UPDATE IN DIAGNOSIS AND TREATMENT OF LATENT TUBERCULOSIS INFECTION

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OBJECTIVES:

• Review epidemiology
• Review updates in diagnosis
• Review updates in treatment
GLOBAL SITUATION

• 2.3 billion people in the world infected with TB (latent TB infection).

• 9 million develop TB every year

• 1.4 - 2 million deaths from TB annually
GLOBAL SITUATION

• TB and HIV
  • 1/3 of people with HIV are infected with Mycobacterium tuberculosis
  • 30 times more likely to progress to active TB compared to those without HIV

• Drug resistant TB
  • Resistance to at least one of the first line drugs
  • Found in virtually every country surveyed by the WHO
In 2013, there were 9,588 new cases.
Rates decreased in both foreign and US-born individuals.
Rates still 11.5 times higher in foreign-born compared to US-born.
Goal of TB elimination is <1/100,000.
• 1.3/100,000 in 2012
• 1.1/100,000 average for 2008 - 2012
• From 2008 - 2012, percentages by county
  • Salt Lake: 55%
  • Weber-Morgan: 10%
  • Bear River: 9%
  • Utah: 8%
• Weber-Morgan rate for 2013 was
LATENT TUBERCULOSIS INFECTION (LTBI)
DEFINITION

• Evidence of having *Mycobacterium tuberculosis* infection:
  • Positive tuberculin skin test (TST) or Interferon Gamma Release Assays (IGRAs).
• No signs or symptoms of disease.
• Normal chest radiograph.
• Able to control the bacteria but unable to completely eradicate it.
1/3 of the world’s population have LTBI
~2.3 billion

11 million in the USA estimated to have it.

10% will progress to active disease/tuberculosis (reactivation).

5-10% will develop active TB within 2 years of infection (primary TB).

Picture courtesy of Sue Wang & Ian Durrant. Statistics courtesy of CDC.
• *Mycobacterium tuberculosis*
  - Belongs to the group *Mycobacterium tuberculosis* of which *Mycobacterium bovis* and *africanum* are members.

• Transmission is via inhalation (airborne)

• Primary tuberculosis
  - Mild, self limited pneumonic illness
Transmission of Tuberculosis and Progression from Latent infection to Reactivated (Active) TB

PREVENTION (BCG vaccination)

- Live attenuated vaccine of *Mycobacterium bovis*.
- Prevents tuberculosis and other mycobacterial infections.
- Duration of protection believed to be about 10-15 years.
- Decreases the incidence of miliary tuberculosis and tuberculous meningitis.
- May contribute to a positive tuberculin skin test.
TESTING

• Targeted
  • Identify, evaluate and treat those at high risk for
    • Having LTBI.
    • Developing active TB disease from LTBI.
    • Increased risk of recent exposure to individuals with active TB disease.

• General population with no risk factors need not be tested.
TESTING

• Two tests:
  • Mantoux tuberculin skin test (TST/Mantoux test)
  • Interferon-gamma release assays (IGRAs)
• 0.1 ml of 5 Tuberculin Units (TU) purified protein derivative (PPD) injected intradermally.
• Produces a wheal of about 6-10 mm
TST

- Read 48-72 hours later.
- Induration and not erythema.
- Positive test can be read up to 7 days later.
- Negative test cannot be read after 72 hours.
TESTING

• > 5 mm
  • Immunosuppressed patients; organ transplant recipients, 15 mg of prednisone for more than a month and patients on TNF-alpha antagonists.
  • Patients with fibrotic changes on x-ray consistent with prior TB disease.
  • HIV patients.
  • Patients with recent exposure to individual with active TB disease.
TESTING

• >10 mm
  • Immigrants (within 5 years)
  • Residents or employees of high risk facilities
  • Intravenous drug users.
  • High risk of progression to active disease.
  • Children below the age of 5 years
  • Infants, children & adolescents exposed to adults in high risk category.
TESTING

• > 15 mm
  • No known risk factors.
Interferon-gamma release assays (IGRAs)

http://www.cellestis.com/IRM/content/compinfo/pic_4_3pic1.gif
IGRAs

• QuantiFERON-TB Gold In-Tube test
  • Measures the change in concentration of interferon
  • Reported as positive (TB likely), negative (TB not likely) or indeterminate.

• T SPOT (ELISpot)
  • Measures the change in the number of cells releasing interferon.

• ESAT-6 and CFP-10 (MTB specific antigens).
IGRAs

• Sensitivity:
  • 80% in untreated culture positive TB
  • Ranges from 56 - 100%
  • Similar to TST sensitivity.

• Specificity:
  • 99%

• Not confounded by BCG or previous exposure to non-tuberculous mycobacterium (NTM).
Use of IGRAs

• History of BCG vaccination
• Contact investigation.
• In all situations where TST can be used.
• 3 regimens:
  • Isoniazid for 6 - 9 months
  • Rifampin for 4 months
  • Rifapentine and Isoniazid for 12 weeks.
TREATMENT

• Isoniazid
  • Efficacy of 93%
  • Poor completion rate
  • Hepatotoxicity
  • Drug resistant *Mycobacterium tuberculosis*.
TREATMENT

• Rifampin
  • 4 months.
  • Higher completion rates
  • Drug interactions.
  • Estimated efficacy of 93%
TREATMENT

• Isoniazid (600 mg) and Rifapentin (900 mg)
  • Weekly for 12 weeks
  • DOT
  • Higher completion rates.
  • Less side effects.
  • Efficacy of 93%.
SUMMARY

- LTBI affects a third of the world’s population with an estimated 11 million in the USA.
- Targeted testing.
- Can use IGRA or TST.
- Treat if positive.
REFERENCES

• www.cdc.gov