5.6. Non-Communicable Disease (NCD)

According to WHO estimates, non-communicable diseases, including hypertension, cardiovascular disease, renal disease, cancer, chronic respiratory disease, diabetes and mental health disorders, account for 63% of global deaths. Low- and middle-income countries bear 86% of the burden of non-communicable diseases.

Compared with the general population, PLHIV have increased risk of developing a range of chronic non-communicable diseases, including cardiovascular disease, hypertension, diabetes, chronic obstructive pulmonary disease, kidney disease and cancer.

Cardiovascular disease is now one of the leading causes of non-AIDS-related morbidity and mortality among PLHIV. Both HIV and non-communicable diseases require health systems that can deliver effective acute and chronic care and support adherence to treatment. Chronic HIV care provides the opportunity for assessing, monitoring and managing non-communicable diseases, especially through primary care.

Integrating interventions such as nutrition assessment, dietary counselling and support, smoking cessation, exercise promotion, blood pressure monitoring and when available cholesterol management as part of HIV care can help to reduce the risks of non-communicable diseases among PLHIV and improve HIV treatment outcomes. Therefore, screening of PLHIV for these comorbidities during every visit is a critical component of care and treatment package.

5.7. HIV and Mental Health Disorders

Globally, Mental Health Disorders (MHD) are more common among PLHIV than among the general population. Depression, Anxiety, PTSD, and Cognitive impairment are common types of MHD in patients following HIV diagnosis or during its progression to AIDS. The magnitude of common MHDs among PLHIV in Ethiopia has been studied and the following results show that the prevalence is significantly high. A meta-analysis has shown that prevalence of depression among PLHIV in Ethiopia was 36.65%, and the prevalence for common mental disorders among PLHIV have been found to be 33% in Hawasa and 24% in Debre Markos.

One of the reasons why mental health problem are more common among PLHIV is that having MHD is one of the risk factor for becoming infected with HIV. People with MHDs are more likely to be exploited by others and less able to negotiate safe sexual relationships including use of condoms with partners. They may be less likely to stay in the kind of steady, long-term relationships in which partners can protect each other from getting HIV.

Furthermore, mental, neurological and substance use disorders (MNS) are important in HIV care because of issues related to adherence, risk of HIV transmission, and overall outcome of HIV care. Evidence also suggests that treatment of co-morbid psychiatric conditions may improve adherence to ART, underlining the importance of recognition and treatment of psychiatric conditions. Evidence further pointed out that there is continued under-recognition and under treatment of these conditions among PLHIV. Factors contributing to the under-recognition of

MNS symptoms related to:

- The overlap between the symptoms of depression and symptoms of HIV disease.
- Related to recognition of certain psychiatric disorders, specifically depression and anxiety, there is a mistaken belief that these symptoms are expected in those diagnosed with HIV disease. Depression or anxiety symptoms that are more severe or that persist beyond the period of initial discovery of HIV infection should prompt evaluation and treatment.
- The neuropsychiatric side effects associated with some ARVs like Zidovudine, abacavir, and efavirenz have been associated with neuropsychiatric symptoms.

The other issue worth mentioning with regard to comorbid HIV and MNS problems is drug-drug interactions (DDIs) between the ARV drugs and psychotropic drugs. DDIs are important to consider in the co-treatment of the two health conditions because they make either group of drugs less effective or toxic.

Therefore, integration of MNS symptom screening into HIV services is important to improve treatment outcome of PLHIV. This has been implemented in Ethiopia using a task-sharing approach among lay healthcare works (case managers) and clinicians. In this model, trained lay case managers proactively screened patients using a mental health screening tool and subsequently linked potential clients with trained clinicians working at HIV clinics for further diagnosis and treatment. A pilot project study conducted in selected sites in Amhara and Tigray regions showed that, of the total PLHIV screened by case managers, clinicians confirmed that about 8% of them had some form of MHD. In this study, the concordance between the case managers' screening results and the clinicians' diagnoses was about 68% over the 15-month pilot implementation period Therefore, the proactive screening of PLHIV for MHD helps to early identification and management PLHIV with co-morbidities. Ten percent or more of people will experience one of the common mental disorders in the course of their life. It includes problems with low mood, excessive worry, or difficult behaviors that do get in the way of daily function.

The rest are categorized as severe mental disorders which are much less common, but much more serious. They include problems with thinking that severely limit function and may make the person a danger to themselves or others.

Below are the common MNS problems integrated into HIV clinic. Please refer to annex 20 for the brief mental health disorders symptom screening and referral tool.

Priority mental health disorders (WHO)

1.Psychosis: this is the collective name for a group of serious disorders characterized by changes in behavior (for example poor self-care, restlessness), strange thoughts or beliefs (for example believing that others wish to do the individual harm) and related dispositions.

2.Mania: a form of severe mental illness in which a person is excessively happy or irritable (experiences extreme mood swings), appears

over-active and sleeps poorly. People with mania have poor reasoning skills (they have difficulty understanding what is good and what is bad), and display excessive self-confidence.

3.Depression: this is the most common priority disorder and is characterized by excessive sadness, loss of interest, lack of energy and related symptoms.

4.Suicide: refers to the intentional ending of one's own life.

5.Abuse of alcohol and other substances: this is the excessive use of these substances to the detriment of one's health.

6.Childhood mental disorders: these are different types of mental disorders related to childhood developments.

7.Dementia: is characterized by memory problems and broader problems with thinking and understanding.

8.Epilepsy: this is a chronic or longstanding condition caused by abnormal electrical conductions in the brain. In its most obvious form, it is characterized by episodic loss of consciousness and repetitive jerky movements of the body.

On the other hand, ACMs/HCWs should prioritize the below PLHIV groups for MHD screening at ART and PMTCT clinic.

- Newly initiated on ART
- Patients with high viral load
- Patients re-engaged into care after treatment interruption
- Patients with problem of ART adherence
- Patients who refused to start ART
- Patients who are on ART preparation for >2 weeks
- Patients with advanced HIV disease
- Patients with other health problems

Mental health aspects of living with HIV

Reaction to the diagnosis

People have many different reactions to learning that they have HIV infection. They may react initially with anger, shock, or denial and these reactions can change or recur over time.

If people **feel guilty** for something that they feel led to their acquisition of HIV:

- Reassure that no one can foresee all the consequences of what they do
- Reassure that life offers many opportunities to do good and they will have many chances in the future feel better about themselves.

For feelings of loneliness and isolation

- Note that there are millions of people living well with HIV, both in Ethiopia and other countries
- Note that they are right to be cautious about who they tell, but that over time they will find many accepting people and develop many close relationships
- Remind them that the ART site and its many services will always be a place that they can turn to for support and care

For feelings of grief and loss

- Acknowledge that this is a big change, that life looks very different
- Be optimistic that the loss will heal with time
- Express your willingness to be of support
- Suggest self-care
- Remind them that this is a treatable problem, and that you and the ART staff will be here to evaluate their concerns.

Mental health side effects of ARV drug

Many of the medications used to treat HIV and related infections have mental health-related side effects. For most medications, these are not common or severe. Some medications to think about in particular are:

- Efavirenz can cause mental health-related side effects in as many as half of patients taking it. Symptoms can begin on the first day of treatment but are likely to resolve after 2-4 weeks. Some can be very troubling, and include confusion, trouble concentrating, and vivid, odd dreams. Hallucinations and mood changes have also been seen, and depression has been reported. There is concern that these side effects can be made worse by alcohol or other substances. INH (used in the treatment of TB) can cause hallucinations, paranoia, and low mood.

Table 5.10. ART-psychotropic/antiepileptic drug interactions

Psychotropic drugs	Interactions
Carbamazepine	Decrease PI and NNRTI levels; use other anticonvulsant. Carbamazepine toxicity possible if combined with RTV.
Diazepam, bromazepam	All PI's can increase levels of diazepam and bromazepam, as can Efavirenz and nevirapine can decrease diazepam levels. Lorazepam, oxazepam, and temazepam are unaffected by ARVs.
Fluoxetine	No specific problems for PIs or NNRTIs. Can be some variation in the level of fluoxetine or the ARVs. But does interact with many other medications.
Haloperidol	PIs can increase haloperidol level; NNRTIs can decrease haloperidol levels.
Phenobarbital	Can decrease PI and NNRTI levels but is ok to use with NRTIs. Not recommended with LPV/r.
Phenytoin	Can decrease PI and NNRTI levels but is ok to use with NRTIs. Not recommended with LPV/r. If must use with LPV, may need higher doses of both medications.
Risperidone	Some PIs may increase risperidone levels. Avoid use with RTV.
Tricyclic antidepressants	OK with NNRTIs and NRTIs. OK with PI's except LPV/r, RTV, – those medications can raise the TCA level to toxic levels (use fluoxetine instead).
Valproic acid	No significant interactions

5.8.HIV related skin and oral conditions

HIV infection increases the prevalence and severity of skin and oral diseases, especially when the person's CD4 cell count declines below 200 cells/mm3. As a result, skin and oral conditions affect up to 90% of adults and children with HIV in resource-limited settings. Adverse drug reactions of the skin are also 100 times more common among people living with HIV than among the general population, and their prevalence increases as immunodeficiency worsens. Immune reconstitution inflammatory syndrome occurs in 10–25% of people living with HIV starting ART.

Different kinds of OI, such as herpes zoster, and other viral, fungal and bacterial infections occur in the skin. Manifestations of adverse drug reactions and non-infectious conditions also occur in the skin. In most instances diagnoses of skin disorders with HIV disease are made on clinical grounds. Most skin disorders in HIV disease can be cured or ameliorated, but a few fail to improve even with good general clinical and immunological responses to ART.

Pruritus is the most common dermatologic symptom in HIV infected patients. It can be localized indicating primary skin lesion, or generalized that may or may not indicate primary skin lesions. In many patients, pruritus may be severe and may not be amenable to available therapy. The most common skin conditions associated with pruritus in patients with HIV include the following:

1.Excessive dryness of the skin (Xerosis cutis)

2.Eczemas like seborrheic dermatitis or contact dermatitis

3.Folliculitis that may include infections by Staphylococcus aureus or hypersensitivity to insects

4.Drug eruptions

5.Scabies

6.Intertrigo (Candida, tinea, herpes simplex)

In most patients, diagnosis can be established by examining the lesions. However, as immune deficiency advances it may be useful to use investigations such as biopsy to diagnose specific dermatosis or use staining and culture to diagnose specific infections.

5.8.1. Etiological classification of skin disorders in HIV disease

Skin disorders in HIV infected patients can occur due to infections, neoplasm, and hypersensitivity to foreign agents including drugs, or to unknown causes. Nevertheless, infections are commonly seen in clinical practice; refer to the following table:

Table 5.11: Common skin infections in HIV disease.

Infections	Disease	Clinical Presentations	Treatment	Remark
Bacterial	Cellulitis	Poorly defined erythema. Pus and crust at the site plus signs of inflammation.	Adult: Amoxicillin 500 mg TID for 5-14 days based on clinical response or erythromycin 500 mg QID if allergic to penicillin. Children: 20-40mg/kg per day on TID basis	Mostly encountered lower extremities and often unilateral.
	Impetigo	Erythematous small papules usually limited to few lesions coalescing in to crusted plaques.	Use topical antibiotics: use Amoxicillin for extensive disease for 5-14 days (see dose above for adults and children) for 7 days	Usually a superficial lesion.
	Carbuncle	Nodular lesion with extensions to the deeper structure. Signs of inflammation present.	Adults: Cloxacillin 500 mg QID for ten days. Children: 50-100 mg/kg/day on QID basis	Involves the trunk as well as extremities.
Viral	Herpes simplex	Painful vesicular lesion around mouth or genitalia. Recurrent and extensive, difficult to eradicate during advanced immune deficiency.	Adults: Acyclovir 400 mg TID for ten days. Children 20 mg/kg/dose 4X/d	
	Herpes zoster	Painful and vesicular eruptions with dermatomal distribution. When healed, scar will remain.	Adults: Acyclovir 800 mg 5X per day for seven days. Monitor renal function. Children: 20–40 mg/kg per dose four times a day.	When it involves the eyes, it is a medical emergency. Do not give Acyclovir* if duration is >72 hours.

Infections	Disease	Clinical Presentations	Treatment	Remark
Viral	Warts / verrucae	Painless flat to raised warts over fingers or genitalia in advanced immune deficiency, they tend to be multiple and exophytic.	Podophyllin, Imiquimod, Cryotherapy, Consult experts	Premalignant and risk for cervical cancer.
	Molluscum Contagiosum	Umbilicated and raised facial lesions that tend to be very big during immunodeficiency state.	May not require therapy;	Contagious
Parasitic infestation	Scabies	Pruritic lesions ranging from pinpointed erythematous papules involving inter digital, axillae and groin areas to varying degrees of hyperkeratotic plaques associated with significant skin thickening and crusting.	BBL, lindane or permethrin to be applied to whole body. Ivermectin 200 microgram/kg stat orally.	Burrows are visible in mild infestations but in crust scabies may not be evident leading to misdiagnosis.
Fungus	Dermatophytosis	Superficial causing ringworm or athlete's foot	Topical antifungal for limited skin affected. Fluconazole for extensive lesion 100mg daily for ten days.	
	Thrush	White plaques on the buccal mucosa including the tongue that can be scraped off leaving red base (bleeding). Can be associated with candida paronychia or intertrigo.	Miconazole gel 2% apply BID Fluconazole 100 mg daily for ten days for recurrent or oropharyngeal thrush.	
	Deep Fungal Infection	Presentation varies from fungating nodules and tumors to ulcers and diffuse papulo nodular disease	Disseminated Cryptococcus can be confused for Molluscum contagiosum. Treat with amphotericin induction and/ or fluconazole maintenance.	

*If patient has ophthalmic involvement refer to ophthalmic specialist.

5.8.2. Pruritic Papular Eruption (PPE)

Pruritic papular eruption is common among HIV infected patients causing substantial morbidity in sub-Saharan Africa. Its prevalence ranges from12-46% and it is uncommon in HIV negative patients (PPV of 82-87% and may play role in diagnosing HIV). The pathogenesis is unknown but it may be related to hypersensitivity to arthropod bites. In extreme form, eosinophilia and eosinophilic infiltrates of the skin are present. Severity of rash often correlates with CD4 count. The clinical manifestation is intensely pruritic, discrete, firm papules with variable stages of development and predilection for extremities, though it can involve trunk and face with significant itching marks. Excoriation results in pigmentation, scarring and nodules. Treat with topical steroid and oral antihistamines. However, it is often refractory to treatment and hence short course prednisolone may be used. ART is often effective.

5.8.3. Dysphagia and odynophagia

Dysphagia (difficulty in swallowing) and odynophagia (painful swallowing) are symptoms of esophagitis occurring at advanced stages of AIDS. They are usually caused by candida, HSV, CMV, and aphthous ulcers. Esophagitis seriously impairs the patient's nutritional status. Therefore, prompt diagnosis and treatment are mandatory to avert nutritional complications and inability to swallow prescribed medications. Children will present with reluctance to eat, excessive salivation, or crying while feeding. If thrush is associated with dysphagia, odynophagia, and/or retrosternal pain, consider oesophageal candidiasis but this can also occur in the absence of oral thrush.

Oral candidiasis presents with oral sores, change in the sense of taste, and when it involves the throat and oesophagus, pain on swallowing; however it can be asymptomatic in some patients. Diagnosis is established clinically when a curd-like membrane is visible on the surface of the tongue and buccal mucosa. Typically the base of the membrane bleeds upon scraping it.

Diagnosis

Diagnosis of oral candidiasis is established clinically when a curd-like membrane is visible on the surface of the tongue and buccal mucosa. Typically, the base of the membrane bleeds upon scraping it.

Oesophagitis is frequently made on clinical grounds, but when facilities are available upper GI endoscopy with or without biopsy or contrast imaging may be done.

Treatment

Oral candidiasis: Oral and pharyngeal thrush are treated with oral miconazole gel 2% applied twice daily; patients should not eat/drink for two hours after applying the gel. If this does not work or is unavailable, use fluconazole 100mg daily for 14 days. Nystatin can also be used in place of miconazole as follows: apply suspension 5 times daily (after each meal and between meals) for 7 days (or until 48 hours after lesion resolves).

Dysphagia and/or odynophagia are treated as oesophageal candida on clinical grounds, in particular when oropharyngeal candida is present. Patients are empirically treated with Fluconazole in presumptive oesophageal

candida. If the response is unsatisfactory, they should be referred or investigated if facilities are available, to rule out other causes.

- Drug of choice: Fluconazole 200 mg (3mg/kg/day in children) PO daily for 14 days.
- Alternative: Ketoconazole 200 mg(3-6mg/kg/day daily in children) twice daily for 4 weeks.

Risk of recurrence after completing treatment may be high. If the patient is on ART, s/he should be investigated for treatment failure. Take necessary precautions regarding drug interactions especially with ketoconazole. Patients may need hospital admission for supportive care till the oesophageal symptoms improve and necessary long term treatments are started. If diagnosis suggests HSV eosophagitis use acyclovir 400mg po five times for 14 to 21 days.

5.9.HIV related Neurological conditions

Neurological manifestations of HIV can occur at any time from viral acquisition to the late stages of AIDS. They are varied and may affect any part of the nervous system including the brain, spinal cord, autonomous nervous system and the peripheral nerves. HIV affects the nervous system in 70-80% of infected patients. The effect may be due to direct effect of the virus, opportunistic infections and/or malignancies. For certain neurological manifestations, a single aetiology is responsible while in others it is due to multiple causes.

Most life-threatening neurological complications of HIV occur during the severe immunodeficiency state and specific aetiological diagnosis in the Ethiopian setting is often a major challenge. Thus, this unit attempts to guide the management of common opportunistic infections and other treatable conditions in the nervous system.

Neurological complications in HIV patients may be due to:

- HIV (HIV encephalopathy)
- OIs (toxoplasmosis, cryptococcal meningitis)
- Neurosyphilis
- Malignancies (primary CNS lymphoma); and
- Drugs (e.g. EFV, etc.)

Diagnosis of neurological disorders in HIV in our setting depends on the history and standard neurological examinations. In view of this, health care providers must be able to perform a physical examination to detect neurological abnormalities.

There can be single or multiple abnormal neurological findings in the same patient necessitating holistic neurological evaluation. Thus, the examination should include assessment of:

- Mental status comprising cognitive function, orientation and memory.
- Cranial nerves.
- Motor function including deep tendon reflexes (DTR).
- Sensation.

5.9.1. Toxoplasma gondii encephalitis

Toxoplasmic encephalitis (TE) is caused by the protozoan Toxoplasma gondii. Disease appears to occur almost exclusively because of reactivation of latent tissue cysts. Primary infection occasionally is associated with acute cerebral or disseminated disease. Sero-prevalence varies substantially in different communities; in Ethiopia, general prevalence is about 80%.

Clinical Manifestations

Among patients with AIDS, 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. Focal neurological abnormalities may be present on physical examination, and in the absence of treatment, disease progression results in seizures, stupor, and coma.

Diagnosis

HIV-infected patients with TE are almost uniformly seropositive for anti-toxoplasma immunoglobulin G (IgG) antibodies. The absence of IgG antibody makes a diagnosis of toxoplasmosis unlikely but not impossible. Anti-toxoplasma immunoglobulin M (IgM) antibodies usually are absent. Quantitative antibody titres are not useful for diagnosis. Definitive diagnosis of CNS toxoplasmosis requires a compatible clinical syndrome; identification of one or more mass lesions by CT, MRI, or other radiographic testing; and detection of the organism in a clinical sample. In the absence of imaging support, empirical treatment is justified when patients present with focal neurological findings and the CD4 count is < 200 cells µl. Failure to respond to conventional therapy, based on presumptive clinical diagnosis within a week or two of initiation of therapy, suggests the diagnosis to be unlikely.

With empirical treatment for toxoplasmosis, nearly 90% of patients will demonstrate clinical improvement within days of starting therapy. Radiological evidence of improvement is usual after 14 days of treatment.

Treatment

First line regimen in the Ethiopia:

- Adult: Trimethoprim/sulfamethoxazole 80/400, oral, 4 tablets 12 hourly for 28 days, followed by 2 tablets 12 hourly for 3 months in adults.
- Children: 10mg of trimethoprim + 50mg of sulfamethoxazole/kg per dose every 12 hours for 28 days followed by maintenance therapy at 50% reduced dosage for three months.

Secondary prophylaxis: use co-trimoxazole 960mg daily for adults and in children. Refer to Table 4.1

Alternative regimen

I. Sulfadiazine, 1-2 gm PO QID for six weeks or 3 weeks after resolution of lesion
Side effects: crystal urea, rash

Contraindication: severe liver, renal and haematological disorders; known hypersensitivity to Sulphonamides.
Dosage/form: 500 mg tablets,

PLUS

Pyrimethamine: loading dose of 200 mg once, followed by 50-75 mg/day.

Side effects: rash, fever and bone marrow suppression (neutropenia and thrombocytopenia).

Contraindication: folate deficiency

Dosage/form: 25 mg tablets

PLUS

Folinic acid (Leucovorin): 10-20 mg/d
Side effects: allergy
Dosage/form: 5 and 10 mg tablets

OR

II. Pyrimethamine and Folinic Acid (Leucovorin): (standard dose)

PLUS

Clindamycin: 600 mg QID

Side effects: toxicities include fever, rash, nausea and diarrhoea (including pseudomembranous colitis or diarrhoea related to Clostridium difficile toxin).

Adjunctive corticosteroids should be used for patients with radiographic evidence of midline shift, signs of critically elevated intracranial pressure or clinical deterioration within the first 48 hours of therapy. Dexamethasone 4 mg every six hours (0.15mg/kg/dose every 6 hours for children) is usually chosen and is generally tapered over several days and discontinued as soon as possible.

Anticonvulsants should be administered to patients with a history of seizures but should not be given routinely for prophylaxis to all patients with the presumed diagnosis of TE. Careful attention needs to be paid to any potential drug interactions.

5.9.2.Cryptococcal infection

Cryptococcal meningitis is one of the most important opportunistic infections and a major contributor to high mortality before and after ART is initiated. The main reasons for this high death rate include delayed presentation, together with poor availability and high cost of treatment. Most HIV-associated cryptococcal infections are caused by Cryptococcus neoformans. 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 mentation, personality changes, and memory loss that are usually a result of increased intracranial pressure, thought to result from impaired CSF absorption, or yeast infection of the brain.

Diagnosis

1. Lumbar puncture (LP) and CSF analysis:

- The opening pressure may be markedly elevated.
- CSF analysis
  - Protein:30-150 mg/dl

- WBC: 0-100 /mm3 (monocyte)
- Culture: positive 95-100%
- Indian ink: positive 60-80%
- Cryptococcal Ag (CrAG) > 95 % sensitive and specific

- If it is not possible or contraindicated to do LP, serum cryptococcal antigen can be used for diagnosis.

Management

Requires hospitalization and evaluation by physician

1.Induction phase

The following is recommended as the **preferred induction regimen.**

A single high dose (10 mg/kg) of Liposomal Amphotericin B with 14 days of flucytosine (100 mg/kg per day divided into four doses per day) and fluconazole (1200 mg/daily for adults; 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily) should be used as the preferred induction regimen.

The following induction regimens are recommended as **alternative options.**

- If Liposomal Amphotericin B is not available: For adults, adolescents and children, a short-course (one-week) induction regimen with Amphotericin B deoxycholate (1.0 mg/kg per day) and flucytosine (100 mg/kg per day, divided into four doses per day) followed by 1 week of fluconazole (1200 mg/day for adults, 12 mg/kg/day for children and adolescents, up to a maximum dose of 800mg daily), is the preferred option for treating cryptococcal meningitis among people living with HIV.

- If no Amphotericin formulation available: Two weeks of Fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents) + Flucytosine (100 mg/kg per day, divided into four doses per day).

- If Flucytosine is not available: Two weeks of Liposomal Amphotericin B (3–4 mg/kg per day) + Fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily).

- If Liposomal Amphotericin B and Flucytosine are not available: Two weeks of Amphotericin B deoxycholate (1.0 mg/kg per day) + Fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily).

2.Consolidation phase (8 weeks)

Option A: Fluconazole 800 mg/day (In children 12mg/kg/day)

Option B: Fluconazole 400-800 mg/day

Maintenance treatment (or secondary prophylaxis)- Fluconazole 200 mg daily (in children 6mg/kg/day).

Additional points about cryptococcal meningitis

1)Management of elevated intracranial pressure (ICP):

Management of increased ICP is critical as >90% of deaths in the first two weeks and 40% of deaths in weeks 3-10 are due to increased ICP. Failure to manage elevated ICP is the most common and most dangerous mistake in management (since the ICP is non-communicating hydrocephalus there is no risk of CSF tapping within the recommended volume).

- Daily serial LP should be done to control increased ICP by drawing 20-30 ml of CSF based on patient's clinical response. Signs of ICP include headache, altered mental status, meningismus and changing in hearing or vision should be closely monitored, if possible opening pressure should be measured.
- There is no role for acetazolamide, mannitol, or corticosteroids to reduce intracranial pressure.

2) Discontinuation of maintenance treatment (secondary prophylaxis)

When patients are stable and adherent to ART and anti-fungal maintenance treatment for at least one year and have a CD4 cell count of greater than or equal to 200 cells/mm3 (two measurements six months apart).

3) Timing of ART initiation

- Immediate ART initiation is not recommended in HIV-infected patients with cryptococcal meningitis due to the high risk of IRIS, which may be life-threatening.
- ART initiation should be deferred until there is evidence of a sustained clinical response to anti-fungal therapy usually 4-6 weeks from the initiation of antifungal treatment.
- Poor prognostic signs
- Extra CNS manifestation (especially pulmonary)
- Altered mental status
- Low CSF WBC count less than 20cells/μL
- High CSF cryptococcal antigen titer

Prevention of cryptococcal disease

According to a pilot study conducted in Ethiopia from June 2015 to July 2016, in 22 high case load facilities in all regions, the proportion of newly enrolled clients with CD4 count less than 100 cells/mm3 was 25.88%. In the same study, the prevalence of clients screened positive for cryptococcal antigenemia was high (9.9%).

The use of routine serum or plasma CrAg screening in ART-naive adults followed by pre-emptive antifungal therapy if CrAg screening is positive to reduce the development of cryptococcal disease, should be considered prior to ART initiation:

- Where patients with a CD4 count less than 100 cells/mm3; and
- Where this populational so has a high prevalence (>3%) of cryptococcal antigenemia.

The following algorithm or decision-making guide shows how to decide whether a patient needs prophylactic fluconazole treatment to CrAg screening positive and asymptomatic patients with CD4 count less than 100 cells/mm3.

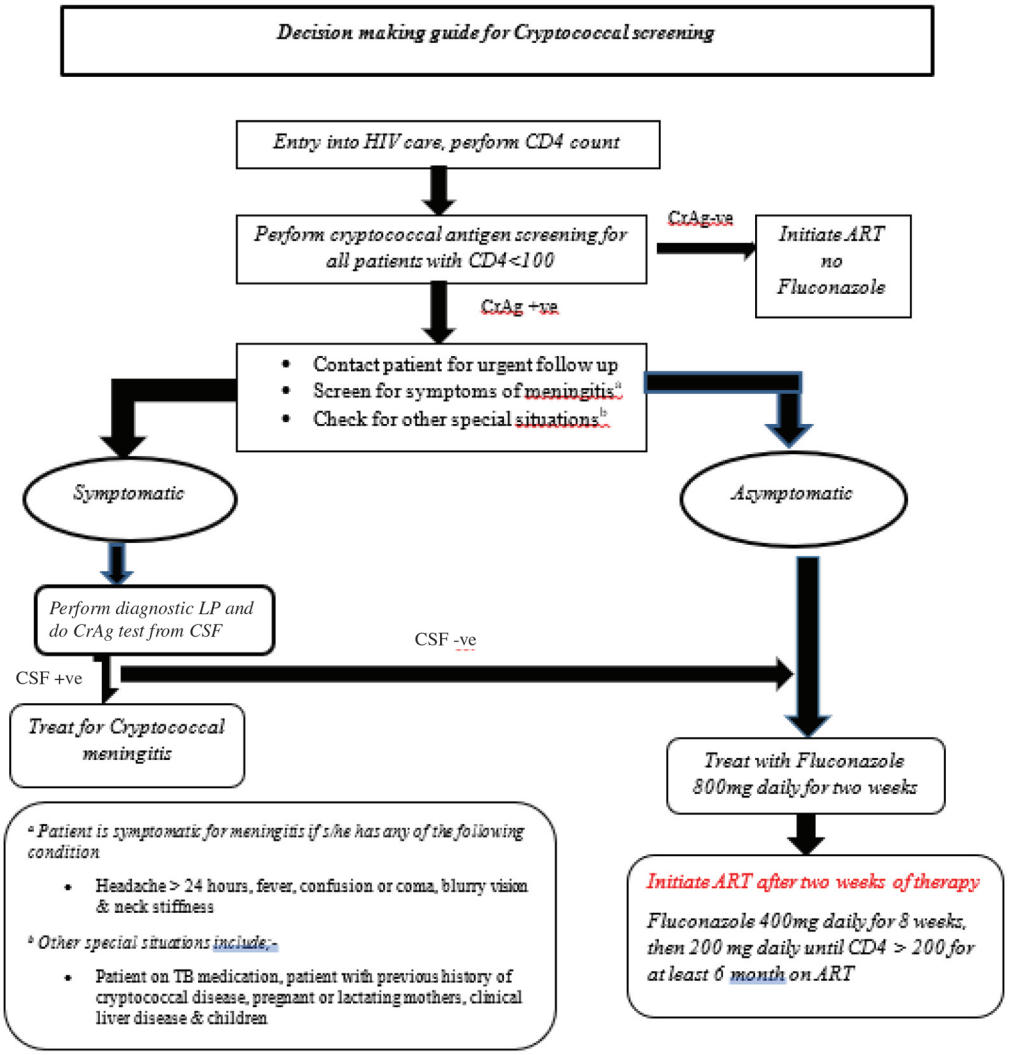

Figure 5.6. Decision-Making Guide for Cryptococcal Screening

When cryptococcal antigen screening is not available, fluconazole primary prophylaxis should be given to adults and adolescents living with HIV who have a CD4 cell count of < 100 cells/mm3.

5.9.3. Peripheral neuropathies

Peripheral neuropathies are among the most common causes of painful legs in HIV infection; they arise as a complication of HIV infection itself, of drug therapy, or of other metabolic or organ dysfunction or nutritional deficiencies.

Distal symmetrical sensory polyneuropathy is the most common presentation but mono-neuropathies can also occur. The neuropathies associated with HIV can be classified as:

- Primary, HIV-associated.
- Secondary causes related to medications (INH), OIs or organ dysfunctions.

Diagnosis

Peripheral neuropathy diagnosis in HIV-infected patients is based on the clinical picture presenting with pain, tingling sensations, paraesthesia or numbness. Physical examination can reveal depressed or absent ankle reflex, decreased sensitivity to different modalities of sensation and in severe cases, difficulty in walking. The feet and sometimes the hands are involved in symmetrical distribution. The diagnosis can be supported by electro diagnostic studies including electromyography (EMG) and nerve conduction studies (NCS) when available. Blood tests are frequently obtained to exclude other causes of neuropathy. In most instances, however, diagnosis is almost always clinical.

Treatment

- Avoid the offending agent if identified.
- Remove other drugs associated with peripheral neuropathy.
- Supplemental vitamin intake for all patients including concomitant administration of pyridoxine with INH.
- Adjuvants for pain management (such as Amitriptyline, carbamazepine) indicated for patients with pain and paraesthesia.

Monitoring of events

- Recognize presence of peripheral neuropathy.
- Assess severity at each clinical visit.
- Avoid drugs causing neuropathy.

5.10. Visceral leishmaniasis

Visceral Leishmaniasis (VL) is a systemic parasitic illness, transmitted primarily by the phlebotomine sand fly from animal or human reservoirs. Visceral Leishmaniasis is endemic in Ethiopia, with patchy distribution in the southern and north-western lowlands. The causative parasite is L. Donovani. VL has emerged as a major OI associated with HIV. In HIV patients, VL represents reactivation of latent infection with Leishmania parasite.

Clinical features

The cardinal signs of VL in patients with HIV infection are unexplained fever, splenomegaly, and pancytopenia (anemia, leucopenia and thrombocytopenia). Presentation may not be typical. The bone marrow is packed with parasites but two-thirds of cases have no detectable anti Leishmanial antibodies. CD4+ cell count in co-infected patients is usually <300cells/ml.

Diagnosis

Parasite Detection-Visualization of the amastigote form of the parasite by microscopic examination of aspirates from lymph nodes, bone marrow or spleen aspiration. *Culture improves the detection of the parasites. However, this technique remains restricted to referral hospitals or research centers.

Antibody Detection-DAT and rK39 have been extensively evaluated and used for the diagnosis of VL in the field and in laboratory settings.

Antigen Detection Test-It is more specific than the antibody-based immunodiagnostic test. Evaluation of the performance of a urine latex agglutination (KATEX) at the Indian subcontinent and East Africa has shown that this test has a good specificity but only a low to moderate sensitivity.

Molecular Techniques-Compared to the other diagnostic techniques available, the molecular approaches remain expensive and technically highly demanding. Their applicability in the endemic areas is highly questionable.

Treatment:

Ambisome at a total dose of 30 mg/kg (5 mg/kgon day 1, 3, 5, 7, 9, 11) and miltefosine 2.5 mg/kg/day for 28 days, starting from day 1 (100 mg/day for patients weighing more than 30 kg, 150 mg/day for patients weighing more than 45 kg).

Please refer to the VL guideline for additional information, second line regimen and specific procedures on the dosage and administration of drugs.

Treatment of relapsed patients: These are patients who are slower to respond and have a higher chance of further relapse and of becoming unresponsive to anti-monial drugs. Treatment is the same as above.