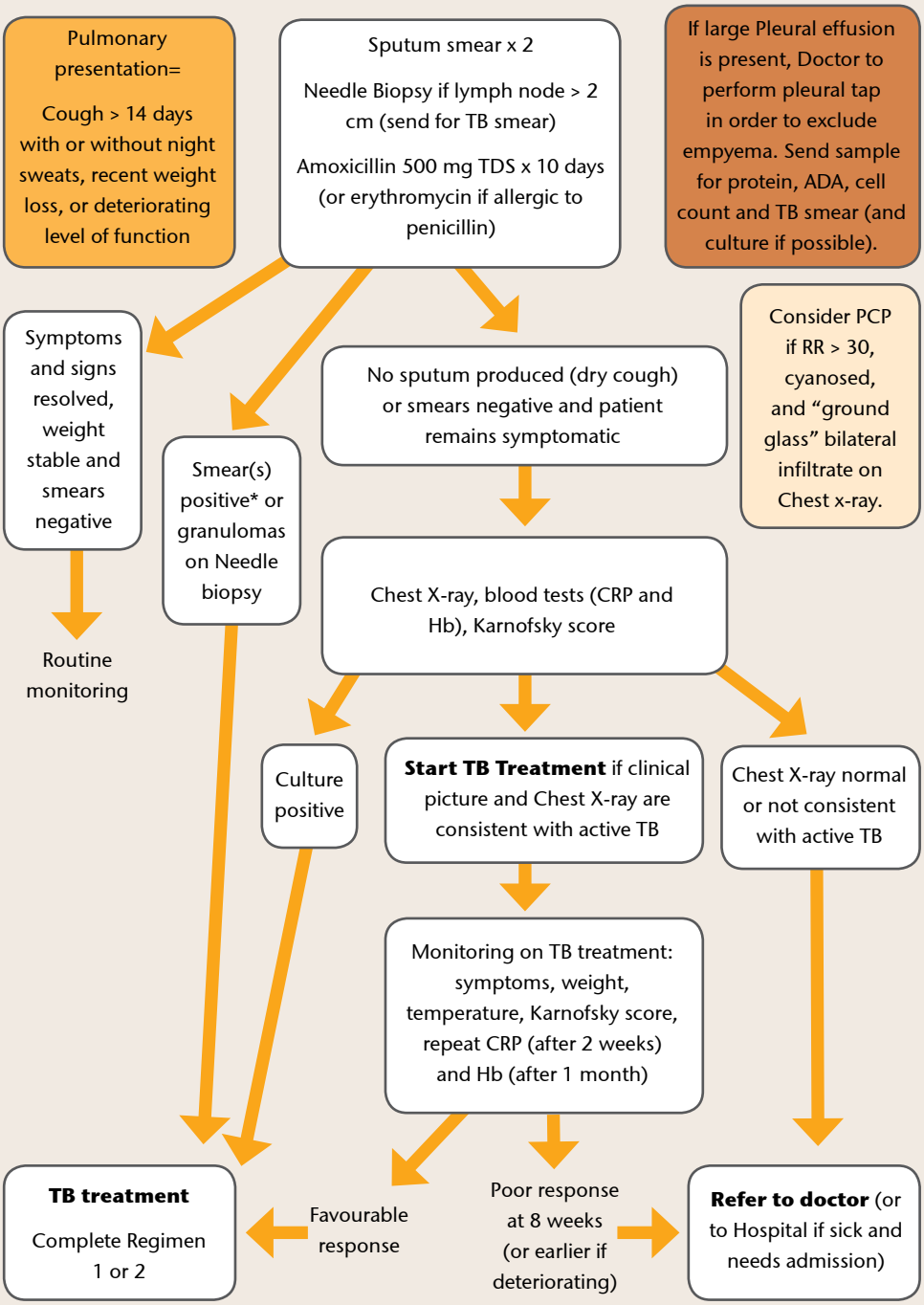
- Improvement of general condition (less sick?)
- Karnofsky performance score (see Appendix 16)
- Improvement of symptoms (cough, night sweats, and appetite)
- Weight gain (another reason to check weight **every** visit)

If the patient is not improving on empiric TB meds, then refer to the doctor for assessment. If the chest x-ray is not consistent with active TB, but the patient is still sick, that is another reason to refer.

NB: TB drugs interact with several other medications. Be particularly careful if the patient is also on warfarin, oral contraceptives, or antiretrovirals.

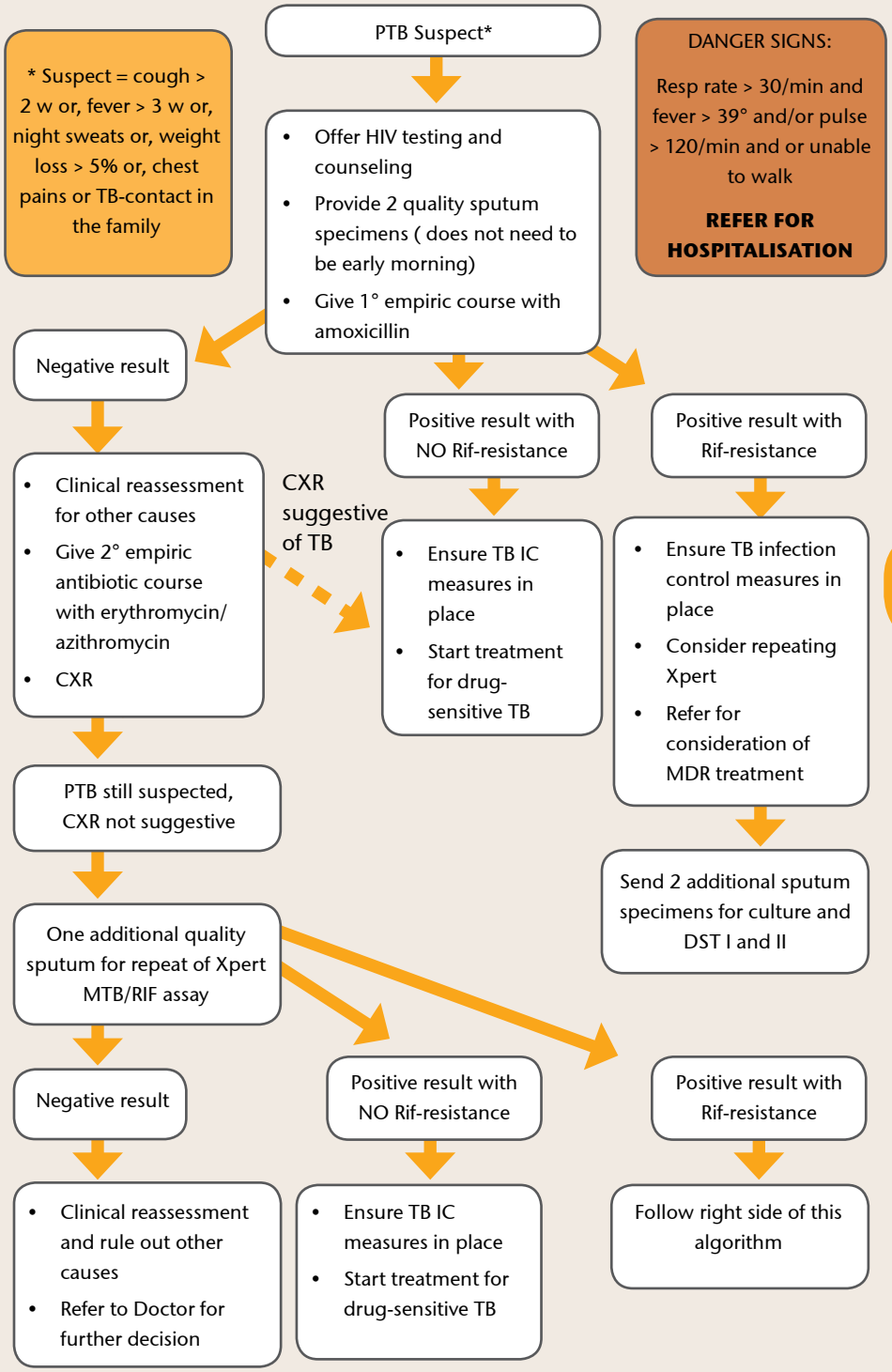
Algorithm 7a: Smear-negative Algorithm for management of HIV patients suspected of having TB (Pulmonary presentation with or without enlarged lymph nodes).

This algorithm to be used if Xpert MTB/Rif is not available for diagnosis.



Source: P Saranchuk, A Boulle, K Hilderbrand, D Coetzee, M Bedelu, G van Cutsem, G Meintjes. Evaluation of a diagnostic algorithm for smear-negative pulmonary tuberculosis in HIV-infected adults. *S Afr Med J* 2007; 97: 517-523.

Algorithm 7b: Diagnostic algorithm for use with Xpert MTB/Rif as first diagnostic tool.



TB Management

TB Treatment regimens

Treatment for TB is different for **new cases** and **retreatment cases**.

New cases are patients who never had TB before. They have to take TB treatment for 6 months, consisting of 2 months of intensive phase with four drugs rifampicin, isoniazid, pyrazinamide and ethambutol (RHZE) and 4 months of continuation phase with rifampicin and isoniazid (RH). Sputum needs to be checked at 2 and 5 months (in all cases of smear-positive PTB or smear-negative/culture-positive PTB).

Retreatment cases are patients who were treated for TB before. Their treatment lasts 8 months and consists of 2 months of RHZE plus streptomycin injections, 1 month of RHZE, and 5 months of RH plus ethambutol. Sputum needs to be checked at 3, 5 and 8 months (in all cases of smear-positive PTB or smear-negative/culture-positive PTB).

Table 3. Frequency of sputum smear/culture follow-up in patients with TB

	End of initial phase		**End of continuation phase**	
	New patient	Retreatment	New patient	Retreatment
Smear-positive PTB	7th week, 1 sputum for smear[1]	11th week, 1 sputum for smear[2]	5th month, 1 sputum for smear[3]	5th and 8th month, 1 sputum for smear[4]
Smear-negative, PTB	7th week, 1 sputum for smear[5]	11th week, 1 sputum for smear[5]	Monitor clinically only	7th month, 1 sputum for smear[4]

Notes:

1. If smear positive at end of month 2 change to continuation phase. Repeat smear at 11th week. If still positive send for culture and DST
2. If smear positive at end of month 3 start continuation phase but send sputum for culture and DST. Repeat smear at 15th week
3. If smear positive send for culture and DST. Register as treatment failure and commence on retreatment regimen
4. If smear positive send for culture and DST and discuss possible empiric MDR treatment with expert

[5] If sputum comes back positive: start continuation phase and send sputum for culture/DST. For further monitoring, cfr. national TB guidelines

Table 4. Regimen 1: New cases, age above 12 years

Pre-treatment weight	Intensive phase (2 months)	Continuation phase (4 months)	
	RHZE (150/75/400/275)	RH (150mg; 75mg)	RH (300mg; 150mg)
30–37kg	2 tablets daily	2 tablets daily	
38–54kg	3 tablets daily	3 tablets daily	
55–70kg	4 tablets daily	4 tablets daily	2 tablets daily
>71kg	5 tablets daily	5 tablets daily	2 tablets daily

Table 5. Regimen 2: Re-treatment cases, age above 12 years (If the facility is able to, streptomycin should be given at weekends too)

Patient's Weight	Intensive Phase (3 months) 2 RHZE S/ 1 RHZE daily (Isoniazid 75mg + Rifampicin 150mg + Pyrazinamide 400mg + Ethambutol 275mg)	Intensive Phase Streptomycin (IM) 2 months	Continuation Phase (5 months) 5 (HRE) daily (Isoniazid 75mg + Rifampicin 150mg + Ethambutol 275mg)
30–39kg	2	0.50g	2
40–54kg	3	0.75g	3
55–69kg	4	1g*	4
70kg+	5	1g*	5
*0.75g if 60 years or over.			

Streptomycin is contraindicated in: pregnant women, patients > 65 years and/or patients with pre-existing renal disease (unless the dosage is adapted to the CrCl of the patient).

Since Streptomycin and TDF can both cause renal toxicity, it is recommended that they **not** be given together. Discuss with doctor if a patient on TDF needs streptomycin.

Table 6a. New TB cases < 12 years old, CAT I: 2 RHZE 4 HR

Weight Band	Intensive Phase R 60 H 30 Z 150 + E 100 (2 months)	Continuation Phase R 60 H 30 (4 months)
≤ 7 kg	RHZ 1.5 + E 1	1.5
8–14 kg	RHZ 2 + E 2	2
15–19 kg	RHZ 3 + E 3	3
20–24 kg	RHZ 4 + E 4	4

(RHZ = Rifampicin Isoniazid Pyrazinamide)

Table 6b. Retreatment TB < 12 years, CAT II: 3 RHZE 5 RHE

Weight Band	Intensive Phase R 60 H 30 Z 150 + E 100 (3 months)	Continuation Phase R 60 H 30 + E 100 (5 months)
≤ 7 kg	RHZ 1.5 + E 1	RH 1.5 + E 1
8–9 kg	RHZ 2 + E 2	RH 2 + E 2
10–14 kg	RHZ 2 + E 2	RH 2 + E 2
15–19 kg	RHZ 3 + E 3	RH 3 + E 3
20–24 kg	RHZ 4 + E 4	RH 4 + E 4

For all patients receiving INH, give pyridoxine (vitamin B6) to avoid peripheral neuropathy:

- adults and children > 5 years: 25 mg OD
- children < 5 years: 12.5 mg OD
- For **treatment (not prevention) of peripheral neuropathy:** pyridoxine 50 mg once daily up to three times daily

TB treatment and ARVs

1. If an adult or child already on ARVs is diagnosed with TB:

   The ARV regimen may need to be modified according to the Table below.

Table 7. Changes to ARV regimen while on treatment for TB

Current regimen includes	Change drug to	Patient group
NVP	EFV	Non pregnant adults Pregnant women in 2nd or 3rd trimester Children > 3 years and > 10 kg
	Double dose LPV/r (see Appendix 7 and 8)	Pregnant women in 1st trimester
	LPV/r super-boosted with additional ritonavir (If LPV/r not available can use NVP up to dose of 200mg/m2 or a triple NRTI regimen) (see Appendices 8 and 9)	Children < 3 years or < 10 kg
LPV/r	Double dose of LPV/r (see Appendices 7 and 8)	Adults Older children (> 5 years)
	LPV/r boosted with additional ritonavir (see Appendices 8 and 9)	Children < 5 years (refer to doctor)
D4T	Consider change to TDF unless patient needs streptomycin or treatment for DR TB with Capreomycin.	Patients 12 years and over (provided CrCl > 50 and Viral load if available is undetectable)

Note: Continue double dose LPV/r (or additional ritonavir) for 2 weeks after stopping the rifampicin-containing TB regimen. Consider changing D4T to TDF to prevent peripheral neuropathy. Do not change D4T to TDF if patient is suspected of virological failure.

2. If TB infection is present before being assessed for ARVs:

   For the choice of ARV regimen, refer to Appendix 8 (adults) and 9 (children). See below for the timing of ARV initiation if TB is present before being assessed for ARVs.

Adults

Table 8: Timing of ARV initiation after the start of treatment for TB

Clinical Situation	Timing of ARV initiation after the start of TB treatment
All cases of MDR/XDR TB	2 weeks
Pregnant women	Initiate within 2–4 weeks (2 weeks if CD4 < 50). If clinically stable, try to wait until the end of the 1st trimester (then initiate with EFV).
All PTB and TB CD4 < 50	Start within 2 weeks of commencing TB treatment.
All PTB and TB CD4 > 50	Start ART within 2–8 weeks of commencing TB treatment.

Children

- All children with TB meet criteria for ART
- Begin ART as soon as TB drugs are tolerated (2–8 weeks into treatment) irrespective of CD4 count and clinical stage. Start after 2 weeks in case of MDR/XDR TB, or a very low CD4 (ie < 5–10 %)
- If the child with lymph node or pulmonary TB is relatively well, and has a high CD4 count (> 25 %), delaying ART initiation beyond 8 weeks may be considered to avoid a high pill burden and potential drug interactions, provided the child is closely monitored. Discuss with doctor.

3. If TB treatment and ARVs are being taken at the same time
    - Make sure that NVP is changed to EFV, or the LPV/r dose is doubled (or super-boosted with additional ritonavir). This should be continued until 2 weeks after the completion of treatment for TB.
    - Monitor for drug interactions
    - Monitor for side effects, especially hepatitis
    - Refer to the doctor if either is suspected
    - Since the patient will be taking a large number of tablets, ensure adequate counseling is done in order to maintain adherence

Special considerations for TB/HIV co-infected children

Active screening

Active screening for TB in children is essential:

- Always ask about contact with an adult with Pulmonary TB
- Common presenting symptoms
  - Persistent cough >14 days
  - Fever > 38 ^{0}C for over 1 week (after excluding other causes of fever)
  - Weight loss (don't forget to look at the "Road to Health card"!)
  - Unusual fatigue
- A visible mass in the neck, not responding to a course of antibiotics and without a visible local cause probably represents lymph node TB

Diagnosis

Diagnosis of TB in children is difficult, especially in the HIV positive child. Other pulmonary conditions may present with symptoms similar to TB (LIP, bacterial pneumonia, fungal pneumonia, etc). Also, if the child is able to produce sputum, it is often paucibacillary (with few germs) so sputum smears are often negative. So, we need to use many pieces of information to make the diagnosis of TB in a child: contact history and clinical presentation are most important. Other investigations may also help: a child over 5 years is generally old enough to try to produce sputum; induced sputum (preferred) or gastric aspirate could help in the younger child. Depending on local resources, CXR, TB skin testing and fine needle aspirate (FNA) of large lymph nodes should be done.

Induced sputum or gastric aspirates help increase the yield of sputum production (see below) in facilities where there are trained staff to do these.

A swelling (raised, thickened area) with a diameter of 5mm or more on a **TB skin test** in an HIV positive child is a positive test, and tells us that the child has been infected with TB. It does not necessarily mean that the child has active TB disease. However, this test result is another clue that we can use to help us make the diagnosis. **Remember, though, that a negative test does not exclude TB.**

CXRs are hard to interpret in the HIV positive child, and can be normal in up to 1/3 of HIV-infected children with active TB. The eye of an experienced clinician is often needed to make a diagnosis and TB should not be diagnosed from the CXR alone. The most common feature on x-ray is hilar lymphadenopathy. Other features may also be present, including: alveolar consolidation, cavitation or miliary pattern.

Note: a miliary pattern in a non-sick looking child most likely means the child has lymphoid interstitial pneumonia (LIP), not TB.

Fine needle aspirate of lymph nodes >= 1 cm should be done when indicated. This is then mounted on a slide and sent for microscopy; AFB or granulomas can be diagnostic.

To improve yield of sputum production, one can use one of the following (in facilities where conditions allow):

- Induced sputum collection- first give a bronchodilator (inhalant 200mcg) then nebulize with hypertonic saline using an ultrasonic nebulizer. An older child can then expectorate the sputum but if unable, suctioning the pharynx also has a good yield. Send for microscopy and culture.
- Gastric washing or gastric aspirates are well used procedures. Requires the child to fast over night. Send for microscopy and culture.

REMEMBER

Remember to keep a high index of suspicion for TB in a child. In other words, if you think the child might have TB, he/she should be investigated further. If CXRs are not available, and the child has chronic symptoms and a known TB contact, refer him/her for TB treatment (sputum collection should be attempted whenever possible). If the HIV positive child has persistent symptoms after a course of antibiotics, refer him/her to the doctor for further evaluation, even if there is no known history of contact and/or TB skin test is negative.

Management:

- Management of TB is the same as for HIV-negative children.
- Children with EPTB may require prolonged treatment of at least 9 months and 4 drugs (including ethambutol) during the intensive phase of treatment.
- In-patient management should be considered for children that are severely affected.
- Nutritional support is very important especially if the child is malnourished
- The child needs CTX prophylaxis and enrolment for ARVs (see **page 92** for timing of ART initiation).
- Pyridoxine: give 12.5 mg daily for those < 5 years, and 25 mg daily for those > 5 years.

REMEMBER **If the child's symptoms worsen despite adequate therapy, the most important questions to ask are:**

- Is the drug dosage correct?
- Is the child adherent?
- Was the child severely malnourished?
- Is there a reason to suspect drug resistant TB (index case has known drug resistant TB, is a relapse case, or is also not responding to therapy)?
- Has the child developed IRIS (if on ARVs)?
- Is there another reason for the child's illness, other than or in addition to TB?

Refer for assessment

REFER

Danger signs requiring urgent hospital referral

- **Severe respiratory distress (TB pneumonia with/without bacterial super infection)**
- **Severe wheezing not responding to bronchodilators (signs of severe airway compression)**
- **Headache (especially if accompanied by vomiting), irritability, drowsiness, neck stiffness and convulsions (signs of TB meningitis)**
- **Big liver and spleen (signs of disseminated TB)**
- **Breathlessness and peripheral oedema (signs of pericardial effusion, 'fluid around the heart')**
- **Distended abdomen with ascites (signs of abdominal TB)**
- **Acute angulation (bending) of the spine (sign of TB in the spine)**

Prevention of TB

INH preventive therapy in the adult

TB can be prevented in HIV-positive patients, especially if there has been recent close contact with someone else coughing with active TB. This is done by prescribing a single TB medication called Isoniazid (INH). For the duration and dose of INH refer to national guidelines.

Before using INH, we must be certain that the person does not have active TB. Or else we may be making things worse, as giving INH monotherapy to a person with active TB would promote resistance of the TB organism against INH!

Of note healthcare workers are a subgroup of adults, where WHO strongly recommends INH preventive therapy.

INH preventive therapy in the child

- Guidelines state that INH prophylaxis may be provided for children with the following criteria:
  - Children under 5 years of age who are household contacts of smear-positive TB patients.
  - Infants and young children with latent M. tuberculosis infection (Mantoux positive) who are at high risk of rapidly developing disease: eg. HIV-infected or malnourished children.

- Infants 2 years of age or younger who are at particularly high risk of developing life-threatening tuberculous meningitis or miliary tuberculosis: e.g. HIV-infected or malnourished children.

- The following criteria exclude a patient from consideration for IPT:
  - Signs and symptoms of TB, i.e., patients who are currently ill with new or worsening cough or sputum production, haemoptysis, night sweats, fever, or measured weight loss of more than 5%
  - Abnormal chest X-ray (even if TB has not been confirmed)
  - Poor prognosis (terminal AIDS)
  - Presence of jaundice or active hepatitis (acute or chronic)
  - Has had TB treatment in the past 2 years
- Children on INH prophylaxis should receive pyridoxine to avoid PN (> 5 years 25mg OD; < 5 years 12.5mg OD)
- The dose of INH for preventive therapy is 10 mg/kg/day for 6 months (see table 9 below)

Table 9. Dosage recommendations for INH preventive therapy in children

Body weight	Daily isoniazid (INH) 100 mg tablet
2–3.4 kg	One quarter of tablet
3.5–6.9 kg	One half tablet
7–9.9 kg	1 tab
10–14.9 kg	1 tab and one quarter
15–19.9 kg	1 tab and one half
20–24.9 kg	2 tabs
25–29.9 kg	2 tabs and one half
≥ 30 kg	3 tabs

TB infection control refers to what can be done to reduce the transmission of TB. Remember that everyone is responsible for TB infection control!

1. Administrative controls. These are the most important and include:

- Prompt identification of infectious TB cases
- Physical separation of patients known or suspected of having TB
- Cough triage
- Fast track for coughing patients
- Coughing patients to wear surgical masks
- Patients to be instructed about cough hygiene
- Infection Control policy and Infection Control Committee to be put in place
- Infection Control risk assessment in all health care facilities to be undertaken

2. Environmental controls

- Maximize natural ventilation
- Avoid being downwind from a patient
- Maximize the amount of natural light in a room.
- In low resource settings mechanical ventilation and UV lamps are not a priority.

3. Personal respiratory protection
    - Patients to wear surgical masks
    - If available staff to wear N95 masks

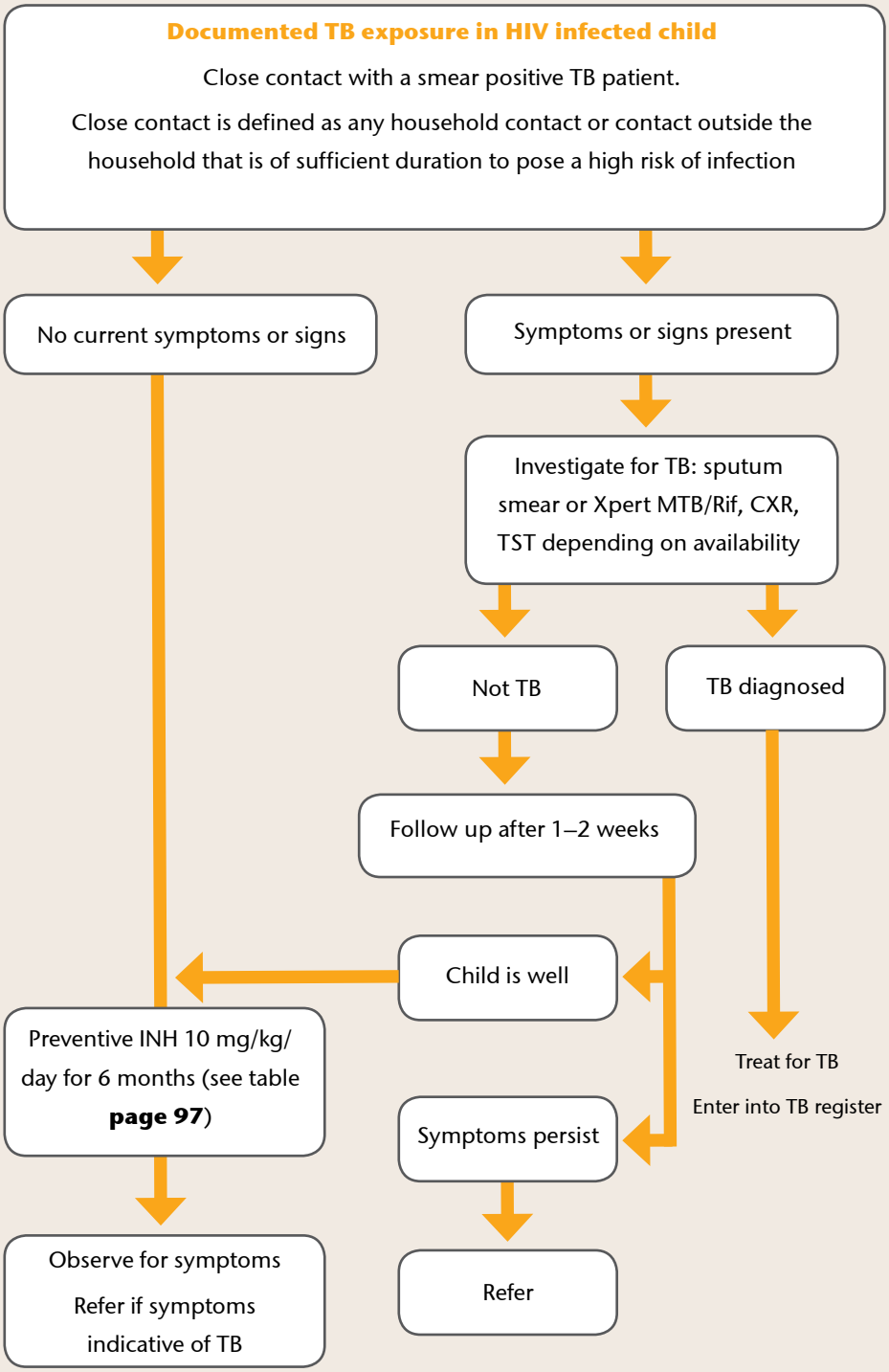
(If a patient is infected with MDR, sleeping in a separate room is advised for the first 2 months of treatment.)

REMEMBER

The "three Is" to reduce the burden of TB among people living with HIV:

1. Intensified case finding for TB
2. Isoniazid preventive therapy
3. Infection control

Algorithm 8: Screening of an HIV infected child with documented TB exposure



Drug Resistant Tuberculosis (DR TB)

If someone on TB treatment has been adherent to their treatment but is not improving, the first diagnosis to think of and to rule out is **Drug Resistant TB.**

Classification of drug resistant TB

Drug resistant TB is classified into 4 categories:

1. Mono Resistant: Resistance to **one** of the first line drugs: Ethambutol (E), Rifampicin* (R), Isoniazid (H), Pyrazinamide (Z)
2. Poly Resistant: Resistance to **two or more** of first line drugs but not R and H together (see next definition)
3. MDR: Resistance to at least R **and** H
4. XDR: Resistance to **R, H and** one or more of the injectable drugs (**capreomycin, kanamycin, amikacin**) and any of the fluoroquinolones (e.g. **ofloxacin**)

During the rest of this section, we will simply talk about drug resistant TB (DR TB) by which we mean at least rifampicin resistance.

Clinical presentation

What are the symptoms of DR TB?

The symptoms of DR TB are the same as those of Drug Sensitive TB (DS TB).

Patients may present with cough, weight loss, fatigue, night sweats, chest pain and/or more atypical symptoms if they are HIV +ve with advanced immunodeficiency.

Who gets DR TB?

Transmission of DR TB is the same as drug sensitive TB. Anyone can get DR TB but certain people are more at risk. Those at increased risk of getting DR TB include:

- Contact of someone with DR TB.
- Those with a history of TB drug use:
  - Relapse
  - Return after default
  - Failure of treatment (greatest risk)
  - History of using poor or unknown quality of drugs
  - History of other medications that interfere with TB drug absorption.
- HIV (increase risk for all TB) and other chronic diseases such as diabetes mellitus.
- Health Care Workers, laboratory workers, prisoners and prison guards, miners.

* Note that Rifampicin mono-resistance is treated similarly to a case of MDR TB

Assessing the patient for DR TB

It is important to ask the patient about previous episodes of TB and if they completed treatment or defaulted. It is also important to know if they have a history of exposure to DR TB or any chronic conditions such as HIV infection, diabetes mellitus, renal disease, malignancies or chronic malabsorption syndrome.

Infection control at the home of the patient along with the patient's psychosocial context need a detailed initial assessment.

How do we diagnose DR TB?

DR TB is a laboratory diagnosis, however it is often suspected clinically. When a patient is suspected of DR TB, sputum is sent for smear, culture and drug sensitivity testing (DST). It is very important that the patient is instructed on how to give a good sputum specimen; otherwise you may just be submitting saliva to the laboratory. (See Appendix 20 for instructions on obtaining a sputum sample).

Smear

Smear microscopy cannot distinguish between drug sensitive or drug resistant TB, however it can evaluate the infectiousness of the patient. It is generally agreed upon that patients who are smear positive are more infectious than patients who are smear negative. However, one needs to remember that smear negative patients may also be infectious and transmit TB.

GeneXpert MTB/RIF

GeneXpert MTB/RIF can detect Rifampicin resistance within 2 hours. If GeneXpert detects Rifampicin resistance, there is a 90% chance of resistance to INH as well. So the probability of MDR is 90%. If Rifampicin resistance is detected, this must be confirmed by DST.

Culture

It takes many weeks to culture the TB mycobacterium, sometimes months. During this time if the patient is deteriorating clinically, refer to the doctor for further evaluation and management.

Drug Sensitivity Testing (DST)

DST is a laboratory test that identifies the TB drugs that the mycobacterium is sensitive and/or resistant to. If 1st line DST is requested, the laboratory will test resistance to Rifampicin and Isoniazid. If Rifampicin resistance is diagnosed, the laboratory will test for resistance to: ethambutol, ofloxacin, ethionamide, and

Amikacin. DST results to these drugs may take up to 2 months to be reported. (NHLS states 100% cross-resistance between Kanamycin and Amikacin).

Whose sputum do we send for culture and DST (or for Xpert MTB/Rif where Xpert is not the first test available)?

- All re-treatment TB cases
- Patients on TB treatment who remain sputum smear positive after 3 months (new cases) or three months (re treatment cases) of first line treatment.
- Symptomatic close contacts of confirmed DR TB cases.
- Symptomatic individuals from known high risk groups, including health care workers, laboratory workers, prisoners, miners.

Management of DR TB

An empiric regimen for treating DR TB is 8 months of Kanamycin, pyrazinamide, levofloxacin, cycloserine,protionomide and followed by 18 months of pyrazinamide, levofloxacin, cycloserine, protionamide.

The two phases of treatment are called the intensive phase (8 months) and the continuation phase which last for a minimum of 18 months. For XDR, duration/ termination of treatment is assessed on a case by case basis. (See Appendix 22 for building a treatment regimen).

If a patient is MDR/HIV co-infected, then Tenofovir is to be avoided to avoid the overlapping nephrotoxicity of Tenofovir and the injectable MDR drugs.

Hospitalization vs. Treatment at the clinics for DR TB?

Ideally patients should receive ambulatory DRTB care. If the patient is very ill or if there are significant psychosocial difficulties they may require initial admission. Infection control measures for MDR should be employed at the admitting site.

The basic principles of treatment are:

- Include first-line drugs to which infecting strain is susceptible
- Include a minimum of **four drugs, preferably five to six**.
- Do not rely on drugs to which resistance is suspected (i.e. if a patient was taking Z and failed SCC (smear and culture positive) then the mycobacterium may be resistant to Z.
- EPTB DR TB is treated using the same strategies and duration of time as DR PTB.

Monitoring of DR TB?

Patients on treatment for DR TB need to be monitored carefully. This is crucial to their outcomes. Drugs for resistant TB are hard to take and can cause many minor and life threatening side effects. It is the responsibility of the HCW to be aware of the side effects of these drugs and monitor their patients appropriately. (See Appendix 23 for a step-by-step approach to managing DR TB clients).

It is also important to monitor patients for the further development of drug resistance, hence the routine monthly monitoring of sputum with smear and culture (and DST if culture remains positive after 4 months of treatment or becomes positive again after conversion).

REMEMBER **Side effects of MDR drugs are more frequent and more severe than with CAT I TB drugs. Early recognition and agressive management of all adverse effects is essential, whether they are minor (non life threatening) or major (life threatening).**

Contact Tracing

All household contacts and persons spending many hours a day with the patient in the same indoor space of DR TB patients are at risk for developing DR TB.

Asymptomatic adult contacts

WHO does not recommend universal use of second-line drugs for preventive therapy in DR TB contacts. Asymptomatic contacts should be advised that they have been exposed to DR TB, advised of the symptoms of TB and, if they develop any TB symptoms, they must go to their clinic and report that they are a DR TB contact. By doing this, they will be investigated for DR TB with smear, culture and DST.

Symptomatic adult contacts

Symptomatic contacts should be screened for DR TB, with smear or Xpert MTB/Rif if available, culture and DST

Paediatric contacts

All paediatric contacts should be evaluated for active TB. This includes:

- History of Symptoms: Symptoms of TB in children can be non-specific, e.g. chronic cough or wheeze, failure to thrive and recurrent fevers.
- Signs of TB on examination e.g. enlarged lymph node, pleural effusion, ascites, respiratory signs

Symptomatic paediatric household contacts of DR TB should be referred to the TB doctor and receive:

1. Clinical examination including weight gain, lymphadenopathy, respiratory signs, etc.
2. Tuberculin skin testing (TST) if available
3. Chest x-ray (Antero-posterior and Lateral)
4. Culture and DST: If the child is very young or cannot expectorate sputum, sputum induction or gastric aspiration should be performed.

Asymptomatic paediatric contacts < 5 years and HIV infected children of any age are to have a TST if available and CXR and be referred to the TB doctor.

REMEMBER **All MDR/XDR TB/HIV co-infected persons should be initiated on ARVs after 2 weeks, no matter the CD4 level.**

Bacterial pneumonia

The most common causative agents for bacterial pneumonia include *Streptococcus pneumoniae* and *Haemophilus influenza*. *Staphylococcus aureus* and gram negative bacteria are less commonly involved. *Pseudomonas aeruginosa* ("sweet smell") is an nosocomial (hospital acquired) infection.

Pneumonia can happen to anyone regardless of HIV status. But those infected with HIV are more likely to suffer from pneumonia (as well as all other infections found frequently in the general population).

Bacterial pneumonia is a rare disease in adults below the age of 40; its occurrence suggests that a person unaware of her/his HIV status might be positive.

Clinical presentation

Typically presents more acutely than TB, with:

- Productive cough, often with yellow or greenish sputum
- High temperature
- Unilateral chest pain
- Localized crepitations on auscultation

Management

- Amoxicillin 500–1000 mg three times daily for 7–10 days or Erythromycin 500 mg four times daily for 7–10 days (if allergic to Penicillin).

Children

Bacterial pneumonia is very common in young children, and even more so in those HIV infected. A child can die from bacterial pneumonia even after ARVs have been started, so you must be vigilant. Use IMCI guidelines to classify pneumonia into simple or severe.

Simple pneumonia

- Fast breathing without chest indrawing or stridor when calm and without any general danger signs (see 'severe pneumonia')
- Treat with Amoxicillin 25 mg/kg/dose three times daily for 7 days
- Follow up within 2 days of starting antibiotics

REMEMBER **Tachypnea (fast breathing) in children is defined as:**

- 60 breaths or more per minute in children < 2 months
- 50 or more in children 2–11 months
- 40 or more in children 12 months–5 years

The respiratory rate should be measured during 1 full minute in young children

Table 10. Amoxicillin dose in children

Given three times a day					
Weight (kg)	**Dose (mg)**	**Syrup 125mg/ 5 ml**	**Syrup 250mg/ 5 ml**	**Capsule: 250mg**	**Age**
3.5–4.9	125	5 ml	2.5 ml		1–2 months
5–6.9	175	7 ml	3.5 ml		3–5 mos
7–10.9	250	10 ml	5 ml	1 caps	6–17 mos
11–13.9	375	15 ml	7,5 ml		18 mos–2 yrs
14–24.9	500	20 ml	10 ml	2 caps	3–6 yrs
25–34.9	750			3 caps	7–10 yrs
≥ 35	1000				≥ 11 yrs

Severe pneumonia

- If a child presents with chest indrawing or stridor when calm or any general danger sign (breathing ≥ 60 breaths per minute in a child less than 2 months, difficulty feeding, convulsions, lethargy, or central cyanosis) he must be referred urgently to the hospital.
- Prior to hospital referral, give the child a first dose of IM Ceftriaxone (75 mg/kg OD). Administer oxygen at 1 L/min and check for hypoglycemia.
  - 3–5 kg: Ceftriaxone 250 mg (1ml)
  - 6–9 kg: 500 mg (2 ml)
  - 10–14 kg: 750 mg (3 ml)
  - 15–25 kg: 1 g (2 ml in each thigh)
- If very severe pneumonia: add Erythromycin 50 mg/kg/day in 2 divided doses to the treatment.
- If Ceftriaxone is unavailable, give Penicillin G IV 50 000 units/kg/dose 6 hourly for 2 days minimum, followed by an oral antibiotic. This needs to be prescribed by a doctor and the first dose monitored closely in case the patient has an allergic reaction.
- For HIV exposed or infected children < 1 year, initiate therapy with high-dose CTX in addition to the treatment described above, since PCP cannot be excluded (and is rapidly fatal if untreated). Continue for 21 days. Severely immuno-depressed children over 1 year who are not on CTX prophylaxis should also be treated for PCP and bacterial pneumonia.
- Total intravenous and oral therapy for treatment of severe bacterial pneumonia is typically 10-14 days.

Pneumocystis jiroveci Pneumonia (PCP)

An opportunistic lung infection caused by the organism Pneumocystis jiroveci. Think of PCP if the chief complaint is progressive **shortness of breath** rather than coughing. The HIV client with CD4 ≤200 is at risk.

Clinical presentation

- **Dyspnoea (shortness of breath)** caused by hypoxemia (low oxygen) is the main symptom. Initially this occurs only on exertion, but later also at rest. The patient can progress to severe dyspnoea quite quickly.
- Tachypnoea (fast breathing)
- Nasal flaring
- Non-productive or “dry” cough which is chronic over several weeks

- Fever is not always present, but when present can be very high.
- Chest X-ray is often **non-specific** (but may show "ground-glass" infiltrate).

Management

If not very hypoxic or dyspnoeic, and strong clinical presumption:

- **High-dose** cotrimoxazole (CTX): dose based on weight: 100 + 20 mg/kg per day in divided doses; typical dose is 4 single-strength tablets every 8 hours for 21 days (adult > 56 kg).
- In patients with an **allergy** to CTX, Dapsone 100 mg/day + trimethoprim 300 mg/day or clindamycin 600mg qid + primaquine 15-30mg od for 14 days may be used.
- Add Prednisone 80 mg/day for 5 days, then 40 mg/day for 5 days, and then taper until discontinued.
- Give Folic acid 5 mg daily whenever a person is taking high-dose cotrimoxazole since CTX depletes the body of folic acid.
- Anticipate CTX-associated rash which is very common. In case of rash, refer!
- See the patient at least **twice per week.**

If severely hypoxic/dyspnoeic or if not responding:

- Refer immediately to hospital since there is a risk of respiratory failure.
- After three weeks of treatment with high-dose cotrimoxazole, don't forget to continue giving a preventive dose of cotrimoxazole (960mg i.e. 2 single-strength tablets), or the PCP can recur. See Table 2 on **page 21** for further details.
- **An adult or child who has suffered from PCP is in the final clinical stage of HIV infection and must be enrolled for ARVs as soon as possible!**

Children

Clinical presentation

- PCP is common in HIV infected children less than 1 year
- In older children, it is seen mainly in severely immune-compromised children not on prophylaxis.
- Present with:
  - Tachypnoea (50 or more breaths per minute in infants 2–11 months, 40 or more in children 12 months to 5 years)

- Dyspnoea, severe difficulty in breathing
- Cyanosis
- Sudden onset of fever (not always present); may be apyrexial (without fever) or have low grade temperature.

- Chest auscultation is less specific and important compared to the degree of respiratory distress. On chest x-ray one might see a diffuse interstitial infiltrate.
- PCP is frequently seen in children who are not taking cotrimoxazole prophylaxis, but being on cotrimoxazole prophylaxis does not exclude the diagnosis, especially in an infant, or a child with low CD4.

Management

- Refer for inpatient management
- Cotrimoxazole 100 + 20 mg/kg/day given three or four times a day for 21 days. Give first dose prior to referral. In hospital, administer CTX intravenously four times a day. In the ambulatory setting, CTX can be administered orally three times daily if this makes adherence easier for the caretaker.
- Treatment with cotrimoxazole can be given in addition to the usual treatment for pneumonia (i.e. amoxicillin).
- In severe cases: add prednisolone 1mg/kg/dose twice daily for 5 days, then 1 mg/kg/dose once daily for 5 days, then 0.5 mg/kg/dose once daily for 5 days
- Cotrimoxazole prophylaxis after completion of treatment (see Table 17 on **page 158**)
- If the child is allergic to cotrimoxazole, dapsone 2 mg/kg/day can be given for partial prophylaxis.

Table 11: High dose CTX (for PCP treatment only)

	Dose given 4 times a day		Dose given 3 times a day	
Weight (kg)	**Syrup (200 + 40 mg/5 ml)**	**480 mg tab**	**Syrup (200 + 40 mg/5 ml)**	**480 mg tab**
Less than 5	2,5 ml		4 ml	
5–9,9	5 ml		7 ml	
10–14,9	7,5 ml		10 ml	1 tab
15–21,9	10 ml	1 tab	15 ml	1½ tab
> 22	15 ml	1½ tab		2 tabs

REFER

- **PCP is often *fatal* unless treated early.**
- **It is *preventable* with cotrimoxazole.**
- **Remember to start the HIV exposed infant on cotrimoxazole starting at 6 weeks of age, since PCP often occurs *early*!**
- **Must keep a high index of suspicion and initiate *immediate treatment* along with usual treatment for pneumonia and refer for in hospital management.**
- **Enrol for ARVs!**

Lymphoid interstitial pneumonia (LIP)

LIP is not an opportunistic infection; it is a chronic condition of the lungs of unknown cause that occurs in HIV infected children. It indicates stage 3 disease.

Clinical presentation

- It is often asymptomatic but at times presents with symptoms
- It is important to recognize this condition because the clinical picture (chronic cough) and chest X-ray (miliary appearance) can easily be mistaken for TB.
- Signs to look for in a child with LIP are: **enlargement of the parotid glands** and **clubbing of the digits**.
- Remember: A child can have both TB and LIP! So making a diagnosis of LIP does not mean that you have excluded the diagnosis of TB! In general, it is helpful to remember that a child with LIP will not be very sick unless he/she has severe progressive LIP (usually this is seen in a child who is not on ARVs).

Management

- LIP improves with ARVs.
- Specific treatment (including oral steroids) is needed only in severe progressive cases (Oxygen saturation consistently < 92% and/or those developing signs of right sided heart failure).
- If febrile or acutely symptomatic, give Amoxicillin 25 mg/kg/dose TDS for 10–14 days (to treat bacterial super-infection)
- If remains symptomatic after multiple courses of antibiotics, rule out TB, then consider prolonged course with oral steroids: prednisolone 1–2 mg/kg/day for 2–6 weeks, then taper. Refer to doctor.

Pulmonary Kaposi sarcoma (KS)

Pulmonary Kaposi sarcoma is a serious diagnosis with a bad prognosis, even in patients on ARVs.

Clinical presentation

- Suspect pulmonary KS whenever a patient with cutaneous or oral KS lesions is having lung symptoms. Pulmonary KS can however occur when cutaneous lesions are absent.
- Pulmonary KS may imitate TB or PCP.
- Pleural effusion is common.
- Chest X-ray is non-specific.

Management

- We still have to rule out PTB in patients with cutaneous or oral lesions who are coughing! Arrange for sputum samples, CXR, and pleural tap if effusion is present.
- If no TB, refer for bronchoscopy and biopsy if possible. Ideally, these patients require chemotherapy at a referral hospital.
- At primary health care level, the management consists of symptom relief:
  - Nebulisation with Sodium Chloride (Na Cl) 0.9% solution;
  - Consider analgesics according to severity of pain (see 'Management of Pain' chapter on **page 185**).
  - Avoid steroid use in those with KS (also avoid steroid use in those with HSV)!

Test yourself

- A 25 year old male with a CD4 count of 120 had all his counseling sessions and is now ready to start ARVs. During TB screening he had the following symptoms; Coughing > 2 weeks, Night sweats and fever, Loss of appetite and weight loss
    - What is your management of the client?

.....

    - If TB is confirmed and TB treatment has been started when should you start ARVs?

.....

- You receive the smear results from a TB suspect you saw last week. The results come back negative but the patient is still coughing and having sweats despite taking antibiotics for the last week. What do you do?

.....

- Name the drugs given for CAT 1 treatment and for what duration the drugs are given for?

.....

- Name 3 possible side effects seen with CAT 1 treatment.

.....

.....

.....

- When are monitoring sputums to be sent for CAT 1 and CAT 2 patients ?

.....

.....

- Which patients should have sputum sent for TB culture and possible drug sensitivity testing?

.....

- What are the three key components of infection control?

.....

.....

.....

- What are the four classifications of drug resistant TB?

- List 3 clinical signs typical of PCP, describe the typical CXR presentation and what treatment should be given

Notes

Neurological Conditions

(Brain, spinal cord, and nerve)

Peripheral neuropathy (PN)

Peripheral neuropathy is a frequent problem affecting HIV-positive individuals and it can have many different causes. It can be associated with HIV infection itself. It can also be a result of vitamin deficiencies (Pyridoxine = vitamin B_6). Peripheral neuropathy can be a side effect of different drugs, including TB drugs (INH) or ARVs (d4T or ddI). Alcohol abuse can also contribute to PN. Drug related neuropathies usually present after the first month of treatment.

Clinical presentation

- Disturbance of sensation in 'glove and stocking distribution' (hands and feet), although feet symptoms are most common (especially the soles)
- Presenting as 'pins and needles', or a burning sensation
- Also described as "cold feet" at night and cramps, mainly in the legs
- Present in one third of patients with CD4 < 200

Prevention of PN

- Try to prevent PN by ensuring that Pyridoxine is always given together with INH
- If an adult (15 years or older) on D4T needs TB treatment, consider changing D4T to TDF (provided CrCl > 50 ml/min). Do not change to TDF if patient needs streptomycin, treatment for DR TB with amikacin or capreomycin, or if there is any suspicion of virological failure.

General management of PN

- Verify symmetrical symptoms. Refer same week to doctor if neuropathy is asymmetrical, associated with other neurological signs or loss of function.
- If an adult is on D4T and develops symptoms of PN, no matter the severity, change D4T to TDF (provided CrCl >50ml/min and if available viral load is undetectable). For the child, change D4T to AZT.
- If the PN is severe, think about checking the lactate level (since PN can be associated with mitochondrial toxicity).
- If the patient is on DDI and develops PN, initiate specific treatment and refer to doctor. (Consider replacing AZT+ddI with TDF+3TC)
- Make sure there is no high alcohol consumption

- Treat according to severity and review after 2 weeks
- If improvement, continue specific treatment
- If no improvement and client not on ARVs, reassess clinical stage, and refer for stronger analgesia and assessment for ARVs. HIV neuropathy is common in advanced HIV.

Management if on TB treatment

- Try to prevent PN by ensuring that Pyridoxine is always given together with INH.
- Pyridoxine (used to both **prevent and treat** PN):
  - Start at 50 mg once daily (at night)
  - Increase pyridoxine up to 150 mg orally once daily if necessary
  - If improvement: Continue pyridoxine until TB treatment is completed.
- If an ARV drug is the culprit, try to change to a new ARV (for example, switch d4T to TDF provided CrCl >50ml/min and if available viral load is undetecable).
- Amitriptyline 25–100 mg at night (if PN is **moderate-severe**). Start with 25 mg at night and increase progressively by 25 mg up to max 100 mg if necessary.
- Always associate amitriptyline with analgesics
- Analgesics:
  - Paracetamol 500–1000 mg four times daily as required, or,
  - Ibuprofen 200–400 mg three times daily as required, or
  - Paracetamol + codeine 1–2 tablets four times daily as required (only if PN is moderate-severe)

Children

- PN is less common in children than in adults but to diagnose peripheral neuropathy (PN) in children is not an easy task. The child sometimes complains of pain in the legs, or refuses to walk.
- The child needs to be referred to a doctor, who will assess motor function against milestones. This would give an indication if the child has PN.
- Prevention of PN in a child on TB treatment
  - Pyridoxine: < 5 years 12.5 mg OD; > 5 years 25 mg OD
- Dosages for treatment:
  - Pyridoxine: < 5 years: 25 mg/day; > 5 years: 50 mg/day
  - Amitriptyline: 6-12 years: 10 mg – 25 mg at bedtime; over 12 years: 25 mg-50 mg plus paracetamol 20 mg/kg three to four times/day
- If the child is on D4T and is assessed as having PN (no matter the severity), change D4T to AZT.

Bacterial meningitis

A bacterial infection causing acute inflammation of the "meninges" (or coverings) of the brain and spinal cord (especially *Neisseria meningitidis* and *Streptococcus pneumoniae*).

Clinical presentation (also see Algorithm 2 on page 33)

Bacterial meningitis is characterised by the following acute symptoms:

- High temperature
- Headache not responding to analgesics
- Vomiting
- Photophobia
- Sometimes a decreased level of consciousness

On physical exam, don't miss:

- Neck stiffness (but not always present!)
- Kernig's (pain in the lower back when the knee is extended with the patient supine and the thigh flexed at the hip) and Brudzinski's (flexion of the hips when the neck is flexed with the patient supine) signs, and
- Petechial rash on the body

Management

A **lumbar puncture** (LP) must be performed as soon as possible at the hospital and the fluid sent for different investigations. Start empiric treatment with an intravenous antibiotic such as Ceftriaxone 1g IV.

If it is not possible to refer for an LP for whatever reason, do not delay in giving an antibiotic if the person is sick and **bacterial** meningitis is suspected! While waiting for the ambulance, start empiric treatment with intravenous Ceftriaxone 1g IV ASAP in order to prevent death!

Children

- Symptoms are: fever, headache, lethargy/coma, irritability, abnormal cry, poor feeding and vomiting, stiffness of the neck, convulsions. For small infants: bulging fontanel (although not always present).
- Children < 2 months: IV ampicillin 50 mg/kg IM/IV QID and gentamycin 7.5 mg/kg IM/IV OD (ampicillin, unlike ceftriaxone, is also active against *Listeria monocytogenes*).
- Children > 2 months: ceftriaxone 100 mg/kg/dose IV or IM during 10 days OR treat according to hospital protocol.

Cryptococcal meningitis

Cryptococcal meningitis is less acute in onset than bacterial meningitis: while most common symptoms might be present, they are usually milder. It is caused by *Cryptococcus neoformans*. It only occurs in AIDS patients with low CD4 counts and places an adult or child into WHO stage 4. It is not contagious.

Clinical presentation

- Progressive mild headache, often frontal (”between the eyes”) not responding to analgesics
- Neck stiffness might be present
- Nausea and vomiting
- Sometimes associated with disorientation, confusion, or seizures
- Temperature slightly increased
- Sometimes Cryptococcal skin lesions appear over the body (these lesions can look similar to those of Molluscum contagiosum)

Diagnosis

- The patient must be referred for a lumbar puncture, Indian ink stain and cryptococcal antigen test (= CLAT = more sensitive) to detect Cryptococcus.

Management

Refer to hospital for amphotericin B IV

- IV Amphotericin B: 0.7 mg/kg/day for 2 weeks, followed by fluconazole 400mg daily for 8 weeks, and then fluconazole 200mg daily as secondary prophylaxis.
- If IV Amphotericin B is not available, give Fluconazole 800mg od for 4 weeks followed by Fluconazole 400mg for 8 weeks followed by secondary prevention with Fluconazole (see below).
- **All patients with Cryptococcal disease must be enrolled to start ARVs as soon as possible but after at least 6 weeks of treatment including Amphotericin or Fluconazole!**

Secondary Prophylaxis

Fluconazole 200 mg daily should be continued in order to prevent Cryptococcal meningitis from coming back. This is referred to as secondary prevention (see **page 19**). This can be discontinued if the patient is on ART, the CD4 > 200 cells/µl and the person has been on fluconazole for at least 6 months. Fluconazole is teratogenic, so women on prophylaxis should be advised to delay any pregnancy until fluconazole prophylaxis can be safely discontinued.

Children

- Refer to hospital for amphotericin B IV
- IV Amphotericin B: 0.5–1mg/kg/day for 2 weeks, followed by fluconazole 12–15 mg/kg daily (max 400 mg) for 8 weeks, and then fluconazole 6 mg/kg daily for secondary prophylaxis.
- Until recently, lifelong secondary prophylaxis was recommended. However, discontinuation should be considered (after being on prophylaxis for at least 6 months) in asymptomatic children aged 6 years or above, on ART with sustained CD4 > 200 cells/µl.

TB meningitis (TBM)

Tuberculosis can infect almost any part of a person's body. When it involves the brain and spinal cord, a person is suffering from tuberculous meningitis (TBM).

Clinical presentation

- Progressive onset (> 5 days usually) with less acute presentation than that of bacterial meningitis
- Headache
- Other signs of disseminated TB or IRIS (if on ARVs)
- High temperature

Diagnosis

- Referral for lumbar puncture is necessary, looking at biochemical markers (high protein and low glucose). Confirmed by acid fast bacilli stain and TB culture though this is often negative.

Management

- Treatment: follow the TB Program guidelines.
- If severe, dexamethasone 0.4 mg/kg/day or alternatively prednisolone 1-2mg/kg/dayis given to reduce intra-cranial pressure

Cerebral toxoplasmosis

Cerebral toxoplasmosis is caused by the reactivation of *Toxoplasma gondii* cysts, which lie dormant in the brain (following a mild 'primary infection' occurring earlier in the person's life).

Clinical presentation

- Headache, and sometimes fever
- Focal signs such as:
  - Hemiplegia (one-sided paralysis)
  - Hemiparesis (one-sided weakness)
  - Ataxia and difficulty walking
- Commonly associated with **new-onset seizures**
- Encephalitis-like symptoms such as decreased levels of consciousness and confusion (less frequent).

Management

Seek doctor's advice. If not available, refer to hospital for lumbar puncture and CT scan.

Because treatment is with oral medication, once the diagnosis is confirmed, the person can be treated at primary care level (unless unstable). If there is no improvement after 2–3 weeks, a follow-up CT scan should be arranged if possible (to rule out other problems such as a Tuberculoma or Lymphoma). **All patients with Cerebral Toxoplasmosis must be enrolled to start ARVs!**

Specific Treatment

For suspected Cerebral Toxoplasmosis, treat with:

- **High-dose** cotrimoxazole: 4 single strength tablets twice daily for 4 weeks, followed by two tablets twice daily for 4–8 weeks.
- Add folic acid 5 mg daily, since high-dose cotrimoxazole quickly depletes folic acid levels.

Secondary prevention

Continue with usual 2 tablets daily cotrimoxazole prophylaxis until Cd4 count > 200 cells/µl for 2 consecutive measures.

Children

- Refer to doctor
- High dose cotrimoxazole 40 +8 mg/kg/dose three times a day during 6 weeks, followed by usual (secondary) prophylaxis with cotrimoxazole.

If an HIV positive patient with focal neurological signs does not respond to empirical anti-toxoplasmosis treatment, cerebral lymphoma or a tuberculoma is another possible diagnosis. The patient should be referred for further assessment.

HIV encephalopathy/dementia

About 10% of HIV positive patients will develop dementia in the late stages of the disease (CD4 < 200). HAART has decreased the risk of dementia. It is a stage 4 (AIDS) diagnosis.

Clinical presentation

Patients will present with:

- Progressive memory loss, low mood and their families may report strange behaviour.
- They may have abnormal walking pattern and poor balance.
- Incontinence may also develop.
- It is very important to exclude any infectious cause (CMV or toxoplasmosis). This is a diagnosis of exclusion.

Management

- Refer patient to hospital for a Lumbar Puncture/CT scan
- If these are normal, start HAART. Refer same week for ARVs.
- Response to ARVs is often good.
- Supportive measures for both patient and family

Children

HIV encephalopathy has a different natural history in children. It is in an important condition to recognize in children because early ARV initiation can significantly diminish the long-term negative consequences that the child will suffer.

Clinical presentation

Suspect if:

- The child's head circumference (HC) is not growing, or
- If the child has lost milestones that he/she had previously acquired or where milestones are delayed. (For example, a child who was able to sit upright and now is unable to).

REMEMBER **This is another reason why it is so important to measure, record, and plot on a graph the HC of every child < 3 years of age, and to assess developmental milestones of all children. Don't forget to ask the caretaker how the child is developing. She/he usually knows best.**

Management

- If suspected, refer to doctor for confirmation and ARV initiation.
- For the child with HIV encephalopathy, a multidisciplinary approach works best (including clinical management, psycho-social support and physiotherapy where feasible).

Test yourself

- John is a taxi driver who tested HIV+ in 2006. His wife is on ARVs but John still can't accept his HIV status. John comes to your clinic because he has a terrible headache that doesn't improve with Paracetomol. Examination reveals; Temp 39, Pulse 100, Bp 150/100, CNS – Neck stiffness present, Chest –Clear , Resp rate- 18
    - How will you manage this client?

.....

    - What are the differential diagnoses?

.....

    - What would be the treatment of cryptococcal meningitis?

.....

- A HIV positive client with a CD4 count of 120 is brought to the clinic by his relatives. Over the last 24 hours he has developed a right sided hemiplegia and has been complaining of a mild headache.
    - Give 3 possible diagnoses

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    - What is your management plan?

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Notes

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Psychiatric Conditions

Mental health problems such as depression, anxiety, psychosis, delirium and substance abuse are more common in PLWHA.

Depression

Depression is very common and under-diagnosed in people living with HIV. It can contribute to weight loss, poor adherence, and those being lost to follow-up.

Clinical presentation

Depression is characterised by:

- Insomnia/hypersomnia
- Reduced motivation/unkept or failing personal hygiene
- Reduced appetite
- Poor concentration, libido (sexual appetite), energy
- Tearful or agitated
- Melancholia (a profound sadness)
- Difficult adherence to their medications
- Increased alcohol intake
- Decreased ability to function on a day to day basis

Management

- Rule out an underlying medical cause for the depression.
- Elucidate potential cause of depression: explore emotional and social issues.
- Refer to a support group, social worker and a psychiatrist if necessary.
- If severe refer same week to doctor for assessment of need for antidepressant medication. (note SSRIs such as fluoxetine can interact with commonly used ARVs. Amitryptilline has fewer interactions)
- Avoid using Efavirenz
- Refer for psychiatric assessment if no improvement

Anxiety

Commonly occurs around the time of testing and diagnosing HIV, as well as with advancing disease

Clinical presentation

- Feeling excessively worried
- Agitated
- Panic attacks
- Obsessive behaviour

- Compulsive thoughts

Management

- Provide psychosocial support: refer for extensive counselling and support group.
- Refer for psychiatric assessment if anxiety persists.

Psychosis

Clients with HIV psychosis usually have advanced stage 3 or 4 HIV disease.

Clinical presentation

- Delusions-fixed false beliefs
- Hallucinations e.g. hearing voices
- Disorganised speech and behaviour
- Social or occupational dysfunction

Management

- **If acute psychotic behaviour: refer same day to hospital!**
- Investigation for any underlying cause. Psychotic behaviour can be the manifestation of an underlying opportunistic infection.
- Exclude fever, focal signs and meningism.

Refer same day for psychiatric assessment

Delirium

This has a high risk of death. Causes include sepsis, hypoxia, alcohol withdrawal, drug toxicity, and hypoglycaemia.

Clinical presentation

- Acute confusion and disorientation
- Agitated and aggressive
- Changing level of consciousness

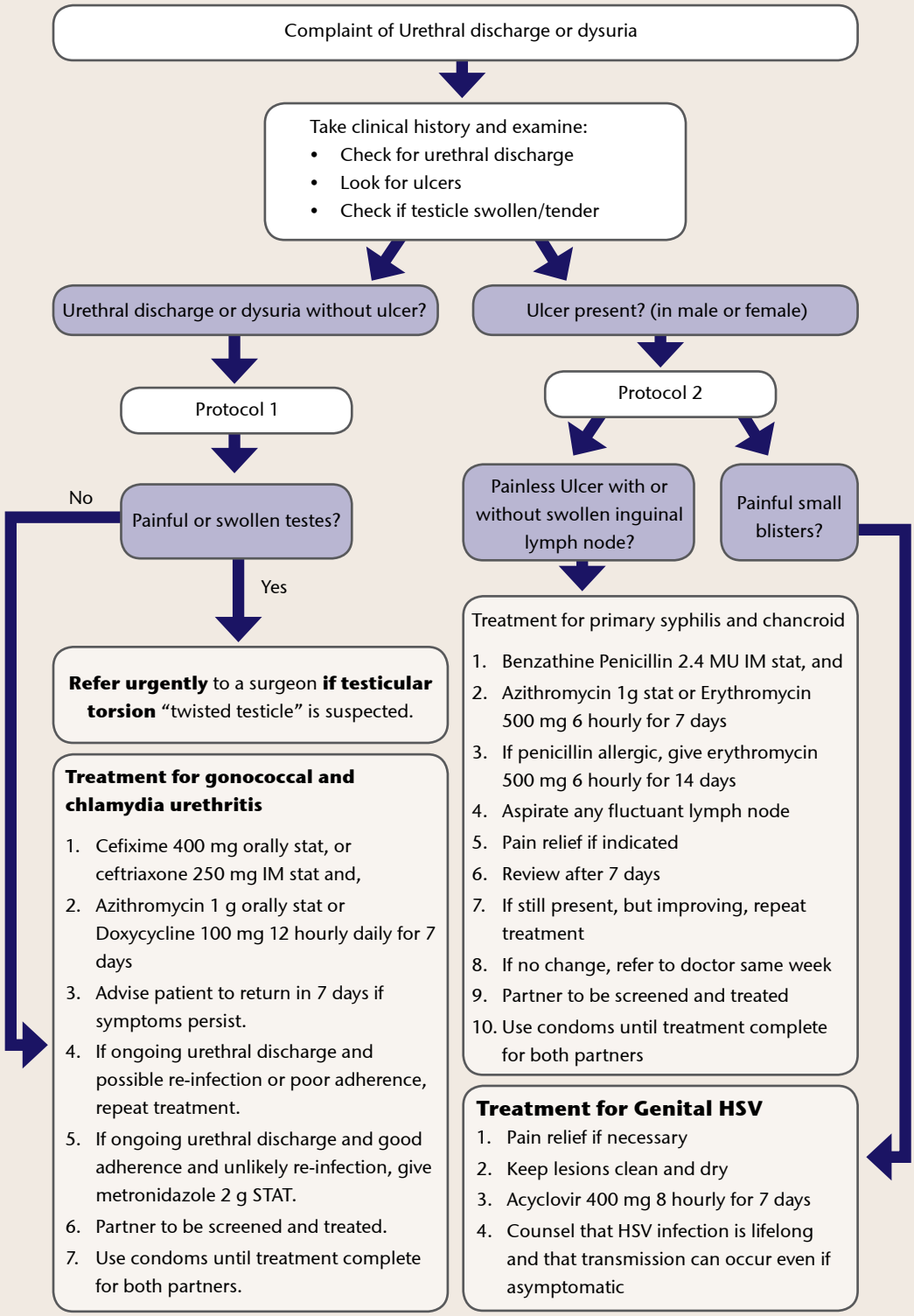
Management

- Manage in a calm environment
- Give Diazepam 5 to 10 mg IM if very agitated or aggressive
- Check blood glucose level and treat if hypoglycaemic (give thiamine = vitamin B_1 orally or by IM injection before starting any glucose infusion, if alcohol withdrawal is suspected)
- Provide face mask oxygen if client hypoxic
- Refer same day to hospital

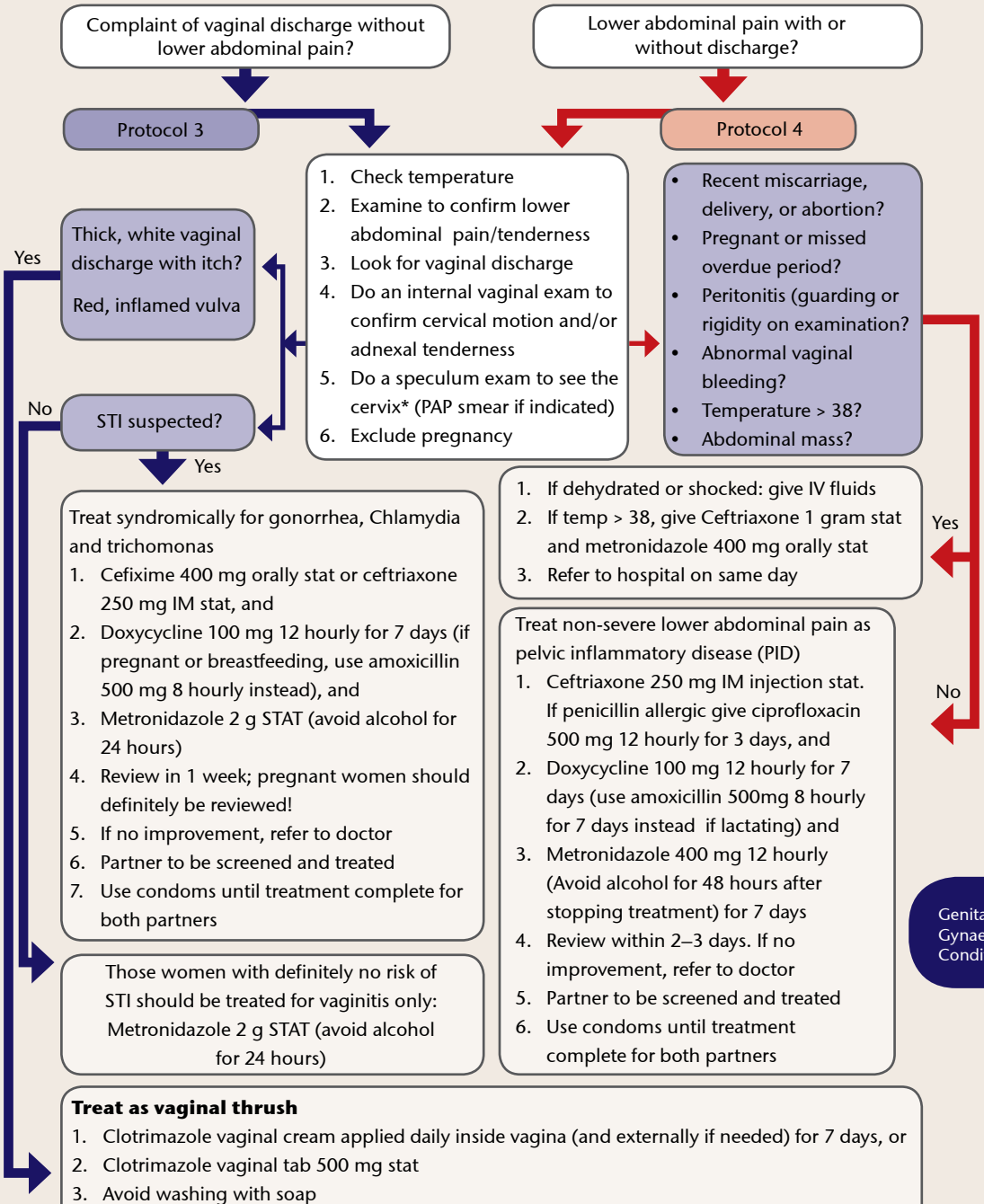
Notes

Genital and Gynaecological Conditions

Algorithm 9: Syndromic STI Management- Protocols 1&2



Algorithm 10: Syndromic STI Management-Protocols 3&4



*If suspicious of cancer, refer the same week.

Sexually Transmitted Infections (STIs)

General principles

It is very important that STIs be diagnosed and treated in the general population, since STIs are a major risk factor for HIV transmission.

A syndromic approach is used for the management of STIs. This means that treatment is based on 'signs and symptoms' (syndromes), without using diagnostic tests to identify the precise cause of the infection. Syndromic management is cost-effective and allows for early treatment of STIs. Since mixed infections are common, syndromic management covers for most possible causes of infection.

A good history is an important part of the following four protocols; assess the person's **risk factors for STI** (age < 21, new partner, or multiple partners) and ask about any symptoms in the partner.

A physical examination should always be done to confirm the symptoms.

Treatment is then provided at the same visit based on results of the history and physical examination. A follow-up appointment in one week for reassessment should be regularly advised. **Partner treatment is essential** to avoid "ping-pong" infections and ensure cure. Family planning, contraception needs (both women and men) should be addressed. Ask about last menstrual period and screen for pregnancy if indicated.

REMEMBER

Always consider the "Six Cs" when dealing with STIs:

- **C**ompletion of prescribed medication and **C**ontact tracing (of partner) to achieve **C**ure.
- **C**ounselling to **C**hange behaviour and encourage **C**ondom use.

Approach to the partner with an STI

- Offer RPR/VDRL and HIV testing to all partners.
- Partners who are symptomatic must be treated syndromically.

Table 12. Asymptomatic partner/s of a client with an STI should be treated based on the client's STI diagnosis

Client diagnosis	Asymptomatic partner treatment
Vaginal discharge syndrome or lower abdominal pain in woman	Cefixime* 400mg orally stat or ceftriaxone* 250 mg IM stat and Azithromycin 1g orally stat or doxycycline 100 mg 12 hourly for 7 days and metronidazole 2g stat
Genital ulcer syndrome	Azithromycin 1g orally stat or benzathine penicillin 2.4 MU IM stat and erythromycin 500mg 6 hourly for 7 days
Male urethritis syndrome or scrotal swelling	Cefixime* 400mg orally stat or ceftriaxone* 250mg IM stat and Azithromycin 1g orally stat or doxycycline 100mg 12 hourly for 7 days and metronidazole 2g stat
RPR/VDRL positive	Benzathine penicillin 2.4 MU IM stat

* If Cefixime and Ceftriaxone not available or concern about allergy use Ciprofloxacin

Resistance of Gonorrhoea against Ciprofloxacin is becoming common. Therefore, Ceftriaxone 250mg by intramuscular injection (or cefixime 400mg daily if available) is recommended to treat Gonorrhoea in place of Ciprofloxacin. Refer if no improvement.

Protocol 1 (Males): Urethral discharge or dysuria

Treat syndromically for gonococcal and chlamydia urethritis:

A man with an STI usually complains of discharge and sometimes also dysuria (painful urination). Testicular pain may also signify an STI in males; rarely, testicular pain can result from torsion and this must not be missed (see below).

Assessment

- Confirm urethral discharge by examination
- If an ulcer is present, use Protocol 2
- If painful or swollen testis is detected, refer to a surgeon at once if testicular torsion ("twisted testicle") is suspected. Testicular torsion is more likely in a boy less than 18 years who is not sexually active, has no history of injury and no discharge on examination.

Management

- Treat urethral discharge or dysuria with: cefixime 400 orally stat or ceftriaxone 250mg IM stat and Azithromycin 1g orally stat or doxycycline 100 mg 12 hourly daily for 7 days. Advise client to return in 7 days if symptoms persist.
- If ongoing urethral discharge or dysuria, ask if possible reinfection or poor adherence.
    - If yes: repeat treatment: cefixime 400mg orally stat or ceftriaxone 250mg IM stat and Azithromycin 1g orally stat or doxycycline 100mg 12 hourly for 7 days
    - If No: Give metronidazole 2g stat. (Avoid alcohol for 24 hours)
- Refer if not resolved.

Protocol 2 (Males or females): Genital ulcer syndrome (GUS)

The most common causes of genital ulcer are genital HSV, syphilis and chancroid.

Assessment

- Confirm ulcer(s) by examination
- Establish first if client has been treated for syphilis. If not, treat syndromically for primary syphilis and chancroid: A single ulcer with or without swollen inguinal lymph nodes. Syphilitic ulcers are painless whilst chancroid ulcers are usually painful

- If there are multiple tiny, very painful blisters (that have become ulcers) and a history of recurrence of these blisters, the diagnosis is more likely to be herpes simplex virus-2 (Genital HSV-2).

Management

Syndromic treatment for primary syphilis and chancroid

In case of a painless single ulcer with or without swollen inguinal lymph nodes:

- Benzathine penicillin 2.4 million units IM injection STAT and
- Azithromycin 1g orally stat or erythromycin 500 mg 6 hourly for 7 days. If penicillin-allergic give erythromycin 500mg 6-hourly for 14 days
- Aspirate any fluctuant lymph node
- Pain relief if indicated
- Review after 7 days
- If still present, but improving, repeat treatment:
  - Azithromycin 1g orally stat or erythromycin 500 mg 6 hourly for 7 days
  - Aspirate any fluctuant lymph node
  - Pain relief if indicated and review after 7 days.
- If no change: refer to doctor same week

Treatment of Genital HSV

- Pain relief if necessary.
- Keep lesions clean and dry.
- Acyclovir 400mg 8 hourly for 7 days
- Explain that herpes infection is lifelong and that transmission can occur even when asymptomatic.
- PLWHA having an episode of genital herpes lasting > 1 month are considered to be in clinical stage 4 and therefore are in need of cotrimoxozole prophylaxis and ART.

Protocol 3 (Females): Vaginal discharge syndrome (VDS)

When a woman complains of a vaginal discharge (and/or burning or itching) it is important to distinguish between vaginitis (inflammation of the vagina) and cervicitis (inflammation 'higher up' of the cervix). It is also important to identify if a woman is pregnant, since some medications should not be used in pregnancy.

Assessment

- Confirm abnormal discharge by examination
- Perform internal examination to check for 'cervical motion tenderness': If lower abdominal or cervical motion tenderness is present, treat for PID (use protocol 4)
- If lower abdominal pain or painful sexual intercourse: treat for PID (use protocol 4)
- Do a speculum examination to see the cervix.
- Do a Pap smear if indicated (see below): If suspicious of cancer, refer same week.

Management

- Those women with definitely **no risk of STI**, treat for **vaginitis only**:
  - If vaginal candidiasis (thrush) is suspected as the cause of the vaginitis (thick, white vaginal discharge with itch), give clotrimazole vaginal cream or tablets (see below).
  - Metronidazole 2g stat. (Avoid alcohol in the first 24 hours. If pregnant give 400mg TDS for 5 days).
- Young, sexually active women should be **treated syndromically for gonorrhoea, chlamydia and trichomonas**:
  - Cefixime 400mg orally stat or ceftriaxone 250mg IM stat and
  - Azithromycine 1 gr stat or doxycycline 100 mg 12 hourly for 7 days (if pregnant or breastfeeding, use amoxicillin 500mg 8 hourly for 7 days instead) and
  - Metronidazole 2g stat (Avoid alcohol for 24 hours. If pregnant give Metronidazole 400 mg TDS for 5 days).
- Pregnant women must definitely be reviewed in one week. If there is no improvement, refer to the doctor.

Protocol 4 (Females): Lower abdominal pain or cervical tenderness

Lower abdominal pain in women can be the result of many different problems. A thorough history and physical examination is necessary to determine the cause, as well as a urine and pregnancy test. Protocol 4 provides syndromic management of **pelvic inflammatory disease (PID)**.

Assessment

- Check temperature
- Is sexual intercourse painful (dyspareunia)
- Examine to confirm lower abdominal pain/tenderness.
- Also do an internal vaginal examination to confirm cervical motion and adnexal tenderness
- Look for vaginal discharge

Management

Severe PID

Refer to hospital on the same day if:

- Patient very ill, cannot walk upright
- Temperature > 38.5 degrees
- Severe abdominal tenderness or pelvic mass
- Abnormal vaginal bleeding
- Pregnant or missed or overdue period
- Recent miscarriage/delivery or abortion
- Abdominal mass

If **dehydrated or shocked**: give IV fluids.

If temp ≥38° C, give ceftriaxone 1g IM stat and metronidazole 400mg orally stat.

Low grade PID

If none of the above symptoms and signs are present, then the P.I.D. can be considered low-grade and treated with:

- Ceftriaxone 250 mg IM injection stat.
- Doxycycline 100 mg 12 hourly for 7 days (use amoxicillin 500mg 8 hourly for 7 days instead if lactating) and

- Metronidazole 400 mg 12 hourly (Avoid alcohol for 48 hours after stopping treatment) for 7 days
- Reassess in 3 days and refer to hospital if not improving!

Vulvo-vaginal candidiasis (also known as vaginal thrush or yeast vaginitis)

Vulvo-vaginal candidiasis is caused by a type of fungus (a yeast called Candida). It can occur in all women regardless of HIV status. It is not an STI.

Vaginal thrush is more common in HIV-positive women for two reasons:

1. HIV-positive women have weaker immune systems and are more likely to suffer from infections in general.
2. HIV-positive women are more often on antibiotics to treat or prevent other infections; this disturbs the normal balance of organisms in a woman's body and allows the Candida yeast to 'overgrow'.

Clinical presentation

- Burning or itching sensation in the vagina
- Associated with a white thick discharge
- The vulva is often inflamed and itchy

Management

There are many possible topical therapies. Any of the following are suitable but depend on what treatments are available in your clinic:

- Clotrimazole vaginal cream applied twice daily inside vagina (and externally if needed) for 7 days
- Clotrimazole vaginal tablet 500mg stat, inserted high inside the vagina at night.
- Avoid washing with soap
- Advise client to return in 7 days if symptoms persist
- If recurrences of vaginal thrush are common (usually > 3 episodes) or the vaginal thrush is resistant to topical therapy:
    - Oral treatment with Fluconazole 150 mg STAT dose should be effective.
    - Fluconazole 50 mg daily for 7–10 days is also effective.
    - Or, repeat clotrimazole.
    - Test for diabetes
- If ongoing discharge, no thrush: consider Protocol 3 (vaginal discharge syndrome).

Human papilloma virus (HPV) infection (Genital warts)

HPV is a sexually-transmitted virus. HPV can cause genital warts in men or women. It can also lead to Cervical Intraepithelial Neoplasia (CIN) in women, which are changes of the cervix that can progress to cancer of the cervix. The incidence of CIN has increased with the HIV epidemic, resulting in the recommendation of a **Pap smear every 12 to 36 months** in HIV infected women in order to screen for any cervical problems. If CIN is found early, these cervical problems can be treated before they develop into cancer.

Clinical presentation

- HPV can present externally as genital warts (also known as 'condyloma acuminata'): They start as small papules, which are often not noticed by the patient.
- Genital warts can grow to become big cauliflower-like tumours!
- CIN changes of the cervix resulting from HPV infection can only be diagnosed by Pap smear and internal examination with a speculum.

Management

- The treatment of external genital warts is not easy: protect surrounding skin with petroleum jelly and give weekly applications of 20% tincture of podophyllin or podophyllotoxin topical solution (5mg/ml).
- Do not apply podophyllin solution internally. Ideally apply twice daily for 3 consecutive days; treatment may be repeated at weekly intervals if necessary for a total of five 3-day treatment courses. If not feasible for patient to self apply then apply weekly at the clinic.
- Cryotherapy is the preferred treatment if available.
- Check for syphylis.
- If the genital wart lesions are too big and/or not responding, or podophyllin not available, the patient must be referred for surgical treatment.
- Do not use Podyphyllin and podophyllotoxin in pregnancy!

Table 13. Cervical screening

• Approximately 1 in every 41 women develops cervical cancer. After breast cancer, it is the most common form of cancer among South African woman. • Papanicolaou (Pap)/cervical smears detect cervical abnormalities which occur before cancer develops. • Cervical cancer is caused by certain types of human papilloma virus (HPV types 16 and 18). HPV is usually transmitted sexually. • Woman who smoke are more likely to have cervical abnormalities. Advise smokers to stop.
• An asymptomatic HIV negative woman should receive 3 smears in her lifetime from age 30, with a 10-year interval between each smear. • An HIV positive woman should receive a Pap smear on diagnosis, regardless of her age. If the result is normal, she needs the next Pap smear in 3 years. • All women with genital warts require a Pap smear. • In pregnancy, Pap smears can be performed safely up to 20 weeks' gestation. • The Ayelsbury spatula is the recommended screening device • If the client has a vaginal discharge, treat the discharge first and then take a Pap smear at the follow up visit.
Manage according to the Pap smear result and national guidelines
Inform client of symptoms of cervical cancer (abnormal bleeding, vaginal discharge) and instruct her to return should they occur.

Syphilis

A non-specific blood test for syphilis (called a RPR or VDRL) is recommended annually on all patients attending the HIV clinic.

Acquired syphilis is a complicated disease in adults with different stages and many different symptoms. Syphilis can also be transmitted from mother to child and is called **congenital syphilis** in the newborn.

Clinical presentation

The different **stages** of acquired syphilis (in adults) include:

- Primary: painless 'chancre' (ulceration) occurring during initial infection; this often goes unnoticed!
- Secondary: various rashes on body several months after primary infection, involves palms and soles
- Latent: asymptomatic stage
- Tertiary: late stage of infection causing skin, heart, and neurological problems

Management

If Syphilis is suggested by a positive RPR/VDRL result (confirmed by a TPHA test) give:

- Benzathine penicillin 2.4 million units IM weekly once a week for 3 weeks
- If allergic to Penicillin: Doxycycline 100 mg twice daily for 14 days, or erythromycin 500 mg four times daily for 14 days
- Late-stage syphilis will require 30 days of oral treatment with Doxycycline or Erythromycin; refer to doctor if unsure of stage of Syphilis infection.
- If **pregnant** and allergic to Penicillin, refer for **assessment by the doctor** since there is an unacceptable risk of transmission of Syphilis to the newborn when using Erythromycin. Seven days of IM or IV treatment with Ceftriaxone 2 gr can be considered.

Sexual assault

Sexual assault is often underreported. An open and non-judgmental attitude is essential. Clients will probably not bring up a history of sexual violence unless they feel at ease. Be aware of more subtle signals that the person may send: for example, the client may look depressed, or not look at you in the eye when talking, etc. The physical and psychological consequences of sexual assault are reduced through the provision of medical and mental health care.

Management of sexual assault

Management of sexual assault includes:

- Taking and documenting history and performing physical examination
- HIV prevention ('PEP') if client presents within the first 72 hours and is HIV negative. Referral to ART treatment centre if patient is HIV positive.
- Testing for pregnancy and prevention of unwanted pregnancy, including emergency contraception (levonorgestrel 1.5 mg single dose).
- STI treatment and prevention (including hepatitis B vaccination if unvaccinated and HBsAg negative or unknown).
- Tetanus vaccination
- Trauma counselling

HIV Post-exposure Prophylaxis (HIV PEP)

A risk assessment will be done to determine risk profile and prevention with ARVs if the client is HIV negative. **A high risk profile** rape includes any of the above:

- Where there have been multiple perpetrators
- Anal penetration
- Obvious trauma to the genital areas
- Female menstruating at time of rape, or with genital ulcerations/sores

For the HIV-negative individual, prophylaxis with ARV's will be given as follows:

- **TDF + 3TC (or FTC) + LPVr for 4 weeks**
- **Alternative regimen: AZT + 3TC + LPVr 400 mg/100mg twice daily for 4 weeks**
- For the choice of ARV regimen, there's no longer any distinction between high and low risk exposure.

STI prevention (Non pregnant adults and children > 12 years)

- Cefixime 400mg stat dose
- Metronidazole 2g stat dose
- Azithromycin 1g stat (or doxycycline 100mg twice a day for 7 days.)

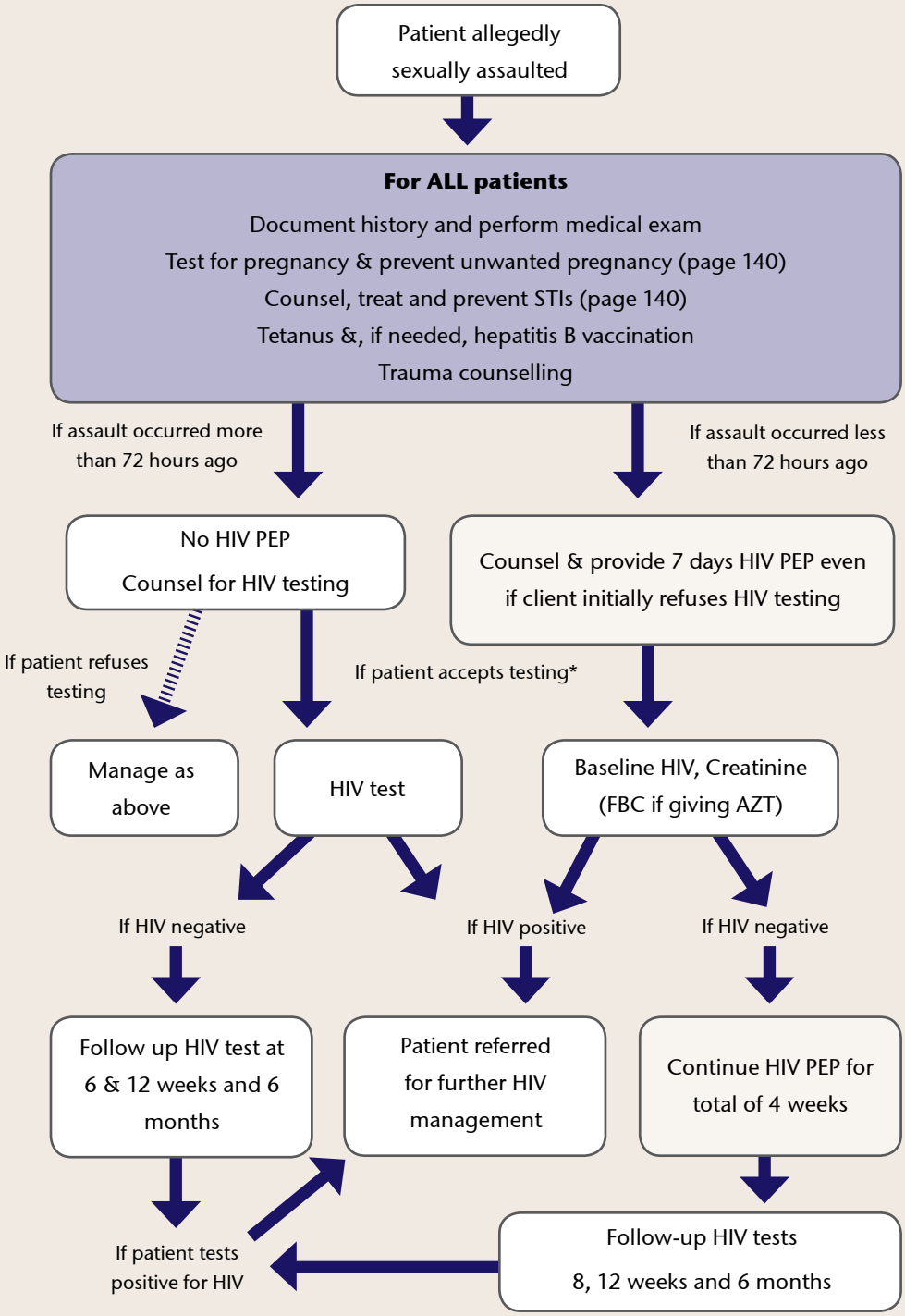
STI prevention (Pregnant adults or pregnant adolescents > 12 years)

- Ceftriaxone 250mg IM stat dose
- Azithromycin 1g stat or erythromycin 500mg 4 times a day for 7 days
- Metronidazole 2g stat dose

Children

- Be aware of legal age of consent for HIV testing and HIV PEP in children.
- For children/adolescents > 12 years, manage as above.
- Children < 12 years preferably need to be managed at a specialized site where there is expertise in dealing with traumatized children and ART in children.
- ARV prophylaxis (PEP) for children < 12 years
  - AZT
  - 3TC
  - Lopinavir/ ritonavir
  - For drug dosages according to weight, refer to Appendix 10.
- STI prophylaxis dosages (children < 12 years)
  - Ceftriaxone: 125 mg IM STAT
  - Metronidazole: 7.5 mg/kg/dose 8 hourly for 7 days
  - Azithromycin 20mg/kg stat dose or Erythromycin: 10 mg/kg 6 hourly for 7 days (give doxycycline if over 8 years).

Algorithm 11: Management of Sexual Assault



* Baseline HIV testing can be done up to 1 week after the assault, provided that the client has been initiated on PEP on time.

Test yourself

- What treatment is given for the syndromic approach to vaginal discharge?

- What treatment is given for the syndromic approach to urethral discharge?

- What treatment is given to a patient presenting with multiple painful blisters developing in the genital area?

- What would be the management and treatment given to a patient presenting with a solitary painless genital ulcer?

- What are the five key steps in managing a victim of a sexual assault?

Notes

Notes

Pregnancy and Children

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Algorithm 12: Management of HIV positive pregnant women

All HIV-positive pregnant women need:

- CD4 and clinical staging
- Folic acid daily in the 1st trimester
- Multivitamin daily
- CTX for stages 2, 3 or 4, or CD4 < 350
- Screening for TB, and when INH prophylaxis available give if active TB is excluded and not eligible for ARVs.
- Screening for syphilis and other STIs
- Ferrous sulfphate (iron) if Hb < 11.0
- Usual antenatal care

Stage 3 or 4 or CD4 < 350

Stages 1 or 2 and CD4 > 350

Treatment of MOTHER with ARVs:

- Pregnancy is in the first trimester and CD4 < 250 start with TDF/3TC and NVP. If CD4 > 250 it is safer to wait until after the first trimester and commence ART with with TDF/3TC and EFV
- TDF + 3TC + EFV except if:
  - CrCl < 50 (Use AZT instead of TDF if Hb > 8 g/dl. Otherwise, use D4T)
- If TB develops while on a ART regimen containing LPV/r, double the dose of LPV/r
- Start ARVs within 2 weeks, unless TB treatment was also started[1]

After delivery, BABY gets:

- NVP at birth[5] then daily for 6 weeks
- Give NVP 1.5 ml if birth weight (BW) ≥ 2.5 kg or NVP 1 ml if BW < 2.5 kg.
- Exclusive feeding (breastfeeding or formula feeding) should be promoted during the 1st 6 months of life
- Mother to continue on ART life-long

For PMTCT[2,3], mother gets:

- AZT[4] 300 mg twice daily from 14 weeks
- At the onset of labour, a single dose of NVP and AZT 300mg/3TC 150mg 12 hourly
- Then, for tail protection after delivery, AZT 300mg/ 3TC 150mg bd for 7 days

After delivery, BABY gets:

- NVP at birth[5] then daily for 6 weeks. If breastfeeding, NVP is continued for the duration of breastfeeding (until 1 week after).
- Give NVP 1.5 ml if birth weight (BW) ≥ 2.5 kg or NVP 1 ml if BW < 2.5 kg. For dosing after 6 weeks of age, see Table 14 on **page 150**.
- Exclusive feeding (breastfeeding or formula feeding) should be promoted during the 1st 6 months of life.

1. In case of treatment for TB, wait 2-4 weeks on TB treatment to start ARVs. If CD4 is very low and woman is in the first first trimester, start with lopinavir/ ritonavir. However, if the CD4 count is higher and patient is otherwise stable, try to wait until the end of the 1st trimester before starting ART and initiate with EFV.
2. The following PMTCT regimen can be given even if the woman presents for the first time during labour.
3. For planned (elective) Caesarien section, ARV prophylaxis (sdNVP + TDF + 3TC) should ideally be given 4 hours prior to the procedure. For an emergency C-section, ensure that the woman receives sdNVP + TDF + FTC/3TC prior to the procedure.
4. Start AZT unless Hb < 8 g/dl or woman is clinically pale. In this case, look carefully for OIs, give iron and refer to doctor. The woman may be eligible for ARVs if no other cause for the anemia is found and the anemia persists despite treatment with iron.
5. If the baby vomits within 1 hour of initial dose, repeat prophylaxis and make sure he doesn't vomit again (observe for at least 1 hour before discharge). If the baby presents for the first time within 72 hours of delivery then NVP should still be given ASAP to the baby and daily for 6 weeks or for the duration of breastfeeding. For late presenters after 72 hours, see Appendix 27.

HIV in pregnancy (including PMTCT)

HIV poses some major challenges to the clinician managing pregnant women. Not only do we want the mother to have a healthy pregnancy, but we also want to prevent the baby from becoming infected with HIV before, during, or after delivery. Different interventions are recommended depending on the woman's CD4 count. Note that there is a difference between treatment and prevention with ARVs.

Diagnosis of HIV in Pregnant Women

- Testing should be done at any ANC visit along with the other usual tests. If testing is refused, individual counselling should be performed, and HIV testing offered at every visit until status is known.
- Testing should be done during labour for all pregnant women with unknown status, or immediately after delivery if not possible during labour
- Testing should be repeated in women who tested negative earlier in pregnancy (every 3 months during pregnancy and the breastfeeding period).
- Partners should be encouraged to test at every visit

Management of HIV positive pregnant women

Treatment versus Prevention

- If a pregnant woman has a CD4 count < 350 or is in stage 3 or 4, then 3 ARVs are given to the mother (HAART, or triple therapy) to **treat** her. Whilst being used for maternal health, this regimen will also help reduce the risk of mother-to-child transmission of HIV by reducing the woman's viral load. This risk can be further reduced if the newborn receives NVP syrup daily for 6 weeks after delivery.
- If a pregnant woman has a high CD4 count >350 then ARVs are given to the mother and newborn to **prevent** mother-to-child transmission (PMTCT) of the virus. ARVs given to the mother will help reduce her viral load and lower the chances of transmitting the virus to the infant.
- Women who seroconvert during pregnancy should be put immediately onto AZT prophylaxis, no matter the CD4. If eligible for ARVs, they should then be started on triple therapy within 2 weeks (fast track).
- HIV can also be transmitted from mother-to-child in breast milk. The risk of transmission in this manner can be reduced if:
    - The mother opts for exclusive formula feeding (no risk of HIV transmission through formula milk), BUT must be affordable, feasible, accessible, safe and sustainable (AFASS) or,

  - The mother opts to exclusively breastfeed for 6 months followed by breastfeeding with complementary feeding up until 12 months (decreased risk of transmission compared to mixed feeding), and NVP prophylaxis is continued throughout the breastfeeding period (unless mother is already on lifelong ART).
- It is very important that infant feeding options be discussed with the pregnant women during her pregnancy (see infant feeding section **page 159**).

REMEMBER **For breastfeeding mothers on effective ARV treatment, the risk of MTCT through breastmilk is minimal, so for mothers not on lifelong ART, eligibility for ARVs should be reassessed regularly (and CD4 repeated at 6 weeks post-partum then every 6 months).**

Monitoring on ARVs

- Toxicity monitoring for the pregnant woman on AZT is essential
- Monitor carefully for signs of liver toxicity on NVP. Check ALT in case of symptoms (jaundice, abdominal pain, unusual fatigue, or fever) and in all cases of rash.

Management of the HIV-positive mother post delivery

- Support the mother's feeding choice. Discourage mixed feeding during the first 6 months of life.
- Arrange for ongoing HIV care for the mother:
  - Client must not interrupt ARVs and cotrimoxazole prophylaxis.
  - All HIV-positive mothers who received AZT prophylaxis should be reassessed for ARV eligibility (by staging and CD4 in the postpartum period at 6 weeks visit)
- Discuss family planning. Encourage dual contraception.
- Discuss care of HIV exposed baby. Remember to write on the infant's child health card if ARVs have been received by the mother and infant and what feeding choice has been made.

Care of the HIV-exposed baby

Routine care

- According to National Guidelines, every infant born to an HIV-positive mother should receive NVP (according to weight) for at least 6 weeks. NVP prophylaxis can be stopped at 6 weeks if the infant is exclusively formula fed or if the mother is on lifelong ART. Otherwise, NVP prophylaxis for the infant should be continued throughout the breastfeeding period (and until 1 week after complete breastfeeding cessation).
- When NVP prophylaxis is continued beyond 6 weeks, NVP dose must be adjusted according to weight and age (see Table 14 on **page 150** for NVP infant dosing).
- For late PMTCT presenters (after 72 hours) who are breastfeeding see specific management in Appendix 27.
- First post-natal visit should occur at day 10 then week 6, 10, 14, 18 and then monthly until one year followed by three monthly visits.
- Weight checks and immunisations as per standard schedule.
- Give **cotrimoxazole** prophylaxis to all HIV exposed babies from 6 weeks, daily according to weight (see Table 17 on **page 158**). This is absolutely essential to prevent early deaths from PCP. CTX prophylaxis continues until the baby has a negative HIV test at least 6 weeks after complete breastfeeding cessation AND does not have any clinical signs of HIV infection (see Table 2 on **page 21** for indications).
- Give multi-vitamins containing vitamin A until HIV infection is excluded or if unavailable, give mega-dose vitamin A as follows:

Age of HIV-exposed or infected child	Dosage of Vitamin A	Schedule
6–12 months	100 000 IU	A single dose between 6 and 11 months of age
> 12 months	200 000 IU	A single dose at 12 months, then every 6 months until the age of 5 years

- Test for HIV as seen in Algorithm 13 on **page 153**.
- Counsel about exclusive feeding (breastfeeding or formula feeding) until 6 months of age. See infant feeding section **page 159** for feeding recommendations during and after the 1st 6 months of life.

If the mother refuses any ARV prophylaxis for the HIV-exposed infant

- Counselor must intervene to explain the risks of MTCT of HIV and the benefits of prophylaxis.
- If the mother continues to refuse, consult the head of the facility, and with his/her permission, provide the necessary treatment in the best interest of the infant.

Table14: NVP Infant Dosing Guide

Drug	Birth Weight or Age	Dose	Quantity
NVP syrup (10 mg/ml)	Birth to 6 weeks < 2,5 kg birth weight	10 mg/day	1 ml
	Birth to 6 weeks ≥ 2,5 kg birth weight	15 mg/day	1,5 ml
	6 weeks to 6 months	20 mg/day	2 ml
	6 months to 9 months	30 mg/day	3 ml
	9 months to end of breastfeeding	40 mg/day	4 ml

Note: Premature babies need reduced dosing.

Care of the baby when maternal status is unknown (including abandoned babies)

- **Abandoned babies:** If judged to be born since less than 72 hours (and the mother's status is unknown), do a HIV rapid test as soon as possible and
  - If rapid test positive, initiate NVP syrup
  - If rapid test negative, do not give NVP syrup, but schedule the baby for a PCR at 6 weeks anyway.
- The above management also applies to other cases in which the maternal status is unknown, including cases in which the mother is indisposed due to severe illness, coma, mental illness or death.

HIV in children

With a little practice you will find that caring for children with HIV is not so difficult, even if they are not simply 'little adults'. As they grow, children's emotional, intellectual and social needs change. Importantly, **doses of medications must be constantly adjusted to the child's weight**. Remember to communicate with children the way you would communicate with them in your home. Making children feel at ease is essential. Simple gestures count, like calling the child by his name, asking her about a favorite hobby or a best friend, and involving him in the discussion (not only the caretaker).

For adolescents (roughly ages 10–19, but definitions vary), peer support becomes increasingly important. If available, adolescents are best managed in specialized clinics attached to paediatric clinics.

Definitions

HIV-exposed

All children born to HIV infected mothers, when the child's status is not yet confirmed. Diagnostic tests are needed to determine the HIV status.

HIV-infected

A definitive test has been done to confirm HIV infection. A positive HIV DNA PCR (which detects viral DNA) is diagnostic in infants and children under the age of 18 months. Ideally a first positive PCR result should be repeated to confirm the result. For children above 18 months of age, 2 positive rapid HIV tests (which detect antibodies) confirm HIV infection. Before 18 months of age, it is not possible to know for sure if the antibodies present in the child's blood are the child's or the mother's.

REMEMBER **The risk of HIV transmission through breastfeeding can be reduced if the HIV-positive mother is on lifelong ART, or if the baby receives NVP prophylaxis throughout the breastfeeding period.**

These children require an age-appropriate HIV test following cessation of breastfeeding after the 'window period' (see Algorithm 13 on page 153). A final rapid test should also be performed at 18 months for all HIV exposed children.

How do children acquire HIV?

More than 90% of HIV infection in children is acquired through mother to child transmission during pregnancy, labour and delivery, and after childbirth through

breastfeeding. This is why we need to implement effective PMTCT! Other ways children can become infected are: through transfusion with contaminated blood, sexual abuse, or injury with contaminated sharp objects such as razors or needles. As children become adolescents, risk factors are the same as for adults.

Disease progression

Infants and children have an immature immune system and are thus less able to suppress HIV viral replication once infected. Hence, HIV disease can progress much more rapidly in infants and children than it does in adults. This is particularly true for infants less than 12 months of age. If untreated, approximately 40% of HIV-infected children will be dead by their first birthday, and 50% will be dead by age 2.

REMEMBER

The goal is to manage HIV-infected infants and children BEFORE they get sick. Since confirmation of HIV diagnosis is commonly delayed in those < 18 months of age, ALL HIV-exposed babies should receive certain interventions (see Algorithm 13).

Which children should be tested for HIV?

Unfortunately, HIV diagnosis in children is often delayed. Frequently, we simply do not think about testing the child! It is important to look out for signs and symptoms that suggest HIV infection; if an infant is not growing and developing well ('failing to thrive') and/or has frequent diarrhoea or lung infections, the infant is probably HIV-positive. When the PCR result is delayed and if the infant has signs of HIV infection, do not wait for the PCR result: Send the child immediately to an ARV treatment centre!

REMEMBER

Remember to initiate counselling and testing for HIV AT LEAST for:

- All HIV exposed children (Algorithm 13)
- Children with HIV positive parents or siblings
- Children diagnosed with TB, severe pneumonia or severe malnutrition
- Orphans, abandoned children, and children in whom maternal status is unknown (see management on page 150)
- Children with signs and symptoms of HIV infection (IMCI classification)
- Children who have experienced or been at risk of sexual assault (see page 140)

Algorithm 13: Management of HIV-exposed babies

All babies[1] born to an HIV-positive mother

- Start NVP prophylaxis to all newborns for at least 6 weeks
- If late presenter (> 72 hours after delivery), see Appendix 27

At 6 weeks (integrated with immunization visit if possible):

- Start prophylaxis with cotrimoxazole (CTX)
- Perform PCR testing[1]
- **Continue NVP prophylaxis only for breastfeeding babies whose mothers are not on lifelong ART**
- Safe infant feeding counseling and support

PCR negative

If breastfed (BF):

- Baby is still at risk
- Continue CTX until BF stopped and infant confirmed HIV neg
- **If mother not on lifelong ART, continue NVP prophylaxis until 1 week after BF stops**
- At 9 months if still breastfeeding check rapid test. If Positive perform PCR
- Repeat age-appropriate[2] HIV test 6 weeks[3] after complete cessation of breast-feeding
- And rapid HIV test at 18 months[4]

If exclusively formula fed:

- Baby is HIV negative but still needs to have rapid HIV test at 18 months of age[4]
- Stop CTX prophylaxis if no clinical signs of HIV infection

Age-appropriate[3] HIV test is negative

Baby is HIV-negative

- Stop CTX prophylaxis and continue routine under 5 care

Age-appropriate[3] HIV test is positive

PCR positive

Baby is HIV-infected:

- If being fast-tracked, initiate ARVs without delay (see Appendix 5)
- Do a confirmatory PCR if possible
- Continue cotrimoxazole
- If still breastfed and on NVP, the NVP should now be stopped
- Continue breast-feeding until 2 years of life
- Ensure well-baby care, including immunizations
- Give multivitamin daily (or a mega-dose of vitamin A every 6 months)
- Prescribe de-worming medication every 6 months
- Clinical staging and developmental assessment every 3 months, with ART referral if eligible (Appendix 5)
- Do a rapid HIV test after 18 months[4] even if prior PCR result was positive

1. PCR should also be done/repeated in an infant of any age (even if < 6 weeks) if clinical features of HIV infection are present, and results fast-tracked to the clinician. Even if result is negative, a PCR should be repeated at 6 weeks. If PCR is unavailable, but clinical features of HIV are present, do not delay ART initiation: follow WHO criteria for presumptive diagnosis of HIV infection (see Appendix 5).
2. Age-appropriate HIV testing = PCR in those ≤ 18 months, and 'antibody tests' (ELISA or rapid HIV testing) in those > 18 months.
3. Consider waiting until 3 months after complete cessation of breast-feeding if only 'antibody' HIV testing is available.
4. All HIV-exposed infants should have an HIV antibody (rapid) test at 18 months (regardless of prior test results).

Assessment and follow-up of HIV exposed and infected children

Birth history

- PMTCT regimen use by mother and baby
- Mode of delivery (C-section or vaginal)
- Complications
- Feeding choice

Interim history

- Changes or new illness since last visit
- Child's appetite and feeding practices
- Any new developmental milestones or loss thereof
- TB and other illnesses in the household
- New medication and adherence to previously prescribed medications (e.g. cotrimoxazole prophylaxis)

Parental concerns

- Note: parents often recognize problems first!

Social and Psychosocial history

- Maternal health
- Source of income and give advice on how to access children's social grant
- Support structures, 2nd care giver
- Disclosure to child and to others (see Appendix 19 for general guidelines on disclosure to children).
- Problems with substance abuse, family violence
- Assess understanding of issues

Tips for the physical Examination

- If possible, examine the child in the presence of caregiver
- Engage the child (not only the caretaker)
- Observation is very important
- Be creative and adaptable; use play when possible
- Perform potentially uncomfortable procedures last (such as mouth and ear examinations)
- Children should be undressed for all physical examinations

Examination

- Identify signs of disease progression
- Look for physical changes indicating HIV involvement (e.g. enlarged liver or spleen, thrush, lymphadenopathy, dermatitis)
- Initial examination must be comprehensive and include all organ systems
- Follow up assessment can be targeted according to history and previous findings
- Annual complete examination for all children

Growth and nutrition

Growth progression is one of the best indicators of a child's overall health

- Monitor weight, length/height and head circumference
- Plot these parameters on growth charts
- Routine deworming:

Age	Weight	Albendazole
12 up to 24 months	< 10 kg	200 mg single dose
> 24 months	10 kg or more	400 mg single dose

- Advise parents about safe food preparation (e.g. washing hands, sterilizing teats and other utensils, clean water, preparing one feed at a time etc.).
- Advise care givers about improving the nutritional value of meals e.g. adding vegetable oil, margarine or peanut butter to the child's porridge, samp, rice or potatoes
- If child is failing to thrive, look for treatable causes and manage these appropriately e.g. chronic diarrhoea, TB, malnutrition.
- Food supplementation where indicated

REMEMBER **Stunting in children**

Stunting means that children are not growing well in height. A child may appear to be proportional (normal weight for height) but still be stunted (height for age < 3rd centile). Chronic malnutrition in the HIV infected child can cause this to happen. This is another reason why it is so important to measure all the growth parameters of children including weight and height (and head circumference for the child < 3 years) and to evaluate these (by plotting them on curves, e.g. weight for age and weight for height or, height for age).

Developmental Assessment

- Measuring and plotting head circumference can help to identify poor brain growth
- Abnormal development should raise concern of disease progression
- Loss of previously attained milestones could be a sign of HIV encephalopathy: in this case, refer immediately for HAART
- Ask the care giver about the child's achievements and their concerns

Table 15. Developmental Checklist

1 month	Raises head, alert to sound, makes crawling movements
2 months	Holds head at midline, lifts chest off the table, smiles
4 months	Rolls front to back, laughs
6 months	Sits supported, babbles
9 months	Pulls to stand
12 months	Walks alone, uses single words
18 months	Can remove garment, scribble, run

Table 16. Developmental Warning Signs

6 weeks	No eye contact, no smile, poor suck, Floppy excessive head lag
6 months	Doesn't reach for object with both hands, no response to sound, poor social response to people
10 months	Unable to sit unsupported, hand preference, fisting Persistence of primitive reflexes
12 months	Unable to bear weight on legs
18 months	No walking No single word with meaning

Dental Evaluation

Dental caries and periodontal disease are common in HIV-infected children of all ages

- Advise and encourage good oral hygiene
- Refer to dentist when indicated

Staging of HIV disease

- Clinical staging every 3–6 months
- According to the revised 2007 WHO staging (see Appendix 2)
- CD4 count evaluation 6 monthly

Children are born with high CD4 counts. CD4 levels gradually decrease to adult levels by 5–6 years of age. This is why we use CD4 percentages to monitor the younger children's (below 5 years) immunological status. The CD4% is a better marker of immune status.

Management of intercurrent medical problems

These include common childhood infections, skin conditions, tuberculosis, etc. They are discussed in prior chapters.

Immunisation

- All children should be immunized according to the national immunisation schedule and according to the WHO Expanded Program on immunization (EPI).
- Is of vital importance in preventing and reducing the severity of some conditions in HIV infected infants.
- BCG vaccination
  - BCG vaccination should routinely be given to newborns at birth except if the mother has pulmonary TB. In this case, INH prophylaxis should be given to the baby, if asymptomatic, for 6 months according to protocol (see **page 96**).
  - If BCG vaccination is delayed because the mother has TB, the HIV-uninfected, exposed infant may receive vaccination after completion of prophylaxis (provided active TB is excluded).
  - The HIV-infected infant should not receive BCG until on ART and having strong immune recovery.
  - HIV exposed or infected children who receive BCG should be closely followed to provide early identification and treatment of any BCG-related complication.

Cotrimoxazole Prophylaxis (also see Table 2 on page 21)

If taken regularly, CTX protects against

- Pneumonia, especially PCP
- Brain infections (toxoplasmosis)
- Certain types of diarrhea
- Other bacterial infections, such as UTI
- Malaria

Table 17. Cotrimoxazole prophylaxis dose

Weight (kg)	Daily preventive dose of Cotrimoxazole dose [given as syrup (240 mg/5 ml) or tablet (single-strength, 480 mg)]
< 5	2.5 ml
5–13.9	5 ml or half a tab
14–29.9	10 ml or one tab
≥ 30	2 tabs

Treatment with ARVs

- ARV enrolment criteria are detailed in Appendix 5
- Follow-up on ART is discussed in the ARV chapter (**page 163)**

Ongoing education and support of families

Provide ongoing counselling for child and caregiver and refer appropriately for specialized care and social and community based programs. Discuss:

- Issues with breast feeding
- Changes in family structure, illnesses
- Financial difficulties
- Disclosure issues (See Appendix 19)

Infant feeding

General considerations:

- Counselling on infant feeding should be started after the first post-test counselling session during pregnancy and infant feeding should be discussed with women at every antenatal visit.
- The decision will depend on her preference, social or family support, availability and affordability of formula, and whether she has regular access to safe, clean water.
- Encourage exclusive feeding during the first 6 months. Discourage mixed feeding as it increases the risk of childhood infections and the risk of HIV transmission.
- Before 6 months of age, the infant does not need any food other than milk to grow. After 6 months, complementary foods are necessary for the infant's growth and should be introduced even though the breastfeeding mother is encouraged to continue breastfeeding beyond 6 months (together with NVP infant prophylaxis if the mother is not on lifelong ART).

i Exclusive breastfeeding during the first 6 months of life means baby gets only breast milk (no formula, tea, water, cereal, traditional medicines), oral polio vaccine and cotrimoxazole prophylaxis. Medications prescribed at the health centre or hospital to treat inter-current medical problems, are also allowed. Likewise, exclusive formula feeding means baby gets only formula (no breast milk!).

Breast feeding (BF)

- The health and child survival benefits of breastfeeding should be emphasized. The risk of transmitting HIV through breast milk is reduced if the mother is on lifelong ART or if infant NVP prophylaxis is given throughout the breastfeeding period (until 1 week after).
- Encourage exclusive breastfeeding for the first 6 months of life
- From 6 months of age, introduce nutritious complimentary foods
- Encourage continued breastfeeding after 6 months of age. Unless the infant is already found to be HIV-positive, it is preferable to stop breastfeeding at 12 months, in order to stop infant NVP. However, if weaning at 12 months would compromise the nutritional status of the child, the mother should be encouraged to continue breastfeeding beyond 12 months (up to 2 years), while the infant continues NVP prophylaxis.

- If the baby's PCR result is positive, the mother should be encouraged to continue breastfeeding until 2 years.
- Mothers who are not on lifelong ART and who decide to stop breastfeeding at any time should do so gradually over 1 month whilst the baby continues to receive daily NVP (until 1 week after all breastfeeding has stopped). Abrupt weaning is no longer recommended.
- Baby should feed on demand
- Within 1 hour of delivery ensure correct latching occurs (enough areola in the mouth) to prevent cracked and sore nipples
- If cracked nipples, mastitis or breast abscess occur, client to stop feeding from the affected breast, express and heat-treat the milk, and cup-feed baby.
- Mother to check the baby's mouth regularly for sores.
- Assess mother's nutritional status. Check BMI. Refer to dietician.
- No bottles, teats or pacifiers.

Formula feeding (FF)

- Formula feeding is **only** an option if it is affordable, feasible, accessible, safe and sustainable (AFASS criteria) or where the mother is too sick to breast feed or where the child has been orphaned
- Ensure client has family support to formula feed exclusively during the first 6 months.
- Advise client to strap breasts to inhibit milk supply
- Advise on management of breast engorgement: express milk, apply cold cloths.
- At each visit ensure client can mix formula properly and is cleaning utensils adequately.
- At 6 months of age, infants with or at risk of poor growth should be referred for continued nutritional monitoring and dietary assistance and for DNA/PCR to exclude HIV-infection.
- Infants weighing < 2 kg should receive a special low birth weight formula (not soy-based) until the infant weighs at least 2 kg.

REMEMBER **If the HIV-positive mother meets AFASS criteria and opts for exclusive FF, safe practices should be discussed at every visit**

- Give clear guidance regarding volumes and frequency of feeding needed at each age
- Discuss dangers associated with bottle-feeding. Discuss and demonstrate cup feeding as a recommended alternative to bottle feeding
- Discuss home support for avoiding all breastfeeding; ensure that the woman has a carer/supporter outside the health facility to help her avoid all breastfeeding.

Test yourself

- What are the criteria to start a pregnant woman on HAART or AZT?

- When should HAART or AZT be started as part of PMTCT?

- What drugs should be given in the minimum package if the mother is on HAART and what are the instructions for the mother if she plans to breast feed?

- What drugs should be given in the minimum package if the mother is on AZT prophylaxis and what are the instructions for the mother if she plans to breast feed?

- When should the mother bring the baby back for the first PCR test?

- A baby presents for the first time to the clinic age 10 months. You test the mother and she is HIV+ve and she has had diarrhea for 6 weeks. You then test the child and the rapid test is positive. What do you need to do for mother and child today?

- What are the criteria to start ART in
  - a child <12 months
  - a child age 36 months
  - a child age 7 years
- What is the first line of choice (give dosing and frequency) if Hb > 8
  - a child age 5 years and 23 kg
  - a child age 2 years and 12kg
  - a baby of 3 months , 6.1kg who has been given PMTCT and is PCR positive at 8 weeks
- A child has been taking triomune junior 1 tablet twice a day. Today he weighs 16 kg. What ART prescription does he need today?

- A 9 month exposed baby who tested negative at 6 weeks but who has been breastfeeding is failing to sit upright without support and is not growing well. What should you do and what could be the underlying cause?

Antiretrovirals (ARVs)

Also known as Antiretroviral Therapy (ART) or Highly Active Antiretroviral Therapy (HAART)

Perspective

Antiretrovirals (ARVs) have become standard treatment for those people infected with HIV. Ideally they should be given to people before their immune systems become severely weakened. i.e ARVS should be started as close to a CD4 count of 350 as possible - this threshold may soon be raised by WHO. ARVs do not eradicate HIV, but block its replication, which then allows the immune system to recover some of its strength. Put more simply, ARVs "stop HIV from growing". By doing so, opportunistic infections become less frequent and less severe, and the person's clinical condition markedly improves. Patients on ARVs might still transmit HIV, but the transmission risk is much lower.

Principles of Therapy with ARVs:

1. **Not all HIV-infected people need ARVs**

   Results of clinical staging and CD4 count testing are used to decide when to start ARVs for adults and older children (see Appendices 3, 4 and 5).

   For infants, the situation is different. **Infants are at a very high risk of dying before the age of 2 years, so early treatment with ARVs should be given to all HIV-positive infants under 12 months, regardless of clinical or immunological status.**

2. **Some HIV-infected people need to be fast-tracked for initiation within 2 weeks**

Require fast track (i.e. ART initiation within 2 weeks of being eligible)
• Pregnant women eligible for lifelong ART OR • Patients with very low CD4 (< 100 cells/µL) OR • Stage 4, CD4 count not yet available OR • All TB patients (after two weeks of TB treatment) and MDR/XDR TB • Children younger than 1 year

3. **ARVs can be given either for treatment (i.e ART) or prevention (PMTCT, Post-exposure prophylaxis, or post-rape).**

4. **HIV can easily develop resistance to individual ARVs.**

   For treatment purposes, three ARV drugs are given together ("Triple therapy") in order to prevent resistance of HIV to individual ARVs. This concept is similar to that seen in TB treatment, where multiple TB drugs are given simultaneously to stop TB (and avoid resistance to TB drugs).

5. **We must do everything possible to prevent resistance from developing.**

   Treatment with ARVs is a life-long treatment. ARVs "stop HIV from growing" only if they are taken faithfully every day. If someone stops ARVs, HIV will start to grow again (and weaken the immune system). ARVs must be taken correctly as prescribed (at the right time, the right dose, and every day!). If they are taken irregularly, 'resistance' will develop and the HIV will once again start to replicate in the presence of the three ARVs. Support is needed to enable a person to take ARVs every day. The person (or caregiver, in the case of a child) must live in a stable, supportive environment, must believe in the usefulness of ARVs and must be motivated to take them! She/he should be encouraged to attend a support group for people living with HIV. She/he should have disclosed her/his HIV status to at least one person in whom they trust.

   Living in denial is a contraindication for ARVs. The development of resistance means that those three ARVs won't be effective ever again for that person, even if they are subsequently taken faithfully. The only chance that person then has to lower the HIV 'viral load' is to start taking three new ARVs (known as 'second line' treatment). **It is better for a person to wait and be ready to start ARVs than to take them incorrectly.**

6. **Change one ARV in case of a severe side effect; change all 3 ARVs if the regimen has failed.**

   Changes may be required for several reasons. Some people may have a major side effect to one ARV. Other times, a whole regimen fails (usually due to earlier problems with adherence).

   The two main reasons for changing are:

   - **Substitution for side effect:** Change only the one "culprit" drug. (always check for symptoms and signs of possible treatment failure first. See Appendix 13.)
   - **Switch for failure:** The whole regimen has to be changed because the HIV in that particular person's body has developed resistance to all three ARVs. The three original ARVs are replaced with three new ARVs (a 'second-line' regimen).

   Changing regimens is a serious decision. The nurse, counsellor and HIV doctor should discuss each case before changing regimens. The first-line regimen is always a person's best chance at maintaining an undetectable viral load; we must help people on 'first-line' ARVs to be faithful to their treatment! Always try to correct a problem with adherence before switching to a 'second-line'

regimen. If the HIV in a person's body has developed resistance against the 'first-line' ARVs because of poor adherence, the same will happen against the 'second-line' ARVs unless the adherence problem is corrected!

7. **Treat any OIs (especially TB) before starting treatment with ARVs.**

   Thoroughly assess for OIs, other HIV-related conditions (such as anaemia and PN), and contraceptive issues before deciding on the first-line regimen. See Appendices 3 and 4. Always try to stabilize the patient as best as possible (by treating TB and other OIs, and improving nutrition) before starting ARVs.

Monitoring on ARVs

Criteria for enrolment for ARV's and 1st and 2nd line regimens in adults are detailed in Appendices 3, 4 and 5. After initiation of ART, patients must be monitored for:

- possible side effects
- efficacy (success) of ART and development of resistance

Monitoring on ART	Purpose
Clinical stage	To monitor response to ART
CD4 at month 6, 1 year on ART and then every 6 months	To monitor response to ART
If available VL at month 3 or 6 (according to local protocol) and then yearly	To monitor response to ART To identify problems with adherence
ALT if on NVP and develops rash or symptoms of hepatitis	To identify NVP toxicity
FBC at month 1, 2, 3 and 6 if on AZT	To identify AZT toxicity
If available and feasible creatinine at month 6, 12 and then every 12 months	To identify TDF toxicity
Fasting cholesterol and triglycerides at month 3, month 12 and then yearly if on LPV/r	To identify LPV/r toxicity

Monitoring for possible ARV-related side effects

Clinical and laboratory monitoring should be performed frequently in the first few months after ART initiation in order to diagnose and manage any short-term side effects early. See Appendices 11, 12, and 13.

Monitoring for Efficacy (Success) of ART

The measurement of the success of treatment with ARVs can be done in three ways:

1. Clinically (by monitoring for subsequent infections)
2. Immunologically (by monitoring CD4 counts) and
3. Virologically (with viral loads).

Clinical monitoring

Allow 4–8 weeks on ARVs until the first positive effects are seen: weight gain, improvement in general health, and fewer new infections. After starting ARVs, opportunistic infections can still occur, especially if CD4count < 100. Infections can also worsen several weeks after ART initiation, a situation called IRIS (Immune reconstitution inflammatory syndrome). Look for signs of infection, particularly TB, at each visit. Check weight. Investigate weight loss > 1.5kg in 4 weeks.

REMEMBER **Note that ARVs do not work instantly so make sure to stabilise your patient before starting ARV's! They slowly stop the HIV from growing and a person gradually feels better. If a person has a very low CD4 count when starting ARVs, that person is still at risk of suffering from serious infections in the first 6 months on treatment. Almost all people who die in the first 6 months on ARVs do so as a result of new serious infections. They do not die from starting ARVs!**

CD4 Lymphocytes

The white blood cells which are targeted by HIV are called CD4 cells. These CD4 cells help a person's immune system to fight infection. In healthy individuals, there are 500–1500 CD4 cells per microlitre of blood. Following infection with HIV, the CD4 cells in a person's body are attacked by the replicating HIV and the CD4 count gradually drops. The speed at which the CD4 count drops is different in different people. The CD4 count will eventually drop down to zero, unless a treatment (ARVs) is started to "fight the HIV". The absolute number of CD4 cells determines the risk for development of HIV-associated diseases (see Table 1 on **page 3**).

Treatment with ARVs interrupts the life cycle of HIV, so HIV "stops growing" and stops killing the CD4 cells. The CD4 count then slowly rises (usually to a level well above 200). However, this can take many months or years, and will only continue if the person is faithfully taking the ARVs. This level of 200 is important, since most OIs occur when the CD4 count is below 200.

Viral Load

This blood test measures how much HIV is in a person's blood. It does not measure how the patient is feeling or how high the CD4 count is. After several months of ARVs (usually no more than six), the HIV viral load should fall to undetectable levels. This undetectable level (also known as LDL or 'lower than detectable' limit) is important since it means that the HIV has stopped growing as a result of the ARVs. Where viral loads are available, they are used to monitor a client's progress and make decisions about switching to second line. In some settings viral load is performed routinely. However if resources are constrained, viral load will only be performed if triggered by clinical, immunological or adherence triggers. (See Algorithm 14 on **page 171**).

A previously undetectable viral load may rise and become detectable again for the following reasons:

- The person is not taking the ARVs faithfully.
- The person is taking the ARVs incorrectly.
- The person is taking another medication, which is reducing the effectiveness of the ARVs (this can occur with both TB meds and traditional medicines).
- The blood sample was mixed up with that of another patient.
- The person is suffering from an intercurrent illness (TB, common cold, etc), which boosts replication of HIV. We call this a "blip" in the viral load.
- Frequent vomiting or diarrhoea, which prevents absorption of ARVs into the body.
- The virus was already resistant or has developed resistance to the antiretroviral medication

Monitoring of children on ART

ARV enrolment criteria and 1st and 2nd line regimens for children are detailed in Appendices 5 and 9.

Four main aspects requiring on-going monitoring are:

- Treatment efficacy: clinical, CD4, (viral load if available)
- Adherence to ART regimen
- Drug toxicity and adverse events
- Developmental and psychosocial progress

Treatment efficacy: clinical, CD4, viral load

We measure success of ARVs in children the same way as we measure it in adults. In children, we often notice clinical improvement quite rapidly. The child will gain weight and he/she will feel much better. Often the caretaker will be the first one to tell you that the child is now playing, not sick as often, and doing things she/he wasn't able to do before. Don't forget to weigh the child at every visit and plot the child's weight on a growth curve. This is one of the most sensitive indicators of treatment success! If the child is getting worse in the first months of treatment instead of getting better, you must suspect IRIS: look carefully for any undiagnosed OI's, especially TB.

As for adults, the child's CD4% should gradually increase on ARVs and the viral load become undetectable. After 1 year on ARVs, the CD4 % in a severely immune-depressed child < 5 years should have risen significantly above its baseline. For a child > 5 years, you should see an increase of at least 50 cells/µl.

Criteria for switching to second line treatment in children are discussed later in this chapter.

Adherence

Adherence poses additional challenges in children for several reasons. Some of these are: the young child is dependent on his/her caretaker to administer the medication at the right time and in the right dosages; fewer fixed dose combinations for children exist; sometimes the child must take syrups which he may not like the taste of, the caretaker can change, etc. Assess adherence at every visit and use every interaction with a caregiver to re-enforce the absolute need for adherence. Also remember that just because a child is adherent today, does not mean that he/she will stay adherent. In particular, as children become adolescents, adherence can become a new challenge.

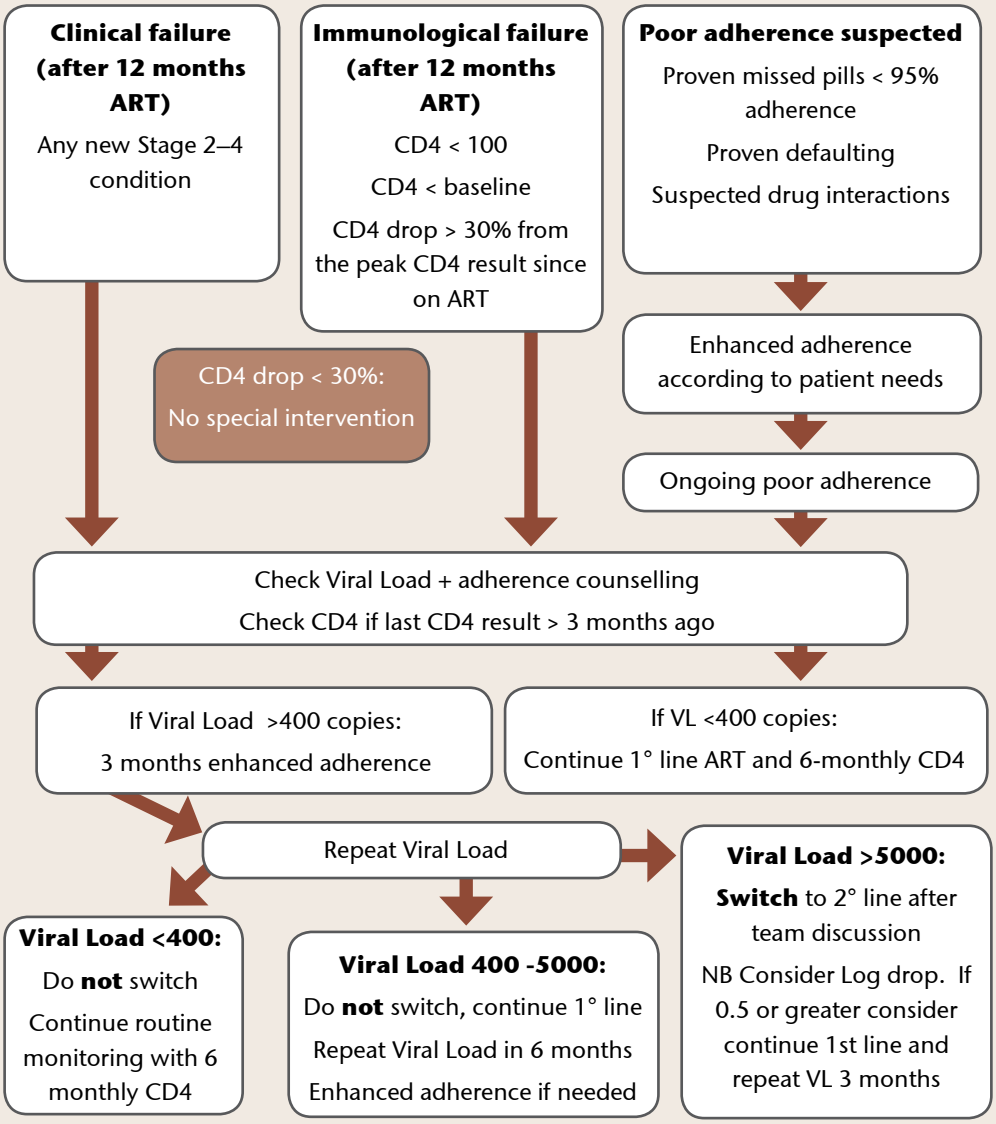
Side Effects

ART associated side effects occur in children as well as adults. Fortunately they are seen a little less commonly in children. However this means that they may be missed when they do occur. Vigilance and proper education given to the caregiver can help avoid this. For more discussion on side effects and management see section on side effects later in this chapter.

Developmental and psychosocial progress

How the child is developing can help us decide when the child needs ARVs (see section on HIV encephalopathy **page 120**). It will also help us see how the ARVs are working. Usually, the caretaker will notice a big improvement in the child's progress once ARVs are started. Also, if adherence is a problem or if the child has developed resistance, we may notice that the child simply is not developing well. This is why it is so important to ask the caretaker how she/he thinks the child is doing. Also clinicians should assess the child's development every 3 months by using the development checklist (**page 156**).

Algorithm 14: Triggered viral load use and switch to second line



The definition of lower than detectable limits (LDL) can vary depending on the laboratory used. All switches to second line should be after a minimum of 12 months on ART.

If TDF is in the first line check Hep B status and consult doctor.

Notes: HBsAg should be checked before considering a discontinuation of TDF, since stopping TDF could cause a serious flare of hepatitis.

If routine viral load becomes available the same algorithm flow will be followed. i.e if VL is detectable 3 months of adherence support will be given and the VL repeated. If VL is > 5000 copies/ml then the patient will be switched to second line. N.B remember to consider the log drop.

Second line treatment in adults

- Give 2nd line treatment if viral load is raised (as described in Algorithm 14: VL > 5000 copies/ml) with or without opportunistic infections and the client is adherent and getting increased adherence support.
- Client to get similar work up as before starting 1st line ARV regimen-steps 1–5 (Appendix 3)
- Discuss all clients who have received ARVs other than the standard regimen with a specialist.
- See Appendix 8 for 2nd line regimens and doses of second line drugs in adults
- Patients failing second line therapy have few treatment options. Failure is almost always due to poor adherence, and every effort should be made to address this, as re-suppression is often possible on the failing drugs.

Criteria for switching to second line treatment in children

The same viral load follow-up criteria apply to children and adults, with the only difference being that, in case the child is failing a PI-based regimen, the adherence re-enforcement must be even stronger, and the cut-off for switching is then VL > 5000 copies/mL. Children can get second line treatment if viral load is raised (Algorithm 14) with or without opportunistic infections and the child is adherent and getting increased adherence support.

Treatment failure should be suspected in children if there is:

- Confirmed return of CD4 percentage (repeated within 1 month) to baseline (CD4 level before starting ARVs) or below, in the absence of concurrent illness to explain CD4 decline.
- A CD4 returning to a count of <200 or CD4% of <10% for a child > 2 years and < 5 years. A CD4 count returning to <100 for a child 5 years of age or older.
- Lack of growth or decline in growth in a child showing initial response to treatment
- Loss of neurodevelopmental milestones or development of HIV encephalopathy
- New evidence of stage 3 or 4 disease after immune reconstitution. (Note: Presentation with TB while on 1st line treatment is not an indication to switch. Also, IRIS is not an indication to switch).

REMEMBER

General considerations prior to defining treatment failure in children:

- At least 24 weeks on therapy
- Always attempt to improve adherence before switching regimens as poor adherence is the commonest cause of virological failure.
- Treat any intercurrent opportunistic infections
- Exclude IRIS
- Ensure adequate nutrition
- First check adherence: if it is not possible to improve adherence, attempt directly observed therapy (DOT) with a health care worker or another adult living in the same house.

Side Effects of ARVs

Important points:

- Not every person starting ARVs will suffer from side effects! Only some people get side effects.
- Side effects are more common in severely immunocompromised (CD4<200) patients.
- Side effects can also be classified into those occurring early and those occurring late (see Appendix 12).
- Side effects can be graded to help differentiate between minor and major problems (See Appendix 13).
- Instruct the patient to report any side effects early and not to stop any drugs without consulting the nurse or doctor first.

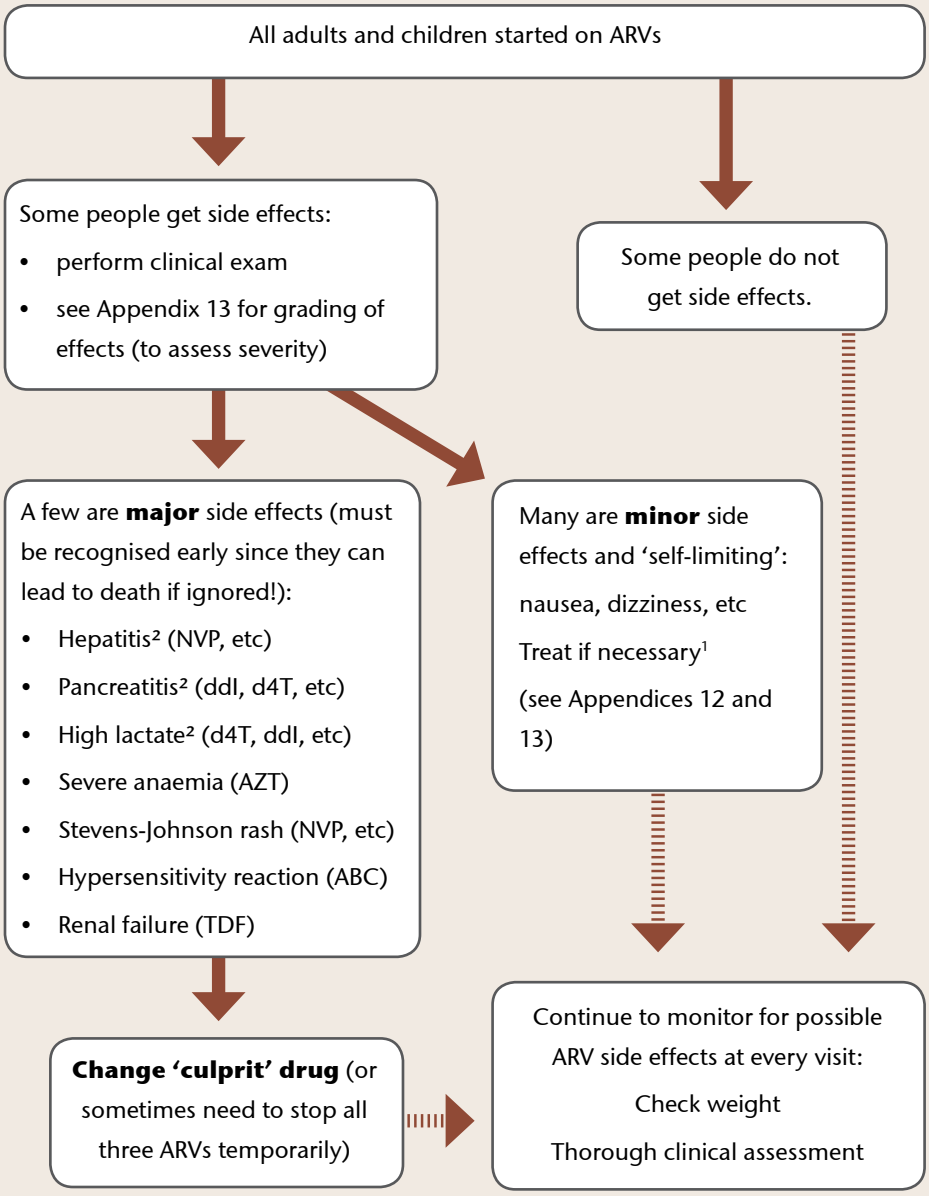
Common side effects of ARVs (Appendices 12 and 13)

The following side effects are more common

Nausea +/- Vomiting

- All drugs can cause this, but it is more common with DDI, AZT, and Protease Inhibitors (PIs)
- Nausea already occurs in all HIV patients to some extent. It can become worse when ARVs are initiated, but ARV-related nausea is usually 'self-limiting' (resolves on its own after several weeks on therapy). There is usually no treatment needed.

Algorithm 15: Managing possible ARV side effects



Notes:

1. Do not change culprit ARV for a minor side effect. Do not systematically prescribe more drugs to treat side effects of ARVs! For example, not all people with nausea need another drug!
2. If someone on ARV's complains of abdominal pain or is losing weight, take blood for relevant tests and refer to doctor

- Metoclopramide 10 mg three times daily as required may help if the nausea is severe.
- Change of drug times may help to some extent (for example, DDI can be tried 2 hours after breakfast instead of one hour before breakfast).
- The more drugs a patient has to take, the more likely there is to be nausea and vomiting (for example, when a person must take ARVs and TB drugs together).
- If the ARVs are vomited, tell the patient to take the pills again after 2 hours. If the vomiting is very severe or does not stop, then consult the doctor.
- Take immediate action (refer for immediate assessment) if the vomiting:
  - Is associated with serious symptoms such as fever, severe rash, and/or jaundice (must **exclude Hepatitis**)
  - Is very severe and does not stop over several days (resulting in dehydration)
  - Is associated with abdominal pain (must **exclude Pancreatitis**)
  - Occurs in patients who are > 4–6 months on ARVs (especially D4T and DDI) and is associated with weight loss (must **exclude high lactate levels before lactic acidosis develops**)

Rash

- Rash is a typical side effect of the NNRTI class of ARVs. Most commonly a concern with NVP; sometimes with Efavirenz or with Cotrimoxazole.
- It occurs during the first 4-8 weeks of treatment, and is much more common with Nevirapine (NVP) than Efavirenz (EFV). For this reason, only half of the usual dose of Nevirapine dose is given during the first 2 weeks of treatment.
- Always recheck the "liver blood test" (ALT) when you see a rash that might be associated with NVP.
- NVP can be continued in the presence of a mild rash (see below) by an experienced nurse or doctor. However, take immediate action (refer to the doctor for assessment and probably a change of the culprit drug) if the rash:
  - Is associated with serious symptoms such as fever, vomiting, or jaundice (must **exclude Hepatitis**)
  - Is associated with a significant increase of ALT (> 5 times the upper limit of normal for ALT, which works out to ALT > 200 in an adult)
  - Progresses and becomes **very severe** (with scaling and skin erosion)
  - **Mucous membranes** are involved ('Stevens-Johnson rash'). These patients need to be referred to hospital ASAP!

- For a mild rash,
  - Continue the 'culprit drug' (usually NVP), consider extending the lead-in dosing, but see the patient every 2-3 days
  - Chlorpheniramine 4 mg three times daily as required may help reduce itching
  - Topical steroid such as Betamethasone ointment may help (but do not use oral steroids!)
  - If in doubt about what to do, consult the doctor.

Dizziness and "light-headedness"

- Can occur with Efavirenz, and AZT
- No specific action needed. This is why Efavirenz is prescribed at bedtime.
- If the dizziness does not disappear after a few weeks, EFV may need to be changed to Nevirapine.
- See Appendix 13 for other possible **psychological** side effects due to EFV.
- If there is a concern about anaemia causing the dizziness (sometimes occurring with AZT), check the Haemoglobin and **refer to the doctor if the Hb is low on AZT.**

Peripheral Neuropathy (PN)

- Occurs most commonly with D4T and DDI
- This possible side effect can become serious!
- Never use D4T and DDI together, since this increases the likelihood of PN.
- If patient is on D4T and has symptoms of PN substitute the D4T for another drug (usually TDF). This change should be made no matter the severity of the PN. It should be made sooner rather than later as clients may have persistent neuropathic pain and/or difficulties walking if left for too long. Always check CrCl if you intend to start TDF.
- Treat PN as described in Appendix 13

Serious side effects of ARVs

The following possible side effects are potentially fatal if missed or ignored!

Hepatitis (inflammation of the liver)

- Hepatitis can occur **acutely** (associated with fever and rash as described above with NVP) or more **chronically** (with D4T or Ritonavir). For acute NVP-induced hepatitis, see also Appendix 13.
- Hepatitis is more common when ARVs are used at the same time as TB medication.
- If the hepatitis is mild, then monitor the ALT regularly to ensure that it is not getting worse.
- If the ALT result is getting progressively higher, then the culprit ARV must be substituted with a new drug.
- If you suspect that a patient has severe hepatitis (jaundice and/or abdominal pain), then **refer to the doctor immediately**.

Pancreatitis

- Didanosine (DDI) is the most common cause (D4T and 3TC occasionally)
- Pancreatitis can be life-threatening!
- Think of it and if possible check the serum amylase +/- lipase level whenever someone on ARVs presents with **abdominal pain**.
- If in doubt, **refer to the doctor**; don't send the person home to return in a month!

Lactic acidosis (which is preceded by high lactate levels or 'hyperlactatemia')

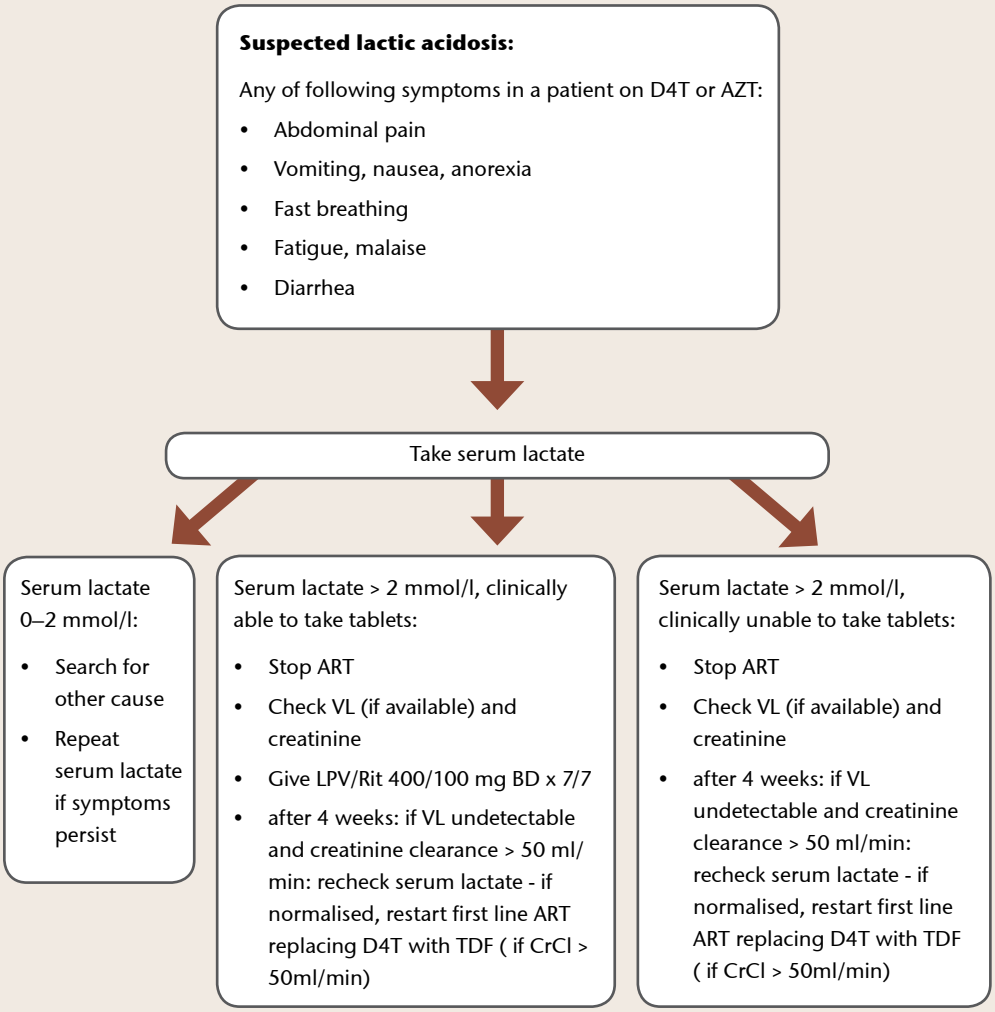
- Can occur with any ARV in the NRTI class, but is most commonly due to D4T or DDI.
- **Monitor clinically for hyperlactatemia** in all patients taking ARVs for more than 3 months, especially obese people (BMI > 28), pregnant women, those on D4T, and those on DDI.
- Watch out for the patient who was stable on ARVs but then starts to feel unwell after 6-9 months (especially when on D4T or DDI).

- The initial symptoms will be non-specific. **If symptoms of high lactate are ignored, then the patient will become sicker and sicker with vomiting, shortness of breath, seizures and even death from lactic acidosis.** This is another reason to check the weight on every single visit!
- Other clinical features of hyperlactatemia:
  - Fatigue
  - Nausea
  - Vomiting
  - Abdominal pain
  - Loss of weight
  - Shortness of breath
- Refer to Algorithm 16 on the next page for the management of suspected hyperlactatemia/lactic acidosis.
- To help prevent this side effect, D4T is no longer used in usual first line regimens (adults and children), and, for adults, DDI is no longer used in usual second line regimens. For individuals already on regimens containing D4T, this drug should be continued unless side effects develop, or the adult client is at high risk of toxicity (i.e., BMI > 28, TB treatment).

i NRTIs cause depletion of mitochondria DNA in the body's cells (mitochondria = "breathing-engines" of our bodies' cells). This may lead to impaired cell function and a metabolic syndrome which involves high lactate levels (hyperlactatemia) which can then progress to lactic acidosis. It is very important to identify this side effect early **before** it progresses to acidosis.

REMEMBER **High lactic acid might also be caused by any situation of circulatory or respiratory failure (e.g. shock, severe infection, severe pneumonia...). All these conditions have to be detected early and managed appropriately in order to prevent mortality.**

Algorithm 16: Management lactic acidosis



Risk factors for lactic acidosis:

- D4T > DDI > AZT > 3TC/ABC/TDF
- Low CD4
- Woman
- Hepatitis B/C or liver disease
- Renal insufficiency
- Obesity

Hypersensitivity reaction

- rare but potentially fatal reaction to Abacavir (ABC)
- see **page 221** for further details

Renal impairment

- may occur with Tenofovir (TDF) (see **page 223**)
- in adults taking TDF, renal function should be routinely monitored by calculating the Creatinine clearance (CrCl)

Other possible late side effects

Lipodystrophy (fat redistribution)

- Can occur with PIs or NRTIs (such as D4T, especially when used in combination with DDI).
- Patient will present with increase of fat around abdomen, breast and/or back of neck. Decrease in fat in face, limbs and buttocks.
- Usually occurs in patients who are on long term therapy.
- Can be disturbing and stigmatising for the patient.
- Changing the offending ARV (D4T to TDF) can lead to improvement (but substitution is allowed only if the latest VL is undetectable and adherence isn't a concern).

Hyperglycaemia and Diabetes mellitus

- Can occur with Protease inhibitors (PIs).
- Consider screening those on LPV/r with yearly fasting glucose levels.
- Management is similar to that of Diabetes.
- The offending ARV may need to be changed (Eg. LPV/r to ATV/r).

Hyperlipidemia

- A person's triglyceride and cholesterol levels often rise when taking a Protease Inhibitor (such as LPV/r). Even if screening for raised lipids is not possible or statins are not available simple advice such as cessation of smoking and the benefits of a healthy diet and exercise should be discussed. This is especially important for patients who have hypertension, diabetes, exisiting cardiovascular disease or a strong family history of cardiovascular disease.

Immune reconstitution inflammatory syndrome (IRIS):

IRIS is a paradoxical phenomenon that occurs when the patient on ARVs begins to have immune recovery in the setting of an untreated or not fully treated OI. This may lead to a transient worsening of symptoms or clinical status, despite favourable recovery of immunological status (CD4 count/percentage). When this occurs, all efforts must be made to find, diagnose and treat the OI.

Clinical presentation

- Usually IRIS occurs within the first 2–9 months of initiating HAART (most cases occur in the first 3 months).
- IRIS is most common in patients with severe immune-suppression (CD4 < 100) and recent diagnosis of OI's before ART was started.
- **TB**, Cryptococcus, Herpes Zoster virus, CMV, NTM, Hepatitis B & C are commonly reported to cause IRIS.
- IRIS syndrome may present in two forms:
  1. The first is the worsening type. This means an OI that was successfully controlled and on continued treatment, worsens a few weeks after start of HAART.
  2. The second is the unmasking type. This means a previously undetected sub clinical infection presents with new and frequently unusual manifestations.

REMEMBER **The possibility of IRIS should be explained to patients prior to the initiation of HAART. This will assist with future adherence and help the patient return early for care and management if symptoms do occur.**

Management

- In general, HAART should not be interrupted if the immune reconstitution syndrome occurs unless a life threatening illness has occurred.
- Treatment of the unmasked OI is essential, and in severe cases a short course of steroids could be considered: prednisolone 40 mg/day for 2 weeks, followed by prednisolone 20 mg/day for 1 week, followed by 10 mg/day for another week (OI guideline MSF, 2006). **It is essential to exclude other diagnoses before prescribing steroids! This should only be done by the doctor.**

REFER

A patient on ARVs needs to be referred to the doctor when presenting with any of the following problems:

- **a severe rash (especially if it involves the mouth and/ or genitals, or is associated with fever, and the patient is feeling sick)**
- **severe abdominal pain**
- **jaundice**
- **loss of weight of more than 2 kg**
- **shortness of breath**
- **severe vomiting with dehydration**
- **severe headache**
- **changes in body shape**
- **numbness ('pins and needles') in hands and feet that does not improve**

Drug interactions

One drug can change the blood or tissue level of another by affecting its absorption, distribution, metabolism (processing in the body) or elimination. Some interactions can result in significant changes in drug levels. This may require the dose of one or more drugs to be changed or to use another drug altogether. See Appendix 14 for some of the most common drug interactions.

Conclusion

The Comprehensive HIV treatment programs will be most accessible to the general population if they are primary health care-based. Nurses at primary health care level should feel comfortable managing HIV-related conditions and advising about ARVs in adults and children. HIV treatment programs should also be closely linked with TB programs, since the most common cause of death in HIV patients continues to be Tuberculosis.

By implementing comprehensive, nurse-based HIV treatment programs across Southern Africa, nurses will prevent many unnecessary deaths from TB and other opportunistic infections.

Test yourself

- What is the first line of choice for (give dosing and frequency) an adult male HIV positive patient weighing 66kg?
    - Whose CrCl is 77ml/min and Hb is 9
    - Whose CrCl is 45ml/min and Hb is 10
    - Whose CrCl is 40 ml/min and Hb is 6
- When do you not give TDF?

- List 3 side effects of D4T?

- List 2 common side effects of Efavirenz

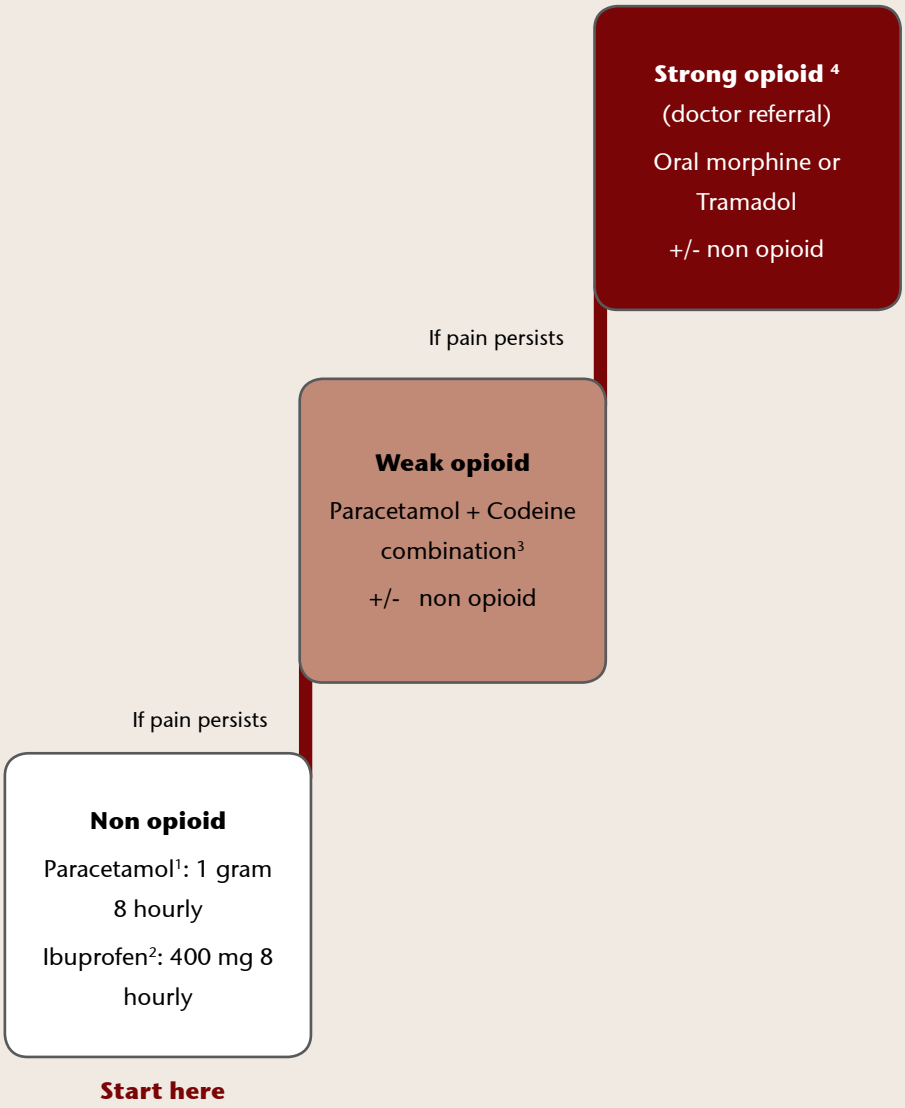
- List the 3 categories of treatment failure and their official definitions

Notes

Notes

Management of Pain

Figure 5: Pain management (The pain ladder)



Notes

1. Refer to Table 18 page 188 for dosage tables of paracetamol for children.
2. This is a non-steroidal anti-inflammatory drug. Do not give if client has a history of gastro-intestinal problems.
3. Refer to Table 19 page 188 for dosage tables of paracetamol and codeine in children
4. Strong and weak opioids should not be combined

General introduction to pain

Chronic pain and pain syndromes are very common (up to 80% at some point during the disease) in HIV positive patients. If not treated properly they can cause much distress for both the patient and their families.

Definition

Pain is an unpleasant sensory or emotional experience because of tissue or nerve damage. Chronic pain may be caused by a dysfunctional nervous system.

Causes

Common causes of pain in HIV patients:

- **Peripheral and sensory neuropathies**
- Post herpetic neuralgia (after Shingles)
- Lactic Acidosis Syndromes

Principles of symptomatic management

- Always treat the underlying cause
  - Eg. add pyridoxine 25–100 mg daily if patients on TB treatment and ARVs
- The World Health Organisation Pain Ladder has been shown to be +/- 90% effective (see previous page and below)

Management Steps of the World Health Organisation Pain Ladder

Step 1

- Use a **Non Opioid** Analgesia: Paracetamol 1g 6 hourly
- Add non steroidal anti inflammatory drugs (NSAIDS) as required (only if no history of gastrointestinal problems): Ibuprofen 400 mg 8 hourly or diclofenac 50 mg 8 hourly

Step 2

- Add a **weak Opioid** analgesic: codeine phosphate 30–60 mg 6 hourly
- Paracetamol and codeine (Panado-Co®) work better as a combination
- Add non steroidal anti inflammatory drugs as above

Step 3

- **Refer to doctor**
- Add a strong Opioid analgesic: Oral Morphine start with 5 mg QID and increase by 5–10 mg increments as necessary. Injectable morphine may be available in some settings. Tramadol is an alternative strong opiod. Start with 50mg up to four times a day and can be increased to 100mg four times a day.

- Add non steroidal anti inflammatory- as above
- Do not use a week Opioid and a strong opioid in combination

Management of pain in children

Pain ladder in children

- Step 1:
  - Paracetamol: 60 mg/kg/day maximum in 3 or 4 divided doses (see Table 18 below)
  - Ibuprofen; Child (> 6 months): 10 mg/kg/day 4 to 6 hourly (max 500 mg/day)
- Step 2: Paracetamol + Codeine (see Table 19 below)
- Step 3: Oral morphine: start with 0.2–0.4 mg/kg/dose 4 to 6 hourly

Table 18. Paracetamol children's dose

Paracetamol 125 mg/5ml syrup; 500 mg tablet				
Weight (kg)	**Dose (mg) 4-6 hourly**	**Syrup (125 mg/5 ml) 4-6 hourly**	**Tab (500 mg) 4-6 hourly**	**Approximate age**
6 to 10 kg	60	2.5 ml	-	3 to 12 months
10 to 18 kg	120	5 ml	-	1 to 5
18 to 25 kg	240	10 ml	Half a tablet	5 to 8
25 to 50 kg	500	-	1	8 to 14
Over 50 kg and adult	1000	-	2	14 and older

Table 19. Paracetamol + Codeine children's dose

Weight	**Age (use only if weight not available)**	**Chronic pain Paracetamol 4-6 hourly (125 mg/5 ml of syrup**	**Chronic severe pain Add codeine phosphate syrup 4 hourly**	
			Min dose	**Max dose**
2–<3 kg	0–3 months	2 ml	0.2 ml	1 ml
3–<6 kg		2.5 ml	0.3 ml	2 ml
6–<10 kg	3-12 months	2.5–5 ml	0.5 ml	3 ml
10–<12 kg	12 up to 24 months	5–7.5 ml	1.0 ml	5 ml
12–<16 kg	24 up to 48 months	7.5–10 ml	1.5 ml	6 ml
16–<25 kg	Over 48 months	10–12.5 ml	2 ml	8 ml

Neuropathic pain

Clinical presentation

Patients complain of a burning, “hot”, tingling sensation – similar to “pins and needles”

Management

Initiate the above steps and add amitriptyline, anticonvulsants, or corticosteroids as described below.

Amitriptyline

- Start with 25 mg at night
- Can increase up to 100 mg at night (doctor to review)
- Give at night as causes drowsiness

Anticonvulsants e.g. gabapentin and carbamazepine

- These require a doctor to review and prescribe

Corticosteroids

- These may be useful to enhance pain relief from nerve pain associated with compression or headaches caused by raised intracranial pressure.
- They need to be used with caution in HIV positive patients.

Notes

Appendices

Appendix 1: WHO Clinical Staging of HIV/AIDS for adults and adolescents with confirmed HIV infection (2007)

Clinical stage 1	• Asymptomatic • Persistent generalized lymphadenopathy (PGL)
Clinical stage 2	• Moderate unexplained weight loss (<10% of presumed or measured body weight)* • Recurrent respiratory tract infections (RTIs, sinusitis, tonsillitis, otitis media, pharyngitis) • Herpes Zoster (Shingles) • Angular cheilitis • Recurrent oral ulcerations • Papular pruritic eruptions (PPE) • Seborrheic dermatitis • Fungal nail infections
Clinical stage 3	• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than 1 month • Unexplained persistent fever (intermittent or constant for longer than 1 month) • Persistent oral candidiasis (thrush) • Oral hairy leukoplakia (OHL) • Pulmonary tuberculosis (current) • Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Unexplained anaemia (< 8.0 g/dL), neutropenia (< 0.5 x 10^9/L), or chronic thrombocytopenia (< 50 x 10^9/L)

* Assessment of body weight in pregnant women needs to consider the expected weight gain of pregnancy

Clinical stage 4	• HIV wasting syndrome: unexplained weight loss > 10% body weight plus either chronic diarrea > 1 month or chronic fever > 1 month • Pneumocystis pneumonia (PCP) • Recurrent severe or bacterial pneumonia • Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration) • Oesophageal candidiasis • Extrapulmonary TB (EPTB) • Kaposi sarcoma (KS) • Central nervous system (CNS) toxoplasmosis • HIV encephalopathy • Extrapulmonary cryptococcosis including meningitis • Disseminated non-tuberculous mycobacteria infection (NTM) • Progressive multifocal leukoencephalopathy (PML) • Candida of trachea, bronchi or lungs • Chronic cryptosporidiosis (with diarrhea) • Chronic isosporiasis • Visceral herpes simplex infection • Cytomegalovirus (CMV) infection (retinitis or infection of other organs) • Any disseminated mycosis (coccidiomycosis or histoplasmosis) • Recurrent non-typhoidal Salmonella bacteremia • Lymphoma (cerebral or B cell non-Hodgkin) or other solid HIV-associated tumours • Invasive cervical carcinoma • Atypical disseminated leishmaniasis • Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

Appendix 2: WHO clinical staging of HIV/AIDS for children with confirmed HIV infection (2007)

(for persons aged under 15 years with confirmed laboratory evidence of HIV infection: HIV antibody if aged 18 months and above; virological (PCR) testing if aged under 18 months)

Clinical Stage 1
• Asymptomatic • Persistent generalized lymphadenopathy (PGL)
Clinical Stage 2
• Unexplained persistent hepatosplenomegaly • Papular pruritic eruption (PPE) • Extensive human papilloma virus infection (warts) • Extensive molluscum contagiosum • Fungal nail infection • Recurrent oral ulceration • Lineal gingival erythema (LGE) • Unexplained persistent parotid enlargement (PPE) • Herpes zoster (shingles) • Recurrent or chronic URTIs (otitis media, otorrhoea, sinusitis, tonsillitis) • Angular cheilitis
Clinical Stage 3
• Unexplained moderate malnutrition (Z score -2) or wasting not adequately responding to nutritional therapy and where TB has been excluded. • Unexplained persistent diarrhoea (two weeks or greater) • Unexplained persistent fever (intermittent or constant, for longer than one month) • Persistent oral candidiasis (after the first 6-8 weeks of life) • Oral hairy leukoplakia (OHL) • Acute necrotizing ulcerative gingivitis/periodontitis • Pulmonary TB • Lymph node TB • Severe recurrent bacterial pneumonia • Unexplained anaemia (< 8.0 g/dL), neutropenia (< 0.5 x 10^9/L), or chronic thrombocytopenia (< 50 x 10^9/L) • Chronic HIV-associated lung disease including bronchiectasis • Symptomatic lymphoid interstitial pneumonitis (LIP)

Clinical Stage 4

- Unexplained malnutrition or wasting (Z score -3), stunting, or severe malnutrition not responding to nutritional therapy and where TB has been excluded
- Pneumocystis pneumonia (PCP)
- Recurrent severe bacterial infection (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)
- Extrapulmonary TB (EPTB)
- Kaposi` s sarcoma (KS)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs)
- CNS toxoplasmosis (outside the neonatal period)
- HIV encephalopathy
- Cytomegalovirus infection: retinitis or CMV infection affecting another organ, with onset at age > 1 month
- Extrapulmonary cryptococcosis including meningitis
- Any disseminated endemic mycosis (coccidiomycosis or histoplasmosis)
- Cryptosporidiosis (with diarrhoea)
- Isosporiasis
- Disseminated non-tuberculous mycobacterial infection (NTM)
- HIV-associated rectovaginal fistula
- Cerebral or B cell non-Hodgkin's lymphoma
- Progressive multifocal leukoencephalopathy (PML)
- Symptomatic HIV-associated cardiomyopathy or HIV-associated nephropathy

Appendix 3:
Enrolment Criteria for ARVs in Adults

Step 1: Start drug readiness training at the same time as clinical workup

- Start counseling sessions as soon as client meets clinical or CD4 criteria for ARV initiation (see Medical criteria on **page 204**). Do not wait until the clinical workup is completed.
- Pre ART counselling sessions should be completed by the date set by the clinician. Duration for C sessions to be completed depends on the level of CD4, whether there is TB coinfection or whether HAART/AZT is for PMTCT. The final session is given on the day of intiation.
- Counselling sessions should include disclosure and positive living, basics of HIV, CD4 , need for cotrimoxazole prophylaxis, ARV treatment plan, adherence and knowledge of side effects.
- Encourage client to attend group sessions and to bring treatment 'buddy' (friend or family member).
- Note that certain patients should be 'fast-tracked' to initiate ART within 2 weeks.

Require fast track (i.e. ART initiation within 2 weeks of being eligible)
• Pregnant women eligible for lifelong ART OR • Patients with very low CD4 (< 100 cells/µL) OR • Stage 4, CD4 count not yet available OR • All TB patients • Children younger than 1 year

Step 2: Exclude TB. Always ask about TB symptoms

- Investigate for TB if any of the following are present:
  - Cough ≥ 2 weeks
  - Weight loss ≥ 1.5kg in 4 weeks
  - Drenching night sweats or fever
  - Chest pain
  - Sputum with or without blood
  - Feeling unwell
- If symptomatic, do not commence ARVs until TB has been excluded, if necessary by a doctor. Send sputa for two smears and Xpert/MTB Rif or culture if possible. (See **pages 86–87** for diagnosing TB).

Step 3: Assess clinically

- Look for opportunistic infections or other HIV related diseases. See table below for conditions that need specific action
- Assess nutritional status, check BMI. If available perform pap smear for all women.

Acute severe illness	HIV emergencies are usually due to opportunistic infections. Stabilise the client before starting ARVs.
CD4 ≤ 100	Aim to start ARVs within 2 weeks.
Kaposi sarcoma	Aim to start within 2 weeks. Ideally, patient should start chemotherapy before starting ARVs. But if chemotherapy is not readily available and the CD4 count is low, better to start ART as soon as possible.
Pregnancy	If > 14 weeks start ARVs as soon as possible with appropriate counselling and adherence support.
Tuberculosis	Aim to start ARVs within 2–4 weeks (See Table 8 on **page 92**). For MDR/XDR TB, aim to start within 2 weeks, irrespective of CD4 count.

Step 4: Discuss contraception and safe sex

- Unsafe sex on ARVs can still transmit HIV and carries the risk of re-infection with different strains of HIV. This can lead to treatment failure.
- Encourage the use of condoms. Encourage your client to have only one partner.
- Discuss your client's plan for a family. If required, advise reliable contraception (e.g., injectable contraceptive plus condoms: remember that the dosing interval of injectable contraceptive is changed in case of NNRTI therapy – see Appendix 14).
- Efavirenz can cause birth defects. Women of child bearing age who need efavirenz must use reliable contraception.
- If pregnant, discuss plans for contraception post delivery.

Step 5: Check baseline blood results

- Take blood for creatinine. Take ALT if nevirapine going to be used.
- Check HBsAg if baseline ALT > 40 (or whenever considering discontinuation of TDF). Note that routine screening for HBsAg is no longer necessary, since the first-line regimen now includes TDF and 3TC, provided that the CrCl is > 50 mL/min.
- Check FBC if the patient is to be started on AZT or there are clinical indications.
- Calculate the creatinine clearance according to formula. It is essential to calculate the CrCl in patients with age > 50 years, weight < 50 kg, or serum creatinine > 100. The following tables allow you to estimate the CrCl if calculation is difficult. Ideally your laboratory should calculate the CrCl.

Formula to calculate creatinine clearance

$$\frac{(140\text{-age}) \times \text{Weight (kg)}}{\text{serum creatinine } (\mu\text{mol/L})} \times c$$

c: in men x 1.23, in woman x 1.04

Creatinine Clearance estimation tables (in ml/min)

N.B Creatinine must be measured in umol/ litre to use these tables

These tables are provided to assist with manual calculation. Ideally this calculation should be done automatically from the lab.

Table 1: Female, age 15-40 years

PCr in µmol/ liter	30-35 kg	36-40 kg	41-45 kg	46-50 kg	51-55 kg	56-60 kg	61-65 kg	66-70 kg
60	52-76	62-87	71-98	80-108	88-119	97-130	106-141	114-152
70	45-65	53-74	61-84	68-93	76-102	83-111	91-121	98-130
80	39-57	47-65	53-73	60-81	66-89	73-98	79-106	86-114
90	35-51	42-58	48-65	53-72	59-79	65-87	70-94	76-101
100	31-46	37-52	43-59	48-65	53-72	58-78	63-85	69-91
110	28-41	34-47	39-53	43-59	48-65	53-71	58-77	62-83
120	26-38	31-43	36-49	40-54	44-60	49-65	53-70	57-76
130	24-35	29-40	33-45	37-50	41-55	45-60	49-65	53-70
140	22-33	27-37	31-42	34-46	38-51	42-56	45-60	49-65
290	11-16	11-18	15-20	16-22	18-25	20-27	22-29	24-31
300	10-15	16-17	14-20	16-22	18-24	19-26	21-28	23-30
350	9-13	13-15	12-17	14-19	15-20	17-22	18-24	20-26
400	8-11	12-13	11-15	12-16	13-18	15-20	16-21	17-23
450	7-10	10-12	10-13	11-14	12-16	13-17	14-19	15-20
500	6-9	9-10	9-12	10-13	11-14	12-16	13-17	14-18
550	6-8	9-9	8-11	9-12	10-13	11-14	12-15	12-17
600	5-8	8-9	7-10	8-11	9-12	10-13	11-14	11-15
650	5-7	7-8	7-9	7-10	8-11	9-12	10-13	11-14
700	7-12	10-14	9-8	7-9	8-10	8-11	9-12	10-13

Table 2: Female, age 41-65 years

PCr in µmol/ liter	30-35 kg	36-40 kg	41-45 kg	46-50 kg	51-55 kg	56-60 kg	61-65 kg	66-70 kg
40	59-90	70-103	80-116	90-129	99-142	109-154	119-167	129-180
50	47-72	56-82	64-93	72-103	80-113	87-124	95-134	103-144
60	39-60	47-69	53-77	60-86	66-94	73-103	79-112	86-120
70	33-51	40-59	46-66	51-74	57-81	62-88	68-96	83-103
80	29-45	35-51	40-58	45-64	50-71	55-77	59-84	73-90
90	26-40	31-46	36-51	40-57	44-63	49-69	53-74	65-80
100	23-36	28-41	32-46	36-51	40-57	44-62	48-67	58-72
110	21-33	26-37	29-42	33-47	36-51	40-56	43-61	53-66
120	20-30	23-34	27-39	30-43	33-47	36-51	40-56	49-60
220	11-16	13-19	15-21	16-23	18-26	20-28	22-30	27-33
230	10-16	12-18	14-20	16-22	17-25	19-27	21-29	25-31
300	8-12	9-14	11-15	12-17	13-19	15-21	16-22	19-24
350	7-10	8-12	9-13	10-15	11-16	12-18	14-19	17-21
400	6-9	7-10	8-12	9-13	10-14	11-15	12-17	15-18
450	5-8	6-9	7-10	8-11	9-13	10-14	11-15	13-16
500	5-7	6-8	6-9	7-10	8-11	9-12	10-13	12-14
550	4-7	5-7	6-8	7-9	7-10	8-11	9-12	11-13
600	4-6	5-7	5-8	6-9	7-9	7-10	8-11	10-12

Table 3: Male, age 15-40 years

PCr in µmol/ liter	30-35 kg	36-40 kg	41-45 kg	46-50 kg	51-55 kg	56-60 kg	61-65 kg	66-70 kg
70	53-77	63-88	72-99	81-110	90-121	98-132	107-143	116-154
80	46-67	55-77	63-86	71-96	78-106	86-115	94-125	101-135
90	41-60	49-68	56-77	63-85	70-94	77-103	83-111	90-120
100	37-54	44-62	50-69	57-77	63-85	69-92	75-100	81-108
110	34-49	40-56	46-63	51-70	57-77	63-84	68-91	74-98
120	31-45	37-51	42-58	47-64	52-70	57-77	63-83	68-90
130	28-41	34-47	39-53	44-59	48-65	53-71	58-77	62-83
140	26-38	32-44	36-49	40-55	45-60	49-66	54-71	58-77
150	25-36	30-41	34-46	38-51	42-56	46-62	50-67	54-72
160	23-34	28-38	32-43	35-48	39-53	43-58	47-62	51-67
170	22-32	26-36	30-41	33-45	37-50	41-54	44-59	48-63
350	11-15	13-18	14-20	16-22	18-24	20-26	21-29	23-31
400	9-13	11-15	13-17	14-19	16-21	17-23	19-25	20-27
450	8-12	10-14	11-15	13-17	14-19	15-21	17-22	18-24
500	7-11	9-12	10-14	11-15	13-17	14-18	15-20	16-22
550	7-10	8-11	9-13	10-14	11-15	13-17	14-18	15-20
600	6-9	7-10	8-12	9-13	10-14	11-15	13-17	14-18
650	6-8	7-9	8-11	9-12	10-13	11-14	12-15	12-17
700	5-8	6-9	7-10	8-11	9-12	10-13	11-14	12-15
750	5-7	6-8	7-9	8-10	8-11	9-12	10-13	11-14
800	5-7	6-8	6-9	7-10	8-11	9-12	9-12	10-13

Table 4: Male, age 41-65 years

PCr in µmol/ liter	30-35 kg	36-40 kg	41-45 kg	46-50 kg	51-55 kg	56-60 kg	61-65 kg	66-70 kg
50	55-85	66-97	76-110	85-122	94-134	103-146	113-158	122-170
60	46-71	55-81	63-91	71-101	78-112	86-122	94-132	101-142
70	40-61	47-70	54-78	61-87	67-96	74-104	80-113	87-122
80	35-53	42-61	47-68	53-76	59-84	65-91	70-99	76-107
90	31-47	37-54	42-61	47-68	52-74	57-81	63-88	68-95
100	28-43	33-49	38-55	42-61	47-67	52-73	56-79	61-85
110	25-39	30-44	34-50	39-55	43-61	47-66	51-72	55-77
120	23-36	28-41	32-46	35-51	39-56	43-61	47-66	51-71
130	21-33	26-37	29-42	33-47	36-52	40-56	43-61	47-66
260	11-16	13-19	15-21	16-23	18-26	20-28	22-30	23-33
300	9-14	11-16	13-18	14-20	16-22	17-24	19-26	20-28
350	8-12	9-14	11-16	12-17	13-19	15-21	16-23	17-24
400	7-11	8-12	9-14	11-15	12-17	13-18	14-20	15-21
450	6-9	7-11	8-12	9-14	10-15	11-16	13-18	14-19
500	6-9	7-10	8-11	8-12	9-13	10-15	11-16	12-17
550	5-8	6-9	7-10	8-11	9-12	9-13	10-14	11-15
600	5-7	6-8	6-9	7-10	8-11	9-12	9-13	10-14

Table 5: Interpretation of blood results

Test	Normal result	Action required if result is abnormal
ALT	< 40 IU/ml	If ALT is abnormally high, consider repeating in order to confirm, and test HBsAg (also investigate alcohol abuse). • If ALT > 100, consider using EFV or LPV/r instead of NVP; also consider monitoring the ALT monthly for 3 months. • If ALT 41-100, also consider monitoring the ALT monthly for the first 3 months on ARVs.
Hb	>10 g/dl	If Hb < 8.0 g/dl, assess carefully for opportunistic infections, especially TB. Consider giving iron and folic acid supplements and repeat Hb in 2-4 weeks. If no OI found, then use tenofovir or d4T instead of AZT when initiating ART.
Hep B s Ag	Negative	Refer to doctor if HBsAg result is positive. Active hepatitis B requires use TDF and 3TC/FTC in the 1st line regimen. Once started, TDF and 3TC/FTC should ideally never be stopped in that person (see **page 75**).
Creatinine clearance	≥ 90 ml/ minute	If CrCl < 50 mL/min, repeat to confirm result after correcting possible causes (dehydration, etc). Discuss with doctor. Adjust doses of AZT, DDI, d4t and 3TC as necessary (see Appendix 31). Avoid tenofovir if CrCl is <50ml/minute or in all cases of chronic renal failure (or renal failure that is new in onset, but not resolving).

Step 6: Assess readiness to start treatment once clinical workup and drug readiness training are complete

When yes to all the below, client is ready to start ARVs.

Medical criteria

- Confirmation of HIV status, AND

Eligible to start ART
• CD4 count <350 cells/µL
• All stage 3 and 4 patients
• All MDR/XDR patients irrespective of CD4

- Tuberculosis and other serious OIs have been diagnosed and treatment started

Social Criteria (not mandatory, but strongly encouraged):

- Patient is ready to commit to long-term antiretroviral therapy
- Patient is willing to disclose HIV status to a person in confidence who agrees to act as the patient's 'Treatment Assistant'. This is the ideal situation but if no treatment assistant is available, this should not be a reason not to start ART.
- No alcohol abuse
- Contraceptives/condoms being used

Adherence Criteria:

- Patient has presented on time to the last four appointments (includes nurse, counsellor, and doctor appointments)
- Patient is able and willing to take tablets regularly*
- Understands the importance of adherence

*Assessment can be based either on adherence to existing treatment (patient is asked to return with remaining cotrimoxazole tablets, or adherence to TB treatment is assessed if on TB medication) or prospectively by using a substitute (for example, vitamins). However, this should never delay ART.

Step 7: Start ARVs- Regimen 1

- Discuss all non-naïves who have previously received ARVs with a specialist.
- Client must have attended all ARV preparation sessions.

- Always prescribe 3 ARVs (see Appendix 7 and 8 for usual adult doses, and Appendix 31 for dose adjustments in case of renal failure). Give TDF, 3TC or FTC, and EFV unless:
  - In 1st trimester of pregnancy or planning a pregnancy (or unable to use/ refusing contraception): Use NVP instead of EFV (provided CD4 is < 250 and not on treatment for TB).
  - In 1st trimester of pregnancy with CD4 > 250: defer ART until 2nd trimester and initiate on EFV if possible. Otherwise use LPV/r instead of NVP (risk of hepatitis on NVP is much higher if CD4 >250).
  - In 1st trimester of pregnancy, on treatment for TB with CD4 < 250: use LPV/r. The dose of LPV/r should gradually be doubled.
  - Creatinine Clearance <50 mL/min: if renal failure persists despite having ruled out and treated possible causes, replace TDF with AZT (provided Hb > 8.0 g/dL) or d4T (if Hb < 8.0 g/dL); long-term use of d4T should be avoided if at all possible, due to its significant risk of long-term toxicity.
- If client will start with NVP, remember step-wise induction (Ie. 200 mg OD for first 2 weeks) to reduce the risk of skin rash and hepatitis.
- Review with client about how to take ARVs and possible side effects.
- Continue cotrimoxazole +/- multivitamins.
- Schedule clinic follow up for 2 weeks.

1st Line for adults		
All new patients needing treatment, including pregnant women	TDF + 3TC + EFV/ NVP	For TB co-infection EFV is preferred. For women of child bearing age, not on reliable contraception, NVP is preferred. However care must be taken if the baseline CD4 is > 250 as the woman is at increased risk of NVP side effects.
Contraindication to TDF: renal disease or CrCl <50ml/ minute	AZT+ 3TC +EFV/ NVP	For TB co-infection EFV is preferred. For women of child bearing age, not on reliable contraception, NVP is preferred.
Contradiction to AZT (if Hb < 8)	D4T+ 3TC+ EFV/ NVP	For TB co-infection EFV is preferred. For women of child bearing age, not on reliable contraception, NVP is preferred.

Appendix 4: ART initiation steps

What is needed before giving a GREEN LIGHT for initiation?

Step 1: Psychologically ready for ART?

Check with counselors

Step 2: Rule out TB

- Cough ≥ 2 weeks
- Weight-loss ≥ 3 kg
- Night sweats ≥ 3 weeks
- Fever ≥ 3 weeks
- Chest pains
- TB-contact

Step 3: Ask for other OI's (current or in the past)

- Skin lesions: Herpes Zoster, PPE, seborreic dermatitis, Kaposi Sarcoma
- Headache, seizures: Meningitis: crypotococcal, TB or bacterial
- Weight-loss > or < 10%
- Fever > 1 month
- Diarrhea > 1 month
- Pain when swallowing or difficult swallowing: oesophageal candidiasis
- Recurrent URTI's?
- Any other problem today?
- Any STI's?

Step 4: Clinical examination

- Mouth: Oral thrush, necrotising gingivitis, oral sores, oral hairy leucoplakia, KS, herpes, angular cheilitis
- Skin: Herpes Zoster (scars), PPE, seborreic dermatitis, KS, Tinea (capitis, corporis, pedis, cruris), Molluscum contagiosum, warts; Genital ulcers or warts?

- Enlarged lymphnodes: TB, persistent generalized lymphadenopathy (PGL)
- Lung exam: crackles, percussion dull (consolidation) or stony dull (effusion)
- Hepatomegaly
- If headache: neck stiffness?
- Children: Weight/Age and Height/Age, developmental milestones

Step 5: Final Staging (Stage III or IV? Or CD4 < 350?)

Step 6: Other conditions or medication?

E.g. epilepsy - drug-interactions

Step 7: Discuss contraception and safe sex

- Efavirenz - must take contraception; if risk for getting pregnant, consider NVP

Step 8: Laboratory

- Creatinine Clearance > 50 ml/min?
- Child < 12 years or Cr Cl < 50 - check Hb for AZT

$$CrCl = \frac{(140 - age) \times W\ (kg)}{Creatinine\ (umol/l)}$$

Women: x 1.04; Men: x 1.23

Appendix 5: Enrolment Criteria for ARVs in Children

Confirmation of HIV status

Depending on age:

- For **children** < 18 months: a positive PCR test
- For **children** > 18 months: Positive on rapid testing

Clinical and Immunological Criteria

Table 21. ART eligibility criteria for HIV-infected children (2010)

WHO stage	< 12 months*	12 to 59 months	≥5 years
1	Treat all	CD4 < 25% or CD4 <750 cells/µL	CD4 < 350 cells/µL
2	Treat all	CD4 < 25% or CD4 <750 cells/µL	CD4 < 350 cells/µL
3	Treat all		
4	Treat all		

* Note that WHO (2010) recommends that ART be initiated in all HIV-infected children up to 2 years of age.

Criteria for expedited ('fast-track') ART initiation (1 to 2 weeks)

- Children younger than 1 year
- CD4 < 100 cells/µL (or < 10 %)
- Stage 4 disease
- All TB coinfected patients

WHO criteria for presumptive diagnosis of HIV infection

Even where DNA PCR testing is not (yet) available, a sick HIV exposed infant should be referred for ART initiation based on the diagnosis of presumptive HIV infection, if he/she fulfils the criteria in the table below:

Criteria for presumptive diagnosis for initiation of HAART in infants < 18 months of age where virological confirmation of infection is not available

- Infant is HIV antibody positive (ELISA or rapid test), and
- Diagnosis of any AIDS-indicator condition(s) can be made, or
- Infant is symptomatic with 2 or more of the following
  - Oral thrush (recurrent or chronic)
  - Severe pneumonia
  - Severe sepsis
- Other supporting factors supporting the diagnosis include:
  - Recent HIV-related maternal death or advanced HIV disease in the mother
  - CD4 < 20%

IMCI definition:

a. Oral thrush: Creamy white to yellow soft small plaques on red or normally coloured mucosa which cannot easily be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender.

b. Severe pneumonia: Cough or difficult breathing in a child with chest indrawing, stridor or any of the IMCI general danger signs; i.e., lethargic or unconscious, not able to drink or breastfeed, vomiting, and presence or history of convulsions during current illness; responding to antibiotics.

c. Severe sepsis: Fever or low body temperature in a young infant with any severe sign such as fast breathing, chest indrawing, bulging fontanel, lethargy, reduced movement, not feeding or sucking breast milk, convulsions

REMEMBER **Do not wait for DNA PCR results to start ARVs in a sick infant who fulfils criteria for presumptive diagnosis of HIV infection. Start ARVs!**

Do not wait for the 6th week to do a PCR in a sick child for whom a presumptive diagnosis of HIV has been made!

Social Criteria

- Must have an adult caregiver who is able to administer medication
- Disclosure to another adult living in the same house is to be encouraged so that there is someone else who can help with the child's ART.
- Caregiver is ready to commit to a support group for caregivers of children on ARVs.

Adherence Criteria

- Child has presented with caregiver on time to the past 4 visits.
- Child is being given current medications (cotrimoxazole or TB meds) regularly.
    - All HIV-positive children should be on cotrimoxazole prophylaxis, and the adherence will be assessed.
- The following 4 key questions should be addressed:
    - Who will be administering the medications
    - What medications will be given
    - When will medications be given
    - How will medications be given

Baseline Clinical and Laboratory Investigations prior to Initiation of ART in Children

- Child's height and weight
- Clinical staging
- Screening for TB symptoms
- Developmental level
- CD4 count, or CD4 % if < 5 years
- FBC for all children at baseline
- ALT (if planning to use an NVP-based regimen)

Appendix 6: Different Classes of ARVs and General Rules

Classes of ARVs

ARVs can be classified according to the different steps where they interrupt the life-cycle of HIV (thereby stopping the replication of HIV).

NRTIs (Nucleoside or Nucleotide Reverse Transcriptase Inhibitors)

- They hinder the enzyme reverse transcriptase
- They include:
  - TDF (Tenofovir)
  - 3TC (or the closely-related FTC)
  - AZT
  - ABC (Abacavir)
  - D4T
  - DDI

NNRTIs (Non-Nucleoside Reverse Transcriptase Inhibitors)

- Also hinder 'reverse transcriptase' but in a different way from NRTI's
- They include
  - Nevirapine
  - Efavirenz

PIs (Protease inhibitors)

- Hinder the enzyme 'protease'
- They include
  - Kaletra (= Lopinavir boosted with ritonavir = LPV/r)
  - Aluvia (= same as Kaletra, but in tablet formulation that does not require refrigeration)
  - Ritonavir (RTV): always given in association to other PIs, in a small dose, just to boost their concentration in the blood
  - Atazanavir (ATV)

Some GENERAL RULES about ARV use:

1. Use EFV instead of NVP if a person is taking TB medication (note that EFV is also preferred in any patient with a higher base-line, E.g. CD4 > 250 in females and > 400 in males*).
2. Don't use EFV if a woman is in the first trimester of pregnancy or at risk of becoming pregnant (i.e. not using reliable contraception).
3. Don't use EFV in children less than 3 years or weighing less than 10 Kg.
4. Don't use TDF if the patient has a CrCl < 50 mL/min, or is younger than 12 years of age.
5. When starting NVP (or re-starting after an interruption lasting > 1 week), use lead-in dosing in order to reduce the risk of side effects: give NVP once a day for the first 2 weeks, and if no side effects, then increase it to twice daily.
6. Don't use AZT if Hb< 8.0 g/dl.
7. Some ARVs are adjusted for weight in adults (EFV and DDI).
8. All ARVs are adjusted for weight in **children, so dosing needs to be double-checked** at every visit as the child grows!
9. Some ARVs require lower dosing in the presence of chronic renal failure, based on the Creatinine Clearance (see Appendix 31).
10. Some ARVs are available in combinations, which reduce the number of pills a person must take every day, and therefore help to improve adherence. Examples include a double combination of TDF + 3TC, AZT + 3TC, D4T + 3TC and a triple combination of TDF + 3TC + EFV, D4T + 3TC + NVP, AZT + 3TC + NVP.
11. Don't use D4T and AZT together in the same regimen!
12. Don't use D4T if a person already has severe peripheral neuropathy!

* Higher baseline CD4 counts (> 250 cells/μL in a female, and > 400 cells/μL in a male) are associated with a much higher risk of NVP-induced hepatitis/allergy!

Appendix 7: The Antiretrovirals

ARV	Formulation	Usual Adult Dose*	Specifics
TDF (Tenofovir)	300 mg tablets	300 mg OD	Usually very well-tolerated. CrCl must be > 50 ml/min. Not to be used if < 12 years.
ABC (Abacavir)	Syrup (20 mg/ml) 300 mg tabs	300 mg twice daily	Potential for severe hypersensitivity reaction (see **page 221**). No food restrictions. Tablet may be crushed (children).
3TC (Lamivudine)	Syrup (10 mg/ml) 150 mg tabs (also in combo with AZT, D4T or TDF)	150 mg twice daily or 300 mg OD with TDF	Normally well-tolerated.
FTC (Emtricit-abine)	Usually in fixed-dose combination with TDF	200 mg OD	Normally well tolerated. Analogue of 3TC.
AZT (Zidovudine)	Syrup (10 mg/ml) 100 mg tabs 300 mg (also in combo with 3TC)	300 mg twice daily	Capsules may be opened (children). Watch for possible side effect of anaemia.
DDI (Didanosine)	25, 50, 100 mg tabs 250, 400 mg caps (enteric coated)	400 mg once daily if > 60 kg; use 250 mg if < 60 kg	TAKE ON AN EMPTY STOMACH. One hour before or two hours after food. Disperse 25 mg and 100 mg tabs in water (or chew). At least 2 tablets of appropriate strength must be used at any one time for adequate buffering.
D4T (Stavudine)	Syrup (1 mg/ml) 15 mg caps 20 mg 30 mg	30 mg twice daily for all adults	All adults should now receive 30 mg of d4T, regardless of weight. Syrup must be refrigerated. Capsules may be opened (children). Watch for possible side effects of high lactate, peripheral neuropathy and lipodystrophy.

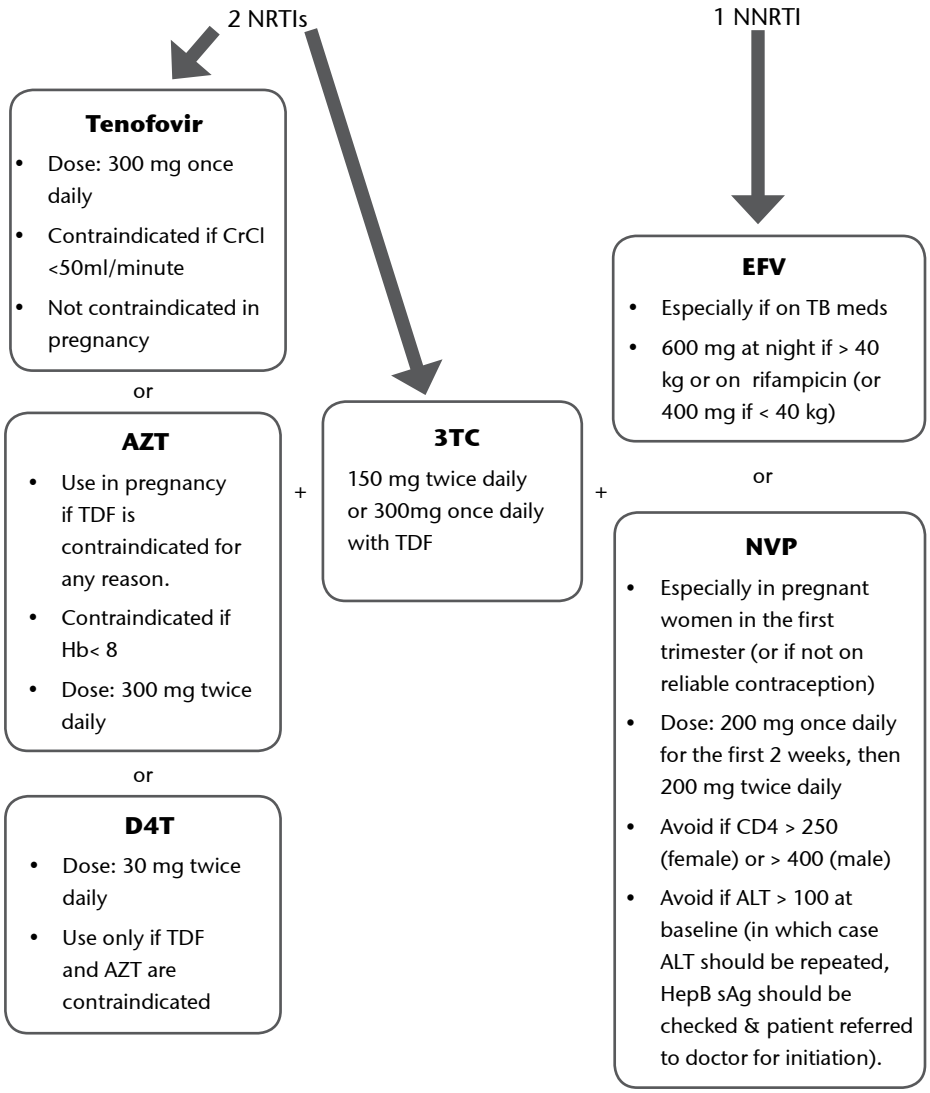
NVP (Nevirapine)	Syrup (10 mg/ml) 200 mg tabs	200 mg once daily for the 1st 2 weeks, then 200 mg twice daily	Tablet may be crushed (children). Watch for rash and hepatitis. Nevirapine induces liver enzymes responsible for its own metabolism. Stepwise introduction helps to reduce the risk of skin rash and hepatitis. Interacts with Fluconazole and TB meds rifampicin.
EFV (Efavirenz)	50 mg tabs or caps 200 mg tabs or caps 600 mg tabs	600 mg at night if > 40 kg; use 400 mg if < 40 kg NB: if on rifampicin, 600 mg should be prescribed.	Taken at night to limit side effects. Avoid taking with fatty foods. Capsules may be opened (children). Tabs may not be chewed, divided or crushed. Avoid in 1st trimester of pregnancy (women must be on reliable contraception).
Kaletra (Lopinavir/ritonavir)	Syrup (80/20 mg/ml) 125 mg tabs LPV 133 mg/r 33 mg caps	400/100 mg (3 caps) twice daily	Combination of Lopinavir/ritonavir. Capsules must be swallowed whole and not chewed, divided or crushed. Syrup and caps (not tabs) must be taken with food to enhance absorption and refrigerated until dispensed. Do not open capsules.
Aluvia = heat-stable Lopinavir/ritonavir (LPV/r)	250 mg tab (LPV 200 mg/r 50 mg)	400/100 mg (= 2 tabs) twice daily	Does not have to be taken with food If patient is on rifampicin-containing TB regimen, the dose of LPV/r must be doubled or 'super-boosted' with additional ritonavir.
ATV (Atazanavir)	150 mg tabs, 200 mg tabs	300 mg (2 tabs of 150 mg) OD, together with 1 cap of 100 mg ritonavir ("boosted ATV") OR 400 mg (2 tabs of 200 mg) OD	To be stored at < 25°C (but keep RTV tabs in the fridge). To be taken with food. Always give boosted dose if associated with use of TDF. Contraindicated in those needing > 20 mg a day of omeprazole. Should not be taken together with anti-acid medications (take ATV 2h before or 1h after). Common side effect is jaundice. Cases of allergic rash (usually not severe) and nephrolithiasis have been reported.

* Paediatric dosages for all of the above ARVs can be determined using children's weights. See Appendix 9 for an example of a simplified table showing weight ranges and the appropriate dosages.

Appendix 8: Typical ARV regimens for adults

1st line ARV regimens for adults.

TDF and 3TC can be combined with EFV or NVP. NVP cannot be combined with TB medication and tends to have more side effects. Both regimens can only be given if the baseline creatinine clearance is > 50ml/minute. Other combinations are possible, always combining two NRTIS together with one NNRTI. Options are shown below



Examples of acceptable first-line regimens for adults:

- Tenofovir + 3TC + EFV (These can all be given once daily)
- Tenofovir + 3TC + NVP
  - morning dose: TDF+ 3TC (300)+ NVP
  - evening dose: Nothing for first two weeks then NVP
- AZT + 3TC + NVP
  - morning dose: AZT + 3TC + NVP
  - evening dose first 2 weeks: AZT + 3TC; then: AZT + 3TC + NVP
- D4T + 3TC + EFV
  - morning dose: D4T + 3TC
  - evening dose: D4T + 3TC + EFV
- D4T + 3TC + NVP
  - morning dose: D4T + 3TC + NVP
  - evening dose first 2 weeks: D4T + 3TC; then: D4T + 3TC +NVP

First line regimen and pregnancy

- EFV is contraindicated during 1st trimester of pregnancy but NVP might also be contraindicated (hepatic disease or previous allergy). Also, NVP is not recommended in pregnant women with CD4 > 250, because of increased risk of toxicity, and during TB treatment. In all those cases, EFV should be replaced by LPV/r, rather than by NVP. (LPV/r is given at double dose during TB treatment: e.g. instead of 400/100 mg BID, give 800/200 mg BID). For a woman in the 1st trimester of pregnancy with TB and a CD4 > 250, consider to wait until the 2nd trimester before starting ART and initiate with EFV.
- If pregnancy is diagnosed in the first trimester in a woman already well established on EFV and the pregnancy is beyond four weeks (the time when neural tube development is completed) it is safer to continue on the EFV than switch regimens. If the woman is in the first four weeks of pregnancy refer to a doctor.
- There is no longer a contraindication to initiation of TDF in pregnant women (provided that CrCl > 50 mL/min), even during the 1st trimester.

First line regimen and TB treatment

- If on rifampicin for TB treatment, substitute NVP with EFV for the duration of TB treatment (or gradually double the dose LPV/r). Two weeks after TB treatment finishes, consider changing EFV back to NVP (an induction dose of NVP is not

necessary when EFV is changed to NVP), or if the dose of LPV/r was doubled, this can be reduced to the normal dose (also after 2 weeks).

Patients currently on a D4T-based regimen

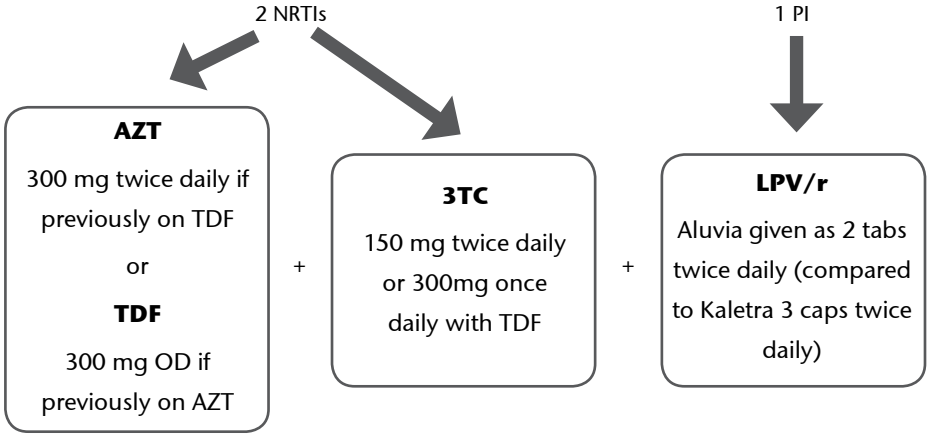
D4T is gradually being replaced with TDF. Consult national guidelines for phasing in process. The priority is for D4T to be promptly changed to TDF in case of any D4T-related toxicity (PN, hyperlactatemia, lactic acidosis, lipodystrophy) or in high-risk patients (BMI > 28, TB treatment), provided that the last VL was LDL (if available) or there are no other signs of treatment failure and there is no problem with adherence.

Second-line ARV regimen for ADULTS

The second-line regimen usually used consists of two NRTIs together with a PI.

Second Line Treatment for adults
Zidovudine (AZT) if previously on TDF; or TDF if previously on d4T or AZT AND
Lamivudine (3TC) (or FTC) AND
Lopinavir + Ritonavir (LPV/r)

If surface hepatitis B antigen positive, do not stop TDF; add the above to TDF.



Heat-stable Aluvia tabs do **not** need to be taken with food (but the Kaletra capsules do).

The patient will thus take:

TDF/3TC (or TDF/FTC) once daily or AZT/3TC twice daily, together with LPV/r twice daily.

3TC (Lamivudine) is maintained in the second line regimen due to its potential stabilizing effect on HIV viral replication, even if resistance to 3TC has already developed.

When switching patients with hepatitis B infection to second-line regimens, **they need to remain on TDF and 3TC!** Stopping TDF could cause a severe flare of the hepatitis. Discuss regimen with an HIV specialist.

If a patient on LPV/r develops diabetes or severe dyslipidemia (see Appendix 18 for reference values), refer to the doctor. A change from LPV/r to Atazanavir/ritonavir (ATV/r) could be considered if high cholesterol, raised fasting glucose, or patient unable to tolerate LPV/r due to gastrointestinal side effects.

LPV/r and TB treatment

- Patients starting rifampicin should have the dose of LPV/r doubled gradually over two weeks (to 800 mg lopinavir/200 mg ritonavir) twice daily. Alternatively, instead of doubling the dose of LPV/r, additional ritonavir (an extra 300 mg 12 hourly in adults to 'super-boost' the existing dose of Lpv/r) may be given while the patient is taking TB drugs.
- Continue with double dose LPV/r (or with boosted LPV/r) for 2 weeks after TB therapy stopped
- If TB is diagnosed while on LPV/r
  - Week 0: Start TB treatment and increase LPV/r to 600 / 150 mg (3 tablets of Aluvia) twice daily
  - Week 1: give LPV/r 800/200 mg (4 tablets of Aluvia) twice daily
- If LPV/r needs to be started while on TB treatment
  - Week 0: Start LPV/r 400/100 mg (2 tablets of Aluvia) twice daily
  - Week 1: Give LPV/r 600 / 150 mg (3 tablets of Aluvia) twice daily
  - Week 3: Give LPV/r 800/200 mg (4 tablets of Aluvia) twice daily

In addition to careful clinical monitoring for symptoms of hepatitis, consider routine monitoring of ALT. If ALT rises above 100, refer to the doctor; if ALT > 200, refer to hospital.

REMEMBER **Patients failing second line therapy have few treatment options. Failure is almost always due to poor adherence, and every effort should be made to detect and address this early, as re-suppression of the VL is often possible using the same drugs.**

Studies have shown clinical benefit in continuing on second line therapy despite virologic failure; if no options exist, the patient should be left on the failing regimen.

Appendix 9: Antiretroviral Therapy Regimens for Children

First and second line regimens in children

First and Second line Regimens in children (SA Paediatric National Guidelines 2010)

First line regimens	Second line regimens
1. Non Nevirapine exposed children Zidovudine (AZT) Lamivudine (3TC) Nevirapine (NVP) **If Hb < 8 replace AZT with stavudine (D4T)** **2. Nevirapine exposed children (starting treatment up to 24 months of age)** Zidovudine (AZT) Lamivudine (3TC) Lopinavir/ Ritonavir (LPV/r) **If Hb < 8 replace AZT with D4T**	**Following a LPV/r based regimen in first line or child <3 years** Refer to doctor **Following AZT/3TC/NVP in first line** Abacavir (ABC) Lamivudine (3TC) Lopinavir/ Ritonavir

Treatment with ARVs and TB drugs in children

ART + rifampicin-based TB treatment in children

< 3 years or < 10kg or any child on a LPV/r regimen	• Boost LPV/r with additional ritonavir • For older children, double the dose of LPV/r
< 3 years or <10 kg and on NVP: and Lopinavir /r not available	Increase dose of NVP to max 200 mg/ m² (WHO 2010)
> 3 years and > 10kg on NVP based regimen	Change NVP to EFV

Additional Ritonavir dose in children taking rifampicin

Extra Ritonavir dose = 0.75 x LPV/r syrup dose in ml (therefore if LPV/r dose = 1 ml, you need to add 0.75 ml of ritonavir, see dosing chart in Appendix 9).

Continue with super-boosted LPV/r for 2 weeks after TB therapy stopped.

Notes on prescribing ARVs in children

- Dosing based on weight or body surface area (BSA)
- ARV dosing charts based on child's weight are available (See Appendix 9)
- NVP is prescribed once daily for 2 weeks then twice daily
- Switch from syrups to tablets or capsules as soon as possible
- Stavudine syrup cannot be given to those with no access to refrigerator
- LPV/r syrup denatures unless it is kept in a cool, dry place at a temperature <25° C (and shouldn't stay out of fridge for more than 42 days). Refrigerate if possible.
- Remember to recalculate doses at each clinic visit according to current body weight and/or body surface area. Giving the child too little medication for his/her weight will cause him/her to develop resistance faster. Giving the child too much medication for her/his weight may lead to more side effects.
- Young children who start on a LPV/r based regimen should remain on the same regimen even after reaching 3 years or 10 kg unless a substitution or switch to second line regimen is indicated for reasons of toxicity or treatment failure.

General comments on individual drugs

Abacavir (ABC)

Tablets can be crushed and mixed with a small amount of water or food and immediately ingested. No food restrictions. Once daily dosing is not yet approved for children.

Caregivers must be warned about potential (but very rare!!) Hyper-Sensitivity Reaction (ABC HSR) which may include:

- fever (80% of cases)
- rash (70%, but often mild, non pruritic and unnoticed)
- gastrointestinal & respiratory symptoms (18% have cough, pharyngitis, dyspnoea)
- constitutional non-specific symptoms (myalgia, generalized malaise).

ABC should be stopped permanently if hypersensitivity reaction occurs, and never re-challenged (recurrence might be fatal).

It's very easy to mistake a common viral infection for an HSR due to ABC, but the following can help:

1. HSR usually occurs in the 1st 6 weeks after initiation on ABC (mainly 1st 10 days)
2. Symptoms worsen just after every new dose (and with every subsequent dose)
3. Symptoms usually resolve after 48h from discontinuation
4. Never initiate ABC if the patient is already having fever or cough
5. NEVER INITIATE A PATIENT ON NVP AND ABC AT THE SAME TIME!! (In case of severe allergy, it would be then impossible to ascertain the culprit drug, and rechallenge would be too dangerous...). A shift to ABC is allowed – when required for example in case of d4T toxicity– only if the patient is stable on NVP-based treatment, for more than 6 weeks
6. Decision about stopping ABC should be made by a health care provider (not by the patient himself)
7. The patient has to be given a "Patient Alert Card" to be shown, in case of symptoms, to any health care provider he/she might consult, to make the HCP aware that he/she is taking ABC.

Didanosine (ddI)

At least 2 tablets of appropriate strength must be used at any one time for adequate buffering. Tablets may be chewed or crushed and dispersed in 30ml water and immediately ingested. Enteric coated tablets (250 mg) are available for once daily use in children > 20 kg. It is recommended to administer ddI on an empty stomach at least 30 minutes before or 2 hours after meals.

Lamivudine (3TC)

Well tolerated, no food restrictions, oral solution may be stored at room temperature. Tablets are scored and can be easily divided; may be crushed and mixed with a small amount of water or food and immediately ingested. Once daily dosing is not yet approved for children. Lamivudine is also active against hepatitis B.

Stavudine (d4T)

Well tolerated & palatable but oral solution requires refrigeration after reconstitution. Discard after 30 days. Capsules may be opened and powder contents dispersed in water (stable in solution for 24 hours) or mixed with a small amount of food (e.g. yoghurt). See dosing chart for further details. Consider early drug substitution if toxicity e.g. neuropathy or lipodystrophy/lypoatrophy develops. Available as FDC with 3TC as baby/junior Lamivir and with 3TC/NVP as baby/junior Triomune.

Zidovudine (AZT)

No food restrictions and oral solution may be stored at room temperature. Use with caution in children with anaemia due to potential for bone marrow suppression. Available as 2-in-1 FDC with 3TC and as 3-in-1 FDC with 3TC and NVP.

Nevirapine (NVP)

Caregivers must be warned about the (small) possibility of a potentially life-threatening rash during the first 3 weeks of treatment with NVP. Once daily 'lead-in' dosing during the first 2 weeks of treatment reduces the frequency of rash. NVP should be permanently discontinued and not restarted in children who develop severe rash especially if accompanied by fever, blistering or mucosal ulceration. If a mild rash occurs during the induction period, continue once daily dosing and only escalate dose to twice daily once the rash has subsided and the dose is well tolerated. No food restrictions. Tablets can be crushed and mixed with a small amount of water or food and immediately ingested. Avoid NVP if rifampicin is being co-administered. Consider drug-drug interactions.

Efavirenz (EFV)

EFV is not approved for children <3years or <10kg. Tablets must not be chewed, divided or crushed; swallow whole with or without food e.g. yoghurt or banana. Capsules may be opened and powder contents dispersed in water or mixed with a small amount of food (e.g. yoghurt) to disguise peppery taste and immediately ingested. Food, especially high-fat meals, increases absorption. Best given at bedtime to reduce CNS side-effects, especially during first 2 weeks.

Lopinavir/ritonavir

Dose is calculated based on lopinavir component. Solution should be taken with food as increases absorption. Oral solution and capsules should be refrigerated but can be stored at room temperature up to 25ºC for 6 weeks. May need techniques to increase tolerance & palatability: coat mouth with peanut butter, dull taste buds with ice, follow dose with sweet foods. Kaletra capsules are soft and may not be opened or crushed and must be swallowed whole. Aluvia tablets must not be chewed, divided or crushed; swallow whole with or without food. Many drug interactions due to RTV inhibition of cytochrome p450.

Ritonavir (RTV)

Only recommended use at present is as booster for lopinavir/ritonavir when being co-administered with rifampicin-containing TB treatment. Should be taken with food. May be stored at room temperature, limited shelf life of 6 months. May need to use techniques described for LPV/r syrup, to improve tolerance of bitter taste.

Tenofovir (TDF)

Very well tolerated drug. Can be stored at room temperature. Daily dosing is 1x 245 mg (= 300 mg Tenofovir disoproxil fumarate) . Exists in a FDC TDF/3TC/EFV which is a 1 pill once daily regimen. Preferably taken with food. Possible side effects include nausea, vomiting, diarrea, dizziness and rash but these are rare. Rarely nephrotoxicity is seen (nephrotic syndrome, Fanconi syndrome). Therefore, TDF should not be prescribed to a patient with a creatinine clearance of < 50 ml/min and substituted if creatinine clearance drops below this level. The combination with DDI should be avoided because of higher risk of virological failure. TDF is also active against Hepatitis B (even more effective in combination with 3TC) and should not be stopped in patients with Hepatitis B because of the risk of a flare.

Appendix 10: Paediatric ART dosing table (May 2010)

Drug	Name	Strength Paediatric tablet	3-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg	Strength Adult tablet	25-34.9kg
INITIATION PHASE (first 2 weeks)									
AZT/3TC/NVP		60/30/50mg tab	1 OD +	1.5 OD +	2 OD +	2.5 OD +	3 OD +	300/150/200mg tab	1 OD +
AZT/3TC		60/30mg tab	1 OD	1.5 OD	2 OD	2.5 OD	3 OD	300/150mg tab	1 OD
D4T/3TC/NVP	Triomune Baby	6/30/50mg tab	1 OD +	1.5 OD +	2 OD +	2.5 OD +	3 OD +	30/150/200mg tab	1 OD +
D4T/3TC	Lamivir S Baby	6/30mg tab	1 OD	1.5 OD	2 OD	2.5 OD	3 OD	30/150mg tab	1 OD
D4T/3TC/NVP	Triomune Junior	12/60/100 mg tab			1 OD +	1 OD +	1.5 OD +	30/150/200 mg tab	1 OD +
D4T/3TC	Lamivir S Junior	12/60 mg tab			1 OD	1.5 OD	1.5 OD	30/150 mg tab	1 OD
MAINTENANCE PHASE (after 2 weeks of initiation)									
AZT/3TC/NVP		60/30/50 mg tab	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	300/150/200 mg tab	1 BD
D4T/3TC/NVP	Triomune Baby	6/30/50 mg tab	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	30/150/200 mg tab	1 BD
D4T/3TC/NVP	Triomune Junior	12/60/100 mg tab			1 BD	1.5 AM + 1 PM	1.5 BD	30/150/200 mg tab	1 BD

Reminder: OD = once per day

BD= twice per day

Drug	Product	Strength Paediatric tablet	3-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg	Strength Adult tablet	25-34.9kg
AZT/3TC	FDC	60/30 mg tab	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	300/150mg tab	1 BD
D4T/3TC	FDC Lamivir Baby	60/30mg tab	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	300/150mg tab	1 BD
D4T/3TC	FDC Lamivir Junior	12/60mg tab			1 BD	1.5 AM + 1 PM	1.5 BD	30/150mg tab	1 BD
ABC/3TC		60/30 mg tab	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	600/300mg tab	0.5 BD[a]
3TC	Lamivudine	Liquid 10mg/ml	3 ml BD	4 ml BD	6 ml BD				
		150mg tab				0.5 BD	1 AM + 0.5 PM	150 mg tab	1 BD
AZT[b]	Zidovudine	Liquid 10mg/ml	6 ml BD	9 ml BD	12 ml BD				
		300 mg tab				0.5 BD	1 AM + 0.5 PM	300 mg tab	1 BD
ABC	Abacavir	Liquid 20mg/ml	3 ml BD	4 ml BD	6 ml BD				
		60mg tab	1 BD	1.5 BD	2 BD	2.5 BD	3 BD	300 mg tab	1 BD
		300mg				0.5 BD	1 AM + 0.5 PM		
NVP[b]	Nevirapine	Liquid 10mg/ml	5 ml BD	8 ml BD	10 ml BD				
		200mg tab				1 AM + 0.5 PM	1 AM + 0.5 PM	200mg tab	1 BD
EFV[c]	Efavirenz	200mg tab			1 OD	1.5 OD	1.5 OD	200mg tab	2 OD
LPV/r	Lopinavir/ ritonavir	Liquid 80/20mg/ml	1 or 1.5 ml BD[d]	1.5ml BD	2 ml BD	2.5ml BD	3 ml BD		
		100/25 tab[e]			2 AM + 1 PM	2 BD	2 BD	100/25 tab[e]	3 BD
ddI	Didanosine	10mg/ml		5 ml BD	6 ml BD				
		25 mg tab		3 AM + 2 PM	3 BD	4 AM + 3 PM	4 BD	25 mg tab	5 BD
		125 or 200mg EC			1 OD (125mg)	1 OD (200mg)	2 OD (125mg)	125 mg EC	2 OD

[a]Not scored – use pill cutter

[b]Doses for HIV treatment. See PMTCT guide for prophylactic doses

[c] EFV should not be used in children <3yrs or <10kg. Ensure effective contraception when used in adolescent girls due to teratogenic risk

[d]LPV/r liquid: 3-3.9kg dose = 1ml BD. 4-5.9kg dose=1.5ml BD

[e]LPV/r tablet MUST NOT be chewed, broken or crushed. LPV should be double boosted with ritonavir if co administered with rifampicin (see TB chapter of paediatric HIV guidelines)

Appendix 11: Monitoring a Patient on ARVs

ARV	Medical Intervention	Before ART initiation	Day of ART initiation	Wk 2	Mo 1	Mo 3	Mo 6	Mo 12	Mo 18	Mo 24	There-after
All ARVs	Informed Consent	X									
	Treatment Assistant (preferred but not mandatory)		X			X	If adherence problems				
	Clinical Exam (history, weight, physical)	X	X	X	X	X	X	X	X	X	6-monthly
	Monitor for possible side effects			X	X	X	X	X	X	X	6-monthly
	CD4 cell count	X					X	X		X	6-monthly
	FBC (only if initiating AZT or if clinically indicated)	X	Required only for AZT at 1, 2, 3, and 6 months								
	HBsAg	Only if baseline ALT > 40 (but mandatory before stopping TDF for any reason)									
Tenofovir	Creatinine (creatinine monitoring can be performed 6 monthly or annually but is not mandatory)	X									
AZT	FBC + differential	X			X	X	X				annually only in children
d4T	Lactate	Lactate should be checked if weight loss, PN, or symptoms of high lactate after 4-6 months on d4T									
ABC	Rule out HSR	Fever +/- rash on ABC requires immediate clinical assessment to rule out a Hypersensitivity reaction (HSR)									
EFV	ALT*		Only if suggested by clinical condition								
NVP	ALT*	X	Only if suggested by clinical condition (rash, jaundice or other symptoms of hepatitis)								
Lpv/r	Lipids (Chol/TG) – fasting					X		X (child)		X (child)	annually only in children
Lpv/r	Glucose – fasting					X					

* If baseline ALT is abnormal, then it should be checked monthly for 3 months if patient is started on NVP or EFV.

Examples:

1. All patients starting TDF + 3TC + EFV should get the following baseline bloods before starting ARVs:
   - CD4 count, creatinine
2. All patients on AZT + 3TC + NVP at 1 month should get the following bloods:
   - FBC + differential
3. All patients on Tenofovir + 3TC + NVP at 6 months should get the following bloods:
   - CD4 (if available and local protocol creatinine)

Appendix 12: Early and late side effects of ARVs

Early side effects possible in the first 3 months

Symptom	Think of...	Important Actions
Rash	Drug-related cause (NVP, cotrimoxazole, or TB drugs)	Grade the rash Treat according to Grade
Nausea	If abdominal pain, think of pancreatitis or hepatitis	See sections below
Vomiting	Pancreatitis Hepatitis	Correct any dehydration Check Lipase and ALT Metoclopramide as required if severe
Abdominal Pain	Pancreatitis Hepatitis	Check Lipase Check ALT
Weight loss	Not a side effect, but probably an undiagnosed OI: (TB, Chronic diarrhoea)	Investigate for TB Send stool sample for investigation
Confusion	Rule out infection before blaming this on Efavirenz!	Refer for L.P. Consider changing Efavirenz to another ARV (if no meningitis found)
Weakness	Anaemia (if on AZT)	Check Haemoglobin (Hb)
Fever, constitutional symptoms, cough, sore throat, rash...	HSR to ABC (See page 221).	If confirmed, stop ABC immediately and never re-try again! If doubtful, allow the pt. to take one more dose and watch him/her carefully.

Late side effects possible after 3-6 months on ARVs

Symptom	Think of...	Important Actions
Nausea +/- Vomiting	High lactate	Check lactate level (+ refer to doctor if lactate level high)
Weight Loss	Tuberculosis High lactate	Investigate for TB Check lactate level Consider need to substitute D4T
Abdominal Pain	High lactate Hepatitis Pancreatitis	Check lactate level Check ALT Check Lipase level
Shortness of breath	High lactate with lactic acidosis	Check lactate level and refer to doctor
Painful, cold feet	Peripheral Neuropathy (due to D4T or DDI)	Grade the P.N. and treat accordingly Consider stopping D4T or DDI
Fat redistribution	Lipodystrophy	Change D4T to another ARV
Weakness	Anaemia (if on AZT)	Check Haemoglobin (Hb)
Creatinine Clearance < 50 ml/min	TDF toxicity	After having ruled out treatable causes of acute renal insufficiency (dehydration due to fever, diarrhea, protracted vomiting, etc), change TDF to AZT.

Appendix 13: Grading of possible side effects to ARVs

Symptom (and diagnoses to consider, plus likely ARV responsible)	Grade 1	Grade 2	Grade 3	Grade 4
Painful feet	Mild, does not worry patient	Moderate, bothers patient	Symptoms day and night	Functional impairment (difficulty walking, etc)
d4T-related peripheral neuropathy (also occurs with ddI)	- Follow D4T phasing out algorithm	- give Amitriptyline 25 mg nocte - Patient should be switched to TDF (follow local protocol)	give Amitriptyline 25 mg nocte - Patient should be switched to TDF (follow local protocol)	URGENT refer to doctor give Amitriptyline 25 mg nocte - Check lactate level to rule out hyperlactatemia
Abdominal pain +/- nausea	Mild and transient (< 24 hr)	Food intake decreased (24–48 hrs)	Minimal food intake (> 48 hrs)	Patient too sick for outpatient treatment
d4T-related pancreatitis (short-term) or high lactate (long-term) NVP-related hepatitis	- No treatment needed, but have patient return early if pain worsens	- Encourage frequent small meals - Give Metoclopramide 10 mg every 12 hours prn - Take blood for ALT and reassess in 2-3 days	- Refer to doctor if ALT 3x normal - Doctor to **check lactate level** if patient has been on d4T for more than 4 months, to rule out high lactate as the cause	- Refer to hospital and doctor

Symptom (and diagnoses to consider, plus likely ARV responsible)	Grade 1	Grade 2	Grade 3	Grade 4
Vomiting	Once per day and/or lasting < 3 days	< 4 episodes per day and not dehydrated	Vomits > 3 times per day, and dehydrated	Dehydrated and too sick for outpatient treatment
d4T-related pancreatitis (short-term) or high lactate (long-term) NVP-related hepatitis	- Reassure patient, but have patient return early if worsens - Consider giving Metoclopramide 10 mg every 12 hours prn	- Give ORT - Encourage frequent small meals - Give Metoclopramide 10 mg every 12 hours prn - Take blood for ALT and reassess in 2–3 days	- Give ORT - Give Metoclopramide 10 mg every 12 hours prn - Refer to doctor - Doctor to **check lactate level** if patient has been on d4T for more than 4 months, to rule out high lactate as the cause	- Refer to hospital and doctor
Psychological	Dizziness	Vivid dreams	Mood changes or persistent disturbing dreams	Acute psychosis, hallucinations, confused behaviour
EFV	- Reassure patient - Confirm EFV is being taken at night	- Reassure patient - Symptom will go away after few weeks	- Confirm EFV is being taken at night and not with fatty foods Refer to doctor if not settling	- refer to hospital - Perform Lumbar Puncture to rule out meningitis - Only restart ARVs when symptoms have fully resolved (use NVP instead of EFV)

Symptom (and diagnoses to consider, plus likely ARV responsible)	Grade 1	Grade 2	Grade 3	Grade 4
Skin rash	Red, itchy	Maculo-papular rash or dry scales	Blisters or moist loss of skin Rash involves mucous membranes or eyes +/- sloughing of skin	
NVP (more commonly) EFV (but also consider TB meds or Co-trimoxazole as possible causes)	- Reassure, but have patient return early if worsens - Consider giving Chlorpheniramine 4 mg every 8 hours prn, if itch is significant	- Give Aqueous cream +/- 0.1% Betamethasone - Consider giving Chlorpheniramine 4 mg every 8 hours prn - Check ALT, and reassess in 2-3 days - Patient to return early if rash worse, or abdominal pain	- URGENT refer to doctor same day Doctor to decide when to Stop ART with tail protection - Give Chlorpheniramine 4 mg every 8 hours as needed - When symptoms have resolved, restart ARVs using a PI	
Creatinine Cleaerance ml/ minute	>50ml/min	30-50ml/min	<30ml/min	
TDF	Continue TDF	Check for urine infection and other reasons for dehydration. Treat possible causes and recheck creatinine after one week	Stop TDF Refer to doctor	
Elevated ALT (in U/L)	50–100	100–200	> 200	
NVP (more commonly) EFV	Continue ARVs, but recheck ALT in 1 month	- Continue ARVs if no other problem - Recheck ALT again after 2 weeks - Switch NVP to EFV (unless patient is in the first trimester of pregnancy)	- refer to hospital - Check ALT frequently to ensure it returns to normal - Restart ARVs with EFV (unless in the first trimester of pregnancy)	

Symptom (and diagnoses to consider, plus likely ARV responsible)	Grade 1	Grade 2	Grade 3	Grade 4
Anaemia (low Haemoglobin, in gm/dl)	8–9.4	6.5–7.9	< 6.5	
AZT	- Examine patient to rule out bleeding, or serious problem (including active TB) - If no problem, continue ARVs - Recheck Hb in 2 weeks	- Examine patient to rule out bleeding, and refer to doctor for assessment **- Stop AZT** **If less than 6 mths on ART change to TDF** **If more than 6 mths on ART change to D4T and then follow d4T phasing out algorithm**	Refer to hospital **- Stop AZT** **If less than 6 mths on ART change to TDF** **If more than 6 mths on ART change to D4T and then follow d4T phasing out algorithm**	
Lipodystrophy	All			
d4T	- Follow D4T phasing out algorithm			

** TAIL-PROTECTION REGIMENS for NNRTI drug interruption:

- Whenever we have to stop EFV or NVP, it's advisable to continue TDF/3TC or d4T/3TC for 7 days, to avoid emergence of HIV resistance.
- Likewise, when we have to stop ALL ARVs (e.g. in case of lactic acidosis), it's better to give a tail-protection with a double dose of Aluvia (that is 4 tabs BD) for 7–10 days. A double dose is given because of an interaction between LPV/r and the NNRTI.
- Stopping TDF in a HBsAg+ pt. is contraindicated and a doctor should manage the case. In case of a life-threatening condition (but different from drug-induced hepatitis!! E.g. emergency surgery), necessitating interruption of all ARVs, withdrawal of TDF for few days is allowed, under surveillance. Re-introduce as soon as possible.

Recommended substitutions for specific severe side effects

Regimen	Toxicity	Drug substitution
TDF/3TC/NNRTI	TDF: renal damage (CrCL < 50 ml/min measured twice)	AZT/3TC/NNRTI*
AZT/3TC/NNRTI	AZT: severe anemia	TDF/3TC/NNRTI
D4T/3TC/NNRTI	D4T: peripheral neuropathy OR lactic acidosis OR lipodystrophy	TDF/3TC/NNRTI (but only if VL below limit of detection and no adherence problems)
NRTI/3TC/EFV	EFV: persistent CNS toxicity	Change EFV → NVP **
NRTI/3TC/NVP	NVP: grade 3 and 4 hepatotoxicity or grade 4 skin toxicity (see also p. 232) - NVP: grade 3 skin toxicity (see also p. 232)	Change NVP → PI (LPV/r) Change NVP → EFV if pt. can be hospitalized; if not → PI

* Permanently stopping TDF in patients with positive HBsAg is contraindicated and might lead to severe reactivation of hepatitis B: refer to doctor

** When changing from EFV to NVP, no need to start with NVP half dose (200mg OD) unless EFV had already been stopped for more than one week (give NVP 200 BID as of the 1st day).

Appendix 14: Common drug interactions

Rifampicin

Co-administration with NVP or PI's reduces ARV drug concentrations. EFV is drug of choice in case of co-administration of TB treatment. In case LPV/r is used, the dosage needs to be doubled (return to the normal dose 2 weeks after the end of anti-TB treatment) or add ritonavir syrup (see **page 218**).

Oral contraceptive pills

Their effectiveness is reduced if taken with NVP, EFV or any of the PI's. Women should be informed to use a barrier method such as condoms.

The effectiveness of Depot contraception may also be affected by NNRTIs. The interval between injections should be reduced from 12 to 8 weeks for medroxyprogesterone (Depo-Provera®) and from 8 to 6 weeks for norethisterone (Noristerat®).

Ketoconazole

Blood levels are significantly lowered with use of NVP. Use of the systemic anti-fungal agent fluconazole is preferred.

Benzodiazepines

Should be avoided with EFV due to increased risk of sedation.

Carbamazepine

Co-administration of carbamazepine with NVP, EFV or LPN/r should be avoided due to changes in drug levels in the blood. In case of PN due to D4T, vitamin B6 and/or amitriptyline should be used instead.

Herbal or traditional treatments

Over-the-counter and traditional herbal treatments should be avoided with all ARV drugs as they might lead to inadequate drug concentrations. For example St John's Wort, a popular herbal remedy for treating mild depression, reduces the plasma concentrations of all ARV drugs.

Warfarin

Interactions can occur between warfarin (used in persons to help prevent clot formation), rifampicin, the PIs, and NNRTIs. Frequent, careful monitoring of the INR is recommended.

Antimalarials

Coadministration of amodiaquine with Efavirenz is contraindicated.There are no interactions between antimalarials and the NRTIS. Levels of artemisinins may be slightly lowered by coadministration with NNRTIs so close observation of patient response is needed.

Appendix 15: Key points for clinical review of symptoms and signs

Ask	Look

If this is the first visit:
Review medical history; particularly for TB, other opportunistic infections, and chronic problems.
For all visits:
• How have you been? What problems have you had?
• Have you had any of the following? If yes, ask for how long:
  • Headache? Fever? Night sweats?
  • Cough?
  • Nausea or vomiting? Poor appetite?
  • Mouth sores?
  • Abdominal pain?
  • Diarrhoea?
  • New skin rash?
  • Fatigue?
  • Signs of STI?
  • Tingling, numb, or painful feet/legs?
  • Any other pain? If yes, where?
• Have you needed urgent medical care? If yes, ask for record/ diagnosis
• Which medications are you taking and how often?
• Assess adherence (if on opportunistic infection prophylaxis and/or ART)
• What problems have you had taking the medicines? How are you taking the medicines?
• Taking any other drugs (traditional remedies, TB, ARV, illicit drugs, etc...)
• How are things at home?
• Has your partner been tested?
• Have your children been tested?
• Who knows about your diagnosis and how do you feel about someone attending with you for appointments?
• Is there anything else you would like to talk about?
• Access to/need for/family planning?
	In all patients:
	• Look for pallor. If present check haemoglobin level.
	• Look at the whites of eyes: are they yellow?
	• If CD4 < 100, examine retinae through dilated pupils
	• Look for oral thrush
	• Listen to the lungs and palpate the abdomen
	• Weigh, calculate, and record weight gain or loss. If weight loss >10%, ask for food intake and assess carefully for TB symptoms.
	• Take the height of adults at the first consultation and calculate BMI. Take the height of children at each consultation and calculate the ratio W/H.
	• Estimate adherence
	• If the patient is sad or has lost interest, assess for depression.
	If any new symptoms:
	• Examine the relevant system and do further assessment of symptoms.
	• Measure temperature.
	• Check lymph nodes
	• Look for a rash
	• Look for evidence of violence.

Recommendations in MSF programmes, Nov 2007; Adapted from: Chronic HIV care with ARV Therapy: Integrated management of adolescents and adults illness interim guide for first-level-facility health workers. Geneva, WHO, December 2003.

Appendix 16: Karnofsky Score

The Karnofsky Score is one way to measure a person's ability to perform activities of daily living. As a person gets sicker, they become less active and less able to care for themselves. As their performance suffers, their Karnofsky Score decreases.

Able to carry on normal activity; requires no special care	**100**	Normal; no complaints of disease
	90	Able to carry on normal activity; minor symptoms or signs of disease
	80	Able to carry on normal activity with some effort; some symptoms or signs of disease
Unable to work; able to live at home and care for most personal needs; requires a varying amount of assistance	**70**	Cares for self; unable to do normal activity or to do active work
	60	Requires occasional assistance but is able to care for most of own needs
	50	Requires considerable assistance and frequent medical care
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly	**40**	Disabled; requires special care and assistance
	30	Severely disabled; hospitalisation indicated although death not imminent
	20	Very sick; hospitalisation necessary; active supportive treatment necessary
	10	Moribund, fatal processes progressing rapidly
	0	Dead

Appendix 17: Desensitization with cotrimoxazole

Desensitization can be offered rapidly or over a longer period of time. Do not desensitize anyone who has had an anaphylactic reaction to cotrimoxazole or a severe skin rash such as Stevens-Johnson syndrome. **Do not attempt in children.** Desensitization is usually about 60% effective. Rapid desensitization ideally should be performed during the day in a setting where emergency resuscitation can be provided and adrenaline can be given. Observations during rapid desensitization should take place every 30 minutes, before each dose is given, and should include temperature, pulse, and blood pressure.

If only mild rash or pruritus occurs, administer antihistamine (e.g., chlorpheniramine or promethazine) and continue. If more serious side effects occur, such as severe wheeze, severe or symptomatic hypotension, severe rash, and so on, discontinue desensitization, manage appropriately, and do not try to restart desensitization.

Once cotrimoxazole has been started, it can be continued indefinitely as long as no reactions are noted, but if the drug is stopped at any time, there may be a risk of reaction when it is restarted.

Using a 1 ml syringe, put 0.5 ml of paediatric cotrimoxazole 240 mg / 5 ml syrup in 1,000 ml of 5% dextrose and mix well.

Give as follows:

Minutes	**Quantity of Above Mixture Given Orally**
0	1 ml (use 10 ml syringe)
30	10 ml (use 10 ml syringe)
60	100 ml (use 10 ml syringe)

Then switch to paediatric cotrimoxazole 240 mg / 5 ml syrup.

Minutes	**Quantity**
90	0.5 ml
120	5 ml
150	480 mg tablet
180	Start full prophylactic or therapeutic dose.

Appendix 18: Introduction to the interpretation of blood results

Explanation of various tests

Liver function tests:

- Albumin is a protein in the blood. Severe damage to the liver could cause the albumin levels to be low. Malnutrition or severe infection could also cause a low albumin (hypoalbuminemia).
- Other tests such as ALT, AST or GGT are also commonly referred to as 'liver function tests' although in reality, they are better indicators of liver 'inflammation' than liver 'function'.
- Some drugs like NVP, Rifampicin and Phenobarbital (hepatic inducers) are accompanied by a slight increase of GGT, which is not worrisome, as long as it's not associated with other LFT abnormalities (such as ALT abnormalities) or symptoms.
- Isolated indirect hyperbilirubinemia is a 'mark' of ATV treatment and, if not associated with any other laboratory abnormality or symptoms, doesn't need any intervention.

Full blood count

- Haemoglobin (Hb) is a protein in red blood cells and it also carries oxygen.
- Mean cell volume (MCV) is a measure of the average red blood cell volume. A low Hb with low MCV (<70-80) may suggest iron deficiency anaemia (microcytic anaemia). A low Hb with high MCV (> 100 = 'macrocytic anaemia') may suggest specific types of vitamin deficiencies (folate, vitamin B12). A macrocytosis is also seen in patients on AZT, but this is not a concern as long as the Hb is not too low. This is a guide only, since chronic diseases such as HIV tend to cause a normocytic anaemia (low Hb with normal MCV) so interpretation may be difficult.
- Platelet count (PLT): platelets are the smallest blood cells and aid in the clotting of blood. They are formed in bone marrow. Trapping of platelets in liver disease could cause the spleen to be enlarged and the platelet count to decrease. That's exactly what happens in case of severe liver disease (cirrhosis). People with a low platelet count (thrombocytopenia) could have the following conditions: untreated HIV or other viral infection, liver disease, or lymphoma.

- White blood cells (WBC's) or leucocytes are cells of the immune system that defend the body against infections and foreign materials.

Kidney tests

Creatinine is a breakdown product of muscle. It is filtered out of the blood into the urine by the kidney. Severe kidney damage could cause the creatinine levels in the blood to be high. However, this test is not suitable for detecting early kidney dysfunction.

Creatinine clearance (CrCl), instead, is a useful test because it helps detect early kidney dysfunction. Creatinine levels in the blood and urine may be used to calculate the creatinine clearance.

Many conditions (not only TDF) can cause reduction of CrCl, acutely (e.g. dehydration due to high fever, heavy diarrhoea, protracted vomiting...) or chronically (hypertension, diabetes, aging... and HIV itself!).Those conditions may warrant a particular treatment and follow-up.

It's always better to check CrCl again after the resolution of an acute disease, if we think that the low result might have been affected by that: we might be able to avoid an unnecessary shift away from TDF!

For severe renal failure, it's advisable to reduce the dose of some of the ARVs (see Appendix 31).

Laboratory test normal values

Full Blood count and Platelets

Test	Normal result (reference range)
White Cell Count	4.0–10.0 x 10^9/L
Red Cell Count	4.5–5.5 x 10^{12}/L
Haemoglobin	10.5–17.0 g/dL
Haematocrit	0.4–0.5 L/L (or 40 – 50%)
MCV	79.1–98.9 fL
MCH	27.0–32.0 pg
MCHC	32.0–36.0 g/dL
Red Cell Distribution Width	11.6–14.0 %
Platelets	137–373 x 10^9/L

Differential Count

Test	Normal result (reference ranges)
Neutrophils	1.5–7.5 x 10^9/L
Monocytes	0.18–0.80 x 10^9/L
Lymphocytes	1.0–4.0 x 10^9/L
Eosinophils	0.00–0.45 x 10^9/L
Basophils	0.00–0.20 x 10^9/L
Absolute CD4	500–2010 cells/µL

Glucose values

Test	Normal result (reference range)
Fasting glucose	3.9–5.5 mmol/L

Liver Function Tests

Test	Normal result (reference ranges)
Bilirubin total	0–21 µmol/L
Bilirubin conjugated	0–6 µmol/L
Alkaline Phosphatase (ALP)	40–120 IU/L
Y-Glutamyl Transferase (GGT)	5–35 IU/L
Alanine Transaminase (ALT)	5–40 IU/L
Aspartate Transaminase (AST)	8–20 IU/L
Int Normalised Ratio (INR)	< 1.2 (in patients on oral anticoagulation for deep venous thrombosis, the target is 2.0–3.0).

Lipid Studies

Test (Need to be fasting bloods)	Normal result (reference ranges)
Fasting	
Total Cholesterol	<5.0 mmol/l
LDL Cholesterol	<3.0 mmol/l
HDL Cholesterol (Males)	>1.0 mmol/l
(Females)	>1.2 mmol/l
Triglycerides	<1.7 mmol/l

Protein studies

Test	Normal result (reference ranges)
CRP Quantitative	<1.0 nmol/L
ESR	15–20 mm/h

Kidney function

Test	Normal result (reference ranges)
Potassium	3.3–5.3 mmol/L
Chloride	99–113 mmol/L
Urea	2.6–7.0 mmol/L
Creatinine clearance	> 90 ml/minute (TDF contraindicated only if < 50)

Appendix 19: Disclosure to children

Disclosure is the **process** by which the child learns about his/her HIV/AIDS status. One can distinguish between **partial** disclosure (giving the child information about what is happening in his body without naming the virus and the disease), and **total** disclosure (telling the child he is infected with HIV and giving him/her all the information needed about HIV/AIDS).

For all children < 12 years, it is usually recommended to go for **progressive** disclosure, starting with partial disclosure. Each child is unique so he/she will also be our guide. Importantly, however, one should make sure that full disclosure is reached before adolescence. Difficult reactions are often seen in adolescents when they find out their diagnosis late. For older children/adolescents, disclosure can also be particularly important to ensure adherence.

Caretakers are often very hesitant to disclose to the child. Some of the common reasons (among many others) are: 1) belief that the child is too young to know 2) fear that the child cannot maintain a secret 3) the mother may feel ashamed to talk to the child about the transmission of the disease.

There are many reasons why to tell children they are HIV positive. Some of these are:

- Child should hear about HIV from caregiver and not from other sources
- Honesty is important in child-caregiver relationship
- Children often know the truth before we expect or think they do
- Children often cope with the truth better than we anticipate
- Secrecy may be associated with increased behavioural problems
- Provide child with a sense of control over their lives
- Child should know why they go to the hospital and have blood taken regularly
- It's their right to know
- Protect others from infection
- Gives child permission to talk openly about HIV with caregivers.

Nurses, doctors, and counsellors have an important role to play in helping caretakers through the process of disclosure. This can take time!

Example of a simple **disclosure** plan:

- Information about hygiene

REMEMBER

Start the disclosure process as early as possible

- At the latest when the child starts asking questions
- The longer we wait, the bigger the risk of losing the child's trust
- The more the secret lasts, the more difficult it will be to break the silence
- Always achieve total disclosure before adolescence

- Information about being sick
- Information about going to the doctor
- Information about the body
- Information about blood circulation
- Information about germs and getting sick
- Information about our defences (immune system)
- Information about immune system needing assistance from drugs
- Information about the specific virus the child has
- Naming the virus and the illness: HIV/AIDS
- Discuss with the child with whom the secret should be shared
- Information about CD4 count (and/or viral load if available)
- Information about transmission & non-transmission of HIV/AIDS
- Information about sexual relations and condoms use

Reference: K. Bosteels and D. Goetghebuer; Patient support for HIV infected children; MSF September 2008.

Appendix 20: Collecting a good sputum sample

A good sputum specimen consists of recently discharged material from the bronchial tree, with minimum amounts of oral or nasal material. Satisfactory quality implies the presence of mucoid or mucopurulent material and is of greater significance than volume.

Procedure

1) Reassure the patient by explaining the reason for sputum collection.
2) Instruct the patient to rinse his/her mouth with water before producing the specimen. This will help to remove food or any contaminating bacteria in the mouth.
3) Give the patient a new sputum container
4) Instruct the patient to take two deep breaths, holding the breath for a few seconds after each inhalation and then exhaling slowly. Ask him/her to breathe in a third time and then forcefully blow the air out. Ask him/her to breathe in again and then cough. This should produce a specimen from deep in the lungs.
5) Ask the patient to hold the sputum container close to the lips and to spit into it gently after a productive cough.
6) Examine the quality of the sputum specimen. Quality ones to be kept are:
    - Purulent or muco-purulent,
    - Thick and mucoid,
    - Fluid, with chunk dead tissue from a lesion in the lung

Thin, clear saliva or nasopharyngeal discharge is not sputum: a new specimen should be collected.

7) Examine the quantity of the sputum specimen. Quality ones to be kept are:
    - 3–5 ml: good,
    - < 3ml: encourage the patient to cough again until a satisfactory specimen is obtained.

Remember that many patients cannot produce sputum from deep in the respiratory tract in a few minutes. Give him/her sufficient time to produce an expectoration, which s/he feels, is produced by a deep cough.

8) Securely close the container,
9) If there is no expectoration, consider the container used and dispose of it in the appropriate manner.
10) Once the first specimen has been collected, give the 2nd container for the collection of the 2nd specimen.
11) Wash hands with soap and water.
12) Send the sample without delay to the laboratory, or store sample in a cool, dark place until transport available.

If patients are unable to produce sputum (especially likely in children) sputum induction using nebulised 5% normal saline should be made available (Appendix 21)

With the introduction of Xpert/MTB/Rif same day diagnosis of TB should be the goal. Therefore Xpert MTB/Rif can be performed on a spot sputum- there is no need to wait for an early morning specimen.

Appendix 21: Sputum induction

Sputum induction is sometimes used in children and adults when sputa cannot be spontaneously expectorated.

Sputum induction may provoke bronchospasm and must be performed under close medical supervision. The patient should be observed for respiratory distress during and for 15 minutes after the procedure. If indicated, 2 puffs of salbutamol and oxygen may be given.

Equipment

- High filtration mask for the operator and carer
- Gloves
- Suction catheter (6, 7, 8F)
- Sputum container
- 50ml syringe, needle
- Mask and tubing for nebulizer

(single use)

- Holding chamber with child's mask (sterilize between each patient)
- Sterile hypertonic solution of 5% sodium chloride (to be kept refrigerated)
- Sterile solution of 0.9% sodium chloride (for the specimen)
- Salbutamol spray
- Oxygen

Procedure

The patient should fast for at least 2 hours before the procedure.

Prior to nebulisation

- Explain the procedure to the patient and / or the person accompanying him.
- Place the patient in a sitting position in the adult's arms.
- Administer 2 puffs of salbutamol via a holding chamber, 10 minutes before nebulisation.
- Prepare a sputum container.

Nebulization

- Fill the nebulizer with 5ml of the 5% hypertonic saline solution (sputum inducer).
- Don an anti-inhalation mask.

- Place the nebulizer mask over the patient's mouth.
- Leave the child to inhale until the reservoir is empty.

Nasopharyngeal suction (a young patient does not expectorate spontaneously)

- Do 1 to 2 minutes of clapping.
- Clean out the nasal cavity.
- During suction, the patient is laid on his side, back to the operator, who is behind him.
- Fit a suction catheter to a 50ml syringe. Lubricate the end of the catheter.
- Measure the distance from the tip of the nose to the angle of the jaw. Insert the suction catheter to that depth.
- When inserting and withdrawing the tube, pull on the plunger of the syringe to create suction.
- Once the syringe is filled with air and mucus, disconnect it from the suction catheter and purge the air (tip facing upward), so that only the mucus is left in the syringe.
- To collect the mucus: draw 2ml of 0.9% saline into the syringe to rinse, then empty contents into the sample container.

Appendix 22: Building a DR TB Treatment Regimen

Step 1

Use any available + One of these + One of these

Group 1: First-line oral	Group 2: Injectables	Group 3: Quinolones
Pyrazinamide	Kanamycin	Levofloxacin
Ethambutol	Amikacin	Moxifloxacin
	Capreomycin	Gatifloxacin
	Streptomycin	Ofloxacin

Step 2

Pick one or more of these

Add Group 4 drugs until you have 4–6 drugs likely to be effective

Group 4: Second-line oral bacteriostatic

Cycloserine/Terizidone

Ethionamide/Protionamide

PAS

Step 3

Consider use of these

Consider adding Group 5 drugs in consultation with an MDR-TB expert if there are not 4–6 drugs available in the above categories

Group 5: Drugs of unclear efficacy

Clofazimine

Linezolid

Amoxicillin/clavulanate

Imipenem/cilastatin

Clarithromycin

High-dose isonaizid

Appendix 23: DR TB Monitoring
(see monitoring table on page 255)

Clinical

Baseline Clinical and Investigations

- Repeat smear, culture and DST prior to starting DR treatment
- Medical history and physical exam by Doctor
- Weight and BMI
- HIV screening and CD4 (if not already done)
- Chest x-ray
- Pregnancy test (child bearing age)
- Audiometry (baseline and monthly during the intensive phase of treatment)
- Potassium
- Serum creatinine and creatinine clearance
- Full blood count
- ALT
- Fasting Blood Glucose (FBG)
- Vision test for colour vision if on Ethambutol (see Ishihara test in Appendix 23).

Intensive Phase Monitoring

- Smear and culture monthly, repeat DST if:
  - Culture remains positive at 4 months
  - Patient is clinically deteriorating
  - If culture becomes positive after conversion (2 negative cultures one month apart)
- At the start of treatment, the patient should be assessed daily by the nurse for side effects to medication. Any concerns should be brought to the attention of the doctor immediately. The doctor should see the patient at least weekly during the first month and more often if any problems are developing. Once the patient is stable, the doctor can see the patient every 2 weeks.

- Patient's weight check each week during the intensive phase.
- Periodic monitoring of ALT every 1–3 months in patients receiving Pyrazinamide, or patients at risk of or with symptoms of hepatitis.
- Creatinine clearance, Hb and potassium monthly during the injectable phase.
- Magnesium if hypokalemia (= low potassium) detected.
- Audiometry monthly during the injectable phase. If audiometry is not available patients must be actively asked if they are experiencing any problems with hearing.
- Repeat Ishihara test monthly if on Ethambutol

Continuation Phase monitoring

- Smear and culture done monthly, DST if patient is deteriorating clinically or culture remains/or becomes positive again after conversion.
- Examination by doctor monthly unless there is a medical necessity to see the patient more often. Other medical team members see the patient between times and signal any concerns to the doctor.
- Patient's weight should be checked monthly.
- ALT, FBC, creatinine if clinically indicated
- TSH levels every 6 months in patients on PAS and/or Ethionamide

Side Effects of Drugs

Second line TB drugs have many more adverse side effects than first-line anti TB drugs. Patients need to be informed of the potential side effects and when to notify the health care provider. Timely and aggressive management of all adverse effects is essential, whether they are minor (non life threatening) or major (life threatening). See Appendix 24 for management of side effects.

Adherence

Each patient who interrupts treatment should be traced immediately and the reasons for interruption should be explored. Every effort should be made to convince the patient to resume treatment.

It is important to have a monitoring system in place to identify defaulters within 1-2 days of non adherence.

If a patient has missed his/her clinic visit, a phone call and/or home visit should be undertaken to determine the reason(s) for non adherence.

Counselling

Counselling of patients is of paramount importance and should be reinforced throughout treatment.

DR TB treatment is very difficult to adhere to for many reasons. Some of these reasons are:

- Psychological distress
- Social problems
- Knowledge and belief regarding treatment purpose
- Separation from family/friends
- Side effects of medication
- Inconsistent immediate effect
- Trust in provider

Strategies to support patients with these numerous difficulties are many, but a basic package of support should include:

- Patients should receive sufficient information and education about their disease and treatment, given by nursing and medical staff to enable the patients to be responsible for their own treatment. It is very important that patients understand that if they do not adhere to their treatment, they are putting themselves at risk of developing resistant TB that is not treatable and they can pass this untreatable resistant TB to their families.
- Psychological support individually and/or in groups.
- Intense medical support to treat side effects of drugs, addictions, other medical conditions, psychiatric disease and other pre-existing conditions or results of treatment.
- Social support, including accommodation, transport and other needs of the patients and their families; and to facilitate access to resources in the community.
- Some flexibility in treatment delivery to enable patients to stay adherent.

Monitoring Drug Resistant TB Patients

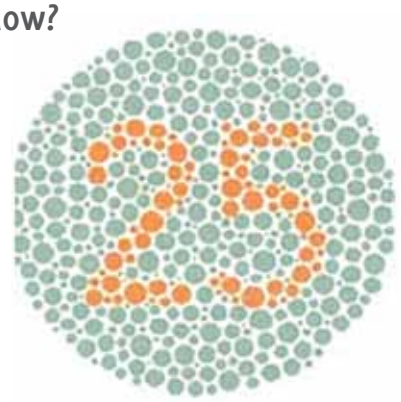
	Baseline	Intensive Phase						Continuation Phase											
MONTH	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18-24**
Smear	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly
Culture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly
DST 1st line	X	Repeat if client clinically deteriorating			X (if culture +ve)			If at any time, culture becomes positive, or patient is clinically deteriorating, repeat 1st line DST and 2nd line DST (patient may now be resistant to more drugs)											
DST 2nd line	X																		
CXR	X						X												
HIV screening	X	If previously -ve repeat at 6 months or if clinically indicated																	
CD4 (HIV +ve)	X						X						X						18 & 24
Audiometry	X	X	X	X	X	X	X												
Evaluation by PHC Doctor	X	Weekly during 1st month Every 2 weeks after 1st month if patient is stable			X	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly
Weight (BMI)	X	Weekly						X	X	X	X	X	X	X	X	X	X	X	Monthly
Urinalysis	X																		
Contraception	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Monthly
Creatinine[1]	X	X	X	X	X	X	X												
Potassium[2]	X	If on Capreomycin MONTHLY in Intensive Phase																	
TSH[3]	X						X						X						18 & 24
ALT[4]	X	If clinically indicated																	
Hb	X	X	X	X	X	X	X												
FBG[5]	X	If clinically indicated																	
Pregnancy test	X	If clinically indicated																	
Colour Vision	X	If clinically indicated																	

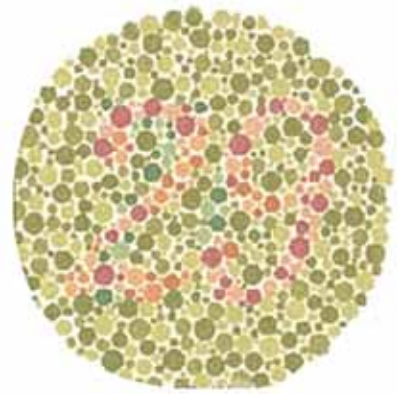
1) While receiving an injectable (Kanamycin, Amikacin, Capreomycin, Streptomycin). Calculate creatinine clearance (see formula on **page 207**)
2) While receiving Capreomycin monthly in Intensive Phase and high risk patients
3) If patient taking PAS or Ethionamide will need baseline monitoring as indicated
4) If clinically indicated
5) Fasting Blood Glucose if clinically indicated

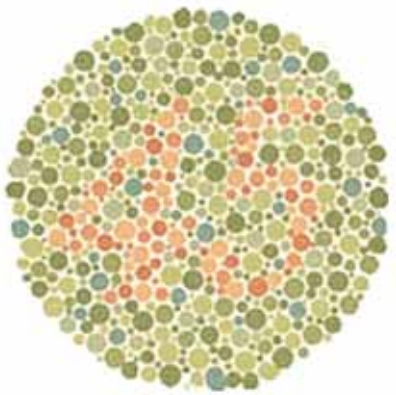
Appendix 24: Ishihara Test for Colour Blindness

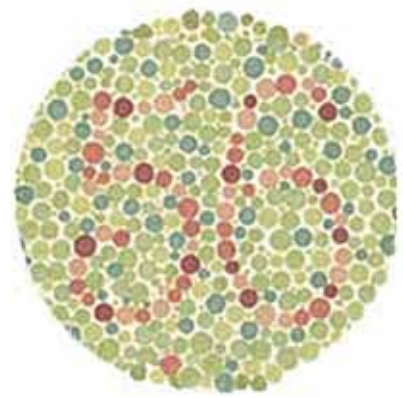
Ethambutol may cause optic neuritis. Colour blindness precedes blindness and can detect early ethambutol toxicity.

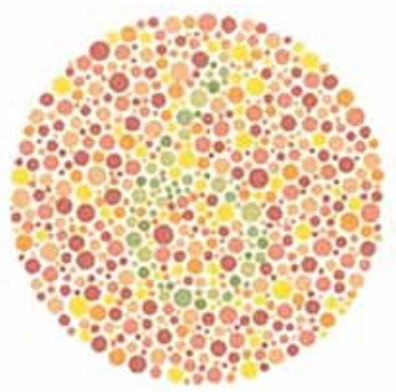
What numbers do you see revealed in the patterns of dots below?

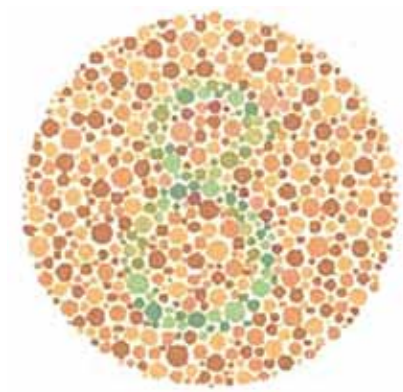






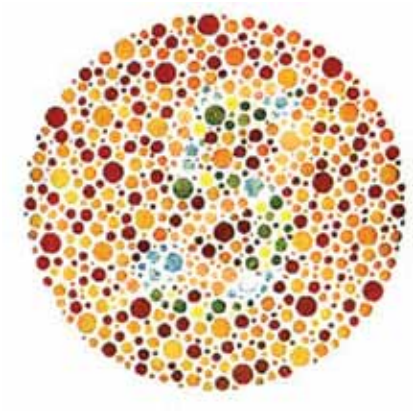






Normal Colour Vision			Red-Green Colour Blind		
	Left	**Right**		**Left**	**Right**
Top	25	29	**Top**	25	Spots
Middle	45	56	**Middle**	Spots	56
Bottom	6	8	**Bottom**	Spots	Spots

Another interesting colour blindness test is below



The test to the left is simpler.
The individual with normal colour vision will see a 5 revealed in the dot pattern.
An individual with Red/Green (the most common) colour blindness will see a 2 revealed in the dots.

Appendix 25: Management of Adverse Effects of DR TB treatment

Common drug adverse reactions and management strategies

(Adapted from: World Health Organization. Guidelines for the Programmatic Management of Drug-resistant Tuberculosis (WHO/HTM/TB/2005.361), World Health Organization: Geneva, Switzerland, 2006).

It is very important to exclude an underlying medical condition for the symptoms and to not automatically blame the drugs for the symptoms!

Adverse reaction	Agent	Management	Comments
Seizures	Cs/Trd FQs	Rule out other likely causes. Treat any suspected causes. Initiate anticonvulsant therapy (e.g. valproic acid 750–1250mg/kg/day; phenytoin 3–5 mg/kg/day; carbamazepine 600–1200 mg/day; phenobarbital 60–120 mg/kg/day). Increase pyridoxine to 300 mg daily. Lower dose of suspected agent. Discontinue suspected agent.	Clinical evaluation generally sufficient unless suspicion high for infectious, malignant, vascular or metabolic cause. Anticonvulsant generally continued until DR-TB treatment completed or suspected agent discontinued. History of prior seizure disorder not a contra-indication to the use of agents listed here if patient's seizures are well-controlled and/or patient is receiving anticonvulsant therapy. Patients with history of prior seizures may be at increased risk for development of seizures during DR-TB therapy. Seizures not a permanent sequela of DR-TB treatment.

Peripheral neuropathy	Cs/Trd S Km Am Eto/Pto E Cm	Increase pyridoxine to 300 mg daily. Begin exercise regimen, focusing on affected regions. Initiate therapy with tricyclic antidepressant drugs. Lower dose of suspected agent. Discontinue suspected agent .	Patients with co-morbid disease (e.g. diabetes, HIV, alcoholism) more likely to develop peripheral neuropathy, but these conditions are not contraindications to the use of the agents listed here. Neuropathy is generally not reversible, although only a minority (approximately 10%) of patients require continued intervention to keep symptoms controlled once DR-TB treatment completed.
Hearing loss	S Km Am Cm	Consider administration 5x or even 3x per week. Lower dose of suspected agent. Discontinue suspected agent.	Patients with prior exposure to streptomycin may have baseline hearing loss. Hearing loss is generally not reversible.
Psychosis Rule out underlying medical cause!	Cs/Trd FQs Eto/Pto	Initiate anti-psychotic drugs (e.g. haloperidol 1–5mg PO IV or IM repeated every hour as needed). Hold suspected agent for short period of time (1-4 weeks) while psychotic symptoms brought under control. Lower dose of suspected agent. Discontinue suspected agent.	Some patients will need to continue anti-psychotic treatment throughout DR-TB therapy. Prior history of psychiatric disease not a contraindication to the use of agents listed here but may increase the likelihood of development of psychotic symptoms. Psychotic symptoms generally reversible upon DR-TB treatment completion or discontinuation of offending agent.

Depression	Cs/Trd FQs Cm Eto/Pto	Rule out side effects of concomitant medications, e.g. amoxycillin-clavulanate, penicillin, benzodiazepines. Institute psychological therapy. Group or individual supportive counselling. Initiate anti-depressant drugs (e.g. amitriptyline (preferable if patient on ARV's), nortriptyline, fluoxetine, sertraline), but use with caution when history of convulsions. Lower dose of suspected agent. Discontinue suspected agent.	Importance of socioeconomic conditions should not be underestimated as contributing factor to depression. Depression and depressive symptoms may fluctuate during therapy. History of prior depression is not a contraindication to the use of the agents listed here; however, these patients may be at increased risk for developing depression during DR-TB treatment.
Nausea and vomiting	Eto/Pto Cm E Z PAS	Rehydration Initiate anti-emetics 30 min prior to DR-TB drugs. Metoclopramide 10 to 20 mg QID, ondansetron 8 mg (up to 24 mg) 30 minutes before dose and 8 hours after dose. Administer Eto in 3 separate doses. Administer Eto at night with short-acting benzodiazepine. Lower dose of suspected agent. Discontinue suspected agent.	Nausea and vomiting ubiquitous in early weeks of therapy and usually abate with supportive therapy. Electrolytes should be monitored and repleted if vomiting severe. Reversible upon discontinuation of suspected agent.

Gastritis	PAS Eto/Pto E Z	Administer DR-TB medications with small amount of food. Avoid caffeine, cigarettes. Proton-pump inhibitors (e.g. omeprazole 20 mg OD or BD). Hold suspected agent(s) for short periods of time (e.g. 1–7 days). Lower dose of suspected agent. Discontinue suspected agent.	Severe gastritis possible, as manifest by hematemesis, melena or hematochezia. Dosing of antacids should be carefully timed so as to not interfere with the absorption of DR-TB drugs. Take fluoroquinolones at least 3 hours apart from antacids. Reversible upon discontinuation of suspected agent(s).
Hepatitis	Z FQs Eto/Pto PAS Cm	Stop therapy if severe. Rule out other potential causes of hepatitis. Re-introduce drugs individually while monitoring liver function, with least likely agent introduced first. Monitor liver function every 1–2 months.	History of prior hepatitis should be carefully analyzed to determine most likely causative agent(s); these should be avoided in future regimens. Generally reversible upon discontinuation of suspected agent.
Nephrotoxicity and renal failure	S Km Am Cm	Follow creatinine, treat symptoms. Reduce dose of medication according to creatinine clearance. Discontinue suspected agent. If on TDF, replace by AZT.	History of diabetes or renal disease not a contraindication to the use of the agents listed here, although patients with comorbidities may be at increased risk for developing renal failure. Renal impairment may be permanent.
Optic neuritis	E	Stop agent	

Arthralgias	Z Ofx	Initiate therapy with non-steroidal anti-inflammatory drugs. Initiate exercise regimen. Lower dose of suspected agent. Discontinue suspected agent.	Symptoms of arthralgia generally diminish over time, even without intervention. Uric acid levels may be elevated in some patients but are of little therapeutic relevance and anti-gout therapy (e.g. allopurinol, colchicine) is of no proven benefit in these patients.
Electrolyte disturbances (hypokalemia, hypomagnesaemia)	Cm Ka Am S	Replete potassium orally or IV. Treat associated vomiting or diarrhoea. Check magnesium levels if potassium levels do not improve Discontinue aminoglycosides if severe.	Hypokalemia can occur without clinical signs and symptoms and may be life-threatening.

Appendix 26: Dosages of DR TB Drugs

Intensive phase: 6–8 months (Includes Kanamycin – or another injectable – for 6 to 8 months) Continuation phase: without the injectable, for a total treatment duration of at least 20 months

Patient weight	Drug	Dosage
<33kg	Kanamycin (OD) Ethionamide (OD) Pyrazinamide (OD) Levofloxacine (in 2 doses) PAS (in 2 doses) Ethambutol (OD) or Terizidone (in 2 doses) Cycloserine (in 2 doses)	15–20 mg/kg 15–20 mg/kg 30–40 mg/kg 15–20 mg/kg 150mg/kg /daily 25 mg/kg 15–20 mg/kg 15–20 mg/kg
33–50 kg	Kanamycin (OD) Ethionamide (OD) Pyrazinamide (OD) Levofloxacine (in 2 doses) PAS (in 2 doses) Ethambutol (OD) or Terizidone (in 2 doses) Cycloserine (in 2 doses)	500–750 mg 500 mg 1000–1750mg 750 mg 8 g 800–1200 mg 500–750 mg 500–750 mg
51–70 kg	Kanamycin (OD) Ethionamide (OD) Pyrazinamide (OD) Levofloxacine (in 2 doses) PAS (in 2 doses) Ethambutol (OD) or Terizidone (in 2 doses) Cycloserine (in 2 doses)	1000 mg 750 mg 1750–2000 mg 1000 mg 8 g 1200–1600 mg 750 mg 750 mg
>70 kg	Kanamycin (OD) Ethionamide (OD) Pyrazinamide (OD) Levofloxacine (in 2 doses) PAS (in 2 doses) Ethambutol (OD) or Terizidone (in 2 doses) Cycloserine (in 2 doses)	1000 mg 750–1000 mg 2000–2500 mg 1000 mg 12 g 1600–2000 mg 1000 mg 750–1000 mg

* Pyridoxine (B6) 150 mg to be given daily to patients on Cycloserine

For Ethionamide and Cycloserine, consider dose escalation (dose ramping) over 2 weeks in order to reduce the likelihood of side effects. For example, a DR-TB patient weighing >50 kg would receive doses according to the following schedule:

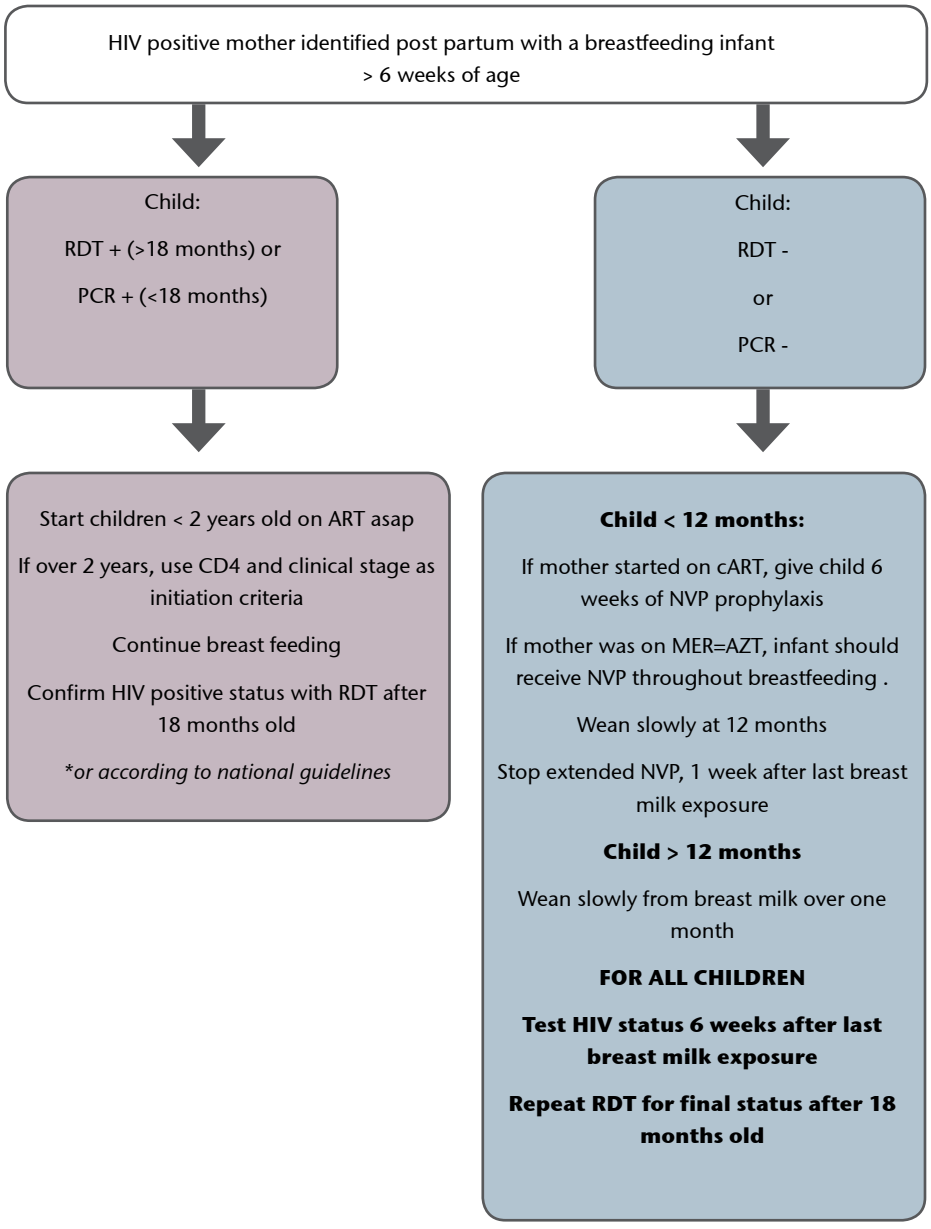
Prothionamide/Ethionamide

Initial dose: 250 mg OD
After 1 week: 250 mg BD
After 2 weeks: 750 mg OD

Cycloserine

Initial dose: 250 mg OD
After 1week: 250 mg BD
After 2 weeks: 250 mg AM – 500 mg PM

Appendix 27: PMTCT in late presenters- HIV positive mothers identified post partum with breastfeeding infants > 6 weeks of age



Appendix 28: Common, serious chest x-ray findings in PLWHA

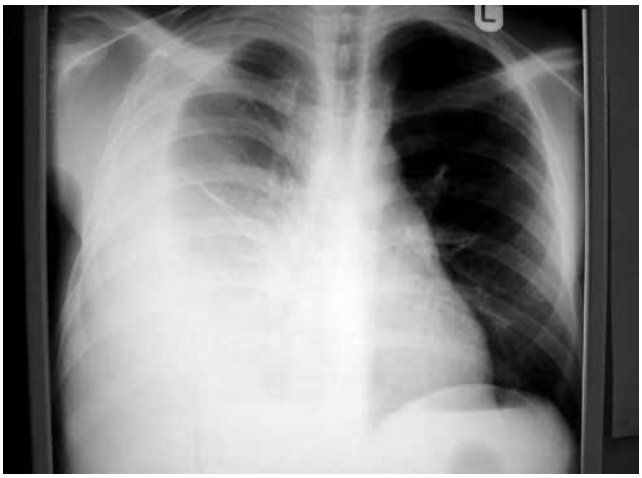


Photo credit: Dr. G. Meintjes

Figure 1: This image shows a **right-sided pleural effusion** which is highly suggestive of tuberculosis (TB) in a person having cough, fever, night sweats, and/or weight loss. If straw-coloured fluid is found during pleuracentesis ('pleural tap'), this helps to confirm the diagnosis. TB treatment should be initiated immediately.

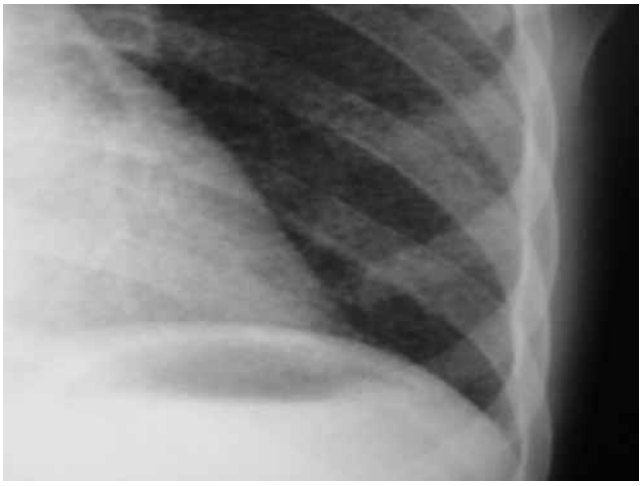


Figure 2: This image demonstrates a **miliary pattern** in a section of the left lung. The hundreds of tiny 'seeds' seen here represent hematogenous spread of TB. Treatment with TB medication should be initiated immediately.

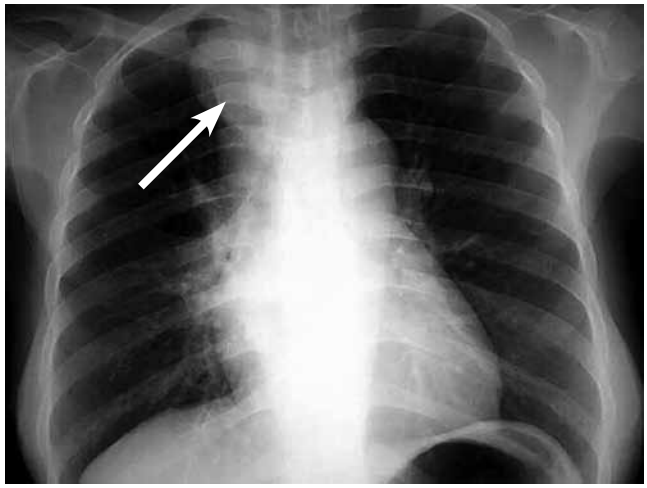


Figure 3: **Enlarged lymph nodes** are seen in the right mediastinum of this woman with severe immunodeficiency (CD4 count = 20 cells/μL). Although her sputum was negative for acid-fast bacilli (AFB), she was started on TB treatment on the basis of her clinical condition and this x-ray result.

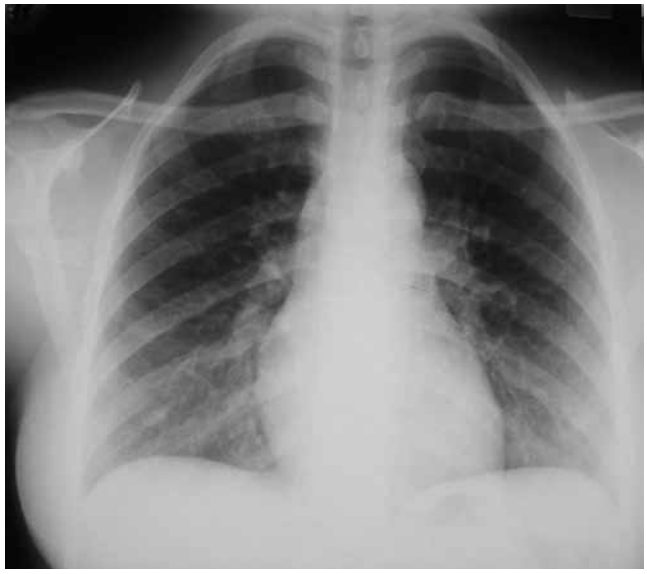


Photo credit: Dr. G. Meintjes

Figure 4: This woman presented with fever, cough, significant shortness of breath, and a low CD4 count. The x-ray shows a widespread interstitial infiltrate with reticulonodular markings that are more pronounced in the lower lobes. The presence of hypoxemia provided further evidence for **Pneumocystis pneumonia (PCP)**. Treatment included high-dose CTX and steroids.

Appendix 29: Common, serious retinal findings in PLWHA

All patients with CD4 < 100 cells/μL should have a retinal examination performed through dilated pupils!

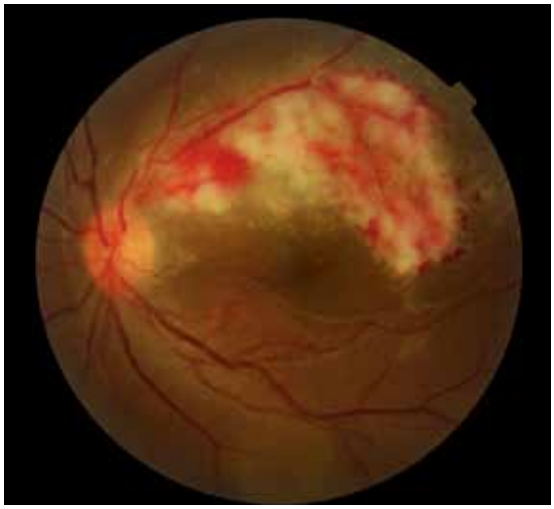


Photo credit: Dr. Gary Holland

Figure 1: **Active CMV retinitis** typically appears as dense retinal whitening with an irregular border having satellite lesions, and sometimes hemorrhage. It tends to follow vessels and as it spreads centrifugally, 'central clearing' can be seen in larger lesions. Blindness is imminent in this case since the retinitis is encroaching on both the fovea and optic disk. CMV retinitis is the most common AIDS-related cause of blindness; much of this blindness could be prevented if all those with CD4 counts < 100 cells/μL receive retinal screening to allow for early diagnosis and CMV-specific treatment.

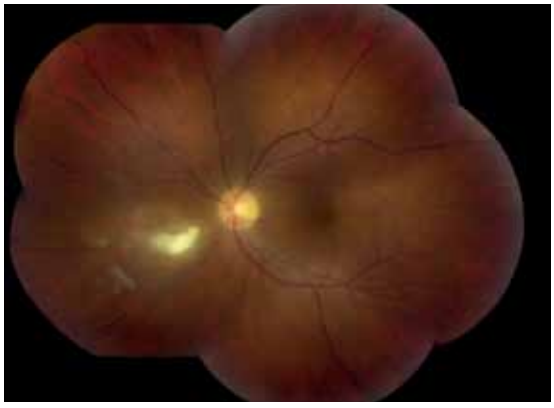


Photo credit: Dr. David Heiden

Figure 2: The area of dense retinal whitening situated inferonasal to the optic disk is a result of **primary toxoplasmosis**. Since this retinal finding could also be due to syphilis, correlation with clinical condition and laboratory results is important.

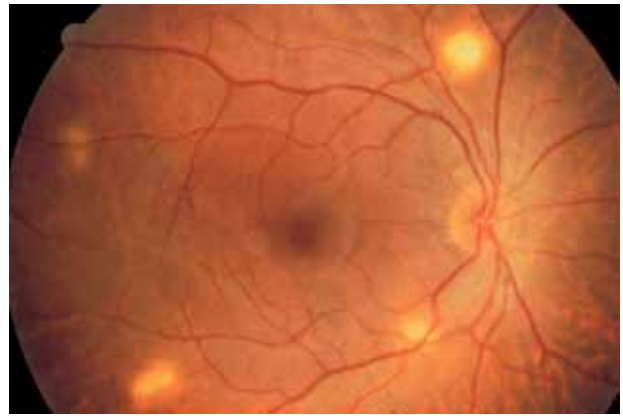


Photo credit: Dr. Emmett Cunningham

Figure 3: Tuberculosis usually affects the choroid through hematogenous spread. The four gray-yellow nodules seen here are **choroidal tubercles**. Since they are deep to the retina, their borders are indistinct; note that the retinal blood vessels can clearly be seen in front of these lesions. There are usually < 5 in number, but may be up to 50. Choroidal tubercles can range from ¼ of a disc diameter to several disc diameters in size.

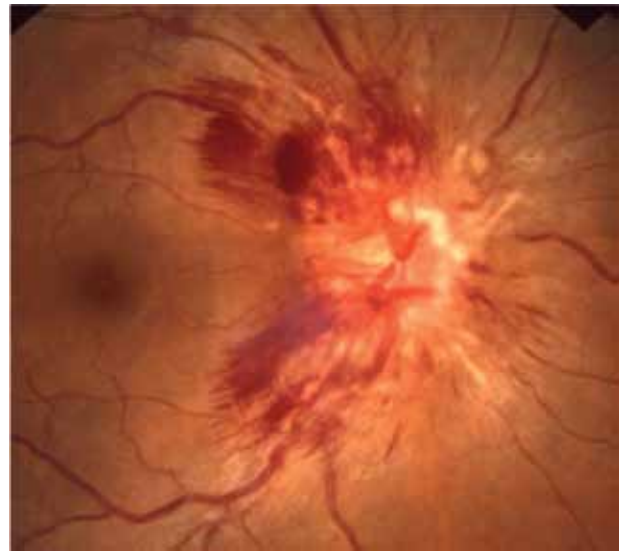


Photo credit: Dr. Richard Imes

Figure 4: **Papilledema** with associated hemorrhage, which in this case was due to Cryptococcal meningitis.

Appendix 30: Fine needle aspiration biopsy (FNAB)

A FNAB allows cellular material from lymph nodes to be examined for microscopic evidence of TB or other pathology (fungal infections, lymphoma, etc).

Equipment needed:

- Gloves
- Povidone-iodine solution (or alcohol swab)
- Sterile gauze
- Sterile needle (23 gauge is best)
- 10 ml syringe
- Sterile water
- 2 microscope slides (frosted at one end)
- Spray fixative
- Pencil

Fine needle aspiration technique:

- Label both microscope slides with patient identification and the date
- Disinfect the skin overlying the lymph node with the povidone-iodine solution (or alcohol swab)
- With the needle attached to the syringe, draw some sterile water into the syringe
- Immediately expel the water from the syringe (so that there is now a small 'coating' of water inside the needle and syringe)
- Immobilizing the lymph node with one hand, insert the needle deep into the lymph node and pull back on the syringe plunger in order to create a vacuum (of about 2 ml)
- Without exiting the lymph node, withdraw and insert the needle several times at different angles in a 'back-and-forth' motion, all the while maintaining constant suction, in order to allow cells from the lymph node to enter the bore of the needle
- Once material (or blood) appears in the needle hub, the aspiration should be stopped; the more cellular material aspirated, the better, since it improves the specificity and sensitivity of this diagnostic intervention

- Release the negative pressure before removing the needle from the lymph node. If not, the aspirated material will enter the barrel of syringe and be less available for introduction onto the microscope slides.
- With the gauze, ask the patient to apply gentle pressure over the entry site

Slide preparation

It is important to prepare the microscope slides *immediately* after aspiration as follows:

- Detach the needle from the syringe
- Gently fill the syringe with air (while the needle is still detached)
- Reattach the needle to the syringe and quickly expel all of the 'air' while the needle tip is touching close to the frosted end of one of the slides. By doing so, moist cellular material will be released onto the slide.
- Gently place the 2nd 'clean' slide face down over the slide with the aspirate on it
- With the two slides now touching each other, move them in opposite directions in order to spread the cellular material across both slides simultaneously. Avoid pressing the slides together forcefully so as to avoid crushing the cells from the lymph node.
- Allow one slide to air dry
- Spray the other slide with fixative

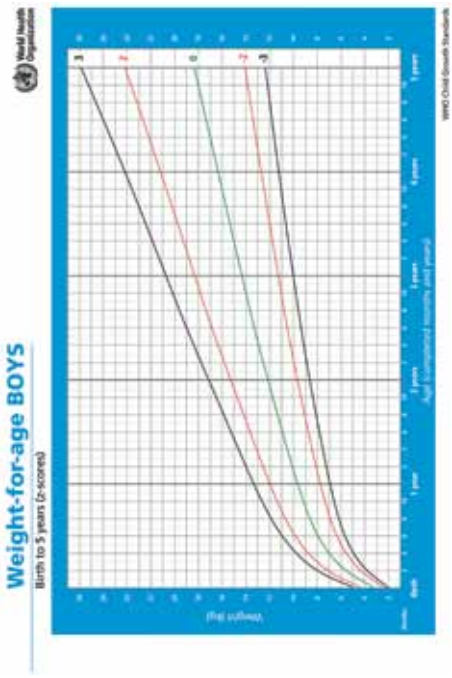
Slide transport

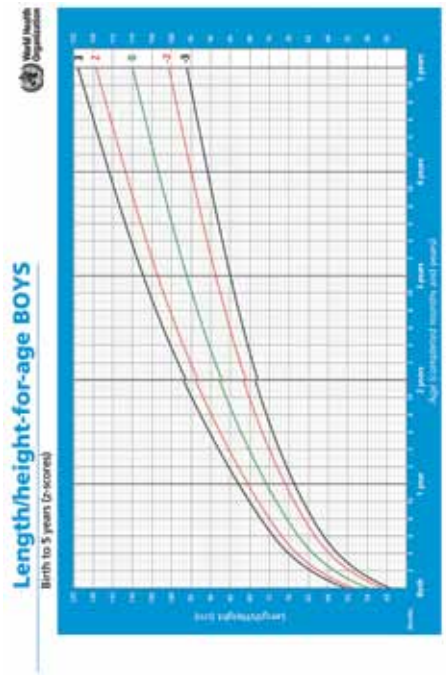
The microscope slides must be well protected during transport to the laboratory.

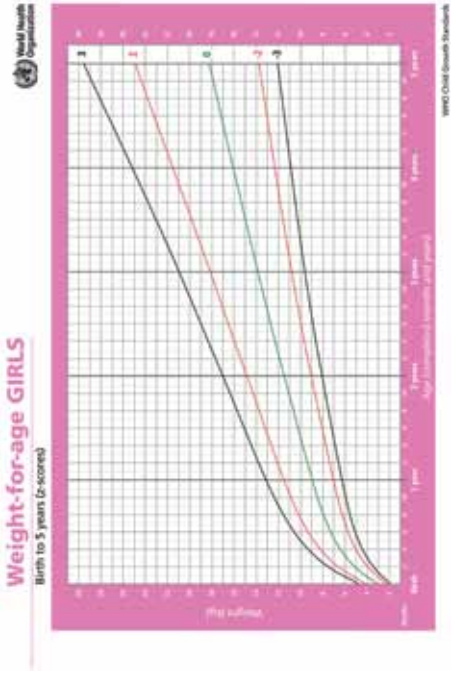
Appendix 31: Dose adjustment of ARVs, CTX and other drugs in case of renal failure

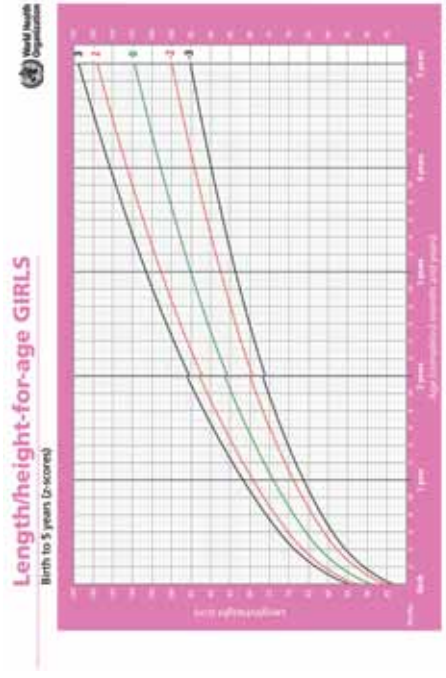
Drug	CrCl > 50	CrCl 10–50	CrCl < 10
CTX-treatment	100%	50%	refer
CTX-prophylaxis	100%	100%	100%
Fluconazole	100%	50%	50%
Acyclovir	400 mg TDS	400 mg BID	200 mg OD
DDI buffered tabs	400 mg OD	200 mg OD	< 60 Kg–100 mg OD > 60 Kg–150 mg OD
DDI coated tabs	400 mg OD	125 mg OD	DO NOT USE
D4T	30 mg BID	30 mg OD	15 mg OD
3TC	300 mg OD or 150 BID	150 mg OD	1/4 of 150 mg tab OD
TDF	300 mg OD	DO NOT USE	
AZT	300 mg BID	300 mg BID	100 mg TDS
NVP, EFV, PIs and ABC	No need for dose reduction		

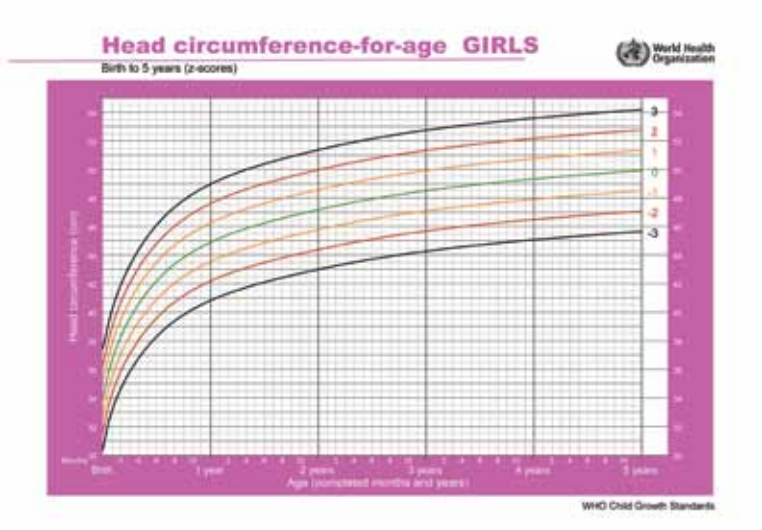
Appendix 32: Growth Charts

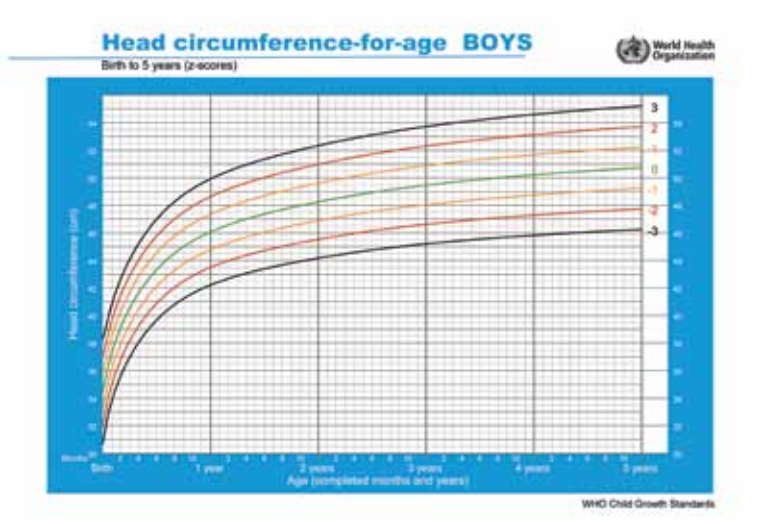









Head circumference-for-age GIRLS
Birth to 5 years (z-scores)
World Health Organization
3
2
1
0
-1
-2
-3
Birth
1 year
2 years
3 years
4 years
5 years
Age (completed months and years)
WHO Child Growth Standards


Head circumference-for-age BOYS
Birth to 5 years (z-scores)
World Health Organization
3
2
1
0
-1
-2
-3
Birth
1 year
2 years
3 years
4 years
5 years
Age (completed months and years)
WHO Child Growth Standards

Appendix 33: Answers

Epidemiology and life cycle

- Name 4 ways HIV can be transmitted

  Sexual; In utero; breastfeeding; contaminated needles; blood products

- List the six main stages of HIV's life cycle

  Attachment; Fusion; Reverse transcription; Integration; Protein production; Maturation

- What regimen should be given for PEP and when

  TDF /3TC /Lop/Rit. If TDF/ 3TC not available use AZT/3TC. To be given as soon as possible

- When should HIV tests be repeated after an accidental exposure to blood

  Within 8 days and then at Month 1, 3 and 6

Assessment and follow up

- Name 2 conditions that are stage 2, 3 and 4 (i.e 2 conditions for each stage)

  Check from Appendix 1

- Which HIV positive adults should start cotrimoxazole prophylaxis

  All stage 2, 3 and 4 and those with a CD4 < 350

- Which children should be given cotrimoxazole prophylaxis

  All exposed babies starting at 6 weeks until proven negative 6 weeks after cessation of breast feeding

  All HIV positive children until the age of 5

  All HIV positive children older than 5 if they are stage 2, 3, 4 or have CD4 <350

- Why is it important to treat all opportunistic infections before starting ART

  To avoid Immune Reconstitution inflammatory syndrome

Symptom Management

- Name two possible causes of weight loss for an HIV positive patient on ART and two causes for an HIV positive patient not on ART. The patient does not have symptoms of TB

  Treatment failure; lipodystrophy

  Oral / oesophageal infections thrush, herpes, CMV; diarrhea

- List 4 indications to perform a lumbar puncture for an HIV positive patient presenting with headache

Fever, CD4 <100; confusion; neck stiffness; vomiting; seizures; change in vision; focal signs

- List three possible causes of meningitis seen in an HIV positive patient

  TB; Cryptococcal meningitis; bacterial; viral; neurosyphilis

Skin conditions

- A 25 year old female complains of a burning, painful rash on the right side of her body for 2 days. During examination a vesicular rash is noted on the right side of her body.
- What is the likely diagnosis for this lady?

  Herpes Zoster
- What is your management of the client?

  Aciclovir 800mg five times a day for 7 days + amitrytilline 25mg nocte +/- ibuprofen 400mg tds
- What is the clinical stage of the client?

  Stage 2
- A 44 year old male comes for a general check up at your clinic. He is HIV positive but clinically well and with a last CD4 count of 400. During examination you notice dark purple papules on the client's skin and similar lesions on the palate.
- From the description what is your likely diagnosis of the lesions?

  Kaposi's sarcoma
- What clinical stage is the client?

  Stage 4
- What is the management of the client?

  Start ART as soon as possible. Refer to the doctor for consideration of chemotherapy.
- What is the treatment of PPE?

  Hydrocortisone 1% or Betamethasone 0.1% bd for 10 days alternating with an emollient +/- an antihistamine e.g promethazine

Mouth Lesions

- A 27 year old male complains of having white patches on his tongue. He tried to brush hard with a toothbrush but it wouldn't go away. The client has been HIV positive since 2007 and the last CD4 count was 380. During examination you find white patches in the mouth and on the tongue.
- What is your most likely diagnosis?

Oral thrush

- What is your management of the client?

  Nystatin oral suspension or miconazole oral gel

- What is the clinical stage of the client?

  Stage 3

- A 30 year old male known HIV positive , tested 2 years ago and never went for follow up care. CD4 count is unknown. When you examine his tongue he has characteristic stripes along the side when scraped with a tongue depressor

- What is the likely diagnosis?

  Oral hairy leucoplakia

- What is the clinical stage of client?

  Stage 3

Gastrointestinal Conditions

- A 17 year old female who is known to be HIV positive attends your clinic, accompanied by her mother. She complains of diarrhoea for 40 days .On examination the client is dehydrated. The Client was rehydrated at the clinic and samples of stools were sent to the laboratory. The stool MC&S reports presence of cryptosporidium.

- What is your management of client?

  Continue rehydration; work up for ART and start as soon as possible

- What clinical stage is client?

  Stage 4

- Does client require fast-tracking?

  Yes

- A patient who is HIV positive presents with a one week history of bloody diarrhea associated with mild abdominal pain. How are you going to manage this patient?

  Rehydrate and ciprofloxacin 500mg bd for five days

Pulmonary conditions

- A 25 year old male with a CD4 count of 120 had all his counseling sessions and is now ready to start ARVs. During TB screening he had the following symptoms; Coughing > 2 weeks, Night sweats and fever, Loss of appetite and weight loss

- What is your management of the client ?

  Screen for TB; send sputum x2 and give one week course of amoxicillin

- If TB is confirmed and TB treatment has been started when should you start ARVs ?

  Within 2-8 weeks

- You receive the smear results from a TB suspect you saw last week. The results come back negative but the patient is still coughing and having sweats despite taking antibiotics for the last week. What do you do?

  Give a further course of antibiotics and refer to have a chest X-Ray performed

- Name the drugs given for CAT 1 treatment and for what duration the drugs are given for?

  Rifampicin, Isoniazid, Pyrazinamide, Ethambutol for 2 mths

  Rifampicin and Isoniazid for 4mths

- Name 3 possible side effects seen with CAT 1 treatment.

  Rash; neuropathy; hepatoxicity/ jaundice; blurring of vision

- When are monitoring sputums to be sent for CAT 1 and CAT 2 patients ?

  Cat 1 7th week and mth 5

  Cat 2 11th week and month 7

- Which patients should have sputum sent for TB culture and possible drug sensitivity testing?

  All retreatment cases, MDR contacts, Health care workers, miners, failing patients on category 1 at mth 3 or 5

- What are the three key components of infection control?

  Administrative; environmental; personal

- What are the four classifications of drug resistant TB?

  Mono resistant; Poly resistant; Multidrug resistant (MDR); Extensively drug resistant (XDR)

- List 3 clinical signs typical of PCP, describe the typical CXR presentation and what treatment should be given

  Tachypnoea, nasal flaring, dry cough,; CXR shows ground glass appearance; high dose cotrimoxazole (100+20mg/kg per day in divided doses) + folic acid 5mg od

Neurological conditions

- John is a taxi driver who tested HIV positive in 2006. His wife is on ARVs but John still can't accept his HIV status. John comes to your clinic because he has a terrible headache that doesn't improve with Paracetomol. Examination reveals; Temp 39, Pulse 100, Bp 150/100, CNS – Neck stiffness present, Chest –Clear,

Resp rate- 18

- How will you manage this client?

  Give analgesia; refer to doctor for lumbar puncture ASAP; check CD4. (If likely delay for lumbar puncture give stat dose of ceftriaxone 2g)

- What are the differential diagnoses?

  Bacterial , TB, Cryptococcal, viral meningitis

- What would be the treatment of cryptococcal meningitis?

  Amphotericin 0.7mg/kg/day for 2 weeks, followed by fluconazole 400mg daily for 8 weeks and then fluconazole 200mg daily as secondary prophylaxis.

- A HIV positive client with a CD4 count of 120 is brought to the clinic by his relatives. Over the last 24 hours he has developed a right sided hemiplegia and has been complaining of a mild headache.

- Give 3 possible diagnoses

  Toxoplasmosis; Tuberculoma; cerebral lymphoma; cerebrovascular accident

- What is your management plan?

  Screen for TB; Trial of high dose cotrimoxazole

Genital and Gynaecological conditions

- What treatment is given for the syndromic approach to vaginal discharge?

  Cefixime 400mg stat or ceftriaxone 250mg im stat; Azithromycine 1 gr stat or Doxycycline 100mg bd for 7 days; metronidazole 2g stat

- What treatment is given for the syndromic approach to urethral discharge?

  Cefixime 400mg stat or ceftriaxone 250mg im stat; doxycycline 100mg bd for 7 days;

- What treatment is given to a patient presenting with multiple painful blisters developing in the genital area?

  Aciclovir 400mg tds for 5-7 days

- What would be the management and treatment given to a patient presenting with a solitary painless genital ulcer?

  Benzathine penicillin 2.4 MU IM stat

- What are the five key steps in managing a victim of a sexual assault?

  Provide emergency contraception; PEP; STI prevention; tetanus vaccination; counselling

Pregnancy and children

- What are the criteria to start a pregnant woman on HAART or AZT?

HAART ; stage 3 and 4 or all with CD4 < 350

AZT; CD4 stage 1 and 2 with > 350

- When should HAART or AZT be started as part of PMTCT?

  HAART as soon as possible (but not EFV in first trimester)

  AZT from 14 weeks

- What drugs should be given in the minimum package if the mother is on HAART and what are the instructions for the mother if she plans to breast feed?

  1 bottle of NVP syrup

  Baby to be given NVP syrup 1.5ml od for 6 weeks

  Child needs to be brought at 6 weeks for PCR and to start cotrimoxazole

- What drugs should be given in the minimum package if the mother is on AZT prophylaxis and what are the instructions for the mother if she plans to breast feed?

  AZT 300mg bd 60 tablets (ongoing therapy until delivery)

  AZT 300/3TC 150 17 tablets

  NVP 200mg one tab

  One bottle of NVP syrup to be given od dose according to weight/age. To continue until one week after cessation of breastfeeding.

  Child needs to be brought at 6 weeks for PCR and to start cotrimoxazole

- When should the mother bring the baby back for the first PCR test?

  At six weeks

- A baby presents for the first time to the clinic age 10 months. You test the mother and she is HIVpositive and she has had diarrhea for 6 weeks. You then test the child and the rapid test is positive. What do you need to do for mother and child today?

  Mother- send CD4 ; start cotrimoxazole; treat diarrhea; stage and assess eligibility for ART

  Child- send PCR; assess for any symptoms/ signs of HIV infection (is there a presumptive diagnosis of HIV)

  Start cotrimoxazole and NVP syrup

  Review in one week

- What are the criteria to start ART in
- a) a child <12 months
- b) a child age 36 months

- c) a child age 7

  a) All

  b) CD4 % < 25% or all stage 3 and 4

  c) CD4 < 350 or all stage 3 and 4

- What is the first line of choice for (give dosing and frequency) if Hb > 8

  a) a child age 5 and 23 kg

  b) a child age 2 and 12kg

  c) a baby of 3 months , 6.1kg who has been given PMTCT and is PCR positive at 8 weeks

  a) AZT 60 3TC 30 3 tabs bd EFV 200mg tab 1.5 nocte

  b) AZT 60 3TC 30 NVP 50 2 tabs bd

  c) AZT 60 3TC 30 1.5 tab bd Lop/Rit 80/20mg/ml 1.5ml bd

- A child has been taking triomune junior 1 tablet twice a day. Today he weighs 16 kg. What ART prescription does he need today?

  Triomune junior 1.5 tablets od + 1 tablet od

- A 9 month exposed baby who tested negative at 6 weeks but who has been breastfeeding is failing to sit upright without support and is not growing well. What should you do and what could be the underlying cause?

  Retest with a rapid test

  If rapid test positive send PCR

  Assess for any other signs of HIV clinically

  Consider presumptive diagnosis of HIV and inititation of ART

  HIV encephalopathy

Antiretrovirals

- What is the first line of choice for (give dosing and frequency) an adult male HIV + patient 66kg

  a) Whose CrCl is 77ml/min and Hb is 9

  b) Whose CrCl is 45ml/min and Hb is 10

  c) Whose CrCl is 40 ml/min and Hb is 6

  a) TDF 300 +3TC 300+ EFV 600mg nocte

  b) AZT 300 bd + 3TC 150 bd + EFV 600mg nocte

  c) D4T 30 bd + 3TC 150 bd + EFV 600mg nocte

- When do you not give TDF?

Under age of 12

When CrCL < 50ml/min

- List 3 side effects of D4T?

  Lactic acidosis,neuropathy, lipodystrophy

- List 2 common side effects of Efavirenz

  Nightmares/sleep disturbance; rash

- List the 3 categories of treatment failure and their official definitions

  Clinical failure- new stage 4 (some 3) event

  Immunological failure – CD4 drop from peak of 50% or more; CD4 below pre therapy baseline after 6 mths on ART ; CD4< 100 after 6 months on ART

  Virological failure – VL > 5000 copies/ml

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