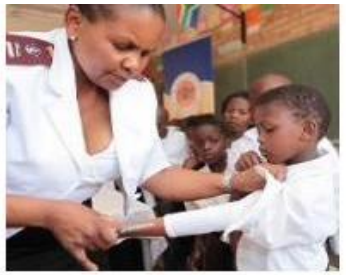
Severe Bacterial Infections in Advanced HIV Disease



Session 7

Updates on the 2026 National Consolidated Guidelines for the Prevention and Management of HIV

Severe Bacterial Infections

Presenter: Dr L Mawela

Clinical Care Platform – 7 September 2026

Global context

The decline in AIDS-related deaths has slowed in recent years, with 680,000 AIDS-related deaths in 2020 and **630,000 in 2024**, missing the global targets set at 500,000.

The proportion of patients presenting with AHD who are at substantially higher risk of dying from OIs has remained largely unchanged even though countries have implemented proactive “treat all” strategies.

While expanded access to antiretroviral therapy (ART) and earlier initiation of treatment has been important in reducing morbidity and mortality among people living with HIV (PLHIV), studies have shown that optimal long-term outcomes are highly dependent on retention in care.

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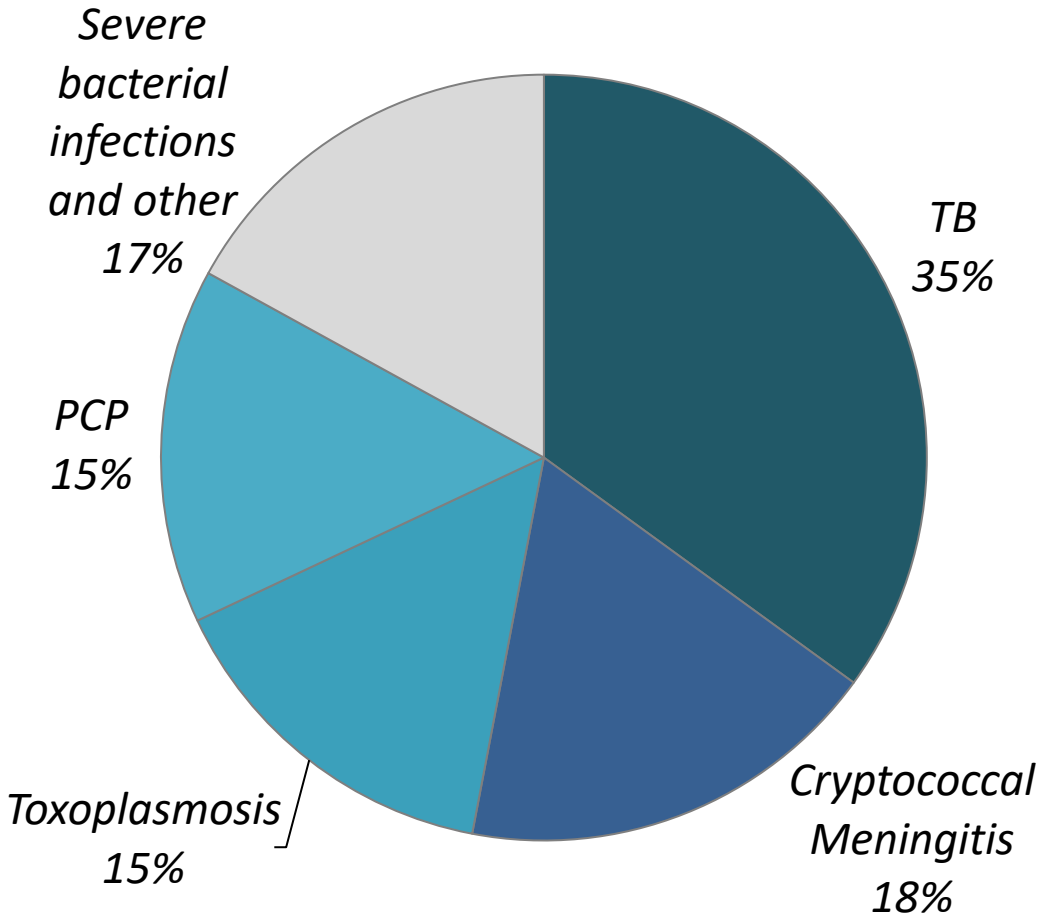
***Ref**: UNAIDS 2025 estimates.*

AIDS-related mortality is driven by a small number of OIs, including tuberculosis (TB), fungal infections like Cryptococcus, and SBIs

Most AIDS-related deaths of hospitalized adults are caused by OIs, including:



TB – 35%

CCM – 18%

SBIs & other infections – 17%

PCP – 15%

Toxoplasmosis – 15%

Source: *[1]REALITY NEJM 2017;377:233-45, [2]Causes of hospitalisation among PLHIV worldwide, 2014-23: a systematic review & meta-analysis . Nathan Ford et al*

Talking point 1 — Classification of OIs and what makes SBIs distinct

Type 1 — AIDS-defining	Almost exclusively in severely immunocompromised patients. Rarely seen in the community. Examples: Cryptococcal meningitis, Pneumocystis jirovecii pneumonia (PJP)
Type 2 — Severe bacterial infections	Routinely seen in non-HIV patients but more frequent and more severe as CD4 falls. Not always AIDS-defining, but major contributors to morbidity and mortality. Now widely considered opportunistic.

SBI examples: bacterial pneumonia · bacterial meningitis (incl. Listeria) · enteric infections · UTI / pyelonephritis · non-typhoidal salmonella bacteraemia · sepsis

Key message: SBIs are NOT a homogeneous group. The pathogen and organ system involved determines the diagnostic workup and treatment. A one-size-fits-all approach will miss diagnoses.

Talking point 2 — Clinical presentation and initial diagnosis

Key rule: Signs of serious bacterial infection can be SUBTLE in HIV patients. A high index of suspicion is essential with any new febrile illness — a normal temperature does not exclude sepsis.

Minimum diagnostic workup:

- Blood cultures in all hospitalised patients
- Sputum, urine, or stool specimens BEFORE antibiotics are started wherever possible
- Full blood count and kidney functions

Treatment principles:

- Empiric antimicrobial therapy must NOT be delayed while awaiting results — it can be life-saving
- Once pathogen is identified, direct therapy at the specific organism
- Co-infections are common — maintain a low threshold for empiric antibiotics
- Pregnant women with AHD are at high risk of sepsis, especially post-caesarean section

When did you last see a patient who was sicker than they looked on presentation?

Talking point 3 — Roles and responsibilities (Table 18)

Nurse at PHC	• Identify danger signs within scope of practice (APC/IMCI guidelines) • Recognise that a patient is unwell and may have a serious bacterial infection • Provide antibiotics before referral to hospital • Refer timeously to a higher level of care
Medical Officer at PHC	• Full history and clinical examination • Assessment and management of SBIs as outpatients where appropriate • Refer to hospital when inpatient care is indicated
Medical Officer at Hospital	• Full assessment and management of SBIs as inpatients • Investigations including blood cultures and imaging • Empiric and directed antimicrobial therapy • Discharge planning and follow-up coordination

What are the most common delays between identifying a sick patient and getting them to hospital at your facility?

Talking point 4a — Acute meningitis: recognition and LP decision

Emergency rule: Acute meningitis is a medical emergency. Antibiotics must NOT be delayed while waiting for a CT scan.

When to suspect meningitis:

- Any 2 of: fever, headache, neck stiffness, confusion
- Other features: rash, photophobia, seizures
- Children: excessive crying, irritability, bulging fontanelle, apnoea in neonates
- TB and Cryptococcus usually cause chronic meningitis but can present acutely

LP contraindications (neurological — CT brain first):

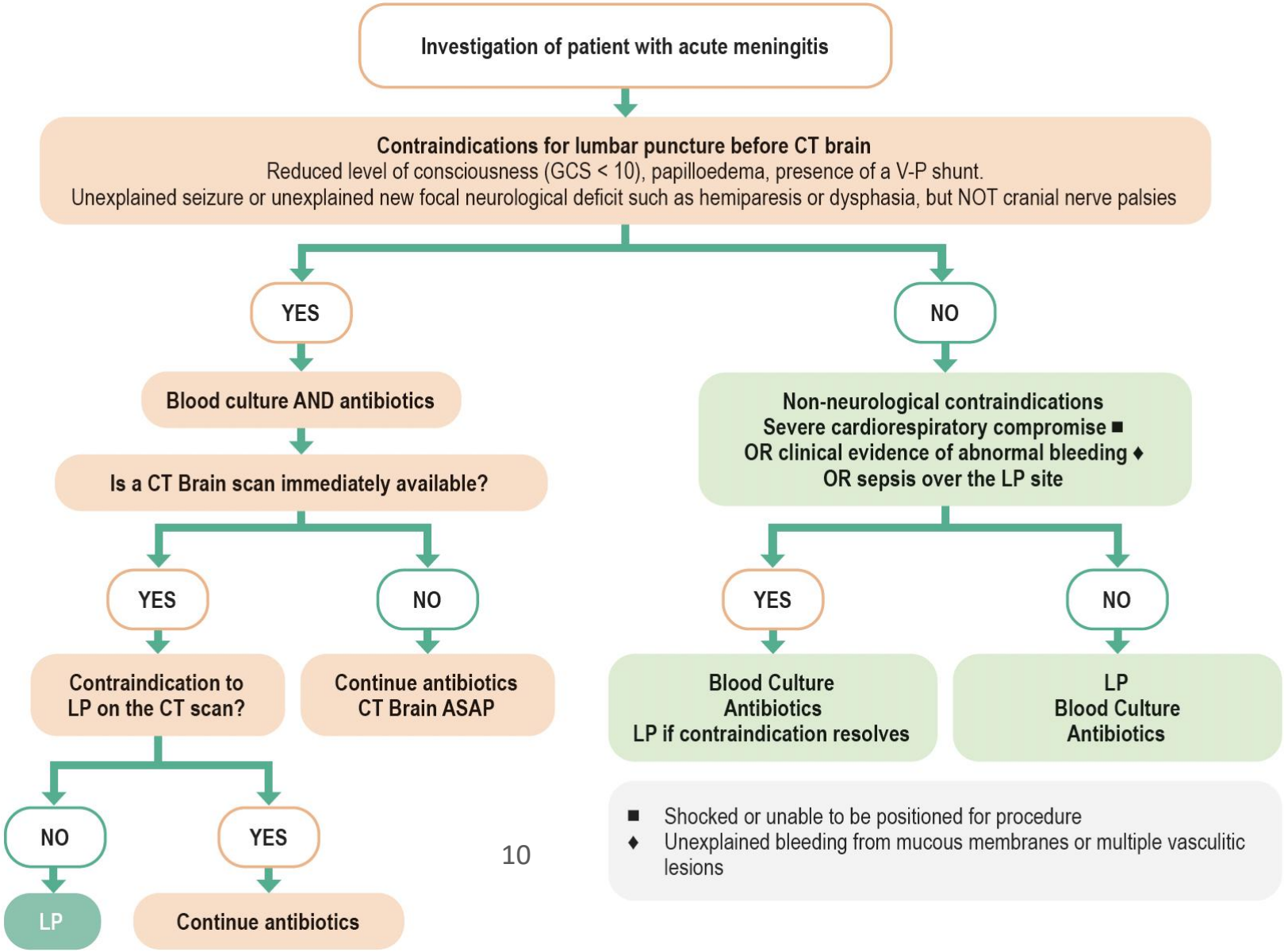
- GCS < 10, papilloedema, V-P shunt
- Unexplained seizure or unexplained new focal neurological deficit (hemiparesis, dysphasia)
- NOTE: cranial nerve palsies alone are NOT a contraindication to LP

Non-neurological LP contraindications:

- Severe cardiorespiratory compromise
- Clinical evidence of abnormal bleeding
- Sepsis over the LP site

Common error: Cranial nerve palsies (e.g. diplopia) are often misidentified as focal neurological deficits and used to delay LP inappropriately. Only unexplained hemiparesis or dysphasia are contraindications.

Investigation of a patient with acute meningitis



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Talking point 4b — Acute meningitis: antibiotic regimens

Ceftriaxone (first-line)

2 g IV 12 hourly for 10 days | Adults
100 mg/kg once daily | Children
IM or IO route if no IV access
Penicillin allergy is NOT a contraindication

Meropenem (if cephalosporin anaphylaxis only)

2 g IV 8 hourly for 7 days
Only if documented cephalosporin anaphylaxis
— NOT for penicillin allergy alone

Add if Listeria suspected (age >50, immunosuppressed, brainstem signs)

Ampicillin 3 g IV 6 hourly × 21 days
+ Gentamicin 5 mg/kg IV daily × 7 days
Consider adding ampicillin in neonates

Corticosteroids are NOT recommended in bacterial meningitis in this patient population.

After the first dose — Figure 13 decision pathway (Consolidated Guidelines p.83):

Gram stain positive	Directed therapy based on culture & sensitivity
Gram –ve, CSF normal	PCT <0.5 (CRP <20) or CrAg +ve → stop antibiotics; seek an alternative diagnosis; cryptococcal guidance if CLAT +ve
At 48–72 hrs	Normalising → continue for the recommended duration. NOT normalising → repeat LP; if still not improving, stop antibiotics and send large-volume CSF for mycobacterial culture/PCR
LP was contraindicated	Continue antibiotics and perform LP when it becomes safe

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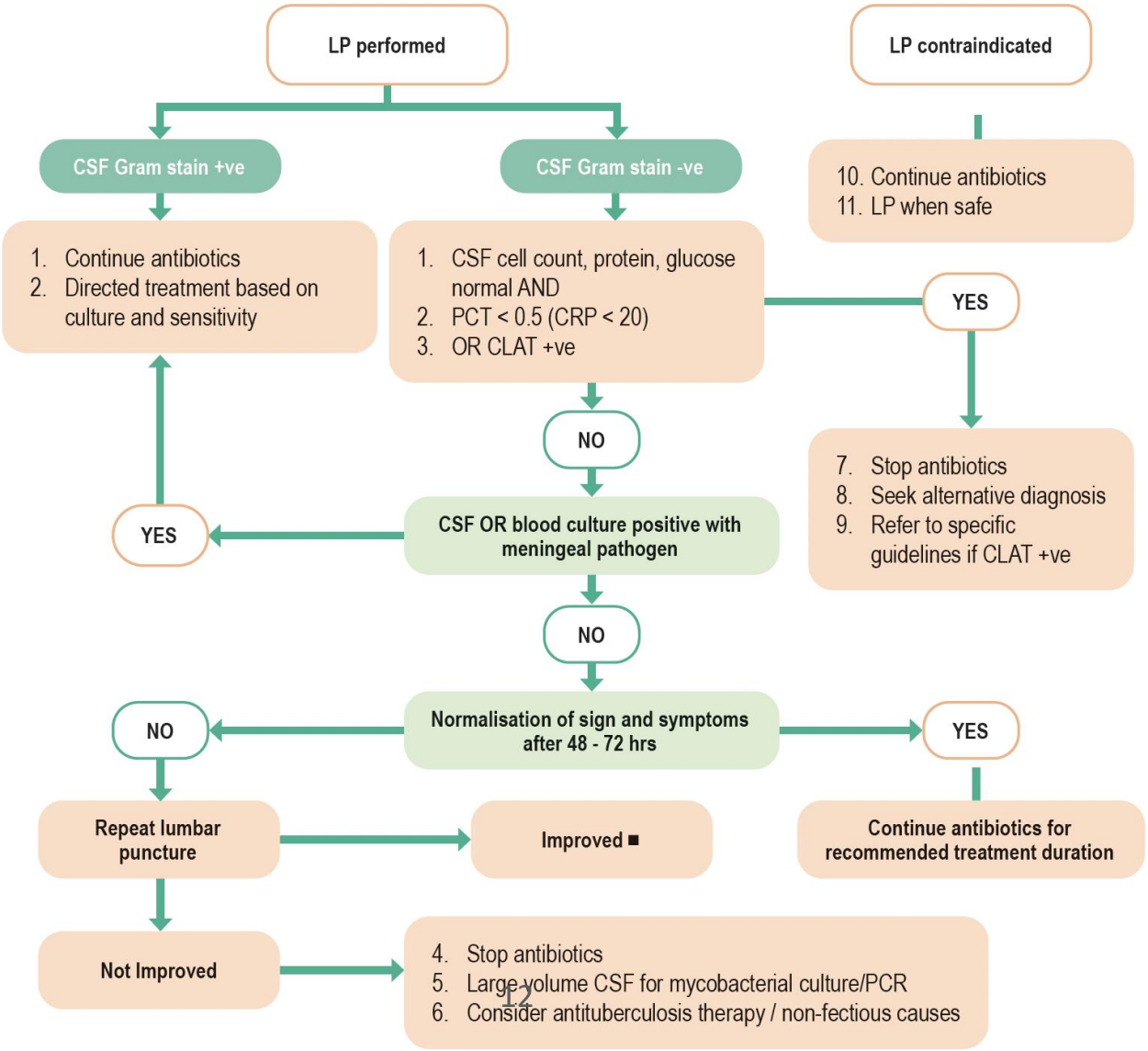
Approach to acute meningitis following the first dose of antibiotics



Talking point 4c — Bacterial pneumonia in AHD (Adult Hospital STG 16.6)

Antibiotic choice	HIV is a named co-morbidity, so ceftriaxone, IV, 2 g daily — not ampicillin — even without severe features. Severe pneumonia (cyanosis, confusion, hypotension or RR >30/min): add azithromycin 500 mg slow IV daily for 3 days.
Step-down and duration	Once haemodynamically stable with RR <25/min and temperature <37.8 °C, switch to amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly. Total duration 5–7 days; minimum 7 days for MRSA or Pseudomonas.
Always exclude TB	Send sputum for TB NAAT MTB/RIF Ultra even in a typical presentation. If response is poor at 48 hours, exclude TB and consider atypical bacterial pneumonia, which requires a macrolide.
Think PJP	Diffuse bilateral interstitial infiltrates with hypoxaemia suggest Pneumocystis jirovecii pneumonia. In a severely ill patient a normal CXR does not exclude pneumonia — repeat at 24–48 hours before ruling it out.

How often do you send an TB NAAT on a patient you are confident has bacterial pneumonia?

Talking point 5 — Diarrhoea in AHD: assessment and algorithm

Diarrhoea affects 40–80% of HIV-infected persons not on ART and is a frequent cause of hospital admission (dehydration, hypokalaemia, significant mortality).

Definitions:

- **Acute diarrhoea**: < 2 weeks · **Chronic diarrhoea**: ≥ 2 weeks
- Small bowel (**enteritis**): **large volume**, watery, bland; nausea/vomiting; often **apyrexial**
- Large bowel (**colitis**): **low volume**, frequent, blood/mucus; tenesmus; **may be pyrexial** with LIF tenderness

Chronic diarrhoea algorithm — 3 key questions (Figure 14):

Q1. Blood/mucus in stool?	Send stool MCS; warm stool for E. histolytica; if C. diff risk factors, request C. diff tests
Q2. Night sweats, weight loss, cough?	TB/MAC investigations: U-LAM, CXR ± sputum TB-NAAT, abdominal U/S, TB blood culture
Q3. Possible medication cause?	Consider switching LPV/r → DTG if eligible; review other implicated drugs

No endoscopy: Trial of empiric Isospora belli treatment; if no response, manage as Cryptosporidium; refer for endoscopy if no response.

Key pitfalls:

- Cryptosporidium: NO specific treatment — only ART. Start in hospital once CM/TBM excluded; never discharge for outpatient ART
- Overuse of loperamide with a protease inhibitor — causes severe ileus. Maximum 1 tablet 12-hourly with a PI
- Failing to send modified auramine stain for Cryptosporidium (standard MCS will miss it)
- No role for antidiarrhoeal medications in acute diarrhoea in children

Key features to identify on history & examination of a client with diarrhoea

Key features	
History	**Examination**
Duration and severity of diarrhoea. Previous episodes.	Hydration status
Stool consistency and presence of mucous or blood.	Blood pressure, pulse
Presence of constitutional symptoms: fever, night sweats, weight loss.	Temperature
Potential drug causes: protease inhibitors, recent antibiotic use.	Signs of TB (adenopathy, chest signs etc.)
Recent travel or possible contaminated water exposure	Abdominal examination: • Tenderness in the left iliac fossa (suggestive of acute colitis) • Other features of generalised tenderness are non-specific
HIV control: if currently taking ARVs, last HIV viral load and CD4	Fundoscopy for features of CMV retinitis (haemorrhages and exudates)

Management of chronic diarrhoea

- Resuscitate patient with oral and/or IVI fluids (normal saline) ± potassium as indicated
- Assess the following 3 things:

1. Is there blood / mucous in stool?

YES

- Send stool MCS
- Send warm stool for E.histolytica
- *If C.diff risk factors♦ also request C.diff tests on stool*

Pathogens present?

NO

Potential CMV colitis (especially if CD4 <50)

- Check for CMV retinitis on fundoscopy
- Arrange flexible sigmoidoscopy & biopsy for CMV

YES

Treat accordingly

See also note below ■

NO

- Send stool MCS + modified auramine stain (up to 3 stools if negative)

Pathogens present?

YES

Add TB/MAC Investigations & treat if positive / suggestive:

- U-LAM
- Chest X-ray +_sputum TB-NAAT
- Abdominal Ultrasound
- TB Blood culture

NO

2. Are there prominent night sweats, weight loss, or cough?

YES

3. Is there a potential medication cause?

YES

- Switch LPV/r to a DTG-containing regimen, if eligible
- Consider changing other medication

NO

No pathogens Identified

If access to endoscopy:

- Flexible sigmoidoscopy
- Colonoscopy
- Gastroscopy & duodenal biopsy
- If all of above negative, do CT abdomen to exclude malignancy

No access to endoscopy:

- Give trial of empiric *Isospora belti* treatment (see table 2)
- If no response, manage ARV's as for *Cryptosporidium* **
- If no response to above, refer for endoscopy.

Infectious causes of diarrhoea in AHD with suggested investigations and treatment

Protozoa	Presentation	Diagnosis	Specific treatment
• Coccidia	Small bowel		
Cryptosporidium		stool modified auramine	Nil
Cystoisospora belli (previously Isospora belli)		stool modified auramine	• Co-trimoxazole (CTX) (80/400mg) 4 tablets orally 12 hourly for 10 days • If allergic to CTX: give instead ciprofloxacin 500mg orally 12 hourly for 10 days.If no response, see section on refractory *Cystoisospora belli*
Microsporidia spp.		Stool calcofluor stain	Albendazole 400mg orally 12 hourly for 4 weeks
• Giardia	Small bowel	Stool microscopy	Metronidazole orally 400mg 8 hourly for 5 days or 2g daily for 3 days
• Amoebiasis	Large bowel	Stool microscopy	Metronidazole 800mg orally 8 hourly for 10 days

Infectious causes of diarrhoea in AHD with suggested investigations and treatment

Bacteria	**Large bowel**		
Salmonella typhi		Stool culture	Fluoroquinolone
Shigella		Stool culture	Fluoroquinolone
Campylobacter		Stool culture	Macrolide
Clostridium difficile (C.diff)		Stool toxin, GDH & C. *diff* PCR	• Metronidazole 400mg orally 8 hourly for 10-14 days • *Second line:* Vancomycin 125mg orally 6 hourly
Mycobacteria	**Small bowel**		
M.TB		Urine LAM Culture/biopsy/ ultrasound	Anti-TB therapy
M. avium-complex (MAC)		Blood or bone marrow TB culture (LAM may also be positive but non-specific)	Azithromycin & Ethambutol
Viral			
CMV	Large bowel	Biopsy	Ganciclovir
HIV	Small bowel	Exclude other causes	Antiretrovirals

Talking point 6 — Deteriorating despite OI treatment: Table 22 (1 of 2)

Drug not reaching the bug	Medication not given/dispensed correctly · Non-adherence (self-reporting unreliable) · Malabsorption from vomiting/diarrhoea (drug levels may assist) · Difficult drug penetration (TB cavities — surgery may be indicated) · Under-dosing for weight
Drug-drug interactions	Especially rifampicin, which significantly reduces levels of many co-administered drugs. Always check the interaction profile when a patient is on both rifampicin and other medications.
Bug resistant to drug	More likely if treatment was empiric or based on a test that does not identify resistance (e.g. urine LAM). Seek microbiological confirmation and drug sensitivities when available.
Incorrect diagnosis	Always reconsider when empiric therapy was started without microbiological confirmation. Co-infections are common in AHD — a second or third pathogen may be the reason for non-response.

Your patient started TB treatment 10 days ago and is not improving. Walk me through your systematic approach.

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Table 22 (2 of 2) — the four categories most often missed

Additional diagnosis	Patients with AHD often have more than one opportunistic infection, or a concurrent malignancy. Consider a second or even a third diagnosis before concluding that treatment has failed.
Adverse drug reaction	A patient may be responding to appropriate treatment yet appear to deteriorate because of an ADR — the guideline's own example is drug-induced liver injury (DILI, the subject of Session 2). Report all ADRs.
Inappropriate expectations	Some OIs improve slowly, and a patient can deteriorate despite correct therapy. TBM and PJP carry approximately 25% mortality even when treated appropriately.
IRIS	The last consideration and a diagnosis of exclusion. Risk factors: low CD4, short interval between OI treatment and ART. Paradoxical TB IRIS occurs in ~18%. Prednisone 1.5 mg/kg for 2 weeks then 0.75 mg/kg for 2 weeks in non-neurological paradoxical TB IRIS; steroids otherwise avoided.

Before you change the diagnosis — have you worked through all eight categories?

Part 2: Case Study Questions

5 Clinical Vignettes — Group Discussion (5–7 minutes each)

Case 1: The febrile patient with subtle signs

Presentation / diagnosis | Difficulty: Foundational

Clinical vignette

Themba is a 38-year-old male with AHD (CD4 52 cells/mm³) presenting to a clinic nurse with a 3-day history of feeling generally unwell, mild headache and reduced appetite. His temperature is 37.6°C. He has no neck stiffness and no cough. The nurse is reassured by the relatively normal temperature and plans to give him a paracetamol prescription and send him home.

Discussion questions:

1. Do you agree with the nurse's plan? What concerns you about this presentation?
2. What minimum workup should this patient receive before any decision is made?
3. What specific infections should be on the differential given his CD4 count?

Case 1 — Model answer (facilitator only)

FACILITATOR USE ONLY — Reveal after group discussion

Model answer

No — the plan is unsafe. Signs of serious bacterial infection in AHD patients can be subtle. A temperature of 37.6°C does not exclude sepsis or meningitis. With a CD4 of 52, Themba is at high risk of multiple serious OIs. Minimum workup: blood cultures, FBC, kidney functions, TB screen (urine LAM), urine MCS. The nurse must not send him home without a medical officer assessment. Top differentials: bacterial sepsis, bacterial or cryptococcal meningitis, TB (urine LAM indicated even without cough at this CD4). This patient should be assessed urgently and almost certainly referred to hospital.

After debrief: Ask participants to identify how this case applies to their own facility context before moving to the next vignette.

Case 2: The meningitis dilemma — LP or CT first?

Acute meningitis | Difficulty: Intermediate

Clinical vignette

Naledi is a 29-year-old HIV-positive woman presenting at hospital with a 2-day history of severe headache, fever (39.1°C), and confusion (GCS 12). She has mild neck stiffness. There is no papilloedema. She had a single generalised seizure 4 hours ago that self-terminated. A CT brain scanner is available at the hospital. The medical officer wants to wait for the CT before giving antibiotics.

Discussion questions:

1. Should the medical officer wait for the CT before starting antibiotics? Justify your answer.
2. Does Naledi have a contraindication to LP before CT? Which contraindication applies?
3. Walk through the initial management steps in the correct order.

Case 2 — Model answer (facilitator only)

FACILITATOR USE ONLY — Reveal after group discussion

Model answer

No — antibiotics must NOT be delayed for a CT scan under any circumstances. Blood cultures must be taken first, then ceftriaxone 2 g IV started immediately. Naledi has an unexplained seizure, which IS a contraindication to LP before CT. However, this does not delay antibiotics. Correct order: (1) Take blood cultures, (2) Give ceftriaxone 2 g IV immediately, (3) Arrange CT brain urgently, (4) If CT shows no contraindication, perform LP with blood cultures and antibiotics already running, (5) Continue antibiotics. Penicillin allergy history should be checked but is not a contraindication to ceftriaxone unless there is documented cephalosporin anaphylaxis.

After debrief: Ask participants to identify how this case applies to their own facility context before moving to the next vignette.

Case 3: The Listeria question

Antibiotic choice | Difficulty: Intermediate

Clinical vignette

Joseph is a 62-year-old male on chronic immunosuppressive medication for a kidney transplant who also has HIV (CD4 110 cells/mm³). He presents with acute meningitis: fever, severe headache, and meningism. He has new-onset brainstem signs including horizontal diplopia. He reports a penicillin allergy documented as 'rash 20 years ago.' The clinician considers starting only ceftriaxone.

Discussion questions:

1. Is penicillin allergy a contraindication to ceftriaxone? What would change the antibiotic plan?
2. Should you add Listeria coverage in this case? Motivate with reference to risk factors.
3. What is the correct antibiotic regimen if Listeria is suspected?

Case 3 — Model answer (facilitator only)

FACILITATOR USE ONLY — Reveal after group discussion

Model answer

Penicillin allergy is not a contraindication to ceftriaxone — a rash 20 years ago is not anaphylaxis. Only documented cephalosporin anaphylaxis warrants substitution, and then with meropenem 2 g IV 8 hourly. Yes, add Listeria cover: Joseph has age >50, chronic immunosuppression for a transplant, and brainstem signs (horizontal diplopia, suggesting rhombencephalitis), on top of HIV. Regimen: ceftriaxone 2 g IV 12 hourly PLUS ampicillin 3 g IV 6 hourly for 21 days AND gentamicin 5 mg/kg IV daily for 7 days (may be prolonged if the response is poor). Note the 21-day ampicillin course is much longer than the 10-day empiric ceftriaxone course. Note also that a VI nerve palsy may equally reflect raised intracranial pressure in cryptococcal disease — it is not a contraindication to LP.

After debrief: Ask participants to identify how this case applies to their own facility context before moving to the next vignette.

Case 4: The chronic diarrhoea investigation

Diarrhoea / workup | Difficulty: Intermediate

Clinical vignette

Lindiwe is a 34-year-old woman with AHD (CD4 88) admitted for severe watery diarrhoea and dehydration lasting 3 weeks. No blood or mucus in stool. She has night sweats and 5 kg weight loss over the past month. No cough. She is on LPV/r-based ART with a VL of 3,200 c/mL. Stool MCS is negative for standard pathogens. The admitting doctor plans to discharge her with oral rehydration and outpatient ART review.

Discussion questions:

1. Is the discharge plan appropriate? What critical diagnostic step has been missed?
2. What additional investigations should be requested given the full clinical picture?
3. If Cryptosporidium is suspected, what is the treatment and why should she not be discharged?

Case 4 — Model answer (facilitator only)

FACILITATOR USE ONLY — Reveal after group discussion

Model answer

No — discharge is inappropriate. Night sweats and weight loss require TB/MAC investigations: U-LAM, CXR ± sputum TB-NAAT, abdominal ultrasound, TB blood culture. Standard stool MCS does not detect Cryptosporidium — a modified auramine stain on up to 3 stools is needed. Her unsuppressed VL on LPV/r and diarrhoea suggests LPV/r as a contributor — switch to DTG if eligible. For Cryptosporidium: there is NO effective specific treatment. The only therapy is immune reconstitution (ART). She must be started on ART in hospital, once contraindications to immediate initiation (cryptococcal and TB meningitis) have been excluded. Discharging for outpatient ART initiation causes frequent re-admission.

After debrief: Ask participants to identify how this case applies to their own facility context before moving to the next vignette.

Case 5: The patient not responding to TB treatment

Table 22 / deterioration | Difficulty: Advanced

Clinical vignette

Siphamandla is a 45-year-old male on TB treatment for 12 days. He was started empirically on TB therapy after a positive sputum TB-NAAT with rifampicin susceptibility confirmed. He remains febrile and his clinical condition has not improved. He is on a PI-based ART regimen. The treating clinician is unsure whether to continue current TB treatment or change management.

Discussion questions:

1. What categories should the clinician work through systematically?
2. What specific drug interaction concern applies to this patient and what should be done?
3. Given rifampicin-sensitive TB-NAAT, how likely is resistance? What else could explain non-response?

Case 5 — Model answer (facilitator only)

FACILITATOR USE ONLY — Reveal after group discussion

Model answer

Systematic Table 22 approach: (1) Drug not reaching the bug — verify medications dispensed and administered correctly; assess adherence; consider malabsorption; check dosing for current weight; (2) Drug-drug interactions — rifampicin dramatically reduces PI levels to sub-therapeutic concentrations; urgent switch to DTG-based ART (with twice-daily DTG dosing) is indicated; (3) Bug resistant to drug — less likely given rifampicin-sensitive NAAT; seek microbiological confirmation if response inadequate; (4) Incorrect diagnosis — consider co-infection (bacterial pneumonia, cryptococcal meningitis, PJP) or non-infectious causes. The PI-rifampicin interaction is the most actionable finding: rifampicin is a potent inducer that reduces PI levels to potentially ineffective concentrations, compromising both ART and indirectly affecting TB treatment response. Then complete the table: additional diagnosis (a second OI is common in AHD), adverse drug reaction, inappropriate expectations (12 days is early — TBM and PJP carry ~25% mortality despite correct treatment), and IRIS as a diagnosis of exclusion.

After debrief: Ask participants to identify how this case applies to their own facility context before moving to the next vignette.

Key messages

1. Subtle signs are the rule in AHD — a high index of suspicion must be maintained for all new febrile illness
2. Antibiotics must NEVER be delayed waiting for CT results — blood cultures first, then antibiotics immediately
3. Penicillin allergy is NOT a contraindication to ceftriaxone. Only cephalosporin anaphylaxis warrants substitution
4. Cryptosporidium has no specific treatment — immune reconstitution (ART in hospital) is the only therapy
5. When a patient deteriorates despite OI treatment, apply the Table 22 framework systematically before changing diagnosis