Review and Update of Tuberculosis
NB/PEI CHICA Chapter

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Dr. Lamont Sweet
Deputy Chief Public Health Officer
MYCOBACTERIA

Three types of mycobacteria are known:

1. Mycobacterium tuberculosis and Mycobacterium bovis
   - Mycobacterium tuberculosis causes human TB and will be the focus of our discussion today.
   - Mycobacterium bovis was common in cows, transferred to humans in milk and no longer a major problem
2. Mycobacterium leprae which causes leprosy and is not found in Canada

3. Atypical Mycobacteria which include many species in the environment in Canada, rarely cause human disease but are common in the lung of humans
   - 75% of Mycobacteria identified from sputum in PEI is in this category
   - Atypical Mycobacteria are not contagious
MYCOBACTERIA

- Mycobacteria are slender, rod-shaped bacteria

- The cell walls are very different from other bacteria because 60% of the cell wall is LIPID
MYCOBACTERIA - ACID FAST BACILLI (AFB)

- If a smear is made of a specimen on a slide, a dye is added and then washed with strong acid-alcohol, the lipid in the wall of mycobacteria retains the dye
- All other bacteria will not retain the dye
- Mycobacteria are therefore called Acid Fast Bacilli (AFB)
- All mycobacteria are acid fast and therefore tuberculosis cannot be distinguished on a slide from atypical mycobacteria
IMPORTANCE OF TUBERCULOSIS

• TB was present in ancient Egypt

• TB can infect any organ but lung is main organ infected

• With growth of cities, crowding increased and so did TB

• In the 1600's and 1700's TB caused 25% of the deaths in Europe
IMPORTANCE OF TUBERCULOSIS

• TB increases with poverty, poor nutrition, crowding, and wars

• TB decreased in 1900’s before antibiotics due to better nutrition

• AIDS resulted in world-wide increase and now one third of world’s population infected with TB
ANTIBIOTIC ERA

• 1946 – Streptomycin introduced – injections needed, deafness a side effect.
• 1952 – INH – more effective, fewer side effects, oral administration.
• 1970 – Rifampin – oral administration
  ▸ Combination therapy with antibiotics common
  ▸ Combination therapy for 2 years effective
  ▸ Recently combined therapy for 6 months effective (if sensitive)
  ▸ INH for 9 months for latent TB infection (LTBI)
SPREAD OF TB

- TB is spread almost always by inhalation of droplets or “droplet nuclei” from the respiratory tract containing the bacteria.

- The bacteria often spread to the lymph nodes and sometimes to the blood.

- If in the blood, any organ can be involved but the kidneys, brain and lymph nodes in the abdomen are the most commonly infected.

- In the lung, anything from no changes to a small density to severe pneumonia can occur.

- Pleuricy used to be common as were cavitation in the lung.
SPREAD OF TB

• More than 90% of those infected fight off the bacteria without ever having any symptoms

• Tuberculin Skin Test (TST) converting to positive can be the only indication of TB infection

• An infected person, or one whose TST test converts to positive, can harbor dormant TB for their lifetime (latent TB infection) and can reactivate with age or decreased immunity

• PEI had highest rate of TB in Canada in 1920's and many seniors will reactivate until 2020
SPREAD OF TB

- Large droplets carrying TB organisms do not reach the lungs and do not result in TB
- Only TB results if in small droplets reach alveoli or the larynx
- TB organisms remain infectious in environment for prolonged periods of time and travel as an aerosol for long distances indoors
SPREAD OF TB

- Laryngeal TB causes hoarseness and is very contagious
- Overall TB is not very contagious
- However TB is very unpredictable
TUBERCULIN SKIN TEST (TST)

• Tuberculin contains 0.1 ml of 5 TU of Purified Protein Derivative (PPD) which is the dead antigen of TB organisms

• A person who breathes in TB organisms tries to fight them off by producing antibodies

• Within 2-8 weeks of breathing in TB organisms, the TB test will convert to positive
TUBERCULIN SKIN TEST

- Many who have a positive Tuberculin test do not have any signs of TB on chest X-ray.

- They have “Latent TB Infection (LTBI)” which can reactivate due to age, stress, illness, alcoholism, cancer, etc.

- Having had BCG (Bacillus Calmette-Guerin) causes a positive Tuberculin Skin Test.

- A course of INH will reduce the chances of TB reactivating by 90% or more but has worrisome rate of adverse reactions particularly INH-induced hepatitis.
INACTIVE TB

- Chest X-ray shows some sign of old or previous TB: scaring, calcification, increased density, pleural thickening, granuloma, etc.

- Immigrants with INACTIVE TB have a significant risk of developing TB in the first two years after arriving in Canada due to stress – particularly if a refugee

- PEI has had immigrant cases from Ethiopia, Philippines, Bhutan and Sudan who reactivated within two years and one from Guatemala after many years

- We arrange follow-up of inactive cases of TB among immigrants and refugees for two years with chest x-rays
DIAGNOSIS OF TB

Lung - Sputum – Halifax

- Can be coughed specimen (X3) or induced (aerosol) or bronchoscop (Bronchoalveolar Lavage-BAL)
- Put on slide and stain for Acid Fast Bacilli
- Reported as:
  ‣ None
  ‣ Rare = 3-9/slide
  ‣ +1 = 1-9/10 fields
  ‣ +2 = 1-9/field
  ‣ +3 = 10-90/field
  ‣ +4 = greater than 90/field
- The more organisms, the more contagious is the patient
- Do not know if diagnosis is TB or Atypical from smear but the more organisms the higher the chance of TB
DIAGNOSIS OF TB

Culture – Halifax

• All specimens incubated
• If organisms grow, which usually occurs in 10 days, they are probed (PCR test) to see if the organism is TB or Atypical Mycobacteria
• Usually 25 % of positive specimens on microscopy are TB with 75 % being Atypical Mycobacterium
• The proportion of Atypical Mycobacterium from smears showing AFB is increasing as TB decreases
Precautions While Waiting for Results

- Often the patient with a positive smear for AFB is put on respiratory precautions in hospital until the culture is back and depending upon the chest x-ray and clinical situation.
- The patient may be started on therapy while awaiting results (usually 3 or 4 anti-TB antibiotics).
- Contact tracing is only started before the PCR result is back if clinical picture is highly suspicious of TB.
- Usually the precautions are only to “play it safe” but often causes great concern to those who have worked with the patient before.
OTHER ORGANS

• TB can be found in many other organs or in lungs at surgery or autopsy

• If active in the lungs, we usually consider the patient contagious and test contacts - a smear is helpful

• TB in most other organs (i.e. lymph nodes) is not contagious and therefore only close/family contacts tested unless rare source is suspected (TB joint)

• Treatment for the patient is longer if it is not in the lungs
SMEAR NEGATIVE, CULTURE POSITIVE TB

- Used to consider that the risk of being contagious was almost zero

- Recently some increased concern about contagiousness

- PEI a bit more aggressive but not as much as some other parts of Canada
DURATION OF CONTAGIOUSNESS OF ACTIVE PULMONARY TB

• For many years respiratory precautions considered necessary for only 10-14 days after a patient with active TB is placed on treatment

• Recently the lab has cultured TB organisms for many weeks while on therapy with precautions extended

• A positive smear for AFB may be due to living or dead TB organisms

• Duration of respiratory precautions varies from 3 to 8 weeks for most TB patients once they have started therapy

• It is not certain that the patients are really contagious for any more than 14 days on therapy if taking medications and sensitive
DURATION OF CONTAGIOUSNESS OF ACTIVE PULMONARY TB

- If patients are taking their medication, follow up testing of sputum should be minimal (some provinces almost too aggressive with follow up testing on patients).

- For protection against TB, Health Care Workers should wear a high level mask (N95's or equivalent).

- Usually a patient with highly contagious TB is immediately admitted to hospital on PEI and cultured for many weeks.
TUBERCULIN TESTING BOOSTER (TWO STEP)

• Child with negative tuberculin exposed to TB in PEI many years ago

• Fights off TB, no signs in lung but TST + in 8 weeks

• With advanced age the TST response declines until it may become negative

• Test the patient 10 days again after the initial and the first tuberculin has booster the response and the test is now positive (called immunological memory) and patient booster positive
TUBERCULIN TESTING BOOSTER (TWO STEP)

• These persons have dormant TB organisms and can reactivate if positive TST due to TB

• In PEI we used to only booster residents over 45 years because rare person under 45 years was exposed to TB as a child and therefore very unlikely to be booster positive

• Immigrants of any age who screen positive on the TST and should have a booster
TUBERCULIN TESTING BOOSTER (TWO STEP)

- BCG often gives positive tuberculin test, usually less than 20 mm and confuses the tuberculin result

- Health care workers most likely to have had BCG

- Many foreign countries give BCG (particularly Central America and the former Yugoslavia)

- Now tend to booster test everyone needing screening because national protocols ask for booster testing

- The IGRA will identify those whose TST + test is due to TB
BCG

- Immunization for TB
- Weakened (attenuated) tuberculosis organisms
- Can lead to widespread disease in immune deficient persons
- Best protection against meningitis and miliary (extensive lung) tuberculosis – child versus adult
- Given intradermally
- Results in positive tuberculin reaction without infection unless immune deficient
- Cannot reactivate years later after receiving BCG
BCG

- BCG was given mainly to young children in areas with high rates of TB (First Nations Communities)
- Also to health care workers in areas of high tuberculin incidence
- Many health care workers in PEI received BCG until 1976 with the school BCG program discontinued in 1966
TB CONTACT INFORMATION

• **Index Case:** patient who has or may have active TB

• **Contacts:** persons breathing in same air as the possible index case in an enclosed space
TB CASE AND CONTACT ASSESSMENT

- Does the Index Case have TB? What is the risk?
  - Weight loss
  - Night sweats
  - Fever
  - **Cough** – how often, how long, any laryngitis?
  - Tuberculin Skin Test – when, results in mm?
  - History of TB – case, family or among contacts?
  - Smear – if positive, how positive?
  - PCR – positive or negative?
  - Chest X-Ray - **cavitation** of major concern
CONTACT INVESTIGATION

- Active Contagious Pulmonary TB is certain
  - Contact Investigation: Identify all contacts who breathed in same air as index case in the last three months, and assess the degree of contact:
    - Household contacts are the highest risk
    - Contacts with immune deficiency are at risk
    - Does the contact already have symptoms of TB?
    - How close and how long was the contact?
    - Was the case coughing during the contact?
    - Has the contact had a previous TB test? When? Result (in mm. if possible)?
    - Did the contact have BCG in the past? When?
CONTACT INVESTIGATION

• Close Versus Casual Contacts
  ‣ Most vital part of any investigation into a case of active pulmonary TB
  ‣ A judgment decision into how long a contact was breathing in air which could contain TB
  ‣ Regular household contacts are close
  ‣ Card playing and eating at same table contacts on a regular basis are close
  ‣ One time contacts usually casual
  ‣ Details of coughing at time of contact important
  ‣ Non-household contacts need assessment for time in contact while case coughing
“CLOSE” AND “CASUAL” ARE MISNOMERS

- Close and casual really means “high risk” and “low-risk” (cannot change centuries of terminology)
- Kiss on the cheek not a close contact
- Distant contacts in an enclosed space can breathe in droplets
- We need close and casual to assess need for prophylaxis
HOSPITAL CONTACTS

• Inquire as to precautions
• Almost always the HCW contact is casual
• Exceptions may be: A) Respiratory therapists  B) Pathologists/histologists
CONTACT INVESTIGATION

• **Close Versus Casual Contacts (Cont’d)**
  `•` Close contacts need INH prophylaxis while casual do not
  `•` All close and casual contacts need TST or chest x-rays
  `•` Remote contact can be tested if they wish
  `•` Contact usually more enthusiastic about being tested when investigation started.
CONTACT INVESTIGATION

• Active Contagious Pulmonary TB is certain (Cont’d)

  ‣ If outside household, recommend an N95 mask
  ‣ Until not contagious anyone entering the home of an active case should wear an N95 and case wear a surgical mask
  ‣ Household or close contacts may need INH prophylaxis
CONTACT INVESTIGATION

- TST first
- If positive, record mm (penalty for not recording mm should be death)
- If negative repeat in 8 weeks
- Do not 2 step or booster test because cannot be certain booster positive is due to previous exposure (another change in policy)
- Any positive tests are followed up by a chest x-ray
CONTACT INVESTIGATION

• Active Contagious Pulmonary TB is NOT certain or likely but the case is under investigation
  ▸ Recommendation is to wear an N95 mask for HCW and non-household contacts and await the test confirmation on the case
  ▸ Almost all will NOT have active contagious infectious TB
  ▸ The mask is a precaution but does result in fear
OTHER TB CONTACT INVESTIGATION EXAMPLES

• How likely is it that possible index case has TB?

  ▶ Patient dies and culture already shows TB:  **Act Now**
  ▶ Smear loaded in AFB organisms, the case is from the Sudan, losing weight for 2 months, large cavity on CX-Ray:  **Act Now**
  ▶ CX-Ray shows a spot, patient is well with no cough, X-Ray screened for Armed Forces, TB test negative, a few organisms on smear:  **Wait for PCR in 10 days**
  ▶ Patient has a mild cough, small spot on lungs, bronchoscopy shows a few AFB organisms. Admission for TB investigation
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<th>Year</th>
<th>Tuberculosis Cases in</th>
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<th>Tuberculosis Cases in</th>
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<td>2</td>
<td>2001</td>
<td>3</td>
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<tr>
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MULTI DRUG RESISTANT TUBERCULOSIS (MDR-TB)

• Multidrug resistance is defined as resistance to Isoniazid and Rifampin
• Became a major concern when AIDS arrived
• The percentage of MDR isolates in Canada has remained below 2% from 1999-2009
• Most MRD isolates are from BC, ON, and PQ
• The Atlantic Provinces, NT and Yukon have never reported a case of MDR Tuberculosis
• Canada rate is 1.2% and world rate is 4.8%
### TOTAL NUMBER OF ISOLATES AND PERCENTAGE MDR IN CANADA: 1999-2009

<table>
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<th>Year</th>
<th>Total number of Isolates</th>
<th>MDR-TB (%)</th>
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<tbody>
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<td>1,415</td>
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<td>2000</td>
<td>1,490</td>
<td>15 (1.0)</td>
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<td>2001</td>
<td>1,475</td>
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<td>1,419</td>
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<td>1,407</td>
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<td>2004</td>
<td>1,378</td>
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<td>2005</td>
<td>1,336</td>
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<td>2006</td>
<td>1,389</td>
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<td>2007</td>
<td>1,267</td>
<td>11 (0.9)</td>
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<td>2008</td>
<td>1,356</td>
<td>15 (1.1)</td>
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<tr>
<td>2009</td>
<td>1,321</td>
<td>18 (1.4)</td>
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<td>TOTAL</td>
<td>15,253</td>
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RISK OF MDR TB IN ATLANTIC PROVINCES

- Most MDR TB in BC, ON, and PQ
- Foreign born 6 times more likely to have MDR TB
- Aboriginal population in Canada and residents of Canada very low rate of MDR
- Aboriginal population in Maritime Provinces have very low rate of TB
- Canadian rate of MDR TB not increasing
- Conclude that significant increase or outbreak of MDR TB in Atlantic Canada not likely in near future unless Immigration increases significantly
DIRECTLY OBSERVED THERAPY (DOT)

• Poor adherence of anti-TB therapy in Canada is commonest reason for treatment failure
• DOT occurs when HCW watches patient swallow the pills
• Usually DOT consists of twice weekly doses of medication
• TB experts in Western and Northern Canada love DOT
ADVANTAGES OF DIRECTLY OBSERVED THERAPY

• More likely to get the prescribed pills
• More likely to achieve cure and decreased chance of spread

DISADVANTAGES OF DIRECTLY OBSERVED THERAPY

• Higher doses may lead to increased chance of adverse reaction if biweekly
• Very time consuming for HCW
• Often chances of non-compliance not explored by nurse
POTENTIAL FOR OUTBREAK OF TB IN ATLANTIC CANADA

• In Maritimes not likely
  ‣ Low rate among Aboriginals
  ‣ Low rate of Immigration
  ‣ Low rate of MDR TB
  ‣ Efficient Public Health Nursing Programs
  ‣ Few remote communities

• Newfoundland and Labrador more likely because of remote communities

• However, outbreak of TB can occur anywhere particularly if delay in diagnosis a case

• Delay in diagnosis on PEI occurred once in 22 years.
NONCOMPLIANCE OF TB CASE FOR PRECAUTIONS

- Occasionally a case of TB will not comply with precaution recommendations and put contacts at risk.

- Quarantine – quarantine means **case** and **contacts** forced to remain separate from others until incubation period over.

- Isolation – separation of active case from contacts during period of communicability with precautions taken to prevent transmission of those who do have contact.
NONCOMPLIANCE OF TB CASE FOR PRECAUTIONS (Cont’d)

- Quarantine appropriate for smallpox, measles and SARS due to short incubation period

- Quarantine not effective for pandemic influenza

- Isolation is appropriate for TB but problems come when case refuses to comply, i.e. homeless on street

- For noncompliance to isolation recommendation for TB case, a Health Order under the Public Health Act is the most common action taken
NONCOMPLIANCE OF TB CASE FOR PRECAUTIONS (Cont’d)

- Specific measures are taken to ensure adherence to specific treatment and control measures are taken.

- Usual action is to admit to hospital where Health Order ensures proper precautions are followed under conditions similar to incarceration.

- This is where Public Health really “means business”.

ONE ISLAND FUTURE

ONE ISLAND HEALTH SYSTEM
MAJOR ADVANCES IN TB

In the past 20 years there have been 2 major advances in investigation of TB:

1. PCR
   - Used to have to await culture for 6-8 weeks
   - Now PCR usually available in 10 days

2. IGRA
   - Great advancement in latent TB infection and contact investigation
WHY HAS TB SURVIVED?

- If low contagiousness, why so widespread global infection in humans?
  1) Difficult to treat: multi-drugs and for months (particularly in third world)
  2) Poverty, overcrowding, poor nutrition and immune deficiency of AIDS
  3) Droplets contagious for long distances and spread by respiratory route
WHY HAS TB SURVIVED?

4) Latent TB: not ill but can reactivate many decades later and are then contagious

5) TB organisms remain contagious in environment for prolonged periods of time and travel long distances indoors