TUBERCULOSIS AND THE EYE

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Course Description

• This course will give an introduction to tuberculosis by some facts and statistics

• This course will provide an overview on tuberculosis transmission, screening, testing, treatment and preventing the transmission of tuberculosis

• This course will also highlight some ocular consequences of being infected with tuberculosis and ocular side effects of tuberculosis medications
Course Objective

• Briefly introduce tuberculosis and its impact as a public health concern
• To learn about tuberculosis’ mode of transmission
• To learn about various screening methods for tuberculosis
• To learn about tools we use to test for tuberculosis
• To learn about what treatment options are available for tuberculosis
• To learn about how to protect yourself from an active tuberculosis patient
• To highlight how a tuberculosis infection relates to optometry and what ocular manifestations you might encounter
Optometric considerations

- Pulmonary disease can increase the risk of ocular disease
  - Dry Eye
  - Glaucoma
  - ARMD
  - Retinal vascular changes
  - Optic nerve head changes

- Pulmonary disease can contraindicate ocular medications
Optometric considerations

- **Medications** taken for pulmonary disease can cause ocular problems
  - Optic atrophy
  - Glaucoma
  - Cataract
  - Blurred vision
  - Tear effects
  - Conjunctivitis
INTRODUCTION TO TUBERCULOSIS
Facts and Data about TB

- **TB is one of the world’s deadliest diseases:**
  - Approximately 1/3 of the world’s population is infected
  - 10.4 million new cases and 1.8 million deaths in 2015
  - TB is a *leading* killer of people who are HIV +

- Intense public health efforts to control TB has caused all time low incidence rates in US to 3 cases per 100,000 (2015)
  - Rates in US have remained stable since 2013

Rising Concerns

Rising concern:

- **Multidrug resistant TB (MDR-TB):** resistant to 2 most potent TB drugs (isoniazid and rifampin)
- **Extensively drug-resistant TB (XDR-TB):**
  - Rare type of MDR-TB
  - MDR-TB + resistant to fluoroquinolone, and at least one of three injectable second-line drugs
  - Increasing worldwide and recent evidence of spread person to person (50% cure rate)

TRANSMISSION
TB transmission

According to CDC: virtually all TB is transmitted by airborne particles

- Released during coughing, sneezing, shouting, or singing

TB CANNOT be spread by:

- Shaking hands
- Sharing food/drinks
- Sharing toothbrushes, drinking glasses, eating utensils
- Touching bed linens, toilet seats, clothes, other surfaces
- Kissing

About 30% of heavily exposed are infected

- % ↑ if patient has DM or HIV+

*Heavy exposure* = being around sick person for 24 hours for 6 months
TB transmission

**Active infection**

- **Latent and noninfectious**
- **Reactivation:**
  - 5% develop infection within 2 yrs
  - 10% over life time
  - Caused by DM, HIV, corticosteroids, stress
  - If HIV+ : risk of 7-10% TB infection per year

Who is at high risk for TB?

**Individuals at higher risk for TB:**

- Close contacts of patients suspected of having TB
- Immune suppressed (HIV, immune modulators, etc)
- Recently exposed
- Health care workers who serve high risk patients
- Residents and employees in long-term care facilities, jails, mycobacteriology labs, homeless shelters
- Recent immigrants from high TB prevalence countries
- Injectable drug users (suppressed immune system)
- Patients with chronic medical conditions
- Children < 4 years of age (less developed immune system)
SCREENING FOR TB
Screening for TB

Screening is often performed with the **Tuberculin Skin Test**

- **AKA:** Mantoux test or PPD

**The Procedure:**
- Purified protein derivative (PPD-S) tuberculin placed intradermal

**The Results:**
- Exposed or not, does **not** give info about active or latent

**The Details:**
- Delayed hypersensitivity response so read 48 - 72 hours later
- Evaluate for size of **induration** not redness
- Measured in **mm transversely** to the long axis of the forearm

Interpretation of TB skin test results depends on risk factors:

Induration of 5 mm or more is positive if:
- Immunosuppressed (HIV or meds) or
- Close contact with person with active TB/recently exposed or
- Chest x-rays show fibrosis consistent with TB

Induration of 10 mm or more is positive if:
- Any high risk individual who does not meet first criteria (includes health care workers)

Induration of 15 mm or more is positive in all
Interpretation of TB skin test

**Positive Test results:**

**Mantoux Conversion**

Either:

- A change from a negative $\rightarrow$ a positive reaction

Or

- An increase of $\geq 10$ mm in size
The 2 step test

CDC recommends **2 step test** for initial test if periodic testing needed

- **Goal**: Prevents interpreting 2\textsuperscript{nd} test (or future test) results as **new** infection
- If infected many years ago few sensitized lymphocytes so no significant response on first test
- Repeat test \(\rightarrow\) larger “**boosted**” response which is considered baseline
- **Drugs are super toxic**, so should only treat those that need it!
Other screening tests

Interferon gamma release assays (IGRAs)
Two types of IGRAs are FDA approved:
1. QuantiFERON®-TB Gold In-Tube Test (QFT-GIT)
2. T-SPOT®.TB tests (T-Spot)

- Blood samples are mixed with TB proteins (antigens) and controls; then incubated for 16-24 hours
- If infection present: WBCs will release interferon-gamma in response to antigens
- Test result interpretation depends on risk factors and general health of patient
**TST vs IGRA**

TST is 3-4 times **less expensive** than IGRA

<table>
<thead>
<tr>
<th></th>
<th>TST</th>
<th>IGRA</th>
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<tbody>
<tr>
<td><strong>Tuberculin</strong></td>
<td>Tuberculin is injected under the skin and produces a delayed-type</td>
<td>Blood is drawn for testing; test measures the immune response to the</td>
</tr>
<tr>
<td></td>
<td>hypersensitivity reaction if the person has been infected with</td>
<td>TB bacteria in whole blood</td>
</tr>
<tr>
<td></td>
<td><em>M. tuberculosis</em></td>
<td></td>
</tr>
<tr>
<td><strong>Requires</strong></td>
<td><strong>Two or more patient visits to conduct the test</strong></td>
<td><strong>One patient visit to conduct the test</strong></td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>48 to 72 hours later</td>
<td>24 hours (depending on the batching of specimens by the laboratory</td>
</tr>
<tr>
<td><strong>Available</strong></td>
<td></td>
<td>and transport)</td>
</tr>
<tr>
<td><strong>Causes</strong></td>
<td><strong>Booster phenomenon</strong></td>
<td><strong>Does not</strong></td>
</tr>
<tr>
<td><strong>Reading</strong></td>
<td><strong>Subjective</strong></td>
<td><strong>Laboratory test not affected by HCW perception or bias</strong></td>
</tr>
<tr>
<td><strong>BCG Vaccination</strong></td>
<td><strong>Can cause false-positive result</strong></td>
<td><strong>BCG vaccination does not cause false-positive result</strong></td>
</tr>
<tr>
<td><strong>A negative</strong></td>
<td><strong>Does not</strong></td>
<td><strong>Does not</strong></td>
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<tr>
<td><strong>reaction</strong></td>
<td><strong>Excludes the diagnosis of</strong></td>
<td></td>
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<tr>
<td><strong>LTBI or TB</strong></td>
<td><strong>Disease</strong></td>
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bacilli Calmette-Guerin (BCG) vaccine for TB
Tested **POSITIVE** for TB...

**Diagnosis of active or reactivated TB:**

- Depends on a **good history** and **clinical evaluation** because the disease tends to start insidiously.
- **Lungs** are most common site of disease (in Canada and US).
- **Classic symptoms** of pulmonary TB (non-specific symptoms):
  
  - Cough with or without hemoptysis
  - Sweats
  - Anorexia/Weight loss
  - Malaise
  - Chills
  - Chest pain (pleuritic disease)
  - Fever

- TB can also affect other sites like **lymphatic system**, bones and joints, **CNS**, **kidney**, etc.
TESTING FOR TB
Chest x-ray

- Posterior-Anterior (PA): standard chest x-ray view
- Since lungs manifests similarly for many diseases:

**Assume TB if:**

1. Tests positive for TB
2. See abnormality in lungs
Sputum sample

- 3 samples 8-24 hours apart with one in AM

**Testing Sputum Samples:**
- **Stain** looking for acid fast bacilli (AFB)
  - Poor sensitivity
- **Culture**
  - Cultures are likely to be positive with smaller #’s of bacilli and are gold standard but very slow (weeks)
- **Perform nucleic acid amplification test (NAA)**
  - More accurate than stains and give results in < 24 hours
<table>
<thead>
<tr>
<th></th>
<th>Latent TB infection</th>
<th>Active or Reactivated TB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TST or IGRA</strong></td>
<td>Usually positive</td>
<td>Usually positive</td>
</tr>
<tr>
<td><strong>Signs/Symptoms</strong></td>
<td>None</td>
<td>Fever, cough, chest pain, weight loss, night sweats, hemoptysis, fatigue, decreased appetite</td>
</tr>
<tr>
<td><strong>Chest x-ray</strong></td>
<td>Typically normal</td>
<td>Usually abnormal (maybe normal in adv immosuppression or extrapulmonary disease)</td>
</tr>
<tr>
<td><strong>Sputum sample</strong></td>
<td>Negative</td>
<td>Positive (negative in extrapulmonary disease or min/early pulmonary disease)</td>
</tr>
<tr>
<td><strong>Spreading TB</strong></td>
<td>Cannot spread to others</td>
<td>May spread to others</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Should consider treatment</td>
<td>Needs treatment</td>
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TREATMENT FOR TB
Treatment

- Currently **10 medications** are approved in US and there are multiple treatment regimens
- Treat both **latent** and **active** but treatment differs
  - Will **ALWAYS** treat **ACTIVE**
  - Will **USUALLY** treat **LATENT**
- Considered latent TB if screening test is **POSITIVE** but there are no signs of active infection by **chest x-ray or sputum culture**
- Cure rate for extensively resistant TB is 50%!
Treatment

What factors to consider for treatment?

- Age
  - Young pts: will likely treat, will have to live with disease for LONG time
  - Elderly pts: drugs very toxic for elderly pts, TB is SLOW growing
- Immune status
- How long ago pt was exposed
  - Will likely treat more recent latent TB vs old latent TB
Treatment

**Goals for Treatment:**
- Cure infection
- Minimize death and disability
- Prevent drug resistance
- Reduce transmission (hit hard in the beginning to prevent spreading!)
Drugs to treat TB

• Rifampin or Rifapentine
• Isoniazid
• Pyrazinamide
• Ethambutol
Drugs to treat TB

• **Rifampin or Rifapentine**
  - Resistant strains develop easily so usually not given alone
  - **Rifapentine**
    - SE: Reddens secretions including urine and tears, stains contact lenses; liver damage, nausea&vomiting, fever

• **Isoniazid**

• **Pyrazinamide**

• **Ethambutol**
Drugs to treat TB

- **Rifampin or Rifapentine**
- **Isoniazid**
  - Most potent of anti-TB drugs
  - Can be administered alone for latent TB treatment
    - Chief risk: hepatotoxicity (d/c other drugs cleared by liver-alcohol, Tylenol)
    - Other SE: anemia, GI symptoms, rash, peripheral neuropathy, subepithelial corneal infiltrates, optic neuritis, visual field defects, EOM paresis
- **Pyrazinamide**
- **Ethambutol**
Drugs to treat TB

• Rifampin or Rifapentine
• Isoniazid
• Pyrazinamide
  • Resistant strains develop easily so usually not given alone
• Ethambutol
Drugs to treat TB

- Rifampin or Rifapentine
- Isoniazid
- Pyrazinamide
- Ethambutol
  - Does not develop resistance as easily
  - Ocular SEs: optic neuritis, macular edema, and pigmentation changes (permanent)

*Note: Care in patients with poor liver function for all TB meds*
To supplement the Treatment of **LATENT TB**

**Pyridoxine (Vitamin B6)**

- Usually co-administered for all latent TB treatments
- Very important for:
  - Pregnant patients
  - Diabetics
  - Alcoholics
  - Elderly
  - Malnourished individuals
- Helps *diminish risk of peripheral neuropathy* from *isoniazid*

*Vitamin C and D* may ↑ speed of TB treatment (kill TB faster)
PREVENTING TRANSMISSION
Preventing TB transmission

**Latent TB**: nothing to worry about

**Active TB or suspected active**:  
- Place patient in isolated room  
- Have patient wear surgical mask (50% effective)  
- Ask them to cover mouth and nose with tissues when they cough or sneeze  
- HEPA mask for health providers per OSHA  
- Once patient treated for 2 weeks, no longer considered infectious

**If believe exposed to disease**  
- Wait 8 weeks to take TB skin test (if known previously negative)
BACK TO OPTOMETRY
Risk of Ocular involvement with TB

• 1-2% of patients with TB have ocular sign (non-HIV+)
• \(\approx 18\%\) if HIV+ patients with TB have ocular signs

• Suggested that patients with TB have ocular exam
• Ocular signs can also be first indication of TB
Ocular Signs of TB

External Eye Structures

- Ulceration of lids with scarring and ectropion
- Cellulitis
- Dacryoadenitis (gland)
- Phlyctenulosis**
- Keratoconjunctivitis
- Interstitial keratitis (also syphilis)
- Episcleritis and Scleritis
Ocular Signs of TB

**Posterior Segment**
- Uveitis
- Choroiditis
- Retinal periphlebitis
- Optic neuritis
- Cranial neuropathy
Eye exams for TB patients

**Optometric involvement**
- Baseline and monthly exams
- Check VA’s
- EOMs
- Amsler grid
- Visual field
- If changes consistent with **optic neuritis**: inform PCP: d/c ethambutol
- Expect improvement in couple weeks to months
THANK YOU
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