


TB or Not TB: Diagnosis of TB Disease and Latent TB Infection



Session Two of a Four-Part Webinar Series
Presented in Partnership with the
BC Lung Association
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Overview

- Review of TB epidemiology, transmission, and pathogenesis (webinar #1)
- Review of risk factors for progression from TB infection to TB disease
- Review of common symptoms of TB disease
- Review of the components of a comprehensive TB assessment
- **Introduction** to methods of testing for TB infection and TB disease
- Veda Peters, Tobacco Education Coordinator, BC Lung Assoc.
- Q & A








Learning Objectives

At the end of this webinar, participants will be able to:

- Describe risk factors for TB exposure and TB infection
- Describe risk factors for progression from TB infection to TB disease
- Explain the differences between latent TB infection (LTBI) and TB disease
- List common symptoms of TB disease
- Identify the components of a comprehensive TB assessment
- Describe current methods of testing for TB infection and TB disease

Abbreviations

- **CXR:** chest X-ray; chest radiograph
- **DST:** drug susceptibility testing
- **IGRA:** interferon gamma release assay
- **LTBI:** latent TB infection
- **NAAT:** nucleic acid amplification tests
- **NTM:** non-tuberculous mycobacteria
- **PHMRL:** Public Health Microbiology & Reference Lab
- **TB bacteria:** bacteria that can cause TB disease
- **TST:** tuberculin skin test

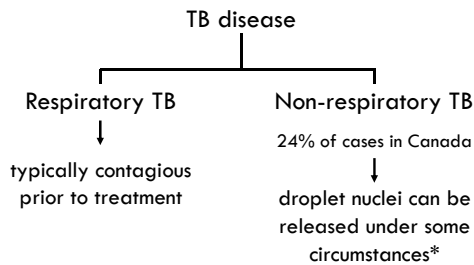


What is Tuberculosis (TB)?

- An infectious disease
- Often (but not always) attacks the lungs
- Almost always curable with appropriate treatment
- Untreated, kills more than 50%
- **Typically, only cases with respiratory forms of TB disease could be infectious**





Types of TB Disease



Note: 2011 data provisional until release of Tuberculosis in Canada, 2011
Source: Public Health Agency of Canada. Tuberculosis in Canada 2011 – Pre-Release. Ottawa (Canada):
Minister of Public Works and Government Services Canada; 2012




TB Tip #1





Non-Respiratory TB Disease:
Peripheral TB Lymphadenitis




- Most common non-respiratory form of TB disease in Canada
- 13% of all TB cases, 55% of all non-respiratory cases
- Single or multiple nodes
- Cervical nodes most often affected

Note: 2011 data provisional until release of Tuberculosis in Canada, 2011

*Source: Public Health Agency of Canada. Tuberculosis in Canada 2011 – Pre-Release. Ottawa (Canada): Minister of Public Works and Government Services Canada; 2012




World Health Organization

- 1/3 of the global population infected with TB
- 8.7 million new cases, 1.4 million deaths (2011)
 - 310 000 cases of MDR-TB (est)
 - 3.7 % of new cases and 20% of previously treated cases MDR-TB
 - 60% of MDR-TB cases: India, China, and Russian Federation
 - 9% of MDR-TB have XDR-TB

Source: http://www.who.int/tb/publications/factsheet_global.pdf


TB in Canada: 2011



- 1 587 new cases
- 4.7 cases per 100 000 population

Note: 2011 data provisional until release of Tuberculosis in Canada, 2011
Source: Public Health Agency of Canada. Tuberculosis in Canada 2011 – Pre-Release. Ottawa (Canada): Minister of Public Works and Government Services Canada; 2012

TB in British Columbia: 2011

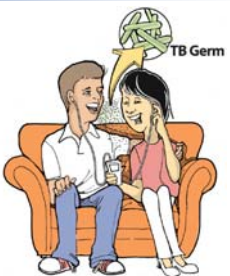


- 268 new cases
- 5.9 cases per 100 000 population

Note: 2011 data provisional until release of Tuberculosis in Canada, 2011
Source: Public Health Agency of Canada. Tuberculosis in Canada 2011 – Pre-Release. Ottawa (Canada): Minister of Public Works and Government Services Canada; 2012

TB Transmission: Inhalation

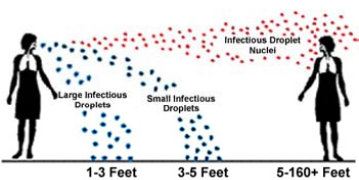
When a person with infectious **TB disease** coughs, sneezes, sings or shouts, TB germs are passed into the air in “**droplet nuclei**”.



People become infected with TB germs by inhaling droplet nuclei.

Centers for Disease Control and Prevention

TB Transmission – Droplet Nuclei

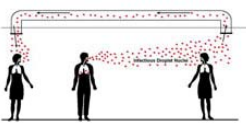


Droplet nuclei (more dangerous) can remain suspended for hours and...

Larger droplets settle to the ground more quickly (less dangerous)

Centers for Disease Control and Prevention



TB Transmission – Droplet Nuclei



...droplet nuclei can travel on air currents!

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TB Tip #2

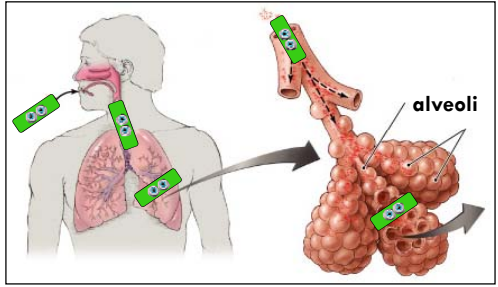
Risk of TB Transmission



Risk of transmission is influenced by:

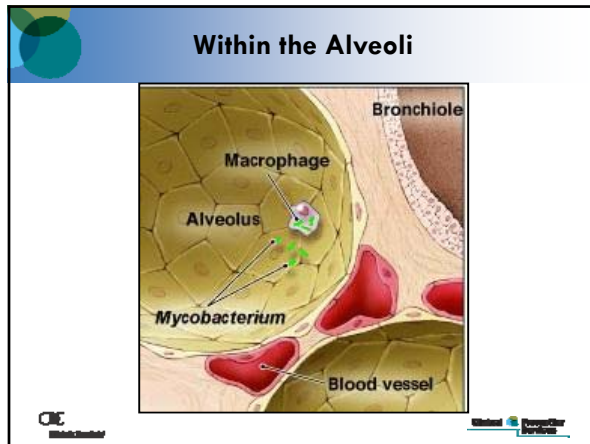
1. Concentration of droplet nuclei
 - Degree of infectiousness of case
 - Exposure environment
2. Duration of exposure/physical proximity to the case
3. Susceptibility of contacts
4. Virulence of the TB bacteria

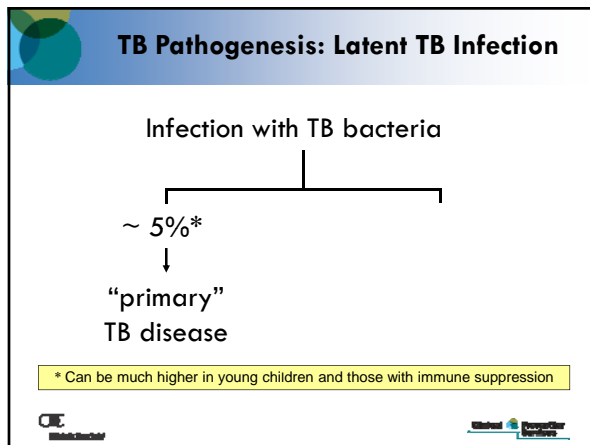



TB Transmission: Inhalation









What is “Primary TB Disease”?

- ~5% of newly infected are unable to limit bacterial replication
- TB disease can develop within 18 to 24 months or sooner (e.g., immune suppressed)
- Pleural TB, TB meningitis, and miliary TB are often presentations of primary TB disease
- Infants, children less than 5 years of age, and HIV infected at very high risk

TB Tip #3

TB Pathogenesis: Latent TB Infection

Infection with TB bacteria

~ 5%*



↓

“primary”
TB disease

~ 95%


↓



latent TB infection
(LTBI)

Latent TB Infection (LTBI)

The term ‘LTBI’ is used to describe the situation when a person is infected with TB bacteria but has not developed TB disease.



Latent TB Infection (LTBI)

Person is infected with TB bacteria but:

- **NO symptoms** of current TB disease
- **NORMAL** clinical examination and chest x-rays (usually)
- **NO TB bacteria** in clinical specimens (e.g., sputum)
- **NOT** contagious
- **NOT** a “case” of TB disease



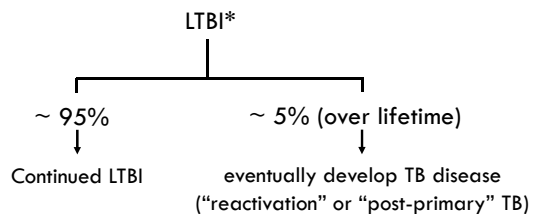
Latent TB Infection (LTBI)



There are medications available to treat LTBI and prevent TB disease!



TB Pathogenesis: Post-Primary TB Disease





* Outcome is influenced by risk factors that might not be present when LTBI is detected (e.g., diabetes, cancer, HIV infection)




Latent TB Infection vs. TB Disease



LATENT TB INFECTION	TB DISEASE
<ul style="list-style-type: none"> • TB bacteria in the body; bacteria are inactive (latent) • Does not feel sick; no symptoms • NOT contagious • Could develop TB disease if TB bacteria become active and begin to multiply • Treatment can PREVENT development of TB disease in future 	<ul style="list-style-type: none"> • TB bacteria in the body; bacteria are active and multiplying • Feels sick; symptoms such as fever, weight loss, fatigue • Could spread TB bacteria if contagious form of disease • Almost always curable if diagnosed in time and treated appropriately

Components of a Comprehensive TB Assessment



1. Health history
2. TB risk assessment
3. Testing for TB infection: TST / IGRA
4. Testing for TB disease: radiography, laboratory testing



 

1. Health History

Two components:

1. TB signs and symptoms review



Should be the **FIRST** component of **EVERY TB** screening!


Signs & Symptoms of TB Disease

- TB disease can involve almost any organ system and can occur in more than one organ system simultaneously
- Presentation depends on site(s) of disease (e.g., TB meningitis, TB lymphadenitis) and host immune response (e.g., children under 5 years of age)
- Diagnosis depends on clients and providers recognizing signs & symptoms of TB disease

THINK TB!

Systemic Symptoms of TB Disease





fever fatigue


night sweats

weight loss loss of appetite

pain and/or dysfunction

Symptoms of Pulmonary TB Disease



cough \geq 2 weeks

shortness of breath



chest pain

hemoptysis

fever fatigue

night sweats

weight loss loss of appetite

TB Tip #4



1. Health History

Two components:

1. TB signs and symptoms review
2. TB history
 - TB exposure history
 - Prior diagnosis/treatment for TB disease or LTBI
 - Results of prior TB screening tests
 - BCG vaccination history



2. TB Risk Assessment



Gather information to help answer:

1. *How likely is it that the client is infected with TB bacteria?*
 2. *How likely is it that the client would develop TB disease if s/he is infected with TB bacteria?*
- Findings influence screening pathway and areas for client education
 - **Incomplete HLTH 939 forms can cause delays and can interfere with the ability of TB physicians to interpret tests results**



Who is at Increased Risk for TB Exposure and Infection with TB Bacteria?



- Close contacts of infectious TB cases
- Immigrants from countries with high TB incidence
- People with social and/or behavioral risk factors such as homelessness and injection drug use
- Employees and other persons who spend time in health care and correctional facilities
- Aboriginal Peoples
- Long-term travelers to high-incidence countries

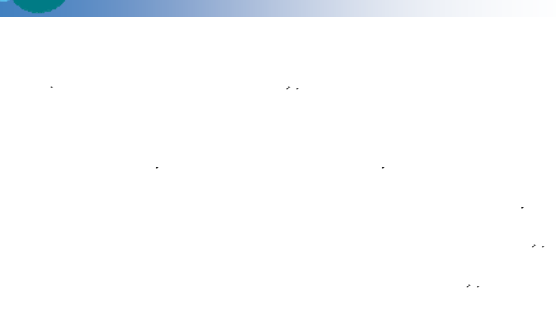
Relative Risk for Development of TB Disease after Infection



Detailed information is available in the *Canadian Tuberculosis Standards*.

- HIV infection, AIDS
- Recent infection (e.g., contact)
- Diabetes
- Infants and young children
- Immune suppressing treatments/medications
- Chronic renal failure
- Alcohol overuse
- Cigarette smoking

TB Tip #5



Testing for TB Infection

1. Tuberculin skin test (TST)

Induces cell-mediated, delayed hypersensitivity reaction in people whose immune systems are "familiar" with TB bacteria due to TB infection or BCG vaccination

2. Interferon gamma release assay (IGRA)

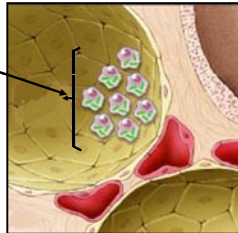
Measures production of interferon-gamma by sensitized T-cells when exposed to TB antigens



Development of Immune Response: Weeks 3 to 8

TB bacteria multiply within macrophages

Cell mediated immunity and delayed-type hypersensitivity (CD4) are stimulated*



Tuberculin Skin Testing

- Intradermal injection of 5 test units (TU) of purified protein **derivative** (*i.e., not the actual bacteria*)
- False negatives for biologic reasons (e.g., host immune suppression) or technical reasons (e.g., improper technique or storage of tuberculin antigen)
- False positives from BCG vaccination, infection with non-tuberculous mycobacteria
- **Reaction size must be interpreted in the clinical context**



Interferon Gamma Release Assay

- Blood test
- More specific than TST because results are **not influenced by BCG vaccine** or most NTM
- Two products available in Canada (QFT-GIT & T-Spot)
- Sensitivity is diminished by HIV and medical immune suppression; T-Spot results may be less influenced
- Access to IGRA testing is available in BC
- **Results must be interpreted in the clinical context**



TB Tip #6



Testing for TB Disease


- Radiography (x-rays)
- Laboratory testing



TST and IGRA are methods for
detecting infection with TB bacteria
NOT for diagnosis of TB disease



Chest Radiography



- Although helpful, can be non-specific
- Typical findings can be absent
- Atypical features more common in young children and those with immune compromising conditions
- Inter-reader variability









Some Indications for Chest X-Ray

- Signs or symptoms consistent with current TB disease
- New “positive” TST or IGRA
- History “positive” TST or IGRA, or prior TB disease and TB screening is required (e.g., pre-employment)
- Admission requirement for residential detox and/or drug and alcohol treatment programs
- **Some** TB contacts (see BCCDC TB Manual)
- Establish baseline for populations at high risk (e.g., HIV+)
- Immigration medication examination (IME) requirements


Chest Radiography Contraindications



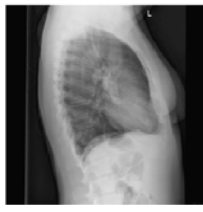



Chest X-Ray Views



Posterior Anterior (PA)





Lateral



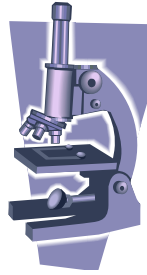
Sensitivity can be improved in children < 5 years old and clients with HIV by reviewing BOTH views



TB Tip #7

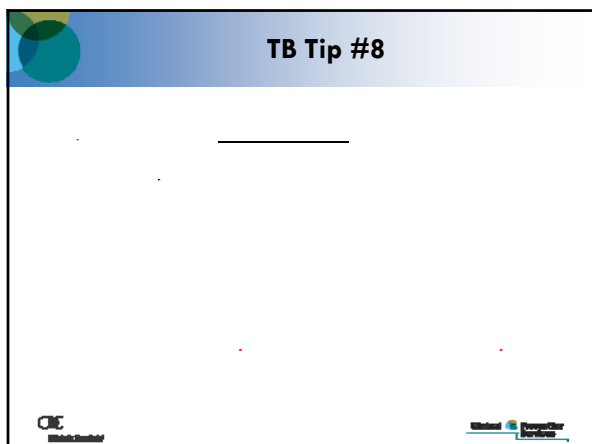



Laboratory Testing





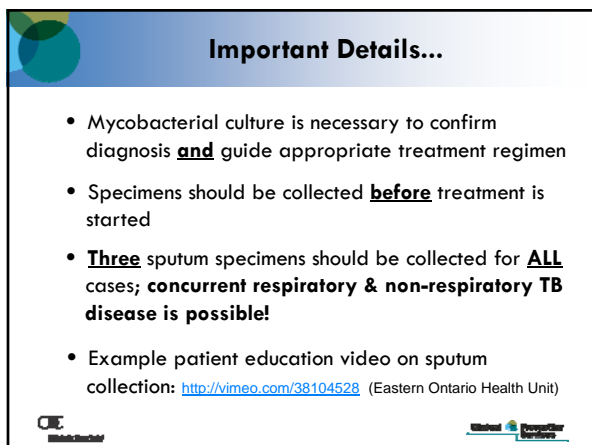
- Smear microscopy (AFB smear)
- Nuclei acid amplification tests (NAAT) (e.g., "PCR", Accuprobe, Xpert MTB/RMP)
- Mycobacterial culture
- Species identification
- Drug susceptibility testing (DST)
- DNA fingerprinting (molecular epidemiology)
- Histopathology (e.g. tissue)





TB Tip #8

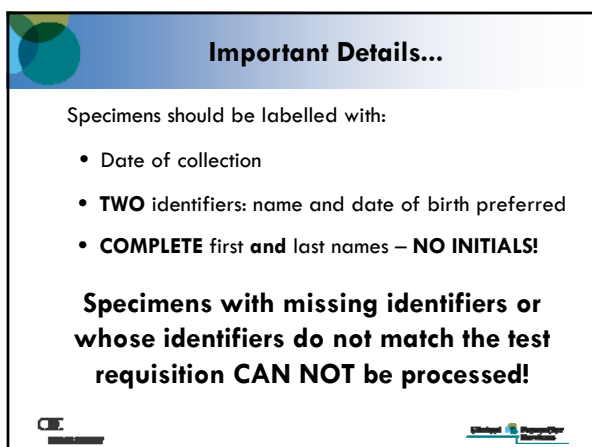
 



Important Details...

- Mycobacterial culture is necessary to confirm diagnosis **and** guide appropriate treatment regimen
- Specimens should be collected **before** treatment is started
- **Three** sputum specimens should be collected for **ALL** cases; **concurrent respiratory & non-respiratory TB disease is possible!**
- Example patient education video on sputum collection: <http://vimeo.com/38104528> (Eastern Ontario Health Unit)





Important Details...

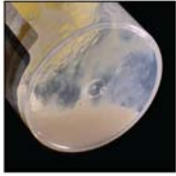
Specimens should be labelled with:



- Date of collection
- **TWO** identifiers: name and date of birth preferred
- **COMPLETE** first **and** last names – **NO INITIALS!**

Specimens with missing identifiers or whose identifiers do not match the test requisition CAN NOT be processed!



TB Tip #9



Smear Microscopy (AFB Smear)

- Available through PHMRL and some hospital laboratories; results in 24-48 hrs
- “STAT” smears are from un-concentrated specimens; this can lead to falsely negative results
- Highly **sensitive** for mycobacteria but not **specific** to TB
- AFB smear positive **respiratory** specimens undergo TB “PCR” testing; a type of nuclei acid amplification test (NAAT) used to detect MTB complex DNA
- PCR results are generally available the next business day



 

Smear Microscopy (AFB Smear)

If AFB are seen (“smear positive”), results are reported semi-quantitatively:

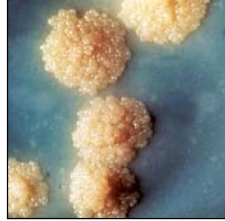
Grading System (in BC)
Negative (no AFB seen)
Few AFB - Repeat
1+
2+
3+
4+

Risk of transmission from cases with respiratory TB disease is generally thought to correlate with degree of smear positivity; the higher the AFB count at time of diagnosis, the more infectious the case.

Mycobacterial Culture

- “**Gold standard**” for diagnosis of TB disease
- Can be performed on **all** specimen types
- Timing of results will vary by bacterial load; generally **more bacteria = faster culture**
- Timing of “negative” report depends on type of culture media; in BC both liquid (6wks) and solid (8wks) media are used

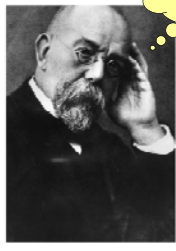


M. tuberculosis growing on solid culture media



Species Identification

TB or not TB?



Dr. Robert Koch

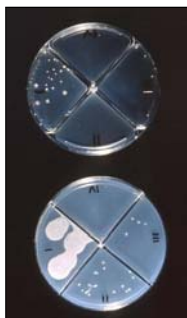
Requires positive culture

Findings help to guide treatment regimen while drug susceptibility tests are pending (e.g., *M. bovis* is PZA resistant) and useful for epidemiologic studies

Results usually available within a few days



Drug Susceptibility Testing (DST)



- **Requires a positive culture**
- Susceptibility to “first-line” TB drugs checked for all **first positive** culture isolates from each **new** case
- Results usually available within 14 days from positive culture
- Can be repeated if acquired drug resistance is suspected (e.g., failure to convert cultures to negative)



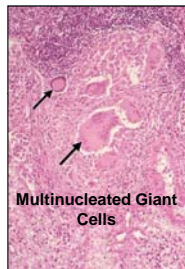
TB Genotyping (DNA Fingerprinting)

- Requires a **positive culture**
- Identify the genetic pattern of the strain of TB bacteria that a person **with TB disease** is infected with
- Can be helpful for:
 - surveillance purposes (e.g., to identify TB outbreaks)
 - identifying relapse vs. disease from re-infection
 - identifying chains of transmission among cases
 - identifying unusual sites of transmission
 - identifying possible cross-contamination among specimens processed in the same laboratory



Histopathology

- Clinical specimens (e.g., biopsies) are examined for findings common to TB disease
- Specimens that are “fixed” in formalin **will not grow** in mycobacterial culture; additional material should **always** be collected and sent for AFB smear and mycobacterial culture



Next Webinar October 4th: “Treatment of LTBI and TB Disease”