CHAPTER FIVE:

PREVENTION, SCREENING, AND MANAGEMENT OF COMMON CO-INFECTIONS AND COMORBIDITIES

ART has reduced mortality and morbidity associated with HIV and transformed HIV into a chronic disease requiring lifetime care. Coinfections and comorbidities, including physical and mental health conditions are common among people living with HIV. Comprehensive HIV care includes combination HIV prevention, the promotion of general health and well-being, maintaining quality of life, ART, the prevention and management of coinfections and comorbidities.

Opportunistic infections are the predominant causes of morbidity and mortality among HIV-infected patients. The level of immunity determines the occurrence and type of OIs. In general, milder infections such as herpes zoster and other skin infections occur early whereas serious life-threatening infections such as CNS toxoplasmosis and Cryptococcal meningitis occur later with severe immune-suppression. Some life-threatening infections, such as pneumonia and TB, may occur early as well as later. When TB occurs later it is atypical, more disseminated and more extra pulmonary. This chapter provides a brief overview of common and important concomitant conditions among people living with HIV. This includes information on co-trimoxazole prophylaxis, the diagnosis, prevention and treatment of TB, pneumonia, viral hepatitis, sexually transmitted infections, cervical cancer prevention and mental health.

Recommended general care for PLHIV

The following package of care and prevention intervention are nationally recommended for adults, adolescents and children living with HIV:

- Psychosocial counselling and support
- Disclosure and partner notification
- Co-trimoxazole prophylaxis
- TB counselling, screening and preventive therapy
- Preventing common fungal infections
- Preventing sexually transmitted infections and supporting reproductive health needs, including preventing and screening for cervical cancer
- Prevention of malaria
- Nutrition
- Family planning
- Prevention of mother-to-child HIV transmission;
- Water sanitation and hygiene
- Orphans and vulnerable children (OVC)

General strategies to prevent opportunistic infections are:

- Reduction of exposure
- Chemoprophylaxis (primary/secondary)
- Immunization and
- Rapid ART initiation

5.1. Co-trimoxazole preventive therapy (CPT)

Co-trimoxazole preventive therapy (CPT) should be implemented as an integral component of a package of HIV-related services. Existing recommendations cover initiation of CPT among adults, adolescents, pregnant women, and children for prevention of pneumocystis pneumonia, toxoplasmosis, bacterial infections and diarrhea caused by Isospora belli or Cyclospora species, as well as benefits for malaria prophylaxis.

Table 5.1 CPT indication for primary prophylaxis

Age	Criteria for initiation	Criteria for discontinuation*	Monitoring approach
HIV exposed infants	In all, starting at 4–6 weeks after birth	Until the risk of HIV transmission ends or HIV infection is excluded	According to the national HEI follow up schedule
<5 years	In all	Discontinue when they become older than 5years of age who are clinically stable, with evidence of immune recovery and/ or viral suppression on ART**	Clinical at 3-month
Intervals ≥5 years, including adults	Any WHO stage and CD4 count ≤ 350 cells/mm3 Or WHO stage 3 or 4, irrespective of CD4 level	Discontinue in those who are clinically stable (those individuals on ART for at least one year without any new WHO clinical stage 2, 3 or 4 events) with; ■ Evidence of immune recovery and/or viral suppression (CD4 count >350 cells/ mm3, with viral load suppression) or ■ Two consecutive CD4 count > 350 cells/mm3 if no VL result	

Contraindications to co-trimoxazole preventive therapy:

- Severe allergy to sulfa drugs
- Severe liver disease
- Severe renal disease and
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency

Table 5.2: Dosage of co-trimoxazole for adults, adolescents, children and infants.

Age(weight)	Suspension (240 mg/5ml co-trimoxazole)	Single strength tab (480 mg of Co-trimoxazole)	Double strength tab (960 mg of co-trimoxazole)
Up to 6month (5kg)	2.5ml/day	¼ tab/day	-
6 months to 5 yr (5-15 kg)	5 ml/day	1/2 tab/day	-
6-14 yr (15-30 kg)	10ml/day	1 tab/day	½ tab/day
>14 yrs (>30 kg)		2 tab/day	1 tab/day

Table 5.3: Adverse effects of CPT and management.

Toxicity	Clinical description	Recommendation
Grade 1	Erythema, pruritis	Prescribe antihistamine and continue CPT and close follow-up.
Grade 2	Diffuse maculopapular rash, dry desquamation	Prescribe antihistamine and continue CPT and close follow-up.
Grade 3	Vesiculation, minor mucosal ulceration	STOP CPT, manage and re-introduce after 2 weeks with observation (desensitize).
Grade 4	Exfoliative dermatitis Steven-Johnson syndrome or erythema multiforme, moist desquamation	STOP CPT NEVER RESTART CO-TRIMOXAZOLE

5.2.Tuberculosis

TB is the most frequent life-threatening OI and a leading cause of death among HIV infected people. TB remains the leading cause of mortality among people living with HIV, despite substantial scale-up of ART, accounting for 30% of the AIDS-related deaths reported in 2019. TB increases HIV replication through the process of immune activation leading to increased viral load and this results in a more rapid progression of HIV disease. On the other hand, HIV increases susceptibility to be infected with M. Tuberculosis, the risk of progression to TB disease and the incidence and prevalence of TB. The lifetime risk of HIV positive individuals to develop TB is 50%, the annual risk is 10%. The WHO recent estimation indicates the risk of developing active TB disease is 18 times higher in PLHIV. In Ethiopia, WHO estimation indicated that 5.3% of TB cases notified in PLHIV in 2019. Moreover, a national level data report indicated that the prevalence of TB in PLHIV is 7.3%. Thus, it is essential for both TB and HIV control programs to synergize their joint efforts and intensify the implementation of TB/HIV collaborative activities to mitigate the dual burden of TB/HIV in populations at risk or affected by both diseases. The rationale for the integration is that tuberculosis and HIV prevention and control programs share mutual challenges of high impact of TB on HIV and vice versa. Therefore, the two programs must collaborate to provide better service for the co-infected patients.

Nationally recommended TB/HIV collaborative activities

A. Strengthen the mechanisms for integrated TB and HIV services delivery

- Strengthen the coordination mechanism for integrated TB/HIV services at all levels;
- Conduct surveillance to determine HIV burden among TB patients and TB burden among HIV patients;
- Carry out joint TB/HIV planning for integrated TB and HIV services delivery; and
- Conduct monitoring and evaluation of collaborative TB/HIV activities.

B. Reduce the burden of TB in HIV infected people and initiate early antiretroviral therapy (the three I's i.e., Intensive case finding, TB preventive therapy and Infection control)

- Intensify TB case finding and ensure quality TB treatment;
- Initiate TB prevention with earlier initiation of ART and TB Preventive therapy (TPT); and
- Ensure tuberculosis infection control in healthcare and congregate settings.

C. Reduce the burden of HIV in patients with presumptive and diagnosed TB.

- Provide HIV testing and counseling to presumptive and confirmed TB patients.
- Provide HIV prevention services for presumptive and confirmed TB patients;
- Provide co-trimoxazole preventive therapy for HIV positive TB patients.
- Ensure HIV/AIDS prevention, treatment, and care for HIV positive TB patients; and
- Provide ART for HIV positive TB patients.

Table 5.4 Timing of ART for adults and children with TB

New HIV positive Patients with signs and symptoms suggesting (presumptive tuberculosis cases)	Patients with tuberculosis found to be HIV positive	HIV positive patients taking ART diagnosed with TB
■ Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment and to people living with HIV with signs and symptoms suggesting TB. Except for central nervous system disease (meningitis), initiate ART while rapidly investigating for TB, with close follow-up within seven days to initiate TB treatment if TB is confirmed.	■ ART should be started in all TB patients, including those with drug-resistant TB, irrespective of the CD4 count. ■ ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 count, among all people living with HIV. (Adult, adolescent and children), except when signs and symptoms of meningitis are present. ■ ART should be delayed at least four weeks (and initiated within eight weeks) after treatment for TB meningitis is initiated. Corticosteroids should be considered adjuvant treatment for TB meningitis. (Note. For people living with HIV with TB meningitis, immediate ART is associated with more severe adverse events compared with initiating ART two months after the start of TB treatment) ■ DTG should be used as the preferred drug in patients starting ART while on Anti-tuberculosis treatment but dose of DTG should be doubled (50 mg BID). ■ When second line is initiated LPV/r is preferable. Note that the dose of the ritonavir should be doubled to counter the effect of Rifampicin on the Protease inhibitors.	■ Start anti-TB ■ Modify ART regimen to avoid drug-drug interaction ■ Evaluate for treatment failure

The 3Is intervention

I. Intensify TB case finding and ensure quality TB treatment

Tuberculosis case finding should be intensified in all HIV testing and counseling services for HIV positive clients by using a set of simple questions for early identification of presumptive TB cases. HIV positive clients coming through HIV testing services should be informed about the advantages of being screened for TB. Once informed about the risk of developing active TB, they should undergo screening for it. Adults and adolescents living with HIV should undergo intensified tuberculosis case finding using symptom-based TB screening questions should be instituted at chronic HIV care and treatment clinics for all people living with HIV. Any HIV positive patient with TB screen positive result should undergo appropriate evaluation and investigation for TB. In addition to symptom based screening, to consider sensitive screening test like CXR for routine screening of TB in PLHIV with no sign and symptoms of TB.

Symptom based TB screening for all PLHIV

All clients living with HIV infection should be screened for active TB with any one of the following symptoms:

Adult and adolescents:

- Current cough
- Fever
- Weight loss or poor weight gain
- Night sweats

Children less than 10 years:

- Current cough,
- Fever,
- Poor weight gain
- Close contact with a person with TB disease

Clients with any one of the above symptoms should be investigated for active TB

Diagnosis of TB in HIV infected people

Although there have been significant improvements in the diagnosis and treatment of TB, there are still limitations in early detection and treatment of all forms of TB cases among PLHIV. A systematic review study that estimated the prevalence of TB in PLHIV studies reported on postmortem testing showed 46% of TB cases remain undiagnosed, which made TB the most prominent opportunistic infection among PLHIV. Moreover, of the total 815,000 estimated HIV-associated TB cases worldwide in 2019, only 56% were notified. This indicates that TB diagnosis is still a challenge in PLHIV, and it is rarely bacteriologically confirmed.

The conventional sputum microscopy is the cheapest and fastest method that is used to diagnose TB since 1882. However, the sensitivity of sputum smear microscopy for the diagnosis of TB is low in PLHIV due to poor quality sputum production and low bacillary concentration.

Particularly in severely immunocompromised patients, the sensitivity of sputum smear microscopy is significantly reduced. Other challenges that make TB diagnosis difficult

include non-specific clinical presentation of TB that is attributable to high prevalence of extra-pulmonary and disseminated forms of TB in individuals with advanced HIV disease.

Currently, rapid, and more accurate molecular technologies have been developed and available to diagnose TB in PLHIV. Polymerase chain reaction (PCR), real-time PCR, and loop-mediated isothermal amplification (LAMP) are the molecular techniques that are commercially available for the diagnosis of TB. However, the diagnostic performance of these technologies has not been fully evaluated for the diagnosis of TB in PLHIV.

Although rapid and accurate molecular assays have significantly reduced the gap in TB case detection among PLHIV, their accessibility continued to be a challenge, due to the infrastructure required and the cost of procurement and maintenance. Thus, access to rapid and accurate diagnostic tests at the point of care is significantly restricted in resource limited settings where the burden of TB/HIV co-infection is high. Moreover, interruption of electricity and inadequate laboratory infrastructure and inefficient sample referral mechanisms are the challenges that limit the accessibility of rapid and accurate molecular diagnostic tests.

To minimize the challenges that are associated to sputum based diagnostic tests, urine based rapid TB diagnostic tests are recommended to detect TB in PLHIV with Advanced HIV Disease. Alere lipoarabinomannan (LAM) assay is one of the urine based rapid diagnostic tests for TB detection in PLHIV. Evidence suggests the importance of LAM in the detection of TB at high TB/HIV burden settings. It is recommended for use as a simple point-of-care test to assist TB diagnosis in HIV positive adult patients with signs and symptoms of TB and with low CD4 cell counts. Based on the generalization of the data from adults, this recommendation is also used in children living with HIV who have signs and symptoms of TB. However, there is limited evidence on the specificity of LAM test in children.

LAM test could decrease mortality through quicker diagnosis and early treatment commencement among PLHIV and severely sick.

Eligible PLHIV for LF-LAM Test

WHO 2019 policy update on LF-LAM recommends the currently available urinary LAM assays have suboptimal sensitivity and are therefore not suitable as general diagnostic tests for TB. However, unlike traditional diagnostic methods, they demonstrate improved sensitivity for the diagnosis of TB among individuals coinfected with HIV. The estimated sensitivity is even greater in patients with low CD4 cell counts.

Therefore, HIV-positive adults, adolescents and children with the following criteria are eligible for Urine LF-LAM test to assist in the diagnosis of active TB:

For inpatient settings

- With signs and symptoms of TB (pulmonary and/or extra pulmonary)
- With advanced HIV disease or who are seriously ill

- Irrespective of signs and symptoms of TB, with a CD4 cell count of less than 200 cells/mm3

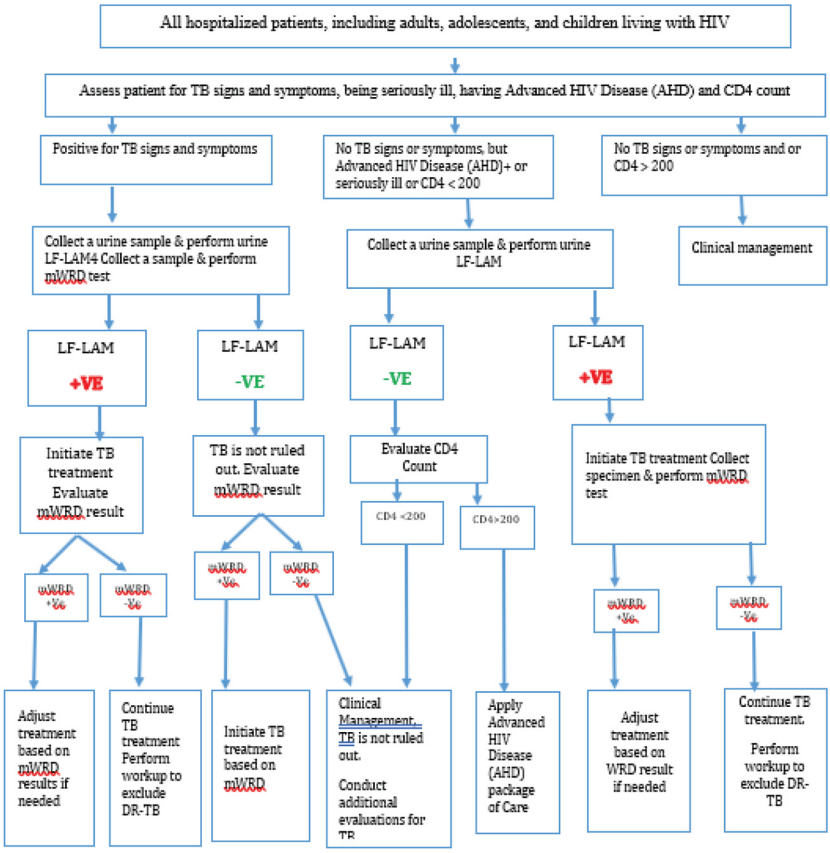
Seriously ill is defined based on four danger signs: respiratory rate of more than 30/minute, temperature of more than 39 °c heart rate of more than 120/minute and unable to walk unaided.

Advanced HIV disease: is defined as a CD4 cell count of less than 200 cells/mm3 or a WHO clinical stage 3 or 4 event at presentation for care for adults, adolescents and children greater than five years. All children with HIV who are aged under 5 years should be considered as having advanced disease.

Figure 5.1. Algorithm for LF-LAM testing to aid in the diagnosis of TB among PLHIV in inpatient settings

For outpatient settings

- With signs and symptoms of TB (pulmonary and/or extra pulmonary) or seriously ill
- Irrespective of signs and symptoms of TB and with a CD4 cell count of less than 100 cells/mm3



In outpatient settings, WHO recommends against using LF-LAM to assist in the diagnosis of active TB in HIV-positive adults, adolescents, and children:

- Without assessing TB symptoms
- Without TB symptoms and unknown CD4 cell count or without TB symptoms and CD4 cell count greater than or equal to 200 cells/mm3
- Without TB symptoms and with a CD4 cell count of 100–200 cells/mm3

Remarks

a.All patients with signs and symptoms of pulmonary TB who can produce sputum should have as their initial diagnostic test at least one sputum specimen submitted for Xpert® MTB/RIF (Ultra) assay. This also includes children and adolescents living with HIV who can provide a sputum sample.

b.LF-LAM should be used as an-add on to clinical judgement in combination with other tests. It should not be used as a replacement or triage test. More details are given in Algorithms for LF-LAM use.

Note for using LF-LAM test for children less than 5 years:

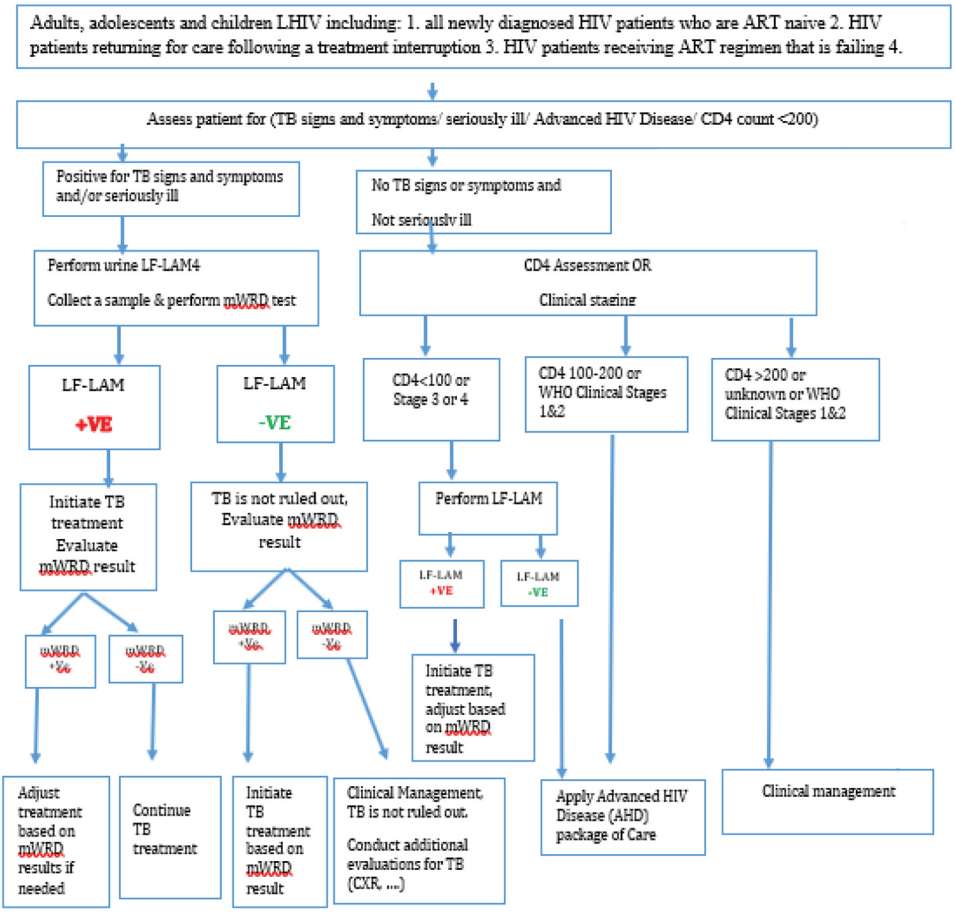
Latest WHO guideline consider all HIV infected children age <5 years old to follow as advanced HIV disease , besides nationally we have a limited number of under 5 children on ART. Hence setting other criteria may limit the Urine LF-LAM utilization. Therefore LF-LAM test should be conducted for all HIV infected children under 5 years at least once as per below criteria:

To offer LF-LAM for all HIV infected <5 years children backlog/currently on treatment once irrespective of clinical stage or CD count/CD 4 percentage

All newly enrolled under 5 HIV infected children (at Enrollment) irrespective of clinical stage or CD4 count/CD4 percentage

Once cleared the backlog, offer LF-LAM at any time when children presented with TB symptoms, or serious illness or advanced HIV stage or CD4 percentage less than 15%.

Figure 5.2. National TB Diagnostic algorithm for PLHIV incorporating Urine LF-LAM testing in outpatient settings



Diagnosis of extra-pulmonary tuberculosis in PLHIV

Extra-pulmonary tuberculosis is more HIV-related than pulmonary tuberculosis. The accurate diagnosis of extra-pulmonary tuberculosis is complex and difficult, particularly in peripheral health facilities with limited diagnostic capacity. Therefore, it is important for healthcare workers to have a high-index of suspicion and critically evaluate through clinical algorithms. It is also recommended to do organ specific investigations.

Note:

- Xpert MTB/RIF test is recommended as diagnostic test for CSF in patients presumed to have TB meningitis.
- One sputum sample for the facility which have Xpert test and two sample for sample referring facilities.

Antibiotic trial: Antibiotic trial has a role to treat concomitant bacterial infection for PLHIV with cough or serious illness. However, antibiotic trial is not helpful in the diagnosis of TB in PLHIV.

Table 5.5: Extra pulmonary TB diagnostic approaches in PLHIV.

Type of TB	Evidence Strongly Suggestive of EPTB	Investigations and recommendations
Lymph Node TB	2cm or more in size, Asymmetrical/localized; Painless swelling; Firm/fluctuated; Cervical location; patient with weight loss, night sweats, fever	LN Aspirate for AFB has 85% yield, if not possible to do FNAC of LN, start anti-TB.
Pleural effusion	Unilateral effusion: Aspirate of fluid is clear and straw colored and clots on standing in a tube without anti-coagulants or pleural fluid analysis shows protein >30g/L &>50% lymphocytes; Patients with weight loss, night sweats, fever, or evidence of TB elsewhere	Start anti-TB as soon as possible.
Tuberculosis Meningitis	Patients with weight loss, night sweats, fever; cerebrospinal fluid clear with high protein, low glucose, and lymphocytes; Cryptococcal antigen (or Indian Ink and fungal culture) negative in CSF, evidence of TB elsewhere	Admit patient, start anti-TB with steroids as soon as possible. Start treatment for cryptococcal meningitis based on clinical or lab evidence.
Pericardial Effusion	Hemodynamically significant pericardial effusion, often with pleural effusions, Lung fields clear and intra-thoracic lymphadenopathy. Usually patients with weight loss, night sweats, fever. N.B. 90% of pericardial effusions in HIV positive patients in high-TB burden areas is due to TB.	CXR, Echocardiograph or chest ultrasound; pericardiocentesis, and pericardial biopsy; routine TB Workup. Start anti-TB as soon as possible
Disseminated TB	Patients with weight loss, night sweats, fever, and cough; Abnormal CXR (which can include miliary pattern); Large spleen/liver, Anemia	Start anti-TB treatment (add antibiotics if critically ill)
TB of the Spine	Pain over localized area, children/adolescents –often thoracic vertebrae. Adults: frequently lumbar vertebrae.	Spinal imaging (e.g. X-Ray, MRI); FNA of vertebral lesions and /or Para spinous abscesses when feasible.

II. TB Prevention Therapy (TPT)

Latent tuberculosis infection (LTBI) is the state of persistent immune response to stimulation of mycobacterium tuberculosis antigens without evidence of clinically apparent active tuberculosis (TB). Estimates show a quarter of the global population is infected with tuberculosis, where most cases are asymptomatic and non-infectious. Studies show that, on average, 5-10% of these latently infected persons have lifetime risk of progressing to develop active TB, usually within the first five years of initial infection. However, risk of progression is dependent on immunological status.

Treatment of LTBI to prevent progression to active disease is one of the global key strategies to ending the TB epidemic. Increasingly, eligible targets and treatment options are expanding, with significant implications in the programmatic management of LTBI. TPT is the use of Isoniazid, rifapentine or other medications to sterilize latent TB infection. Screening for exclusion of active TB in HIV infected persons is the single most important step that should precede the decision to initiate TPT. Concerns regarding the development of INH resistance should not be a barrier to providing TPT.

The selection of treatment options for LTBI by programs and clinicians should consider the characteristics of the clients who are to receive treatment and acceptability of treatment for higher completion rate. The benefits of all the treatment options outweigh the potential harm. Shorter TPT regimens have been shown to be as effective and better tolerated than longer regimens, and thus may be preferable for individuals receiving treatment, clinicians providing treatment, and program managers.

For adults and adolescents living with HIV, TPT should be provided to those who are unlikely to have active TB based on appropriate clinical algorithm, irrespective of CD4 count, ART status, pregnancy status or history of treatment for prior episode of TB before THREE years. Children and infants less than 1 year of age should be provided preventive therapy only if they have a history of household contacts with pulmonary TB and active TB in the child has been excluded in investigation.

Clinicians should follow the algorithms for initiation and selection of regimen for the specific population groups eligible for TPT as indicated in section below.

Figure 5.3. Algorithm for initiating TPT in adults and adolescents ≥15 years living with HIV

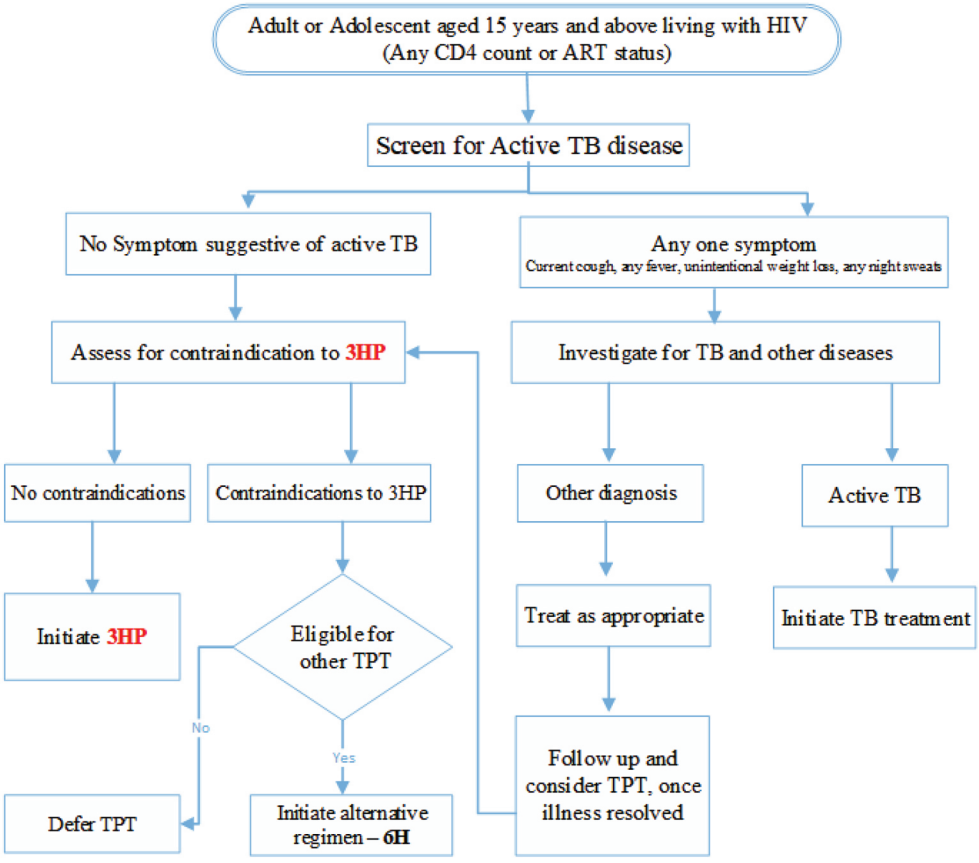


Figure 5.4. Children <15 years living with HIV and without household TB exposure

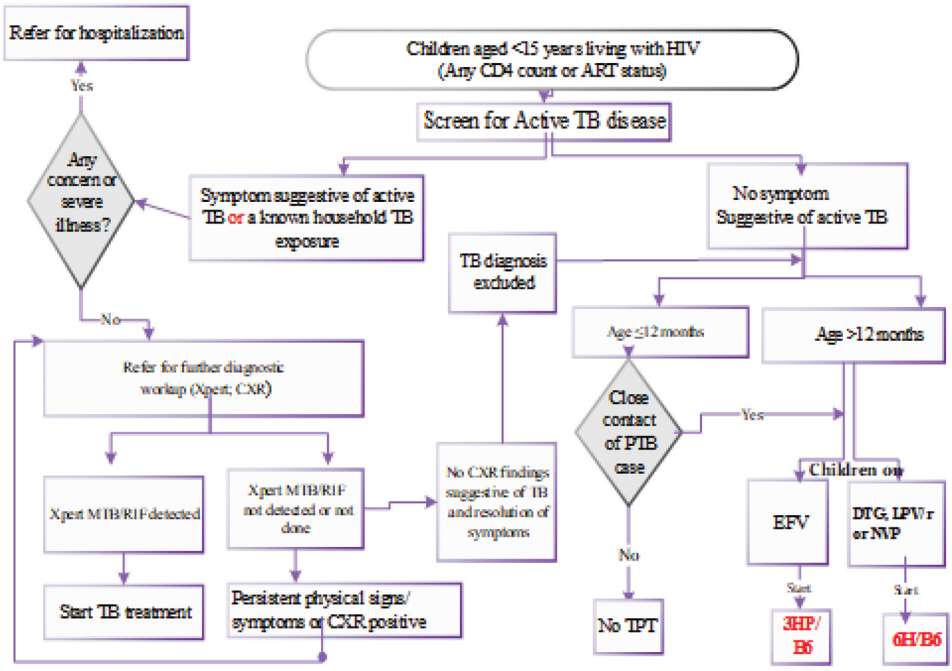
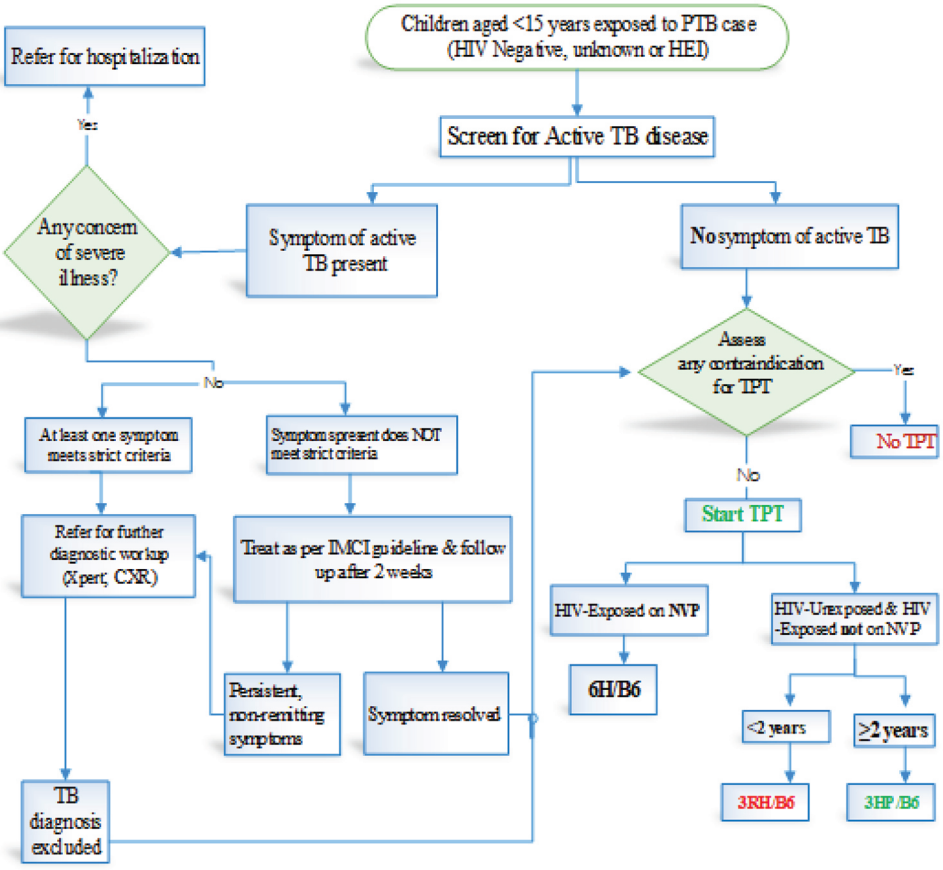


Figure 5.5. HIV-exposed Children and HIV negative children and adolescents <15 years of age with household exposure to PTB case



Regimen and dosage for treatment of LTBI

Table 5.6. Regimen for treatment of latent TB infection.

Population group	Age group and ART regimen	Selection of TPT regimen	
Persons living with HIV		Preferred regimen	Alternative regimen
	Adults, adolescents, children, and infants of all ages taking a **PI-based ART regimen**	Daily isoniazid preventive treatment for 6 months (6H)	
	Children and adolescents aged <15 years taking a **DTG-based ART regimen**	Daily isoniazid preventive treatment for 6 months (6H)	
	Children and adolescents aged <15 years taking **EFV-based ART regimen**	Weekly isoniazid Plus rifapentine for 3 months (3HP*).	■ Daily isoniazid preventive treatment for 6 months (6H) ■ Daily rifampicin Plus isoniazid for 3 months (3RH).
	Adolescents and adults living with HIV (≥ 15 years of age) taking non-**PI based ART regimen**	Weekly isoniazid Plus rifapentine for 3 months (3HP).	■ Daily isoniazid preventive treatment for 6 months (6H)
HIV-negative persons	Infants and children <2 years of age)	Daily rifampicin Plus isoniazid for 3 months (3RH).	-Daily isoniazid preventive treatment for 6 months (6H)
	Eligible adolescents and children aged between ≥2 -14 years (refer to eligibility criteria specified above)	Weekly isoniazid Plus rifapentine for 3 months (3HP).	-Daily isoniazid preventive treatment for 6 months (6H) -3RH will be used as alternative to 3HP
*3HP: should be taken with food to prevent GI upset; if patients are unable to swallow tablets (due to age or illness), the tablets can be crushed and added to a small amount of semi-solid food			

Drug-drug interactions with antiretroviral medicines

Drug-drug interactions should be cautiously considered in using rifampicin and rifapentine in persons who are receiving antiretroviral treatment (ART). Both rifampicin and rifapentine should not be administered in persons who are receiving nevirapine or Protease Inhibitor (PI) based regimen. A three-month weekly rifapentine plus isoniazid can safely be used in patients receiving efavirenz-based antiretroviral regimen without the need for dose adjustment. Studies show that co-administration of rifapentine with raltegravir and dolutegravir based regimen is both safe and well tolerated in HIV infected adults and adolescents aged ≥ 15 and do not need any dose adjustment.

Monitoring adverse events

Routine clinical monitoring of persons receiving TPT is necessary to ensure adherence and continuity of care. Adverse effects, including those considered as medically "minor", may be a barrier for adherence in a person who is otherwise well. TPT related adverse events (AEs), identified during treatment should be properly monitored, managed and reported per national recommendation, using health facilities reporting systems.

Management of adverse events (AEs)

Individuals receiving TPT do not have active disease and therefore their risk for adverse events during treatment must be minimized. Moreover, the regimen can be withheld while an AEs is assessed, and there is time for the regimen to be recommenced and completed if safe to do so. Overall, 3HP is a safe and effective treatment for latent TB infection. Clinically significant drug reactions are rarely experienced by patients receiving 3HP, and even less commonly require discontinuation of treatment. Severe reactions are particularly rare. Nonetheless, healthcare workers should be familiar with the important drug reactions so that they can recognize rare occurrences and manage them appropriately.

Therefore, in general: If an AE occurs while a patient is receiving 3HP, they should be advised not to take any further doses and contact the ART providers and TB focal persons of the health facilities as appropriate.

Minor adverse events are likely to occur in a small proportion of individuals/patients. Rarely serious adverse events may occur, and hence both the health care provider and patient should be vigilant and manage such events rapidly. This can be achieved by careful assessment of the patient prior to commencing 3HP, and routine monitoring during treatment as indicated below:

Table 5.7. Baseline assessment and monitoring during TPT

Drug interactions	The most common drug reactions with 3HP are: ■ Liver toxicity (less common than for 6H) ■ Flu-like reactions (more common than for 6H) Drug reactions are usually mild and self-limiting, but occasionally they can be severe. Children usually tolerate 3HP very well and have much lower rates of drug reactions.
Baseline assessment	Active TB must be ruled out before commencing TPT. 3HP is currently not recommended in: ■ Pregnancy ■ Age <2years ■ Information on baseline liver function is important in the following: ■ HIV+ (done as part of ART assessment but not mandatory) ■ Daily alcohol consumption ■ Liver disorders including viral hepatitis ■ Postpartum period (≤3 months after delivery) ■ Concomitant use of other hepatotoxic substances Individuals at higher risk of peripheral neuropathy should be offered vitamin B6 (pyridoxine) supplementation with 3HP; if B6 is not available, this should not delay starting a course of 3HP
Counselling for AEs	Red/orange discoloration of urine and other body fluids while receiving 3HP is normal and completely harmless. If patients experience any symptoms concerning for an AE: ■ Do not take any further doses of3HP ■ Contact a healthcare provider for advice ■ Only continue receiving 3HP if advised to do so by a healthcare provider Individuals should be alert to the following symptoms: ■ Weakness, fatigue, loss of appetite, persistent nausea (early symptoms of ■ hepatotoxicity) ■ Flu-like, or other acute symptoms appearing shortly after receiving a dose of 3HP ■ Symptoms of active TB (appendix1)

Adherence support and monitoring

Clients receiving TPT should be supported at home level, either by adherence case managers, HEWs or family supporter. They should have monthly scheduled follow up that is coordinated with other services, such as HIV care, child and maternal health services, as necessary. At each follow-up visit, the healthcare provider should:

- Educate clients and their families about the benefit of TPT, potential side effects, and importance of returning back to a health facility for new symptom/sign or any concern.
- Evaluate and counsel clients on importance of treatment adherence and completion. Case managers, adherence supporters, and HIV care and child health service providers should support treatment adherence and monitoring, as part of comprehensive HIV care and child health services.
- Evaluate and routinely monitor drug side effects, including hepatitis, peripheral neuropathy or rash. Stop TPT if serious adverse effect is identified and manage the patient.
- Evaluate for signs and symptoms of active TB, other opportunistic infections (OIs) or diseases.
- Stop TPT, if active TB is diagnosed, which requires immediate start of anti-TB treatment

Contraindications for TPT

Individuals with any one or more of the following conditions should not receive TPT:

- Symptoms compatible with tuberculosis even if the diagnosis is not yet confirmed;
- Active hepatitis (chronic or acute);
- Regular and heavy alcohol consumption;
- Prior allergy or intolerance to medicine(s) in the regimen; and
- Symptoms of peripheral neuropathy

In addition, rifapentine is not currently indicated for children below 2 years, PLHIV receiving PI or NVP based ART regimens, and pregnant and breastfeeding women.

Patient management after treatment interruption:

TPT is said to be completed when a person completed a full course of treatment within the specified period. Completion of ITP is defined as "completed" if a patient completed the full course of therapy within nine months period (i.e. the six months of doses should be finished in nine months). If a patient has interrupted TPT without medical personnel advice, the client should be traced by health extension workers (HEW) or through the index person or other family member who is already enrolled in care, and treatment must be resumed. It is important to identify barriers and support treatment adherence. However, concerns about adherence should not be a barrier to the use of TPT. If the

client discontinues isoniazid-based TPT for a period of less than three months: Resume the same course by adding for the missed doses at the end. If the client discontinues treatment for a period of more than three months, then re-initiate new course of treatment.

Completion for 3HP is defined when the patient took at least 11 doses of treatment in 16 weeks.

TB preventive treatment in Newborns

Once a pregnant woman with TB has been on treatment for TB for several weeks before delivery, it is less likely that the baby will become infected. The risk is highest if a mother is diagnosed at the time of delivery or shortly thereafter. If a pregnant woman is found to have pulmonary TB shortly before delivery, then the baby, and if possible, the placenta, should be investigated for evidence of congenital TB infection. If the result is positive, the newborn should be treated accordingly. If asymptomatic, the newborn should receive TB preventive treatment followed by BCG immunization. Breastfeeding can be safely continued during this period.

TPT service provision amid COVID19:

At TPT initiation, all PLHIV will receive standardized comprehensive education and counseling on benefits of TPT, importance of adherence, TPT-related AEs, with clear instructions to present for evaluation at onset of any sign or symptoms indicative of TPT-related AEs. All patients will be placed on three months TPT MMD (both for clients on daily isoniazid for 6 months [6H] and rifapentine and isoniazid weekly for 3 months [3HP]). TPT MMD will be aligned with ART MMD to reduce unnecessary facility visits. Facility level follow up visit & adherence monitoring will be aligned with TPT dispensation at initiation and month three. Documentation of TPT completion will be aligned to clinical visit following expected TPT completion at month six (for 6H) and at month three (for 3HP).

III. TB Infection, prevention, and control

PLHIV are at increased risk of acquiring TB in health care facilities and congregate settings. Each health care facility should have a TB infection control plan for the facility that includes administrative, environmental, and personal protection measures to reduce the transmission of TB in health care and congregate settings and to provide surveillance of TB disease among workers. Health care workers with HIV should be provided with ART and TPT if they are eligible. TB can affect everyone, but specific population groups, including PLHIV and healthcare workers, have a higher risk of acquiring TB infection and progressing to disease once infected.

Summary of recommendations for key actions for infection control

Administrative (facility-level infection control committee and protocols):

A set of administrative controls is the first and most important component of any IPC strategy. These key measures comprise specific interventions aimed at reducing exposure and therefore reducing transmission of M. tuberculosis. These include:

- Triage and patient separation systems (i.e. management of patient flows to promptly identify and separate presumptive TB cases);
- Prompt initiation of effective treatment; and
- Respiratory hygiene including cough etiquette.

Health workers and care providers

- Surveillance and information
- Package of care for HIV-positive workers (ART and TB preventive therapy)
- Protective equipment (particulate respirator masks that meet or exceed N95 standards)
- Relocation for health care workers living with HIV to a lower-risk area

Environmental

To reduce the risk of transmission of M. tuberculosis, air can be made less infectious through the use of three principles: dilution, filtration and disinfection. Environmental controls are aimed at reducing the concentration of infectious droplet nuclei in the air. This is achieved by using special ventilation systems to maximize airflow rates or filtration, or by using germicidal ultraviolet (GUV) systems to disinfect the air. Ventilation systems can also be used to control the direction of airflow to reduce the spread of infection; for example, through the use of exhaust fans to generate negative pressure gradients. Environmental controls are used in combination with other IPC measures to help prevent the spread of M. tuberculosis

Respiratory protection

Respiratory protection controls are designed to further reduce the risk of exposure to M. tuberculosis (and other airborne pathogens) for health workers in special areas and circumstances. The recommendations given here are aimed at strengthening these controls, and preventing the inadequate implementation of respiratory protection programs that may lead to a false sense of security and therefore increase the risk to health care staff.

- Ensure presumptive and TB patients do not walk along rooms in which susceptible individuals are evaluated (Eg. ART clinic)
- Enforcing cough etiquette; health education is given to cover mouth and nose with soft paper, cloth or using one's arm while coughing or sneezing.
- Properly implementing cough etiquette to contain the dispersal of respiratory secretions and practicing respiratory hygiene maneuvers to properly dispose used tissues and masks are important preventive measures hence;
- HCWs should give health education on the prevention and control of TB.
- Posting of pictures showing precautions at waiting area is essential.
- Issuing face masks for MDR-TB patients and providing health education to overcome MDR TB- associated stigma is also important.

To reduce exposure in households:

- Houses should be adequately ventilated, particularly rooms where people with infectious TB spend considerable time (natural ventilation may be sufficient to provide adequate ventilation);
- Anyone who coughs should be educated on cough etiquette and respiratory hygiene so as to behave accordingly at all times; while infectious TB patients should:
  - Spend as much time as possible outdoors;
  - Sleep in an adequately ventilated room;
  - Minimize contact with children(< 5yrs) and immune-suppressed individuals; and
  - Spend as little time as possible in congregate and public transport market.
- Reduce the burden of HIV in patients with presumptive and confirmed TB
- Provide HIV testing and counseling to presumptive and confirmed TB patients

HIV testing is an entry point for HIV care and treatment services including ART. This equally applies to TB patients. Significant proportions of TB patients are co-infected with HIV. Among TB patients who are also HIV-infected, other OIs are significant causes of morbidity and mortality even with a successful treatment of TB. Hence, HIV testing and counseling should be routinely offered to all TB patients.

Presumptive treatment of TB for people living with HIV

The rationale for presumptive TB treatment is to prevent the death of people with HIV in situations where expedited diagnosis of TB is not possible or feasible due to the clinical condition of the patient or limited access to TB diagnostic services. While there is no case definition of presumptive TB, WHO algorithms include initiation of TB treatment for people with HIV in peripheral facilities based exclusively on clinical suspicion (without TB investigations) for seriously sick patients (with respiratory distress) based on the judgement of the clinician.

This approach is based on expert opinion and emphasizes that every effort should be made to confirm the diagnosis of TB after initiation of presumptive treatment and that treatment should be stopped only if there is bacteriological, histological or strong clinical evidence of an alternative diagnosis.

Introduce HIV prevention interventions for presumptive and confirmed TB patients

All clients attending TB clinics should be screened for STI using a set of simple questions. Those with symptoms of STI should be treated or referred to the treatment providers. (Refer to the National Guideline for the Treatment of STI using the Syndromic Approach.) Condoms should be made available in TB clinics.

Provide co-trimoxazole preventive therapy for HIV positive TB patients

Co-trimoxazole is a safe and broad-spectrum antibiotic with activity against a broad range of bacterial, fungal and protozoal infections that are common cause for morbidity and mortality in HIV infected populations. Therefore, CPT is recommended to all TB/HIV co-infected patients regardless of their CD4 Count. All PLHIV with TB and receiving CPT should be registered on the unit TB register, as well as the Pre ART/ ART Register. They should also be monitored monthly.

Ensure HIV prevention, treatment, and care for HIV positive TB patients

Referral linkages between TB and HIV services must be strengthened to provide comprehensive HIV prevention services for TB patients and their families. Tuberculosis control program should implement procedures for prevention of occupational and nosocomial exposure to HIV infection in their services. Health units should be equipped with protective materials and routinely follow standard precautions to prevent HIV transmission in the healthcare settings. Linkage should be ensured for pregnant and non-pregnant HIV positive clients to access services for prevention of mother to child transmission. TB clinics should establish linkage with HIV services to provide the continuum of care and support for HIV positives during and after completion of anti-TB treatment.

Management consideration for TB/HIV Co-infections

In the management of TB/HIV confection, treatment of tuberculosis is always given priority over ART. As soon as HIV is identified in a TB patient, the patient should be enrolled to HIV chronic care. Ideally, the HIV care can be delivered at the TB clinic for the duration of TB treatment.

In settings where this is not possible, there should be a strong referral system in place to link the TB/HIV co-infected patient to the HIV clinic promptly. Appropriate clinical, psychosocial and laboratory evaluations (including complete blood count, chemistry tests and CD4 count tests) as per the national guidelines for ART should be performed as soon as possible. Patients should be initiated on CPT and ART regardless of CD4 count or WHO clinical stage and ART regardless of CD4 count or WHO clinical stage. ART is recommended for all HIV infected TB patients regardless of CD4 count or WHO clinical stage. CD4 cells count shall preferably be determined for all HIV infected TB patients. The preferred regimen for TB/HIV co-infected adult patients is TDF+3TC+DTG (adjust dose of dose of DTG to 50mg BID, for children use appropriate weight band), regardless of pregnancy status.

Multidrug-resistant TB and HIV

Multidrug-resistant TB (MDR-TB) is defined as TB that is resistant to at least isoniazid and rifampicin. Patients with both HIV and MDR-TB face complicated clinical management, fewer treatment options and poor treatment outcomes.

Outbreaks of MDR-TB among people with HIV have been documented in hospital and other settings, especially in Eastern Europe and in Southern African countries with a high HIV prevalence. People with HIV with suspected drug-resistant TB should be tested using Xpert MTB/RIF where possible, since this test is more sensitive for detecting TB among people with HIV and rapidly detects rifampicin resistance, thus greatly shortening the time to diagnose and treat MDR-TB.

The burden of MDR-TB can be reduced by strengthening HIV prevention, improving infection control and improving collaboration between HIV and TB control activities, with special attention to the groups at the highest risk of MDR-TB and HIV infection, such as people who inject drugs and those exposed in congregate settings.

5.3. Pneumonia

5.3.1.Bacterial Pneumonia

This can occur in immune-competent individuals but in HIV-infected patients, particularly those infected with S. pneumoniae; incidence of bacteremia accompanying pneumonia is increased compared with individuals who are not HIV infected. Bacterial pneumonia occurs during the whole spectrum of HIV disease but tends to be more severe and recurrent as the CD4 counts drops significantly. In addition, pneumonia can concomitantly present with sinusitis and/or bacteremia. If not treated promptly, extra pulmonary complications like empyema, meningitis, pericarditis, hepatitis and arthritis can follow. Streptococcus pneumonia and Hemophilus influenzae are the most common etiologies of community acquired pneumonia.

Clinical manifestation

Typically, the patient presents with sudden onset of cough, sputum production, chest pain, fever and/or shortness of breath.

Diagnosis

The clinical suspicion is based on a history of acute symptoms presented over days to a few weeks and/or abnormal physical signs of systemic infection and consolidation in the affected lung/s. Radiologic imaging can assist in confirming the diagnosis of pneumonia.

Treatment

For adults

For less sever pneumonia,

- Amoxicillin 500mg TID OR erythromycin 500 mg QID OR doxycycline 100 mg BID for seven days (Avoid doxycycline in pregnancy).
- Alternative, azithromycin 500 mg per day for three days OR clarithromycin 500 mg twice daily for seven days.
- If not improving after three days with good adherence to the antibiotics, review and consider switching to IV regimen:
    - Ceftriaxone 1-2gm IV once per day plus erythromycin 500 mg oral (if not taken earlier) or IV four time a day for 7 days.

For pediatric age groups:

For less sever pneumonia Amoxicillin 40mg/kg divided in to three doses per day for seven days. In children and infants allergic to penicillin, use erythromycin; for infants aged one month up to two years, erythromycin 125 mg four times daily for seven days; for age groups2-8 years, erythromycin 250 mg four time per day for seven days; for age groups above 8 years give erythromycin adult dose. If not improving after three days and if patient is adherent to the antibiotic, review and consider switching to IV ceftriaxone 75-100gm per kg IV/IM once a day or equally divided dosed twice a day for 7 to 10 days. Maximum dose 2-4gm per day for seven days.

Table 5. 8. Management of less severe pneumonia in PLHIV

Management of less severe pneumonia			
Age	First line treatment	If allergic to penicillin	If not improving after 3 days and good adherence
All ages	Amoxicillin 40mg/kg in three divided doses for 7 days	-	Ceftriaxone IV/IM: 75 mg/kg, once a day or in two divided doses for 7-10 days (Max dose: 2-4 gm/day)
1month-2 years	-	Erythromycin: 125 mg, QID, 7 days	
2-8 years	-	Erythromycin: 250 mg, QID, 7 days	
Above 8 years	-	Erythromycin: 500 mg, QID, 7 days	

When the patient has presented with clinical evidence of severe pneumonia, admit for parenteral antibiotic treatment and supportive therapy or refer the patient if admission is impossible. Signs of severe pneumonia include:

Children:

- Chest in-drawing, grunting and presence of danger signs in children

Adults:

- Tachypnea, old age (>65 years), cyanosis, hypotension, systolic blood pressure <80mm Hg, multi-lobar involvement and altered mental status,

The respiratory rate in tachypnea is summarized as below:

S. No.	Age-group	Respiratory Rate (RR)
1	Birth to 2 months	>60/minute
2	2 months to 1 year	>50/minute
3	1 year to 5 years	>40/ minute
4	5 years and above	>30/minute

5.3.2.Pneumocystis pneumonia

Pneumocystis pneumonia is caused by Pneumocystis jiroveci, formerly known as pneumocystis carini pneumonia, a ubiquitous organism that is classified as a fungus but also shares biologic characteristics with protozoa. It commonly occurs when patients have significant immune suppression (adults: CD4<200cells/mm3 or children: CD4 percentage < 14%).

Clinical manifestation

Typical clinical presentations are characterized by insidious onset of low grade fever, dry cough, and dyspnea exacerbated by exertion. Physical examination reveals fever, tachypnea, tachycardia and scattered rales in the lungs, but examination of the lungs can appear normal in some patients. In children highest incidence is seen between 2-6 months of age and is characterized by abrupt onset of fever, tachypnea, dyspnea and cyanosis.

Diagnosis

Presumptive diagnosis of PCP is based on clinical judgement and typical chest X-ray findings revealing a perihilar interstitial infiltration with tendency to spread outwards. Note that the chest X-ray can be normal in 20% of patients. Definitive diagnosis of PCP is based on demonstration of the organism from an induced sputum sample using special stains like Giemsa or methylamine silver stains, but these tests are not routinely done in Ethiopia.

Treatment

- Use Trimethoprim 15-25 mg/kg, three or four times daily for 21 days.
- Close monitoring is necessary during the initial five days of treatment and if patient grows sicker, administration of oxygen is useful.
- In severely ill patients with marked respiratory distress and extensive chest X-ray findings:
  - Children: add prednisolone - 2mg/kg per day for the first 7 - 10 days followed by a tapering regimen for the next 10 - 14 days.
  - Adults: add prednisolone - 80mg for the first five days, 40 mg until 11 days and 20 mg until completion of intensive co-trimoxazole therapy.
- Toxicity of co-trimoxazole, like skin rash, bone marrow suppression, hepatitis and renal failure can be troublesome in some patients with advanced HIV disease and requires close monitoring.

Secondary prophylaxis after completion of the course of treatment with co-trimoxazole should be continued. (Refer Table 4.1).

The alternative regimens for mild to moderate cases of PCP include:

- Clindamycin 600 mg qid plus primaquine 15 mg bid; or
- Clindamycin 600 mg qid plus dapsone 100 mg daily.

Consider spontaneous pneumothorax in patients with sudden deterioration in clinical condition.

5.3.3.Lymphoid Interstitial Pneumonitis

Lymphoid interstitial pneumonitis (LIP) is one of the most common chronic lower respiratory conditions occurring in up to 25% of children with HIV/AIDS.

Clinical manifestations

It ranges from asymptomatic disease with isolated radiographic findings to bullous lung disease with pulmonary insufficiency. Symptomatic children present with insidious onset of tachypnea, cough, and mild to moderate hypoxemia with normal auscultatory findings or minimal rales or wheezing. Progressive disease is accompanied by digital clubbing and symptomatic hypoxemia. Associated physical findings include generalized lymphadenopathy, hepatosplenomegaly and parotid enlargement.

Diagnosis

It is usually based on findings of clinical examination. Diffuse bilateral reticulonodular infiltrate on X-ray with mediastinal lymphadenopathy. It is important to exclude tuberculosis and other infectious etiology.

Treatment

Provide symptomatic treatment (hydration, oxygen). Use antibiotics if there is a superimposed bacterial infection. Bronchodilators may be helpful in mild to moderate disease. Corticosteroids are usually reserved for children with significant hypoxemia and symptoms of pulmonary insufficiency. Give prednisolone 1 – 2 mg/kg/24 hrs for 6 – 8 weeks and then taper as tolerated.

5.4. Hepatitis B and C

Introduction

Chronic Hepatitis B and C Virus infection are major global public health problems. WHO estimates that, in 2019, 71 million people had chronic HCV infection and 257 million people chronic HBV worldwide, and 820 000 people died from HBV and 290 000 from HCV, mainly from cirrhosis or hepatocellular carcinoma. In 2019, there were 1.5 million new chronic HCV infections. In Ethiopia, over 30 studies have been conducted since 1980's, to determine a sero-prevalence of various hepatitis viruses in the country. It is reported that 12% of the hospital admissions and 31% of mortality in medical wards were due to all causes of chronic liver

disease. The National sero-survey conducted by MoH and EPHI in 2017 shows the prevalence of HBsAg was estimated to be 9.4 among the general population aged 15 years and above with regional variations; the highest being in the Afar region (28.8%). The pooled prevalence of anti-hepatitis C virus antibody (anti HCV) was 3.1%. Unlike HBV, anti HCV virus prevalence in HIV infected individuals were higher, 5.5%.

Early identification of people with chronic HBV or HCV infection enables them to receive the necessary care and treatment to prevent or delay the progression of liver disease. Testing also provides an opportunity to link people to interventions to reduce transmission, through counselling on risk behavior and provision of prevention commodities and HBV vaccination.

In our set up systematic screening for viral hepatitis B and C is prioritized for the following population groups:

- People who have received medical or dental interventions in settings where infection control practices are substandard
- Pregnant women
- Children born to HBV or HCV positive mothers
- People with injecting drugs
- People living with HIV
- Health care workers exposed to biological fluids
- People who ever received blood or blood products
- Inmates of correctional facilities
- Household and sexual contacts of HBsAg positive people
- Female Sex workers
- History of multiple sexual partners or STIs
- Patients undergoing renal dialysis
- People needing immunosuppressive therapy

Chronic HBV is defined as persistence of HBsAg for more than six months and chronic HCV infection is HCV antibody positive with viremic HCV infection.

5.4.1.HBV/HIV co-infection management

HIV co-infection has been shown to have a profound impact on almost every aspect of the natural course of HBV infection and includes more rapid progression to cirrhosis and hepatocellular carcinoma (HCC), higher liver-related mortality, and decreased treatment response compared with persons without HIV coinfection.

HIV/HBV co-infected persons also demonstrate more rapid HIV disease progression compared to those who are HIV-infected alone, and have an impaired recovery of CD4 cells. HIV clients are among the high risk groups for HBV and should be given priority for screening. i.e all HIV clients should get screened for HBV and evaluated for chronic infection as per the national viral hepatitis prevention and control guideline. After test result, vaccination or treatment and care for reactive patients are recommended when resources permit.

Treatment options for patients with HIV/HBV co-infection:

- ART should be started rapidly.
- If treatment is indicated for HBV, TDF+3TC + DTG as a preferred regimen.
- The use of lamivudine as mono-therapy in any of these diseases is contraindicated due to high YMDD resistance.
- When switching treatment in patients with HIV on ART failure, the second line regimen should contain TDF + 3TC to continue the treatment against HBV.
- If tenofovir-associated renal toxicity occurs, the dose of tenofovir should be adjusted according to the renal clearance.
- Note: treatment of HIV without the use of TDF in the regimen may lead to flares of hepatitis B due to ART-associated immune reconstitution.
- Similarly, treatment discontinuation, especially of 3TC, has been associated with HBV reactivation, ALT flares and, in rare cases, hepatic decompensation.

NB: For further reference please consult the national Viral Hepatitis prevention and control guidelines.

5.4.2.HCV HIV co-infection management

HIV patients are among high risk groups for HCV and should be given priority for screening. Therefore, all HIV patients should be screened and confirmation VL test should be done for HCV screened positives.

Anti-HCV rapid diagnostic test (RDT) or immunoassay (IA) can be used for screening and HCV RNA viral load test using either quantitative or qualitative PCR should be used to confirm chronic HCV infection.

Persons with HIV/HCV coinfection generally have more rapid disease progression than mono-infected persons. Even among persons in whom ART leads to successful control of HIV infection (i.e. undetectable HIV viral load), the risk of hepatic decompensation among coinfected persons is higher than among persons with HCV mono-infection.

All chronic HCV infected individuals should be treated to eradicate the virus and achieve cure so that complications can be avoided. Follow up quantitative or qualitative HCV RNA viral load is required to confirm if the patient has achieved Sustained Virologic Response (SVR).

HCV treatment outcomes with DAAs are comparable in persons with HIV/HCV coinfection to those with HCV mono-infection. Because DAAs are safe and effective for people with HIV/HCV, there is no longer any need to consider them as a special or difficult-to-treat population. However, there are important drug-drug interactions and shared side effects like headache, fatigue and anemia with pan-genotypic HCV regimens and ART. Therefore,

checking for drug-drug interactions and side effects between HIV and HCV medications needs to be given appropriate attention. The HCV treatment for children is differed until 12 year of age and treatment with interferon-based regimens should no longer be used.

For adolescents (12–17 years), the treatment at this time still requires genotyping to identify the appropriate regimen. This include:

- Sofosbuvir/ledipasvir 12 weeks in genotypes 1, 4, 5 and 6
- Sofosbuvir/ribavirin 12 weeks in genotype 2
- Sofosbuvir/ribavirin 24 weeks in genotype 3

For adults without cirrhosis, the following pan-genotypic regimens is recommended for use in adults 18 years of age or older can be used:

- Sofosbuvir/velpatasvir for 12 weeks
- Sofosbuvir/daclatasvir for 12 weeks
- Glecaprevir/pibrentasvir 8 weeks3

For adults with compensated cirrhosis, the following pan-genotypic regimens can be used:

- Sofosbuvir/velpatasvir for 12 weeks
- Glecaprevir/pibrentasvir for 12 weeks
- Sofosbuvir/daclatasvir for 24 weeks

Refer the national viral hepatitis prevention and control guideline for further information

5.5. Sexual Transmitted Infection and Cervical Cancer

The epidemiological synergy between HIV and sexually transmitted infections is well established, and they frequently coexist. Most of these infections are asymptomatic, especially among women. However, even asymptomatic STIs can cause complications, be transmitted to sexual partners and enhance HIV transmission. STI services should be an integral part of comprehensive HIV care among adults and adolescents. Refer the revised STI guideline for syndromic management of STIs.

Prevention of cervical cancer:

Cancer of the cervix is the second most common cancer, among women in Ethiopia with over 6,200 new cases every year and with a mortality close to 5,000 (Globocan 2018). According to Addis Ababa Population Based Cancer Registry (2012-2015), the leading cause cancer type among women is breast cancer (32.3%) followed by cervical cancer (14.5%).

Cervical cancer is a preventable disease and is curable if diagnosed and treated early. 99% of cervical cancer is caused by high risk human papilloma viruses (HPV) types. Types 16 and 18 cause 70 percent of cervical cancer. Women living with HIV (WLHIV) are about six times more at risk of developing pre-cancerous lesions and invasive cervical cancer. The risk and persistence of HPV infection increases with low CD4 count and high HIV viral load.

Target Population:

Women Living with HIV (WLHIV) are at a much greater risk for developing cervical cancer and require a more frequent screening. Start screening at the time of HIV diagnosis, regardless of age, once sexually exposed (15-49 is recommended).

Screening Frequency:

WLHIV should be screened every two years as part of routine care for HIV-positive women, regardless of whether they are on antiretroviral. Following abnormal results and/or treatment, repeat screening at 6months. If follow-up screening is normal, return to screening every two years.

Screening methods:

Depending on the availability of resources, this guideline recommends the following types of screening methods (refer annex 19 and 20 for the algorithm).

1. Visual inspection: with acetic acid (VIA) or Lugol's iodine (VILI)

2. HPV DNA test

3. Cytology:

   - conventional (Pap smear)
   - liquid-based cytology(LBC)

Treatment of Precancerous Lesions:

a.Cryotherapy

Cryotherapy is the treatment of choice for precancerous lesions that meet eligibility criteria. Treatment is to be offered without requiring biopsy diagnosis (screen and treat) in a single visit approach whenever feasible. Only providers who have demonstrated clinical competencies in cryotherapy are permitted to perform the procedure. Treat using a double-freeze (three minutes freeze, five minutes defrost, three minutes freeze) technique to achieve a 3-5 mm ice ball around the cryo-tip. Follow-up screening with VIA for those VIA positive is in one year.

NB: Do not treat with cryotherapy during pregnancy. Reschedule the woman when she is more than 12 weeks postpartum.

b.Thermal ablation

Thermal ablation is another novel ablative treatment of option for precancerous lesions, and is sometimes called "cold coagulation" or "thermocoagulation". The equipment is fairly simple, and treatment is based on a 20–30 second application of a reusable metallic probe that is electrically heated to approximately 100 °C, leading to epithelial and stromal destruction of the lesion. The treatment time is shorter with thermal ablation and also the use of thermal ablation overcomes one major disadvantage of cryotherapy which is the need for a refrigerant gas (N2O or CO2). The gas containers are bulky and heavy to transport and some areas of LMIC may have supply issues. In addition, frequent refilling of freezing gas can be costly. The use of thermocoagulation for the treatment

of CIN is as effective as other methods, such as cryotherapy and LEEP, with the advantage of being rapid and is also associated with low occurrence of side effects

c. Loop Electrosurgical Excision Procedure (LEEP)

LEEP is reserved for precancerous lesions that are not eligible for cryotherapy or thermal ablation. It should be done by providers who have demonstrated clinical competence in the procedure. LEEP requires anesthesia and is to be performed only in settings that can handle potential urgent complications related to the procedure (e.g., heavy bleeding).Follow-up screening with VIA in one year.

d. Conization (Cone Biopsy)

Conization is recommended for the treatment of lesions that cannot be treated with cryotherapy and unclear type of cervical abnormality to rule out invasive cervical cancer. It involves the removal of a cone-shaped area from the cervix, including portions of the outer cervix (ecto-cervix) and inner cervix (endo-cervix) and is usually done in the operating room under general or regional (spinal or epidural) anesthesia.

Linkage and Integration of services:

ART clinics should be closely linked with VIA clinics or sites providing cervical cancer prevention services, or ideally, provide the services at the unit.

Table 5.9. Healthcare delivery level by type of service and type of health care workers

Healthcare delivery level	Service provided	Type of health care workers
Tertiary hospital	VIA/cryotherapy/thermal ablation, PAP smear, colposcopy, LEEP biopsy, histopathology radiotherapy, radical surgery chemotherapy and palliative care	Nurse, midwives, health officer, MD residents and specialists (gyn/obn, gyn-oncologists)
Regional/general hospitals	VIA/cryotherapy/thermal ablation, PAP smear, colposcopy LEEP biopsy histopathology, radical surgery and palliative care	Nurse, midwives, health officer, MD residents and specialists (gyn/obs, gyn-oncologists)
District hospitals / primary hospitals	VIA/cryotherapy/ thermal ablation, biopsy, palliative care	Nurse, midwives, health officer, MD
Health centers	VIA/cryotherapy/ thermal ablation, palliative care	Nurse, midwives, health officer

For details on prevention, screening and treatment, refer to guideline for cervical cancer prevention and control in Ethiopia, 2021.