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LEARNING OBJECTIVE

Mycobacterial Infections – Presentation, Diagnosis, and Management

Understand the clinical presentation, diagnosis, and management of common mycobacterial infections

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Background

Mycobacterial infections in children are caused by *Mycobacterium tuberculosis* (TB) or nontuberculous mycobacteria (NTM). NTM are environmental organisms (water, soil) that typically cause localized disease in immunocompetent children, especially cervicofacial lymphadenitis. Common species include *M. avium* complex (MAC), *M. haemophilum*, and *M. marinum*. Some NTM (*M. marinum*, *M. kansasii*, *M. szulgai*) can cause **false-positive IGRA** results.

Clinical Features / Presentation

Cervicofacial Lymphadenitis

Typical NTM pattern: Immunocompetent child **aged 1 to 5 years** with a **unilateral**, nontender submandibular or anterior cervical node that enlarges slowly over weeks. Overlying skin becomes tethered and may change from pink to **violaceous** and parchment-like. May suppurate or form a sinus tract. Fever and systemic symptoms are uncommon. Poor response to routine antibiotics.

TB lymphadenitis pattern: More common in **older children and adolescents**, often with epidemiologic risk factors (TB-endemic birth, travel, residence, or household contact). More likely to have **systemic symptoms** (fever, weight loss, night sweats) and **bilateral or posterior cervical** involvement.

Chronic Skin and Soft Tissue Infection

NTM clues:

- Direct inoculation through wounds, surgical sites, or cosmetic procedures
- Rapidly growing mycobacteria (*M. abscessus*, *M. fortuitum*, *M. chelonae*) cause nodules, pustules, or abscesses with **less tenderness** than typical pyogenic infections
- *M. marinum* causes “swimming pool granuloma” after freshwater or saltwater exposure
- Medical tourism for cosmetic surgery is a risk factor

Pulmonary Disease

TB pulmonary disease by age: **Infants** may have cough, wheezing (airway obstruction from lymphadenopathy), fever, and poor weight gain. **School-aged children** are often asymptomatic or have mild cough; chest radiograph shows perihilar adenopathy with or without infiltrate. **Adolescents** may have classic symptoms (prolonged fever, productive cough, night sweats, weight loss) and can have cavitary upper lobe disease.

Children **younger than 10 years are usually not contagious**; adolescents with cavitary disease are more likely to transmit TB.

Nontuberculous Mycobacterial Pulmonary Disease

Rare in healthy children; occurs primarily in those with cystic fibrosis or other bronchiectasis.

Extrapulmonary and Disseminated TB

TB meningitis is the most severe form; occurs in 0.5% to 2% of TB infection cases, more common in children **younger than 2 years** and in immunocompromised hosts. **Early recognition is critical**. Prognosis depends on prompt treatment initiation.

Miliary TB is disseminated disease with involvement of 2 or more organ systems; presents with malaise, anorexia, weight loss, and fever. Chest radiograph shows diffuse nodular “millet seed” pattern. Meningitis develops in **20% to 40%**.

Differential Diagnosis

Cervicofacial Lymphadenitis Quick Compare

FEATURE	NTM LYMPHADENITIS	TB LYMPHADENITIS	NEXT STEP
Age	1 to 5 years	Older children and adolescents	Age shifts likelihood; neither excluded by age alone
Systemic symptoms	Absent or rare	More common	If present, escalate TB concern
Skin findings	Violaceous, thinning, tethering, sinus tract	Less characteristic	Skin changes strongly support NTM
TB risk context	Usually absent	Often present	If TB risk present, prioritize TB evaluation pathway
TST/IGRA	TST may be +; *IGRA usually –	TST + and IGRA + more likely	Obtain CXR when TB concern exists or TB testing is +
Chest radiograph	Typically normal	May show adenopathy or infiltrates	Helps separate TB infection from TB disease

*Most NTM causing lymphadenitis (*MAC*, *M. haemophilum*) do not cross-react with IGRA. Some species (*M. marinum*, *M. kansasii*, *M. szulgai*) may cause false-positive IGRA.

Consider NTM in skin/soft tissue when nodules, pustules, or abscesses follow water exposure, surgery, or cosmetic procedures and **persist or recur despite routine therapy**.

Evaluation and Diagnosis

History

TB epidemiologic risk factors (birth in or travel to a TB-endemic country, household contact, exposure to high-risk populations); **NTM exposure context** (age 1 to 5, environmental water exposure, dental procedures, cosmetic surgery abroad); duration and progression of adenopathy; response to prior antibiotics; **constitutional symptoms** (fever, weight loss, night sweats, cough).

Physical Examination

Node location (anterior or submandibular suggests NTM; posterior cervical or bilateral suggests TB); **overlying skin changes** (violaceous discoloration, thinning, tethering, sinus tract favors NTM); tenderness and fluctuance; hepatosplenomegaly or generalized adenopathy (suggests disseminated disease).

Imaging

For NTM lymphadenitis, imaging is not routinely required but may help evaluate alternative diagnoses. **Chest radiograph (PA and lateral) is indicated when TB is suspected or TB testing is positive** to distinguish TB infection from TB disease.

TB Testing Quick Reference

Two tests detect TB infection: the tuberculin skin test (TST) and an interferon-gamma release assay (IGRA).

TST Positive Thresholds by Risk

INDURATION	POSITIVE IF ANY OF THESE APPLY
≥5 mm	Close TB contacts; suspected TB disease (abnormal CXR or clinical evidence); HIV; immunosuppressed (transplant, TNF- α inhibitors, prolonged corticosteroids)
≥10 mm	Birth, residence, or travel to TB-endemic area; age <4 years; high-risk exposures (homelessness, incarceration, injection drug use); certain medical conditions (diabetes, chronic renal failure)
≥15 mm	No identified risk factors

IGRA vs TST Comparison

CHARACTERISTIC	IGRA	TST
Visits required	1	2 (placement and reading)
BCG cross-reaction	No	Yes (false positives)
NTM cross-reaction	No for most (MAC, <i>M. haemophilum</i>)*	Yes (many species)
Specificity	Higher (92%–97%)	Lower in BCG-vaccinated populations
Boosting phenomenon	No	Yes
Reader variability	Minimal	Significant
Age considerations	Acceptable all ages per AAP (2024)	All ages

*Cross-reaction may occur with *M. marinum*, *M. kansasii*, and *M. szulgai*.

Negative IGRA or TST is **unreliable in infants younger than 3 months**. In immunocompromised patients, sensitivity of both tests is decreased.

For suspected mycobacterial lymphadenitis, **perform TST and IGRA on the same day**. Interpret results in the context of TB risk factors and clinical features.

After any positive TB test, review for symptoms of active TB disease (cough, fever, weight loss, night sweats) and **obtain a chest radiograph** to distinguish TB infection from TB disease.

Microbiologic Confirmation

- **AFB smear:** Rapid but **low yield** in many pediatric specimens (e.g., <10% in gastric aspirates); cannot speciate or reliably distinguish TB from NTM
- **Culture: Gold standard;** may take weeks (often **6+ weeks** for NTM). Yield from excised lymph nodes is 50%–80%
- **Molecular testing (Xpert MTB/RIF):** Rapid confirmation for TB. Sensitivity is 65%–73% depending on specimen; does not replace culture
- **Speciation/susceptibility:** Guides therapy for NTM and for suspected drug-resistant TB

Approach to Chronic Unilateral Cervicofacial Lymphadenitis

- 1 **Recognize the NTM pattern** (young child 1 to 5 years, unilateral nontender node, violaceous skin changes, poor response to routine antibiotics)
- 2 **Assess TB risk and perform TB testing** (TST plus IGRA on the same day)
- 3 **Interpret results with key caveats** (decreased sensitivity in immunocompromised patients; IGRA may cross-react with certain NTM) and obtain a chest radiograph if TB concern exists or TB testing is positive
- 4 **Choose specimen strategy:** excision is preferred when safe and provides both diagnosis and treatment; fine needle aspiration is an alternative when facial nerve risk is high
- 5 **Determine management:** excision is preferred for NTM; antimicrobials are used when excision is not feasible; **avoid incision and drainage** because it increases risk of chronic sinus tracts and recurrence

Management and Treatment

Nontuberculous Mycobacterial Lymphadenitis

Surgical excision is preferred: Complete excision achieves high cure rates (**92%–96%**) with rapid healing and good cosmetic results, and it provides diagnostic tissue.

Do not do: Avoid incision and drainage. It commonly leads to chronic draining sinus tracts and recurrence.

Antimicrobial therapy (if excision not feasible): Consider when **facial nerve risk** is high (preauricular or intraparotid nodes) or when surgery is not acceptable. Regimens typically include a **macrolide** (azithromycin or clarithromycin) plus one or more additional agents (e.g., a rifamycin and/or ethambutol) for several months. Cure rates are lower than excision, and some patients ultimately require surgery.

Without treatment, eventual resolution can occur over months, but fistula formation is common with prolonged drainage. Surgical excision carries **facial nerve palsy risk**, especially with preauricular or intraparotid disease; when it occurs, it is usually transient.

Nontuberculous Mycobacterial Skin and Soft Tissue Infection

Obtain species identification and susceptibility testing because treatment varies by organism. Source control (e.g., debridement, foreign body or catheter removal) is important when relevant. Prolonged multidrug therapy is typically required (months). **Infectious disease consultation is recommended.**

Tuberculosis Infection (TBI)

Definition: Positive TST or IGRA with normal chest radiograph and no symptoms.

Why treat: Risk of progression to TB disease is **~10% overall**, with higher risk in the **first 2 years** after infection and in young children and immunocompromised patients.

TBI Regimen Selection

REGIMEN	WHO IT FITS BEST	DURATION/FREQUENCY	KEY CONSTRAINTS
3HP	Preferred for age ≥2 years	3 months (12 weeks), once weekly	Not approved <2 years; drug interactions; higher pill burden; cost
4R	Preferred for age <2 years; isoniazid-resistant TB contact	4 months (120 doses), daily	Drug interactions (rifampin)
3HR	When 3HP and 4R not available	3 months, daily	Drug interactions
9H or 6H	Alternative when rifamycins contraindicated	9 months (US preferred) or 6 months, daily or twice weekly	Long duration; poorer completion rates

3HP = isoniazid plus rifapentine; 4R = rifampin; 3HR = isoniazid plus rifampin; 9H/6H = isoniazid.

Tuberculosis Disease

Regimen notation: Number = months; **H** = isoniazid; **R** = rifampin; **Z** = pyrazinamide; **E** = ethambutol.

Standard 6-month regimen (2HRZE/4HR): Intensive phase (**2 months**) with isoniazid, rifampin, pyrazinamide, and ethambutol, followed by continuation phase (**4 months**) with isoniazid and rifampin.

4-month regimen (2HRZE/2HR): Acceptable for children **aged 3 months to 16 years** with nonsevere, paucibacillary TB disease (e.g., peripheral lymph node TB; intrathoracic adenopathy without airway obstruction; uncomplicated pleural TB; noncavitary disease confined to <1 lobe).

Adverse effects of TB medications:

- **Hepatotoxicity** (INH, rifampin, pyrazinamide): Monitor LFTs; avoid alcohol
- **Optic neuropathy** (ethambutol): Baseline eye exam; report visual changes promptly
- **Peripheral neuropathy** (INH): Give **pyridoxine (B6)** prophylaxis, especially in adolescents, malnourished, or pregnant patients
- **Drug interactions** (rifampin): Potent CYP450 inducer; check anticonvulsants, anticoagulants, antiretrovirals

If **less than 1 year old** with TB disease, must have a **lumbar puncture** to evaluate for TB meningitis, even if no CNS symptoms present.

TB meningitis requires **9 to 12 months** of therapy. Use ethionamide or a fluoroquinolone (levofloxacin, moxifloxacin) as the fourth drug instead of ethambutol for better CNS penetration. **Corticosteroids are strongly recommended.**

Drug-resistant TB: Specialist consultation is required for suspected or confirmed MDR-TB or XDR-TB.

TB and HIV: All patients with HIV must also be screened for TB infection.

Guidance and Counseling

Children **younger than 5 years** and immunocompromised children exposed to active TB should **receive prophylaxis immediately** (isoniazid or rifampin). Repeat TB testing **8 to 10 weeks** after last exposure; if negative, prophylaxis may be discontinued. If positive, complete full TBI treatment.

TB disease (not TBI alone) is **reportable**. Directly observed therapy (DOT) is recommended to support adherence and completion.

JUST IN CASE (CURATED EXAM-DAY SUPPORT)

- [Nontuberculous Mycobacterial Infections in Children](#) – AAP Pediatrics in Review
- [Update in the Diagnosis and Treatment of Tuberculosis](#) – AAP Pediatrics in Review
- [Nontuberculous Mycobacterial Lymphadenitis in Children](#) – UpToDate

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