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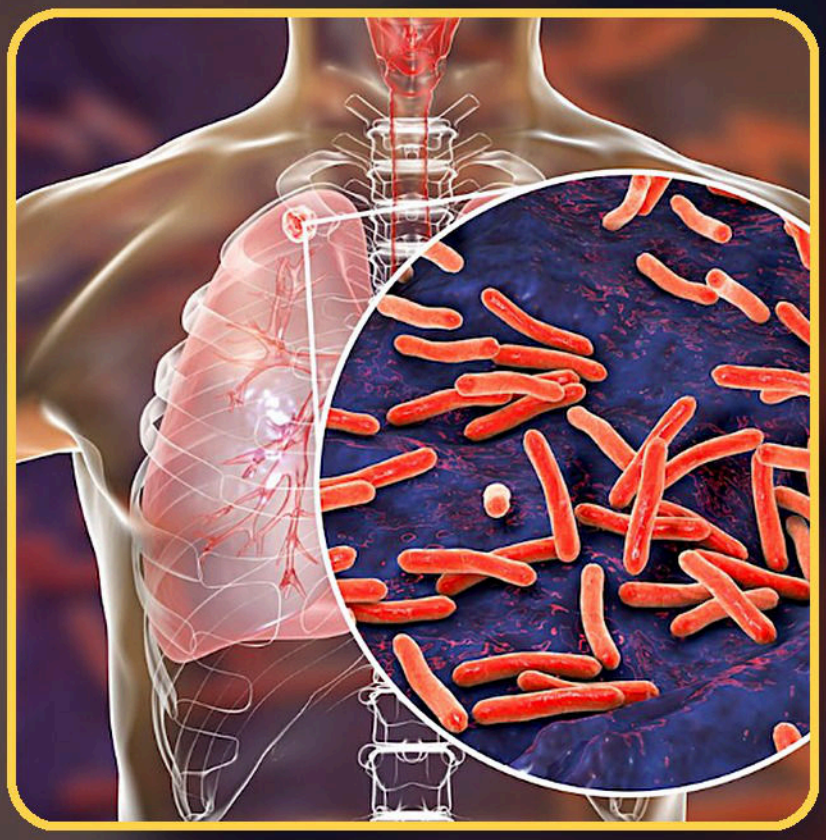
TUBERCULOSIS AT YOUR FINGERTIPS

Guidelines-Based Tuberculosis Manual for Clinicians & Examinees

MD Pulmonary Medicine · DNB Respiratory Medicine · MD General Medicine · NTEP Medical Officers

Dr. Gireesh Kumar K P

WHO Consolidated Guidelines 2025 · NTEP India · Index-TB · ATS/CDC/ERS/IDSA · Exam-pattern questions



EXPLORE BY SECTION — TAP TO JUMP

- 1 Tuberculosis Guidelines at a Glance
- 2 Tuberculosis — History, Epidemiology & Risk
- 3 Bacteriology — Clinical Overview
- 4 Pathology & Pathogenesis
- 5 Natural History & Prognosis
- 6 Pulmonary Tuberculosis
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NMC TB competencies — tap to open · Question bank · Contents

Amrita School of Medicine · Amrita Institute of Medical Sciences, Kochi

First Edition · 2027

FOREWORD

Foreword

From Dr. Gireesh Kumar K. P. · To postgraduates in Respiratory Medicine, General Medicine and every doctor who treats tuberculosis



Dear colleague,

Tuberculosis is the one disease that every Indian doctor will meet, whatever specialty they choose. It walks into the emergency department as massive haemoptysis, into the neurology ward as a confused young man with a cranial-nerve palsy, into the gynaecology clinic as infertility, into the orthopaedic OPD as back pain and into the ICU as miliary ARDS. It remains the world's leading infectious killer, and India still carries roughly a quarter of the global burden.

The last five years have changed TB care more than the previous fifty. Molecular tests have replaced the microscope as the first test, a 4-month regimen now exists for drug-susceptible disease, injections have disappeared from drug-resistant TB, and 6-month all-oral regimens — BPaLM and BDLLfxC — cure most MDR/RR-TB. Preventive treatment has become as important as treatment itself, and nutrition has been proven, in our own country, to reduce TB.

Tuberculosis at Your Fingertips follows the house style of *Pulmonary Medicine at Your Fingertips*. It is organised exactly as you think at the bedside: guidelines first, then the organism, the pathology, the natural history, pulmonary disease, every extrapulmonary organ on its own page, investigations, management and complications. Each topic opens with its competencies and closes with exam-pattern questions; algorithms let you think under pressure, tables let you revise at speed, and the guideline boxes keep you current with WHO 2025 and the National TB Elimination Programme.

Use this book to pass your examinations — but, more importantly, use it to finish every patient's treatment. A cured patient is the only real end point in tuberculosis.

With best wishes,

Dr. Gireesh Kumar K. P.
Principal, Amrita School of Medicine
Director, Academy for Emergency, Trauma & Critical Care Medicine (AETCM), Kochi
Kochi · 2027

How to use this manual

- **Guidelines first.** Section 1 summarises every WHO module and the NTEP; later topics refer back to it.
- **One organ, one page.** Section 7 gives every extrapulmonary site a single, complete page — ideal for last-minute revision.
- **Think in algorithms.** Flowcharts follow the NTEP and WHO decision pathways.
- **Navigate by tapping.** Cover, contents, section pages, topic buttons, the question bank, the curriculum and the index are all hyperlinked; every page footer links back to the cover, contents and index.

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How to Use This Book

This manual covers tuberculosis from the organism to the programme. Content is written in the clean, high-yield house style of the AETCM *At Your Fingertips* series and is aligned to the WHO consolidated guidelines on tuberculosis (Modules 1–6, 2024–2026 updates), the National TB Elimination Programme (NTEP) technical and operational guidelines, the Index-TB guidelines for extrapulmonary tuberculosis and the ATS/CDC/ERS/IDSA clinical practice guidelines.

Element	What it gives you
CBME competencies	What the postgraduate must be able to do for the topic, with the matching NMC syllabus area
In brief	A two-line summary that can open any long answer
Tables	Classification, differential diagnosis, investigations and drugs — fastest revision format
Algorithms	Step-by-step decisions based on NTEP and WHO pathways (colour key below)
Guideline snapshot	The current WHO / NTEP recommendation in one box
Recent advances	Updates from 2022 to 2026 — examiners' favourite "recent advances" questions
Clinical pearls	Bedside and viva points; common exam traps
Landmark trials	The evidence behind each recommendation (STREAM, Nix-TB, ZeNix, TB-PRACTECAL, endTB, BEAT-TB, Study 31, SHINE, RATIONS…)
Red flags	Situations where delay kills or disables
Imaging links	Every X-ray, CXR, CT, HRCT and MRI mention is a dotted blue link to Radiopaedia — it opens image cases for that topic's condition
Exam-pattern questions	Long-answer, short-note and case questions in the pattern of MD/DNB papers, also gathered in the question bank

Flowchart colour key

Start / end | Decision | Action | Urgent step | Information / alternative

Abbreviated regimen notation

The number before the letters is the duration in months; letters are drugs: **H** isoniazid, **R** rifampicin, **Z** pyrazinamide, **E** ethambutol, **P** rifapentine, **M** moxifloxacin, **Lfx** levofloxacin, **B/Bdq** bedaquiline, **Pa** pretomanid, **L/Lzd** linezolid, **D/Dlm** delamanid, **C/Cfz** clofazimine, **Cs** cycloserine, **Eto** ethionamide, **Am** amikacin. Thus **2HRZE/4HR** = 2 months of HRZE then 4 months of HR; **3HP** = 12 weekly doses of isoniazid + rifapentine.

Important note

Doses are for adults with normal renal and hepatic function unless stated. Guidelines change — confirm current NTEP circulars and the latest WHO operational handbooks before prescribing. This book supports, but does not replace, clinical judgement, programme guidance and supervised training.

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NMC Syllabus Map

Each section is mapped to the tuberculosis content of the National Medical Commission competency-based postgraduate curricula — MD Respiratory Medicine (Pulmonary Medicine), MD General Medicine and related specialties — and to the paper in which it is most often examined.

Book section	NMC syllabus content covered	Usual paper
1. Guidelines at a Glance	National TB Elimination Programme, WHO End TB Strategy, case definitions, programmatic management, notification, TB–HIV collaboration, recent guidelines	Paper IV
2. Tuberculosis: History, Epidemiology & Risk	Epidemiology of tuberculosis in India and the world, social determinants, risk groups, screening	Paper I / IV
3. Bacteriology	Microbiology of mycobacteria, transmission, molecular basis of drug resistance, NTM	Paper I
4. Pathology & Pathogenesis	Immunology of TB, granuloma, primary and post-primary disease, hypersensitivity phenomena	Paper I
5. Natural History & Prognosis	Spectrum of TB infection and disease, risk of progression, outcomes, post-TB lung disease	Paper I / II
6. Pulmonary Tuberculosis	Clinical features, radiology, miliary TB, TB in children, HIV, diabetes and pregnancy, differential diagnosis	Paper II
7. Extrapulmonary TB — Organ by Organ	Pleural, lymph node, pericardial, CNS, spinal, osteoarticular, abdominal, genitourinary, cutaneous, ocular and other forms	Paper II / III
8. Investigations	Smear, culture, DST, molecular tests, IGRA/TST/TBST, LAM, ADA, imaging, diagnostic algorithms	Paper II / IV
9. Management	Antituberculosis drugs, DS-TB and DR-TB regimens, adverse reactions, special situations, preventive treatment, infection control, vaccines	Paper II / IV
10. Complications	Haemoptysis, post-TB lung disease, aspergilloma, pneumothorax, respiratory failure, IRIS and paradoxical reactions	Paper II / III
11. Landmark Trials — Theory & References	Research methodology, evidence base for current regimens, prevention, diagnostics, steroids and ART timing	Paper IV

Clinical examination: TB features in nearly every long case (fibrocavitary disease, pleural effusion, collapse, bronchiectasis, empyema). Practise the summary statement, the differential diagnosis and the investigation plan given in Sections 6–8.

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SECTION 1

Tuberculosis Guidelines at a Glance

Paper IV · Programme, policy and recent advances

The four WHO consolidated guideline modules — Module 1 Prevention (TB preventive treatment, 2nd edition 2024), Module 2 Screening (2021), Module 3 Diagnosis (4th edition 2025) and Module 4 Treatment and care (2025) — summarised recommendation by recommendation, with definitions, the End TB Strategy and the National TB Elimination Programme (NTEP). Every later section builds on these pages.

1.1 The Global Framework — End TB Strategy & the WHO Guideline Modules 7
1.2 Definitions, Case Classification & Treatment Outcomes 9
1.3 WHO Module 1 — TB Preventive Treatment (2nd edition, 2024) 10
1.4 WHO Module 2 — Systematic Screening for TB Disease (2021) 12
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1.1 The Global Framework — End TB Strategy & the WHO Guideline Modules

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Programme management; End TB Strategy; UN high-level meeting targets
- ✓ State the vision, goal, pillars and milestones of the WHO End TB Strategy
- ✓ List the six WHO consolidated guideline modules and what each covers
- ✓ Explain the GRADE language — strong vs conditional recommendations and certainty of evidence

IN BRIEF The End TB Strategy (2015–2035) aims to end the global TB epidemic: by 2035, a 90% fall in TB incidence and a 95% fall in deaths compared with 2015, and no family facing catastrophic costs. WHO now issues all TB policy as modular "consolidated guidelines", each paired with an operational handbook.

End TB Strategy — vision, goal and targets

Milestones and targets (baseline 2015)

Indicator	2020 milestone	2025 milestone	2030 (SDG)	2035 target
Fall in TB deaths	35%	75%	90%	95%
Fall in TB incidence rate	20%	50%	80%	90%

Indicator	2020 milestone	2025 milestone	2030 (SDG)	2035 target
Households facing catastrophic costs	0%	0%	0%	0%

- **Pillar 1 — integrated, patient-centred care and prevention:** early diagnosis with universal DST, systematic screening of contacts and high-risk groups, treatment of all people with TB including DR-TB, TB/HIV collaboration, preventive treatment and vaccination.
- **Pillar 2 — bold policies and supportive systems:** political commitment and resources, engagement of communities and private providers, universal health coverage, notification, vital registration, drug quality, social protection and action on determinants.
- **Pillar 3 — intensified research and innovation:** new tools (diagnostics, drugs, vaccines) and implementation research.
- **Four principles:** government stewardship and accountability; coalition with civil society; human rights, ethics and equity; adaptation at country level.

UN high-level meeting on TB (2023) — commitments for 2023–2027

- Reach **90%** of people who develop TB with quality-assured diagnosis and treatment; provide TPT to at least **45 million** people (2024–2027).
- Use WHO-recommended rapid tests as the first test for all people with presumptive TB; deliver a health and social benefits package to all people with TB; licence a new safe, effective vaccine within five years.

The WHO consolidated guidelines — module map

Module	Topic (latest edition)	Pages	Headline content
Module 1 ›	Prevention — TB preventive treatment (2nd ed., 2024); infection prevention and control (2022); BCG	21 recs	Who gets TPT, ruling out disease, TST/IGRA/TBST, 6H, 3HP, 3HR, 1HP, 4R; **6Lfx** for MDR/RR-TB contacts
Module 2 ›	Screening — systematic screening for TB disease (2021)	17 recs	Target groups, symptom screen, CXR, **CAD**, CRP, mWRD
Module 3 ›	Diagnosis (4th ed., 2025)	21 recs	**Class-based** NAAT recommendations, concurrent testing (sputum + stool + urine LF-LAM), tNGS, LPA, TBI tests
Module 4 ›	Treatment and care (2025)	DS-TB, DR-TB, care & support	2HRZE/4HR, **4-month HPMZ**, child 4-month regimen, **BPaLM, BDLLfxC**, 9-month regimens, Hr-TB, adherence models
5	Children and adolescents (2022)	—	Treatment decision algorithms, 4-month regimen for non-severe TB, 6-month intensive TBM regimen
6	Comorbidities, vulnerable populations and people-centred care (TB & HIV, mental health, undernutrition, diabetes)	—	Integrated care; nutritional assessment and support

Reading a WHO recommendation

- **Strong** recommendation ("should") — desirable effects clearly outweigh harms; applies to most patients. **Conditional** ("may", "WHO suggests") — balance is closer; adapt to setting, values and resources.
- **Certainty of evidence (GRADE):** high, moderate, low, very low — independent of strength (e.g. BPaLM is conditional, very low certainty, yet regimen of choice).
- **Good practice statements** cover actions so obviously beneficial that grading is unnecessary (e.g. DST before retreatment).

◆ GUIDELINE SNAPSHOT

- Treatment recommendations live in Module 4 (2025), which consolidates and **supersedes** the 2022 DR-TB update; diagnosis is consolidated in Module 3 (2025), which for the first time merges tests for TB infection, disease and drug resistance in one document.
- The 2HRZE/6HE regimen and the retreatment "Category II" regimen (2HRZES/1HRZE/5HRE) are obsolete — retreatment is guided by rapid DST.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Describe the WHO End TB Strategy — vision, pillars and targets. *[Long answer · MD/DNB pattern]*
2. WHO consolidated guidelines on tuberculosis — modules and key recent changes. *[Short note]*

1.2 Definitions, Case Classification & Treatment Outcomes

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Case definitions; programmatic management; outcome reporting
- ✓ Define bacteriologically confirmed and clinically diagnosed TB, new and previously treated cases
- ✓ Define RR-TB, MDR-TB, Hr-TB, pre-XDR-TB and XDR-TB as per current WHO definitions
- ✓ Assign treatment outcomes including sustained treatment success

IN BRIEF Classification is by anatomical site, bacteriological status, history of previous treatment, HIV status and drug resistance. The 2021 definitions of pre-XDR and XDR-TB (now used in Module 4, 2025) replaced the injectable-based definitions, and treatment outcomes were simplified for both DS- and DR-TB.

Case definitions (WHO Module 4, 2025)

Term	Definition
Presumptive TB	A person with symptoms or signs suggestive of TB, or who screens positive (CXR, CRP in PLHIV, mWRD)
Bacteriologically confirmed	Specimen positive by smear microscopy, culture or a WHO-recommended rapid diagnostic test (WRD) — must be notified whether or not treatment starts
Clinically diagnosed	Not bacteriologically confirmed, but a medical practitioner decides to give a full course of TB treatment (includes cases diagnosed on X-ray, histology or clinical grounds)
Pulmonary TB (PTB)	Involves lung parenchyma or tracheobronchial tree; a person with both PTB and EPTB is classified as PTB
Extrapulmonary TB (EPTB)	Organs other than lungs — pleura, lymph nodes, abdomen, genitourinary tract, skin, bones and joints, meninges. Isolated pleural effusion and mediastinal/hilar nodes without lung lesion = EPTB
Severe EPTB	Miliary TB, TB meningitis, osteoarticular or pericardial TB; in children < 15 years, any EPTB other than peripheral lymphadenopathy or isolated mediastinal mass without compression
Extensive (advanced) PTB	Bilateral cavitary disease or extensive parenchymal damage on CXR; in children, cavities or bilateral disease
New case	Never treated, or took TB drugs for < 1 month
Previously treated	≥ 1 month of TB drugs in the past — subgrouped as recurrent (relapse/reinfection), treatment after failure, treatment after loss to follow-up, and other previously treated

Drug-resistance categories

Category	Definition
Hr-TB	Isoniazid-resistant, rifampicin-susceptible
RR-TB	Resistant to rifampicin (± isoniazid or others) — managed exactly like MDR-TB ("MDR/RR-TB")
MDR-TB	Resistant to at least rifampicin **and** isoniazid
Pre-XDR-TB	MDR/RR-TB **plus** resistance to any fluoroquinolone (levofloxacin or moxifloxacin)
XDR-TB	MDR/RR-TB **plus** fluoroquinolone resistance **plus** resistance to at least one other Group A drug (bedaquiline or linezolid)
Mono / poly-resistance	Resistance to one / more than one first-line drug other than both H and R

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Treatment outcome definitions (WHO 2021 — same for DS- and DR-TB)

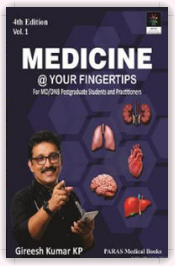
Outcome	Definition
Cured	Bacteriologically confirmed PTB at start; completed treatment as recommended by national policy with evidence of bacteriological response and no evidence of failure
Treatment completed	Completed treatment; no evidence of failure, but no record of bacteriological response
Treatment failed	Regimen terminated or permanently changed to a new regimen or treatment strategy (e.g. lack of response, adverse reactions, new resistance)
Died	Death from any cause before or during treatment
Lost to follow-up	Did not start treatment, or treatment interrupted for **2 consecutive months or more**
Not evaluated	No outcome assigned (includes "transferred out" with unknown outcome)
Treatment success	Cured + treatment completed
Sustained treatment success	Assessed **6 months (DS-TB) or 12 months (DR-TB)** after successful treatment: alive and free of TB

★ **CLINICAL PEARLS & EXAM FOCUS**

- Bacteriological response = culture (or smear for DS-TB) conversion; culture conversion needs **two consecutive negative cultures taken ≥ 7 days apart**.
- "Defaulter" and "relapse" as outcome labels are obsolete — use "lost to follow-up" and "recurrent".
- Pre-XDR is defined by the fluoroquinolone (not the injectable) — a favourite exam trap.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Define pre-XDR and XDR-TB. Why were the definitions revised in 2021? *[Short note]*
2. Treatment outcome definitions in tuberculosis — what is sustained treatment success? *[Short note]*



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1.3 WHO Module 1 — TB Preventive Treatment (2nd edition, 2024)

‹ NMC curriculum | Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Prevention; TB infection; TPT
- ✓ List the population groups who should receive TPT and how TB disease is ruled out first
- ✓ Choose between TST, IGRA and TBST to test for TB infection
- ✓ Prescribe the recommended TPT regimens, including 6Lfx for contacts of MDR/RR-TB

IN BRIEF About a quarter of the world is infected; 5–10% progress to disease over a lifetime, mostly within 5 years. TPT (60–90% efficacy) is a core End TB intervention. The 2024 edition has 21 recommendations across four steps: identify, rule out disease, test for infection, treat.

Source document: WHO consolidated guidelines on tuberculosis. Module 1: Prevention — tuberculosis preventive treatment, 2nd edition (2024) ›

Step 1 — who should receive TPT

Population	Recommendation	Strength
Adults & adolescents with HIV	TPT for all in whom TB is unlikely — including those on ART, pregnant women and previously treated, **even if TBI testing unavailable**	Strong
Infants < 12 months with HIV	TPT if in contact with a TB patient and disease excluded	Strong
Children ≥ 12 months with HIV	TPT in high-transmission settings regardless of contact	Strong
Child with HIV who completed TB treatment	May receive TPT	Conditional
Household contacts < 5 years	TPT even if TBI testing unavailable (contact of bacteriologically confirmed PTB)	Strong
Household contacts ≥ 5 years	May be given TPT	Conditional
Anti-TNF therapy, dialysis, transplant candidates, silicosis	Systematically **test and treat** TBI	Strong
Prisoners, health workers, migrants from high-burden countries, homeless, people who use drugs	Test-and-treat **may be considered**	Conditional

Step 2 — rule out TB disease before TPT

- PLHIV: **WHO four-symptom screen** (current cough, fever, weight loss, night sweats); CXR, **CRP > 5 mg/L** and mWRD may be added. Children with HIV: poor weight gain, fever, current cough or contact history.
- HIV-negative contacts ≥ 5 years and other risk groups: **no symptoms + normal CXR** rules out disease.
- Contacts < 15 years: cough, fever or poor weight gain, or CXR, or both.

Step 3 — testing for TB infection

- **TST or IGRA** can be used (strong); **M. tuberculosis antigen-based skin tests (TBST — e.g. Cy-Tb, C-Tb, Diaskintest)** may be used (conditional). Testing is desirable but must never be a barrier for PLHIV and child contacts < 5 years.

Step 4 — TPT regimens (Recs 19–21)

Regimen	Drugs & frequency	Strength	Points
6H / 9H	Daily isoniazid 6 or 9 months	Strong	Cheapest; hepatotoxicity; low completion
3HP	Weekly rifapentine + isoniazid × 12 doses	Strong	Usable with dolutegravir; flu-like reactions
3HR	Daily isoniazid + rifampicin × 3 months	Strong	Preferred child formulation available
1HP	Daily rifapentine + isoniazid × 28 days	Conditional (alternative)	Age ≥ 13 years in most programmes
4R	Daily rifampicin × 4 months	Conditional (alternative)	Good for INH intolerance; interactions
6Lfx	Daily levofloxacin × 6 months	Strong (contacts of MDR/RR-TB)	NEW 2024 — based on **VQUIN** and **TB-CHAMP** trials

✦ RECENT ADVANCES & GUIDELINE UPDATES

- 2024 changes: 6Lfx recommended for contacts of MDR/RR-TB in all settings; TBST added; CXR with CAD, CRP and mWRD added to rule out disease; recommendation against TBI testing in diabetes, alcohol use, smoking and underweight withdrawn and replaced by guidance text; 36-month isoniazid for PLHIV withdrawn.

★ CLINICAL PEARLS & EXAM FOCUS

- Previous TB treatment, pregnancy and ART are **not** reasons to deny TPT in PLHIV.
- Rifapentine regimens must not be given with protease inhibitors or NNRTIs other than efavirenz; dolutegravir is acceptable with 3HP.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Programmatic management of TB preventive treatment — candidates, regimens and the role of levofloxacin. *[Long answer]*
2. Compare TST, IGRA and the new antigen-based skin tests. *[Short note]*

1.4 WHO Module 2 — Systematic Screening for TB Disease (2021)

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Active case finding; screening tools
- ✓ Identify populations that should be systematically screened
- ✓ Choose screening tools — symptom screen, CXR, CAD, CRP, mWRD
- ✓ Distinguish screening from diagnosis and triage

IN BRIEF Systematic screening is the organised, active search for TB disease in people who have not sought care. Module 2 contains 17 recommendations: 8 on whom to screen and 9 on tools. Screening never replaces diagnosis — a positive screen must be followed by a WHO-recommended rapid diagnostic test.

Source document: WHO consolidated guidelines on tuberculosis. Module 2: Screening — systematic screening for tuberculosis disease (2021) ›

Whom to screen

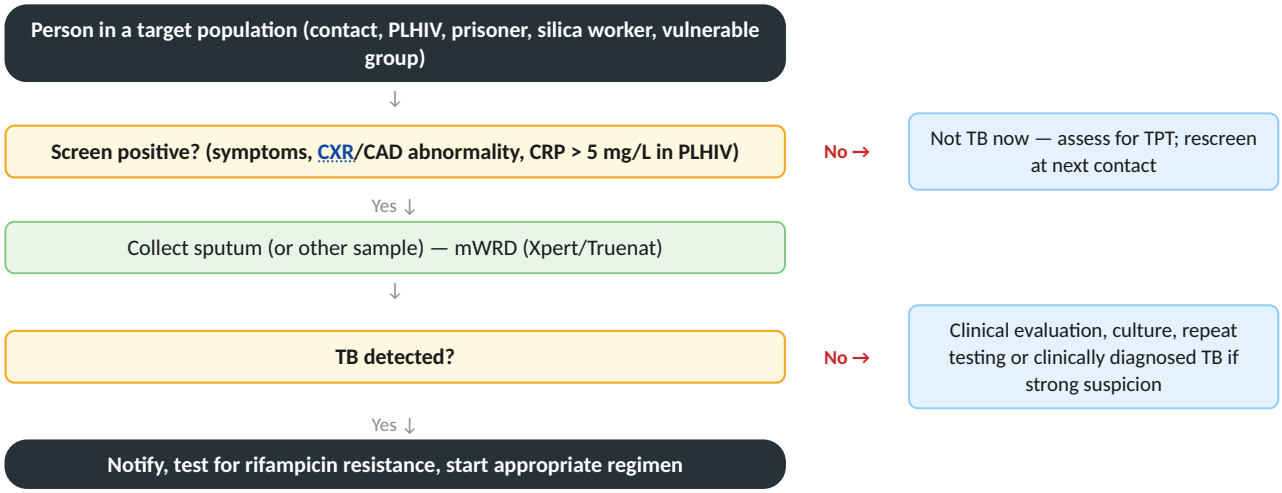
Population	Recommendation	Strength
General population where TB prevalence ≥ 0.5%	May be screened	Conditional
Structural risk groups — urban poor, homeless, remote/isolated, indigenous, migrants, refugees, displaced	May be screened	Conditional
People living with HIV — at every facility visit	Should be screened	Strong
Household and close contacts	Should be screened	Strong
Prisons and penitentiary institutions	Should be screened	Strong
Current and former silica-exposed workers	Should be screened	Strong
People with a clinical risk factor seeking care, where prevalence ≥ 100/100 000	May be screened	Conditional
Untreated fibrotic lesion on CXR	May be screened	Conditional

Screening tools

Tool	WHO position
Symptom screen	Any cough ≥ 2 weeks (prolonged cough) is specific but insensitive; **any cough** more sensitive; PLHIV — **four-symptom screen** (current cough, fever, weight loss, night sweats), strong
Chest X-ray	Most sensitive screening tool; any abnormality → test; ≥ 15 years and PLHIV
CAD software	May **replace human readers** for digital CXR screening and triage in people ≥ 15 years (conditional, low certainty) — needs local threshold calibration
C-reactive protein	PLHIV: cut-off **> 5 mg/L** may be used (conditional)
mWRD (e.g. Xpert)	May be used to screen high-risk groups and PLHIV; **inpatients with HIV in wards with TB prevalence > 10% should be tested** with mWRD (strong)
Children < 15 years (contacts)	Any one of cough, fever or poor weight gain, or CXR, or both (strong)
Children < 10 years with HIV	Current cough, fever, poor weight gain or close TB contact (strong)

AETCM Academy for Emergency, Trauma & Critical care Medicine

Algorithm 1.1 · Screening cascade (WHO Module 2 / NTEP active case finding)



★ CLINICAL PEARLS & EXAM FOCUS

- Number needed to screen (NNS) is lowest in contacts, PLHIV, prisoners and people with prior TB.
- India's 100-day TB Mukt Bharat Abhiyaan used handheld AI-enabled X-ray units to screen vulnerable groups irrespective of symptoms — a programmatic application of Module 2.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Active case finding in tuberculosis — principles, target groups and tools. *[Long answer]*
2. Computer-aided detection (CAD) for chest radiography in TB. *[Short note]*

1.5 WHO Module 3 — Diagnosis (4th edition, 2025)

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Diagnosis of TB infection, disease and drug resistance
- ✓ List the classes of WHO-recommended NAATs and their indications
- ✓ Apply concurrent testing strategies in PLHIV and children
- ✓ Choose molecular tests for detection of drug resistance (LPA, LC-aNAAT, tNGS)

IN BRIEF The 2025 edition is the first to combine guidance on TB infection, disease and drug resistance. It establishes test **classes** rather than products: low-complexity automated NAATs (LC-aNAAT — Xpert MTB/RIF, Xpert Ultra, Truenat MTB Plus/ MTB-RIF Dx) and low-complexity manual NAATs (LC-mNAAT — TB-LAMP). Smear and culture are no longer initial tests.

Source document: WHO consolidated guidelines on tuberculosis. Module 3: Diagnosis, 4th edition (2025) ›

The 21 recommendations — grouped

No.	Recommendation (condensed)	Strength / certainty
1	Adults & adolescents with symptoms or screen-positive: **LC-aNAAT on respiratory samples** as the initial test, rather than smear or culture	Strong, high
2	Bacteriologically confirmed TB: LC-aNAAT for initial detection of rifampicin resistance, rather than culture DST	Strong, high
3	Suspected TB meningitis: LC-aNAAT on **CSF** as initial test	Strong, moderate
4	Suspected EPTB: LC-aNAAT on lymph-node aspirate, pleural tissue/fluid, synovial, peritoneal or pericardial fluid	Strong, low–very low

No.	Recommendation (condensed)	Strength / certainty
5	Moderate-complexity automated NAATs (e.g. Abbott RealTime, BD MAX, cobas MTB) for TB and R/H resistance	Conditional, moderate
6	LC-mNAAT (TB-LAMP) on respiratory samples as initial test	Strong, high
7	Adults/adolescents with HIV (symptomatic, seriously ill or advanced HIV): **concurrent LC-aNAAT on sputum + urine LF-LAM**	Strong, low
8	Children HIV-negative/unknown: **concurrent LC-aNAAT on respiratory + stool** samples	Strong, low
9	Children with HIV: concurrent respiratory + stool NAAT **+ urine LF-LAM**	Conditional, low
10	LC-aNAAT (Xpert MTB/XDR) for isoniazid and fluoroquinolone resistance	Conditional, moderate
11–12	LC-aNAAT for ethionamide (inhA promoter) and amikacin resistance in RR-TB	Conditional
13	First-line LPA on smear-positive sputum or isolate for R and H resistance	Conditional, moderate
14–15	Second-line LPA in MDR/RR-TB for fluoroquinolone and SLID resistance	Conditional
16	High-complexity reverse-hybridisation NAAT on isolates for pyrazinamide resistance	Conditional, very low
17	**Targeted next-generation sequencing (tNGS)** on respiratory samples for R, H, FQ, Z, E resistance	Conditional
18	tNGS in RR-TB for H, FQ, **bedaquiline, linezolid, clofazimine**, Z, E, amikacin, streptomycin	Conditional
19	TBST may be used for TB infection	Conditional, very low
20	TST or IGRA can be used for TB infection	Strong
21	IGRA and TST **should not be used** in LMICs to diagnose active TB	Strong

✦ RECENT ADVANCES & GUIDELINE UPDATES

- Box A changes (2025): two new NAAT classes replace product-specific recommendations; concurrent testing of respiratory and non-respiratory samples for PLHIV and children; TB infection tests moved into Module 3.
- 2026: WHO announced first recommendations on **near point-of-care NAATs**, **tongue swabs** and **sputum pooling** — to be incorporated in the next Module 3 edition.

★ CLINICAL PEARLS & EXAM FOCUS

- Universal DST = every bacteriologically confirmed patient is tested at least for rifampicin; every RR-TB patient is tested at least for fluoroquinolones (and ideally bedaquiline, linezolid).

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. WHO-recommended rapid diagnostic tests for TB — classes and indications. *[Long answer]*
2. Concurrent testing strategies for TB in people living with HIV and children. *[Short note]*

1.6 WHO Module 4 — Drug-Susceptible TB Treatment & Care (2025)

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Treatment of DS-TB; HIV; steroids; care and support
- ✓ State the recommended regimens for drug-susceptible TB in adults and children
- ✓ Describe the eligibility for the 4-month HPMZ regimen
- ✓ Time ART in TB–HIV co-infection and use adjuvant steroids appropriately

IN BRIEF The 6-month 2HRZE/4HR regimen, given daily as fixed-dose combinations, remains the standard. Two 4-month options exist: 2HPMZ/2HPM for people ≥ 12 years, and 2HRZ(E)/2HR for children 3 months–16 years with non-severe TB.

Source document: WHO consolidated guidelines on tuberculosis. Module 4: Treatment and care (2025) — Chapters 1 and 3 ›

Chapter 1 — DS-TB recommendations

No.	Recommendation	Strength / certainty
1.1	New pulmonary TB: 6 months of rifampicin — **2HRZE/4HR** (applies also to EPTB except CNS, bone and joint, where longer therapy is suggested)	Strong, high
1.2	Daily dosing throughout	Strong, high
1.3	Thrice-weekly dosing **not recommended** in either phase	Conditional, very low
1.4	**Fixed-dose combinations** preferred over separate drugs	Conditional, low
1.5	Smear-positive at end of intensive phase: **do not extend** the intensive phase	Strong, high
2.1	≥ 12 years, DS pulmonary TB: **2HPMZ/2HPM** (isoniazid, rifapentine, moxifloxacin, pyrazinamide)	Conditional, moderate
2.2	Children 3 months–16 years, **non-severe** TB: **2HRZ(E)/2HR**	Strong, moderate
3.1	PLHIV: at least the same duration as HIV-negative	Strong, high
3.2	**ART within 2 weeks** of starting TB treatment, regardless of CD4 (in TB meningitis ART is usually deferred 4–8 weeks — see [[t-7-5	7.5]])
4.1	TB meningitis: **dexamethasone or prednisolone tapered over 6–8 weeks**	Strong, moderate
4.2	TB pericarditis: adjuvant steroids **may** be used	Conditional, very low

Chapter 3 — care and support

- Health education and counselling for all (strong); a **package of adherence interventions** with a suitable administration option (conditional).
- Adherence tools: tracers (SMS, calls, home visits), **digital medication monitors**, **material support** (food, cash, transport), psychological support, staff education.
- **Community- or home-based treatment support** preferred over facility-based or unsupervised; trained lay providers or health workers preferred over family; **video-supported treatment** may replace in-person support.
- MDR-TB: mainly **ambulatory**, **decentralised** care. Children: decentralised, **family-centred** integrated models.

◆ **GUIDELINE SNAPSHOT**

- The term "DOT" is replaced by **treatment support** — people-centred, without coercion.

★ **CLINICAL PEARLS & EXAM FOCUS**

- 2HPMZ/2HPM is not for weight < 40 kg, EPTB, pregnancy or PLHIV with CD4 < 100 (excluded in **Study 31/A5349**); rifapentine interacts with most ART except efavirenz.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Recent WHO recommendations for treatment of drug-susceptible TB, including 4-month regimens. *[Long answer]*

1.7 WHO Module 4 — Drug-Resistant TB Treatment (2025)

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Treatment of DR-TB; programme management of DR-TB
- ✓ List the 6-month, 9-month and longer regimens for MDR/RR-TB and their eligibility
- ✓ Classify second-line drugs into Groups A, B and C
- ✓ Manage Hr-TB, HIV and HCV co-infection and surgery in DR-TB

IN BRIEF Module 4 (2025) supersedes the 2022 update. Two 6-month all-oral regimens are now first choice — **BPaLM** (age ≥ 14, not in pregnancy) and the new **BDLLfxC** (all ages, including pregnancy and children). Three modified 9-month regimens (BLMZ > BLLfxCZ > BDLLfxZ) join the original 9-month bedaquiline regimen for fluoroquinolone-susceptible disease.

Source document: WHO consolidated guidelines on tuberculosis. Module 4: Treatment and care (2025) — Chapter 2 ›

The DR-TB recommendations

No.	Recommendation	Strength / certainty
1.1	**BPaLM** — bedaquiline, pretomanid, linezolid 600 mg, moxifloxacin × 6 months for MDR/RR-TB; **BPaL** if FQ-resistant (pre-XDR)	Conditional, very low
1.2	**BDLLfxC** — bedaquiline, delamanid, linezolid 600 mg, levofloxacin, clofazimine × 6 months, MDR/RR-TB with or without FQ resistance (NEW)	Conditional, very low
2.1	9-month all-oral bedaquiline regimen when FQ resistance excluded	Conditional, very low
2.2	Modified 9-month regimens **BLMZ, BLLfxCZ, BDLLfxZ** (preference in that order) when FQ resistance excluded (NEW — endTB trial)	Conditional, very low
2.3	**Against** 9-month DCLLfxZ or DCMZ	Conditional
3.1–3.17	Longer (18–20 month) individualised regimens built from Groups A, B, C	Mixed
4.1	Hr-TB: **6 months of rifampicin, ethambutol, pyrazinamide, levofloxacin (6REZLfx)**; no injectables (4.2)	Conditional
5.1	Longer regimens: sputum culture plus smear for monitoring, **monthly**	Strong
6.1	ART in all HIV + DR-TB, as early as possible (**within 8 weeks**)	Strong
7.1	Elective partial lung resection may be used with a recommended regimen	Conditional
8.1	MDR/RR-TB with HCV: **co-administer** HCV and TB treatment (NEW)	Conditional

Eligibility — the two 6-month regimens

Criterion	BPaLM / BPaL	BDLLfxC
Age	≥ 14 years	**All ages** including children
Pregnancy / breastfeeding	**Not recommended** (pretomanid safety data limited)	**Can be used**
FQ resistance	BPaL (drop M)	Drop Lfx → **BDLC**; if FQ-susceptible drop clofazimine → **BDLLfx**
Disease site	PTB and EPTB except CNS, osteoarticular, disseminated multi-organ	Same exclusions
Prior exposure	< 1 month to B, Pa, L, D (or resistance excluded)	< 1 month to B, L, D, C
Evidence	**TB-PRACTECAL** (89% vs 52% success), ZeNix, Nix-TB	**BEAT-Tuberculosis** trial

Grouping of medicines for longer regimens

Group	Medicines and rule
A	**Levofloxacin/moxifloxacin, bedaquiline, linezolid** — include all three
B	**Clofazimine, cycloserine/terizidone** — add one or both
C	Ethambutol, delamanid, pyrazinamide, imipenem–cilastatin or meropenem (with clavulanate), amikacin (or streptomycin), ethionamide/prothionamide, p-aminosalicylic acid — to complete the regimen

- Start with **at least four likely effective drugs**, keep **at least three** after bedaquiline stops. Kanamycin and capreomycin are **not** used; clavulanic acid alone is not counted.
- Duration **18–20 months**, or **15–17 months after culture conversion**; injectable intensive phase 6–7 months if amikacin used.

★ CLINICAL PEARLS & EXAM FOCUS

- Linezolid is 600 mg once daily in BPaLM/BDLLfxC — peripheral and optic neuropathy, myelosuppression need monitoring.
- The 9-month regimen with **linezolid** (2 months) instead of ethionamide can be used in pregnancy.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Discuss the WHO 2025 recommendations for treatment of MDR/RR-TB. *[Long answer · Recent advances]*
2. BPaLM versus BDLLfxC — eligibility and evidence. *[Short note]*

1.8 National TB Elimination Programme (NTEP) — India

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** NTEP; National Strategic Plan; Ni-kshay; TB Mukt Bharat
- ✓ Describe the structure, strategy and key schemes of NTEP
- ✓ Apply NTEP diagnostic and treatment policies in daily practice
- ✓ Explain notification, Ni-kshay and patient-support schemes

IN BRIEF The Revised National TB Control Programme was renamed the **National TB Elimination Programme** in 2020. Under the National Strategic Plan (Detect–Treat–Prevent–Build), India aims at TB elimination ahead of the SDG 2030 target, backed by free molecular diagnosis, daily FDC treatment, DBT nutrition support and community support (Ni-kshay Mitra).

Evolution

Year	Milestone
1962	National TB Programme (BCG, domiciliary treatment, District TB Centres)
1997	RNTCP — DOTS nationwide by 2006
2012	TB made a **notifiable disease** (private sector included); Nikshay launched
2017	Daily FDC regimen nationwide; NSP 2017–25 (Detect, Treat, Prevent, Build)
2018	**Ni-kshay Poshan Yojana** (DBT nutrition support)
2020	Renamed **NTEP**
2022	**Pradhan Mantri TB Mukt Bharat Abhiyaan** — Ni-kshay Mitra community support
2024	NPY increased to **₹1000/month** for the whole treatment; household contacts covered by Ni-kshay Mitra; nationwide **BPaLM** rollout approved; 100-day TB Mukt Bharat Abhiyaan (from 7 Dec 2024)
2025	TB Mukt Bharat Abhiyaan extended to all districts

Key NTEP policies

- **Presumptive TB:** cough ≥ 2 weeks, fever, weight loss, night sweats, haemoptysis, or any CXR abnormality; in PLHIV, contacts, diabetics and other vulnerable groups — symptoms of **any duration**.
- **Upfront NAAT** (CBNAAT/Truenat) for all presumptive TB as far as possible; **universal DST** — every diagnosed patient tested for rifampicin resistance, RR-TB reflexed to **FL-LPA, SL-LPA/Xpert XDR** and culture DST.
- **DS-TB:** 2HRZE/4HRE daily weight-band FDCs (continuation phase includes ethambutol in India); extension by 3–6 months in selected EPTB.
- **Hr-TB:** 6(Lfx)REZ. **MDR/RR-TB:** shorter oral bedaquiline-containing regimen, **BPaLM** for eligible ≥ 14 years, longer oral regimen for the rest.
- **TPT:** 6H or 3HP for PLHIV and household contacts after ruling out disease; levofloxacin-based TPT for contacts of MDR/RR-TB as per programme guidance.
- **Patient support:** Ni-kshay Poshan Yojana ₹1000 per month by DBT; energy-dense nutrition supplementation for BMI < 18.5; Ni-kshay Mitra food baskets; transport support for tribal patients; treatment supporter honorarium; Ni-kshay Sampark helpline **1800-11-6666**.
- **Digital adherence:** 99DOTS, MERM boxes, video-observed therapy; all cases recorded on **Ni-kshay**.

India — burden snapshot (WHO Global TB Report 2025)

- Incidence fell from **237 to 187 per lakh** (2015→2024, ~21%), mortality from **28 to 21 per lakh**; treatment coverage > 90%; India still carries about a quarter of global cases and the largest share of MDR/RR-TB.

★ **CLINICAL PEARLS & EXAM FOCUS**

- Notification of every TB case (public or private, including clinically diagnosed) is mandatory — notify on Ni-kshay.
- India keeps ethambutol in the continuation phase (2HRZE/4HRE), unlike WHO 2HRZE/4HR.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. National TB Elimination Programme — components and recent initiatives. *[Long answer]*
2. Ni-kshay Poshan Yojana and Pradhan Mantri TB Mukt Bharat Abhiyaan. *[Short note]*

1.9 Other Guidelines You Must Quote — Index-TB, ATS/CDC/ERS/IDSA & NICE

‹ NMC curriculum | Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Comparative guidelines
- ✓ Summarise the Index-TB guidelines for extrapulmonary TB
- ✓ Compare key differences between WHO, NTEP and ATS/CDC/ERS/IDSA recommendations

IN BRIEF The WHO modules set global policy; national and society guidelines adapt them. Index-TB (India, 2016) remains the reference for extrapulmonary TB; the ATS/CDC/ERS/IDSA guideline (2025 update) and NICE NG33 guide practice in low-incidence settings.

Index-TB guidelines (ICMR–WHO Country Office, 2016)

- Specialty-wise guidance for EPTB: lymph node, pleural, abdominal, CNS, musculoskeletal, genitourinary, pericardial, cutaneous and ocular TB.
- Key messages: obtain tissue/fluid for **NAAT, culture and histology**; **6 months** treatment for most EPTB; **12 months** for CNS TB and **12 months** for spinal TB (may extend clinically); steroids in TBM and pericarditis; avoid empirical treatment of female genital TB based on endometrial PCR alone; do not treat ocular inflammation on IGRA alone.

How the guidelines differ

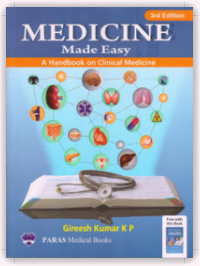
Issue	WHO 2025	NTEP India	ATS/CDC/ERS/IDSA
DS-TB continuation phase	4HR	**4HRE**	4HR (E stopped once susceptible)
4-month HPMZ	Yes, ≥ 12 years	Not programme policy	Yes (≥ 12 years, weight ≥ 40 kg)
TBM duration	Longer therapy (commonly 2HRZE/10HR); 6-month intensive regimen in children	12 months	9–12 months
Bone & joint TB	Longer therapy suggested	Up to 12 months	6–9 months
Steroids in pericarditis	Conditional	Selected patients	Not routinely
MDR/RR-TB	BPaLM / BDLLfxC	BPaLM; shorter oral Bdq regimen	BPaLM preferred
LTBI test	TST/IGRA/TBST	TST/IGRA	IGRA preferred (BCG-vaccinated)

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- **Study 31/A5349 (2021)** — 4-month HPMZ non-inferior to 6-month standard regimen.
- **SHINE (2022)** — 4 months non-inferior to 6 months for non-severe childhood TB.
- **TB-PRACTECAL, ZeNix, Nix-TB** — BPaL(M) regimens; **BEAT-Tuberculosis** — BDLLfxC; **endTB** — modified 9-month regimens.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Compare WHO, NTEP and ATS/CDC/ERS/IDSA recommendations for treatment of TB. *[Short note]*



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SECTION 2

Tuberculosis — History, Epidemiology & Risk

Paper I / IV · Epidemiology and public health

From Egyptian mummies to the WHO Global TB Report 2025: the burden of TB worldwide and in India, the determinants that drive it, and the people at highest risk.

2.1 History of Tuberculosis — From Phthisis to Pretomanid 20
2.2 Global & Indian Epidemiology (WHO Global TB Report 2025) 21
2.3 Social Determinants & Risk Factors for TB 22
2.4 High-Risk & Vulnerable Populations 23

2.1 History of Tuberculosis — From Phthisis to Pretomanid

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** History of medicine; milestones
- ✓ Narrate the key historical milestones in the understanding and control of TB
- ✓ Relate historical treatments (sanatoria, collapse therapy) to modern practice

IN BRIEF TB has accompanied humans for at least 9000 years. Koch's discovery (1882), BCG (1921), streptomycin (1944), the MRC trials and rifampicin (1960s) created modern short-course chemotherapy; the 2010s–2020s brought molecular diagnosis and all-oral regimens.

Milestones

Year	Event
~7000 BCE	Mycobacterial DNA in skeletons from the eastern Mediterranean; spinal TB in Egyptian mummies (Pott's lesions)
460 BCE	Hippocrates describes **phthisis** — the commonest disease of his time
1689	Richard Morton coins "tubercles"; consumption, "the captain of all these men of death" (Bunyan)
1779	Percivall Pott describes spinal TB with paraplegia
1819	Laennec invents the stethoscope, describes TB pathology — himself dies of TB
1854	Hermann Brehmer opens the first **sanatorium** (Görbersdorf)
1865	Villemin proves TB is transmissible (rabbits)
24 Mar 1882	**Robert Koch** announces *M. tuberculosis* — now **World TB Day**; Koch's postulates
1890	Koch's "tuberculin" — failed as therapy, became a diagnostic test (Mantoux 1907, von Pirquet)
1895	Röntgen discovers X-rays — radiological diagnosis
1921	**BCG** first given (Calmette & Guérin, attenuated *M. bovis*)
1944	**Streptomycin** (Schatz & Waksman); 1948 — first randomised controlled trial in medicine (MRC streptomycin trial)
1952	**Isoniazid**; 1956 — Madras Study (Tuberculosis Chemotherapy Centre, Chennai): home treatment as effective as sanatorium

Year	Event
1960s	**Rifampicin** (1963), ethambutol; short-course chemotherapy
1993	WHO declares TB a **global emergency**; DOTS strategy
2010	**Xpert MTB/RIF** endorsed
2012–19	Bedaquiline (2012), delamanid (2014), pretomanid (2019) — first new TB drugs in 40 years
2022–25	BPaLM, 4-month regimens, BDLLfxC; India's NTEP, Ni-kshay Poshan and TB Mukt Bharat

Indian contributions

- **Tuberculosis Chemotherapy Centre, Madras (1956)** — now ICMR–National Institute for Research in Tuberculosis (NIRT): domiciliary treatment, intermittent regimens, BCG Chingleput trial (1968–) which showed BCG gave no protection against adult pulmonary TB in South India.
- **National TB Institute, Bangalore (1959)** — the National TB Programme model (1962).
- **RATIONS trial (2023, Jharkhand)** — food support to household contacts reduced incident TB by ~40%.

★ **CLINICAL PEARLS & EXAM FOCUS**

- Collapse therapy (artificial pneumothorax, thoracoplasty, plombage) explains the "old TB chest" — rib resection, Lucite balls and calcified pleura on CXR of elderly patients.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. History of tuberculosis — milestones in diagnosis and treatment. *[Short note]*

2.2 Global & Indian Epidemiology (WHO Global TB Report 2025)

‹ NMC curriculum | Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Epidemiology; burden of disease
- ✓ Quote current global and Indian TB incidence, mortality and MDR/RR-TB burden
- ✓ Interpret incidence, prevalence, notification and case-fatality indicators

IN BRIEF In 2024 an estimated **10.7 million** people fell ill with TB and **1.23 million** died — the first decline since COVID-19, yet TB remains the world's leading infectious killer. India contributes about a quarter of all cases and the largest share of deaths and MDR/RR-TB.

Global burden — 2024 estimates

Indicator	Value (WHO Global TB Report 2025)
Incident TB	**10.7 million** (≈ 131 per 100 000) — 5.8 million men, 3.7 million women, 1.2 million children
Deaths	**1.23 million** (including HIV-positive); case-fatality ≈ 11.5%
Newly diagnosed and notified	8.3 million (~78% of estimated incidence)
TPT given	5.3 million people at high risk (2024)
Trend 2015→2024	Incidence ↓ ~12%, deaths ↓ ~29% — far short of the 2025 milestones (50% and 75%)
Trend 2023→2024	Incidence ↓ ~2%, deaths ↓ ~3%
TB/HIV deaths	Down ~76% since 2010
MDR/RR-TB	Roughly 0.4 million incident cases; treatment success ~71% (2022 cohort)

Indicator	Value (WHO Global TB Report 2025)
Geography	South-East Asia ~ 45%, Africa ~ 25%, Western Pacific ~ 17%; 30 high-burden countries ≈ 87%
Top countries	India, Indonesia, Philippines, China, Pakistan ≈ 55% of global cases

India

- **Incidence** 237 → **187 per lakh** (2015→2024, ↓ 21% — nearly double the global decline); **mortality** 28 → **21 per lakh**.
- **Treatment coverage** rose from 53% (2015) to > 90% (2024); ~26 lakh notified in 2024 against an estimated ~27 lakh.
- **Treatment success** ~ 90% for DS-TB; India has the largest number of MDR/RR-TB patients and ~28% of global TB deaths.
- **National TB Prevalence Survey (2019–21):** microbiologically confirmed PTB prevalence 312 per lakh (≥ 15 years); ~64% of people with symptoms had not sought care — the case for active case finding.

Epidemiological indicators

Indicator	Meaning
Incidence	New + relapse cases per 100 000 per year — the End TB metric
Prevalence	All existing cases at a point in time — measured by prevalence surveys; ≈ incidence × duration
Notification rate	Cases reported to the programme — depends on access and private-sector reporting
Annual risk of TB infection (ARTI)	Proportion infected per year; in India historically ~1.5%; ≈ 50 new smear-positive cases per 100 000 per 1% ARTI (Styblo's rule, now outdated)
Case-fatality ratio	Deaths ÷ incidence — reflects late diagnosis and poor treatment
Catastrophic cost	Total costs > 20% of annual household income — End TB target 0%

★ **CLINICAL PEARLS & EXAM FOCUS**

- About a quarter of the world's population is infected with *M. tuberculosis* (WHO Modules 1 and 3).
- The "missing millions" — the gap between estimated incidence and notifications — are people undiagnosed or diagnosed but not notified (often in the private sector).

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Burden of tuberculosis in India and the world — current status and challenges. *[Long answer]*

2.3 Social Determinants & Risk Factors for TB

‹ NMC curriculum

Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Determinants of health; risk factors
- ✓ List the five major risk factors driving TB incidence and their relative risks
- ✓ Explain the bidirectional links between TB and undernutrition, diabetes, HIV, smoking and alcohol

IN BRIEF TB is a disease of poverty. Infection depends on exposure (crowding, ventilation, contact duration); disease depends on host immunity. WHO attributes most incident TB to five risk factors: **undernutrition, HIV, alcohol use disorders, smoking and diabetes** — undernutrition contributes the largest number of cases in India.

Risk factors for progression from infection to disease

Risk factor	Approximate relative risk	Comment
HIV infection (untreated)	15–20× (higher with low CD4)	ART lowers but does not abolish risk; TB is the leading cause of death in PLHIV

Risk factor	Approximate relative risk	Comment
Silicosis	~30×	Screen and test workers; TB–silicosis has poor outcomes
Recent infection (< 2 years)	Highest risk period	Half of lifetime risk in first 2 years
Anti-TNF therapy (infliximab > etanercept)	4–25×	Test and treat before starting
Transplant, dialysis, CKD	10–25×	Immunosuppression
Undernutrition (BMI < 18.5)	~3×	Largest attributable fraction in India; RATIONS trial
Diabetes mellitus	~3×	Poor glycaemic control; higher failure, relapse and death
Smoking	~2×	Also more cavitation, relapse, mortality
Alcohol use disorder	~3×	Poor adherence, DILI
Fibrotic lesions on CXR (untreated old TB)	6–19×	Screen
Infants < 2 years, adolescents, elderly	Variable	Disseminated disease in infants
Gastrectomy, jejuno-ileal bypass, malignancy (head & neck, haematological), steroids ≥ 15 mg/day prednisolone ≥ 1 month	2–5×	

Determinants of exposure and transmission

- **Crowding and poor ventilation** — urban slums, prisons, hostels, hospitals; **indoor air pollution** (biomass fuel).
- **Delayed diagnosis** — stigma, cost, distance, private-sector diagnostic delays.
- **Occupational:** health-care workers, miners (silica), sex workers, migrants.
- **Structural:** poverty, illiteracy, gender norms, homelessness, incarceration.

TB–diabetes: a bidirectional relationship

- DM triples the risk of TB; TB and rifampicin worsen glycaemia (rifampicin induces metabolism of sulfonylureas, DPP-4 inhibitors); TB causes stress hyperglycaemia.
- **NTEP bidirectional screening:** every TB patient screened for diabetes (RBS/HbA1c); every diabetic screened for TB symptoms.
- DM–TB: more lower-lobe disease, cavitation, delayed conversion, relapse and death — tight control, consider insulin.

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- **RATIONS (Bhargava et al., Lancet 2023)** — monthly food baskets to household contacts reduced incident TB by 39–48%; nutritional support to patients reduced deaths and improved weight gain.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Social determinants of TB and the role of nutrition. Discuss the RATIONS trial. *[Long answer]*
2. TB and diabetes mellitus — bidirectional screening. *[Short note]*

2.4 High-Risk & Vulnerable Populations

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Vulnerable populations; screening priorities
- ✓ Identify populations requiring systematic screening and preventive treatment
- ✓ Plan TB services for health-care workers, prisoners, migrants and PLHIV

IN BRIEF High-risk groups need active case finding (Module 2), TPT (Module 1) and adapted care. In India the NTEP lists contacts, PLHIV, diabetics, malnourished, smokers, alcohol users, people with past TB, elderly, prisoners, miners, slum dwellers and tribal populations as vulnerable.

Vulnerable populations and actions

Group	Why at risk	Programme action
Household contacts	Highest exposure; children < 5 progress fast	Screen all; TPT (all < 5 y; ≥ 5 y after excluding disease); 6Lfx if index MDR
People living with HIV	Impaired cellular immunity	4-symptom screen every visit; CRP, CXR, mWRD; TPT; LF-LAM
Health-care workers	Occupational exposure, especially undiagnosed patients	Baseline and periodic screening; administrative and environmental controls; N95 respirators
Prisoners	Crowding, HIV, drug use	Entry and periodic screening
Miners / silica workers	Silicosis	Screen current and former workers; TPT
Diabetics, smokers, alcohol users	Immune impairment	Bidirectional screening; cessation support
Elderly	Immunosenescence, atypical symptoms	Low threshold for CXR; DILI risk
Pregnant women	Postpartum risk ↑; worse outcomes	Screen in antenatal care; TPT
Tribal, migrants, homeless	Poor access	Mobile vans, NAAT, transport support

Health-care workers

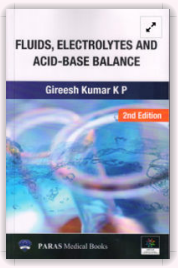
- TB incidence in Indian health-care workers is several times the general population; students and nurses at highest risk.
- Hierarchy of controls: **administrative** (triage, cough etiquette, fast-track diagnosis) > **environmental** (ventilation ≥ 12 ACH in airborne isolation, UVGI) > **respiratory protection** (fit-tested N95).

★ CLINICAL PEARLS & EXAM FOCUS

- An undiagnosed patient is far more infectious than one on effective treatment — infectiousness falls rapidly within days of starting appropriate therapy.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. TB in health-care workers — risks and prevention. *[Short note]*



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SECTION 3

Bacteriology — Clinical Overview

Paper I · Clinical microbiology

What the clinician needs to know about the organism to order and interpret tests correctly: acid-fast staining, slow growth and culture timelines, TB versus non-tuberculous mycobacteria, and how resistance is reported by the laboratory.

3.1 The Organism at a Glance — What Matters at the Bedside 25

3.2 Non-Tuberculous Mycobacteria — The Great Mimic 26

3.1 The Organism at a Glance — What Matters at the Bedside

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Clinical microbiology of mycobacteria
- ✓ Explain why TB diagnosis relies on acid-fast staining, culture and molecular tests
- ✓ Interpret laboratory reports — smear grade, culture result, time to positivity, DST report
- ✓ Know when to suspect non-tuberculous mycobacteria in a "TB" patient

IN BRIEF Tuberculosis is caused by organisms of the *Mycobacterium tuberculosis* complex. For the clinician, three properties shape practice: the bacilli are **acid-fast** (smear microscopy), they **grow slowly** (culture takes weeks, so molecular tests come first), and other mycobacteria (**NTM**) can look identical on a smear.

Clinically relevant properties and their consequences

Property	What it means in practice
Acid-fast staining	Ziehl–Neelsen (light microscopy) or auramine (LED fluorescence) smear detects bacilli — but needs a high bacillary load and cannot separate TB from NTM
Slow growth	Solid culture takes 3–8 weeks, liquid culture (MGIT) 1–3 weeks — hence **NAAT first**, culture for confirmation, monitoring and DST
MTB complex vs NTM	NAAT and line-probe assays identify the TB complex; a smear-positive, NAAT-negative sample suggests NTM
M. bovis	Associated with unpasteurised milk; naturally not susceptible to pyrazinamide — matters for abdominal/cervical node TB in cattle-rearing communities
BCG vaccine strain	Can cause local abscess, regional lymphadenitis or disseminated disease in immunodeficient infants

Reading a laboratory report

- **Smear:** graded scanty, 1+, 2+, 3+ — higher grade = more infectious and higher bacillary load; a negative smear does **not** exclude TB.
- **NAAT (Xpert/Truenat):** "MTB detected — high/medium/low/very low/trace" with "rifampicin resistance detected / not detected / indeterminate".
- **Culture:** positive/negative with **time to positivity** (shorter = higher load); contamination rates should be < 5% (MGIT) — high rates suggest poor processing.
- **DST report:** lists each drug as susceptible or resistant; molecular DST may list specific resistance results by drug — act on rifampicin and fluoroquinolone results first (see 8.4).

★ CLINICAL PEARLS & EXAM FOCUS

- Always send a sample for culture as well as NAAT in previously treated patients, EPTB and suspected DR-TB — culture enables full DST and treatment monitoring.
- A patient "failing" TB treatment with smear-positive, NAAT-negative sputum may have NTM disease — speciate before escalating TB drugs.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Laboratory diagnosis of tuberculosis — role of smear, culture and molecular tests. *[Short note]*

3.2 Non-Tuberculous Mycobacteria — The Great Mimic

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** NTM lung disease; differential diagnosis of TB
- ✓ Distinguish NTM pulmonary disease from TB on clinical, radiological and laboratory grounds
- ✓ Apply diagnostic criteria for NTM pulmonary disease

IN BRIEF NTM are environmental mycobacteria (water, soil). In India, many patients labelled "smear-positive, non-responding TB" have NTM. Diagnosis needs clinical, radiological **and** microbiological criteria — one positive sputum culture is not enough.

TB versus NTM lung disease

Feature	Tuberculosis	NTM pulmonary disease
Source	Person-to-person	Environment (water systems, soil); person-to-person spread unusual
Host	Anyone; HIV, diabetes, undernutrition	Structural lung disease (bronchiectasis, COPD, old TB), cystic fibrosis, thin elderly women
Radiology	Upper-lobe cavities, nodules, tree-in-bud	Fibrocavitary (upper lobe) or **nodular-bronchiectatic** (middle lobe, lingula)
Smear	AFB	AFB — indistinguishable
NAAT for MTB	Positive	**Negative**
Public health	Notifiable; contact screening	Not notifiable; no contact tracing
Treatment	Standard TB regimens	Species-specific macrolide-based regimens for 12 months after culture conversion

Diagnostic criteria for NTM pulmonary disease (ATS/ERS/ESCMID/IDSA 2020)

- **Clinical:** pulmonary symptoms, with other diagnoses excluded.
- **Radiological:** nodular or cavitary opacities, or bronchiectasis with multiple small nodules on HRCT.
- **Microbiological:** positive culture from **≥ 2 separate expectorated sputum** samples, or ≥ 1 bronchial wash/BAL, or biopsy with granulomatous histology plus positive culture.

Common NTM species

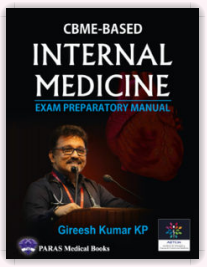
Species	Notes
M. avium complex (MAC)	Commonest worldwide; nodular-bronchiectatic disease; disseminated in advanced HIV
M. abscessus	Rapid grower; hard to treat; also post-procedure skin infections
M. kansasii	Most TB-like; responds to rifampicin-based therapy
M. fortuitum, *M. chelonae*	Skin and soft-tissue infections after injections, surgery or cosmetic procedures

★ CLINICAL PEARLS & EXAM FOCUS

- Suspect NTM when: AFB-positive but NAAT-negative; no response despite adherence to TB therapy with susceptible results; nodular bronchiectasis in a non-smoking older woman.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Non-tuberculous mycobacterial lung disease — diagnosis and differentiation from tuberculosis. *[Long answer]*



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SECTION 4

Pathology & Pathogenesis

Paper I · Pathology and immunology

How infection becomes disease: the granuloma, primary and post-primary tuberculosis, the classic named lesions examiners love, and the hypersensitivity phenomena that mimic other diseases.

4.1 Host Response & the Tuberculous Granuloma 28
4.2 Primary Tuberculosis — Ghon Focus & Ranke Complex 29
4.3 Post-Primary (Reactivation) Tuberculosis 30
4.4 Hypersensitivity Phenomena & Tuberculids 31

4.1 Host Response & the Tuberculous Granuloma

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Immunopathology; granuloma
- ✓ Outline the cell-mediated immune response to TB at a clinical level
- ✓ Describe the histology of the tuberculous granuloma and caseous necrosis
- ✓ Explain why TNF-α blockers, HIV and steroids increase TB risk

IN BRIEF Inhaled bacilli are taken up by alveolar macrophages. Containment depends on **cell-mediated immunity** — CD4 T-helper 1 cells, interferon-γ and TNF-α activate macrophages and organise the **granuloma**. Anything that weakens this axis (HIV, anti-TNF therapy, steroids, undernutrition) allows disease.

The immune response — clinically relevant points

- **Innate phase:** alveolar macrophages and dendritic cells ingest bacilli; a proportion of people clear infection early.
- **Adaptive phase (2–8 weeks):** antigen-specific CD4 Th1 cells release **IFN-γ**; macrophages release **TNF-α** — this is when TST and IGRA turn positive.
- **Clinical corollaries:** HIV (CD4 depletion), **anti-TNF agents**, high-dose steroids and inherited IL-12/IFN-γ pathway defects (Mendelian susceptibility to mycobacterial disease) all predispose to severe or disseminated TB.

Anatomy of the granuloma

Component	Description
Centre	**Caseous necrosis** — cheesy, eosinophilic, granular, acellular debris
Epithelioid cells	Activated macrophages with elongated nuclei and pale cytoplasm
Langhans giant cells	Fused macrophages — nuclei arranged in a **horseshoe at the periphery**
Lymphocyte cuff	CD4 and CD8 T cells, B cells
Fibroblasts	Peripheral fibrosis → healing, calcification

Fate of a lesion

- **Healing:** fibrosis and calcification (Ghon focus seen on CXR years later).
- **Liquefaction of caseum:** discharge into a bronchus → **cavity** — high bacillary load, infectious.

- **Spread:** bronchogenic (tree-in-bud), lymphatic (nodes), haematogenous (miliary, EPTB), direct (pleura, pericardium).

Granulomatous diseases — differential on histology

Disease	Distinguishing features
Tuberculosis	Caseating granulomas; AFB ± ; NAAT/culture positive
Sarcoidosis	Non-caseating, "naked" tight granulomas; asteroid and Schaumann bodies; no AFB
Fungal (histoplasmosis)	Organisms on GMS/PAS stain
Leprosy	Neural involvement; foamy macrophages in lepromatous form
Crohn's disease	Non-caseating, small, mucosal; skip lesions
Cat-scratch, tularaemia	Stellate necrotising granulomas

★ **CLINICAL PEARLS & EXAM FOCUS**

- Caseation strongly suggests TB but is not diagnostic — confirm with NAAT/culture of tissue (send part of every biopsy fresh in saline, not all in formalin).

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Describe the morphology of the tuberculous granuloma and the factors that determine its fate. *[Short note]*

4.2 Primary Tuberculosis — Ghon Focus & Ranke Complex

‹ NMC curriculum | Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Primary TB; childhood TB pathology
- ✓ Describe the Ghon focus, Ghon complex and Ranke complex
- ✓ List the outcomes of primary infection

IN BRIEF Primary TB is the response to first infection, typically in children. A subpleural focus, usually in the lower part of the upper lobe or upper part of the lower lobe (**Ghon focus**), plus enlarged draining hilar nodes forms the **Ghon complex**; when calcified, it is the **Ranke complex**.

Named lesions

Lesion	Description
Ghon focus	1–1.5 cm subpleural parenchymal focus, mid-zone (lower upper lobe / upper lower lobe)
Ghon (primary) complex	Ghon focus + lymphangitis + caseous hilar/mediastinal nodes
Ranke complex	Calcified, healed Ghon complex
Simon foci	Apical seeding during primary bacillaemia — later source of reactivation
Weeker's focus	Haematogenous seeding of the renal cortex during primary infection

Outcomes of primary infection

- **Healed** in > 90% (immunocompetent) — positive TST/IGRA only (TB infection).
- **Progressive primary TB** (infants, HIV, malnutrition): enlarging consolidation, cavitation.
- **Lymph-node complications:** compression or erosion of bronchi → collapse (middle-lobe syndrome — **Brock's syndrome**), obstructive emphysema, endobronchial TB.
- **Pleural effusion** (hypersensitivity, adolescents and young adults, 3–7 months after infection).
- **Haematogenous spread:** miliary TB and **TB meningitis** within 6–12 months — commonest in children < 2–3 years.
- **Wallgren's timetable:** primary complex 3–8 weeks; pleural effusion 3–7 months; miliary/meningitis up to 1 year; bone and joint 1–3 years; renal 5–8 years or more.

★ CLINICAL PEARLS & EXAM FOCUS

- In children, mediastinal/hilar lymphadenopathy is the radiological hallmark of primary TB.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Primary complex — morphology and fate. *[Short note]*

4.3 Post-Primary (Reactivation) Tuberculosis

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Post-primary TB; cavitation
- ✓ Explain why post-primary TB favours the apices
- ✓ Describe the pathology of cavitation, fibrosis and bronchogenic spread
- ✓ Recognise named lesions — Assmann focus, Puhl's lesion, Rasmussen aneurysm

IN BRIEF Post-primary TB follows reactivation of dormant foci or reinfection in a sensitised host. Strong delayed hypersensitivity causes caseation and **cavitation**, typically in the **apical and posterior segments of the upper lobes** and the superior segment of lower lobes, where high oxygen tension and poor lymphatic clearance favour bacillary growth.

Pathological sequence

- **Exudative phase** → caseous pneumonia → **liquefaction** → erosion into a bronchus → **cavity** (bacilli up to 10^8–10^9 per cavity).
- **Bronchogenic spread** → acinar nodules ("tree-in-bud") in other lobes and the opposite lung.
- **Healing** by fibrosis → volume loss, upper-lobe retraction, traction bronchiectasis, hilar elevation.

Named lesions in post-primary disease

Lesion	Description
Assmann focus	Infraclavicular early infiltrate of adult reinfection TB
Puhl's lesion	Apical reinfection focus
Rasmussen aneurysm	Pseudo-aneurysm of a pulmonary artery branch in a cavity wall → **massive haemoptysis**
Tuberculoma	Encapsulated caseous nodule, often calcified, 1–4 cm
Aspergilloma	Fungal ball in an old healed cavity — air-crescent sign
Tuberculous bronchiectasis	Upper-lobe traction bronchiectasis ("dry bronchiectasis" with haemoptysis)

Primary vs post-primary — comparison

Feature	Primary	Post-primary
Host	Non-sensitised (children)	Sensitised (adults)
Site	Mid/lower zones, subpleural	Apices, posterior upper lobes
Nodes	Prominent hilar/mediastinal	Uncommon (except HIV)
Cavitation	Rare	Characteristic
Infectiousness	Low	High (cavities)
Healing	Calcified Ghon/Ranke complex	Fibrosis, volume loss, bronchiectasis

★ CLINICAL PEARLS & EXAM FOCUS

- In advanced HIV, post-primary TB looks "primary" — lower zones, lymphadenopathy, no cavities, frequent dissemination.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Pathogenesis of cavitation in pulmonary tuberculosis. *[Short note]*

4.4 Hypersensitivity Phenomena & Tuberculids

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Immune phenomena in TB
- ✓ Recognise immune-mediated manifestations that accompany TB
- ✓ Differentiate tuberculids from true cutaneous TB

IN BRIEF Some manifestations of TB are driven by hypersensitivity to mycobacterial antigens rather than by bacillary invasion. They are usually paucibacillary (AFB rarely found), resolve with antituberculosis treatment and often appear early after infection.

Hypersensitivity manifestations

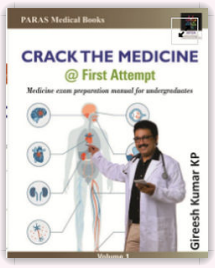
Manifestation	Features
Erythema nodosum	Tender red shin nodules with primary infection (also sarcoid, streptococcal, drugs)
Phlyctenular keratoconjunctivitis	Nodules at the limbus in children with primary TB
Poncet's disease	Reactive polyarthritis of large joints during active TB — sterile joint, resolves with treatment
Tuberculous pleural effusion	Largely a hypersensitivity response to a few bacilli entering the pleural space
Papulonecrotic tuberculid	Symmetrical necrotic papules on extensor surfaces
Lichen scrofulosorum	Grouped lichenoid papules on the trunk in children
Erythema induratum (Bazin)	Nodular vasculitis of the posterior calves, often in women
Eales disease	Retinal periphlebitis and recurrent vitreous haemorrhage in young men — linked to TB hypersensitivity

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Tuberculids: strongly positive TST/IGRA, biopsy shows granulomatous vasculitis, AFB/culture negative, NAAT sometimes positive — and they resolve with ATT.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculids and Poncet's disease. *[Short note]*



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SECTION 5

Natural History & Prognosis

Paper I / II · Spectrum of disease and outcomes

TB is a spectrum — from cleared infection through incipient and subclinical disease to symptomatic TB — and untreated it kills about half of those it affects. This section covers progression, outcomes with and without treatment, and the long tail of post-TB lung disease.

5.1 The Spectrum of TB — Infection to Disease 32
5.2 Risk & Timing of Progression 33
5.3 Outcomes of Untreated & Treated TB — Prognosis 33
5.4 Post-TB Lung Disease & Life After Cure 34

5.1 The Spectrum of TB — Infection to Disease

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Spectrum of TB infection and disease
- ✓ Describe the states along the TB spectrum, including incipient and subclinical TB
- ✓ Explain why "latent TB" has been replaced by "TB infection" in WHO terminology

IN BRIEF The old binary of "latent vs active" has been replaced by a **dynamic spectrum**. WHO now uses **TB infection (TBI)** — a persistent immune response to *M. tuberculosis* antigens without clinically manifest disease. Movement can occur in both directions along the spectrum.

States along the spectrum

State	Description	Tests
Exposure, cleared	Infection eliminated by innate or acquired immunity	TST/IGRA negative or revert
TB infection (TBI)	Viable bacilli contained; no symptoms; not infectious	TST/IGRA/TBST positive; CXR normal
Incipient TB	Early changes likely to progress; no symptoms or radiology	Research biomarkers (blood transcriptomic signatures)
Subclinical TB	Bacteriological or radiological disease **without symptoms** — may transmit	CXR abnormal; sputum NAAT/culture positive
Clinical (symptomatic) TB	Symptoms + evidence of disease	Microbiology, imaging

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Prevalence surveys show that a large proportion of people with bacteriologically confirmed TB **do not report cough** — the rationale for CXR-based screening (Module 2).
- ▸ Positive TST/IGRA does not distinguish infection from disease, and a negative test does not exclude disease (Module 3, Rec. 21).

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Spectrum of tuberculosis — concept of incipient and subclinical TB. *[Short note]*

5.2 Risk & Timing of Progression

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Natural history of TB infection
- ✓ Quantify lifetime risk of progression and the effect of risk factors
- ✓ Explain why recent contacts and young children are priorities for TPT

IN BRIEF About **5–10%** of infected people develop disease in their lifetime, usually within **5 years** — about half within the first 2 years. The risk is far higher with HIV, young age, recent infection, silicosis and immunosuppression.

Risk of progression by age (after infection)

Age at infection	Risk of disease	Type of disease
< 1 year	30–50%	Pulmonary 30–40%; miliary/TBM 10–20%
1–2 years	10–20%	Pulmonary 10–20%; miliary/TBM 2–5%
2–5 years	~5%	Mostly pulmonary/nodal
5–10 years	~2% (the "safe school age")	Pulmonary
> 10 years	10–20% (adolescents)	Adult-type cavitary disease

Key points

- People with HIV not on ART: risk of ~5–10% **per year**, not per lifetime.
- **Reinfection** contributes substantially to disease in high-transmission settings (India) — prior infection gives only partial protection.
- Most TB in high-burden settings is from recent transmission; in low-incidence countries, most is reactivation (migrants, elderly).

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Children < 5 years: highest risk of severe disease after infection — therefore TPT without waiting for a TBI test (Module 1, Rec. 5).

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Natural history of TB infection in children. *[Short note]*

5.3 Outcomes of Untreated & Treated TB — Prognosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Prognosis; mortality predictors
- ✓ State the outcome of untreated pulmonary TB
- ✓ List predictors of death, failure and recurrence during and after treatment

IN BRIEF Before chemotherapy, about **70% of smear-positive patients died within 10 years** (≈ 50% within 5 years), about 20% of smear-negative patients died, and some self-cured with chronic disease. With treatment, > 85% of DS-TB patients are cured; death remains concentrated in the first 2 months among those diagnosed late.

Natural history of untreated pulmonary TB (pre-chemotherapy cohorts)

Outcome at 10 years	Smear-positive	Smear-negative
Died	~70%	~20%

Outcome at 10 years	Smear-positive	Smear-negative
Spontaneous cure	~20–25%	Majority
Chronic infectious disease	~5–10%	Few

Predictors of poor outcome

Domain	Predictors
Patient	Age > 60, HIV (especially CD4 < 100, not on ART), BMI < 16, diabetes, alcohol, smoking, CKD, liver disease
Disease	Extensive bilateral cavitation, high smear grade, miliary TB, TB meningitis (stage III), pericardial TB
Drug resistance	MDR/RR-TB, pre-XDR/XDR-TB, unrecognised Hr-TB
Health system	Diagnostic delay, poor adherence, loss to follow-up, unaddressed comorbidity
Recurrence	Cavitation + positive culture at 2 months, low BMI, poor adherence, smoking, HIV, shorter regimens in high-risk patients

TB meningitis prognosis — British MRC staging

Stage	Features	Approximate outcome
I	GCS 15, no focal deficit	Best — most survive without disability
II	GCS 11–14, or GCS 15 with focal deficit	Intermediate
III	GCS ≤ 10	Up to half die; survivors often disabled

★ CLINICAL PEARLS & EXAM FOCUS

- Most deaths during DS-TB treatment occur in the intensive phase — screen for advanced HIV, severe undernutrition and comorbidities at diagnosis (NTEP "differentiated TB care").

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Prognostic factors in pulmonary tuberculosis. *[Short note]*

5.4 Post-TB Lung Disease & Life After Cure

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Post-tuberculosis lung disease; sequelae
- ✓ Define post-TB lung disease and list its patterns
- ✓ Plan follow-up and rehabilitation of TB survivors

IN BRIEF Microbiological cure is not health. Many survivors are left with **post-TB lung disease (PTLD)** — airflow obstruction, restriction, bronchiectasis, cavities, fibrosis, pulmonary hypertension, chronic aspergillosis — and higher mortality than the general population. Recurrent TB is also common in the first years after treatment.

Patterns of post-TB lung disease

Pattern	Features
Airway disease	Fixed airflow obstruction ("TB-associated obstructive pulmonary disease"), bronchiectasis, bronchostenosis
Parenchymal	Fibrosis, volume loss, residual cavities, **destroyed lung**
Pleural	Pleural thickening, fibrothorax, trapped lung, calcification

Pattern	Features
Vascular	Pulmonary hypertension, bronchial artery hypertrophy → haemoptysis
Infection	Chronic pulmonary aspergillosis, aspergilloma, NTM, recurrent bacterial infection
Systemic	Cor pulmonale, frailty, depression, catastrophic costs

Follow-up of survivors

- Post-treatment follow-up (NTEP): clinical review every 6 months for 2 years; sputum/CXR if symptomatic.
- Spirometry at end of treatment; pulmonary rehabilitation; vaccination (influenza, pneumococcal); smoking cessation.
- Haemoptysis or new cavity after cure: rule out recurrent TB (NAAT + culture), aspergilloma (Aspergillus IgG), bronchiectasis, and lung cancer.

✦ RECENT ADVANCES & GUIDELINE UPDATES

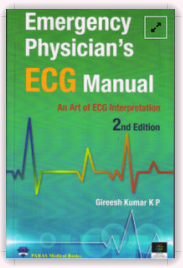
- The International Post-Tuberculosis Symposium consensus (2019, updated 2023) introduced the term PTLD and recommended routine end-of-treatment assessment of lung function and symptoms.

★ CLINICAL PEARLS & EXAM FOCUS

- Xpert may remain positive for months to years after cure (dead bacilli) — in previously treated patients, confirm recurrence with culture and clinical evaluation.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Post-tuberculosis lung disease — patterns and management. *[Long answer]*



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SECTION 6

Pulmonary Tuberculosis

Paper II · Clinical respiratory medicine

The commonest and the only routinely infectious form of TB — symptoms, signs, radiology, miliary disease, and the special patterns seen in children, people with HIV, diabetes, pregnancy and old age.

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6.2 Radiology of Pulmonary TB 37
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6.8 Approach to Presumptive TB & Differential Diagnosis 43

6.1 Clinical Features of Pulmonary TB

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Clinical presentation of PTB
- ✓ Elicit the symptoms and signs of pulmonary TB and judge their diagnostic value
- ✓ Identify presumptive TB as per NTEP and WHO
- ✓ Present a TB long case with a complete summary and differential diagnosis

IN BRIEF Pulmonary TB typically presents with **cough for ≥ 2 weeks**, evening fever, night sweats, weight loss and haemoptysis, but no symptom is sensitive enough to rule TB out — a substantial share of prevalent TB is subclinical. Signs are often minimal compared with radiological extent.

Symptoms and their meaning

Symptom	Points
Cough	Most common; dry → productive; ≥ 2 weeks defines presumptive TB (NTEP); **any duration** in PLHIV, contacts, diabetics
Fever	Low-grade, evening rise; may be absent in elderly
Night sweats	Drenching; non-specific
Weight loss / anorexia	"Consumption"; BMI < 18.5 common; predicts mortality
Haemoptysis	Streaky to massive; also after cure (bronchiectasis, aspergilloma, Rasmussen aneurysm)
Chest pain	Pleuritic — pleural involvement
Breathlessness	Extensive disease, effusion, pneumothorax, post-TB lung disease
Others	Hoarseness (laryngeal TB), amenorrhoea, fatigue

Signs

Finding	Significance
General	Pallor, wasting, clubbing (advanced, cavitary or associated bronchiectasis), lymphadenopathy, erythema nodosum, phlyctenules
Apical crepitations	Post-tussive crepitations ("crackles after a short cough") — classic for early apical disease
Cavity	Amphoric / cavernous breath sounds, whispering pectoriloquy
Fibrosis	Tracheal deviation **towards** the lesion, flattening, drooping shoulder, crowded ribs, reduced movement
Effusion	Stony dull note, absent breath sounds, trachea away (if large)
Collapse / consolidation	Bronchial breathing, dullness

Presenting a TB long case — model summary

"A 45-year-old diabetic smoker presents with productive cough of 6 weeks, evening fever, 8 kg weight loss and one episode of streaky haemoptysis. Examination shows a left drooping shoulder, trachea deviated to the left, and post-tussive crepitations with amphoric breath sounds in the left infraclavicular area — suggesting **left upper-lobe fibrocavitary disease, most likely pulmonary TB**, with differentials of NTM disease, chronic pulmonary aspergillosis, lung abscess and carcinoma."

★ CLINICAL PEARLS & EXAM FOCUS

- No cough does not mean no TB — screen with CXR in high-risk groups.
- Signs underestimate disease — always get a CXR.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Clinical features of pulmonary tuberculosis — symptom screen and its limitations. *[Short note]*

6.2 Radiology of Pulmonary TB

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Chest radiography and CT in TB
- ✓ Describe CXR patterns of primary, post-primary and miliary TB
- ✓ Use CT findings to assess activity and complications
- ✓ Distinguish active from inactive disease radiologically

IN BRIEF CXR is the most sensitive screening tool but not specific. Active post-primary TB shows upper-lobe consolidation, **cavitation** and bronchogenic spread; CT shows **tree-in-bud** nodules (endobronchial spread — the best CT marker of activity), centrilobular nodules and cavities.

CXR patterns

Pattern	Features
Primary TB	Hilar/mediastinal lymphadenopathy (right paratracheal), consolidation in any lobe, effusion; Ghon focus, Ranke complex when healed
Post-primary TB	Apical/posterior upper-lobe and superior lower-lobe infiltrates, **cavities** (thick-walled, no air-fluid level usually), fibrosis, volume loss, hilar elevation
Miliary	Innumerable 1–3 mm nodules uniformly distributed — "millet seeds"; may be invisible early (CT more sensitive)
Tuberculoma	Well-defined nodule 0.5–4 cm, central calcification, satellite nodules
Pleural	Effusion (often unilateral), empyema, pleural thickening, calcification

Pattern	Features
Complications	Pneumothorax, bronchopleural fistula, aspergilloma (air crescent), destroyed lung
HIV (low CD4)	Lower-zone infiltrates, lymphadenopathy, effusion, miliary — or **normal** CXR

CT signs of activity

Active	Inactive / healed
Tree-in-bud nodules, centrilobular nodules	Calcified nodules, Ranke complex
Consolidation, thick-walled cavities	Thin-walled cavities, fibrotic bands
Necrotic (rim-enhancing) nodes	Calcified nodes
Miliary nodules	Traction bronchiectasis, volume loss, pleural calcification

Practical rules

- Radiology alone must never be the basis to label TB "active" or "cured" — always attempt microbiology.
- Radiological improvement lags behind clinical improvement; residual lesions are common.
- For images see Radiopaedia — pulmonary tuberculosis.

★ CLINICAL PEARLS & EXAM FOCUS

- Air-fluid level in a "TB cavity" → think secondary bacterial infection, lung abscess or carcinoma.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Radiological features of pulmonary TB — distinguishing active from healed disease. *[Long answer]*

6.3 Miliary & Disseminated Tuberculosis

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Miliary TB
- ✓ Recognise miliary TB clinically and radiologically
- ✓ Plan investigations to confirm disseminated TB
- ✓ Identify complications — ARDS, TBM, adrenal insufficiency, HLH

IN BRIEF Miliary TB is haematogenous dissemination producing 1–3 mm granulomas in many organs. It affects infants, PLHIV, the elderly and immunosuppressed. Presentation is often non-specific (pyrexia of unknown origin); **choroid tubercles**, CT chest, and NAAT/culture of multiple samples clinch the diagnosis.

Clinical forms

- **Acute miliary TB** — fever, weight loss, breathlessness, hepatosplenomegaly; may progress to ARDS and multi-organ failure.
- **Cryptic miliary TB (elderly)** — PUO with normal CXR, anaemia, raised ALP.
- **Non-reactive (areactive) miliary TB** — overwhelming bacillaemia, minimal granulomas; mimics sepsis; pancytopenia.

Investigations

- **Fundoscopy** — choroid tubercles (pathognomonic).
- **CT chest** — random/uniform miliary nodules even when CXR is normal.
- Samples for NAAT and culture: sputum/induced sputum, gastric aspirate, BAL, **urine**, CSF (lumbar puncture in all — TBM coexists in up to a third), bone marrow, liver biopsy, blood culture (MGIT) in HIV.
- Urine **LF-LAM** in PLHIV; TST often negative (anergy).
- Blood: anaemia, pancytopenia, hyponatraemia (SIADH or adrenal), raised ALP, transaminases.

Differential diagnosis of a miliary pattern

Cause	Clue
Miliary TB	Fever, constitutional symptoms, choroid tubercles
Miliary metastases	Thyroid, renal, melanoma, choriocarcinoma; no fever
Fungal	Histoplasmosis, cryptococcosis, talaromycosis (HIV)
Sarcoidosis	Perilymphatic nodules, bilateral hilar nodes, well patient
Pneumoconiosis	Occupational history, upper-zone predominance
Varicella pneumonia (healed)	Calcified small nodules

Treatment points

- Standard DS-TB regimen; **extend to 12 months if CNS involvement**; steroids if TBM, adrenal insufficiency or severe hypoxaemia/ARDS (expert opinion).
- Screen for and treat HIV; check cortisol if hypotension or hyponatraemia.

⚠ RED FLAGS — DO NOT MISS

- Breathless miliary TB with falling SpO_2 — may progress rapidly to ARDS; admit to HDU.
- Every patient with miliary TB needs a lumbar puncture.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Miliary tuberculosis — clinical features, diagnosis and management. *[Long answer]*

6.4 Tuberculosis in Children & Adolescents

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Paediatric TB
- ✓ Recognise the presentations of childhood TB and its diagnostic difficulty
- ✓ Apply WHO treatment-decision algorithms and concurrent testing in children
- ✓ Prescribe the 4-month regimen for non-severe TB

IN BRIEF Children account for about 1.2 million cases a year; most are paucibacillary and cannot expectorate. WHO now recommends **concurrent NAAT on respiratory samples and stool** (Module 3, Rec. 8), treatment-decision algorithms for clinical diagnosis, and a **4-month regimen (2HRZ(E)/2HR)** for non-severe TB (Module 4, Rec. 2.2).

Presentations

- **Intrathoracic lymphadenopathy** — commonest; persistent cough, wheeze (bronchial compression), collapse.
- **Progressive primary disease**, **adult-type cavitary TB** in adolescents.
- **Severe forms:** miliary TB and **TB meningitis** in < 3 years — irritability, vomiting, failure to thrive.
- **Peripheral lymphadenitis** (cervical), spinal TB, abdominal TB.

Diagnosis

- Contact history with an infectious adult — the single most important clue.
- Persistent unremitting cough > 2 weeks, fever > 2 weeks, weight loss/failure to thrive, lethargy.
- Specimens: **gastric aspirate**, **induced sputum**, **nasopharyngeal aspirate**, **stool**, string test; Xpert Ultra preferred (detects low bacillary loads).
- CXR: hilar/paratracheal nodes, airway compression, miliary pattern.
- TST/IGRA supports infection but does not diagnose disease.

Non-severe vs severe TB (eligibility for 4-month regimen)

Non-severe (4 months)	Severe (6 months or longer)
Peripheral lymph-node TB	Miliary TB, TBM, osteoarticular TB
Intrathoracic nodes without airway obstruction	Airway obstruction by nodes
Uncomplicated pleural effusion	Complicated effusion, empyema
Paucibacillary, non-cavitary disease confined to one lobe	Cavitary disease, more than one lobe, bilateral disease
Without miliary pattern	Spinal TB, abdominal TB, pericardial TB

★ CLINICAL PEARLS & EXAM FOCUS

- TB meningitis in children: WHO also allows an intensive **6-month regimen (6HRZEto)** as an alternative to 12 months (Module 5).
- Use dispersible child-friendly FDCs (NTEP: H50/R75/Z150 + E100) by weight band.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Diagnosis of pulmonary tuberculosis in children — current WHO approach. *[Long answer]*

6.5 TB–HIV Co-infection

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** TB–HIV collaborative activities
- ✓ Describe the effect of HIV on the presentation and diagnosis of TB
- ✓ Time ART, choose compatible regimens and anticipate IRIS
- ✓ Implement the "Three I's" and TB–HIV collaborative activities

IN BRIEF TB is the leading cause of death in people with HIV. Lower CD4 counts bring atypical radiology, extrapulmonary and disseminated disease, smear-negative sputum and higher mortality. WHO recommends **LC-aNAAT + urine LF-LAM concurrently**, **ART within 2 weeks** of TB treatment (except TBM), TPT for all PLHIV without disease, and co-trimoxazole prophylaxis.

Presentation by CD4 count

CD4 (cells/µL)	Pulmonary picture	Other
> 350	Typical upper-lobe cavitary TB	Similar to HIV-negative
200–350	Mixed	More EPTB
< 200	Lower-zone infiltrates, adenopathy, effusion, normal CXR, miliary	Disseminated TB, mycobacteraemia, LAM positive, high mortality

Key management rules

- **ART timing:** within 2 weeks of starting TB treatment regardless of CD4 (Module 4, Rec. 3.2); in **TB meningitis delay ART by 4–8 weeks** (higher mortality with early ART in TBM trials). DR-TB: within 8 weeks.
- **Drug interactions:** rifampicin lowers dolutegravir — give **dolutegravir 50 mg twice daily** during and 2 weeks after rifampicin; avoid protease inhibitors with rifampicin (use **rifabutin**).
- **Co-trimoxazole prophylaxis** for all HIV-TB patients.
- **IRIS** — paradoxical worsening after ART; prednisone prophylaxis (40 mg × 2 weeks, 20 mg × 2 weeks) reduces IRIS in high-risk patients with CD4 ≤ 100 starting ART (**PredART trial**).
- Duration: same as HIV-negative (Module 4, Rec. 3.1).

"Three I's" and collaborative activities

- **Intensified case finding** — four-symptom screen at every visit, CRP/CXR/mWRD.

- **Isoniazid/TB preventive therapy** — 6H, 3HP (with dolutegravir), 1HP.
- **Infection control** in ART centres.
- In India: single-window services, ICTC–DMC linkage, all TB patients offered HIV testing; ART at ART centres with NTEP coordination.

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- **SAPiT, CAMELIA, STRIDE** — early ART reduces mortality in TB-HIV, especially CD4 < 50; **TBM trials (Török 2011)** — immediate ART in TBM did not help and increased severe adverse events.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Management of TB–HIV co-infection — timing of ART, drug interactions and IRIS. *[Long answer]*

6.6 TB in Diabetes, Pregnancy, the Elderly & Other Special Hosts

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Special situations in PTB
- ✓ Modify the diagnosis and treatment of TB in diabetes, pregnancy, elderly, CKD and liver disease
- ✓ Identify drug safety issues in each group

IN BRIEF Comorbidities change the presentation, drug choice and prognosis of TB. Diabetes delays conversion and increases relapse; pregnancy alters drug safety; elderly patients present atypically and have more adverse reactions; renal and hepatic disease require dose changes (see 9.7).

Special hosts at a glance

Host	Presentation	Treatment points
Diabetes	Lower-lobe disease, cavities, more bacilli, slower conversion	Optimise glycaemia (insulin preferred if uncontrolled); rifampicin reduces sulfonylurea/DPP-4i levels; pyridoxine (neuropathy)
Pregnancy	Same; postpartum flare; congenital TB rare	Standard **HRZE safe**; pyridoxine; avoid aminoglycosides (ototoxic), ethionamide; HPMZ not studied; BPaLM avoided; **BDLLfxC can be used**
Breastfeeding	—	Continue; drugs in milk are low; infant gets TPT if mother infectious, plus BCG
Elderly	Fewer symptoms, lower zones, atypical CXR, misdiagnosed as pneumonia/cancer	Higher DILI and ADRs; check renal function, drug interactions
Silicosis	Upper-zone nodules mask TB	Prolonged therapy often advised
Post-transplant / anti-TNF	Disseminated, extrapulmonary	Rifampicin lowers calcineurin inhibitors — use rifabutin or monitor levels
Malignancy	Coexistent lung cancer in old TB scars	Biopsy suspicious lesions; don't attribute everything to TB

Congenital TB (Cantwell criteria)

- Proven TB lesion in the infant **plus** one of: lesions in the first week of life, primary hepatic complex/caseating hepatic granulomas, placental or endometrial TB, or exclusion of postnatal transmission.

★ CLINICAL PEARLS & EXAM FOCUS

- Oral contraceptives are inactivated by rifampicin — advise barrier or IUD contraception.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculosis in pregnancy — diagnosis and management. *[Short note]*
2. TB and diabetes — clinical features and management issues. *[Short note]*

6.7 Unusual Pulmonary Forms — Endobronchial, Lower-Lobe, Tuberculoma, Pneumonic

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Atypical pulmonary TB
- ✓ Recognise endobronchial TB, lower-lobe TB, tuberculoma and TB pneumonia
- ✓ Prevent bronchostenosis in endobronchial TB

IN BRIEF Atypical forms are missed because they do not look like "apical cavities". Lower-lobe TB is common in diabetes, pregnancy and the elderly; endobronchial TB mimics asthma or cancer and causes stenosis; TB pneumonia mimics bacterial pneumonia.

Atypical forms

Form	Features	Management points
Endobronchial TB	Barking cough, wheeze (localised, monophonic), haemoptysis; bronchoscopy — caseating, oedematous or fibrostenotic types	Standard ATT; steroids controversial; stenosis may need dilatation or stenting
Lower-lobe TB	Diabetes, elderly, pregnancy, HIV; mimics pneumonia	Sputum NAAT for every "non-resolving pneumonia"
Tuberculoma	Coin lesion, calcification, satellite nodules; mimics carcinoma	Biopsy if growing or no calcification; ATT if active
TB pneumonia (caseous)	Acute lobar consolidation, high fever	NAAT on sputum/BAL; non-response to antibiotics is a clue
Tracheobronchial TB in children	Node compression, ball-valve emphysema	Steroids may help airway compression
Laryngeal TB	Hoarseness, odynophagia; highly infectious	ATT; isolate

Non-resolving pneumonia — always think of TB

- Persisting radiological shadow > 4–6 weeks despite antibiotics → sputum NAAT/culture, CT, bronchoscopy with BAL NAAT.
- **Avoid fluoroquinolones** for community-acquired pneumonia when TB is possible — they mask TB, delay diagnosis and select fluoroquinolone resistance.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Fluoroquinolone exposure before diagnosis is a risk factor for FQ-resistant TB.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Endobronchial tuberculosis. *[Short note]*

6.8 Approach to Presumptive TB & Differential Diagnosis

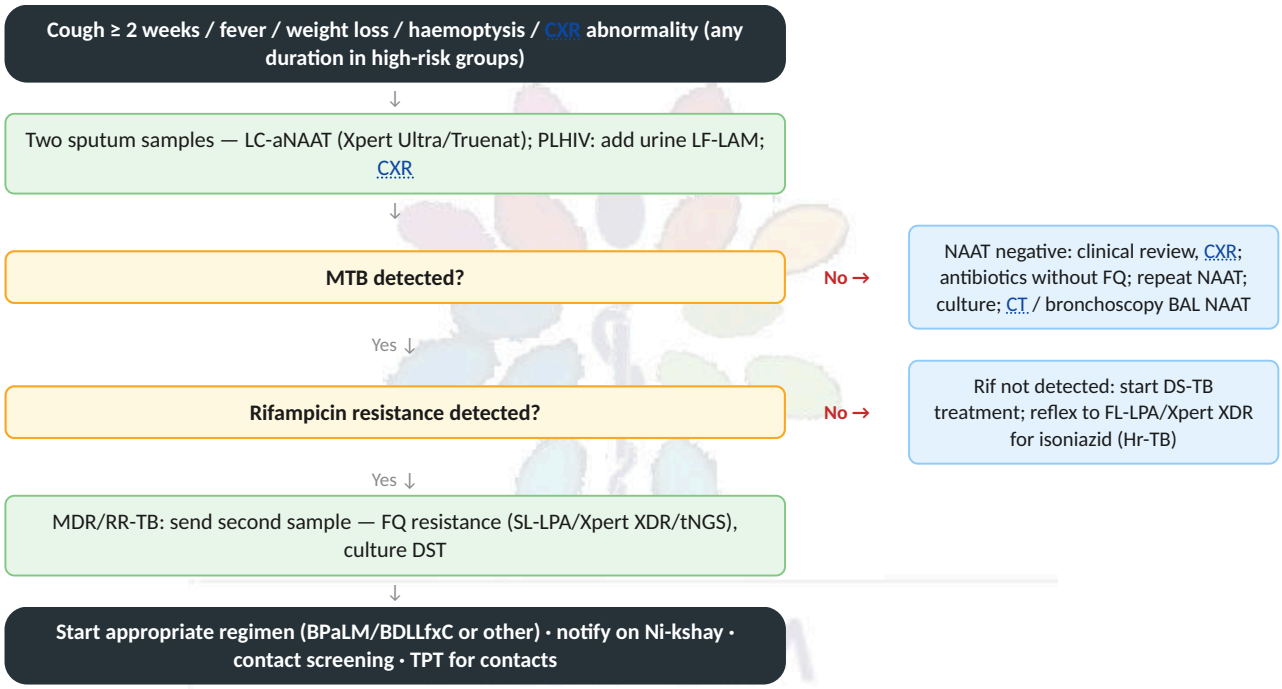
‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Differential diagnosis of PTB; diagnostic approach
- ✓ Apply a stepwise approach to a patient with presumptive pulmonary TB
- ✓ Differentiate TB from its common mimics

IN BRIEF The diagnostic goal is **bacteriological confirmation with rifampicin-resistance status at the first visit** — an LC-aNAAT on sputum. When NAAT is negative but suspicion remains, repeat testing, culture, CT and bronchoscopy come before empirical treatment.

Algorithm 6.1 · Presumptive pulmonary TB in an adult (WHO Module 3 / NTEP)



Differential diagnosis

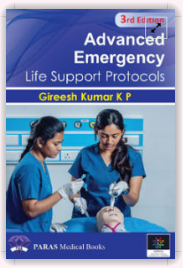
Condition	Distinguishing points
Bacterial pneumonia / lung abscess	Acute onset, response to antibiotics; abscess — air-fluid level, foul sputum
NTM lung disease	NAAT negative, culture NTM, bronchiectasis (see [[t-3-2
Lung cancer	Smoker > 40, haemoptysis, mass, nodes; may coexist with TB
Chronic pulmonary aspergillosis	Old cavity, pleural thickening, fungal ball, Aspergillus IgG positive
Fungal (histoplasmosis, paracoccidioidomycosis)	Travel/endemic exposure; fungal stains
Sarcoidosis	Bilateral hilar nodes, perilymphatic nodules, non-caseating granulomas
Melioidosis	Diabetes, monsoon, rice-field exposure; upper-lobe cavities; *Burkholderia pseudomallei* culture — important in coastal India
Paragonimiasis	Crab ingestion, haemoptysis, eosinophilia (North-East India)
GPA (Wegener's)	Cavitating nodules, sinus/renal disease, c-ANCA
Pneumoconiosis	Occupational history; TB often superimposed

★ CLINICAL PEARLS & EXAM FOCUS

- A clinically diagnosed TB patient should still have NAAT, culture and HIV test documented — and response reviewed at 2 months.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Approach to a patient with presumptive pulmonary TB and negative NAAT. *[Long answer]*
2. Differential diagnosis of cavitary lung lesions. *[Short note]*



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SECTION 7

Extrapulmonary TB — Organ by Organ

Paper II / III · One organ, one page

Extrapulmonary TB forms about a fifth of notified TB in India and more in children and PLHIV. Each organ has one complete page: presentation, the right sample and test, treatment duration, adjuncts and the exam pearl. Diagnosis follows WHO Module 3 (Rec. 3 and 4 — LC-aNAAT on CSF, aspirates and fluids) and the Index-TB guidelines.

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7.1 EPTB — General Principles & Sampling Guide

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Extrapulmonary TB; Index-TB guidelines
- ✓ Choose the right specimen and tests for each extrapulmonary site
- ✓ Decide treatment duration and need for adjunctive steroids or surgery

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IN BRIEF EPTB is paucibacillary — tissue or fluid must go for **NAAT, liquid culture and histopathology together**. Always look for coexisting pulmonary TB (sputum NAAT, CXR) and test for HIV. Most EPTB is treated for 6 months; CNS TB 12 months; osteoarticular TB often longer.

Sampling guide

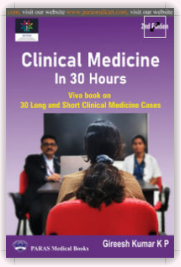
Site	Best specimen	Key tests	Duration (NTEP/Index-TB)
Lymph node	FNA / excision biopsy	NAAT, culture, cytology/histology	6 months
Pleura	Pleural fluid; pleural biopsy (thoracoscopy)	ADA, lymphocytic exudate; NAAT on tissue > fluid	6 months
Pericardium	Pericardial fluid; biopsy	ADA, unstimulated IFN-γ, NAAT	6 months + steroids (conditional)
Meninges	CSF ≥ 6 mL	Xpert Ultra, culture, cell count, glucose, protein	12 months + steroids
Spine/bone	CT-guided biopsy / pus	NAAT, culture, histology	12 months (may extend)
Abdomen	Ascitic fluid, peritoneal/bowel biopsy	ADA, NAAT, histology	6 months
Urinary	3 early-morning urine samples	NAAT, culture	6 months
Female genital	Endometrial biopsy (premenstrual), laparoscopy	Histology, culture, NAAT	6 months
Skin	Punch biopsy	Histology, culture, NAAT	6 months
Eye	Aqueous/vitreous tap	NAAT (PCR)	6–9 months (ophthalmology-guided)

General rules

- **Do not diagnose TB on IGRA/TST** in a high-burden country (Module 3, Rec. 21).
- Send fresh tissue in **saline** for NAAT/culture, the rest in formalin for histology.
- Paradoxical reactions (enlarging nodes, new effusion, tuberculomas) are common in EPTB — not treatment failure.
- Universal DST applies to EPTB: every NAAT-positive sample has rifampicin status reported.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Approach to diagnosis of extrapulmonary tuberculosis. *[Long answer]*



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7.2 Tuberculous Lymphadenitis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Lymph node TB
- ✓ Diagnose TB lymphadenitis by FNAC/biopsy with NAAT
- ✓ Manage abscess, sinus and paradoxical enlargement

IN BRIEF Commonest EPTB in India. Painless, slowly enlarging, matted **cervical** nodes (posterior triangle, supraclavicular) in young adults and children; may soften to a **cold abscess** and discharge as a **sinus** ("scrofula"). Mediastinal and abdominal nodes occur in HIV.

Clinical stages (Jones and Campbell)

Stage	Description
1	Enlarged, firm, mobile discrete nodes — reactive hyperplasia
2	Larger rubbery nodes fixed to surrounding tissue (periadenitis) — **matting**
3	Central softening — abscess formation
4	**Collar-stud abscess** — pus breaks through deep fascia into subcutaneous plane
5	**Sinus** formation — chronic discharge, undermined bluish edges

Diagnosis

- **FNAC** — epithelioid granulomas ± caseation, AFB; **NAAT (Xpert Ultra) on aspirate** (Module 3, Rec. 4) — detects rifampicin resistance.
- Excision biopsy if FNAC inconclusive: histology + NAAT + culture.
- USG: matting, intranodal necrosis, peripheral vascularity; CXR and HIV test in all.

Differential diagnosis

Condition	Clue
Reactive / pyogenic	Acute, tender, responds to antibiotics
Lymphoma	Rubbery, non-tender, B symptoms, generalised nodes — biopsy
Metastatic carcinoma	Hard, older age, primary in head and neck
NTM lymphadenitis	Children < 5 years, unilateral submandibular, violaceous skin; excision curative
Kikuchi disease	Young women, tender nodes, fever, necrotising histiocytic lymphadenitis
Sarcoidosis, toxoplasmosis	Non-caseating granulomas; serology

Management

- **6 months** of standard regimen (2HRZE/4HRE — NTEP). Aspirate fluctuant nodes; avoid incision and drainage (sinus).
- Surgical excision for persistent abscess, NTM, or diagnostic doubt.
- **Paradoxical upgrading reaction** (new or enlarging nodes during treatment) in up to 20–25% — continue same regimen; aspirate; consider short steroid course; exclude drug resistance by NAAT.
- Residual small nodes at the end of treatment are common and **do not** need extended therapy.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Nodes may remain palpable after cure — residual nodes are not failure. Judge response clinically, not by complete disappearance.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculous cervical lymphadenitis — stages, diagnosis and treatment. *[Short note]*

7.3 Tuberculous Pleural Effusion & Empyema

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Pleural TB
- ✓ Diagnose TB pleurisy using fluid analysis, ADA and pleural biopsy
- ✓ Manage TB empyema and prevent pleural thickening

IN BRIEF The commonest cause of exudative effusion in young Indians. Largely a hypersensitivity response; typically unilateral, moderate, **lymphocytic exudate with high ADA**. Fluid NAAT and culture have low yield; **pleural biopsy** (granulomas + culture/NAAT) gives the highest yield.

Clinical

- Fever, pleuritic chest pain, dry cough, breathlessness; acute presentation in young adults; ~ one-third to half have parenchymal disease on CT.

Pleural fluid analysis

Test	Typical TB finding
Appearance	Straw-coloured exudate; protein > 3 g/dL; Light's criteria exudate
Cells	**Lymphocyte predominant** (> 50%; often > 80%); early neutrophilic phase possible
Mesothelial cells	**< 5%** (scarce)
ADA	**> 40 U/L** supports TB in high-prevalence settings (sensitivity/specificity ~ 90%); ADA2 isoform more specific; ADA > 250 → think empyema/lymphoma
Unstimulated IFN-γ	High — similar accuracy to ADA
Glucose, pH	Normal or mildly low (< 60 mg/dL in ~20%)
Fluid AFB / NAAT / culture	Smear < 10%; NAAT ~ 30–50%; liquid culture ~ 30–60%
Pleural biopsy (thoracoscopic)	Granulomas > 80–95%; send tissue for NAAT and culture

Differential of lymphocytic exudate with high ADA

- Lymphoma, rheumatoid pleurisy, empyema (neutrophilic), mesothelioma rarely — biopsy if atypical.

TB empyema

- Thick pus, often with active parenchymal disease or bronchopleural fistula; frequently mixed bacterial infection.
- **Intercostal drain**, intrapleural fibrinolytics (tPA–DNase per MIST-2 principle), VATS decortication if loculated or trapped lung.

Management

- Standard 6-month regimen; therapeutic aspiration for symptomatic large effusions improves dyspnoea.
- **Steroids are not recommended routinely** (no reduction in residual pleural thickening; increased risk in HIV).
- Residual pleural thickening > 10 mm in ~ 20–50% — physiotherapy; decortication for trapped lung.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Young patient + lymphocytic exudate + ADA > 40 + no other cause → treat as TB in India (Index-TB) — but obtain a biopsy if age > 40, atypical features, or no response.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculous pleural effusion — diagnosis and role of ADA. *[Long answer]*

7.4 Tuberculous Pericarditis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Pericardial TB
- ✓ Recognise effusive, constrictive and effusive-constrictive TB pericarditis
- ✓ Perform the diagnostic work-up and choose adjuncts

IN BRIEF The commonest cause of pericardial effusion in high-burden settings and in HIV. Presents as large effusion, tamponade or **constrictive pericarditis**. Diagnosis is often probable rather than definite; **pericardial fluid ADA, unstimulated IFN-γ and NAAT** help. Steroids may be used (Module 4, Rec. 4.2).

Clinical stages

Stage	Features
Dry (fibrinous)	Pericardial rub, chest pain, fever
Effusive	Large effusion, raised JVP, pulsus paradoxus, tamponade
Effusive-constrictive	Persistently raised RA pressure after pericardiocentesis
Constrictive	Kussmaul sign, pericardial knock, ascites/oedema out of proportion, thick ± calcified pericardium

Diagnosis

- ECG: low voltage, electrical alternans; echo: effusion, fibrin strands, tamponade, septal bounce in constriction; CT/MRI: thickening > 4 mm.
- **Pericardiocentesis:** exudate, lymphocytes; **ADA > 40 U/L**; **unstimulated IFN-γ** (best single test); NAAT (Xpert) and culture; pericardial biopsy.
- **Tygerberg score** (probable TB): fever, night sweats, weight loss, globulin > 40 g/L, WBC < 10 × 10^9/L.
- Look for TB elsewhere (sputum, nodes, pleural fluid); HIV test.

Management

- Standard 6-month regimen (NTEP may extend).
- **Steroids** (conditional): prednisolone tapered over 6 weeks — reduce constriction (IMPI trial) but not death; **avoid in HIV** (increased Kaposi sarcoma risk in IMPI).
- Pericardiocentesis for tamponade; pericardiectomy for persistent constriction despite 6–8 weeks of ATT.

⚠ RED FLAGS — DO NOT MISS

- ▸ Tamponade — echo-guided pericardiocentesis immediately; do not wait for diagnosis.

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- ▸ **IMPI trial (Mayosi, NEJM 2014)** — prednisolone did not reduce the composite of death, tamponade or constriction, but reduced constriction and hospitalisation; increased cancers in HIV.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculous pericarditis — diagnosis and role of corticosteroids. *[Short note]*

7.5 Tuberculous Meningitis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** CNS TB — meningitis
- ✓ Diagnose TBM using clinical, CSF, imaging and NAAT criteria
- ✓ Treat TBM with ATT, dexamethasone and management of hydrocephalus and hyponatraemia

IN BRIEF The most lethal form of TB. Subacute meningitis (> 5 days) with fever, headache, vomiting, cranial-nerve palsies (VI), altered sensorium and focal deficits. CSF shows **lymphocytic pleocytosis, high protein, low glucose**; **Xpert Ultra on CSF** is the initial test (Module 3, Rec. 3). Treat for 12 months with steroids.

CSF in meningitis

Parameter	TB	Bacterial	Viral
Cells/µL	50–500, lymphocytes	> 1000, neutrophils	< 500, lymphocytes
Protein	**1–5 g/L** (very high in block)	High	Normal/mild ↑
Glucose ratio	**< 0.5** (often < 0.3)	Very low	Normal
Other	ADA > 10 U/L; cobweb clot; Ultra ~ 70% sensitive	Gram stain, culture	PCR

Imaging (MRI preferred)

- **Basal meningeal enhancement**, hydrocephalus, **infarcts** (basal ganglia — "TB zone"), tuberculomas.
- Uniform research case definition (Marais 2010) scores clinical, CSF and imaging criteria (definite / probable / possible TBM).

Management

- **ATT 12 months:** 2HRZE + 10HRE (NTEP; WHO 2HRZE/10HR); children — option of 6-month intensive regimen.
- **Dexamethasone** 0.4 mg/kg/day tapered over 6–8 weeks (Module 4, Rec. 4.1) — reduces death in HIV-negative adults.
- **ART:** delay 4–8 weeks in HIV-positive TBM.
- Hydrocephalus: communicating — trial of acetazolamide/furosemide, serial LP; obstructive or deteriorating → **VP shunt / ETV**.
- **Hyponatraemia:** cerebral salt wasting (volume-depleted — saline ± fludrocortisone) vs SIADH (euvolaemic — fluid restriction).
- Aspirin may reduce infarcts (trial evidence emerging); manage seizures, raised ICP.

⚠ RED FLAGS — DO NOT MISS

- ▸ Do not wait for microbiology — start ATT and steroids empirically when TBM is suspected; delay worsens outcome.

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- ▸ **Thwaites (NEJM 2004)** — dexamethasone reduced mortality in TBM (HIV-negative). **ACT HIV (NEJM 2023)** — dexamethasone did not reduce mortality in HIV-positive adults. Intensified regimens (high-dose rifampicin) remain investigational in adults.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculous meningitis — CSF findings, staging and management. *[Long answer]*

7.6 CNS Tuberculoma, TB Abscess & Spinal Arachnoiditis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** CNS TB — parenchymal and spinal
- ✓ Distinguish tuberculoma from neurocysticercosis and tumour on imaging
- ✓ Manage paradoxical tuberculomas and spinal TB arachnoiditis

IN BRIEF Parenchymal CNS TB presents with **seizures**, focal deficits or raised ICP. Tuberculomas are often multiple, ring-enhancing lesions with a T2 hypointense core; they may appear or enlarge during treatment (paradoxical). Spinal arachnoiditis causes radiculomyelopathy and paraparesis.

Ring-enhancing lesions — differential

Feature	Tuberculoma	Neurocysticercosis	Tumour/abscess
Size	Usually > 2 cm, irregular	< 2 cm, round	Variable
Scolex	No	**Eccentric scolex**	No
T2 core	**Hypointense** (caseous)	Hyperintense cyst	Variable
MR spectroscopy	**Lipid peak**	Succinate, alanine	Choline peak (tumour)
Midline shift	Often	Rare	Often
Other	Basal meningitis, chest TB	Calcified dots, endemic diet	Abscess: DWI restriction

Management of tuberculoma

- ATT for **12–18 months**, guided by MRI resolution; steroids for perilesional oedema; antiepileptics.
- Surgery for large lesions with mass effect, obstructive hydrocephalus or diagnostic doubt.
- **Paradoxical tuberculomas** (new/enlarging during ATT) — continue ATT, steroids; thalidomide or anti-TNF in refractory cases (specialist).

Tuberculous abscess

- True abscess with pus and bacilli; larger, multiloculated, rapid progression — needs surgical drainage plus ATT.

Spinal TB arachnoiditis (tuberculous radiculomyelitis)

- Subacute paraparesis, radicular pain, sphincter disturbance; may follow TBM.
- MRI: clumping of roots, CSF loculation, intradural enhancement; CSF very high protein (Froin's syndrome).
- ATT + steroids; surgery rarely helps.

Spinal intramedullary tuberculoma

- Rare; myelopathy; MRI target sign; ATT ± surgery.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ In India, a solitary small ring-enhancing lesion with seizures is more often neurocysticercosis — but a large irregular lesion with a lipid peak and chest TB suggests tuberculoma.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Intracranial tuberculoma — imaging differential and treatment. *[Short note]*

7.7 Spinal Tuberculosis (Pott's Disease)

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Osteoarticular TB — spine
- ✓ Recognise spinal TB clinically and on MRI
- ✓ Manage Pott's paraplegia and decide when surgery is needed

IN BRIEF The spine is involved in about half of osteoarticular TB — commonly **lower thoracic and upper lumbar** vertebrae. Typical **paradiscal** destruction of two adjacent vertebrae with disc involvement, cold abscess (paravertebral, psoas) and **gibbus**. MRI is the investigation of choice; CT-guided biopsy confirms.

Clinical

- Back pain, local tenderness, stiffness, constitutional symptoms; **gibbus** (knuckle kyphosis); cold abscess (psoas — groin swelling, flexion deformity of hip; retropharyngeal in cervical spine).
- **Pott's paraplegia:** early-onset (active disease — abscess, granulation tissue, sequestra; good prognosis with treatment) vs late-onset (healed disease — internal gibbus, fibrosis; poor prognosis).
- Patterns: **paradiscal** (commonest), central (concertina collapse, mimics tumour), anterior (subligamentous scalloping), posterior (neural arch — more deficit).

Imaging

- X-ray: disc-space narrowing, end-plate erosion, collapse, paravertebral shadow (bird-nest), kyphosis.
- **MRI:** marrow oedema, subligamentous spread, skip lesions, abscess with thin smooth enhancing wall, cord compression. Disc relatively preserved early (vs pyogenic).
- Biopsy (CT-guided): **NAAT, culture, histology** — essential for DST.

TB vs pyogenic vs malignant spine

Feature	TB	Pyogenic	Metastasis
Disc	Destroyed late	Destroyed early	**Spared**
Abscess	Large, thin wall, calcified	Small, thick wall	Rare
Course	Slow (months)	Acute	Older, primary known
Levels	Multiple, skip lesions	One level	Pedicle involvement

Management

- **ATT 12 months** (NTEP/Index-TB; may extend clinically); bracing; rest in early phase.
- **Surgery** (decompression + stabilisation) for: neurological deficit not improving or worsening on ATT, severe/progressive kyphosis, instability, large abscess, diagnostic biopsy, no response.
- **Middle-path regimen** (Tuli): ATT + surgery reserved for specific indications.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Pott's paraplegia with active disease often recovers with ATT ± decompression — do not label it permanent.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Pott's spine — clinical features, imaging and indications for surgery. *[Long answer]*

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7.8 Peripheral Osteoarticular Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Bone and joint TB
- ✓ Recognise TB of hip, knee and other joints and tuberculous osteomyelitis
- ✓ Plan biopsy, ATT and joint rehabilitation

IN BRIEF Peripheral osteoarticular TB is usually a **monoarthritis of a large weight-bearing joint** (hip, knee) with insidious pain, swelling and wasting. Early synovial disease can be cured with preserved function; late disease destroys the joint. Synovial fluid NAAT and synovial biopsy confirm the diagnosis.

Common sites

Site	Features
Hip	Limp, pain referred to knee, **Babcock triangle** tenderness; stages from synovitis (flexion, abduction, external rotation, apparent lengthening) to destruction (flexion, adduction, internal rotation, shortening, wandering acetabulum)
Knee	Boggy synovial swelling, wasting, "doughy" feel; triple deformity in late stages
Ankle/foot, wrist	Chronic swelling, sinuses
Spina ventosa	Fusiform expansion of short tubular bones of hands/feet in children (dactylitis)
Tuberculous osteomyelitis	Metaphyseal lytic lesions crossing the growth plate, minimal sclerosis
Tenosynovitis / bursitis	Compound palmar ganglion — melon-seed bodies

Phemister triad (X-ray)

- **Juxta-articular osteoporosis**, **peripheral (marginal) erosions** and **gradual joint-space narrowing** (preserved longer than in pyogenic arthritis).

Diagnosis

- Synovial fluid: lymphocytic exudate, low glucose; **NAAT on synovial fluid** (Module 3, Rec. 4); synovial biopsy — histology + NAAT + culture.
- MRI: synovial thickening, erosions, abscesses.

Management

- ATT for 9–12 months (Index-TB: 12 months for most osteoarticular TB).
- Splintage in functional position early, then active mobilisation.
- Surgery: synovectomy, debridement, arthrodesis or arthroplasty in healed disease.

Differential diagnosis

- Septic arthritis, rheumatoid monoarthritis, pigmented villonodular synovitis, haemophilic arthropathy, fungal arthritis, Poncet's disease (reactive, sterile).

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Monoarthritis of the knee or hip in a young adult with juxta-articular osteopenia — biopsy the synovium before calling it "seronegative arthritis".

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculosis of the hip joint — stages and management. *[Short note]*

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7.9 Intestinal (Gastrointestinal) Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Abdominal TB — gut
- ✓ Recognise ileocaecal TB and differentiate it from Crohn's disease
- ✓ Manage obstruction, perforation and strictures

IN BRIEF The **ileocaecal region** is involved in most intestinal TB (lymphoid-rich, stasis, absorption). Presents with chronic abdominal pain, weight loss, altered bowel habit, a right iliac fossa mass or subacute obstruction. Distinguishing TB from **Crohn's disease** is a major challenge in India.

Pathological types

- **Ulcerative** (transverse girdle ulcers → stricture), **hypertrophic** (mass), **ulcero-hypertrophic** (commonest at ileocaecal region), fibrous strictures.

TB vs Crohn's disease

Feature	Intestinal TB	Crohn's disease
Duration	Shorter history	Long, relapsing
Ulcers	**Transverse**, circumferential	**Longitudinal**, aphthous, cobblestoning
Ileocaecal valve	Patulous, gaping	Narrowed
Perianal disease	Rare	Common
Granulomas	Large, confluent, **caseating**	Small, non-caseating, sparse
CT	Necrotic nodes, short segment, ascites	Comb sign, fibrofatty proliferation, skip lesions
Chest	Active/old TB	Usually normal
Tests	AFB, NAAT, culture, IGRA (supportive)	ASCA, calprotectin (non-specific)

Investigations

- **Colonoscopy with ileal intubation** and multiple biopsies — histology, NAAT, culture.
- CT enterography: thickening, strictures, necrotic nodes; CXR and HIV test.
- If uncertain: a **therapeutic trial of ATT** with objective reassessment at 8 weeks (mucosal healing) — not before excluding malignancy and lymphoma.

Complications

- Subacute/acute **intestinal obstruction** (strictures, adhesions), **perforation** (usually ileum, during treatment), haemorrhage, malabsorption, fistula.

Management

- **ATT 6 months** (randomised trials show 6 months = 9 months for abdominal TB).
- Strictures: many resolve on ATT; endoscopic balloon dilatation; **strictureplasty or limited resection** for persistent obstruction.
- Perforation — surgery (resection; avoid extensive resections).

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Starting steroids for presumed Crohn's in undiagnosed intestinal TB can be disastrous — exclude TB first.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Ileocaecal tuberculosis versus Crohn's disease. *[Long answer]*

7.10 Peritoneal Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Abdominal TB — peritoneum
- ✓ Diagnose TB peritonitis using ascitic fluid analysis, ADA and laparoscopy
- ✓ Recognise wet, dry and fibrotic types

IN BRIEF TB peritonitis presents with insidious **ascites**, fever, weight loss and abdominal distension; the "doughy" abdomen is a classic sign. Ascitic fluid is a **lymphocytic exudate with high ADA and low SAAG**; laparoscopy with peritoneal biopsy is the most accurate test.

Types

Type	Features
Wet (ascitic)	Commonest; free or loculated ascites
Fixed fibrotic	Omental thickening ("omental cake"), matted bowel loops, masses
Dry (plastic)	Dense adhesions, doughy abdomen, nodules, subacute obstruction

Ascitic fluid

Test	TB finding
SAAG	**< 1.1 g/dL** (unless coexisting cirrhosis)
Protein	> 2.5–3 g/dL
Cells	500–1500/µL, **lymphocyte predominant**
ADA	**> 39 U/L** — high accuracy (lower in cirrhosis and HIV)
AFB / NAAT / culture	Smear rarely positive; NAAT low–moderate sensitivity; culture up to ~ 50% with large volumes

Investigations

- Ultrasound/CT: ascites with septations, peritoneal thickening, omental thickening, necrotic nodes, clumped bowel loops.
- **Laparoscopy:** white "miliary" tubercles on parietal peritoneum, adhesions; biopsy for histology, NAAT, culture — near-diagnostic.
- CA-125 is raised in TB peritonitis as in ovarian cancer — do not over-interpret.
- **Differentials of high-protein, low-SAAG ascites:** peritoneal carcinomatosis, ovarian cancer (very high CA-125), pancreatic ascites (high amylase), secondary bacterial peritonitis (neutrophils), chylous ascites (triglycerides > 200 mg/dL).

Management

- **ATT 6 months**; corticosteroids not routinely recommended; surgery for obstruction.
- Cirrhotic patients: ADA less reliable; DILI risk high — choose hepatotoxicity-sparing regimen if decompensated.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Young woman, ascites, raised CA-125 and "omental cake" — laparoscopic biopsy before staging laparotomy for ovarian cancer.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Peritoneal tuberculosis — diagnosis. *[Short note]*

7.11 Hepatobiliary, Splenic & Pancreatic Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Abdominal TB — solid organs
- ✓ Recognise TB of the liver, spleen and pancreas and its mimics
- ✓ Plan image-guided sampling

IN BRIEF Solid-organ abdominal TB is usually part of disseminated or miliary disease (granulomatous hepatitis), but local forms — tuberculous liver abscess, splenic microabscesses, and pancreatic TB mimicking carcinoma — occur in immunocompetent hosts in India.

Forms

Form	Features	Diagnosis
Granulomatous hepatitis (miliary)	Fever, hepatomegaly, **raised ALP** disproportionate to transaminases	Liver biopsy — caseating granulomas; NAAT
Tuberculoma / TB liver abscess	Fever, RUQ pain, solitary or multiple hypodense lesions	USG/CT-guided aspirate — NAAT, culture
Biliary TB	Obstructive jaundice from nodes at porta hepatis or biliary strictures	MRCP, EUS-FNA of nodes
Splenic TB	Fever, splenomegaly, **multiple hypodense microabscesses** ("starry sky"/snow-storm)	Splenic aspirate rarely needed; nodes or other sites
Pancreatic TB	Mass in head of pancreas, peripancreatic necrotic nodes, obstructive jaundice — mimics **pancreatic carcinoma**	**EUS-guided FNA** — granulomas, NAAT; avoids Whipple surgery

Granulomatous hepatitis — differential

- TB, sarcoidosis, drug-induced (allopurinol, sulfonamides), brucellosis, Q fever, histoplasmosis, lymphoma, primary biliary cholangitis, BCG infection after intravesical therapy.

Management

- Standard 6-month ATT; drainage of large abscesses; biliary stenting for obstruction.
- **Liver involvement is not a contraindication to standard ATT** — baseline LFTs and close monitoring; distinguish TB-related ALP elevation from DILI.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Pancreatic mass + necrotic peripancreatic nodes + young patient from an endemic area → EUS-FNA with NAAT before surgery.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Hepatic tuberculosis — forms and diagnosis. *[Short note]*

7.12 Genitourinary (Renal & Urinary Tract) Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Genitourinary TB — urinary tract
- ✓ Diagnose renal TB with urine NAAT/culture and imaging
- ✓ Recognise sterile pyuria and its causes

IN BRIEF Renal TB follows haematogenous seeding years after primary infection. It presents with **irritative voiding symptoms, sterile pyuria, haematuria** and loin pain; constitutional symptoms are often absent. Progressive ureteric and bladder fibrosis causes obstruction, a **thimble bladder** and renal failure.

Clinical features

- Frequency (most common), dysuria, nocturia, haematuria, loin pain; recurrent "UTI" not responding to antibiotics.
- **Sterile pyuria** (pus cells without growth on routine culture) — classic.

Investigations

- **3–5 early-morning urine samples** (whole first void) — NAAT and mycobacterial culture.
- CT urography: papillary necrosis, calyceal irregularity ("moth-eaten"), infundibular stenosis (**phantom calyx**), **hydronephrosis**, ureteric strictures (**beaded/corkscrew ureter**, "pipe-stem"), small contracted bladder.
- End-stage: **autonephrectomy** — small calcified non-functioning kidney (**putty kidney**).
- Cystoscopy and bladder biopsy (avoid in acute cystitis).

Causes of sterile pyuria

Infective	Non-infective
Genitourinary TB	Renal calculi
Partially treated UTI	Interstitial nephritis (analgesic, drugs)
Chlamydia, gonorrhoea, Ureaplasma	Papillary necrosis, polycystic disease
Fungal (Candida)	Bladder/renal tumour, foreign body, catheter

Management

- **ATT 6 months**; monitor renal function; dose-adjust ethambutol and pyrazinamide in CKD.
- **Ureteric stricture:** watch with imaging at 3–6 weeks; **DJ stent** or nephrostomy if obstruction; steroids debated.
- Surgery: reconstruction (ureteric reimplantation, augmentation cystoplasty for thimble bladder) after ≥ 6 weeks of ATT; nephrectomy for non-functioning infected kidney with pain or hypertension.

⚠ RED FLAGS — DO NOT MISS

- ▸ Ureteric strictures can worsen in the first weeks of ATT (healing fibrosis) — repeat imaging early to protect renal function.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Recurrent "UTI" with sterile pyuria and haematuria in a young adult → urine NAAT and mycobacterial culture before cystoscopy.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Renal tuberculosis — clinical features and imaging. *[Short note]*

7.13 Female Genital Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Genital TB — female
- ✓ Recognise female genital TB as a cause of infertility and menstrual disturbance
- ✓ Avoid over-diagnosis based on PCR alone

IN BRIEF A major cause of **tubal infertility** in India. Fallopian tubes are almost always involved (bilateral salpingitis), followed by endometrium and ovaries. Many women are asymptomatic apart from infertility; diagnosis requires histology, culture or NAAT — **not** a positive PCR/IGRA alone (Index-TB).

Clinical features

- **Infertility** (most common), oligo/amenorrhoea or menorrhagia, chronic pelvic pain, adnexal masses, post-menopausal bleeding, ascites.
- **Asherman syndrome** (intrauterine adhesions) from endometrial destruction.

Investigations

- **Premenstrual endometrial biopsy** (or menstrual blood) — histology (granulomas), mycobacterial culture, NAAT.
- **Hysterosalpingography** (only after excluding active disease): beaded tubes, rigid "lead-pipe" tubes, **tobacco-pouch** distal end, **cornual block**, calcification, uterine synechiae.
- **Laparoscopy:** tubercles, adhesions, caseous nodules, tubo-ovarian masses, **Fitz-Hugh–Curtis**-like perihepatic adhesions; biopsy.
- USG: tubo-ovarian masses, thin endometrium.

Diagnostic pitfalls

- Endometrial **PCR is highly sensitive but poorly specific** — false positives lead to unnecessary ATT (Index-TB discourages ATT based on PCR alone).
- IGRA/TST positivity reflects infection, not genital TB.

Management

- **ATT 6 months**.
- Fertility: tubal damage is often irreversible — **IVF** is usually needed; surgery for tubo-ovarian abscess; hysteroscopic adhesiolysis for synechiae.
- Pregnancy after genital TB carries a higher ectopic risk.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Treat genital TB only on robust evidence — granulomas, positive culture or NAAT (Xpert) on tissue — and counsel that ATT rarely restores tubal patency.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Female genital tuberculosis — diagnosis and management of infertility. *[Short note]*

7.14 Male Genital Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Genital TB — male
- ✓ Recognise TB epididymo-orchitis and prostatic TB
- ✓ Differentiate TB from testicular tumour and bacterial epididymitis

IN BRIEF Male genital TB usually accompanies renal TB (descending infection) or haematogenous spread. The **epididymis** (globus minor/tail) is most commonly involved, producing a **firm, craggy, painless or mildly painful scrotal swelling**, often with a beaded vas and a posterior scrotal sinus.

Sites and features

Site	Features
Epididymis	Craggy nodular swelling of the tail; **beaded vas deferens**; cold abscess; **posterior scrotal sinus**
Testis	Secondary to epididymal disease; mass mimicking tumour
Prostate & seminal vesicles	Perineal pain, haemospermia, low-volume ejaculate, nodular prostate, calcification
Penis / urethra	Ulcers, strictures — rare

Investigations

- Urine NAAT/culture (3 early-morning samples), semen culture, CT urography for renal involvement.
- Scrotal USG: heterogeneous enlarged epididymis, abscess, calcification, sinus tract.
- FNAC/biopsy: granulomas, NAAT; **inguinal orchidectomy** if tumour cannot be excluded (avoid scrotal approach to a possible tumour).
- Transrectal USG for prostatic abscess.

Differential of scrotal swelling

Condition	Clue
Bacterial epididymo-orchitis	Acute, painful, responds to antibiotics
Testicular tumour	Painless mass of testis; raised AFP/β-hCG/LDH
Filarial epididymitis/funiculitis	Endemic area, hydrocele, microfilariae
Brucella orchitis	Livestock contact, serology
Spermatocele, varicocele	Typical USG features

Management

- **ATT 6 months**; drainage of abscess; epididymectomy or orchidectomy for refractory disease or sinus.
- Infertility from obstructive azoospermia — assisted reproduction.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ A craggy epididymis + beaded vas + sterile pyuria → genitourinary TB until proved otherwise.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculous epididymo-orchitis. *[Short note]*

7.15 Cutaneous Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Skin TB
- ✓ Classify cutaneous TB by route of infection and immune status
- ✓ Diagnose skin TB by biopsy with histology, culture and NAAT

IN BRIEF Cutaneous TB is uncommon but varied. In India the commonest forms are **scrofuloderma** and **lupus vulgaris**. Classification depends on whether bacilli reach the skin from outside (exogenous) or from within (endogenous), and on host immunity (multibacillary vs paucibacillary).

Classification

Route	Form	Features
Exogenous (inoculation)	Tuberculous chancre	Painless ulcer + regional nodes in non-immune host
Exogenous	**Tuberculosis verrucosa cutis**	Warty plaque on hands/feet/buttocks in previously sensitised host ("prosector's wart")
Endogenous — contiguous	**Scrofuloderma**	Breakdown of skin over node/bone/joint; sinuses, undermined edges, cord-like scars
Endogenous — autoinoculation	Orificial TB	Painful ulcers around mouth/anus in advanced visceral TB
Haematogenous	**Lupus vulgaris**	Slowly spreading plaque, face/buttocks; **"apple-jelly" nodules on diascopy**; scarring; risk of squamous carcinoma
Haematogenous	Miliary skin TB, gumma	Immunosuppressed; papules, abscesses
Hypersensitivity	Tuberculids	Papulonecrotic tuberculid, lichen scrofulosorum, erythema induratum (see [[t-4-4

Diagnosis

- **Skin biopsy** — tuberculoid granulomas (paucibacillary forms rarely show AFB); culture and NAAT on fresh tissue.
- Look for underlying node, bone or lung TB; strongly positive TST/IGRA supportive.

Differential diagnosis

Lesion	Mimics
Lupus vulgaris	Discoid lupus, sarcoidosis, leprosy, leishmaniasis, psoriasis
TB verrucosa cutis	Warts, chromoblastomycosis, sporotrichosis, hypertrophic lichen planus
Scrofuloderma	Actinomycosis, hidradenitis, NTM, deep fungal infection

Management

- **ATT 6 months**; response is often dramatic (a therapeutic clue); surgery for residual scars/deformity.
- Watch for **squamous cell carcinoma** in long-standing lupus vulgaris (Marjolin-type change).

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Lupus vulgaris: diascopy shows apple-jelly nodules; scarring at the centre with activity at the edge.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Cutaneous tuberculosis — classification and lupus vulgaris. *[Short note]*

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7.16 Ocular Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Eye TB
- ✓ Recognise the ocular manifestations of TB
- ✓ Apply the COTS approach before starting ATT for uveitis

IN BRIEF Ocular TB is most often a **posterior or intermediate uveitis** (choroiditis, serpiginous-like choroiditis, retinal vasculitis) in a patient without active systemic TB. Diagnosis is usually presumptive — ocular phenotype plus evidence of TB infection and exclusion of other causes — guided by the **Collaborative Ocular TB Study (COTS)** consensus.

Ocular manifestations

Manifestation	Features
Choroidal tubercles	Yellowish nodules — with miliary TB (diagnostic clue)
Choroidal tuberculoma	Solitary mass; mimics tumour
Serpiginous-like choroiditis	Multifocal, progressive choroiditis — typical in India
Retinal vasculitis	Occlusive periphlebitis; **Eales disease** (young men, vitreous haemorrhage)
Anterior uveitis	Granulomatous — "mutton-fat" keratic precipitates, Koeppe/Busacca nodules
Intermediate uveitis	Vitritis, snowballs
External	**Phlyctenular keratoconjunctivitis** (hypersensitivity), scleritis, eyelid/orbital TB
Optic nerve	Optic neuritis, papillitis (also from TBM); **ethambutol optic neuropathy** — drug toxicity

Diagnosis

- Clinical phenotype + positive **IGRA/TST** and/or chest CT evidence of TB + exclusion of syphilis, sarcoidosis, toxoplasmosis, viral retinitis, lymphoma.
- **Aqueous/vitreous NAAT** (PCR) when feasible.
- Fundus fluorescein angiography, OCT, ICG angiography.

Management (ophthalmologist-led)

- **ATT 6–9 months** with **corticosteroids** (topical, periocular or systemic) and immunosuppressants as needed; COTS consensus recommends ATT for specific phenotypes (e.g. serpiginous-like choroiditis, tubercular retinal vasculitis) with positive immunological tests.
- **Paradoxical worsening** may occur in the first weeks of ATT — increase steroids.
- Baseline visual acuity and colour vision (Ishihara) before ethambutol.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Do not start ATT for "uveitis + positive IGRA" without the ophthalmologist confirming a TB-compatible phenotype — IGRA positivity is common in India.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Ocular tuberculosis — clinical forms and management. *[Short note]*

7.17 Ear, Nose, Throat & Oral Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Head and neck TB (non-nodal)
- ✓ Recognise laryngeal, middle-ear and oral TB
- ✓ Appreciate the infectivity of laryngeal TB

IN BRIEF Head-and-neck TB beyond the lymph nodes includes **laryngeal TB** (the most infectious form), **tuberculous otitis media**, nasal and nasopharyngeal TB and **oral ulcers**. They mimic carcinoma and chronic infections; biopsy with NAAT and culture is essential.

Sites

Site	Features	Diagnosis/treatment points
Larynx	Hoarseness, odynophagia, cough; posterior larynx/ interarytenoid ulcers, "turban epiglottis"; usually with cavitary PTB	Laryngoscopy + biopsy; sputum NAAT — **highly infectious, isolate**
Middle ear	Painless chronic otorrhoea, **multiple tympanic perforations**, pale granulations, early severe hearing loss, facial palsy	Biopsy of granulations; NAAT; mastoid surgery if needed
Nose / nasopharynx	Nasal obstruction, crusting, septal perforation (cartilaginous); nasopharyngeal mass	Biopsy; differentiate from lymphoma, NPC, rhinosporidiosis
Oral cavity	Painful **undermined ulcer on tongue** (lateral border/tip), lips, gingiva	Biopsy; mimics squamous cell carcinoma
Tonsil, salivary glands	Enlargement, masses (parotid)	FNAC/biopsy
Thyroid	Rare; nodule, abscess	FNAC

Differential diagnosis of chronic oral/laryngeal ulcer

Condition	Clue
Squamous cell carcinoma	Tobacco, indurated everted edge, older age
Syphilis	Serology; painless
Traumatic ulcer	Sharp tooth, heals on removal
Fungal (histoplasmosis)	Immunosuppressed; fungal stain
Behçet's disease	Recurrent oral and genital ulcers, uveitis

Management

- **ATT 6 months**; voice rest; rapid symptomatic response in laryngeal TB.
- Airborne infection control for laryngeal TB (N95, isolation until sputum improves and on effective treatment).
- Hearing rehabilitation; mastoid exploration for complications.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ "Multiple perforations of the tympanic membrane" in chronic painless otorrhoea is the classic exam clue to tuberculous otitis media.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Laryngeal tuberculosis. *[Short note]*

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7.18 Breast Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Breast TB
- ✓ Recognise tuberculous mastitis and differentiate it from carcinoma and idiopathic granulomatous mastitis
- ✓ Plan core biopsy with NAAT and culture

IN BRIEF Breast TB is rare but well recognised in Indian women of reproductive age, often lactating or multiparous. It presents as a **lump**, **abscess** or **sinus** and is frequently mistaken for carcinoma or idiopathic granulomatous mastitis (IGM). Core biopsy with histology, NAAT and culture is decisive.

Clinical forms

Form	Features
Nodular	Slow-growing painless lump, often upper outer quadrant; may mimic carcinoma (skin fixation)
Disseminated	Multiple nodules, sinuses, skin ulceration
Sclerosing	Elderly; fibrosis, nipple retraction
Abscess / sinus	Recurrent "breast abscess" not healing after drainage; axillary nodes in up to half

Investigations

- USG: irregular hypoechoic mass, fluid collection, fistulous tracts; mammography not specific.
- **Core-needle biopsy** (preferred to FNAC): caseating granulomas; NAAT; culture; exclude malignancy.
- Pus: NAAT and culture; CXR; HIV test.

Granulomatous mastitis — TB vs IGM vs carcinoma

Feature	Breast TB	Idiopathic granulomatous mastitis	Carcinoma
Age	20–40, lactating	Young parous women, recent lactation	Older
Granulomas	Caseating, AFB/NAAT ±	Lobulocentric, non-caseating, neutrophilic microabscesses	None
Nodes	Axillary common, matted	Uncommon	Hard nodes
Treatment	ATT	Steroids/methotrexate	Oncological

Management

- **ATT 6 months** (may extend for extensive disease); aspiration or drainage of abscesses; excision of residual sinus/mass after ATT.
- Lactation: continue breastfeeding from the unaffected side; infant needs evaluation and TPT if mother infectious.

★ CLINICAL PEARLS & EXAM FOCUS

- ▸ Never treat a non-healing breast abscess as "IGM" with steroids until TB is excluded on core biopsy with NAAT.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculosis of the breast. *[Short note]*

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7.19 Adrenal & Endocrine Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Adrenal TB; endocrine complications
- ✓ Recognise primary adrenal insufficiency due to TB
- ✓ Anticipate rifampicin-induced adrenal crisis

IN BRIEF TB is a leading cause of **Addison's disease** in India. Bilateral adrenal destruction (> 90% of cortex) produces glucocorticoid and mineralocorticoid deficiency. Early disease shows **enlarged adrenals** with necrosis; late disease shows small, **calcified** glands. Rifampicin can precipitate crisis in borderline patients.

Clinical features of adrenal insufficiency

- Fatigue, weight loss, anorexia, abdominal pain, postural hypotension, **hyperpigmentation** (buccal mucosa, palmar creases, scars), salt craving.
- Labs: **hyponatraemia, hyperkalaemia**, hypoglycaemia, eosinophilia, mild hypercalcaemia.

Diagnosis

- **Morning cortisol** (< 3–5 µg/dL suggests insufficiency); **ACTH stimulation test** (synacthen — cortisol < 18 µg/dL at 30–60 min); high ACTH, high renin.
- CT: bilateral enlarged adrenals with central necrosis and peripheral rim enhancement (active) → atrophy and calcification (chronic).
- CT-guided biopsy rarely needed if TB proven elsewhere.

Endocrine involvement in TB

Condition	Notes
Adrenal insufficiency	Addison's — lifelong replacement usually needed
SIADH	With TBM, pulmonary TB — euvolaemic hyponatraemia
Hypopituitarism, diabetes insipidus	Hypothalamic–pituitary TB, basal TBM
Hypercalcaemia	Granulomatous 1α-hydroxylase activity — uncommon
Thyroid TB	Rare; nodule, abscess, thyroiditis
Rifampicin effects	Increases metabolism of cortisol, levothyroxine, oral hypoglycaemics, oral contraceptives

Management

- **Hydrocortisone** 15–25 mg/day in divided doses (double dose while on rifampicin) + **fludrocortisone** 50–100 µg/day.
- **Adrenal crisis:** IV hydrocortisone 100 mg stat then 200 mg/day, IV saline and dextrose.
- ATT 6 months; adrenal function rarely recovers; sick-day rules and steroid card.

⚠ RED FLAGS — DO NOT MISS

- ▸ Unexplained hypotension, hyponatraemia or vomiting after starting rifampicin — think adrenal crisis.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Adrenal tuberculosis — diagnosis and management. *[Short note]*

SECTION 8

Investigations

Paper II / IV · Diagnostic tests and algorithms

From the sputum cup to sequencing: how to collect the right sample, which test to order first, how to read every result, and the NTEP/WHO algorithms that tie them together (WHO Module 3, 4th edition 2025).

8.1 Specimen Collection — Getting the Right Sample 65
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8.8 Integrated Diagnostic Algorithms — DS & DR-TB 72

8.1 Specimen Collection — Getting the Right Sample

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Specimen collection and transport
- ✓ Collect good-quality sputum and alternative respiratory samples
- ✓ Choose specimens for children, non-expectorating adults and EPTB

IN BRIEF The best test fails on a poor sample. Two sputum specimens (one early-morning) of **3–5 mL of purulent material** give the best yield. When patients cannot expectorate — children, PLHIV, early disease — use induced sputum, gastric aspirate, stool, BAL or urine LF-LAM.

Specimen options

Specimen	Method	Use
Expectorated sputum	Deep cough after mouth rinse with water; spot + early-morning	Standard for adults
Induced sputum	Nebulised 3–5% hypertonic saline after salbutamol, in a ventilated room/booth	Non-expectorating adults and children
Gastric aspirate	Early morning, fasting, via NG tube; neutralise with sodium bicarbonate if delayed	Young children
Nasopharyngeal aspirate	Suction catheter	Infants
Stool	Small sample; processed for Xpert Ultra	Children — concurrent with respiratory sample (Module 3, Rec. 8–9)
Bronchoscopy — BAL, bronchial wash, post-bronchoscopy sputum	Under infection control	Smear-negative, non-expectorating, suspected endobronchial disease

Specimen	Method	Use
Urine	LF-LAM (PLHIV); 3 early-morning samples for NAAT/culture (renal TB)	Advanced HIV; GU TB
Tongue swab	Swab of tongue dorsum	New WHO option (2026) for near point-of-care NAATs
Tissue / fluid	Fresh in saline for NAAT/culture; formalin for histology	EPTB

Transport and safety

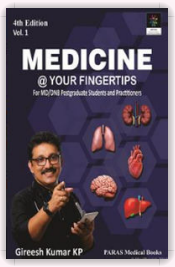
- Leak-proof screw-cap containers, triple packaging, cold chain (2–8 °C); process for culture within 3–5 days (CPC transport medium if longer).
- Collect sputum **outdoors or in a ventilated area**, never in a closed room or toilet.

★ CLINICAL PEARLS & EXAM FOCUS

- Saliva is not sputum — reject and re-collect; label the request "presumptive TB / DR-TB / follow-up" so the laboratory chooses the right test.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Methods of obtaining samples for TB diagnosis in children. *[Short note]*



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8.2 Sputum Smear Microscopy

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Smear microscopy; AFB grading
- ✓ Describe Ziehl–Neelsen and fluorescence microscopy and their limits
- ✓ Grade smears and use microscopy for treatment monitoring

IN BRIEF Smear microscopy is cheap and specific in high-burden settings but **insensitive** — about 5000–10 000 bacilli/mL are needed. WHO no longer recommends it as the initial diagnostic test (Module 3, Rec. 1), but it remains useful for grading infectiousness and **monitoring** DS-TB treatment.

ZN vs fluorescence (LED) microscopy

Feature	Ziehl–Neelsen	Auramine/LED-FM
Stain	Carbol fuchsin, heat, acid-alcohol decolourisation, methylene blue counterstain	Auramine O
Appearance	Red, slightly curved rods on blue background	Yellow-green fluorescent rods on dark background
Magnification	1000× (oil immersion)	200–400× — scans faster
Sensitivity	Baseline	~10% higher

Feature	Ziehl–Neelsen	Auramine/LED-FM
Use	Peripheral labs	Higher-volume labs (Designated Microscopy Centres)

IUATLD/WHO grading (ZN)

Report	Count
Negative	No AFB in 100 fields
Scanty	1–9 AFB in 100 fields (record exact number)
1+	10–99 AFB in 100 fields
2+	1–10 AFB per field (examine 50 fields)
3+	> 10 AFB per field (examine 20 fields)

Limitations

- Cannot distinguish TB from NTM or dead from live bacilli; no DST; poor in children, HIV, EPTB.
- Follow-up smears may remain positive with dead bacilli — smear positivity at 2 months does **not** justify extending the intensive phase (Module 4, Rec. 1.5).

★ CLINICAL PEARLS & EXAM FOCUS

- A smear-positive, NAAT-negative result → think NTM or laboratory error; send culture.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Grading of sputum smear microscopy and its role in the NAAT era. *[Short note]*

8.3 Culture & Phenotypic Drug Susceptibility Testing

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Mycobacterial culture; phenotypic DST
- ✓ Compare solid and liquid culture systems
- ✓ Explain the role of phenotypic DST alongside molecular tests

IN BRIEF Culture is the reference standard for diagnosis and is needed for treatment monitoring in DR-TB (Module 4, Rec. 5.1) and for phenotypic DST of drugs without reliable molecular tests. **Liquid culture (MGIT)** is faster and more sensitive than solid **Löwenstein–Jensen (LJ)** medium.

Culture systems

Feature	Solid (LJ)	Liquid (MGIT 960)
Medium	Egg-based with malachite green	Middlebrook 7H9 broth with fluorescent oxygen sensor
Detection limit	~ 100 bacilli/mL	~ 10 bacilli/mL
Time to result	3–8 weeks	1–3 weeks (reported negative at 6 weeks)
Contamination	Lower (~ 2–5%)	Higher (~ 5–10%)
Colonies	Rough, buff, dry ("rough, tough and buff")	Growth detected by fluorescence; cords on smear
Identification	MPT64 antigen test, NAAT/LPA	Same

Phenotypic DST

- Tests growth at a WHO **critical concentration** of each drug; results in 2–6 weeks (liquid).

- Still required for bedaquiline, linezolid, delamanid, pretomanid and clofazimine where molecular tests are limited; tNGS increasingly fills this gap (Module 3, Rec. 18).
- **Culture conversion:** two consecutive negative cultures ≥ 7 days apart (WHO 2021).

When culture is mandatory

- Previously treated patients, all MDR/RR-TB (baseline and monthly on longer regimens), EPTB samples, children, suspected NTM, treatment failure and discordant results.

★ CLINICAL PEARLS & EXAM FOCUS

- Time to culture positivity is a surrogate of bacillary load — shorter time means higher load and higher relapse risk.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Liquid versus solid culture for Mycobacterium tuberculosis. *[Short note]*

8.4 Molecular Tests — NAATs, LPA, Xpert XDR & Sequencing

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** WHO-recommended rapid diagnostic tests
- ✓ Choose the right molecular test for detection of TB and drug resistance
- ✓ Interpret Xpert/Truenat results including "trace" and "indeterminate"
- ✓ Order second-line molecular DST in RR-TB

IN BRIEF Molecular WHO-recommended rapid diagnostic tests (mWRDs) are now the **initial test for everyone with presumptive TB**. LC-aNAATs (Xpert MTB/RIF Ultra, Truenat) give TB detection and rifampicin resistance in under 2 hours; reflex tests (Xpert MTB/XDR, LPA, tNGS) then detect isoniazid, fluoroquinolone and other resistance.

The test classes (WHO Module 3, 2025)

Class	Examples	Use
LC-aNAAT (low-complexity automated)	**Xpert MTB/RIF, Xpert Ultra, Truenat MTB Plus / MTB-RIF Dx**	Initial test on sputum, CSF, nodes, fluids, stool; rifampicin resistance
LC-mNAAT (low-complexity manual)	TB-LAMP	Initial detection only (no resistance)
Moderate-complexity automated NAAT	Abbott RealTime MTB/INH-RIF, BD MAX MDR-TB, cobas MTB/MTB-RIF/INH, FluoroType	High-throughput labs; TB + R + H resistance
LC-aNAAT for H/FQ (and Eto, Am)	**Xpert MTB/XDR**	Reflex test after TB detected — isoniazid, fluoroquinolones, ethionamide, amikacin
Line probe assays	FL-LPA (R, H); SL-LPA (FQ, SLID)	Smear-positive sputum or culture isolate; reference labs
Targeted NGS	Deeplex Myc-TB, AmPORE-TB, TBseq	Comprehensive resistance including bedaquiline, linezolid, clofazimine (Rec. 17–18)
Near point-of-care NAAT	New class (WHO 2026)	Peripheral health facilities; tongue swabs

Interpreting Xpert results

Result	Action
MTB detected, Rif not detected	Start DS-TB treatment; reflex for isoniazid (Xpert XDR/FL-LPA)
MTB detected, Rif resistance detected	Treat as RR-TB; second sample to confirm in low-prevalence groups; reflex FQ testing
MTB detected, Rif indeterminate	Repeat test on a fresh sample

Result	Action
MTB trace detected (Ultra)	Treat as TB in PLHIV, children, EPTB samples; in others, repeat test — trace in previously treated may be old DNA
MTB not detected	Does not exclude TB — clinical review, culture, repeat NAAT, other samples
Error / invalid	Repeat on a new sample

Practical points

- Xpert Ultra detects ~ 15 CFU/mL (vs ~ 130 for MTB/RIF) — better in smear-negative, paediatric, HIV and CSF samples.
- NAAT positivity can persist after cure — do **not** use NAAT to monitor treatment or diagnose recurrence without culture/clinical correlation.
- Discordance (molecular resistant, phenotypic susceptible) occurs with certain low-level resistance — treat according to the molecular result for rifampicin and seek expert review.

★ **CLINICAL PEARLS & EXAM FOCUS**

- Never start a fluoroquinolone-containing MDR regimen without sending a sample for FQ resistance testing (SL-LPA/Xpert XDR/ tNGS).

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Xpert MTB/RIF Ultra — principle, advantages and interpretation of results. *[Long answer]*
2. Role of targeted next-generation sequencing in drug-resistant TB. *[Short note]*

8.5 Tests for TB Infection — TST, IGRA & TBST

‹ NMC curriculum | Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Tests for TB infection
- ✓ Perform and read a Mantoux test with correct cut-offs
- ✓ Compare TST, IGRA and the new antigen-based skin tests
- ✓ Explain why these tests should not diagnose active TB

IN BRIEF All TB infection tests measure **immune memory**, not bacilli. They cannot distinguish infection from disease, are falsely negative in immunosuppression and severe disease, and **must not be used to diagnose active TB in high-burden countries** (Module 3, Rec. 21). TST or IGRA can be used for TBI; TBSTs combine the convenience of a skin test with IGRA-like specificity.

Mantoux TST

- **5 TU PPD-S or 2 TU PPD RT23**, 0.1 mL intradermally on the flexor forearm (wheal 6–10 mm); read **induration** (not erythema) across the forearm at **48–72 hours**.

Induration	Considered positive in
≥ 5 mm	PLHIV, recent close contacts, fibrotic lesions on CXR, transplant/immunosuppressed (≥ 15 mg prednisolone), anti-TNF
≥ 10 mm	General population in India; health-care workers; children < 4 years; diabetes, silicosis, CKD
≥ 15 mm	Low-risk individuals in low-incidence settings

- False negatives: HIV, malnutrition, steroids, measles/live vaccines, severe/miliary TB, sarcoidosis, technical errors. False positives: BCG (wanes after infancy), NTM.
- **Booster phenomenon** — two-step testing in health-care workers; **conversion** = increase ≥ 10 mm within 2 years.

IGRA vs TST vs TBST

Feature	TST	IGRA (QFT-Plus, T-SPOT.TB)	TBST (Cy-Tb, C-Tb, Diaskintest)
Antigens	PPD (many shared with BCG, NTM)	ESAT-6, CFP-10 (± TB7.7)	ESAT-6, CFP-10
BCG cross-reaction	Yes	No	No
Visits	Two	One (blood)	Two
Lab	None	Laboratory needed	None
Cost	Low	High	Low–moderate
WHO status	Strong (TBI)	Strong (TBI)	Conditional (Module 1 & 3)

★ CLINICAL PEARLS & EXAM FOCUS

- India's **Cy-TB** (Serum Institute) is a TBST read like a Mantoux (induration ≥ 5 mm positive) but without BCG cross-reactivity.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Interferon-gamma release assays — principle, advantages and limitations. *[Short note]*
2. Mantoux test — technique, interpretation and causes of false results. *[Short note]*

8.6 LF-LAM, ADA, Biomarkers & Histopathology

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Adjunctive diagnostic tests
- ✓ Use urine LF-LAM in people with advanced HIV
- ✓ Interpret ADA and unstimulated IFN-γ in body fluids
- ✓ Recognise the histopathology of TB and its mimics

IN BRIEF Several adjunctive tests help where microbiology is weak: **urine LF-LAM** in seriously ill PLHIV, **ADA** and **unstimulated IFN-γ** in serous fluids, and **histopathology** of tissue. None replace NAAT and culture; each has a defined niche.

Adjunctive tests

Test	Use and cut-off	Limitations
Urine LF-LAM (Determine TB LAM Ag)	PLHIV with symptoms, seriously ill, advanced HIV, or CD4 ≤ 200 inpatients; **concurrent with NAAT** (Module 3, Rec. 7) — reduces mortality	Low sensitivity in HIV-negative; no DST
ADA — pleural	> 40 U/L	False positives: empyema, lymphoma, RA
ADA — peritoneal	> 39 U/L	Lower in cirrhosis
ADA — pericardial	> 40 U/L	
ADA — CSF	> 10 U/L (not standardised)	Overlap with bacterial meningitis, lymphoma
Unstimulated IFN-γ	Pleural/pericardial fluid — highly accurate	Cost, availability
CRP	> 5 mg/L as screening in PLHIV (Module 2)	Non-specific
Serology (antibody tests)	**Not recommended** — WHO negative recommendation (2011)	Inaccurate; banned in India (2012)
Blood transcriptomic signatures	Research — incipient TB	Not yet recommended

Histopathology

- **Caseating granulomas** with epithelioid cells and Langhans giant cells; AFB on ZN stain (low yield in tissue).

- Differentials: sarcoidosis, fungal, leprosy, NTM, cat-scratch, Crohn's, granulomatous mastitis, foreign body reaction.
- Always send a portion of tissue **fresh in saline** for NAAT and culture.

Other baseline investigations at diagnosis (NTEP)

- HIV, blood glucose/HbA1c, LFT, creatinine, haemogram; hepatitis B/C in high-risk; pregnancy test; ECG and electrolytes for DR-TB regimens; audiometry if aminoglycoside.

★ **CLINICAL PEARLS & EXAM FOCUS**

- Serological antibody tests for TB are banned in India — never order "TB IgG/IgM".

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Role of ADA in diagnosis of extrapulmonary tuberculosis. *[Short note]*
2. Lateral-flow urine LAM assay. *[Short note]*

8.7 Imaging Beyond the Chest X-ray — CT, MRI, PET & Ultrasound

‹ NMC curriculum

Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Imaging in TB
- ✓ Choose the right imaging modality for each site
- ✓ Use computer-aided detection and point-of-care ultrasound appropriately

IN BRIEF CXR (with CAD) is the screening workhorse; CT defines activity and complications; MRI is best for CNS and spine; ultrasound guides aspiration and detects abdominal and pericardial disease; PET-CT helps biopsy targeting but cannot separate TB from cancer.

Modality by question

Question	Best imaging
Screening / triage	CXR with **CAD** (≥ 15 years, Module 2)
Activity, cavities, endobronchial spread	HRCT/CECT chest — tree-in-bud, necrotic nodes
Miliary TB with normal CXR	HRCT
TB meningitis, tuberculoma	**Contrast MRI brain** — basal enhancement, hydrocephalus, infarcts; MRS lipid peak
Spine and joints	**MRI** — abscess, cord compression, skip lesions
Abdomen	**CECT abdomen**, CT enterography; USG for ascites, nodes, splenic lesions
Pericardium	Echo; CT/MRI for thickening
Renal tract	CT urography
Biopsy targeting, response assessment	18F-FDG PET-CT (avid in both TB and cancer)

Point-of-care ultrasound — FASH protocol (HIV)

- **Focused Assessment with Sonography for HIV-associated TB:** pericardial effusion, pleural effusion, ascites, abdominal lymph nodes (> 1.5 cm), hypoechoic **splenic** and **liver** lesions.

Computer-aided detection (CAD)

- Software (e.g. qXR, CAD4TB, Lunit) gives an abnormality score; calibrate threshold locally; use for screening and triage in ≥ 15 years, not for diagnosis.

★ CLINICAL PEARLS & EXAM FOCUS

- A normal CXR does not exclude TB in PLHIV, children or endobronchial disease.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Role of imaging in extrapulmonary tuberculosis. *[Short note]*

8.8 Integrated Diagnostic Algorithms — DS & DR-TB

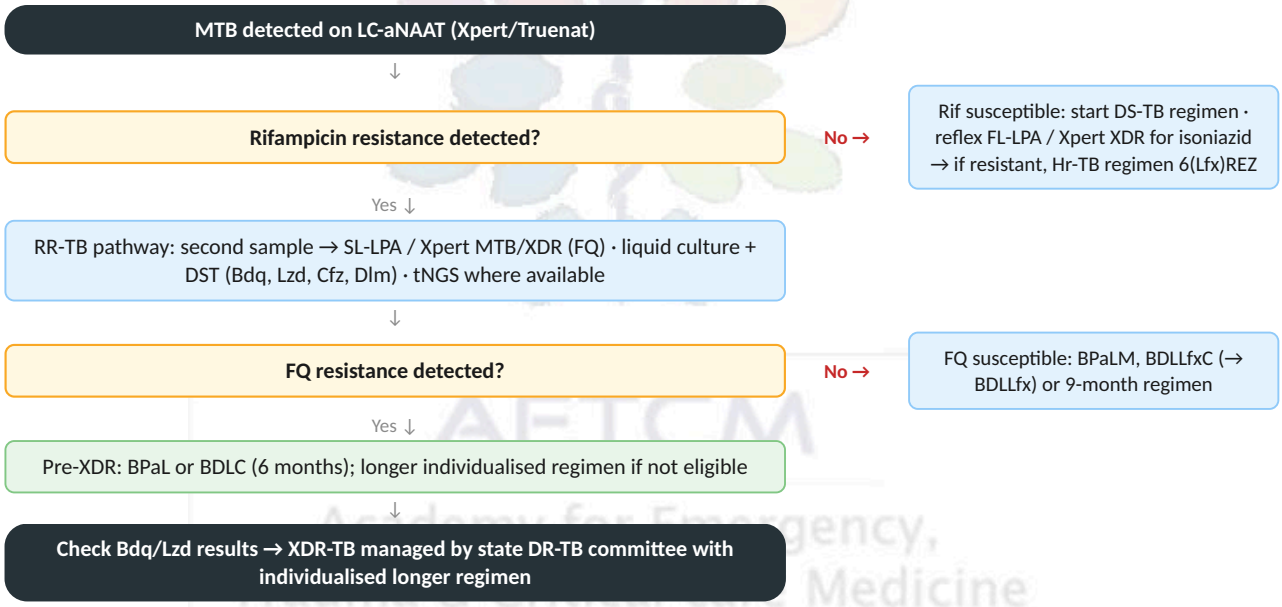
‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** NTEP integrated algorithm; universal DST
- ✓ Apply the NTEP integrated diagnostic algorithm
- ✓ Plan universal DST pathways for RR-TB and Hr-TB

IN BRIEF The aim is a confirmed diagnosis **and** a resistance profile before or within days of starting treatment. NTEP uses NAAT up front, reflexes isoniazid testing for rifampicin-susceptible TB, and second-line testing for every RR-TB patient.

Algorithm 8.1 · Universal DST pathway after a positive NAAT



Who needs which test (NTEP)

Patient	Tests
Every presumptive TB	NAAT (Xpert/Truenat) on sputum or relevant specimen; CXR
Rif-susceptible TB	FL-LPA or Xpert XDR for isoniazid
RR-TB	SL-LPA/Xpert XDR for FQ; culture + DST including bedaquiline, linezolid
Previously treated, contacts of DR-TB, non-responders	NAAT + culture + full DST
PLHIV	NAAT + urine LF-LAM; CD4; consider blood/urine culture
Children	NAAT on respiratory + stool; gastric aspirate; CXR
Follow-up DS-TB	Smear at end of IP and treatment; culture if positive
Follow-up DR-TB	Smear and culture monthly (longer regimens) or per regimen schedule

★ CLINICAL PEARLS & EXAM FOCUS

- Do not wait for the full DST to start treatment — start on the best regimen supported by rapid tests and adjust.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. NTEP integrated diagnostic algorithm for drug-susceptible and drug-resistant TB. *[Long answer]*

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SECTION 9

Management

Paper II / IV · Treatment, prevention and patient support

Drugs, regimens, monitoring and adverse reactions for drug-susceptible and drug-resistant TB, special situations, adjuncts, adherence support, preventive treatment, infection control and vaccines — aligned to WHO Module 4 (2025), Module 1 (2024) and NTEP. Ends with the drug chart.

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9.1 First-Line Antituberculosis Drugs

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Pharmacology of first-line drugs
- ✓ Describe the action, dose and adverse effects of isoniazid, rifampicin, pyrazinamide and ethambutol
- ✓ Explain the roles of each drug — early bactericidal, sterilising and resistance-preventing

IN BRIEF Short-course chemotherapy rests on four drugs. **Isoniazid** gives the most rapid early bactericidal kill; **rifampicin** and **pyrazinamide** are the key **sterilising** drugs that make 6 months possible; **ethambutol** protects against unrecognised resistance in the intensive phase.

First-line drugs (adult daily doses)

Drug	Mode of action	Dose (max)	Key adverse effects	Notes
Isoniazid (H)	Inhibits mycolic acid synthesis	5 mg/kg (300 mg)	Hepatitis, peripheral neuropathy, lupus-like syndrome, rash	**Pyridoxine 10–25 mg** in risk groups; slow acetylators ↑ toxicity

Drug	Mode of action	Dose (max)	Key adverse effects	Notes
Rifampicin (R)	Inhibits bacterial RNA polymerase	10 mg/kg (600 mg)	Hepatitis (cholestatic), orange secretions, flu-like syndrome, thrombocytopenia, renal failure (intermittent use)	**Potent CYP3A4 inducer**; stains contact lenses
Pyrazinamide (Z)	Active in acidic environment; sterilising	25 mg/kg (2 g)	Hepatitis (most hepatotoxic), **hyperuricaemia/gout**, arthralgia, rash	Avoid in severe liver disease
Ethambutol (E)	Inhibits arabinogalactan synthesis	15 mg/kg	**Optic neuritis** (red–green colour vision, acuity)	Dose by weight; reduce in CKD; colour vision check
Rifapentine (P)	As rifampicin, long half-life	1200 mg (4-month regimen); 900 mg weekly (3HP)	Hypersensitivity, flu-like	Interactions as rifampicin
Rifabutin	As rifampicin, weaker inducer	5 mg/kg (300 mg)	Uveitis, neutropenia	Use with protease inhibitors (150 mg daily)
Streptomycin (S)	Aminoglycoside	15 mg/kg	Ototoxicity (vestibular), nephrotoxicity	No longer in DS-TB regimens

Paediatric doses (mg/kg/day)

- **H 10 (7–15), R 15 (10–20), Z 35 (30–40), E 20 (15–25)** — use dispersible FDCs by weight band.

★ CLINICAL PEARLS & EXAM FOCUS

- Remember the trio for each drug in viva: **H** — neuropathy, hepatitis; **R** — interactions, orange urine, flu-like; **Z** — gout, hepatitis; **E** — eyes.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Pharmacology of rifampicin — mechanism, adverse effects and drug interactions. *[Short note]*

9.2 Drug-Susceptible TB Regimens

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Treatment of DS-TB
- ✓ Prescribe 2HRZE/4HR(E) by weight band using FDCs
- ✓ Choose 4-month regimens (HPMZ; 2HRZ(E)/2HR in children) for eligible patients
- ✓ Decide durations for extrapulmonary TB

IN BRIEF Standard treatment is **2 months HRZE (intensive phase) followed by 4 months HR** daily (WHO; NTEP gives **HRE** in the continuation phase). FDCs are preferred; thrice-weekly dosing is no longer used. The **2HPMZ/2HPM** regimen is an option for people ≥ 12 years with pulmonary TB.

NTEP adult weight bands (daily FDCs)

Weight (kg)	Intensive phase — HRZE (75/150/400/275 mg)	Continuation — HRE (75/150/275 mg)
25–34	2 tablets	2 tablets
35–49	3 tablets	3 tablets
50–64	4 tablets	4 tablets
65–75	5 tablets	5 tablets
> 75	6 tablets	6 tablets

Regimen options

Regimen	For whom	Notes
2HRZE/4HR (NTEP 2HRZE/4HRE)	All new and previously treated DS-TB	Standard (Module 4, Rec. 1.1); IP is not extended for positive smear at 2 months
2HPMZ/2HPM	≥ 12 years, pulmonary DS-TB	**Study 31/A5349**; not if weight < 40 kg, EPTB, pregnancy, CD4 < 100; rifapentine interactions
2HRZ(E)/2HR	Children 3 months–16 years, **non-severe** TB	**SHINE** trial; E added where HIV or isoniazid resistance prevalence is high
2HRZE/10HR(E)	TB meningitis, CNS tuberculoma; osteoarticular (NTEP/Index-TB up to 12 months)	Steroids for TBM
6HRZEto	Children with TBM (alternative)	Intensive short regimen (Module 5)

Extension and special rules

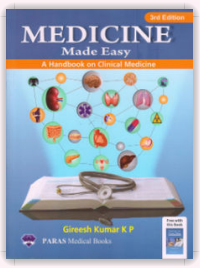
- NTEP permits extension of the continuation phase by 3–6 months in selected EPTB/slow responders on clinical grounds.
- **Previously treated** patients: same regimen once rifampicin (and preferably isoniazid) susceptibility is confirmed — Category II with streptomycin is abolished.
- Missed doses: if interruption ≥ 2 months, the patient is "lost to follow-up" — re-evaluate with NAAT/culture and DST before restarting.

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- **Study 31/A5349 (Dorman, NEJM 2021)** — 4-month rifapentine–moxifloxacin regimen non-inferior to standard 6-month regimen. **SHINE (Turkova, NEJM 2022)** — 4 months non-inferior for non-severe childhood TB. **TRUNCATE-TB (2023)** — strategy of 2 months' treatment with extended follow-up non-inferior; not yet a WHO recommendation.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Treatment regimens for drug-susceptible TB — current WHO and NTEP recommendations. *[Long answer]*



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9.3 Monitoring During & After Treatment

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Treatment monitoring; follow-up
- ✓ Plan clinical, bacteriological and laboratory monitoring for DS-TB
- ✓ Recognise and respond to non-response

IN BRIEF Response is judged clinically (weight, symptoms), bacteriologically (smear at end of IP and end of treatment for PTB; culture when positive) and by adverse-event monitoring. Persistent positivity raises suspicion of non-adherence, drug resistance, malabsorption, wrong diagnosis (NTM) or comorbidity.

NTEP monitoring schedule (DS-TB)

Time	Action
Baseline	Weight, NAAT + DST (universal), HIV, RBS/HbA1c, LFT if risk, creatinine, CBC; visual acuity/colour vision; counselling; Ni-kshay registration, bank details for NPY
Every month	Weight (adjust dose band), adherence, adverse events, symptom review
End of IP (2 months)	Sputum smear (PTB); if positive → NAAT/LPA + culture DST — **do not extend IP**
End of treatment	Sputum smear/culture; CXR; assign outcome
Post-treatment	Follow-up at 6, 12, 18, 24 months for recurrence; spirometry/rehabilitation if PTLD

Assessing non-response

- Check adherence (Ni-kshay/99DOTS records, pill counts); correct weight band.
- Repeat NAAT with rifampicin result, **FL-LPA/Xpert XDR for isoniazid**, culture DST.
- Consider NTM, malignancy, aspergillosis, HIV/diabetes control, paradoxical reaction (EPTB).

Monitoring DR-TB regimens (summary)

- Monthly smear and culture (longer regimens; Module 4, Rec. 5.1); clinical review each visit.
- **ECG (QTcF)** at baseline, 2, 4, 8, 12 and 24 weeks for bedaquiline/delamanid/clofazimine/FQ regimens; electrolytes (K, Mg, Ca).
- **CBC** (linezolid) monthly or more often; **peripheral neuropathy** screening; **visual acuity and colour vision** monthly on linezolid/ethambutol.
- LFT, creatinine, TSH (ethionamide/PAS), audiometry (aminoglycosides).

★ **CLINICAL PEARLS & EXAM FOCUS**

- Weight gain is the simplest and most reassuring sign of response — record weight every visit.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Monitoring of a patient on treatment for drug-susceptible pulmonary TB. *[Short note]*

9.4 Drug-Induced Liver Injury (DILI)

‹ NMC curriculum | Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

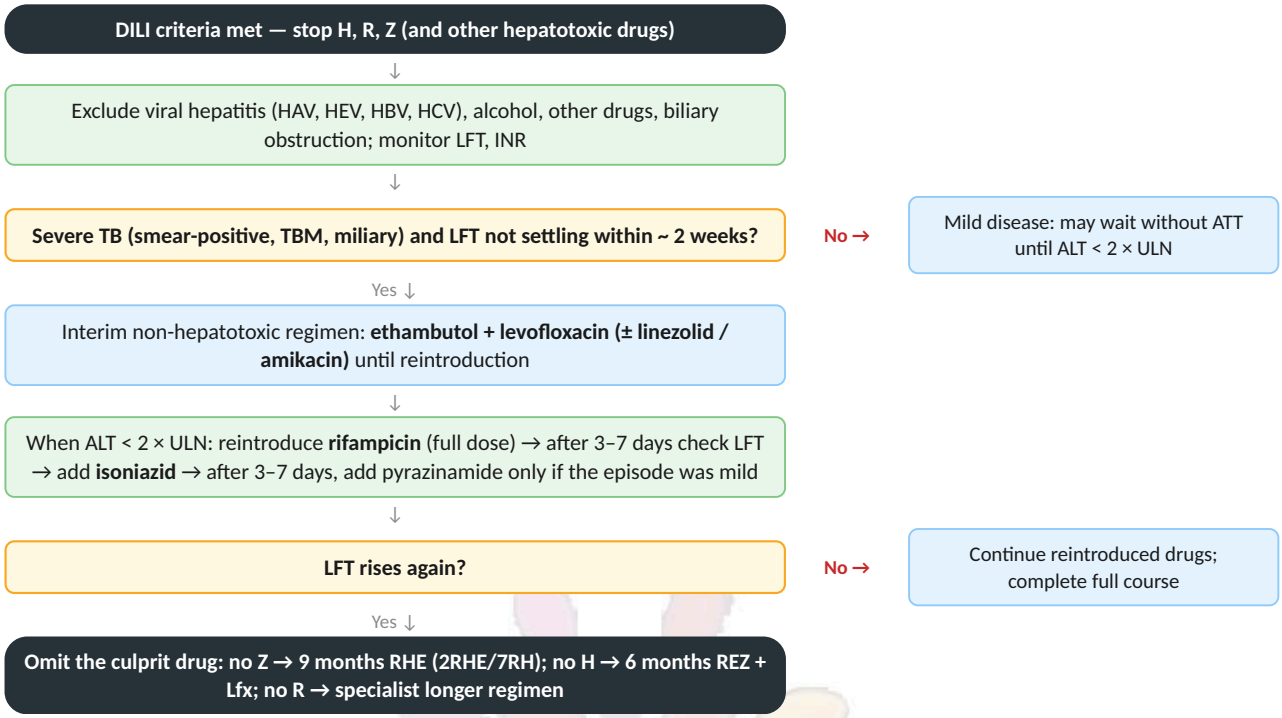
- ✓ **NMC syllabus area:** Hepatotoxicity of antituberculosis drugs
- ✓ Define DILI thresholds that require stopping ATT
- ✓ Reintroduce drugs sequentially and choose interim liver-safe regimens

IN BRIEF Hepatotoxicity is the most important adverse effect of first-line therapy (pyrazinamide > isoniazid > rifampicin). Risk factors: age > 35, alcohol, chronic hepatitis B/C, HIV, malnutrition, slow acetylators, female sex, concomitant hepatotoxic drugs. Most DILI occurs in the first 2 months.

When to stop ATT (ATS/BTS; NTEP)

Situation	Action
ALT < 3 × ULN, no symptoms	Continue with closer monitoring (adaptation)
ALT ≥ 3 × ULN with symptoms (nausea, vomiting, abdominal pain, jaundice)	**Stop hepatotoxic drugs**
ALT ≥ 5 × ULN without symptoms	**Stop**
Bilirubin > 2 × ULN / clinical jaundice	**Stop**

Algorithm 9.1 · Management of antituberculosis DILI



Regimens without one first-line drug

Drug omitted	Regimen (adult DS-TB)
Pyrazinamide	2HRE/7HR (total 9 months)
Isoniazid	6 months RZE + levofloxacin (as Hr-TB)
Rifampicin	Longer FQ-based regimen (12–18 months) — specialist

★ **CLINICAL PEARLS & EXAM FOCUS**

- Isolated raised bilirubin with normal ALT early in therapy may be rifampicin's effect on bilirubin uptake — check before stopping all drugs.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Management of antituberculosis drug-induced hepatotoxicity. *[Long answer]*

9.5 Other Adverse Reactions & Drug Interactions

‹ NMC curriculum
Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Adverse drug reactions; interactions
- ✓ Manage cutaneous, neurological, ocular, renal and haematological adverse reactions
- ✓ Anticipate rifamycin and QT-prolonging drug interactions

IN BRIEF Most adverse effects are minor and managed without stopping treatment. Serious ones — severe cutaneous reactions, optic neuritis, thrombocytopenia, acute kidney injury, QTc prolongation, linezolid myelosuppression — need prompt drug withdrawal. Rifampicin's enzyme induction is the most common source of clinically important interactions.

Common adverse effects and management

Effect	Likely drug	Management
Gastrointestinal upset	Z, R, H, ethionamide, PAS	Give with food or at bedtime; antiemetic; check LFT
Pruritus / mild rash	Any	Antihistamine; continue
Severe rash, SJS/TEN, DRESS	H, R, Z, E, FQ	**Stop all**; supportive; rechallenge one by one (except in SJS/TEN with culprit identified) under supervision
Peripheral neuropathy	H, linezolid, cycloserine	Pyridoxine (higher dose); dose reduction/stop linezolid
Arthralgia, gout	Z	NSAIDs; uric acid not routinely monitored; allopurinol not effective for Z-induced hyperuricaemia
Optic neuritis	E, linezolid	**Stop immediately**; ophthalmology review
Flu-like, thrombocytopenia, haemolysis, AKI	R (esp. intermittent)	Stop rifampicin permanently if serious
QTc prolongation	Bdq, Dlm, Cfz, Mfx	Stop if QTcF > 500 ms; correct K/Mg
Myelosuppression, lactic acidosis	Linezolid	Hold/reduce dose (300 mg); transfuse if needed
Psychosis, depression, seizures	Cycloserine, H, FQ	Pyridoxine; psychiatric review; dose reduce
Hypothyroidism	Ethionamide, PAS	Levothyroxine
Skin discolouration	Clofazimine	Reversible; counsel
Ototoxicity, nephrotoxicity	Amikacin, streptomycin	Audiometry; stop if hearing loss

Key rifampicin interactions

- **Reduces levels of:** oral contraceptives, warfarin, sulfonylureas, DPP-4 inhibitors, corticosteroids (double the dose), levothyroxine, calcineurin inhibitors, azoles, methadone, protease inhibitors, dolutegravir (give 50 mg twice daily), nevirapine, many anticonvulsants and anti-arrhythmics, opioids.
- **Isoniazid** raises phenytoin and carbamazepine levels.
- **Fluoroquinolones:** absorption reduced by antacids, iron, calcium, zinc — separate by 2 hours.

⚠ RED FLAGS — DO NOT MISS

- Rash with fever, mucosal involvement or eosinophilia — stop all drugs immediately.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Adverse reactions to antituberculosis drugs — recognition and management. *[Long answer]*

9.6 Principles of DR-TB Management & Hr-TB

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Programmatic management of DR-TB; Hr-TB
- ✓ Apply principles of regimen design for drug-resistant TB
- ✓ Treat isoniazid-resistant, rifampicin-susceptible TB

IN BRIEF DR-TB management rests on **rapid detection of resistance**, a regimen with enough **likely effective drugs**, **all-oral** shorter regimens where eligible, active drug-safety monitoring (aDSM), and strong patient support. Hr-TB is treated with **6 months of rifampicin, ethambutol, pyrazinamide and levofloxacin** (Module 4, Rec. 4.1).

Principles

- Never **add a single drug** to a failing regimen — it amplifies resistance.

- Base regimen on the patient's DST (and the index case's DST for contacts); start immediately on the best available regimen and modify.
- Prefer shorter all-oral regimens: **BPaLM/BDLLfxC (6 months) > 9-month regimens > longer individualised (18–20 months)**.
- **Active drug-safety monitoring and management (aDSM):** systematic ECG, CBC, neuropathy, vision and LFT monitoring; report to pharmacovigilance.
- **Ambulatory, decentralised care** (Module 4 care chapter); hospitalise only the sick.
- Treat comorbidities: HIV (ART within 8 weeks), HCV (co-treat), diabetes, nutrition, mental health, substance use.

Isoniazid-resistant TB (Hr-TB)

- Regimen: **6(Lfx)REZ** — 6 months levofloxacin + rifampicin + ethambutol + pyrazinamide; no injectables (Rec. 4.2).
- Exclude rifampicin and FQ resistance first; if FQ-resistant or intolerant → 6REZ.
- NTEP: Hr-TB detected on FL-LPA/Xpert XDR → 6(Lfx)REZ; extend in selected cases.

Classification of second-line drugs for longer regimens (Module 4)

- **Group A:** levofloxacin/moxifloxacin, bedaquiline, linezolid. **Group B:** clofazimine, cycloserine/terizidone. **Group C:** ethambutol, delamanid, pyrazinamide, imipenem/meropenem + clavulanate, amikacin (streptomycin), ethionamide/prothionamide, PAS.

★ CLINICAL PEARLS & EXAM FOCUS

- Rifampicin resistance detected → assume MDR until proven otherwise; start an MDR/RR-TB regimen even before isoniazid results.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Principles of management of drug-resistant tuberculosis. *[Long answer]*
2. Isoniazid-resistant tuberculosis — diagnosis and treatment. *[Short note]*

9.7 MDR/RR-TB Regimens in Practice

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Treatment of MDR/RR-TB and pre-XDR/XDR-TB
- ✓ Prescribe BPaLM and BDLLfxC with correct doses and monitoring
- ✓ Choose 9-month or longer regimens for those not eligible
- ✓ Manage linezolid and QT toxicity

IN BRIEF For most patients with MDR/RR-TB or pre-XDR-TB, a **6-month all-oral regimen** cures about 9 in 10. BPaLM (age ≥ 14, not pregnant) and BDLLfxC (all ages, including pregnancy) are the regimens of choice; 9-month regimens serve FQ-susceptible patients not eligible for 6-month regimens; longer individualised regimens are for extensive resistance, intolerance or severe EPTB.

Regimens and doses (adults)

Regimen	Composition and adult dose	Duration
BPaLM	Bedaquiline 400 mg daily × 2 weeks then 200 mg thrice weekly × 22 weeks (or 200 mg daily × 8 weeks then 100 mg daily) + pretomanid 200 mg daily + linezolid 600 mg daily + moxifloxacin 400 mg daily	26 weeks (extendable to 39 weeks)
BPaL	As above without moxifloxacin — pre-XDR-TB	26 weeks
BDLLfxC	Bedaquiline (as above) + delamanid 100 mg twice daily + linezolid 600 mg daily + levofloxacin (750–1000 mg by weight) + clofazimine 100 mg daily → **BDLLfx** if FQ-susceptible, **BDLC** if FQ-resistant	6 months

Regimen	Composition and adult dose	Duration
9-month Bdq regimen	4–6 Bdq-Lfx/Mfx-Cfz-Z-E-Hh-Eto (or 2 months Lzd instead of Eto) / 5 Lfx/Mfx-Cfz-Z-E (Bdq 6 months)	9–11 months
BLMZ (preferred), BLLfxCZ, BDLLfxZ	Bedaquiline-linezolid-moxifloxacin-pyrazinamide and variants (endTB)	9 months
Longer regimen	All 3 Group A + ≥ 1 Group B (≥ 4 effective drugs); Group C to complete	18–20 months (15–17 after conversion)

Linezolid toxicity — practical management

- Baseline and monthly CBC, neuropathy screening (brief peripheral neuropathy screen), visual acuity and colour vision.
- Anaemia/thrombocytopenia or neuropathy grade ≥ 2 → hold, then reduce to **300 mg** daily or stop if severe; optic neuropathy → stop permanently.

QT monitoring

- ECG baseline and at weeks 2, 4, 8, 12, 24; **QTcF > 500 ms** → stop QT-prolonging drugs, correct electrolytes; 450–500 ms → closer monitoring.

Contacts of MDR/RR-TB

- Screen; **6 months of levofloxacin** TPT once disease excluded (Module 1, Rec. 21).

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

▸ **TB-PRACTECAL (Nyang'wa, NEJM 2022)** — BPaLM 89% vs 52% favourable outcome. **ZeNix (2022)** — linezolid 600 mg × 26 weeks as effective with less toxicity. **BEAT-Tuberculosis (South Africa)** — BDLLfxC non-inferior to standard of care. **endTB (2024)** — three 9-month regimens non-inferior. **STREAM stage 2** — all-oral bedaquiline short regimen superior to injectable-containing regimen.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. BPaLM regimen — composition, eligibility, monitoring and evidence. *[Long answer]*
2. Management of pre-XDR and XDR tuberculosis. *[Short note]*

9.8 Special Situations — Renal, Hepatic, Pregnancy & HIV

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Treatment in special situations
- ✓ Adjust ATT in CKD, dialysis and liver disease
- ✓ Choose safe regimens in pregnancy, breastfeeding and HIV

IN BRIEF Most special situations need adjustment rather than avoidance of standard drugs. Rifampicin and isoniazid are hepatically cleared; ethambutol, pyrazinamide, levofloxacin and aminoglycosides need renal dose adjustment. Pregnancy does not change the DS-TB regimen.

Renal impairment (CrCl < 30 mL/min or dialysis)

Drug	Adjustment
Isoniazid, rifampicin	No change (pyridoxine for H)
Pyrazinamide	25 mg/kg **three times weekly**
Ethambutol	15 mg/kg **three times weekly** (optic toxicity risk)
Levofloxacin	750–1000 mg three times weekly
Amikacin / streptomycin	Avoid; if essential 12–15 mg/kg 2–3 times weekly with levels

Drug	Adjustment
Bedaquiline, linezolid, pretomanid, delamanid, clofazimine	No change (monitor)

- Give doses **after haemodialysis**.

Liver disease

Situation	Regimen
Stable chronic liver disease, normal ALT	Standard regimen with close LFT monitoring
Moderate disease / ALT > 3× ULN at baseline	Avoid Z: **2HRE/7HR**, or 2 hepatotoxic drugs
Decompensated cirrhosis (Child B–C)	One or no hepatotoxic drug: e.g. **R + E + Lfx** (12–18 months) or **E + Lfx + linezolid/ amikacin** — specialist care

Pregnancy and breastfeeding

- **HRZE safe**; pyridoxine supplementation; breastfeeding continues.
- Avoid: aminoglycosides (fetal ototoxicity), ethionamide (teratogenic in animals), rifapentine/moxifloxacin 4-month regimen (not studied), **pretomanid (BPaLM)**.
- DR-TB in pregnancy: **BDLLfxC** or 9-month regimen with linezolid; delay not justified.

HIV

- Rifampicin with **dolutegravir 50 mg twice daily**; efavirenz standard dose; avoid protease inhibitors (use rifabutin 150 mg daily); ART within 2 weeks (8 weeks for DR-TB), delayed 4–8 weeks in TBM.
- Bedaquiline: avoid efavirenz (lowers levels) — use dolutegravir-based ART.

★ CLINICAL PEARLS & EXAM FOCUS

- Rifampicin is the most valuable drug — try hardest to keep it in renal, hepatic and HIV situations.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Treatment of tuberculosis in a patient with chronic kidney disease on haemodialysis. *[Short note]*

9.9 Adjunctive Therapy — Steroids, Surgery & Nutrition

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Adjuncts in TB treatment
- ✓ State evidence-based indications for corticosteroids
- ✓ List indications for surgery in pulmonary and extrapulmonary TB
- ✓ Provide nutritional assessment and support

IN BRIEF Adjuncts improve outcomes in selected patients: **steroids** in TB meningitis (strong) and pericarditis (conditional), **surgery** for complications and selected DR-TB, and **nutrition** for everyone — undernutrition increases mortality and relapse, and food support reduces TB in families (RATIONS).

Corticosteroids

Indication	Evidence	Regimen
TB meningitis	Strong (Module 4, Rec. 4.1)	Dexamethasone 0.4 mg/kg/day tapered over 6–8 weeks
TB pericarditis	Conditional (Rec. 4.2)	Prednisolone 60 mg tapered over 6 weeks (avoid in HIV)
IRIS (severe) and prevention	PredART	Prednisone 40 mg × 2 weeks, 20 mg × 2 weeks

Indication	Evidence	Regimen
Paradoxical reactions, tuberculoma oedema, spinal cord compression, airway compression by nodes (children), adrenal insufficiency, severe hypoxaemia in miliary TB	Expert opinion	Individualised
Pleural TB	Not recommended	—

Surgery

Site	Indications
Lung	Massive or recurrent haemoptysis, destroyed lobe, persistent cavity with DR-TB (Module 4, Rec. 7.1 — elective partial resection), aspergilloma, bronchopleural fistula, empyema/trapped lung
Spine	Neurological deficit not improving, instability, severe kyphosis, abscess
Abdomen	Obstruction, perforation, fistula, strictures
Others	Constrictive pericarditis, hydrocephalus (VP shunt), ureteric strictures, non-healing abscess/sinus

Nutrition

- Assess BMI/MUAC at diagnosis; **BMI < 18.5** = undernutrition; < 16 = severe (admit, monitor refeeding).
- NTEP: **Ni-kshay Poshan Yojana ₹1000/month**, energy-dense nutrition supplementation for BMI < 18.5, Ni-kshay Mitra food baskets for patients and household contacts.
- Counsel: 1.2–1.5 g/kg protein, 35–40 kcal/kg/day; micronutrients; alcohol and tobacco cessation.

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- **RATIONS trial (Lancet 2023, Jharkhand)** — food baskets reduced TB incidence in household contacts; nutritional support reduced mortality among patients.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Role of corticosteroids in tuberculosis. *[Short note]*
2. Indications for surgery in pulmonary tuberculosis. *[Short note]*

9.10 Adherence & Patient-Centred Care

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Treatment support; digital adherence technologies
- ✓ Apply WHO care-and-support recommendations
- ✓ Use digital adherence technologies and NTEP support schemes
- ✓ Counsel patients and address stigma

IN BRIEF Treatment support has replaced the term DOT. WHO recommends health education and counselling for all, a package of adherence interventions, community- or home-based support, video-supported treatment and material support (Module 4, Chapter 3). India adds DBT nutrition support, Ni-kshay Mitras and digital adherence tools.

Adherence tools

Tool	Description
Treatment supporter	Trained community volunteer/ASHA/health worker (honorarium under NTEP)
99DOTS	Pill packs with hidden phone numbers; patient gives a missed call after each dose
MERM	Medication event reminder monitor — pill box that records openings, audio/visual reminders

Tool	Description
Video-supported treatment (VST)	Patient records dose intake; recommended as replacement for in-person support (Module 4, Rec. 1.4c)
Family-based observation	Acceptable; trained lay providers/health workers preferred
Ni-kshay Sampark	Helpline 1800-11-6666 — counselling and follow-up

Counselling checklist (first visit)

- Disease, curability, duration, side effects, need to complete treatment.
- Cough hygiene, ventilation, masks in early weeks; family screening and TPT.
- Nutrition, alcohol/tobacco cessation, HIV and diabetes testing.
- Entitlements: free drugs and tests, NPY, transport, Ni-kshay Mitra.
- Address **stigma** and mental health — depression is common in TB; screen and refer.

★ CLINICAL PEARLS & EXAM FOCUS

▸ Most loss to follow-up happens in the first 2 months and after symptoms improve — reinforce counselling at both points.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Patient-centred approaches to improve adherence in tuberculosis. *[Short note]*

9.11 TB Preventive Treatment in Practice

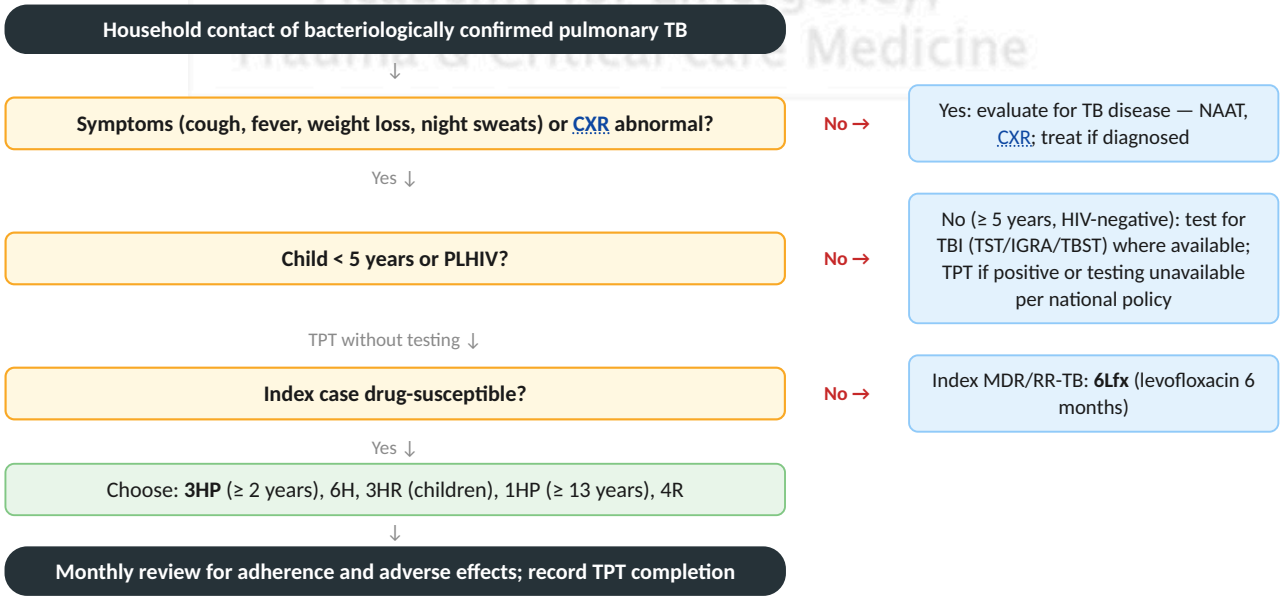
‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** TPT; contact management
- ✓ Evaluate household contacts and select a TPT regimen
- ✓ Monitor TPT for adverse effects and completion

IN BRIEF The cascade is: identify contacts and risk groups → screen and **rule out TB disease** → test for infection where required → start a short rifamycin-based regimen where possible → support completion (Module 1, 2024). For contacts of MDR/RR-TB, **6 months of levofloxacin** is recommended.

Algorithm 9.2 · Household contact management (WHO Module 1 / NTEP)



TPT doses (adults)

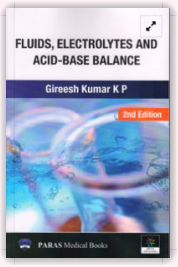
Regimen	Dose	Points
6H	Isoniazid 5 mg/kg (300 mg) daily	+ pyridoxine
3HP	Isoniazid 900 mg + rifapentine 900 mg weekly × 12	Weight ≥ 30 kg doses; hypersensitivity in ~ 4%
1HP	Isoniazid 300 mg + rifapentine 600 mg daily × 28 days	≥ 13 years
3HR	Isoniazid 5 + rifampicin 10 mg/kg daily × 3 months	Child FDC (H50/R75)
4R	Rifampicin 10 mg/kg daily × 4 months	Isoniazid intolerance/resistance
6Lfx	Levofloxacin 750–1000 mg daily (15–20 mg/kg children) × 6 months	Contacts of MDR/RR-TB

★ **CLINICAL PEARLS & EXAM FOCUS**

- Ruling out disease is the critical step — giving TPT to someone with active TB breeds resistance.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. TB preventive therapy for household contacts — evaluation and regimens. *[Long answer]*



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9.12 Infection Prevention & Control and Vaccines

‹ NMC curriculum

Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Infection control; BCG; vaccine pipeline
- ✓ Apply the hierarchy of TB infection control in health facilities
- ✓ Describe BCG — effectiveness, complications — and the vaccine pipeline

IN BRIEF WHO infection-prevention guidelines (2019, part of Module 1) recommend **triage, isolation, prompt effective treatment and cough etiquette** (administrative), **ventilation and upper-room UVGI** (environmental) and **respirator programmes** (personal). BCG protects infants against severe forms but gives variable protection against adult pulmonary TB.

Hierarchy of controls

Level	Measures
Administrative (most important)	Triage and fast-tracking of coughing patients, separation, prompt NAAT and **effective treatment** (rapidly reduces infectiousness), cough etiquette, surgical masks for patients, staff screening
Environmental	Natural/mechanical ventilation (airborne infection isolation ≥ 12 air changes/hour, negative pressure), upper-room ultraviolet germicidal irradiation
Respiratory protection	**N95/FFP2 respirators** with fit-testing for staff in high-risk areas (bronchoscopy, sputum induction, DR-TB wards)

BCG

- Live attenuated *M. bovis*; 0.1 mL (0.05 mL in < 1 month in some products) intradermally over left deltoid at birth (India, UIP).

- Protects against **TB meningitis and miliary TB in children** (~ 70–80%); protection against adult pulmonary TB variable (0–80%; Chingleput trial — none).
- Complications: local ulcer, abscess, regional lymphadenitis, **disseminated BCG** in SCID/HIV — contraindicated in symptomatic HIV and immunodeficiency.

Vaccine pipeline (2026)

Candidate	Status
M72/AS01E	Subunit vaccine; ~ 50% efficacy in phase 2b in infected adults; phase 3 trial (2024–) in adolescents and adults
MTBVAC	Live attenuated *M. tuberculosis* — infant phase 3
VPM1002	Recombinant BCG — trials including India (household contacts)
BCG revaccination	India adult BCG study (2024–25) in high-burden districts
mRNA and viral-vector vaccines	Early-phase trials

★ **CLINICAL PEARLS & EXAM FOCUS**

- Effective treatment is infection control — infectiousness drops quickly once the patient is on an appropriate regimen, which is why rapid DST matters.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Infection control measures for tuberculosis in health-care settings. *[Short note]*
2. BCG vaccine and newer TB vaccines. *[Short note]*

9.13 Drug Chart — Antituberculosis Medicines at a Glance

‹ NMC curriculum | Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** Drug chart: class, drug, dose, indication, caution
- ✓ Revise every antituberculosis drug with dose, indication and key caution

IN BRIEF One-page chart for quick revision before ward rounds and examinations. Doses are adult daily doses unless stated; adjust for weight, age, renal and hepatic function as per 9.8.

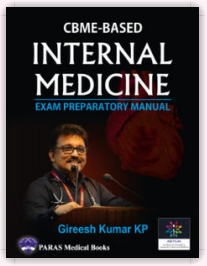
Drug chart — class · drug · dose · indication · caution

Class	Drug	Dose (adult)	Indication	Caution
First-line	Isoniazid	5 mg/kg (300 mg); TPT 300 mg; 3HP 900 mg weekly	DS-TB, TPT	Hepatitis, neuropathy — pyridoxine
First-line	Rifampicin	10 mg/kg (600 mg)	DS-TB, Hr-TB, 3HR/4R TPT	Interactions; hepatitis; orange fluids
First-line	Pyrazinamide	25 mg/kg	DS-TB IP, Hr-TB, some DR regimens	Hepatitis, gout
First-line	Ethambutol	15 mg/kg	DS-TB, Hr-TB	Optic neuritis; renal dosing
Rifamycin	Rifapentine	1200 mg daily (HPMZ); 900 mg weekly (3HP)	4-month DS-TB, TPT	Interactions; flu-like
Rifamycin	Rifabutin	150–300 mg	HIV on protease inhibitors	Uveitis, neutropenia
Group A (FQ)	Levofloxacin	750–1000 mg	Hr-TB, MDR regimens, 6Lfx TPT	QT, tendinopathy, dysglycaemia

Class	Drug	Dose (adult)	Indication	Caution
Group A (FQ)	Moxifloxacin	400 mg	BPaLM, HPMZ, BLMZ	QT prolongation
Group A	Bedaquiline	400 mg × 2 wk → 200 mg TIW × 22 wk	MDR/RR-TB	QT; hepatotoxicity; avoid efavirenz
Group A	Linezolid	600 mg daily	BPaLM, BDLLfxC, longer regimens	Myelosuppression, neuropathy, optic neuritis
Nitroimidazole	Pretomanid	200 mg daily	BPaL(M)	Hepatotoxicity; not in pregnancy
Group C	Delamanid	100 mg twice daily	BDLLfxC, longer regimens, children	QT
Group B	Clofazimine	100 mg daily	BDLLfxC, 9-month and longer regimens	Skin discolouration, QT
Group B	Cycloserine / terizidone	10–15 mg/kg (max 1 g)	Longer regimens	Psychosis, seizures — pyridoxine
Group C	Ethionamide	15–20 mg/kg (max 1 g)	Longer regimens	GI, hypothyroidism
Group C	PAS	8–12 g/day	Last resort	GI, hypothyroidism
Group C	Amikacin	15 mg/kg (≥ 18 years, susceptible)	Longer regimens when needed	Ototoxicity, nephrotoxicity
Group C	Meropenem + clavulanate	1 g TDS + amox-clav 125 mg	Longer regimens (XDR)	IV access
Adjunct	Pyridoxine	10–50 mg (higher for neuropathy)	With H, cycloserine, linezolid	—
Adjunct	Dexamethasone / prednisolone	0.4 mg/kg dexa tapered 6–8 wk; prednisolone 60 mg taper	TBM, pericarditis, IRIS	Infections; hyperglycaemia

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Write a drug chart for second-line antituberculosis drugs with doses and major toxicities. *[Short note]*



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SECTION 10

Complications of Tuberculosis

Paper II / III · Complications and sequelae

Complications appear during disease, during treatment and long after cure: haemoptysis, aspergilloma, pneumothorax and empyema, respiratory failure, paradoxical reactions and IRIS, systemic complications, and treatment failure or recurrence.

10.1 Haemoptysis in Tuberculosis — Including Massive Haemoptysis 88
10.2 Chronic Pulmonary Aspergillosis & Aspergilloma 89
10.3 Pneumothorax, Bronchopleural Fistula & Empyema 90
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10.7 Treatment Failure, Recurrence & Non-Response — An Approach 93

10.1 Haemoptysis in Tuberculosis — Including Massive Haemoptysis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Haemoptysis; bronchial artery embolisation
- ✓ Identify the causes of haemoptysis in active and treated TB
- ✓ Resuscitate and manage massive haemoptysis

IN BRIEF Haemoptysis occurs in active TB (cavity erosion, **Rasmussen aneurysm**) and after cure (bronchiectasis, **aspergilloma**, broncholith, recurrent TB, carcinoma). Massive haemoptysis kills by **asphyxia**, not exsanguination — airway first. **Bronchial artery embolisation (BAE)** is the definitive first-line procedure in most cases.

Causes in TB

Cause	Clue
Active cavitary TB	Fever, sputum NAAT positive
Rasmussen aneurysm	Pulmonary artery pseudo-aneurysm in cavity wall — CT angiography
Post-TB bronchiectasis	Dry bronchiectasis of upper lobes; recurrent episodes
Aspergilloma / CPA	Fungal ball, Aspergillus IgG positive
Broncholithiasis	Calcified node eroding a bronchus — "stone-spitting"
Recurrent TB, carcinoma in scar	Weight loss, new lesion

Algorithm 10.1 · Massive haemoptysis (≥ 100–600 mL/24 h, or any amount causing airway compromise or instability)

Large-volume haemoptysis — call senior help, ICU and interventional radiology

↓

Protect airway: position bleeding side down; high-flow oxygen; suction; intubate with large tube (≥ 8.0) if failing — selective intubation of non-bleeding lung if needed

↓

Two large-bore IV lines, crossmatch, correct coagulopathy; IV tranexamic acid (± nebulised); stop anticoagulants; cough suppression cautiously

↓

Stable enough for imaging?

No → Unstable: rigid/flexible bronchoscopy — cold saline, adrenaline, balloon tamponade, endobronchial blocker

Yes ↓

CT angiography — localise bleeding side and vessels (bronchial, non-bronchial systemic, Rasmussen pulmonary artery)

↓

Bronchial artery embolisation (success 80–90%; recurrence 10–30%)

↓

Treat cause: ATT (NAAT/culture/DST), antifungal for CPA, surgery (resection) for localised disease or recurrent bleeding in fit patients

⚠ RED FLAGS — DO NOT MISS

- Do not send an unstable patient to CT; do not do bronchoscopy without the ability to secure the airway.

★ CLINICAL PEARLS & EXAM FOCUS

- Spinal artery arising from a bronchial artery (anterior spinal artery — artery of Adamkiewicz) must be identified before embolisation — risk of paraplegia.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Management of massive haemoptysis in a patient with treated pulmonary TB. *[Long answer]*

10.2 Chronic Pulmonary Aspergillosis & Aspergilloma

‹ NMC curriculum | Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Post-TB fungal complications
- ✓ Classify chronic pulmonary aspergillosis and diagnose it in TB survivors
- ✓ Distinguish CPA from relapsed TB

IN BRIEF Residual TB cavities are the commonest substrate for **chronic pulmonary aspergillosis (CPA)** in India. CPA mimics recurrent TB — cough, haemoptysis, weight loss, upper-lobe cavities — and many patients receive repeated courses of ATT. **Aspergillus-specific IgG** and imaging make the diagnosis.

Spectrum of CPA

Form	Features
Simple aspergilloma	Single fungal ball in a cavity, minimal symptoms, stable for months

Form	Features
Chronic cavitary pulmonary aspergillosis	One or more cavities ± fungal balls, pericavitary infiltrates, symptoms > 3 months, progressing
Chronic fibrosing pulmonary aspergillosis	End-stage destruction and fibrosis of two or more lobes
Aspergillus nodule	Nodule(s) mimicking cancer
Subacute invasive (chronic necrotising)	Immunocompromised; progression over 1–3 months

Diagnosis (ERS/ESCMID criteria)

- Compatible imaging for ≥ 3 months: thick-walled cavity, **air-crescent (Monod) sign**, mobile fungal ball, **pleural thickening** adjacent to cavity.
- **Aspergillus IgG** positive (most sensitive), or *Aspergillus* in sputum/BAL culture or histology.
- Exclude TB recurrence (NAAT + culture) and NTM.

Management

- Simple aspergilloma: observe; **surgery** for haemoptysis in fit patients; BAE for bleeding.
- CCPA: **oral itraconazole or voriconazole for at least 6 months**; monitor drug levels and liver function; note interaction — **rifampicin drastically lowers azole levels** (avoid co-administration).
- Tranexamic acid for minor haemoptysis; BAE for significant bleeding.

★ CLINICAL PEARLS & EXAM FOCUS

- "Recurrent smear-negative TB" with a cavity and pleural thickening → check Aspergillus IgG before restarting ATT.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Chronic pulmonary aspergillosis as a sequel of tuberculosis. *[Short note]*

10.3 Pneumothorax, Bronchopleural Fistula & Empyema

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Pleural complications of PTB
- ✓ Manage secondary pneumothorax and bronchopleural fistula in TB
- ✓ Treat TB empyema and recognise empyema necessitatis

IN BRIEF Rupture of a subpleural cavity causes a **secondary spontaneous pneumothorax**, often with a **bronchopleural fistula (BPF)** and pyopneumothorax. These are high-risk because lung reserve is poor and the lung may not re-expand. Drainage, ATT and early surgical referral are key.

Complications and management

Complication	Management
Secondary pneumothorax	Intercostal drain (not aspiration alone) for most; admit; ATT; thoracic surgery referral if air leak > 5–7 days or non-expansion
Bronchopleural fistula	Persistent air leak; drainage, nutrition, ATT; endobronchial valves/occlusion, surgical closure, muscle flap, Eloesser window or thoracoplasty in selected
Pyopneumothorax	Drain; cover secondary bacteria; ATT
TB empyema	Drain (wide-bore if thick), fibrinolytics, VATS/open decortication for loculation or trapped lung (see [[t-7-3
Empyema necessitatis	Pus tracking through chest wall forming subcutaneous swelling — drain + ATT

Complication	Management
Fibrothorax / trapped lung	Decortication when restriction is disabling and lung beneath is healthy

Investigations

- CXR/CT for extent; pleural fluid NAAT, culture (TB + bacterial); sputum NAAT; PFT before decortication.

★ CLINICAL PEARLS & EXAM FOCUS

- TB pyopneumothorax may need prolonged drainage — prepare the patient for weeks, not days.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Bronchopleural fistula in tuberculosis. *[Short note]*

10.4 Respiratory Failure, ARDS & Cor Pulmonale

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Critical care in TB
- ✓ Recognise TB as a cause of ARDS and respiratory failure
- ✓ Manage TB patients in the ICU with infection control

IN BRIEF TB causes acute respiratory failure through **miliary TB/ARDS**, extensive TB pneumonia, massive haemoptysis and pneumothorax, and chronic failure through **destroyed lung and cor pulmonale**. ICU mortality is high (often > 50%); late diagnosis and drug absorption problems contribute.

Acute respiratory failure

- **TB-ARDS:** miliary or extensive bronchogenic disease; lung-protective ventilation (VT 6 mL/kg PBW, plateau < 30 cmH_2O, prone positioning).
- Diagnosis in ventilated patients: tracheal aspirate/BAL NAAT and culture; urine LF-LAM in PLHIV.
- ATT by **nasogastric tube** (crushed FDCs); IV options if no enteral route — IV rifampicin (where available), IV isoniazid, levofloxacin/moxifloxacin, linezolid, amikacin.
- Screen for adrenal insufficiency, HIV, hyponatraemia; consider steroids in severe miliary disease (expert opinion).

Chronic respiratory failure and cor pulmonale

- Destroyed lung, fibrothorax, TB-associated obstructive lung disease → hypoxaemia, hypercapnia, pulmonary hypertension.
- Management: long-term oxygen therapy, home NIV for hypercapnia, bronchodilators, pulmonary rehabilitation, vaccinations, treat right heart failure.

Infection control in ICU

- Closed suction, HEPA/bacterial–viral filter on the expiratory limb, airborne isolation room, N95 for staff during aerosol-generating procedures.

★ CLINICAL PEARLS & EXAM FOCUS

- A ventilated patient with ARDS and pancytopenia in an endemic area — think miliary TB, send BAL NAAT and look at the fundus.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Tuberculosis in the intensive care unit. *[Short note]*

10.5 Paradoxical Reactions & TB-IRIS

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Paradoxical reactions; immune reconstitution inflammatory syndrome
- ✓ Define paradoxical reactions and TB-IRIS
- ✓ Differentiate them from treatment failure and drug resistance
- ✓ Treat with steroids and continue ATT

IN BRIEF A **paradoxical reaction** is clinical or radiological worsening of pre-existing lesions or new lesions in a patient improving on appropriate ATT, after excluding other causes. In PLHIV starting ART it is **TB-IRIS** (paradoxical or unmasking). Both reflect recovering immunity against mycobacterial antigens.

TB-IRIS (INSHI case definition — summary)

Element	Criteria
Antecedent	TB diagnosed and improving on ATT before ART
Onset	Within 3 months of starting ART (commonly 2–4 weeks)
Major criteria	New/enlarging nodes, abscesses, or other focal lesions; new/worsening radiological TB; new/worsening CNS TB; new/worsening serositis
Minor criteria	New/worsening fever, night sweats, weight loss; cough, dyspnoea; abdominal pain with hepatomegaly/ascites
Exclusions	Poor adherence, **drug resistance**, another opportunistic infection, drug toxicity

Common paradoxical reactions (HIV-negative too)

- Enlarging lymph nodes or new abscesses (most common), new pleural effusion, new/enlarging **tuberculomas**, worsening pulmonary infiltrates.
- Usually 2–12 weeks into treatment.

Management

- **Continue ATT and ART**; confirm adherence; repeat NAAT on new samples to exclude resistance.
- Mild: NSAIDs, aspiration of nodes/abscesses.
- Moderate–severe: **prednisone 1.5 mg/kg/day × 2 weeks then 0.75 mg/kg/day × 2 weeks** (Meintjes trial).
- Prevention: **prednisone 40 mg × 2 weeks then 20 mg × 2 weeks** when starting ART with CD4 ≤ 100 (PredART).
- Life-threatening CNS IRIS: high-dose steroids; neurosurgery for mass effect.

LANDMARK TRIALS & GUIDELINES · full trial summaries & references ›

- ▸ **Meintjes (AIDS 2010)** — prednisone reduced hospital days and procedures in paradoxical TB-IRIS. **PredART (NEJM 2018)** — prophylactic prednisone reduced IRIS by 30% without excess harm.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. TB-IRIS — definition, diagnosis and management. *[Long answer]*

10.6 Systemic Complications of Tuberculosis

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Systemic and metabolic complications
- ✓ Recognise haematological, metabolic, renal and other systemic complications of TB

IN BRIEF TB is a systemic disease. Beyond organ damage it causes **anaemia of inflammation**, **hyponatraemia** (SIADH, adrenal insufficiency, cerebral salt wasting), **hypercalcaemia**, **secondary (AA) amyloidosis**, **haemophagocytic lymphohistiocytosis (HLH)** and thromboembolism — several of which are life-threatening and easily missed.

Systemic complications

Complication	Key points
Anaemia	Anaemia of chronic disease; also haemolysis/thrombocytopenia from rifampicin; marrow infiltration in miliary TB
Hyponatraemia	SIADH (pulmonary TB, TBM), cerebral salt wasting (TBM), adrenal insufficiency — assess volume status
Hypercalcaemia	Granulomatous calcitriol production — mild; vitamin D supplementation may unmask
AA amyloidosis	Long-standing untreated or chronic TB (bronchiectasis, osteomyelitis); proteinuria, nephrotic syndrome, CKD — rectal/fat-pad biopsy
HLH	Fever, pancytopenia, splenomegaly, very high ferritin, hypertriglyceridaemia — TB is a leading infectious trigger in India; ATT ± dexamethasone/etoposide (specialist)
Venous thromboembolism	Increased risk in active TB, especially in hospital — prophylaxis; rifampicin lowers warfarin and DOAC levels
Malabsorption / undernutrition	Intestinal TB, cachexia — nutritional rehabilitation
Renal	Interstitial nephritis (rifampicin), glomerulonephritis, obstructive uropathy, amyloid
Depression, cognitive decline	Common; screen and support

Practical checklist for the admitted TB patient

- Sodium, potassium, calcium, glucose, creatinine, CBC, LFT, albumin, HIV; cortisol if hypotensive/hyponatraemic; ferritin and triglycerides if cytopenias.

★ CLINICAL PEARLS & EXAM FOCUS

- Persistent fever with pancytopenia during ATT — consider HLH, drug-induced cytopenia, IRIS, and drug resistance before "slow response".

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Secondary amyloidosis and HLH as complications of tuberculosis. *[Short note]*

10.7 Treatment Failure, Recurrence & Non-Response — An Approach

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Failure and recurrence
- ✓ Approach a patient who is not responding to TB treatment
- ✓ Distinguish relapse from reinfection and manage recurrent TB

IN BRIEF Not every non-responder has drug resistance. The commonest causes are **non-adherence**, **unrecognised resistance**, **wrong diagnosis** (NTM, CPA, cancer), **paradoxical reaction** and **comorbidity** (HIV, diabetes, undernutrition, malabsorption). Recurrence after cure is either relapse (same strain) or reinfection (new strain) — always repeat DST.

Algorithm 10.2 · Approach to non-response or suspected failure

Persistent symptoms, smear/culture positive at month 2 onwards, or clinical deterioration

↓

Adherence confirmed (records, pill counts, interview)?

No → Poor adherence: counsel, treatment support, address barriers; re-evaluate DST

Yes ↓

Repeat NAAT with rifampicin result + FL-LPA/Xpert XDR (isoniazid, FQ) + liquid culture DST; tNGS if available

↓

Resistance detected?

No → No resistance: consider NTM (speciate), CPA (Aspergillus IgG), cancer, paradoxical reaction, HIV/DM control, malabsorption, wrong weight band

Yes ↓

Switch to the appropriate DR-TB regimen (Hr-TB, MDR/RR-TB, pre-XDR) — never add a single drug

Recurrent TB

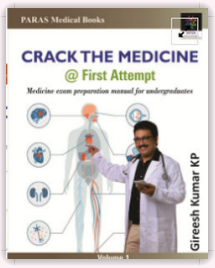
Point	Detail
Definition	TB after being declared cured/completed (WHO: "recurrent" — relapse or reinfection)
Timing	Most relapses within 6–12 months; reinfection more likely later in high-transmission settings
Diagnosis	**Culture** (NAAT may detect old DNA); full DST; exclude CPA, NTM, bronchiectasis infection
Treatment	DS-TB regimen if rifampicin-susceptible (no Category II); DR regimen per DST
Risk factors	Cavitary disease, 2-month culture positivity, low BMI, smoking, diabetes, HIV, poor adherence, shorter regimens in high-risk patients

★ CLINICAL PEARLS & EXAM FOCUS

- Xpert positivity in a previously treated patient with a negative culture may reflect residual DNA — base decisions on culture and the clinical picture.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Approach to a patient with failure of first-line antituberculosis treatment. *[Long answer]*
2. Recurrent tuberculosis — relapse versus reinfection. *[Short note]*



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SECTION 11

Landmark Trials in Tuberculosis — Theory & References

Paper IV · Evidence base and recent advances

The trials behind every recommendation in this book: what question each asked, how it was designed, what it found and how it changed WHO and NTEP policy. Each topic ends with full references — tap a reference to open it in PubMed.

11.1 How to Read a TB Trial — Design, Endpoints & Non-Inferiority 95
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11.5 TB–HIV & Corticosteroid Trials — SAPiT, CAMELIA, STRIDE, PredART, Thwaites, ACT HIV & IMPI 100
11.6 Prevention, Diagnosis & Nutrition Trials — PREVENT TB, BRIEF-TB, VQUIN, TB-CHAMP, Xpert, M72 & RATIONS 101

11.1 How to Read a TB Trial — Design, Endpoints & Non-Inferiority

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Research methodology applied to TB trials
- ✓ Explain why most modern TB treatment trials are non-inferiority trials
- ✓ Define the composite "unfavourable outcome" endpoint and its components
- ✓ Interpret mITT and per-protocol analyses and the non-inferiority margin

IN BRIEF Standard TB treatment already cures about 85–95% of trial participants, so new regimens aim to be **shorter, safer or simpler while not being meaningfully worse**. Most landmark trials since 2010 are therefore **non-inferiority** RCTs with a composite **unfavourable outcome** endpoint measured 12–18 months after randomisation.

Key concepts

Concept	Meaning in TB trials
Superiority trial	Tests whether the new regimen is **better** (e.g. MRC streptomycin 1948, STREAM stage 2 for some outcomes, TB-PRACTECAL)
Non-inferiority trial	Tests whether the new regimen is **not worse by more than a pre-set margin** (e.g. Study 31, SHINE, ZeNix, endTB)
Non-inferiority margin	Largest acceptable loss of efficacy — usually **6–12 percentage points** in unfavourable outcome; the upper 95% CI of the difference must lie below it
Unfavourable outcome	Composite of **treatment failure, relapse (recurrence), death, and loss to follow-up/withdrawal** — sometimes with "bacteriological failure" defined by culture
Follow-up	Relapse is captured only with long follow-up (typically 12–24 months after randomisation)
mITT	Modified intention-to-treat — all randomised eligible participants (excluding those found ineligible, e.g. resistant at baseline); conservative for superiority

Concept	Meaning in TB trials
Per-protocol	Only those who completed the assigned regimen adequately — the more conservative analysis for **non-inferiority**; both analyses should agree
Open-label design	Common because regimens differ in pill number and duration; objective microbiological endpoints reduce bias
Adaptive / seamless phase 2–3	TB-PRACTECAL selected the best arm in stage 1 before continuing to stage 2
Single-arm studies	Nix-TB — no comparator; justified because outcomes of XDR-TB were very poor; weaker evidence (hence "very low certainty" GRADE)

Why do WHO recommendations say "very low certainty" for regimens that work so well?

- GRADE downgrades for **indirectness** (trial population differs), **imprecision** (small numbers of events), **risk of bias** (open label, single-arm) — so even BPaLM (89% success) carries very low certainty, yet a conditional recommendation **in favour** because benefits clearly outweigh harms.

Reading checklist (viva)

- Population (age, HIV, cavitation, resistance), regimen and duration, comparator, primary endpoint and its timing, margin, mITT vs per-protocol results, adverse events grade ≥ 3, relapse rate, generalisability to India.

★ **CLINICAL PEARLS & EXAM FOCUS**

- "Non-inferior" does not mean "equal" — it means "not worse than the margin"; always quote the margin and the confidence interval.

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Non-inferiority trials in tuberculosis — concepts with examples. *[Short note]*

11.2 Foundation Trials — Streptomycin, Madras & Chingleput

‹ NMC curriculum
Previous-year Qs ›

◉ **CBME COMPETENCIES — the postgraduate should be able to:**

- ✓ **NMC syllabus area:** History of TB trials
- ✓ Describe the MRC streptomycin trial as the first randomised controlled trial
- ✓ Explain the importance of the Madras home-versus-sanatorium study and the Chingleput BCG trial

IN BRIEF Three studies built modern TB policy: the **MRC streptomycin trial (1948)** — the first properly randomised clinical trial in medicine; the **Madras study (1959)** — which proved home treatment as effective as sanatorium care; and the **Chingleput (Tiruvallur) BCG trial** — which showed BCG did not protect against adult pulmonary TB in South India.

MRC streptomycin trial (1948)

Element	Details
Question	Does streptomycin plus bed rest improve acute progressive bilateral pulmonary TB compared with bed rest alone?
Design	Randomised (sealed envelopes with random sampling numbers), controlled; radiologists and clinicians assessing films blinded
Participants	107 young adults with acute progressive bilateral PTB
Result	Deaths at 6 months: 7% (streptomycin) vs 27% (control); more radiological improvement
Lesson	Rapid emergence of **streptomycin resistance** with monotherapy — led to combination therapy (PAS + streptomycin, then isoniazid)

Madras home vs sanatorium study (Tuberculosis Chemotherapy Centre, 1956–59)

Element	Details
Question	Is domiciliary treatment as effective as sanatorium treatment in poor urban patients?
Design	193 patients randomised to 12 months isoniazid + PAS at home or in a sanatorium
Result	Similar bacteriological quiescence (~ 86–92%); **no excess TB among family contacts** of home-treated patients
Impact	Ended the sanatorium era worldwide; basis of the National TB Programme (1962) and ambulatory care — echoed today in WHO's decentralised MDR-TB care recommendation

Chingleput BCG prevention trial (1968–)

Element	Details
Design	~ 260 000 people in Chingleput district (Tamil Nadu) randomised to two BCG strains/doses or placebo
Result	**No protection** against adult bacillary pulmonary TB at 15-year follow-up; some protection in children with low-dose BCG
Explanations	Prior exposure to environmental NTM, high infection pressure, reinfection; strain differences
Impact	BCG kept at birth for protection of infants against severe forms; drive for new vaccines

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3. Tuberculosis Research Centre (ICMR), Chennai. Fifteen year follow up of trial of BCG vaccines in south India for tuberculosis prevention. *Indian J Med Res* 1999;110:56–69. PubMed ›

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Contribution of the Madras study and the Chingleput BCG trial to TB control. *[Short note]*

11.3 Shortening Drug-Susceptible TB Treatment — REMoxTB, Study 31, SHINE & TRUNCATE-TB

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Trials of DS-TB regimens
- ✓ Explain why 4-month fluoroquinolone regimens failed in REMoxTB but succeeded in Study 31
- ✓ Describe the SHINE trial and the 4-month regimen for non-severe childhood TB
- ✓ Discuss the strategy approach of TRUNCATE-TB

IN BRIEF For forty years, 6 months was the floor for DS-TB treatment. **REMoxTB (2014)** showed that simply replacing one drug with moxifloxacin for 4 months led to more relapses; **Study 31/A5349 (2021)** succeeded by adding **high-dose daily rifapentine** to moxifloxacin; **SHINE (2022)** shortened treatment to 4 months in children with non-severe TB; **TRUNCATE-TB (2023)** tested a strategy of 2-month treatment with monitoring.

Trial summaries

Trial	Design & population	Arms	Result & impact
REMoxTB (2014)	Phase 3 non-inferiority, 1931 adults with smear-positive DS-PTB	4-month moxifloxacin (replacing E or H) vs 6-month HRZE/HR	Unfavourable outcome higher with 4-month arms (relapse) — **not non-inferior**; showed culture conversion is a poor surrogate for cure

Trial	Design & population	Arms	Result & impact
Study 31/A5349 (2021)	Phase 3 non-inferiority, 2516 participants ≥ 12 years, 13 countries, incl. PLHIV CD4 ≥ 100	2HPZM/2HPM vs 2HPZE/2HP vs 2HRZE/4HR	**HPZM non-inferior** to standard; rifapentine-ethambutol arm not non-inferior → **WHO 2022 conditional recommendation** (Module 4, Rec. 2.1)
SHINE (2022)	Phase 3 non-inferiority, 1204 children < 16 years with non-severe, smear-negative TB (Africa, India)	4 vs 6 months of standard first-line drugs	4 months **non-inferior** (unfavourable 3% vs 4%) → **WHO strong recommendation** (Rec. 2.2)
TRUNCATE-TB (2023)	Adaptive phase 2–3, 674 adults, Asia/Africa	Strategy: 8-week high-intensity regimens, extended follow-up, retreatment if needed vs 6-month standard	Bedaquiline–linezolid strategy **non-inferior**; total time on treatment much shorter — not yet a WHO recommendation

Theory — why rifapentine worked

- Rifapentine's long half-life gives **higher rifamycin exposure**; combined with moxifloxacin it improves sterilising activity enough to shorten therapy.
- Study 31 used daily 1200 mg rifapentine with food; pharmacokinetic and safety data supported once-daily outpatient use.

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PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Trials of treatment shortening in drug-susceptible TB. *[Long answer · Recent advances]*

11.4 Drug-Resistant TB Trials — STREAM, Nix-TB, ZeNix, TB-PRACTECAL, endTB & BEAT-TB

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Trials of MDR/RR-TB regimens
- ✓ Summarise the design and results of the trials behind BPaLM, BDLLfxC and the 9-month regimens
- ✓ Explain how linezolid dosing was optimised (ZeNix)
- ✓ Link each trial to the WHO 2025 recommendation it supports

IN BRIEF In a decade, MDR-TB treatment moved from 20+ months with injections and ~ 50–60% success to **6 months, all-oral, ~ 90% success**. STREAM tested the 9-month injectable regimen and then an all-oral bedaquiline version; Nix-TB and ZeNix created BPaL; TB-PRACTECAL proved BPaLM against standard care; endTB and BEAT-Tuberculosis added new 9- and 6-month options.

Trial summaries

Trial	Design & population	Regimen tested	Result → WHO impact
STREAM stage 1 (2019)	Phase 3 non-inferiority, 424 MDR-TB patients with FQ/SLID-susceptible disease	9–11 month injectable regimen vs 20-month WHO regimen	Favourable 78.8% vs 79.8% — non-inferior; QT prolongation more common → 9-month regimen

Trial	Design & population	Regimen tested	Result → WHO impact
STREAM stage 2 (2022)	Phase 3, 588 patients	All-oral 40-week bedaquiline regimen vs injectable short regimen	Bedaquiline regimen **superior** (favourable 83% vs 71%), fewer hearing losses → **all-oral 9-month regimen**
Nix-TB (2020)	Single-arm, 109 patients with XDR-TB or treatment-intolerant/non-responsive MDR-TB, South Africa	BPaL (linezolid 1200 mg) × 26 weeks	**90% favourable** at 6 months post-treatment; neuropathy 81%, myelosuppression 48%
ZeNix (2022)	Partially blinded RCT, 181 patients	BPaL with linezolid 1200 vs 600 mg for 26 vs 9 weeks	**600 mg × 26 weeks**: 91% favourable with far less neuropathy/ myelosuppression → linezolid 600 mg in BPaLM
TB-PRACTECAL (2022)	Seamless phase 2–3 open-label RCT, 552 adults ≥ 15 years with RR-TB, Belarus, South Africa, Uzbekistan	BPaLM 24 weeks vs local standard of care (9–20 months)	Unfavourable 11% vs 48%; favourable **89% vs 52%**; fewer grade ≥ 3 AEs → **WHO 2022: BPaLM** (Module 4, Rec. 1.1)
endTB (2025)	Phase 3 non-inferiority, 754 participants with FQ-susceptible RR-TB, 7 countries	Five 9-month regimens (BLMZ, BLLfxCZ, BDLLfxZ, DCLLfxZ, DCMZ) vs WHO standard	Three bedaquiline-containing regimens non-inferior → **WHO 2025 modified 9-month regimens** (Rec. 2.2); DCLLfxZ, DCMZ not recommended (Rec. 2.3)
BEAT-Tuberculosis (South Africa, NCT04062201)	Phase 3 RCT including adolescents, children, PLHIV and pregnant women	6-month BDLLfxC (adjusted to FQ result) vs WHO 9-month/longer regimens	Similar efficacy and safety, shorter, fewer pills → **WHO 2025: BDLLfxC** (Rec. 1.2) for all ages and pregnancy

Theory — what made 6 months possible

- **Bedaquiline** (ATP-synthase inhibitor) and **pretomanid/delamanid** (nitroimidazoles) are new drug classes with no pre-existing resistance in most patients.
- **Linezolid** is highly active but dose- and duration-dependent toxic — ZeNix showed the efficacy–toxicity balance at 600 mg.
- Removing injectables removed permanent deafness and nephrotoxicity, improving adherence and outcomes.

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PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Evidence behind the BPaLM regimen — Nix-TB, ZeNix and TB-PRACTECAL. *[Long answer · Recent advances]*
2. STREAM trial — stage 1 and stage 2. *[Short note]*

11.5 TB–HIV & Corticosteroid Trials — SAPiT, CAMELIA, STRIDE, PredART, Thwaites, ACT HIV & IMPI

‹ NMC curriculum
Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Trials guiding ART timing and steroids
- ✓ Explain the evidence for early ART in TB–HIV and the exception in TB meningitis
- ✓ Summarise steroid trials in TBM, pericarditis and IRIS

IN BRIEF Three trials (SAPiT, CAMELIA, STRIDE) established **early ART** — especially when CD4 < 50 — and one (Török 2011) showed **no benefit of immediate ART in TB meningitis**. Steroid trials showed **mortality benefit in HIV-negative TBM (Thwaites 2004)** but not in HIV-positive TBM (ACT HIV 2023), **no mortality benefit in pericarditis (IMPI)**, and **prevention of IRIS with prednisone (PredART)**.

ART timing trials

Trial	Population	Comparison	Result → impact
SAPiT (2010, 2011)	642 South African adults, smear-positive TB, CD4 < 500	ART during vs after TB treatment; early (within 4 weeks) vs later	ART during TB treatment reduced mortality by 56%; early ART benefited CD4 < 50
CAMELIA (2011)	661 Cambodian adults, CD4 ≤ 200 (median 25)	ART at 2 vs 8 weeks	Mortality 18% vs 27% — **early ART saves lives** in advanced HIV
STRIDE (ACTG A5221, 2011)	806 adults, CD4 < 250	ART within 2 vs 8–12 weeks	No overall difference; benefit when **CD4 < 50**; more IRIS with early ART
Török et al. (2011)	253 Vietnamese adults with HIV-associated TBM	Immediate vs deferred (2 months) ART	No survival benefit; **more grade 4 adverse events** → defer ART 4–8 weeks in TBM

Steroid trials

Trial	Population	Comparison	Result → impact
Thwaites (2004)	545 Vietnamese adults with TBM	Dexamethasone (tapered over 6–8 weeks) vs placebo	Mortality at 9 months reduced (RR 0.69); no reduction in severe disability → **WHO strong recommendation** (Module 4, Rec. 4.1)
ACT HIV (2023)	520 HIV-positive adults with TBM, Vietnam & Indonesia	Dexamethasone vs placebo	**No mortality benefit** at 12 months
IMPI (2014)	1400 adults with TB pericarditis (Africa), ~ two-thirds HIV-positive	Prednisolone vs placebo; M. indicus pranii immunotherapy	No reduction in death/tamponade/constriction composite; **less constriction and hospitalisation**; more HIV-associated cancers → WHO conditional recommendation (Rec. 4.2)
Meintjes (2010)	110 patients with paradoxical TB-IRIS	Prednisone 4 weeks vs placebo	Fewer hospital days and procedures, faster symptom improvement
PredART (2018)	240 HIV-positive adults with TB, CD4 ≤ 100, starting ART	Prednisone 40 mg → 20 mg over 4 weeks vs placebo	IRIS 32.5% vs 46.7% (RR 0.70), no excess severe infections or cancers

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2. Blanc FX et al. Earlier versus later start of antiretroviral therapy in HIV-infected adults with tuberculosis. *N Engl J Med* 2011;365:1471–81. PubMed ›

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6. Donovan J et al. Adjunctive dexamethasone for tuberculous meningitis in HIV-positive adults. *N Engl J Med* 2023;389:1357–67. PubMed ›

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8. Meintjes G et al. Randomized placebo-controlled trial of prednisone for paradoxical tuberculosis-associated immune reconstitution inflammatory syndrome. *AIDS* 2010;24:2381–90. PubMed ›

9. Meintjes G et al. Prednisone for the prevention of paradoxical tuberculosis-associated IRIS. *N Engl J Med* 2018;379:1915–25. PubMed ›

PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. Timing of antiretroviral therapy in TB–HIV co-infection — evidence from trials. *[Long answer]*
2. Corticosteroids in tuberculous meningitis and pericarditis — trial evidence. *[Short note]*

11.6 Prevention, Diagnosis & Nutrition Trials — PREVENT TB, BRIEF-TB, VQUIN, TB-CHAMP, Xpert, M72 & RATIONS

‹ NMC curriculum

Previous-year Qs ›

◉ CBME COMPETENCIES — the postgraduate should be able to:

- ✓ **NMC syllabus area:** Trials of TPT, diagnostics, vaccines and nutrition
- ✓ Summarise the trials behind 3HP, 1HP and 6Lfx preventive treatment
- ✓ Describe the Xpert validation study and the M72/AS01E vaccine trial
- ✓ Explain the RATIONS trial and its relevance to India

IN BRIEF Short rifapentine regimens (**PREVENT TB → 3HP; BRIEF-TB → 1HP**) transformed TB prevention; **VQUIN and TB-CHAMP** led to 6 months of levofloxacin for contacts of MDR-TB (WHO 2024). The **Xpert MTB/RIF** validation study (2010) began the molecular era, **M72/AS01E** gave the first vaccine signal in adults, and the Indian **RATIONS** trial proved that food prevents TB.

Trial summaries

Trial	Population	Comparison	Result → impact
PREVENT TB (TBTC Study 26, 2011)	7731 high-risk contacts and others with TB infection	3HP (12 weekly doses, directly observed) vs 9H	TB rates 0.19% vs 0.43% — **non-inferior**; higher completion (82% vs 69%) → **3HP** recommended
BRIEF-TB (A5279, 2019)	3000 PLHIV in high-burden settings	1HP vs 9H	**Non-inferior**; higher completion, less hepatotoxicity → **1HP** alternative
VQUIN (2024)	Household contacts of MDR-TB, Viet Nam	6 months levofloxacin vs placebo	Lower TB incidence (not statistically significant alone)
TB-CHAMP (2024)	Child household contacts of MDR-TB, South Africa	6 months levofloxacin vs placebo	Reduced TB incidence (not significant alone); combined meta-analysis with VQUIN showed ~ 60% reduction → **WHO 2024: 6Lfx** (Module 1, Rec. 21)
Xpert MTB/RIF validation (Boehme, 2010)	1730 patients with suspected TB, 5 countries	Single Xpert vs culture	Detected 98% of smear-positive and 73% of smear-negative culture-positive TB; rifampicin resistance sensitivity 98% → **WHO endorsement 2010**

Trial	Population	Comparison	Result → impact
M72/AS01E (Tait, 2019)	3573 HIV-negative adults with TB infection (Kenya, South Africa, Zambia)	Two doses vs placebo	Vaccine efficacy **49.7%** against active pulmonary TB at 3 years → phase 3 trial now under way
RATIONS (Bhargava, 2023)	2800 patients with PTB and 10 345 household contacts, Jharkhand, India	Monthly food baskets to contacts (+ nutrition for all patients) vs patient-only support	Incident TB in contacts reduced by **39% (all forms) and 48% (microbiologically confirmed)**; patients: lower mortality, better weight gain → NTEP Ni-kshay Mitra support for contacts

Theory — lessons

- Shorter rifamycin-based TPT works because **completion** drives effectiveness as much as drug efficacy.
- RATIONS is a **cluster-randomised** trial — the unit of randomisation was the patient's household cluster/TB unit; it shows that addressing a **social determinant** is a TB-prevention intervention.
- Xpert validation trials measure **diagnostic accuracy** (sensitivity/specificity vs culture), not patient outcomes; later pragmatic trials (e.g. TB-NEAT) showed faster treatment but little mortality benefit — the reason LF-LAM (which reduced mortality in STAMP/LAM RCT) is paired with NAAT in advanced HIV.

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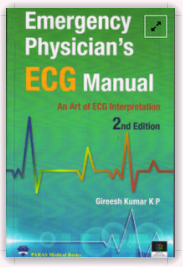
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PREVIOUS-YEAR & EXAM-PATTERN QUESTIONS ON THIS TOPIC · full list ›

1. RATIONS trial and the role of nutrition in TB control. *[Short note]*
2. Evidence for short-course TB preventive treatment regimens. *[Short note]*



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PART II

Previous-Year & Exam-Pattern Question Bank

Long-answer, short-note and case-based questions in the pattern of MD Respiratory Medicine, DNB Respiratory Diseases and MD General Medicine examinations — tap a topic to jump to its answer

Section 1 · Tuberculosis Guidelines at a Glance

1.1 The Global Framework — End TB Strategy & the WHO Guideline Modules ›

1. Describe the WHO End TB Strategy — vision, pillars and targets. *[Long answer · MD/DNB pattern]*
2. WHO consolidated guidelines on tuberculosis — modules and key recent changes. *[Short note]*

1.2 Definitions, Case Classification & Treatment Outcomes ›

1. Define pre-XDR and XDR-TB. Why were the definitions revised in 2021? *[Short note]*
2. Treatment outcome definitions in tuberculosis — what is sustained treatment success? *[Short note]*

1.3 WHO Module 1 — TB Preventive Treatment (2nd edition, 2024) ›

1. Programmatic management of TB preventive treatment — candidates, regimens and the role of levofloxacin. *[Long answer]*
2. Compare TST, IGRA and the new antigen-based skin tests. *[Short note]*

1.4 WHO Module 2 — Systematic Screening for TB Disease (2021) ›

1. Active case finding in tuberculosis — principles, target groups and tools. *[Long answer]*
2. Computer-aided detection (CAD) for chest radiography in TB. *[Short note]*

1.5 WHO Module 3 — Diagnosis (4th edition, 2025) ›

1. WHO-recommended rapid diagnostic tests for TB — classes and indications. *[Long answer]*
2. Concurrent testing strategies for TB in people living with HIV and children. *[Short note]*

1.6 WHO Module 4 — Drug-Susceptible TB Treatment & Care (2025) ›

1. Recent WHO recommendations for treatment of drug-susceptible TB, including 4-month regimens. *[Long answer]*

1.7 WHO Module 4 — Drug-Resistant TB Treatment (2025) ›

1. Discuss the WHO 2025 recommendations for treatment of MDR/RR-TB. *[Long answer · Recent advances]*
2. BPaLM versus BDLLfxC — eligibility and evidence. *[Short note]*

1.8 National TB Elimination Programme (NTEP) — India ›

1. National TB Elimination Programme — components and recent initiatives. *[Long answer]*
2. Ni-kshay Poshan Yojana and Pradhan Mantri TB Mukt Bharat Abhiyaan. *[Short note]*

1.9 Other Guidelines You Must Quote — Index-TB, ATS/CDC/ERS/IDSA & NICE ›

1. Compare WHO, NTEP and ATS/CDC/ERS/IDSA recommendations for treatment of TB. *[Short note]*

Section 2 · Tuberculosis — History, Epidemiology & Risk

2.1 History of Tuberculosis — From Phthisis to Pretomanid ›

1. History of tuberculosis — milestones in diagnosis and treatment. *[Short note]*

2.2 Global & Indian Epidemiology (WHO Global TB Report 2025) ›

1. Burden of tuberculosis in India and the world — current status and challenges. *[Long answer]*

2.3 Social Determinants & Risk Factors for TB ›

1. Social determinants of TB and the role of nutrition. Discuss the RATIONS trial. *[Long answer]*
2. TB and diabetes mellitus — bidirectional screening. *[Short note]*

2.4 High-Risk & Vulnerable Populations ›

1. TB in health-care workers — risks and prevention. *[Short note]*

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Section 3 · Bacteriology — Clinical Overview

3.1 The Organism at a Glance — What Matters at the Bedside ›

1. Laboratory diagnosis of tuberculosis — role of smear, culture and molecular tests. *[Short note]*

3.2 Non-Tuberculous Mycobacteria — The Great Mimic ›

1. Non-tuberculous mycobacterial lung disease — diagnosis and differentiation from tuberculosis. *[Long answer]*

Section 4 · Pathology & Pathogenesis

4.1 Host Response & the Tuberculous Granuloma ›

1. Describe the morphology of the tuberculous granuloma and the factors that determine its fate. *[Short note]*

4.2 Primary Tuberculosis — Ghon Focus & Ranke Complex ›

1. Primary complex — morphology and fate. *[Short note]*

4.3 Post-Primary (Reactivation) Tuberculosis ›

1. Pathogenesis of cavitation in pulmonary tuberculosis. *[Short note]*

4.4 Hypersensitivity Phenomena & Tuberculids ›

1. Tuberculids and Poncet's disease. *[Short note]*

Section 5 · Natural History & Prognosis

5.1 The Spectrum of TB — Infection to Disease ›

1. Spectrum of tuberculosis — concept of incipient and subclinical TB. *[Short note]*

5.2 Risk & Timing of Progression ›

1. Natural history of TB infection in children. *[Short note]*

5.3 Outcomes of Untreated & Treated TB — Prognosis ›

1. Prognostic factors in pulmonary tuberculosis. *[Short note]*

5.4 Post-TB Lung Disease & Life After Cure ›

1. Post-tuberculosis lung disease — patterns and management. *[Long answer]*

Section 6 · Pulmonary Tuberculosis

6.1 Clinical Features of Pulmonary TB ›

1. Clinical features of pulmonary tuberculosis — symptom screen and its limitations. *[Short note]*

6.2 Radiology of Pulmonary TB ›

1. Radiological features of pulmonary TB — distinguishing active from healed disease. *[Long answer]*

6.3 Miliary & Disseminated Tuberculosis ›

1. Miliary tuberculosis — clinical features, diagnosis and management. *[Long answer]*

6.4 Tuberculosis in Children & Adolescents ›

1. Diagnosis of pulmonary tuberculosis in children — current WHO approach. *[Long answer]*

6.5 TB–HIV Co-infection ›

1. Management of TB–HIV co-infection — timing of ART, drug interactions and IRIS. *[Long answer]*

6.6 TB in Diabetes, Pregnancy, the Elderly & Other Special Hosts ›

1. Tuberculosis in pregnancy — diagnosis and management. *[Short note]*
2. TB and diabetes — clinical features and management issues. *[Short note]*

6.7 Unusual Pulmonary Forms — Endobronchial, Lower-Lobe, Tuberculoma, Pneumonic ›

1. Endobronchial tuberculosis. *[Short note]*

6.8 Approach to Presumptive TB & Differential Diagnosis ›

1. Approach to a patient with presumptive pulmonary TB and negative NAAT. *[Long answer]*
2. Differential diagnosis of cavitary lung lesions. *[Short note]*

Section 7 · Extrapulmonary TB — Organ by Organ

7.1 EPTB — General Principles & Sampling Guide ›

1. Approach to diagnosis of extrapulmonary tuberculosis. *[Long answer]*

7.2 Tuberculous Lymphadenitis ›

1. Tuberculous cervical lymphadenitis — stages, diagnosis and treatment. *[Short note]*

7.3 Tuberculous Pleural Effusion & Empyema ›

1. Tuberculous pleural effusion — diagnosis and role of ADA. *[Long answer]*

7.4 Tuberculous Pericarditis ›

1. Tuberculous pericarditis — diagnosis and role of corticosteroids. *[Short note]*

7.5 Tuberculous Meningitis ›

1. Tuberculous meningitis — CSF findings, staging and management. *[Long answer]*

7.6 CNS Tuberculoma, TB Abscess & Spinal Arachnoiditis ›

1. Intracranial tuberculoma — imaging differential and treatment. *[Short note]*

7.7 Spinal Tuberculosis (Pott's Disease) ›

1. Pott's spine — clinical features, imaging and indications for surgery. *[Long answer]*

7.8 Peripheral Osteoarticular Tuberculosis ›

1. Tuberculosis of the hip joint — stages and management. *[Short note]*

7.9 Intestinal (Gastrointestinal) Tuberculosis ›

1. Ileocaecal tuberculosis versus Crohn's disease. *[Long answer]*

7.10 Peritoneal Tuberculosis ›

1. Peritoneal tuberculosis — diagnosis. *[Short note]*

7.11 Hepatobiliary, Splenic & Pancreatic Tuberculosis ›

1. Hepatic tuberculosis — forms and diagnosis. *[Short note]*

7.12 Genitourinary (Renal & Urinary Tract) Tuberculosis ›

1. Renal tuberculosis — clinical features and imaging. *[Short note]*

7.13 Female Genital Tuberculosis ›

1. Female genital tuberculosis — diagnosis and management of infertility. *[Short note]*

7.14 Male Genital Tuberculosis ›

1. Tuberculous epididymo-orchitis. *[Short note]*

7.15 Cutaneous Tuberculosis ›

1. Cutaneous tuberculosis — classification and lupus vulgaris. *[Short note]*

7.16 Ocular Tuberculosis ›

1. Ocular tuberculosis — clinical forms and management. *[Short note]*

7.17 Ear, Nose, Throat & Oral Tuberculosis ›

1. Laryngeal tuberculosis. *[Short note]*

7.18 Breast Tuberculosis ›

1. Tuberculosis of the breast. *[Short note]*

7.19 Adrenal & Endocrine Tuberculosis ›

1. Adrenal tuberculosis — diagnosis and management. *[Short note]*

Section 8 · Investigations

8.1 Specimen Collection — Getting the Right Sample ›

1. Methods of obtaining samples for TB diagnosis in children. *[Short note]*

8.2 Sputum Smear Microscopy ›

1. Grading of sputum smear microscopy and its role in the NAAT era. *[Short note]*

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8.3 Culture & Phenotypic Drug Susceptibility Testing ›

1. Liquid versus solid culture for Mycobacterium tuberculosis. *[Short note]*

8.4 Molecular Tests — NAATs, LPA, Xpert XDR & Sequencing ›

1. Xpert MTB/RIF Ultra — principle, advantages and interpretation of results. *[Long answer]*
2. Role of targeted next-generation sequencing in drug-resistant TB. *[Short note]*

8.5 Tests for TB Infection — TST, IGRA & TBST ›

1. Interferon-gamma release assays — principle, advantages and limitations. *[Short note]*
2. Mantoux test — technique, interpretation and causes of false results. *[Short note]*

8.6 LF-LAM, ADA, Biomarkers & Histopathology ›

1. Role of ADA in diagnosis of extrapulmonary tuberculosis. *[Short note]*
2. Lateral-flow urine LAM assay. *[Short note]*

8.7 Imaging Beyond the Chest X-ray — CT, MRI, PET & Ultrasound ›

1. Role of imaging in extrapulmonary tuberculosis. *[Short note]*

8.8 Integrated Diagnostic Algorithms — DS & DR-TB ›

1. NTEP integrated diagnostic algorithm for drug-susceptible and drug-resistant TB. *[Long answer]*

Section 9 · Management

9.1 First-Line Antituberculosis Drugs ›

1. Pharmacology of rifampicin — mechanism, adverse effects and drug interactions. *[Short note]*

9.2 Drug-Susceptible TB Regimens ›

1. Treatment regimens for drug-susceptible TB — current WHO and NTEP recommendations. *[Long answer]*

9.3 Monitoring During & After Treatment ›

1. Monitoring of a patient on treatment for drug-susceptible pulmonary TB. *[Short note]*

9.4 Drug-Induced Liver Injury (DILI) ›

1. Management of antituberculosis drug-induced hepatotoxicity. *[Long answer]*

9.5 Other Adverse Reactions & Drug Interactions ›

1. Adverse reactions to antituberculosis drugs — recognition and management. *[Long answer]*

9.6 Principles of DR-TB Management & Hr-TB ›

1. Principles of management of drug-resistant tuberculosis. *[Long answer]*
2. Isoniazid-resistant tuberculosis — diagnosis and treatment. *[Short note]*

9.7 MDR/RR-TB Regimens in Practice ›

1. BPaLM regimen — composition, eligibility, monitoring and evidence. *[Long answer]*
2. Management of pre-XDR and XDR tuberculosis. *[Short note]*

9.8 Special Situations — Renal, Hepatic, Pregnancy & HIV ›

1. Treatment of tuberculosis in a patient with chronic kidney disease on haemodialysis. *[Short note]*

9.9 Adjunctive Therapy — Steroids, Surgery & Nutrition ›

1. Role of corticosteroids in tuberculosis. *[Short note]*
2. Indications for surgery in pulmonary tuberculosis. *[Short note]*

9.10 Adherence & Patient-Centred Care ›

1. Patient-centred approaches to improve adherence in tuberculosis. *[Short note]*

9.11 TB Preventive Treatment in Practice ›

1. TB preventive therapy for household contacts — evaluation and regimens. *[Long answer]*

9.12 Infection Prevention & Control and Vaccines ›

1. Infection control measures for tuberculosis in health-care settings. *[Short note]*
2. BCG vaccine and newer TB vaccines. *[Short note]*

9.13 Drug Chart — Antituberculosis Medicines at a Glance ›

1. Write a drug chart for second-line antituberculosis drugs with doses and major toxicities. *[Short note]*

Section 10 · Complications of Tuberculosis

10.1 Haemoptysis in Tuberculosis — Including Massive Haemoptysis ›

1. Management of massive haemoptysis in a patient with treated pulmonary TB. *[Long answer]*

10.2 Chronic Pulmonary Aspergillosis & Aspergilloma ›

1. Chronic pulmonary aspergillosis as a sequel of tuberculosis. *[Short note]*

10.3 Pneumothorax, Bronchopleural Fistula & Empyema ›

1. Bronchopleural fistula in tuberculosis. *[Short note]*

10.4 Respiratory Failure, ARDS & Cor Pulmonale ›

1. Tuberculosis in the intensive care unit. *[Short note]*

10.5 Paradoxical Reactions & TB-IRIS ›

1. TB-IRIS — definition, diagnosis and management. *[Long answer]*

10.6 Systemic Complications of Tuberculosis ›

1. Secondary amyloidosis and HLH as complications of tuberculosis. *[Short note]*

10.7 Treatment Failure, Recurrence & Non-Response — An Approach ›

1. Approach to a patient with failure of first-line antituberculosis treatment. *[Long answer]*
2. Recurrent tuberculosis — relapse versus reinfection. *[Short note]*

Section 11 · Landmark Trials in Tuberculosis — Theory & References

11.1 How to Read a TB Trial — Design, Endpoints & Non-Inferiority ›

1. Non-inferiority trials in tuberculosis — concepts with examples. *[Short note]*

11.2 Foundation Trials — Streptomycin, Madras & Chingleput ›

1. Contribution of the Madras study and the Chingleput BCG trial to TB control. *[Short note]*

11.3 Shortening Drug-Susceptible TB Treatment — REMoxTB, Study 31, SHINE & TRUNCATE-TB ›

1. Trials of treatment shortening in drug-susceptible TB. *[Long answer · Recent advances]*

11.4 Drug-Resistant TB Trials — STREAM, Nix-TB, ZeNix, TB-PRACTECAL, endTB & BEAT-TB ›

1. Evidence behind the BPaLM regimen — Nix-TB, ZeNix and TB-PRACTECAL. *[Long answer · Recent advances]*
2. STREAM trial — stage 1 and stage 2. *[Short note]*

11.5 TB–HIV & Corticosteroid Trials — SAPiT, CAMELIA, STRIDE, PredART, Thwaites, ACT HIV & IMPI ›

1. Timing of antiretroviral therapy in TB–HIV co-infection — evidence from trials. *[Long answer]*
2. Corticosteroids in tuberculous meningitis and pericarditis — trial evidence. *[Short note]*

11.6 Prevention, Diagnosis & Nutrition Trials — PREVENT TB, BRIEF-TB, VQUIN, TB-CHAMP, Xpert, M72 & RATIONS ›

1. RATIONS trial and the role of nutrition in TB control. *[Short note]*
2. Evidence for short-course TB preventive treatment regimens. *[Short note]*

CURRICULUM

NMC Curriculum — Tuberculosis Competencies

What the competency-based postgraduate curriculum expects on tuberculosis, mapped to the pages of this book

Area	The postgraduate should be able to…	Covered in
K1	Describe the epidemiology of tuberculosis in India and the world, risk factors and the social determinants of disease	Section 2
K2	Describe the microbiology of *M. tuberculosis* and NTM, transmission and the molecular basis of drug resistance	Section 3
K3	Explain the immunopathogenesis, granuloma biology and the primary/post-primary patterns of disease	Section 4
K4	Describe the spectrum and natural history of TB infection and disease, prognosis and post-TB lung disease	Section 5
S1	Elicit the history and signs, and interpret the chest radiograph, in pulmonary and miliary TB, including TB in children, PLHIV, diabetes and pregnancy	Section 6
S2	Diagnose and manage extrapulmonary TB of every organ system, choosing the right sample and test	Section 7
S3	Choose, perform or interpret smear, culture, DST, NAAT, LPA, tNGS, IGRA/TST/TBST, LF-LAM, ADA and imaging	Section 8
S4	Prescribe and monitor regimens for drug-susceptible and drug-resistant TB, manage adverse reactions and special situations	Section 9
S5	Recognise and manage complications — massive haemoptysis, pneumothorax, empyema, respiratory failure, IRIS, CPA and post-TB lung disease	Section 10
P1	Implement NTEP policies — notification, Ni-kshay, universal DST, TPT, infection control and patient support	1.8, Section 9
A1	Counsel patients and families with empathy, address stigma, obtain consent and support adherence	Section 9

Reference documents — tap to open

Document	Title
Module 1	WHO consolidated guidelines on tuberculosis. Module 1: Prevention — tuberculosis preventive treatment. 2nd edition. Geneva: WHO; 2024.
Module 2	WHO consolidated guidelines on tuberculosis. Module 2: Screening — systematic screening for tuberculosis disease. Geneva: WHO; 2021.
Module 3	WHO consolidated guidelines on tuberculosis. Module 3: Diagnosis. 4th edition. Geneva: WHO; 2025.
Module 4	WHO consolidated guidelines on tuberculosis. Module 4: Treatment and care. Geneva: WHO; 2025.
Report	WHO Global Tuberculosis Report 2025.
NTEP	Central TB Division, MoHFW — NTEP guidelines and circulars (tbcindia.mohfw.gov.in)
Images	Radiopaedia — pulmonary tuberculosis image collection

Abbreviations

ADA	Adenosine deaminase
AFB	Acid-fast bacilli
ART	Antiretroviral therapy
BAL	Bronchoalveolar lavage
BCG	Bacille Calmette–Guérin
BDLLfxC	Bedaquiline, delamanid, linezolid, levofloxacin, clofazimine
BPaLM	Bedaquiline, pretomanid, linezolid, moxifloxacin
CAD	Computer-aided detection
CBNAAT	Cartridge-based NAAT (Xpert)
CPA	Chronic pulmonary aspergillosis
CRP	C-reactive protein
DILI	Drug-induced liver injury
DR-TB	Drug-resistant TB
DS-TB	Drug-susceptible TB
DST	Drug susceptibility testing
EPTB	Extrapulmonary TB
FDC	Fixed-dose combination
FL/SL-LPA	First/second-line line probe assay
FQ	Fluoroquinolone
Hr-TB	Isoniazid-resistant, rifampicin-susceptible TB
IGRA	Interferon-γ release assay
IRIS	Immune reconstitution inflammatory syndrome
LC-aNAAT	Low-complexity automated NAAT
LF-LAM	Lateral-flow urine lipoarabinomannan
LTFU	Lost to follow-up
MDR-TB	Multidrug-resistant TB
MGIT	Mycobacteria growth indicator tube
mWRD	Molecular WHO-recommended rapid diagnostic test
NAAT	Nucleic acid amplification test
NPY	Ni-kshay Poshan Yojana
NTEP	National TB Elimination Programme
NTM	Non-tuberculous mycobacteria
PLHIV	People living with HIV
PTB	Pulmonary TB
RR-TB	Rifampicin-resistant TB
TBM	Tuberculous meningitis
TBST	TB antigen-based skin test
tNGS	Targeted next-generation sequencing
TPT	TB preventive treatment
TST	Tuberculin skin test
UDST	Universal drug susceptibility testing
XDR-TB	Extensively drug-resistant TB

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