A Guide to HIV Care Services & Management of Opportunistic Infections

2017 November

Ministry of Health
Sri Lanka

National STD/AIDS
Control Programme
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Guideline on HIV care services and Management of Opportunistic Infections

National STD and AIDS control programme

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Contents

Acronyms

ANA - Anti Nuclear Antibody
ART - Anti Retroviral Treatment
ASCUS - Atypical Squamous Cells of Undetermined Significance
ATT - Anti Tuberculosis Treatment
AUC - Area Under Curve
AZT - Zidovudine
BAL - Bronchoalveolar lavage
BASHH - British Association of Sexual Health and HIV
BHIVA - British HIV Association
CDI - Clostridium Dificille Infection
CIN - Cervical Intraepithelial Neoplasia
CMV - Cytomegalovirus
CMV - Cytomegalovirus
COPD - Chronic Obstructive Pulmonary Disease
Cr Ag - Cryptococcal Antigen
CRP - C Reactive Protein
CSF - Cerebro Spinal Fluid
CT - Computed Tomography
CVD - Cardiovascular Disease
DMAC - Disseminated Mycobacterium Avium Complex
DS - Double Strength
e GFR - Estimated GFR
ESR - Erythrocyte Sedimentation Rate
FBC - Full Blood Count
FBS - Fasting blood sugar
GI - Gastro Intestinal
HAART - Highly Active Antiretroviral Treatment
HBV - Hepatitis B Virus
HRCT - High Resolution Computed Tomography
HSIL - High grade Squamous Intraepithelial Lesion
HSV - Herpes Simplex Virus
IGRA - Interferon Gamma Releasing Assay
IPT - Isoniazid Preventive Therapy
IRIS - Immune Reconstitution Inflammatory Syndrome
IRU - Immune Reconstitution Uveitis
KS - Kaposi Sarcoma
LDH - Lactate Dehydrogenase
LFT - Liver Function Test
LFU - Loss to Follow Up
LSIL - Low grade Squamous Intraepithelial Lesion
MAC - Mycobacterium Avium Complex
MRI - Magnetic Resonance Imaging
NC - Neuro cognitive
NCDs - Non Communicable Diseases
NHL - Non Hodgkin's Lymphoma
NNRTI - Non Nucleoside Reverse Transcriptase Inhibitor
NSACP - National STD AIDS Control Programme
OI - Opportunistic infections
PCP - Pneumocystis Carinii Pneumonia
PCR - Polymerase Chain Reaction
PDHS - Provincial Director Health Services
PHI - Public Health Inspector
PHNS - Public Health Nursing Sister
PI - Protease Inhibitor
PLHIV - People Living With HIV
PMTCT - Prevention of Mother To Child Transmission
PPE - Papular Pruritic Eruption
PUO - Pyrexia of Unknown Origin
RBC - Red Blood Cells
RDHS - Regional Director Health Services
RFT - Renal Function Test
Rh - Rheumatoid
SLE - Systemic Lupus Erythematosus
SSHA - Society for Sexual Health Adviser
STI - Sexually Transmitted Infections
TB - Tuberculosis
TCA - Trichloro Acetic Acid
TDF - Tenofovir Disoproxil Fumarate
TE - Toxoplasma Enchepalitis
TEN - Toxic Epidermal Necrolysis
TIBC - Total Iron Binding Capacity
TMP-SMX - Trimethoprim – Sulfamethoxazole
TPHA - Treponema Pallidum Haemagglutination
TPPA - Treponema Pallidum Particle Agglutination
TST - Tuberculin Skin Test
USS - Ultrasound Scan
VDRL - Venereal Disease Research Laboratory test
VZV - Varizella Zoster Virus
WHO - World Health Organization

Guideline on

HIV care services and

Management of

Opportunistic Infections

1. Pyrexia of Unknown Origin (PUO)

Dr. Chaminda Dodampegamage

HIV related PUO is defined as a pattern of fever with temperature >38.3^0 C on several occasions over 4 weeks or more for out- patients or more than 3 days in hospital, in which the diagnosis remains uncertain after an initial diagnostic work up, including at least 2 days of incubation of microbiological cultures for in-ward patients.

1. **Common causes of PUO in PLHIV** are but not limited to,

• Infections -	-TB, MAC, PJP, Cryptococcal infections, Hep B and C, CMV, HSV, Toxoplasmosis, Histoplasmosis, Endocarditis, Salmonellosis and Shigellosis.
• Malignancies	-Lymphomas, KS
• Multisystem diseases	-Connective tissue disorders (eg; SLE, Rheumatoid disease), Rheumatic disease, Vasculitis, Sarcoidosis
• IRIS	-MAC, TB, Cryptococcus, Viral Hepatitis
• Other	-Drug induced

Multiple aetiologies may exist in a single patient.

2. Clinical evaluation

A detailed history including the duration and development of symptoms, travel and residence history, contact history, vaccination and prophylactic treatment history, other medications, recreational drug use, previous infections and treatment history, occupational history, sexual history and family history should be obtained.
Documentation of Temperature and fever pattern is very important. Thorough general and systemic examination should be carried out focusing on differential diagnosis and should be examined and observed regularly as new clinical features may develop.

3. Investigations may include,

- FBC with Differential Count, CD4 count.
- LFT, RFT, LDH
- CRP/ESR
- Mantoux test
- Microscopy - sputum, urine, stools
- Culture - Blood, sputum, urine, stools (including mycobacterial and fungal cultures,)
- Chest X ray, USS abdomen and pelvis, CT brain
- Syphilis serology, Cryptococcal Antigen
- Hepatitis screening, CMV and Toxoplasma antibodies
- ANA, Rh Factor
- 2D Echo if endocarditis suspected
- Arterial blood gases if indicated

Depending on the clinical features and initial test results, may need the following –

- Bronchoscopy and BAL
- Cytology/Histology from Lymph Nodes, Liver, Bone marrow, lung(pleural)
- Lumbar Puncture and CSF examination
- CT/MRI of chest, abdomen and pelvis

2. Anaemia in HIV infection

Dr. Chaminda Dodampegamage

Anaemia is a common condition found in HIV patients; about one third of PLHIV have anaemia at diagnosis and 60 -80% of PLHIV in late stages have anaemia of any degree.
Anaemia is an independent prognostic factor in ART naive HIV patients.
It is multifactorial and occurs as a result of decreased or ineffective red cell production, increased red cell destruction or blood loss or combination of those.

Common causes for Anaemia in HIV infected people are but not limited to –

- Iron, Folate and Vit B 12 deficiencies due to poor dietary intake and malabsorption
- Medication -AZT, gangciclovir/ valgangciclovir, amphotericin B, co-trimoxazole, Interferon, dapsone, sulphadiazine, pyrimethamine, chemotherapy
- Blood loss - eg; mainly from GI tract due to infections (eg; CMV Colitis) and parasitic infestations and malignancies (eg; KS, NHL)
- Bone marrow suppression due to HIV infection itself
- Infiltration of the bone marrow by neoplasms (eg; NHL) or infections (eg: MAC, TB, Parvo Virus B19 infection, Cryptococcosis, Histoplasmosis)
- Decreased production of Erythropoietin
- Haemolytic Anaemia due to RBC Autoantibodies

Clinical evaluation

Conduct a general evaluation of anaemia. Analysis of systemic symptoms of infections and malignancies, dietary and alcohol history, medication, menstrual history and evidence of blood loss are important.

Investigations may include,

- Full blood count with differential count, CD4 count
- Blood picture
- ESR/CRP
- Chest X ray
- Renal Functions
- USS abdomen
- Stool for occult blood
- Serum Bilirubin
- Liver Function tests
- Serum Vitamin B12 and Folate levels
- Serum Ferritin and TIBC
- LDH
- Direct and indirect Coomb's tests

- Bone Marrow biopsy - cytology
- Blood and Bone marrow culture for MAC, TB and Fungal infections
- Parvo Virus B 19 PCR - if available
- Thyroid functions
- Endoscopy

Principles of management - Depends on the severity of anaemia

- Correct haematinic deficiencies
- Blood transfusion if indicated.
- Treat the underlying infection or malignancy
- Stop or change responsible medication
- Modify ART if necessary

3. Cryptococcal infection

Dr. Nalaka Abeygunasekara

Most HIV-associated cryptococcal infections are caused by *Cryptococcus neoformans* and are observed in patients who have CD4 cell counts <100 cells/µl.

1. Clinical presentation

In HIV-infected patients, cryptococcosis commonly presents as a subacute meningitis or meningoencephalitis with fever, malaise and headache. Classic meningeal symptoms and signs, such as neck stiffness and photophobia, occur in only one-quarter to one-third of patients. Some patients experience encephalopathic symptoms, such as lethargy, altered mental status, personality changes, and memory loss that are usually a result of increased intracranial pressure. Isolated skin lesions and pulmonary infection also can occur.

2. Diagnosis

- Serum cryptococcal antigen (CrAg)
- India ink stain of CSF
- CSF cryptococcal antigen
- Cryptococcal culture of CSF

3. Treatment

Treatment for cryptococcosis consists of 3 phases: induction, consolidation, and maintenance therapy.

<table>
<tr><td colspan="2">Induction therapy – (for at least 2 weeks)</td></tr>
<tr><td>Preferred
Liposomal amphotericin B 3–4 mg/kg IV daily + flucytosine 25 mg/kg orally 6hrly.</td><td>Alternative
Amphotericin B deoxycholate 0.7–1.0 mg/kg IV daily + flucytosine 25 mg/kg orally 6hrly or
Liposomal amphotericin B 3–4 mg/kg IV daily + fluconazole 800 mg orally or IV daily. or
Amphotericin B deoxycholate 0.7-1.0 mg/kg IV daily + fluconazole 800 mg orally or IV daily. Or
Amphotericin B lipid complex 5 mg/kg IV daily + flucytosine 25 mg/kg orally 6hrly or
IV/Oral fluconazole 1200mg daily (if unable to use amphotericin)</td></tr>
</table>

Consolidation therapy – (for at least 8 weeks) Commence after at least 2 weeks of successful induction therapy (defined as substantial clinical improvement and a negative CSF culture after repeat LP) • Fluconazole 400mg orally once daily
Maintenance therapy • Fluconazole 200mg orally (for at least 1 year)

Stopping maintenance therapy

Maintenance therapy can be stopped, once the following criteria are fulfilled

- Completed initial (induction, consolidation) therapy, and at least 1 year of maintenance therapy and
- Remain asymptomatic from cryptococcal infection and
- CD4 count ≥100 cells/µL for ≥3 months and suppressed HIV RNA in response to effective ART

4. Other considerations

- Measures to decrease intracranial pressure should be used for all patients with signs of increased intracranial pressure (confusion, blurred vision, papilloedema, lower extremity clonus etc). Drainage of CSF via lumbar puncture is recommended. Remove 20–30 ml of CSF daily until symptoms and signs improve. Corticosteroids and mannitol are not recommended.
- Patients treated with amphotericin B formulations should be monitored for dose-dependent nephrotoxicity and electrolyte disturbances. Pre-infusion administration of 500 to 1000ml of normal saline appears to reduce the risk of nephrotoxicity.
- ART administration should be considered between 2 and 10 weeks after the start of antifungal therapy with the precise starting dates based on individual conditions.
- An estimated 30% of HIV-infected patients with cryptococcal meningitis experience IRIS. Appropriate management of IRIS is to continue both ART and antifungal therapy and reduce elevated intracranial pressure, if present. In patients with severe symptoms of IRIS, some specialists recommend a brief course of steroids.
- Treatment of non CNS, extra pulmonary and diffuse pulmonary disease is same as CNS disease.
- For localized non-meningeal disease, or in patients with isolated serum CrAg positivity (where cryptococcal meningitis has been excluded) fluconazole 800 mg/day for two weeks, then 400mg/day for 8 weeks, and continued maintenance with fluconazole 200 mg/day for one year. (WHO – 2016, pg 206)

4. Toxoplasmosis

Dr. Nalaka Abeygunasekara

Toxoplasmic encephalitis (TE) is caused by the protozoan Toxoplasma gondii. Clinical disease is mostly seen among the patients with CD4 less than 200 cells/ µl.

1. Clinical presentations

Among patients with HIV, the most common clinical presentation of T. gondii infection is focal encephalitis with headache, confusion, or motor weakness and fever. Patients may also present with non-focal manifestations, including only non-specific headache and psychiatric symptoms. In the absence of treatment, disease progression results in seizures, stupor and coma.

2. Diagnosis

- Contrast enhanced CT scan of brain - multiple contrast-enhancing lesions in the grey matter of the cortex or basal ganglia, often with associated oedema.
- MRI scan of brain
- Toxoplasma antibodies - negative serology make toxoplasmosis unlikely
- CSF toxoplasma PCR – if safe and feasible, but low sensitivity

3. Treatment

Acute therapy - for at least 6 weeks

Preferred therapy	Alternative therapy
• Pyrimethamine 200mg oral loading dose then 50-75mg once a day + Sulfadiazine 1–1.5 g 6hrly	• Pyrimethamine 200mg oral loading dose then 50-75mg once a day + clindamycin 600 mg orally 6hrly or • TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) orally bd

Chronic maintenance therapy - After completion of the acute therapy (at least for 6 weeks), all patients should be continued on chronic maintenance therapy as outlined below till immune recovery.

Preferred therapy	Alternative therapy
• Pyrimethamine 25–50mg orally daily+ Sulfadiazine 2000–4000mg orally daily (in 2 to 4 divided doses)	• Clindamycin 600mg orally 8hrly + Pyrimethamine 25–50 mg orally daily or • TMP-SMX 960 mg bd

Discontinuing chronic maintenance therapy

Successfully completed initial therapy, remain asymptomatic of signs and symptoms of toxoplasma encephalitis and CD4 count >200 cells/µl for >6 months in response to ART.

4. Other considerations

- Initiate ART within 2 to 3 weeks after the diagnosis of toxoplasmosis.
- Patients with toxoplasmosis should be monitored routinely for drug adverse events and clinical and radiologic improvement.
- Anticonvulsants should be administered to patients with seizures and continued at least through the period of acute treatment.
- IRIS associated with TE has been reported but appears to be rare.

5. Pneumocystis pneumonia

Dr. Nalaka Abeygunasekara

Pneumocystis pneumonia (PCP) is caused by fungus Pneumocystis jirovecii. Approximately ninety percent of the PCP cases are seen among patients withCD4 count less than 200 cells/µl.

1. Clinical presentation

The most common manifestations of PCP are subacute onset of progressive exertional dyspnoea, fever, non-productive cough and chest discomfort that worsens within days to weeks. In mild cases, pulmonary examination usually is normal at rest. With exertion; tachypnoea, tachycardia and diffuse crepitations may be observed.

2. Diagnosis

- Chest X ray -Chest radiograph typically demonstrates diffuse, bilateral, symmetrical interstitial infiltrates emanating from the hilar in a butterfly pattern. In early stages, chest radiograph may be normal. Atypical presentations also occur such as lobar consolidation, pneumothorax etc. However, pleural effusion and lymphadenopathy are rare. If present, consider an alternative diagnosis.
- HRCT of chest shows patchy ground-glass attenuation.
- Definitive diagnosis is by demonstrating the organisms in broncho-alveolar lavage fluid or induced sputum. Demonstrate organisms with silver stain or immunofluorescence.

Oxygen saturation of <94% indicates moderately severe or severe disease.

3. Treatment

For moderate to severe PCP—Total duration 21 Days

Preferred Therapy:	Alternative Therapy:
• TMP-SMX : TMP 15–20 mg and SMX 75–100 mg)/kg/day IV given 8hrly. may switch to oral therapy after clinical improvement	• Pentamidine 4 mg/kg IV once daily infused over at least 60 minutes or • Primaquine 30mg orally once daily + clindamycin IV 600mg 6hrly

For mild to moderate PCP—Total Duration 21 days

Preferred Therapy:	Alternative Therapy:
• TMP-SMX: (TMP 15–20 mg and SMX 75–100 mg) /kg/day given orally in 3 divided doses or • TMP-SMX –3 SS tablets tds	• Dapsone 100 mg orally daily + TMP 15 mg/kg/day orally (3 divided doses) or • Primaquine 30 mg orally daily + clindamycin orally 600mg 8hrly or • Atovaquone 750 mg orally bd

Adjunctive Corticosteroids

Corticosteroid therapy is necessary for moderate to severe PCP.

- Prednisolone should be started as early as possible within 72 hours of PCP therapy and continue for 21 days.
  - 40mg bd for 5days
  - 40mg daily for 5days
  - 20mg daily for 11 days

Secondary Prophylaxis

Secondary prophylaxis should be started after completing the treatment for acute condition with 3 weeks of therapy and continue till immune recovery.

- TMP-SMX - 1 DS tablet orally daily
  Or
- Dapsone 100 mg orally daily
  Or
- Pentamidine aerosole 300mg nebulization once a month

Secondary Prophylaxis should be continued till CD4 count increased to >200 cells/µl for >3 months as a result of ART. However, discontinuation can be considered if CD4 count 100-200 cells/µl and HIV RNA remain below limits of detection for at least 3-6 months.

4. Other considerations

ART should be initiated, when possible, within 2 weeks of diagnosis of PCP.

6. Tuberculosis

Dr. Ganga Pathirana

Globally, it is estimated that 14.8% of all new Tuberculosis [TB] cases among adults are attributable to HIV infection. Among people living with Human Immunodeficiency Viral [HIV] infection, TB is the most frequent life-threatening opportunistic infection and a leading cause of death.

A. Intensified TB case finding:

1. Refer to District Chest Clinic for TB case finding and management

    a) Every newly diagnosed person with HIV
    b) ALL HIV infected adults, adolescents and children should be evaluated with symptom-based TB screening as explained in Table 01 at each visit and if evaluation suggestive of active TB
    c) ALL HIV infected adults, adolescents and children who are close contacts of smear positive TB patients

Table 1 - Symptom based TB screening for PLHIV

PLHIV	Symptoms	Remarks
Children	Cough Fever Poor weight gain Fatigue Loss of appetite	If one or more symptoms positive which may indicate active TB disease
Adults and adolescents	Cough Fever Loss of weight Night sweats Fatigue Loss of appetite	If one or more symptoms positive which may indicate active TB disease

2. At each visit of HIV/TB co-infected patients to HIV clinic, Consultant Venereologists and MO/STDs should counsel them and emphasize the importance of adherence to TB treatment and motivate them to attend the chest clinic and HIV clinic regularly.

3. All patients on ATT should be given pyridoxine 10mg. If peripheral neuropathy occurs the dose of pyridoxine can be increased up to 50mg three times a day.

4. Document the symptom based evaluation, action taken and instructions given in each visit.

B. Isoniazid Preventive Therapy [IPT]:

HIV infected people with latent TB infection are much more likely to progress to active TB than HIV uninfected people. Detection and treatment of latent TB infection is therefore important. Active TB disease has to be excluded before considering treatment for latent infection.

1. **IPT is recommended to following PLHIV without active TB**,

    a) All HIV infected adult /children who are close contacts of smear positive TB patients without active TB
    b) HIV infected Adults/ children with a tuberculin test > or = to 5mm or positive Interferon gamma releasing assay [IGRAs] without active TB

    In Sri Lankan context, decision on IPT prophylaxis in the absence of active TB will be taken at the discretion of the Consultant Chest Physician. Above mentioned PLHIV without active TB should receive at least six months of IPT as a part of a comprehensive package of HIV care. IPT can be given to such individuals irrespective of the degree of immune-suppression, to patients on ART, those who have previously been treated for TB and also to pregnant women.

2. At each visit to HIV clinic, Consultant Venereologists or MO/STDs should counsel them and emphasize the importance of adherence to IPT and motivate them to attend the chest clinic and HIV clinic regularly.

3. Peripheral neuropathy may occur in patients with HIV infection. This can be prevented or minimized by supplementary pyridoxine 10 mg daily.

4. Document compliance to IPT, duration of IPT and instructions given in each visit.

    Steps should be taken to minimize transmission of TB in HIV clinic settings.

Important points to consider in managing HIV/TB co-infected Patients:

1. Latent TB and IPT

Tuberculin Skin Test [TST] and Interferon- Gamma release assays [IGRAs] are used to detect latent TB infection. However, TST is less useful in HIV patients with low CD4 counts. IGRAs are more sensitive than TST especially in BCG vaccinated subjects.

2. Active TB disease, Anti-Tuberculosis Treatment [ATT] and HAART

3. Routine co-trimoxazole prophylaxis should be given to all HIV infected patients with active TB disease regardless of CD 4 cell count.

When to start ART for PLHIV on ATT:

In TB/HIV coinfection, priority is to treat TB. TB treatment should be commenced first and ART commenced subsequently as soon as possible but within the first 8 weeks of starting anti TB treatment. In case of severe immunosuppression (CD4<50 cells/µl) and in very ill patients ART should be commenced within 2 weeks.
Caution is needed in people living with HIV and TB meningitis as immediate ARV is significantly associated with more severe adverse events when compared with initiation of ART two months after start of ATT.

Drug Interaction between ATT and ART

Most interactions between ART and ATT are through induction or inhibition of metabolic enzymes in the liver and intestine. The most important family of enzymes is CYP450. Rifampicins are potent inducers of CYP3A4 and have clinically important interactions with Protease Inhibitors [PIs], Non-Nucleoside Reverse Transcriptase Inhibitors [NNRTIs], CCR5 inhibitors and Integrase Inhibitors.

There are no major interactions between rifampicin or rifabutin and Nucleoside/Nucleotide Reverse Transcriptase Inhibitors. (Annexure 8.)

Because of its potency, simplicity, and proven clinical efficacy, use of efavirenz 600mg with 2 NRTIs, is the preferred ART regimen for co-treatment of HIV and tuberculosis where rifampicin is part of ATT.

If efavirenz cannot be given, raltegravir/dolutegravir can be considered. Rifampicin is known to significantly lower plasma concentrations of Dolutegravir, and increasing the dose to a twice daily schedule may be necessary.
When people with HIV related TB are receiving boosted PI, Rifampicin may need to be substituted with Rifabutin. If Rifabutin is not available, LPV/r can be used for the duration of TB treatment by doubling the standard dose of LPV/r to 800/200 mg. (WHO guideline 2016, pg 151,155)

Adverse Effects of commonly used drugs for HIV/TB co-infected patients:

1. Rash, fever and hepatitis are common side effects of ATT drugs especially rifampicin, isoniazid and pyrazinamide. NNRTIs and co-trimoxazole cause similar adverse reactions. Physicians have to face difficult clinical management decisions if these side effects occur in a patient on both ATT and HAART.

2. PLHIV on ATT and ART needs liver function tests prior to start of ART/ATT treatment and need to be rechecked at 2 weeks after starting ART/ATT and then monthly till completion of ATT.

3. Hepatotoxicity is a common and potentially serious adverse event. It is defined as

    a. Serum AST or ALT more than three times of the upper limit of normal in the presence of symptoms or
    b. Serum AST or ALT more than five times of the upper limit of normal in the absence of symptoms.

Reference:

Tuberculosis. Clinical Guidance Across the Continuum of Care: managing common co-infections and co-morbodities. Consolidated Guidelines on the use of Anti-Retroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Geneva. World Health Organization. June 2013; 158 - 165

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7. Mycobacterium avium complex

Dr. Ganga Pathirana

Mycobacterium avium complex:

Mycobacterium avium complex [MAC] organisms are present throughout the environment. MAC is the predominant atypical mycobacterium that affects PLHIV.

1. Presentation:

Disseminated MAC infection [DMAC] typically occurs in advanced immunosuppression where CD4 cell count is less than 50 cells/micro liter. They have non-specific symptoms like fever, night sweats, fatigue, weight loss, anorexia and diarrhea. Common signs include splenomegaly, hepatomgaly and lymphadenopathy. Laboratory abnormalities include anaemia, leucopenia, raised alkaline phosphatase levels and hypoalbuminaemia. More unusual focal manifestations of MAC include palatal and gingival ulceration, septic arthritis and osteomyelitis, endophthalmitis, pericarditis, pulmonary and focal lymphadenitis.

2. Diagnosis:

Diagnosis requires culture of the organism in blood or from a bone marrow aspirate or fluid from a normally sterile site or biopsy specimen.

3. Treatment:

Antimicrobial treatment of DMAC requires combination therapy that should include a macrolide [clarithromycin or azithromycin] and ethambutol with or without rifabutin. Treatment should be continued at least for 12 months.

ART should be initiated within one to two weeks of initiation of DMAC antimicrobial therapy.

Focal MAC tends to occur at higher CD4 cell counts and in the presence of effective ART. Most clinicians would recommend a three drug regimen for a duration of at least 12 months and possibly for 24 months.

Table 5: Drug therapy for treatment and chronic maintenance therapy of AIDS-associated opportunistic infections in adults and adolescents -**Disseminated *Mycobacterium avium* complex (MAC) disease** [Source: CDC MMWR March 2009]

Preferred therapy, duration of therapy, chronic maintenance	**Alternative therapy**	**Other options/issues**
Preferred therapy for disseminated MAC At least 2 drugs as initial therapy with • Clarithromycin 500 mg PO bid + • Ethambutol 15 mg/kg PO daily Addition of rifabutin may also be considered: • Rifabutin 300 mg PO daily (dosage adjusted may be necessary based on drug-drug interactions) **Chronic maintenance therapy (secondary prophylaxis)** Same as treatment drugs and regimens Duration: till immune recovery (CD4 >100 cells/µl for >6 months) on ART	**Alternative therapy for disseminated MAC**(e.g., when drug interactions or intolerance precludes the use of clarithromycin) • Azithromycin 500–600 mg + • Ethambutol 15 mg/kg PO daily Addition of a third or fourth drug should be considered for patients with advanced immunosuppression (CD4+ count <50 cells/μL), high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART • Amikacin 10–15 mg/kg IV daily; or • Streptomycin 1 gm IV or IM daily; or • Ciprofloxacin 500–750 mg PO bid; or • Levofloxacin 500 mg PO daily; or • Moxifloxacin 400 mg PO daily	Testing of susceptibility to clarithromycin and azithromycin is recommended In ART-naïve patients, may consider withholding initiation of ART until after 2 weeks of MAC treatment to lessen drug interactions, reduce pill burden, and potentially lower occurrence of IRIS NSAIDs may be used for patients who experience moderate to severe symptoms attributed to ART-associated IRIS If immune reconstitution inflammatory syndrome (IRIS) symptoms persist, short term (4–8 weeks) of systemic corticosteroid (equivalent to 20–40 mg of prednisone) can be used

Primary MAC Prophylaxis:

Prophylaxis with Azithromycin 1250mg weekly can be considered for individuals with CD4 counts less than 50 cells/micro litre. Primary prophylaxis can be stopped in the presence of a sustainable virological and immunological response to ART for at least three months.

Reference:

M Fisher, E. Ong, A. Pozniak. Mycobacterium avium complex and Mycobacterium kansasii. HIV Medicine. United Kingdom. British HIV Association. 2011;12 [suppl.2]:75 – 82

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8. Diarrhoea

Dr. Manjula Rajapakshe

If the diarrhoea is watery and large volume, it is more likely to be due to small bowel pathology,
If the diarrhoea is small volume, with cramping lower abdominal pain, mucous, blood, fever or rectal symptoms, it is more suggestive of a large intestinal pathology.
Diarrhoea persisting for more than one month duration is defined as chronic diarrhoea.

1. Causes

Infective

- Virus -Cytomegalovirus, Adenovirus, Herpes simplex virus, Rotavirus
- Bacteria -Salmonella spp. Shigella, Campylobacter, *Clostridium difficile*, TB Mycobacterium avium complex(MAC)
- Protozoa -*Giardia lamblia*, Cryptosporidia spp. Microsporidia, *Entamoeba histolitica*, Cyclospora, *Strongyloides stercoralis*
- Nematodes

Other causes

- Fat malabsorption
- HIV enteropathy
- ART and other medications
- Inflammatory bowel disease
- Systemic disease – Thyrotoxicosis
- Malignancies

2. Diagnosis

- Fecal microscopy, examination for ova, cysts and parasites including Cryptosporidia, Cyclospora and Isospora within 10 days (at least 3 samples should be tested).
- Stool culture - Bacterial culture including Clostridium difficile toxin and culture.
- Bacterial blood cultures (specially diarrhoea with fever), including blood cultures specific for MAC.
- Gastroscopy and duodenoscopy with duodenal biopsy (if symptoms suggestive of small bowel pathology).
- Sigmoidoscopy and/or colonoscopy with biopsy of macroscopically abnormal areas (symptoms suggest large bowel pathology).
- Biopsy specimens should be examined with special stains such as Giemsa and modified Ziehl-Neelsen, and immunohistochemistry, viral and mycobacterial cultures, LGV PCR.

3. Treatment

General Considerations

- Oral or IV rehydration therapy (if indicated) should be given to patients with diarrhea.
- Antimotility agents should be avoided if there is concern about inflammatory infectious diarrhea, including Clostridium difficile infection.
- Diagnostic fecal specimens should be obtained prior to initiation of empiric antimicrobial therapy.
- If stool sample is obtained, antibiotic susceptibilities should be performed.
- Risk of a bacterial enteric infection increases as CD4 count declines, with the greatest risk in patients with CD4 counts <200 cells/µl. Risk of bacteremia also increases with decreasing CD4 count. If no clinical response after 3 to 4 days, consider follow up stool culture with antibiotic susceptibility testing and other methods to detect enteric pathogens (e.g., toxin assays, molecular methods), alternative diagnosis, antibiotic resistance, or drug-drug interactions.
- Effective ART may reduce the frequency, severity, and recurrence of bacterial enteric infections.

Symptomatic treatment

- loperamide 4-32 mg daily by mouth in divided doses if inflammatory causes excluded.

Empiric Treatment of Bacterial Enteric Infections (Pending Diagnostic Studies)

For patients with advanced HIV (CD4 count <200 cells/µl or concomitant AIDS-defining illnesses) and clinically severe diarrhea (≥6 liquid stools/day or bloody stool and/or accompanying fever or chills).

Preferred Therapy:	Alternative Therapy:
• Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h (AIII)	• Ceftriaxone IV 1 g q24h or • Cefotaxime IV 1g q8h

Table 6 - Specific treatment for bacterial and parasitic organisms

Organism	diagnosis	Treatment
Salmonella	Stool culture Blood culture Urine culture	Preferred therapy • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h Alternative Therapy • Levofloxacin 750 mg (PO or IV) q24h or • Moxifloxacin 400 mg (PO or IV) q24h or If susceptible, alternatives to fluroquinolone may include one of the following: • Trimethoprim 160 mg/sulfamethoxazole 800 mg (PO or IV) q12h (BIII), or • Ceftriaxone IV 1g q24h or • Cefotaxime IV 1g q8h Duration of Therapy for Gastroenteritis Without Bacteraemia - If CD4 count >200 cells/mm3: 7–14 days - If CD4 count <200 cells/mm3 particularly if primary illness was severe: 2–6 weeks Duration of Therapy for Gastroenteritis with Bacteraemia - If CD4 count >200 cells/mm3: 14 days; longer duration if bacteraemia persists or if the infection is complicated (e.g., metastatic foci of infection are present)

Shigella	Stool culture	Preferred Therapy • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h Alternative Therapy (Depending on Susceptibility Results): • Levofloxacin 750 mg (PO or IV) q24h or • Moxifloxacin (PO or IV) 400 mg q24h • Trimethoprim 160 mg/sulfamethoxazole 800 mg PO or IV q12h • Azithromycin 500 mg PO daily for 5 days (Note: Azithromycin is not recommended for Shigella bacteraemia) Duration of Therapy - Gastroenteritis: 7–10 days (except azithromycin, treat for 5 days) - Bacteraemia: ≥14 days • Recurrent Infections: up to 6 weeks (BIII)
Clostridium difficile	Clostridium difficile toxin and culture	Preferred Therapy • Vancomycin 125 mg (po) four times per day X 10-14 days Alternative Therapy • For mild, outpatient disease: metronidazole 500 mg (po) three times per day
Campylobacter	Stool culture	**Mild to Moderate Disease** Preferred Therapy • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h —if susceptible, or • Azithromycin 500 mg PO daily for 5 days (BIII) (Not recommended for bacteraemia) Alternative Therapy (Depending on Susceptibility Results): • Levofloxacin 750 mg PO or IV q24h, or • Moxifloxacin 400 mg PO or IV q24h **Bacteraemia** • Ciprofloxacin 500–750 mg PO (or 400 mg IV) q12h **+** an aminoglycoside in bacteraemic patients to limit the emergence of antibiotic resistance

		<u>Duration of Therapy</u> - Gastroenteritis: 7–10 days [5 days if azithromycin is used] - Bacteraemia: ≥14 days • Recurrent bacteraemic disease: - 2–6 weeks
Cryptosporidia	Microscopic identification of the oocysts in stool or tissue with modified acid-fast staining or direct immunofluorescence, PCR	<u>Preferred Management Strategies</u> - Initiate or optimize ART for immune restoration to CD4 count >100 cells/mm^3. - Aggressive oral and/or IV rehydration and replacement of electrolyte loss, and symptomatic treatment of diarrhoea with antimotility agent. - Tincture of opium may be more effective than loperamide as an anti-diarrheal agent.
		<u>Alternative Management Strategies:</u> No therapy has been shown to be effective without ART. Trial of these agents may be used in conjunction with, but not instead of, ART: • Nitazoxanide 500–1000 mg PO BID with food for 14 days + optimized ART, symptomatic treatment, and rehydration and electrolyte replacement, or alternatively • Paromomycin 500 mg PO QID for 14 to 21 days + optimized ART, symptomatic treatment and rehydration and electrolyte replacement
Microsporidia	Stool microscopy	Initiate or optimize ART with immune restoration to CD4 count >100 cells/mm^3. For Gastrointestinal Infections Caused by Enterocytozoon bieneusi - The best treatment option is ART and fluid support. - No specific therapeutic agent is available for this infection. • Fumagillin 60 mg PO daily and TNP-470 are two agents that have some effectiveness, but neither agent is available in the United States. • Nitazoxanide may have some effect, but the efficacy is minimal in patients with low CD4 cell count, and cannot be recommended.

		For Intestinal and Disseminated (Not Ocular) Infection Caused by Microsporidia Other Than E. bieneusi and Vittaforma corneae: • Albendazole 400 mg PO BID, continue until CD4 count >200 cells/mm3 for >6 months after initiation of ART
Cyclospora	ZN or auramine staining of faeces. Oocysts can also be seen using phase contrast microscopy, and PCR-based diagnostic methods have been developed	<u>Preferred therapy</u> • TMP-SMX 960mg bd for 7 days <u>Alternatives</u> • Ciprofloxacin 500mg bd but response slower and incomplete ***Remarks**: Antibiotic prophylaxis required until effective response to ART*
Entamoeba histolytica	Faecal microscopy with or without faecal antigen/PCR or colonic biopsy. Serology and imaging for extraintestinal disease	• Metronidazole 800mg tid for 10 days; or Tinidazole 2g once a day for 3 days • Followed by either Diloxanide fuorate 500mg tid po for 10 days or Paromomycin 30mg/kg/day in three divided doses po for 10 days
Giardia lamblia	Faecal microscopy or faecal antigen detection ELISA. Rarely, duodenal biopsy or duodenal fluid sample for microscopy	• Metronidazole 400mg tid for 7 days or 1g daily po for 3 days Alternative • Tinidazole 2g po once only or 500mg bd for 7 days

Isospora belli	Direct microscopy of iodine-stained faecal smears or fluorescence microscopy, but most laboratories rely on faecal stains including ZN, auramine or safranin-methylene blue	<u>Preferred</u> • TMP-SMX 960mg bd for 7 days <u>Alternatives</u> • TMP-SMX 960mg qid for 10 days or ciprofloxacin 500mg bd but response is slower and incomplete with ciprofloxacin ***Remarks:*** *Antibiotic prophylaxis required until effective response to ART*
Strongyloides stercoralis	Stool culture to detect larvae in faeces. It may be found in duodenal biopsies or by string test	<u>Preferred choice</u> • Oral Ivermectin (200µg/ kg once or twice only). <u>Alternatives</u> • Albendazole 400mg bd for 3 days

Reference

- CDC Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents 2016
- HIV Management in Australasia 2009
- British HIV Association and British Infection Association Guidelines for the Treatment of Opportunistic Infection in HIV-seropositive Individuals 2011

9. Oral manifestations in HIV

Dr. Darshani Wijewickrama

9.1 Oral candidiasis

There are four types.

1. Pseudomembranous
2. Erythematous
3. Angular chelitis
4. Hyperplastic

The most common manifestation is pseudo-membranous candidiasis.

Treatment

- Fluconazole 100mg/d for 7-14d
- itraconazole 100mg bd for 7-14d (itraconazole oral solution has better bioavailability than capsule)
- Clotrimazole topical therapy

9.2 Oesophageal Candidiasis

Empirical diagnosis is based on the presence of oral candidiasis (80%) with odynophagia. Endoscopy recommended with atypical presentations or failure to respond to empirical treatment.

Treatment

Preferred Treatment
O. Fluconazole 200mg daily up to 800mg daily for 14-21 days

Alternative regimen
IV Ampotericine B 0.3-0.7 mg/kg/day for 14-21 days
O. Itraconazole 200mg/day for 14-21days

Secondary prophylaxis
Only with relapsing disease
Oral Fluconazole 100-200mg/day (discontinue when CD4 >200 cells/µl.)

9.3 Oral hairy leukoplakia

Caused by Epstein bar virus

Seen as asymptomatic white, hyperkeratotic, corrugations over the lateral border of the tongue.

Diagnosis

Clinically (does not rub off as in pseudo-membranous candidiasis)
Can be confirmed by histology.

Treatment

No treatment is needed usually as the lesions are asymptomatic.
Responds to ART.

9.4 Gingivitis

a) **Gingival erythema** (Characterized by 1-3mm erythematous band along gingival margin)

Usually asymptomatic
May bleed and cause pain

Management
- Dental referral
- Dental scaling, chlorhexidine rinses

b) **Necrotizing ulcerative gingivitis**
Characterized by ulceration of interdental papilla, pain, halitosis
Usually occurs in late HIV infection, more severe with ulceration extending to alveolar bone, rapid loss of bone and loss of teeth can occur)

Management

- Dental referral
- Topical anaesthetics
- 0.2% chlorhexidine mouth rinses bd
- Metronidazole 400mg three times daily, Co-amoxiclav 375mg or 625 mg tablet three times daily, or Clindamycin (one 300-mg tablet three times daily) should be added to the treatment regimen

9.5 Oral ulceration

Aphthous ulceration

Multiple, oval, shallow ulcers on non keratinized oral mucosa
Major aphthous ulcers-associated with severe immune deficiency
Can be very painful

Treatment

- Topical regimens may include the following:

- Topical corticosteroids, including dexamethasone, triamcinolone, fluocinonide, and clobetasol
- Immunomodulatory agents, including retinoids, cyclosporine.
- Antimicrobials, including tetracycline, chlorhexidine gluconate, and dilute hydrogen peroxide
- Anaesthetics such as topical lidocaine or benzocaine

- Systemic agents may include the following:

- Systemic steroids such as prednisone and dexamethasone
- Immunomodulatory agents such as colchicine, azathioprine, montelukast and Thalidomide.
  Close follow-up, including nerve conduction studies and electromyography every 6 months, is recommended in patients using thalidomide

Other oral ulcers

a) Herpes simplex type 1 (uncommonly type 2)

Can be Primary, or recurrent
Treatment

- Acyclovir 400mg 8h orally 7-10 days

b) Herpes zoster

Oral herpes zoster generally causes skin lesions. Following a prodrome of pain, multiple vesicles appear on the facial skin, lips, and oral mucosa. Skin and oral lesions are frequently unilateral and follow the distribution of the maxillary and/or mandibular branches of the trigeminal nerve. The skin lesions form crusts and the oral lesions coalesce to form large ulcers. The ulcers frequently affect the gingiva, so tooth pain may be an early complaint.

Management

- Acyclovir 800mg 5 times/d 7-10 days

c) Primary and secondary syphilis

Can present as a chancre, mucous patch or a snail track ulcer. Diagnosed with VDRL and

TPPA/TPHA.

Treatment

Benzathine penicillin 2.4mu im stat dose

9.6 Kaposi sarcoma

May occur intraorally, either alone or in association with skin and disseminated lesions. Intraoral lesions have been reported at other sites and may be the first manifestation of late-stage HIV disease

KS can appear as a red, blue, or purplish lesion. It may be flat or raised, solitary or multiple. The most common oral site is the hard palate, but lesions may occur on any part of the oral mucosa, including the gingiva, soft palate, and buccal mucosa and in the oropharynx. Occasionally, yellowish mucosa surrounds the KS lesion. Oral KS lesions may enlarge, ulcerate, and become infected. Good oral hygiene is essential to minimize these complications.

Local treatment

Appropriate for large oral KS lesions that interfere with eating and talking. Oral KS can be treated surgically or with localized intralesional chemotherapy.

Surgical removal

Suitable for small, well-circumscribed lesions such as gingival or tongue lesions. Intra lesional chemo therapy.

Intralesional vinblastine is useful for treating small lesions, particularly on the palate or gingiva.

Radiation therapy

Indicated for large, multiple lesions.

9.7 Lymphoma

Diffuse, undifferentiated non-Hodgkin's lymphoma (NHL) is a frequent HIV-associated malignancy. Most are of B cell origin, and Epstein-Barr virus occurs in cells from several cases. Lymphoma can occur anywhere in the oral cavity and there may be soft tissue involvement with or without involvement of underlying bone. The lesion may present as firm, painless swelling that may be ulcerated. Some oral lesions may appear as shallow ulcerations. Oral NHL may appear as solitary lesions with no evidence of disseminated disease.

Treatment

Oncology referral

9.8 Oral warts

HPV lesions in the oral cavity may appear as solitary or multiple nodules. They may be sessile or pedunculated and appear as multiple, smooth-surfaced raised masses resembling focal epithelial hyperplasia or as multiple, small papilliferous or cauliflower-like projections. The lesions will improve with ART. For treatment of warts, refer STI management guidelines by Sri Lanka college of venereologists.

References

CDC guidelines on Management of HIV -2016
Medscape –management of apthous ulcerations -2016
HIV insite –Oral manifestations of HIV

10. Cytomegalovirus (CMV)

Dr. Manjula Rajapaksha

Cytomegalovirus (CMV) is in the human herpes virus family that can cause disseminated or localized end-organ disease in HIV-infected patients with advanced immunosuppression.

Most clinical disease occurs in individuals previously infected with CMV (seropositive) and therefore represents either re-activation of latent infection or re-infection with a novel strain.

End-organ disease caused by CMV occurs in patients with advanced immunosuppression, typically those with CD4 count <50 cells/mm3.

1. Clinical Manifestations

a) Retinitis:

Retinitis is the most common clinical manifestation of CMV end-organ disease in HIV-infected patients. It occurs as unilateral disease in two-thirds of patients at presentation, but disease ultimately is bilateral in most patients in the absence of therapy or immune recovery.

Peripheral retinitis present with floaters, scotomata, or peripheral visual field defects. Central retinal lesions or lesions impinging on the macula or optic nerve are associated with decreased visual acuity or central field defects. Delay in diagnosis and treatment can lead to retinal detachment and blindness.

b) Colitis:

Usual presenting features are weight loss, anorexia, abdominal pain, debilitating diarrhoea, and malaise. In the colon, and especially in the cecum, CMV can produce perforation and present as an acute abdomen. Haemorrhage and perforation can be life-threatening complications.

c) Oesophagitis:

Occur in small percentage. Presents with odynophagia, nausea, and occasionally mid epigastric or retrosternal discomfort.

d) CMV neurologic disease

This includes CMV dementia, ventriculoencephalitis, and polyradiculomyelopathies.

Patients with dementia caused by CMV encephalitis typically have lethargy, confusion, and fever.

Patients with ventriculoencephalitis have a more acute course, with focal neurologic signs, often including cranial nerve palsies or nystagmus, and rapid progression to death.

CMV polyradiculomyelopathy causes a Guillian-Barre–like syndrome characterized by urinary retention and progressive bilateral leg weakness. Clinical symptoms usually progress over several weeks to include loss of bowel and bladder control and flaccid paraplegia.

e) Pneumonitis:

CMV is detected frequently in the bronchoalveolar lavage. However, as CMV pneumonitis is extremely uncommon, should search for a more likely causative agent.

2. Diagnosis

CMV detection by antigen, PCR and culture

Blood tests to detect CMV by antigen detection, culture, or PCR are supportive but may not be diagnostic of CMV end-organ disease because of their poor positive predictive value. Viraemia as detected by one of these assays can be present in disease-free patients with low CD4 cell counts, in the absence of end-organ disease. Also, a negative serum or plasma PCR assay does not rule out CMV end-organ disease. CMV PCR can be particularly useful in assessing CSF or vitreous or aqueous humor specimens; a positive result is highly suggestive of that CMV is the cause of end organ disease.

CMV antibodies

Presence of serum antibodies to CMV is not diagnostically useful, although a negative immunoglobulin-G antibody level indicates that CMV is unlikely to be the cause of the disease process.

a) Retinitis:

Clinically diagnosed (95% PP value) with recognition of characteristic retinal changes observed through a dilated pupil during an ophthalmoscopic examination performed by an experienced ophthalmologist.

It is a full thickness necrotizing retinitis. *Retinal changes include fluffy, yellow-white retinal lesions, with or without intraretinal hemorrhage characteristic brushfire pattern, with a granular, white leading edge.*

Can perform PCR of aqueous or vitreous specimens for CMV, HSV, VZV and toxoplasma in difficult cases to differentiate.

b) Colitis:

In colitis, computed tomography (CT) may show colonic thickening.

Demonstration of mucosal ulcerations on endoscopic examination, combined with histopathologic demonstration of characteristic intranuclear and intracytoplasmic inclusions.

c) Oesophagitis

CMV esophagitis is diagnosed by presence of ulcers of the distal esophagus and biopsy evidence of intranuclear inclusion bodies in the endothelial cells with an inflammatory reaction at the edge of the ulcer.

d) CMV neurological disease.

Usually diagnosed with compatible clinical syndrome, and the presence of CMV PCR in CSF or brain tissue often evaluated by PCR.

In addition, following features in CSF and imaging can be seen

i. Encephalitis

Cerebrospinal fluid (CSF) typically demonstrates lymphocytic pleocytosis (although a mixture of neutrophils and lymphocytes might be evident), low-to-normal glucose levels, and normal-to-elevated protein levels

ii. Ventriculoencephalitis

Periventricular enhancement of computed tomography(CT) or magnetic resonance images(MRI) is highly suggestive of CMV ventriculoencephalitis rather than HIV-related neurologic disease.

iii. Polyradiculopathy

The CSF in CMV polyradiculopathy usually demonstrates neutrophilic pleocytosis (usually 100–200 neutrophils/µL and some erythrocytes) accompanied by low glucose and elevated protein

e) Pneumonitis:

The diagnosis of CMV pneumonitis is difficult and requires consistent clinical and radiological findings (i.e., diffuse pulmonary interstitial infiltrates, fever, and cough or dyspnea), identification of multiple CMV inclusion bodies in lung tissue or cytology, and the absence of any other pathogens that are more commonly associated with pneumonitis like TB and PCP.

3. Treatment

Retinitis

CMV retinitis should ideally be treated with the active participation of an ophthalmologist who is familiar with the diagnosis and management of retinal disease.

Preferred Therapy	Alternative Therapy	Other Comments
Induction Therapy (followed by Chronic Maintenance Therapy): *For Immediate Sight-Threatening Lesions* • Intravitreal injections of ganciclovir (2mg) or Foscarnet (2.4mg) for 1-4 doses over a period of 7-10 days to achieve high intraocular concentration faster; plus • Valganciclovir 900 mg PO BID for 14–21 days, then 900mg once daily *For Peripheral Lesions*: • Valganciclovir 900 mg PO BID for 14–21 days, then 900 mg once daily (AI) *Chronic Maintenance*: • Valganciclovir 900 mg PO daily for 3-6 months until ART induced immune recovery	*For Immediate Sight-Threatening Lesions* -Intravitreal therapy as listed in the Preferred section, plus one of the following *Alternative Systemic Induction Therapy (followed by Chronic Maintenance Therapy):* • Ganciclovir 5 mg/kg IV 12h for 14–21 days or • Foscarnet 90 mg/kg IV 12h or 60 mg/kg 8h for 14–21 days or • Cidofovir 5 mg/kg/week IV for 2 weeks; saline hydration before and after therapy and probenecid, 2 g PO 3 hours before dose, followed by 1 g PO 2 hours and 8 hours after the dose (total of 4 g). (Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid.) *Chronic Maintenance (for 3-6 months until ART induced immune recovery* • Ganciclovir 5 mg/kg IV daily or • Foscarnet 90–120 mg/kg IV once daily or	The choice of therapy for retinitis should be individualized, based on location and severity of the lesions, level of immunosuppression, and other factors (e.g., concomitant medications and ability to adhere to treatment). Systemic therapy prevents contralateral eye involvement, reduces CMV visceral disease and improves survival. Whenever feasible, treatment should include systemic therapy. The ganciclovir ocular implant, which is effective for treatment of CMV retinitis, is no longer available. For sight threatening retinitis, intravitreal injections of ganciclovir or foscarnet can be given to achieve higher ocular concentration faster.

	• Cidofovir 5 mg/kg IV every other week with saline hydration and probenecid as above	Routine (i.e., every 3 months) ophthalmologic follow-up is recommended after stopping chronic maintenance therapy for early detection of relapse or Immune Reconstitution Uveitis (IRU), and then periodically after sustained immune reconstitution. IRU may develop in the setting of immune reconstitution. Treatment of IRU • Periocular corticosteroid or short courses of systemic steroid.

Monitoring of Response to Therapy and Adverse Events (Including IRIS)

Indirect ophthalmoscopy through a dilated pupil should be performed at the time of diagnosis of CMV retinitis, 2 weeks after initiating therapy, and monthly thereafter while the patient is on anti-CMV treatment. The purpose of such examinations is to evaluate efficacy of treatment and to detect complications such as retinal detachment.

CMV neurological disease

Therapy for well-documented neurologic disease also has not been extensively studied. Some experts would initiate therapy with both IV ganciclovir and IV foscarnet, despite the substantial toxicities associated with such an approach. Optimizing ART is important, as in all types of CMV disease. The optimal duration of therapy and the role of oral valganciclovir have not been established.

Treatment should be initiated promptly.

Preferred Therapy

Ganciclovir 5 mg/kg IV 12h + foscarnet 90 mg/kg IV 12h or 60 mg/kg IV 8h to stabilize disease and maximize response, continue until symptomatic improvement and resolution of neurologic symptoms

Colitis or esophagitis

For patients who have colitis or esophagitis, many HIV specialists recommend anti-CMV therapy for 21 to 42 days or until signs and symptoms have resolved. Some HIV specialists would withhold therapy for mild disease if ART is to be initiated soon or can be optimized. IV ganciclovir generally is the therapy of choice; therapy can be switched to oral valganciclovir once the patient can tolerate oral medications

Preferred Therapy	**Alternative Therapy**	**Other Comments**
• Ganciclovir 5 mg/kg IV 12h; may switch to valganciclovir 900 mg PO 12h once the patient can tolerate oral therapy • Duration: 21–42 days or until symptoms have resolved • Maintenance therapy is usually not necessary, but should be considered after relapses .	• Foscarnet 90 mg/kg IV 12h or 60 mg/kg 8h for patients with treatment-limiting toxicities to ganciclovir or with ganciclovir resistance, or • Valganciclovir 900 mg PO 12h in milder disease and if able to tolerate PO therapy, • Duration: 21–42 days or until symptoms have resolved • For mild disease, if ART can be initiated without delay, consider withholding CMV therapy	Initial therapy in patients with CMV retinitis, esophagitis, colitis, and pneumonitis should include initiation or optimization of ART.

CMV Pneumonitis

Experience in treating well-documented CMV pneumonia in patients with HIV infection is limited and anecdotal. Treatment with IV ganciclovir, or alternatively, with foscarnet, is logical. The optimal duration of therapy and the role of oral valganciclovir have not been established.

Anti retroviral treatment

Do not delay ART for more than two weeks after starting anti CMV therapy for retinitis or other end organ diseases caused by CMV.

Reference

CDC Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV Infected Adults and Adolescents 2016

HIV Management in Australasia 2009

British HIV Association and British Infection Association Guidelines for the Treatment of Opportunistic Infection in HIV-seropositive Individuals 2011

11. Progressive multifocal leukoencephalopathy

Dr. Nalaka Abeygunasekara

Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection of the central nervous system (CNS), caused by the JC virus (a polyoma virus). Unlike some of the other CNS opportunistic infections that are prevented when CD4 cell counts are maintained above 100 to 200 cells/mm^3, PML can still appear in such patients. The cardinal pathological feature is demyelination of white matter, which is irreversible.

1. Clinical presentation

PML manifests as focal neurological deficits, usually with insidious onset and steady progression. Because the demyelinating lesions can involve different brain regions, specific deficits vary from patient to patient. Aphasia, hemi-paresis, hemi-sensory deficits, ataxia and loss of vision are common presentations. Seizures develop in nearly 20% of PML patients. Headache and fever are not characteristic features of PML.

2. Diagnosis

- Magnetic resonance imaging (MRI) of brain
- JC virus detection by PCR in CSF
- Brain biopsy

3. Treatment

No specific therapy exists for PML. The main approach to treatment is antiretroviral therapy (ART) to reverse the immunosuppression that interferes with the normal host response to this virus. ART should be started as soon as PML is diagnosed. Treatment response should be monitored with clinical examination and MRI. Neuro-imaging can be repeated 6 to 8 weeks after ART initiation.

PML-Immune Reconstitution Inflammatory Syndrome

PML has been reported to occur within the first weeks to months after initiating ART. Clinical and radiographic features are different from classical PML. Clinical course is more rapid with oedema and mass effect. Neuro imaging shows contrast enhancement. Corticosteroids have been used empirically to treat this with reported benefits.

12. Malignancies

Dr. Priyantha Weerasinghe

HIV infection is associated with three AIDS-defining malignancies (Kaposi sarcoma, high grade B-cell non-Hodgkin lymphoma and invasive cervical cancer) as well as an increased risk of many other malignancies such as Hodgkin lymphoma, anal cancer and others. Management of PLHIV with malignancies requires multi disciplinary team approach with many other specialties.

1. AIDS related Non Hodgkin Lymphoma

This is the second most common cancer among PLHIV, and can be divided into three types based on area of involvement.

Systemic NHL : commonly diffuse large B cell lymphoma (DLBCL) accounts for more than 80% cases, and usually with late HIV infection, and to a lesser degree Burkitt's lymphoma (BL) which may develop with sustained CD4 levels.

Primary central nervous system lymphoma (PCNSL) : This is a NHL confined to cranio-spinal axis without systemic involvement, and tends to develop at CD4 count less than 50 cells/ ml

Primary effusion lymphomas ("body cavity lymphoma") : is an unusual rare form of HIV-associated non-Hodgkin lymphoma. Growth in a liquid phase is observed in serous body cavities such as the pleura, peritoneum and pericardial cavities without identifiable tumour masses or lymphadenopathy.

Clinical features

Systemic NHL commonly present with ("B") symptoms which include fever, weight loss greater than 10%, and night sweats and enlarged lymph nodes, Further, it may present with extra-nodal involvement, including bone marrow.

PCNSL typically presents with a focal mass lesion in more than 50% of cases and systemic B symptoms are rare. Patients may present with headache, blurred vision, muscular weakness, sensory deficits, personality changes, depression, apathy, confusion, memory impairment, and cranial neuropathies. Some may be present with sub-acute focal neurological signs.

Diagnosis

The diagnosis of NHL should be based on a tissue biopsy and excisional lymph node biopsy in the case of NHL. Apart from basic investigations Serum LDH, CT whole body and Bone marrow aspiration with trephine biopsy are recommended to stage the disease.

CT Scan of PCNSL may show typical single mass with ring enhancement in as many as half the cases. Stereotactic Biopsy is the only confirmatory test. Patients with PCNSL cannot be reliably separated from toxoplasma encephalitis by CT/MRI. However, lesions that are single, have a periventricular location or demonstrate sub-ependymal spread are suggestive of PCNSL.

Treatment

DLBCL - There is no optimal 'gold-standard therapy' as limited published data in the era of ART.

First-line treatment includes chemotherapy regimens such as CHOP or infusional therapies such as EPOCH.

Chemotherapy regimens should be combined with ART therapy.

Concomitant administration of rituximab in Patients with CD4 cell counts <50 cells/µL require additional monitoring.

PCNSL - Patient should be started on ART. High dose methotrexate-containing chemotherapy regimen is recommended for patients with an adequate performance status. Whole brain radiotherapy is a useful palliative treatment modality for control of symptoms when other agents are considered unacceptable.

The treatment of HIV-associated primary cerebral lymphoma is poor with median survival rarely reported at greater than 9 months.

Kaposi sarcoma

Kaposi sarcoma is the most common tumour in PLHIV and HHV-8 is associated with all forms of KS (i.e., classic, endemic, transplant-related, and AIDS-related) . KS is described most frequently among PLHIV with more advanced immunosuppression (CD4+ counts of <200 cells/µL), although they can occur at any CD4+ count.

Clinical presentation :

Characteristic skin lesions patch, plaque or nodular lesions, predilection to the mouth, face and lower limbs. Visceral involvement is uncommon, but 14% have at the time of diagnosis.

Diagnosis : Is by histology. CT scans, bronchoscopy and endoscopy are not generally indicated in the absence of symptoms.

Treatment :

Introduction of ART is associated with considerable decline of incidence of KS.

Initiation of ART alone could result in regression of the lesions, and combine with other options can be considered depending on the site of involvement. ART might result in paradoxical KS.

Local radiotherapy or intralesional vinblastine for early stage with ART and Liposomal anthracycline is considered as first line chemotherapy in advanced KS.

Hodgkin's Lymphoma

Hodgkin lymphoma (HL) is one of the commonest tumours with a 10- to 20-fold increased incidence among PLHIV, and is EBV driven. HL occurs most commonly at CD4 cell counts below 200 cells/μL.

Clinical features:

HL in HIV patients tends to present more frequently in advanced stage at diagnosis, with extranodal involvement, especially bone marrow infiltration, commonly with B symptoms and poor performance status. This makes bone marrow a mandatory investigation among PLHIV with HL.

Treatment

Patients should receive ART during chemotherapy and recommend to avoid PI/ritonavir-boosted regimens due to addictive vinblastine mediated neurotoxicity and neutropenia.

Anal Cancer

The incidence of anal cancer in PLHIV is up to 40 times higher compared to general population and generally occurs at a much younger age, and highest risk is among HIV infected MSMs.

Clinical Presentation

Presentation can vary from rectal bleeding and anal pain to features of incontinence depending on the extension, importantly some can be asymptomatic.

Diagnosis

Diagnosis is by examination under anaesthetic (EUA) of the anal canal and rectum with biopsy. Staging for anal cancer needs CT of the chest, abdomen and pelvis and MRI of the pelvis in order to assess regional lymph nodes and tumour extension.

The management of anal cancer PLHIV patients require a multidisciplinary team (MDT) approach.

Recommendation is chemoradiotherapy (CRT) with 5-fluorouracil and mitomycin C and ART should be started with opportunistic infection prophylaxis. Salvage surgery may be considered for patients with loco-regional disease persistence or relapse following CRT.

Prevention: anal cytology screening of HIV-seropositive MSM and of women might be useful preventive strategies, but needs further evaluation on management of abnormal results. Some specialists recommend an annual digital rectal examination as an important procedure to detect doubtful masses.

Multi-Centric Castlemen's disease (MCD)

This is a rare lymphoproliferative disorder associated with HHV-8 most commonly diagnosed among PLHIV, clinically present with fever, anaemia and multifocal lymphadenopathy.

Cervical cancer

Almost all cases of invasive cancer are associated with infection with oncogenic types of human papilloma virus (HPV). Incidence of cervical cancer has not changed significantly even after ART, many cases can be prevented by regular cervical screening tests.

Diagnosis is based on histopathological examination of cervical biopsies. Radiological assessment is required for staging process.

In general, Invasive cervical cancer is usually treated by radical hysterectomy with lymph node dissection or by radiation therapy for advanced disease. If cone biopsy or loop excision reveals microinvasive cervical cancer with clear margins, a simple hysterectomy can be done. An alternative for women with microinvasive lesions who want to preserve their fertility may be managed with local surgical procedure such as LEEP or cone biopsy with careful follow-up.

Reference

British HIV Association Guidelines for HIV associated malignancies 2014
Medscape emedicine.medscape.com/article/1389907-overview (accessed July 2017)
CDC Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents 2009

13. Cervical cancer screening

Dr. G. Weerasinghe

Screening for cervical cancer is of particular importance for women with human immunodeficiency virus (HIV). The incidence of CIN, as confirmed by colposcopy, is four to five times higher in HIV-positive women and adolescents compared to HIV-negative women with high-risk sexual behaviours. CIN is common in HIV-infected women because:

- Both HIV and HPV are sexually transmitted
- HIV-infected women are more likely to have persistent HPV infection
- Persistent infection with one or more oncogenic HPV subtypes is a major factor in the pathogenesis of premalignant and malignant cervical disease

All women who are diagnosed as HIV should undergo PAP smear at baseline and annually thereafter if baseline PAP smear is normal.
For management of abnormal PAP smears please follow national guideline for cervical cancer screening.

Table - Management of cervical lesions classified according to Modified Bethesda Classification System

Category	**Recommendation**
Negative	Routine annual re-screening
LSIL (CIN 1)	Refer to a gynaecologist
HSIL (CIN 11 or 111)	Refer to a gynaecologist
ASCUS-low grade	Refer to gynaecologist
ASCUS-high grade	Refer to a gynaecologist
Glandular cell atypia	Refer to a gynaecologist
Squamous or glandular malignancy	Urgent referral to a gynaecologist
Inadequate sample	If two repeat pap smears are inadequate refer to a gynaecologist.

Treatment

Patients with Pap smear reports of dysplasia or intraepithelial neoplasia require colposcopy and may require cone biopsy or surgery (please follow national guideline). Adjuvant therapy (chemotherapy/radiotherapy) may be required. Therefore, refer to a gynaecologist.

HPV DNA-based screening methods

- New screening procedures are based on the detection of high-risk HPV DNA in vaginal or cervical smears.
- Detection of high-risk HPV does not necessarily mean that a precancerous lesion or cancer is present; it indicates simply that there is HPV infection.
- HPV test has a greater sensitivity for CIN 2 and above lesions.

14. Prevention, screening and management of non-communicable diseases in people living with HIV

Dr. Chaminda Dodampegamage

People living with HIV are at increased risk of developing a range of non communicable diseases (NCDs), including cardiovascular disease (CVD), hypertension, diabetes, chronic obstructive pulmonary disease (COPD), kidney disease and cancers. This has been strongly influenced by availability of effective ART, lifestyle factors, long-term complications of ART and other disease conditions associated with ageing. Therefore, it is very important to screen, manage and refer the patient to appropriate specialists when necessary.

14.1 Cardiovascular disease

Cardiovascular disease (CVD) is a significant contributor to the excess risk of non-AIDS disease and death in HIV-positive populations. This may be due to smoking, inactivity, an ageing HIV-positive cohort, increased prevalence of surrogate markers of CVD (such as dyslipidaemia), HIV viraemia, immune dysfunction and the pro-inflammatory state associated with HIV infection.

Some classes of ARV drugs (PIs and Efavirenz) can cause lipid abnormalities and may increase the risk of premature CVD. However, **the overall beneficial role of ART on HIV morbidity and mortality has been demonstrated to outweigh potential CVD risks in people with HIV.**

Individuals who are at higher CVD risk

- Those with established atherosclerotic CVD
- People with known hypertension or diabetes mellitus over the age of 40 years
- Waist circumference >90 cm in women and >110 cm in men, high BMI
- Family history of diabetes mellitus or premature CVD
- Hypercholesterolemia
- An estimated glomerular filtration rate (eGFR) <60ml/min/1.73m2 and/ or albuminuria
- A high calculated CVD risk (Annexure ….)

What ARV drugs to start in individuals with higher CVD risk

- Lopinovir/r and Abacavir should be avoided when suitable alternatives are available.
- First-line ARV therapy with tenofovir plus emtricitabine or lamivudine is preferred
- Adverse effects of lipid parameters should be considered when selecting a regimen.

Modification of CVD risk factors

In patients with high CVD risk it is highly recommended to advice to modify all possible modifiable risk factors

- Smoking cessation
- Exercise
- Maintenance of ideal body weight
- Dietary modifications
- Control of high blood pressure

14.2 HIV and renal disease

Dr. Darshini Mallikarachchi, Dr. Geethani Samaraweera

Renal disease is one of the most important comorbidity associated with HIV infection. This is even more important in Sri Lankan context as chronic kidney disease is common among Sri Lankans. Hence when managing patients with HIV infection it is crucial to carry out an initial assessment of the patient for presence of already established renal impairment and risk factors, which predict development of renal disease in future. In addition, new onset kidney diseases can occur at any time due to anti-retroviral therapy (ART), other comorbidities and opportunistic infections. Therefore, it is important to do regular monitoring of renal function.

Initial evaluation of HIV infected patient for kidney disease

All HIV infected patients should be evaluated for kidney disease at the time of entry in to the HIV care.

- Detail history on present or past acute/chronic renal disease, risk factors for renal disease and clinical symptoms and signs should be taken at the initial evaluation. Following categories are at higher risk of developing renal disease.
  - Patients with diabetes mellitus
  - Patients with hypertension.
  - Patients with family history of renal disease
  - Elderly patients
  - HIV infected patients with low baseline CD4 count (<200 cells/μL)
  - Patients having AIDS defining illnesses
  - HIV infected patients with high viral load
  - Patients with Hepatits B and C infection
  - Patients from areas with high prevalence of kidney disease
  - Patients who are already on nephrotoxic drugs (eg. Aminoglycoside antibiotics, pentamidine, acyclovir, foscarnet, amphotericin, tenofovir, adefovir, and cidofovir)
  - Patients with obesity, dyslipidaemia and smoking

- Following investigations to detect renal problems are recommended routinely for all patients at the entry in to HIV care[1,2]
  - Urine analysis
  - Serum electrolytes
  - Serum creatinine
  - BUN
  - Estimated GFR
  - FBS /HBA1c

- If screening shows following abnormalities the patient should be referred to a Nephrologist[1].
  - creatinine clearance (CrCl) or estimated GFR (eGFR) <60 mL/min/1.73 m2
  - Persistent proteinuria ≥1+ or haematuria in urinanalysis (urine dipstick analysis or UFR). However, Dipstick UA is insensitive for microalbuminuria

- Anatomical abnormality in the USS- abdomen

- In patients with high risk of developing kidney disease following tests need to be done to detect microalbuminuria as that may be the first indication of renal dysfunction.
  i. **Random urinary albumin-to-Cr ratio: AlbuminUrine [mg/dL]/ CrUrine [mg/dL]**. Highly sensitive for microalbuminuria; normal is <0.03. Should be used at initial screening and for follow-up, if microalbuminuria is diagnosed.
  ii. **Random urinary protein-to-Cr ratio: ProteinUrine [mg/dL] / CrUrine [mg/dL]** Highly sensitive for proteinuria, but not for microalbuminuria; normal is <0.15.

  If there is no evidence of proteinuria at initial evaluation, high risk patients preferably should undergo annual screening.

Use of ART in HIV infected patients with kidney disease

ART should be given to patients with renal disease, though most NRTIs must be dosed according to renal function and some ARVs should be avoided.

If patient is diagnosed as having a chronic kidney disease it is always better to avoid nephrotoxic drugs such as tenofovir disoproxil fumarate (TDF), atazanavir (ATV) as they may further increase the risk of kidney disease[1].

Rilpivirine, DTG, COBI and RTV and possibly RTG although not intrinsically nephrotoxic, affect the clinically useful relationship between serum creatinine and eGFR and result in difficulty in interpreting the results. If using these medication, renal function is assessed after 4 weeks of starting of these drugs to establish the new 'eGFR setpoint' as a reference to compare subsequent measurements. Furthermore, eGFR declines of 10–20% can be anticipated with these drugs and should not immediately raise concern if non-progressive and seen in isolation. Patients with substantial eGFR reduction at 4 weeks should have this rechecked a month later to ensure that no further decline has occurred[3].

Table 1. Renal adverse effects of commonly used ART[1]

Drug	Disorder/ Pathology	Findings	Comments/ Suggestions
TDF	TDF-associated renal insufficiency	↑ Cr, usually small; slight decrease in eGFR over time	• Of unclear clinical significance, but warrants monitoring of renal function. • May be associated with duration of HIV infection, concomitant RTV-boosted PIs (which boost TDF levels), pre-existing renal dysfunction, or diabetes. • Check serum electrolytes and eGFR every 3-6 months on TDF; check UA every 6 months. Consider more frequent monitoring in patients with eGFR ≤90 mL/min/1.73 m^2, renally secreted drugs, RTV-boosted PIs, diabetes, or hypertension. • Adjust TDF dosage based on steady-state CrCl. • Usually resolves with discontinuation of TDF, but can lead to permanent damage, ESRD.
	Proximal tubular injury (ATN)	Fanconi syndrome (metabolic acidosis, ↑ Cr, ↓ serum $K^+$and phosphate, ↑ urine bicarbonate, phosphate, and glucose)	
ATV	Nephrolithiasis	Symptoms of renal colic, dysuria, urgency; mild ↑ Cr; ATV-containing stones	Treat with hydration; if symptoms do not resolve, or if symptoms recur, may need to discontinue drug.

Preferred regimens in patients with kidney disease

1. ABC+ 3TC/FTC+ EFV/NVP
2. AZT +3TC/FTC+ EFV/NVP

Several NRTIs (including TDF, lamivudine and emtricitabine) may need to be dose adjusted if using when no alternatives are available in subjects with renal impairment.

When there is renal insufficiency, NRTI dose adjustments are indicated as mentioned below.

Table 3. NRTI Dosing for Patients with Decreased Renal Function (based on CrCl)[1]

Drug	Standard Dosage	Adjusted Dosage/Notes

Adapted from McNicholl IR, Rodriguez RA. Dosing of Antiretroviral Drugs in Adults with Renal Insufficiency and Hemodialysis. San Francisco: University of California San Francisco, Center for HIV Information; 2010. Accessed April 1, 2011.

ABC	300 mg PO BID	Dosage adjustment for renal insufficiency does not appear necessary	
FTC	200 mg PO QD	CrCl (mL/min)	
		≥50	200 mg QD
		30-49	200 mg Q48H
		15-29	200 mg Q72H
		<15	200 mg Q96H
		Hemodialysis	200 mg Q96H, give after dialysis
3TC	150 mg PO BID or 300 mg PO QD	CrCl (mL/min)	
		≥50	150 mg BID or 300 mg QD
		30-49	150 mg QD
		15-29	150 mg first dose, then 100 mg QD
		5-14	150 mg first dose, then 50 mg QD
		<5	50 mg first dose, then 25 mg QD
TDF	300 mg PO QD	Experience in patients with CrCl <60 mL/min is limited. Preliminary data suggest:	
		CrCl (mL/min)	
		≥50	300 mg QD
		30-49	300 mg Q48H
		10-29	300 mg twice weekly
		Hemodialysis	300 mg weekly
AZT	300 mg PO BID	CrCl (mL/min)	
		<15	100 mg Q6-8H
		Hemodialysis	100 TID

Follow up

In patients with high risk of developing renal disease, renal function should be monitored every 6 months.

In patients who have established renal disease after starting non nephrotoxic ART regimen, the renal function should be monitored as requested by the nephrologist. If having CKD

- Maintain blood pressure at ≤125/75 mmHg.
- Initiate ACEIs or ARBs for patients with hypertension or proteinuria
- Screen for and/or maximize treatment for diabetes and dyslipidaemia
- Screen for and treat hematologic abnormalities
- Advise on protein- and salt-restricted diet; refer to renal dietician.
- Refer for substance abuse counselling, when appropriate, to decrease risk of nephropathy associated with use of heroin or other illicit substances.

Dialysis and the placement of arterio-venous fistula should not be withheld for patients solely because of HIV infection.

Renal transplant may be considered for patients with end stage renal disease.

ART should not be withheld from patients simply because of the severity of their renal dysfunction.

Addition of ACE inhibitors/angiotensin receptor blockers and prednisolone should be considered in patients with HIVAN if ART alone does not result in improvement of renal function.

Reference

- U.S Department of veterans affairs, Renal disease in HIV/AIDS https://www.hiv.va.gov/provider/manual-primary-care/renal-disease.asp (accessed 25th June 2017)
- British HIV association guidelines. British HIV Association guidelines for the routine investigation and monitoring of adult HIV-1-positive individuals 2016. file:///C:/HIV%20and%20kidney%20disease/2016-BHIVA-Monitoring-Guidelines.pdf (accessed 6th June 2017)
- Jean C. Yombi; Anton Pozniak; Marta Boffito; Rachael Jones; Saye Khoo; Jeremy Levy; Frank A. Antiretrovirals and the Kidney in Current Clinical Practice http://www.medscape.com/viewarticle/821748_2(accessed 5th June 2017)

14.3 HIV-associated neurocognitive (NC) impairment

All patients with HIV should be evaluated for evidence of HIV associated neuro-cognitive impairment. This NC deficit may present with a wide spectrum of clinical symptoms and typically includes patterns involving ineffective learning and difficulties in decision making or executive function, rather than pure difficulties in formulating new memory (the cortical defect typical of Alzheimer's disease). They may be asymptomatic with abnormal neuropsychiatric tests or may have mild, moderate or severe symptoms.

Risk factors for the development of NC disorders are poorly understood and are likely to be multifactorial including both HIV disease factors and concomitant diseases.

When to start ART

It is recommended for individuals with symptomatic HIV-associated neurocognitive disorders to start ART immediately, irrespective of CD4 cell count.

What to start with

- It is recommended to start combination anti-retroviral therapy for all individuals with HIV associated NC disorders.
- Efavirenz containing regimens are better avoided in individuals with HIV associated NC disorders.
- Although it was believed in early years that including AZT in combination anti retroviral therapy in individuals with HIV associated NC disorders has a clear benefit over other ARV, new evidence do not support any such benefit of one antiretroviral regimen over the others.

In individuals who show continuing or worsening NC impairment despite ART, it is recommended to reassess patients to find any confounding factors. If facilities are available, assessment of CSF HIV RNA and genotyping of CSF HIV RNA is also recommended.

14.4 Depression

People living with HIV are at high risk of mental, neurological and substance-use disorders. Depression has clear negative impact on optimal treatment adherence. Therefore, it is important to screen HIV infected individuals for clinical evidence of depression at diagnosis and regularly thereafter and refer to psychiatrists for further management. Efavirenz should be avoided in PLHIV having suicidal risk.

14.5 Drug use and drug use disorders

People living with HIV who use drugs may experience a range of disorders related to drug use, including drug dependence, intoxication, withdrawal and overdose. Although injecting drug use is uncommon in Sri Lanka it is associated with a range of diseases and infections, including viral hepatitis, TB, septicaemia and bacterial endocarditis, in addition to HIV. Drug use behaviour can significantly affect treatment adherence and they can interact with ARV. Therefore, it is important to take a detail history about substance abuse and refer to psychiatrists for necessary management.

15. Dermatological manifestations in HIV infection

15.1 Spectrum of dermatological manifestation in HIV infection

Rash morphology	Differential diagnosis
Follicular	Bacterial, eosinophilic folliculitis, pityrosporum folliculitis, follicular eczema
Eczematous	Dermatitis, drug eruptions, Seborrhoeic dermatitis
Papular	Molluscum contagiosum, HPV, Scabies, Cryptococcosis, Histoplasmosis, Kaposis sarcoma
Macular/Maculopapular	Secondary syphilis, Parvo virus B19, HBV, Dissaminated candidiasis, widespread scabies and drug reactions. Consider OI with skin manifestations such as cryptococcosis, histoplasmosis, penicilliosis and coccidiomycosis
Vesicular	Herpes zoster, Varicellar infection, herpes simplex and drug reactions
Petechial and pustular	Bacterial causes such as disseminated gonococcal infection, pseudomonal, staphylococcal sepsis, infective endocarditis, listeriosis Viral causes such as Parvo virus B19, cutaneous vasculitis and drug reactions
Nodular	Prurigo nodules from persistent scratching, basal and squamous cell carcinoma, Kaposis sarcoma, mycobacteria, bartonella, histoplasmosis, coccidiomycosis
Psoriasiform lesions	Psoriasis, Reiter's syndrome

15.2 Clinical Diagnosis and Management of Skin Conditions

1. ***Non infectious diseases***

Condition	Clinical features	Diagnosis	Treatment
Eosinophilic folliculitis	Erythematous, pruritic, follicular papules (centred around follicles)/ pustules on face, upper trunk, upper arms, Intense itching; This can lead to excoriation with secondary bacterial infections, prurigonodularis, lichen simplex chronicus and post-inflammatory hyperpigmentation.	Clinical	Treat mild disease with topical steroids and oral antihistamines Treat moderate to severe disease with oral Itraconazole, isotretinoin, or phototherapy
Pruritic papular eruptions (PPE)	Hyperpigmented, hyperkeratotic papules and nodules which are usually symmetrically distributed on the arms, legs, lower back, buttocks	Clinical	Treatment- Topical steroids, systemic antihistamines to relieve the itching that often accompanies this condition. If secondary impetigo occurs topical or systemic antibiotics may be needed. Phototherapy is also recommended. The condition improves with immune recovery on ART but scarring from old lesions may be permanent
Xerosis	Dry and rough skin, sometimes with fine cracks	Clinical	A moisturising skin lotion can be used to relieve dryness and antihistamine for itching (chlorpheniramine). Emmollients including urea, lactic acid or salicylic acid. The condition impoves with immune restoration on ART
Seborrhoeic dermatitis	Erythematous plaques with greasy scaling on the scalp, face, postauricular, area and chest	Clinical	<u>In mild cases</u> Scalp – ketoconozole shampoo Body and face – Ketoconozole If not responding or moderate/severe cases

			Scalp - betamethasone lotion Face – 1% hydrocortisone cream Body – betamethasone cream <u>Refractory cases</u> oral ketoconazole 200mg/day for 7-14 days
Infection	Clinical features	Diagnosis	Treatment
Drug reaction	HIV infected people have a higher incidence of drug reactions. Generalized erythematous, pruritic rash with or without fever and signs of hepatotoxicity. Severe drug reactions (Stevens-Johnson syndrome and TEN-toxic epidermal necrolysis) result in blistering of skin and or mucous membranes, typically in the first days to weeks of commencing the new drug *Use of ART can cause lichenoid eruptions, mobiliform eruptions, genital and oral ulceration	Clinical	Stop the causative drug. Give antihistamines and topical moisturising creams. Hospitalization with cardiorespiratory support may be needed for patients with SJS and TEN. Most experts recommend the use of short course of systemic steroids in case of sever drug reactions. Start with prednisone. 0.5mg/kg per day, and reduce the dose over 5-10d Once suspected dermatological referral is needed For severe cases immunoglobuline can be used.
Primary HIV infection	Generalized maculopapular rash usually with fever and systemic symptoms	Serology for HIV RNA or DNA may be negative in early primary infection	No specific treatment is indicated for the rash or for primary infection. Patient counselling, education and behaviour modification are necessary
Psoriasis	This can present for the first time at the progression to AIDS. Well defined salmon pink plaques bearing large, centrally adherent silvery white polygonal scales. There are different types- Plaque psoriasis, scalp, guttate, flexural, palmar, plantar and pustular. There can be nail	Clinical	Topical applications- coal tar, dithranol, cacineurin inhibitors Flexural psoriasis steroids can be used When extensive methotrexate can be given, but ciclosporine is better avoided in immunosuppression UV radiation, PUVA, retinoids, biological agents

	changes such as thimble pitting, onycholysis and sub-ungual hyperkeratosis. In addition can be complicated with psoriatic arthropathy.		
*2. **Viral infections***			
Infection	Clinical features	Diagnosis	Treatment
Primary varicella or chickenpox	Crops of pruritic vesicles that becomes generalised. Malaise, headache, fever, myalgia. Greater incidence of complications as encephalitis, pneumonitis and hepatitis	Clinical Culture DFA/PCR Tzanck smear	Acyclovir 800mg 5 times daily7 days Valacycovir tds / Famcyclovir 500mg tds - 5-7 days Prevention with vaccination
Herpes zoster	Typically painful blisters in clusters along dermatomes. Can involve the eye. HIV infection should be suspected if lesions are multi dermatomal or episodes are recurrent. Prodromal symptoms include paraesthesia and or pain in the dermatomes a few days before the rash appear. Fever, malaise and headache may precede the outbreak of blisters	Clinical Tzanck smear	Acyclovir 800mg 5 times daily for 7 days should be started within 72 hours of onset of the blisters. Famiciclovir and Valacyclovir are alternatives. For ophthalmic zoster, acyclovir ointment can be applied in the eye every 4 hours Pain is managed with paracetamol 1g 6 hourly; stronger analgesics can be used if necessary. Amitriptyline 25-50mg before bedtime or gabapentin is useful for the control of the neuropathic pain and for post herpetic neuralgia, which may persist for months after the episode.

Herpes simplex	Typical blisters, with pain and tingling, usually genital area or face. Chronic HSV infection presents as progressive, shallow, clean based ulcers on genitalia, perianal, perioral areas	Clinical/Isolation in cell culture Presumptive presence of multinucleated giant cells in scrapings stained with Giemsa stain/Tzanck smear ®Serology may be helpful	Saline wash-2-4 times a day Analgesics Keep the area clean and dry Acyclovir 400mg 3 times daily - 7days Valacyclovir 500mg bd - 7d Famcyclovir 250 tds-7d Secondary bacterial infections- Cotrimoxazole or ciprofloxacin Fungal infections- fluconazole (avoid topical) In immunosuppressed HSV can be chronic and invasive (esophagitis and encephalitis) Recurrence- suppressive therapy- refer STI management guidelines
Molluscum contagiosum	Raised dome shaped, flesh coloured papules with central umbilication containing caseous material lesions usually on face, neck, genital area, axilla and groins	Clinical Biopsy of lesions- molluscum bodies on Giemsa staining	Cryotherapy, curettage, TCA, Imiquimod under occlusion, topical cidofovir in recalcitrant disease, often improves with ART

*3. **Fungal infections-superficial***

Infection	Clinical features	Diagnosis	Treatment
Dermatophyte infections	Tinea cruris, corporis, onychomycosis Proximal nail white onychomycosis is also a marker of HIV infection Can present as deep dermal morphologies as multiple fluctuant erythematous nodules on extremities	Clinical Microscopy of scrapings with (KOH) preparations Culture	Superficial disease with topical applications Wide spread disease with systemic antifungals Fluconazole and Itraconazole Onychomycosis with terbinafine

Malassezia furfur (Pityriasisversicolor)	Pruritic papules and macules on the face, chest, back and shoulders	Microscopy of scrapings with KOH	Topical Clotrimazole, if fails systemic Fluconazole, itraconazole
4. ***Parasitic infestations and infections***			
Infection	Clinical features	Diagnosis	Treatment
Scabies	Rash and excoriations on torso; burrows in web spaces, and wrist; face spared	Microscopy of skin scrapings, KOH or mineral oil preparation	Permethrin cream 5%: Apply from chin to toes and take a shower 10-12 hours later; repeat after 1 week Or 25% benzyl benzoate solution: Apply below head. The application is left to dry on the skin and then repeated for 3 consecutive days. Itching can be relieved by taking chlorpheniramine tablets and applying crotomitone cream locally. Clothes and bedding should be washed/boiled and kept separately for 3 days to prevent re-infestation. Household contacts should be treated. After treatment, all the clothes and bed linen should be washed/boiled and dried. Clothes which cannot be washed has to be tied up in bags for 2-3 weeks Household and other close contacts require the same treatment. In severe cases ivermectin administered in a single oral dose of 200µd/kg may be considered
Norwegian scabies	Extensive crusting (psoriasis like lesions) with thick hyperkeratotic scales on elbows, knees, palms and soles		

Leishmaniasis	Cutaneous disease is usually accompanied by visceral disease. Cutaneous manifeststions are common. Skin lesions present as papules modules or plaques mainly on the exposed areas and. Muco-cutaneous disease affect the nasal, buccal and pharyngeal areas with disfiguring. Bone marrow, liver, spleen, lymph nodes, GI and respiratory involvement occur in visceral disease. Visceral disease has been reported but rare in Sri Lanka	Demostration of parasite in blood, tissue, scrapings, skin biopsy, Culture, PCR	Pentavalent antimonial salts/ Sterbogluconate

16. Provision of General care services

16.1 HIV transmission, the law and the clinical team

Dr. Lilani Rajapaksa

An underlying principle in the provision of clinical care for people with HIV is the need for a secure and confidential environment in which extremely sensitive matters can be frankly and fully discussed. Maintaining the rights and dignity of people who have been diagnosed or are at risk of HIV infection creates a conducive environment for successful prevention, treatment and care services.

Confidential information

- (In law, Confidentiality is not absolute.) The public interest in maintaining confidentiality may sometimes be outweighed by another public interest favouring disclosure to third parties. Ultimately the public interest is decided by the courts.
- A healthcare worker must maintain the confidentiality of patient information unless the patient has consented to disclose, disclosure is necessary in the public interest or is required by a court of law.
- A failure to maintain confidentiality may give rise to legal liability.

A healthcare worker should explain to the patient:

- The nature of the disease
- Its medical, social and occupational implications, as appropriate.
- Ways of protecting others from infection
- **The importance of giving the information about the patient's disease or condition to other care givers to facilitate management.**

Make sure the patient understands that practitioners cannot provide adequate clinical management and care without knowledge of their patients' conditions.

Recommendations for Clinical Practice

- Normally, the overall responsibility for the patient rests with the consultant of record, who should in all cases be clearly identified.
- All healthcare professionals working with people with HIV must be familiar with the ways in which data is stored and the confidentiality of medical information is maintained within their service and be able to explain this to patients as required.

The particular roles of health care professionals in this area are:

- To advise PLHIV appropriately about HIV infection and the implications for themselves and others.
- To support patients with HIV appropriately
- To ensure confidentiality of medical information

Advice that should be provided by the clinical team to all patients diagnosed with HIV infection

- All advice given to people with HIV should be fully documented in the clinical record and advice must be up to date.
- Advice given by members of the multidisciplinary team to people living with HIV must be consistent and advice should be provided in both verbal and written forms in appropriate language, ensuring the patient understands. (taking into account language, cultural sensitivities, educational level, literacy and other factors)
- Clinicians should discuss sexual behaviour regularly with patients and ensure that advice given is appropriate for the current state of affairs.

Clinical documentation

It is important to observe proper practice in documentation of the clinical process and discussions with and about patients as follows:

- Document clearly in the notes the name of the consultant with overall responsibility for a patient's clinical care.
- Maintain full, contemporaneous notes that are **dated and signed**.
- Document advice given to patients by whatever route – telephone conversations, letters, visits and print and file copies of emails
- Document discussions that are held about the patient with third parties and other professionals keeping copies of all letters in the main clinical file.

The duty to properly advise

Healthcare practitioners must properly advise a patient on ways of protecting their sexual partners from infection. A failure to do this may give rise to legal liability if the patient's sexual partner becomes infected as a result.

Circumstances in which a breach of confidentiality would probably be considered to be in the public interest, and therefore lawful.

- When the infected person and the partner both are under the care of the same institution/ care giver, as there is a duty to care for own patients, failure to disclose will be breach of duty.
- If the close contact is not a patient of the health care practitioner, there is no legal duty. However, disclosure would be lawful because of the public interest in protecting the contact from infection. There is power to disclose but no legal obligation to do so. (eg- martial partners)

Disclosure to other healthcare professionals

- A doctor should explain to the patient that other care givers cannot provide adequate clinical management and care without knowledge of their patients' conditions. Where the patient is prepared to consent to third party disclosure, no legal issue should arise.
- If you are in doubt about whether disclosure is appropriate, you should seek advice from an experienced colleague/ legal and ethical committee.
- You should inform patients before disclosing information.
- you must be prepared to justify a decision to disclose information against a patient's wishes.
- These should be documented early.

PLHIV should be advised that that there have been successful prosecutions when transmission of HIV has been proved to have taken place and that the risk of prosecution is likely to be higher if the patient

- has not disclosed the fact of his/her HIV infection to the sexual partner before having intercourse
- has only disclosed his/her HIV infection after having sex
- has given false information to a partner
- has not used condoms.

Support for the process of disclosure to sexual partners after diagnosis.

- Disclosing HIV infection to sexual partners can be very difficult. It is important that individuals are given enough time and appropriate support.
- Disclosure should be seen as a process rather than an event and patients should be given support throughout that process. There should be discussion and agreement about an appropriate time frame for disclosure wherever possible.
- The clinical team should give patients information about, and where necessary direct referral to, additional sources of support, peer groups and other agencies to get help in disclosure.
- In circumstances of non-disclosure, this should be discussed sensitively on an individual basis to establish barriers that exist and provide support in addressing these.
- In complex cases of continued non-disclosure and failure to follow medical advice will require assessment to be made on a case by case basis at a higher level (ethical and legal committee).

Disclosing information in court

- Although medical evidence is confidential it is not legally privileged.
- This means that if a health care professional is required to testify in court under oath all information must be disclosed.
- Failure to give such information would be in contempt of court.

Disclosing information to the police

- If an adult patient has become HIV-positive as a result of potentially criminal actions by a third party, it is that patient's choice whether or not to bring it to the attention of the police.
- It is for the patient to decide to take that decision and to initiate it with appropriate legal guidance, NOT the health care provider.
- Health care professionals have no duty to answer questions that the police ask about their patients **unless the request is sanctioned by a court order**.
- Medical records are the property of the individual hospital. Any request for access to health care records by an outside agency, including the police should be directed to the Director/ NSACP or RDHS/PDHS/ hospital director.

16.2 Partner disclosure in HIV

Dr. Darshani Wijewickrama

- Health care professionals should advise and support patients in decision making according to professional guidance and the law.
  Advice must include the routes of HIV transmission and how to prevent transmission, with information about safer sexual practices, the use of condoms and suppression of viral load. Advice must be given in a non-judgmental way.
- In Sri Lanka, it is an offence to knowingly infect another person. (Sri Lankan penal code, marginal notes 262,263)
- When considering breaching confidentiality, it is important to weigh up all potential harms as there may be situations where disclosure of HIV status to protect a sexual partner results in considerable harm to an individual. e.g. domestic violence.
- In situations where a health care professional believes that an HIV positive individual continues to put sexual contacts at risk, their duties and subsequent action depend upon the type of contact.
- No information should be released to the police unless patient's consent has been verified or there is a court order in place.
- It is up to an individual person to make a decision about complaining to the police that they have become infected with HIV, and health care workers should remain impartial during discussions with patients.
- A healthcare worker must maintain the confidentiality of patient information unless the patient has consented to disclosure or disclosure is necessary in the public interest. A failure to maintain confidentiality may give rise to legal liability.
- A healthcare worker must properly advise a patient on ways of protecting their sexual partners from infection. A failure to do this may give rise to legal liability if the patient's sexual partner becomes infected as a result. Liability may also arise where a healthcare worker negligently fails to diagnose the patient as having the infection.
- The health care professional may disclose information to a known sexual contact of a patient with a HIV, if the health care professional has a reason to think that the partner is at risk of infection and that the patient has not informed the partner and cannot be persuaded to do so. In such circumstances, the patient should be informed before the disclosure, if it is practicable and safe to do so. Health care professional must be prepared to justify a decision to disclose personal information without consent.
- If the sexual contact is also a patient of the healthcare professional it is considered likely that the courts would recognise a duty by a doctor to disclose the HIV diagnosis to the sexual contact. A failure to disclose might therefore be a breach of the duty owed to the sexual contact, if the contact became HIV-positive as a result.

[Reference - BHIVA 2013]

16.3 Partner notification in HIV

Dr. Darshani Wijewickrama

HIV partner notification is a process in which contacts of people with HIV are identified and offered HIV testing.
There are two main contact categories.

- Contacts whose HIV status is known
- Contacts whose HIV status is unknown

Status-known contacts:

These include known HIV positive contacts and known HIV negative contacts. (Contacts who have a negative result on a fourth generation HIV test performed 4 weeks or more after the exposure are highly unlikely to have HIV infection).

Status-unknown contacts:

These are divided into two groups based on whether or not we know enough details of the partners.

a) Contactable

People who have enough information to be identified

Eg: working mobile number or email address, and sufficient demographic data like name and address.

All information sources should be used with index case agreement in attempting to identify contacts.

b) Uncontactable:

People for whom the index case (or HCP) has no means of contact.

1. Partner notification process should be initiated by the consultant/doctor.

2. Every newly diagnosed HIV positive patient should be referred to the PHI/PHNS for partner notification interview. Partner notification process should be continued, if the index patient is transferred to another STD clinic also.

3. It is important that the patients are not forced to reveal the names of partners for the purpose of contact tracing. Partner notification should be mentioned in post-test counselling and should be regularly discussed as there may be additional partners identified over time. It is essential the privacy and confidentiality of the index patients ensured at all times. The PHI/PHNS need to support and assist the patient in informing his or her contacts in practical terms. (eg; making a plan on notification) The index patient's identity and sexuality should not be revealed to the contacts

being notified unless the index patient requests to do so. Likewise, the outcomes and results of the partner notification should not be revealed to the index patient.

4. The outcomes of the partner notification should be recorded in the patient's notes by the PHI/PHNS. If the patient declines to see the PHI/PHNS, the doctor should raise the issue of partner notification with the patient and record it in the notes.

5. When the patient feels unable to inform his or her contacts, the PHI/PHNS can offer provider referral. This may be carried out by:
    a) The PHI/PHNS offering to inform the contacts in the presence of the index patient, or in the absence of the index patient, when the contact is available in the clinic after being informed to come by the index patient
    b) The PHI/PHNS informing the contacts without divulging the index patient's identity

    In provider referral, it is essential to discuss each case on its own merit to decide whether provider referral is appropriate, for example if there may be significant harm to the index patient and/ or their contacts. Any decisions taken should be clearly documented in the index patient's notes.
    It is crucial that the contact is given sufficient information to make an informed decision to test or not.
    Where there is an ongoing risk of HIV transmission to a contact, and the contact is unaware of the patient's HIV positive status, there may be different legal and ethical considerations. eg: law on wilful HIV transmission where the risk to an individual may outweigh the confidentiality of the index patient. The consultant has to decide on an appropriate course of action
    [Ref - SSHA Manual for sexual health advisers, UK -2004]

Look back period in HIV

An estimate, based on a risk assessment, of when infection is likely to have occurred should be made and all contacts since, and in the three months prior to this estimate, should be notified. If this is not possible, all previous partners should be contacted and offered HIV testing. The risk assessment should consider sexual history, HIV testing history (including antenatal and blood transfusion service testing history), and history of possible seroconversion illness.
[BASHH statement on partner notification for STIs -2012]

References

- BASHH and BHIVA statement on HIV partner notification 2015
- SSHA Manual for sexual health advisers, UK -2004
- BASHH statement on partner notification for STIs -2012

16.4 Defaulter tracing

Dr. Shyama Somawardana

1. When a patient comes for care, follow- up date is given and follow- up date is entered in the diary.
2. All the files due on the day are selected according to the registration number in the diary.
3. When the patient visits for follow- up the number in the diary is marked in red.
4. Other files which indicate patients who did not attend for the follow- up on the given date are selected as defaulters.
5. The defaulted files are kept for one week to see whether the patients attend for follow- up.
6. At the end of one week period, Registrar/ Senior registrar goes through all these files, paying more attention to those on ART.
7. Defaulter tracing action is decided- phone calls, letter or visit in urgent cases.
8. If they do not attend within 3 months, files are labelled as lost to follow-up (LFU)
9. Before labelling files as LFU every possible effort will be made to trace the patient and to get back them for services.

Annexure 1 Check list for follow up visits of HIV positive patients

Dr. Shyama Somawardana

please check the following aspects of care at each and every visit. plan investigations at appropriate intervals

1. Ask for symptoms of OIs and Tubercolosis
2. Any other symptom
3. Performance scale
4. Adherence issues
5. ART Side effects
6. Drugs in hand, Pill count if possible
7. Last sexual exposure
8. Condom usage
9. LMP
10. Contraception
11. Partner sero status
12. Investigations (CD4 VL FBC LFT RFT Lipid profile FBS
13. Annual STI Screening
14. Annual PAP smear
15. Dietary habits and advice
16. Exercise
17. Advice on smoking and alcohol usage
18. Non -communicable disease and follow-up
19. Other medical conditions
20. Serious non-AIDS conditions (non-AIDS malignancies, Cardiovascular disease and end stage kidney failure
21. Safer sex counselling
22. Adherence counselling
23. Condom counselling
24. Any psychosocial issues

Annexure 2 Counselling for initial visits and before starting ART

Dr. Piyumi Perera, Dr. Dulari Liyanage

For initial visits

1. Explain the natural history of HIV
    a. What HIV/ AIDS is
    b. Natural history and progression (CD4/ Viral load/ OI)
    c. Modes of transmission and myths related
2. Discuss importance of early diagnosis
3. Briefly discuss the availability of ART, other health care facilities and importance of regular follow up.
4. Advise for healthy life style measures
    a. Dietary advises/ nutrition
    b. Regular exercise
    c. Stop alcohol and smoking
    d. Regarding other substance abuse
5. For female patients - pregnancy issues, pap smears, family planning methods
6. Prevention
    a. Sexual exposures - safe sex and condom demonstration
    b. Mother to child transmission
    c. Blood and body fluids - safe handling and first aid, not to donate
7. Prevention of infection – availability of prophylaxis treatment, hygienically prepared food and sanitary hygiene, vector born infection
8. Discuss disclosure related issues and the support available
    a. Need for partner and children screening and PMTCT

Before starting ART

1. Explain the need to start ART & objectives of treatment (increase immunity, prevent OIs, improve survival & quality of life)
2. Adherence counselling – please refer A Guide to antiretroviral therapy, 2016 by NSACP, section 1.9 (page 19)
3. In addition, discuss-
    a. The importance of informing regarding possible drug interactions, concurrent use of other medications including ayurvedic treatment
    b. The need to attend HIV clinic regularly for monitoring of efficacy and adherence.
    c. Issues of storage and keeping drug stocks for emergency situations. Eg ; travelling for long distances or staying overnight outside home
4. Reassess treatment support, partner screening.
5. If treatment supporter is present, discuss his/ her role in supporting treatment.

Annexure 3 Protocol for screening partners of HIV positive patients

1. All the HIV positive patients who are registered for HIV services should be advised and counselled on the importance of partner screening.
2. When a patient brings the partner he/ she should be registered at the STD clinic as a anew patient and full STI screening and counselling should be done depending on the situation.
3. In instances where the patient is reluctant to bring his/ her partner/s to the STD clinic due to confidentiality issue etc., the doctor should communicate with the public health staff at the STD clinic and take appropriate measures with the consent of the index patient.
4. The necessary screening need to be carried out by the medical Officer at the STD clinic while maintaining confidentiality.
5. Please seek advice from the Consultant Venereologist whenever necessary.

Annexure 4 Hepatitis B Vaccination Guidelines – STD clinics

Dr. G. Weerasinghe

Vaccination schedule for Hepatitis B using monovalent vaccine

Vaccination schedule	Comment
Standard Schedule 0,1, 6 months	Standard schedule which gives a higher antibody titre is recommended for routine vaccination *If vaccine schedule interrupted, the vaccine series does not need to be restored.* If interrupted after the 1st dose patient need to be contacted and 2nd dose should be administered as soon as possible. If there is at least 8 weeks interval between the 2nd dose and scheduled 3rd dose, give the 3rd dose as scheduled. If not make sure that 2nd and 3rd doses are separated by an interval of at least 8 weeks. If only 3rd dose is delayed, patient should be contacted as soon as possible and give the 3rd dose.
Ultra Rapid Schedule - emergency 0, 7, 21, and 12 months **Accelerated Schedule** 0,1, 2, 12 months	Ultra rapid and accelerated schedule are given in special situations. Decision has to be made following discussion with a Consultant Venereologist.

Note:

Pre vaccination serological testing is not recommended at routine practice.

If facilities are available it reduces the number of unnecessary vaccination of people who are already immune to HBV infection and provide an opportunity to refer people with chronic hepatitis B for care and treatment.

Post vaccination testing for immunity is not recommended as routine practice.

However it is recommended for following groups ;

1. People at risk of occupationally acquired infection
2. Infants born to HBsAg – positive mothers
3. People infected with HIV and other immune compromised people

4. Sex partners or needle sharing partners of people who are HBsAg positive

Post vaccination antibody testing should be performed 1- 2 months after administration of the last dose of the vaccine series for detection of a protective concentration of anti HBs (> 10 m IU/ ml)

Annexure 5 Guideline to the TB/ HIV reporting and recording

Dr. A. Azran, Dr. D.I. Rajapaksha

Referral forms :

1. National Programme for TB Control and Chest Diseases (TB/ HIV 1) (version : June 2014)
   This format is designed to refer the TB patients to STD clinic by the chest clinic doctors.
   Original form (White copy) to be sent to the STD clinic. This should be sent with the patient and should be compiling in STD clinic.
   Copy (yellow copy) of that will be retained at the STD clinic.

2. National STD/ AIDS Control Programme (TB/ HIV 2) – This format is designed to refer HIV patients to the chest clinic by the STD doctors.
   - Original form (White copy) has to be sent to the chest clinic. This should be sent with the patient and should be compiling in STD clinic.
   - Copy (yellow copy) of that will be retained at the STD clinic.

Back referral forms

1. National Programme for TB Control & Chest Diseases (TB/ HIV 1a) (version : June 2014)
   This format is designed to back refer the TB patients from the STD clinic, which has been referred by the chest clinic doctors to the STD clinic. This form includes the result of the HIV screening, confirmatory test and other related information.
   - Original form (White copy) – has to be sent to the chest clinic as usual, confidentially addressed to the chest clinic doctor and will be handed over to the patient.
   - Copy (yellow copy) of that will be retained at the STD clinic.

2. National STD/ AIDS Control Programme (TB/ HIV 2 a) (version : June 2014)
   This format is designed to back refer the HIV patients from the chest clinic, who have been referred by the STD clinic doctors. This form includes the result of the TB screening, the treatment given and other related information.
   - Original form (White copy) – has to be sent to the STD clinic with the patient.
   - Copy (yellow Copy) – of that will be retained at the chest clinic.

Register of HIV/ TB Co infection (TB/ HIV 3) (version: June 2014)

This register has to be maintained at each district chest clinics., All the patients with HIV/ TB Co infection will be registered and the register will be kept confidentially. These data will be used to prepare the quarterly return and to trace the patients whenever advised by the in charge.

Annexure 6 Cardiovascular risk calculator - Framinghum Risk score

Framingham Risk Score

Risk assessment tool for estimating a patient's 10-year risk of developing cardiovascular disease

Age:	Years
Gender:	Female Male
Total cholesterol:	mmol/L
HDL cholesterol:	mmol/L
Smoker:	Yes No
Diabetes:	Yes No
Systolic blood pressure:	mm Hg
Is the patient being treated for high blood pressure?	Yes No

Calculate risk

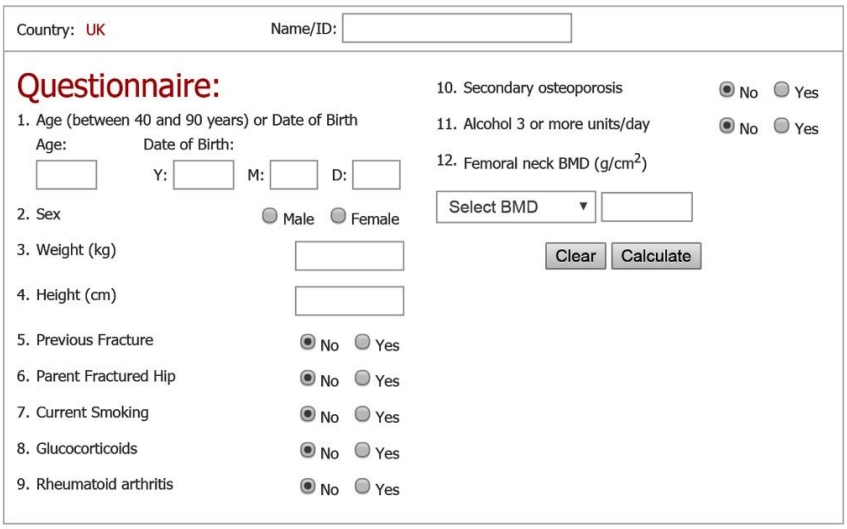
This online assessment tool is intended as a clinical practice aid for use by experienced healthcare professionals. Results obtained from this tool should not be used alone as a guide for patient care.

The risk assessment tool above uses information from the Framingham Heart Study as recommended by the 2009 CCS Canadian Cholesterol Guidelines to predict a person's chance of developing cardiovascular disease in the next 10 years, modified for family history (double the CVD risk percentage if any CVD present in a first degree relative before age 60). In men over 50 or women over 60 of intermediate risk whose LDL-C does not already suggest treatment, hsCRP can be used for risk stratification. Please enter your patient's information in the fields below.

Annexure 7 FRAX® Fracture Risk Assessment Tool

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.



Risk factors

For the clinical risk factors a yes or no response is asked for. If the field is left blank, then a "no" response is assumed. See also notes on risk factors.

The risk factors used are the following:

Age	The model accepts ages between 40 and 90 years. If ages below or above are entered, the programme will compute probabilities at 40 and 90 year, respectively.
Sex	Male or female. Enter as appropriate.
Weight	This should be entered in kg.
Height	This should be entered in cm.
Previous fracture	A previous fracture denotes more accurately a previous fracture in adult life occurring spontaneously, or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture. Enter yes or no (see also notes on risk factors).
Parent fractured hip	This enquires for a history of hip fracture in the patient's mother or father. Enter yes or no.
Current smoking	Enter yes or no depending on whether the patient currently smokes tobacco (see also notes on risk factors).
Glucocorticoids	Enter yes if the patient is currently exposed to oral glucocorticoids or has been exposed to oral glucocorticoids for more than 3 months at a dose of prednisolone of 5mg daily or more (or equivalent doses of other glucocorticoids) (see also notes on risk factors).
Rheumatoid arthritis	Enter yes where the patient has a confirmed diagnosis of rheumatoid arthritis. Otherwise enter no (see also notes on risk factors).
Secondary osteoporosis	Enter yes if the patient has a disorder strongly associated with osteoporosis. These include type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition, or malabsorption and chronic liver disease
Alcohol 3 or more units/day	Enter yes if the patient takes 3 or more units of alcohol daily. A unit of alcohol varies slightly in different countries from 8-10g of alcohol. This is equivalent to a standard glass of beer (285ml), a single measure of spirits (30ml), a medium-sized glass of wine (120ml), or 1 measure of an aperitif (60ml) (see also notes on risk factors).

Table 04: Substantial pharmacokinetic drug-drug interactions between Anti-Retroviral Drugs and Rifampicin/Rifabutin

Drug	Interacting with	Mechanism/effects	Recommendations
Rifampicine	Atazanavir	Substantial decrease in Atazanavir AUC even with double dosing or boosting with ritonavir	Avoid this combination
	Darunavir	Substantial decrease in darunavir concentration	Avoid this combination
	Efavirenz	Efavirenz decreased 22%	No dose adjustment needed
	Etravirine	Significant reduction in etravirine concentration	Avoid this combination
	Indinavir	Indinavir AUC decreased 89%	Avoid this combination
	Boosted Lopinavir	Lopinavir AUC decreased 75%	Avoid this combination
	Maraviroc	Maraviroc AUC decreased 63%	Avoid this combination
	Nevirapine	Nevirapine AUC decreased >50%	Used with caution. Monitor ART response
	Raltegravir	Raltegravir AUC decreased 40%	Increase Raltegravir dose to 800mg bd orally
	Ritonavir 600mg bd	Ritonavir AUC decreased 35%	Monitor ART activity of Ritonavir
	Tipranavir	Significant reduction in Tipranavir concentration	Avoid this combination
	Zidovudine	Zidovudine AUC decreased 47%	Monitor zidovudine efficacy
Rifabutin	Atazanavir	Rifabutin AUC increased to 210%	Decrease Rifabutin dose to 150mg three times a week
	Darunavir	Inhibit metabolism of Rifabutin	Decrease Rifabutin dose to 150mg three times a week
	Efavirenz	Rifabutin AUC decreased 38%	Increased rifabutin dose to 450 – 600mg/day
	Etravirine	Rifabutin AUC decreased by 17%	Use standard dose of rifabutin 300mg daily
	Boosted Lopinavir	Rifabutin AUC increased 303%	Decrease Rifabutin dose to 150mg three times a week
	Ritonavir	Rifabutin AUC increased 430%	Decrease Rifabutin dose to 150mg three times a week

Annexure 8 Drug interactions with Rifampicin

Substantial pharmacokinetic drug-drug interactions between Anti-Retroviral Drugs and Rifampicin/Rifabutin

Drug	Interacting with	Mechanism/effects	Recommendations
Rifampicine	Atazanavir	Substantial decrease in Atazanavir AUC even with double dosing or boosting with ritonavir	Avoid this combination
	Darunavir	Substantial decrease in darunavir concentration	Avoid this combination
	Efavirenz	Efavirenz decreased 22%	No dose adjustment needed
	Etravirine	Significant reduction in etravirine concentration	Avoid this combination
	Indinavir	Indinavir AUC decreased 89%	Avoid this combination
	Boosted Lopinavir	Lopinavir AUC decreased 75%	Avoid this combination
	Maraviroc	Maraviroc AUC decreased 63%	Avoid this combination
	Nevirapine	Nevirapine AUC decreased >50%	Used with caution. Monitor ART response
	Raltegravir	Raltegravir AUC decreased 40%	Increase Raltegravir dose to 800mg bd orally
	Ritonavir 600mg bd	Ritonavir AUC decreased 35%	Monitor ART activity of Ritonavir
	Tipranavir	Significant reduction in Tipranavir concentration	Avoid this combination
	Zidovudine	Zidovudine AUC decreased 47%	Monitor zidovudine efficacy
Rifabutin	Atazanavir	Rifabutin AUC increased to 210%	Decrease Rifabutin dose to 150mg three times a week
	Darunavir	Inhibit metabolism of Rifabutin	Decrease Rifabutin dose to 150mg three times a week
	Efavirenz	Rifabutin AUC decreased 38%	Increased rifabutin dose to 450 – 600mg/day
	Etravirine	Rifabutin AUC decreased by 17%	Use standard dose of rifabutin 300mg daily
	Boosted Lopinavir	Rifabutin AUC increased 303%	Decrease Rifabutin dose to 150mg three times a week
	Ritonavir	Rifabutin AUC increased 430%	Decrease Rifabutin dose to 150mg three times a week

Annexure 9 Renal adverse effects of drugs commonly used in HIV infection

Table 2

Renal adverse effects of drugs commonly use in HIV infection[1].

Drug	Disorder/ Pathology	Finding	Comments
Acyclvior	Crystalluria	May precipitate ARF	Treat with hydration; avoid rapid intravenous bolus; adjust dosage for renal function.
Amphotericin B	Increased tubular permeability and/or renal vasoconstriction	↑ Cr, ↓ serum K^+ and Mg^{++}, ↓ urine bicarbonate; distal renal tubular acidosis; non-anion-gap metabolic acidosis	More severe renal failure likely with concurrent nephrotoxins (aminoglycosides, foscarnet), diuretic use, hypovolemia, chronic renal failure. Hydration with normal saline is somewhat protective. Switch to lipid formulation of amphotericin B for rise in Cr of >2.5 mg/dL while on conventional amphotericin B; continue to monitor electrolytes.
Cidofovir	Proximal tubular injury	(See TDF, above)	Incidence reduced with hydration (normal saline)• and probenecid, which blocks absorption of drug by tubular epithelial cells. Check Cr and urine protein within 48 hours before each dose and reduce dosage for decreased CrCl or eGF. Discontinue drug for either Cr ≥0.5 mg/dL above baseline or proteinuria ≥3+ on dipstick analysis.
Foscarnet	ATN Crystal deposition	↑ Cr, ↓ serum Ca^{++}, Mg^{++}, phosphorus; *so metimes*↑ serum $Ca^{++}$and phosphorus	Cr generally increases after 1-2 weeks of foscarnet therapy. Renal toxicity is reduced with infusion of 0.5-1 liter of normal saline with or before foscarnet.

			Toxicity is more likely with concomitant nephrotoxins.
Pentamidine	Tubular toxicity (ATN)	↑ Cr, ↑ serum K^+; ↓ serum Mg^{++} and Ca^{++}	Discontinuation of pentamidine reverses toxicity, although that process can take several weeks. Usually seen with high-dose therapy (eg, PCP treatment), but sometimes seen with lower dosages. Hyperkalemia more common with pre-existing renal insufficiency.
TMP-SMX	Hyperkalemia caused by blockage of Na^+ channel in collecting tubule Impaired tubular secretion of Cr	↑ Serum K^+ ↑ Cr	Usually seen with high-dose therapy (eg, PCP treatment), but sometimes seen with lower dosages. Hyperkalemia more common with pre-existing renal insufficiency. Hyperkalemia often appears after 1 week of therapy. Consider monitoring serum K^+, especially with high-dose therapy.

Annexure 10 Disclosure of serostatus of children

Dr. Lilani Rajapaksa

There are obvious health benefits such as improving access to HIV care, treatment and adherence and reduced risk of death from disclosure of their own HIV status to HIV infected children. Disclosure is not just a single event but an important step in the process of adjustment by the infected child, family and the care givers to a chronic illness with life challenges.

Disclosure decisions are complex due to stigma, social support concerns, family relationship and support concerns and concerns about child's ability to understand and cope with the nature of the illness.

When to disclose depends on the age, cognitive level and emotional maturity of the infected child. Should occur at a time when the child is clinically and emotionally stable and the caregiver is ready to disclose. Disclosure of HIV status is usually a process involving on-going discussions as the child matures physically, cognitively and emotionally.

Who will disclose to the child should be guided by the quality of the relationship with the child and level of competency in disclosure. Serostatus of the child can be disclosed by the parents/caregivers, Health care workers or both parties together. If disclosure is done by parents/caregivers, they should be guided by well trained HCWs.

Important points -

- HCWs should work with caregivers to develop an individualised disclosure plan that meets needs of the child and the family. They should discuss caregiver's concerns about disclosure, importance of on-going communication with the child regarding health issues, benefits and risks of disclosure and potential harm that can result from nondisclosure.
- Counselling and language used should be appropriate to the age, developmental and cognitive level of the child.
- Medical facts can be explained minimally at the beginning and add later on. Information on HIV infection, care and support available and psychosocial aspects need to be addressed.
- Explore child's knowledge on their own health and HIV/AIDS, assess their coping skills, family and peer support, school/work progress and interests/ambitions.
- Children who are emotionally unstable or who have poor coping skills may need closer post-disclosure follow-up.

Post disclosure plan for assessment of the child's emotional well-being and functioning at each visit (school functioning, interests, mood and behaviour) and provision of continuous support is very important.

Annexure 11 Bone mineral density (BMD) issues with TDF

Bone mineral density (BMD)	(BMD) Please select the make of DXA scanning equipment used and the enter the actual femoral neck BMD (in g/cm2). Alternatively, enter the T – score based on the NHANES iii female reference data. In patients without a BMD test, the field should be left blank (see also notes on risk factors) (provided by Oregon Osteoporosis Center)

Notes on risk factors

Previous fractures

A special situation pertains to a prior history of vertebral fracture. A fracture detected as a radiographic observation alone (a morphometric vertebral fracture) counts as a previous fracture. A prior clinical vertebral fracture or a hip fracture is an especially strong risk factor. The probability of fracture computed may therefore be underestimated. Fracture probability is also underestimated with multiple fractures.

Smoking, alcohol, glucocorticoids

These risk factors appear to have a dose- dependent effect. i.e the higher the exposure, the greater the risk. This is not taken in to account and the computations assume average exposure. Clinical judgement should be used for low or high exposures.

Rheumatoid arthritis (RA)

RA is a risk factor for fracture. However, osteoarthritis is, if anything, protective. For this reason reliance should not be placed on a patient's report of 'arthritis' unless there is clinical or laboratory evidence to support the diagnosis.

Bone mineral density (BMD)

The site and reference technology is DXA at the femoral neck. T – scores are based on the NHANES reference values for women aged 20-29 years. The same absolute values are used in men.