Extrapulmonary TB

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Overview

Brief Overview of TB history, transmission, pathophysiology, clinical presentation and treatment

Discuss the frequency of extrapulmonary TB compared with pulmonary TB

Identify the population with increased risk of extrapulmonary TB

Review the common sites and diagnostic challenges of extrapulmonary TB

Review the infection control aspects of extrapulmonary TB

Review of Tuberculosis

Five stages of in the history of TB

- Prehistoric era
- Classical era
- Industrial era
- Re-emergence
- Contemporary era

Currently about 11 million new cases of TB annually worldwide with 2 million deaths

- Incidence gradually decreasing

Review of Tuberculosis

TB is a bacteria with unique properties

- Low rate of division, mycolic acid cell wall (stains AFB)

Transmission through aerosolized droplets.

- Cough: pulmonary and laryngeal
- Aerosol generating procedures: intubation, BAL, irrigation of wounds, autopsy.

Infection though inhalation of bacilli into alveoli

- Macrophages and trigger of immune response: Ghon focus

Review of Tuberculosis

If disease develops within 2 years

- **Primary TB** – 5 % in otherwise health adult

If infection goes quiescent:

- It remains dormant: **latent TB** – 95%
- If it remerges and becomes active: reactivation TB ~ 5% lifetime risk.

Risk of primary and reactivation TB increases in certain cases:

- **High Risk**: AIDS, HIV, organ transplant, head and neck cancers
- **Moderate**: ESRD, DM, fibronodular disease, other cancers
- **Low**: alcoholism, malnutrition, heavy smoking

Review of Tuberculosis

We diagnose active TB

- Clinically: weight loss, night sweats, cough, other
- Radiologically: CXR, other
- Micro: smear, culture, molecular probe: sputum or other

We treat active TB with

- **Intensive phase**: IREZ x daily or 5 x a week x 2 months
- **Continuation phase**: IR (if sensitive) 3 x a week x 4 to 10 months

Review of Tuberculosis

We diagnose latent TB

- TST
- IGRA

We treat latent TB with

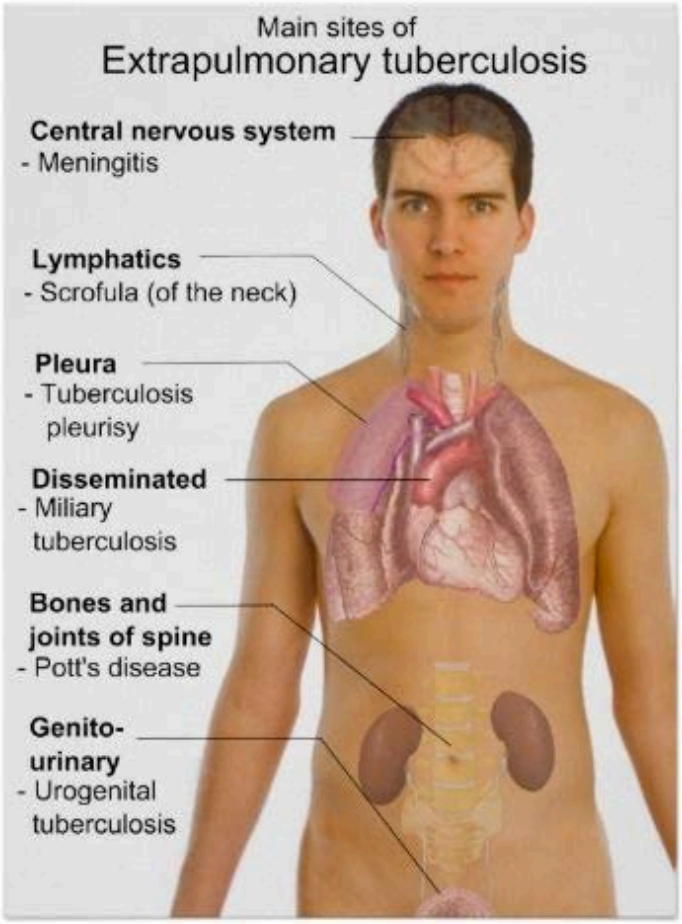
- INH daily or 3x a week for 6 to 9 months
- RMP daily x 4 months
- I+R 2 x a week x 4 months

What is Extra-pulmonary TB?

Contrast with:

- **Pulmonary TB** which includes lungs, airways
- **Respiratory TB** which includes pulmonary TB as well as the pleura (pleural TB, TB effusion) and anywhere else in the respiratory tract (sinuses, nasopharynx, mediastinal lymph nodes.)

Can be the result of progressive primary infection or via reactivation of a latent focus which then spreads


Main sites of
Extrapulmonary tuberculosis
Central nervous system
- Meningitis
Lymphatics
- Scrofula (of the neck)
Pleura
- Tuberculosis pleurisy
Disseminated
- Miliary tuberculosis
Bones and joints of spine
- Pott's disease
Genito-urinary
- Urogenital tuberculosis

Epidemiology

Canadian TB Standards:

1970s	17% of all TB cases were non-respiratory
2010	25% of TB cases in Canada are extra-pulmonary

Table 1. Anatomic site of disease and population groups of patients with TB, Canada 2010

Disease site	Aboriginal*		Canadian-born (other)		Foreign-born		Unknown		Total	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
Respiratory†	270	81.8	144	78.7	660	63.6	14	53.7	1,088	69.0
Nonrespiratory	36	10.9	33	18.0	310	29.9	10	38.4	389	24.7
Both	24	7.3	6	3.3	68	6.6	2	7.7	100	6.3
TOTAL	330	100	183	100	1038	100	26	100	1,577	100

*Includes Status and Non-Status Indians, Métis and Inuit.

†Includes primary, pulmonary, pleural and "other" respiratory TB.

Risk Factors for Extrapulmonary TB

HIV/AIDS

Malignancy

Immunosuppressive agents

- Chemotherapy, Corticosteroids, Anti-TNF alpha drugs

Renal failure

DM

ETOH abuse

pregnancy

Clinical presentation

TB lymphadenitis

Genitourinary TB

Miliary/disseminated TB

Bone/joint/spinal

Abdominal – gastrointestinal, peritoneal

CNS – meningitis, tuberculoma, ocular TB

Cardiac – TB pericarditis

Other – skin, bone marrow, glandular tissue (breast), great vessels

Table 3. Number of TB cases and incidence per 100,000 population by main diagnostic site, Canada 2010

Disease site	Cases		Incidence per 100,000
	n	(%)	population
Respiratory	1,088	(70.0)	3.2
Nonrespiratory	389	(24.7)	1.1
Peripheral lymph nodes	196	(12.4)	0.50
Miliary/disseminated	16	(1.0)	0.04
Meninges/central nervous system	22	(1.4)	0.06
Abdominal	39	(2.5)	0.1
Bones and joints	39	(2.5)	0.1
Genitourinary	24	(1.5)	0.07
Other*	53	(3.4)	0.16
Both	100	(6.3)	0.19
Total	1,577	100	4.64

*Includes 8 cases with more than one nonrespiratory site identified.

Peripheral TB Lymphadenitis

Common for intrathoracic lymph nodes to become involved with most forms of TB

12% of all TB cases in 2010 in Canada

- Common sites – neck, supraclavicular, axillary
- **Scrofula** – cervical lymph node with a sinus tract to skin surface

Common in immigrants from Asian countries

In Canada, more common in older Aboriginal women

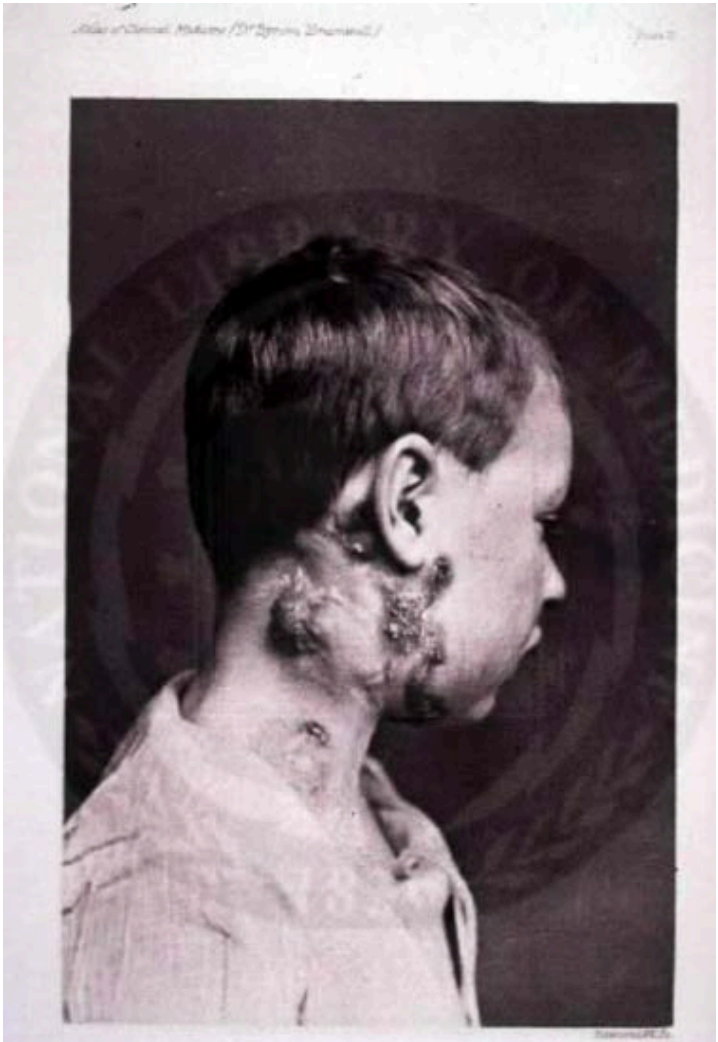
Diagnosis and Management

Fine Needle Aspiration (FNA or biopsy)

- sensitivity of 77%
- specificity of 62%

If non-diagnostic, may require excisional biopsy

Treatment – 6 months of anti-TB therapy



SCROFULA

Genitourinary TB

1.5% of all cases of TB in Canada

Presents with hematuria

More common in men and patients on dialysis

Urinary tract

Genital tract

- May be secondary to urinary tract disease
  - Associated with vesical BCG treatment for bladder cancer
- Female – fallopian tubes (most common, risk of infertility), cervical, vulvovaginal
- Male – epididymorchitis (most common), rarely penile and prostatic

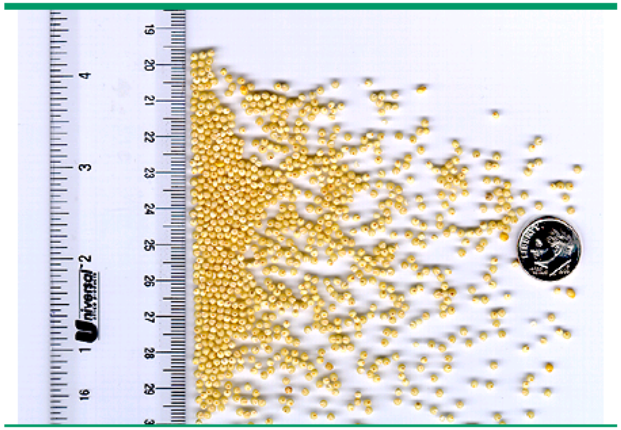
Miliary/disseminated TB

Widespread hematogenous dissemination

Bacteremia occurs during initial infection or during a reactivation

Often have “miliary” pattern on CXR – small nodules 1-5mm in size

Comparative size of millet seeds



Millet seeds from which the name miliary tuberculosis derives compared to the size of a dime (right) and a centimeter scale (left). These correspond to the approximate size of miliary lesions seen on chest radiograph.
Courtesy of Nesli Basgoz, MD.

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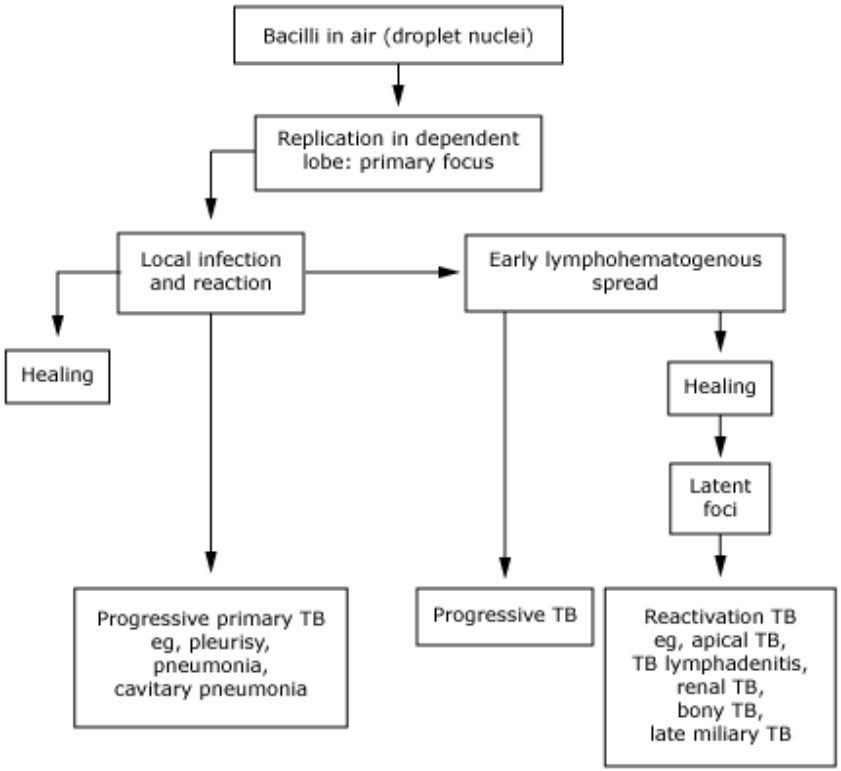
Miliary tuberculosis of the spleen

Miliary tuberculosis of the spleen. The cut surface shows numerous gray-white granulomas.

Pathogenesis of tuberculosis and miliary tuberculosis



TB: tuberculosis.

Courtesy of Nesli Basgoz, MD.

Miliary TB

Miliary TB is rare – only 16 cases in Canada in 2010

Becoming more common in the US due to increased rates of HIV

- When TB incidence is high, more common in early childhood
- When TB incidence is low, more common in immuno-compromised adults

Miliary TB

Difficult to diagnose

- often nonspecific presentation
- leads to delays in diagnosis
- variable infectiousness
- high mortality rate (~20%)

Treatment

- may require longer treatment, especially in children and immunocompromised

Bone and Joint TB

2.5% of all cases

Spinal/vertebral (Pott's disease)

- Vertebral bodies are vascular
- Slowly progressive back pain
- Nonspecific radiographic findings, MRI most helpful
  - anterior vertebral involvement, discitis of intervening discs, preserved disc until late
- Important to establish culture diagnosis – AFB smear and TB culture
  - (CT guided biopsy, surgical bx if needed)

Bone and Joint TB

Joint

- Usually mono-arthritis of hip or knee
- Often soft tissue abscesses around infected joint, can develop draining sinuses late in disease
- Synovial fluid
  - AFB microscopy only has 19% yield
  - Cultures 79% sensitivity
- Improved diagnostic accuracy with synovial biopsy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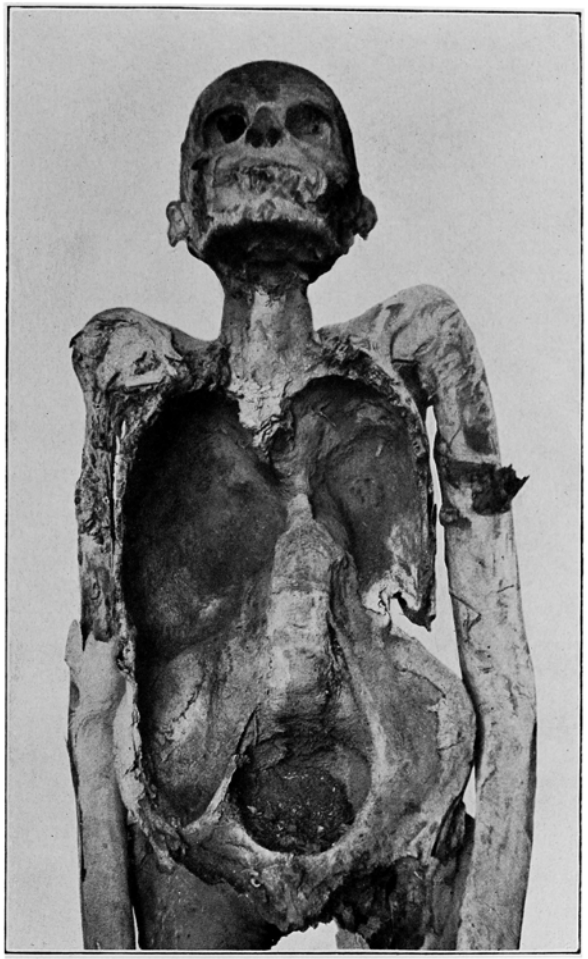

Abdominal TB

2.5% of cases

2nd most common site of Extra-pulmonary TB

Gastrointestinal

- Most commonly ileocecal, jejunoileal, anorectal areas
- Can appear similar to Crohn's disease
- Diagnosis
  - stool for AFB smear and culture
  - colonoscopy with biopsy (histopath, AFB smear, culture)

Abdominal TB

Peritoneal

- Present with abdominal pain, swelling, fever
- Peritoneum becomes lined with tubercles that leak fluid – leads to ascites
- Ascitic fluid usually smear negative, but cultures often positive
- Peritoneal biopsy for definitive diagnosis

Central Nervous System

Meningitis

- One of few TB emergencies – high morbidity and mortality
- Starts as a tubercle that ruptures and spreads in the subarachnoid space
- Can lead to from headache and fever to cranial nerve palsies, seizures, infarct, coma and death

Central Nervous System

Meningitis

- Diagnosis – Lumbar Puncture
  - Low glucose, high protein, lymphocytic
  - Poor sensitivity, increased if serial LP
- DO NOT delay treatment if TB meningitis suspected
- TB therapy with good CSF penetration PLUS steroids
  - Use of iv therapy in most cases initially

Central Nervous System

Tuberculomas

- Various neurologic presentations

Ocular TB

- Rare in Canada
- Difficult to diagnose due to trouble obtaining specimens to culture

TB pericarditis

Due to hematogenous spread from primary infection or from reactivation disease that has disseminated

Pericardial effusion – exudative, bloody, neutrophilic

Can progress to cardiac tamponade/constriction

TB pericarditis

Diagnosis

- Pericardial fluid assessment –
  - AFB smear poor test
  - TB culture and histopathologic analysis better

Treatment

- Usual treatment AND steroids
- Pericardiocentesis, pericardial window or pericardectomy

Other

TB can affect any organ system

Diagnostic Challenges of Extrapulmonary TB

Presentation of Extra pulmonary TB is nonspecific and variable (contrast with pulmonary TB)

Diagnostic tests including imaging may be nonspecific

AFB smear, culture, and PCR have variable and in some cases reduced accuracy when compared with sputum analysis for pulmonary TB

Sites involved may not be easily accessible and could require invasive procedures (ie ocular TB, spinal TB)

Case 1

45 year old man from Philippines, truck driver

Has a generalized seizure while unloading his truck.

CT head is normal

MRI shows some minor enhancement of meninges on parietal area.

LP: low glucose, high protein, and lymphocytic pleocytosis

negative smear for bacteria and AFB and negative Gene Xpert.

Case 1

Started on INH, RMP, PZA and EMB.

- No steroids given as there was no tuberuloma, no increase in ICP

Weeks later: AFB isolated on culture.

- Once speciated: NTM therefore likely a contaminant

Patient treated for 1 year with IREZ + anticonvulsant.

Complete resolution but needs life long levetiracetam.

Case 2

67 year old Caucasian man from northern SK community with a bowel obstruction.

OR for colonic resection with planned later re-anastamosis.

- Pathology: necrotizing granuloma and no malignancy.

Sample not sent in saline and so no culture could be performed.

- No opportunity to collect new sample as all affected tissue removed.

Patient started on IREZ and treated 2 + 4 months for cure.

Case 3

6 year First Nations boy from northern SK presents with dyspnea and fever.

Noted to have left sided pleural effusion.

Thoracentesis: neutrophil predominant fluid with negative AFB smear, Gene Xpert and culture.

Code Blue due to cardiac tamponade after the procedure.

- Survived code and went for emergency pericardiocentesis.

Case 3

Pericardial fluid: lymphocyte predominant, AFB smear, Gene Xpert negative.

Started on IREZ + steroids for presumed pericardial TB.

TB meds stopped when TB culture was negative.

Began to deteriorate again went to Edmonton for Pericardectomy.

All TB investigations there including pericardial tissue culture were negative for TB.

Completed 9 months of IREZ and had complete recovery.

Infection Control and extrapulmonary TB

Airborne isolation indicated if:

Concomitant pulmonary TB is present

Open wound or draining lesion that is infected and will be manipulated or irrigated.

- Wound care, surgical procedures

Once the wound is closed or dressed, it is no longer an infectious risk.

Room reopened after adequate number of air exchanges

- Relate to room size, airflow etc.

Time required for removal of infectious particles

ACH	Minutes for 99% removal	MIn for 99.9% removal
2	138	207
4	69	104
6	46	69
12	23	35
15	18	28
20	14	21
50	6	8

Other procedures

Notify department and schedule to minimize exposure.

Post appropriate signage

Those engaged in procedure wear N95 masks

Routine cleaning after room is reopened

Infection Control and extrapulmonary TB

Airborne isolation discontinued:

Pulmonary TB is ruled out: CXR reviewed

Tissue infected will not be irrigated or manipulated

Two weeks of effective therapy has been taken.

- Airborne isolation requirement maybe be extended at the discretion of TB physician
  - Lack of improvement, uncertainty of drug penetration at site, concerns regarding drug resistance.

Summary of Key Points

TB can affect any organ or organ system in the body

Require a high index of suspicion

Gold standard for diagnosis is to obtain microbiologic confirmation but important not to delay therapy if suspicious (esp with TB meningitis)

Summary of Key Points

Diagnosis of extrapulmonary TB should prompt:

- Evaluation for concomitant pulmonary TB
- Evaluation for predisposing factors (HIV etc)

Majority of EPTB cases the standard 6 month therapy is reasonable, may need longer in some cases, add steroids for TB meningitis or pericarditis

Questions?

References

Canadian Tuberculosis Standards, 7th Edition

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