**FRCPath Part 2 Revision Notes – *Mycobacterium*** *(Integrated from UK‑SMI B 40 i7.3, ATS/ERS/ESCMID/IDSA 2020, BTS 2017, WHO TB Consolidated Guidelines 2024/25, NICE NG33 2024, CLSI M24‑A4 2024, UKHSA WGS & TB Action Plan)*

## **1 Taxonomy & Key Pathogens**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Runyon** | **Growth rate / Pigment** | **Representative species** | **Typical disease** | **Exam pearls** |
| **I Photochromogens** | Slow, yellow‑orange after light | *M. kansasii*,  *M. marinum* | Pulmonary cavitary (kansasii); fish‑tank granuloma (marinum) | *M. kansasii* rif‑susceptible, niacin‑neg |
| **II Scotochromogens** | Slow, pigment in dark | *M. gordonae*  *M. scrofulaceum*, | Contaminant (gordonae)  Cervical nodes (scrofulaceum); | Gordonae = “tap‑water” bacillus |
| **III Non‑photochromogens** | Slow, non‑pigmented | *M. avium* complex,  *M. xenopi*,  *M. haemophilum* | Chronic lung, disseminated AIDS (MAC);  nodular bronchiectasis (xenopi);  skin (*haemophilum)* | *M. haemophilum* grows at 30 °C with Fe³⁺ |
| **IV Rapid growers** | Colonies ≤7 d | *M. abscessus* complex,  *M. fortuitum*,  *M. chelonae* | SSTI, CF bronchiectasis, device infections | Check **erm(41)** for inducible macrolide R |
| **MTB complex** | Slow, non‑pigmented | *M. tuberculosis*,  *M. bovis*,  *M. africanum*,  *M. canettii*,  *M. caprae* | Pulmonary & extra‑pulmonary TB | Niacin +/-, NAP inhibited |

## **2 Biosafety & Infection‑control**

* Hazard Group 3 (ACDP) for MTBC and most NTMs – work in CL3 if aerosol‑generating (smear prep, MGIT positives).
* Class II MSC, sealed buckets ≥3000 g 15 min, negative‑pressure rooms for induced sputum.
* Decontaminate work surfaces with 1 % hypochlorite (10 000 ppm) or 70 % ethanol followed by UV.

## **3 Specimen Collection & Transport**

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| Specimen | Points |
| **Sputum** | ≥2 (ideally 3) early‑morning, 5 mL, tight‑lidded pot. |
| **BAL / washings** | For smear‑neg or non‑productive; avoid tap‑water contamination. |
| **Gastric aspirate (children)** | Neutralise with Na₂CO₃ if delay > 4 h. |
| **Sterile fluids / tissue** | No decontamination; send fresh (no formalin). |
| **Urine** | Three consecutive early‑morning, no boric acid. |
| **Blood / bone‑marrow** | Culture in Myco/F Lytic bottle. |
| Transport within 24 h, refrigerate 4 °C if delayed. |  |

## **4 Laboratory Diagnosis Workflow**

### **4.1 Front‑end Molecular Tests**

* **Xpert MTB/RIF Ultra**: LoD ~16 CFU/mL; detects *rpoB* Rif R.
* **Xpert MTB/XDR (2023 UK roll‑out)**: adds isoniazid (*katG*, *inhA)*, quinolone (*gyrA/B)*, aminoglycoside (*rrs/eis)*; 90 min.
* Positive rifampicin‑resistant or smear‑positive specimens proceed to **WGS** for full resistance prediction and cluster typing (UKHSA).

### **4.2 Homogenisation / Decontamination**

* Preferred: **NALC–NaOH** (final 1 % NaOH, 0.5 % NALC) 15 min → neutralise pH 6.8 phosphate buffer, centrifuge 3000 g 15 min.
* Alternative: 5 % oxalic acid for heavily P. aeruginosa‑contaminated CF sputum.

### **4.3 Microscopy**

* Auramine‑phenol primary (LED fluorescence) → Ziehl‑Neelsen less sensitive but gives morphological detail.
* Report grading (WHO/IUATLD): 0, scanty (1–9 AFB/100 fields), 1+, 2+, 3+.

### **4.4 Culture**

* **Liquid**: MGIT 960 (⁓10 d positivity), VersaTREK.
* **Solid**: Löwenstein–Jensen / Middlebrook 7H10 & 7H11; incubate 37 °C (and 30 °C if *M. haemophilum* suspected), retain 8 wks.
* Contamination action limit ≤5 % (MGIT); monitor monthly.

### **4.5 Identification**

* MALDI‑TOF (Bruker database v11+),
* line‑probe assays (GenoType Hain),
* 16S/hsp65/rpoB sequencing.

### **4.6 Drug‑Susceptibility Testing (DST)**

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| Method | Organisms | Notes |
| **MGIT 960 SIRE/PZA** | MTBC | Critical conc per CLSI M24‑A4; QC *H37Rv* ATCC 27294. |
| **Broth microdilution (Sensititre RAPMYCO)** | NTM | Test macrolide & amikacin for MAC/abscessus; report MICs. |
| **Rapid molecular** | GeneXpert, LPAs, tNGS/WGS | Interpret mutations (e.g. *katG S315T* high‑level INH R). |

Quality control: weekly QC strains (*M. avium* ATCC 700898, *M. kansasii* ATCC 12478), MGIT positive & negative controls each run; document under ISO 15189.

## **5 Public Health & Genomics**

* **Statutory notification** of TB within 24 h (online ETS).
* **WGS**: SNP cut‑off ≤5 SNPs suggests recent transmission; triggers incident meeting.
* **Contact tracing**: concentric circles, risk matrix (smear ++, cavitary, household, paediatric). Follow 2021–26 UKHSA TB Action Plan.
* **EQA**: UK NEQAS AFB smear, culture, identification & DST schemes.

## **6 Treatment & Management**

### **6.1 Drug‑susceptible TB (adults)**

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| Phase | Regimen | Duration |
| Intensive | R + H + Z + E | 2 months |
| Continuation | R + H | 4 months |

### **6.2 DR‑TB (WHO Module 4, Apr 2025)**

* **Short all‑oral regimen (BPaLM)**: bedaquiline 400 mg qd 2 wks then 200 mg thrice‑weekly + pretomanid 200 mg qd + linezolid 600 mg qd + moxifloxacin 400 mg qd for 6–9 mo.
* Monitor ECG (QTc >500 ms), LFTs, weekly FBC for linezolid.

### **6.3 Non‑tuberculous Mycobacteria**

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| Scenario | Preferred regimen | Comments |
| **MAC – nodular/bronchiectatic** | 3× weekly azithro 500 mg + rifampicin 600 mg + ethambutol 25 mg/kg | ≥12 mo post‑conversion |
| **MAC – cavitary / severe** | Daily azithro 250–500 mg  + rifampicin  + ethambutol  **± IV amikacin** first 2–3 mo | Add ALIS if culture‑pos ≥6 mo |
| **M. kansasii** | Daily rifampicin  + ethambutol  + INH *or* azithro | 12 mo total |
| **M. xenopi** | Rifampicin  + ethambutol  + moxifloxacin/macrolide  **± IV amikacin** | High relapse |
| **M. abscessus (erm neg)** | **Intensive ≥2 mo**:  IV amikacin  + imipenem/cefoxitin  + azithro  **Continuation**:  azithro  + clofazimine  ± inhaled amikacin | ≥12 mo neg |
| **M. abscessus**  **(erm pos / mac‑R)** | Same IV backbone, macrolide for immunomodulation only; consider tigecycline, bedaquiline, linezolid; surgical resection | Specialist input |

Refer also to **BTS Pulmonary NTM PD Guideline 2017** for UK surgical thresholds & airway clearance

### **6.4 Monitoring & Toxicity**

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| Drug | Monitoring | Major toxicities |
| Rifampicin | Baseline/ monthly LFT,  drug‐interactions | Hepatitis, thrombocytopenia |
| Isoniazid | LFT,  neuropathy prophylaxis with pyridoxine | Hepatitis, neurotoxicity |
| Ethambutol | Visual acuity/colour monthly | Optic neuritis |
| Pyrazinamide | LFT, uric acid | Hepatotoxicity, arthralgia |
| Bedaquiline | ECG baseline & monthly | QT prolongation |
| Linezolid | Weekly FBC,  visual symptoms | Cytopenias, neuropathy |
| Amikacin | Creatinine monitoring,  audiogram | Nephro‑/ototoxicity |

## **7 Surgery & Adjuncts**

* Consider lobectomy/pneumonectomy for localised cavitary or mac‑R disease with good reserve.
* Corticosteroids only for paradoxical IRIS.
* ALIS (amikacin liposome inhalation) licensed for refractory MAC.

## **8 Quality & Accreditation (ISO 15189 hot points)**

* IQC logs: smear pos/neg, MGIT growth control, lot acceptance.
* Contamination index ≤5 % (liquid); action if > 10 %.
* Staff competency, risk assessments, annual CL3 airflow validation.

## **9 High‑Yield Exam Pearls**

1. **NALC–NaOH ≤15 min** – most mycobacteria survive.
2. *M. kansasii* = photochromogen, nitrate +, rif‑S.
3. Inducible **erm(41)** causes macrolide R in *M. abscessus* after 14 d incubation.
4. **Xpert Ultra ‘trace’** → treat as TB if high pre‑test probability.
5. **BPaLM** now first‑line for MDR/RR‑TB in adults ≥14 y.
6. MGIT PZA false‑R if pH >6 or inoculum >0.5 McF.
7. Visual monitor ethambutol if >15 mg/kg or paediatric.
8. WGS SNP distance ≤5 suggests recent transmission in UKHSA algorithm.

### **Key Documents to Read**

* UK‑SMI B 40 i7.3 (Oct 2020)
* WHO TB Consolidated Guidelines – Module 3 (Mar 2024) & Module 4 (Apr 2025)
* NICE NG33 Tuberculosis (Feb 2024 update)
* ATS/ERS/ESCMID/IDSA NTM Guideline 2020 (ciaa241)
* BTS Guideline 2017 – NTM Pulmonary Disease
* CLSI M24‑A4 2024 – Susceptibility Testing of *Mycobacteria*
* UKHSA TB WGS & Cluster Investigation Handbook 2022