UPDATE IN DIAGNOSIS AND TREATMENT OF LATENT TUBERCULOSIS INFECTION

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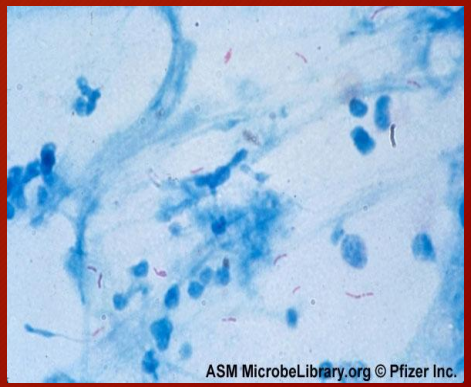
OBJECTIVES:

- Review epidemiology
- Review updates in diagnosis
- Review updates in treatment

EPIDEMIOLOGY OF TUBERCULOSIS

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



MMWR weekly, July 6, 2012/61 (26);484-489

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

World Health Organization: Fact sheet on Tuberculosis.

USA

- 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.

MMWR weekly: March 21, 2014/63(11);229-233

UTAH

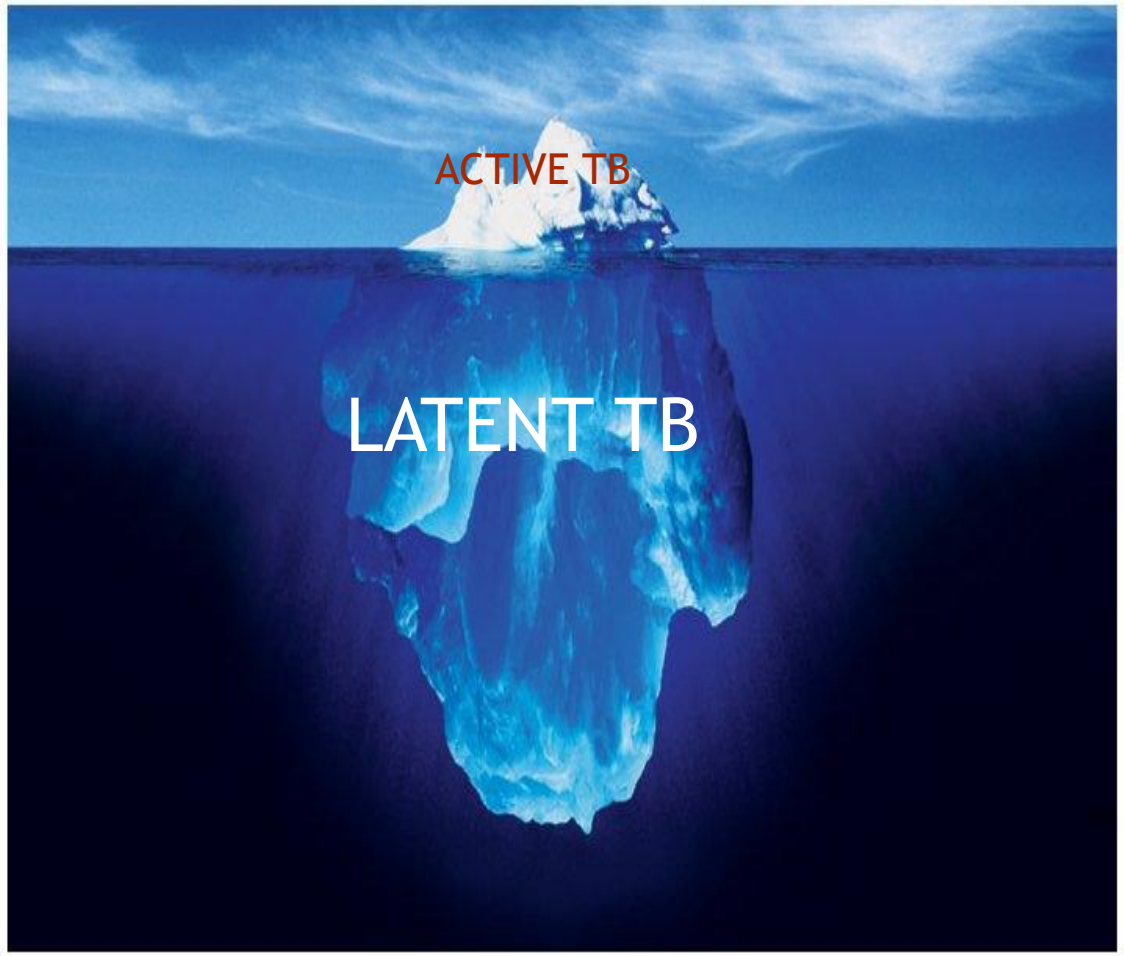
- 1.3/100,000 in 2012
- 1.1/100,000 average for 2008 – 2012
- From 2008 – 2012, percentages by county
  - Salt Lake: 55%
  - Weber-Morgan: 10%
  - Bear River: 9%
  - Utah: 8%
- Weber-Morgan rate for 2013 was

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).

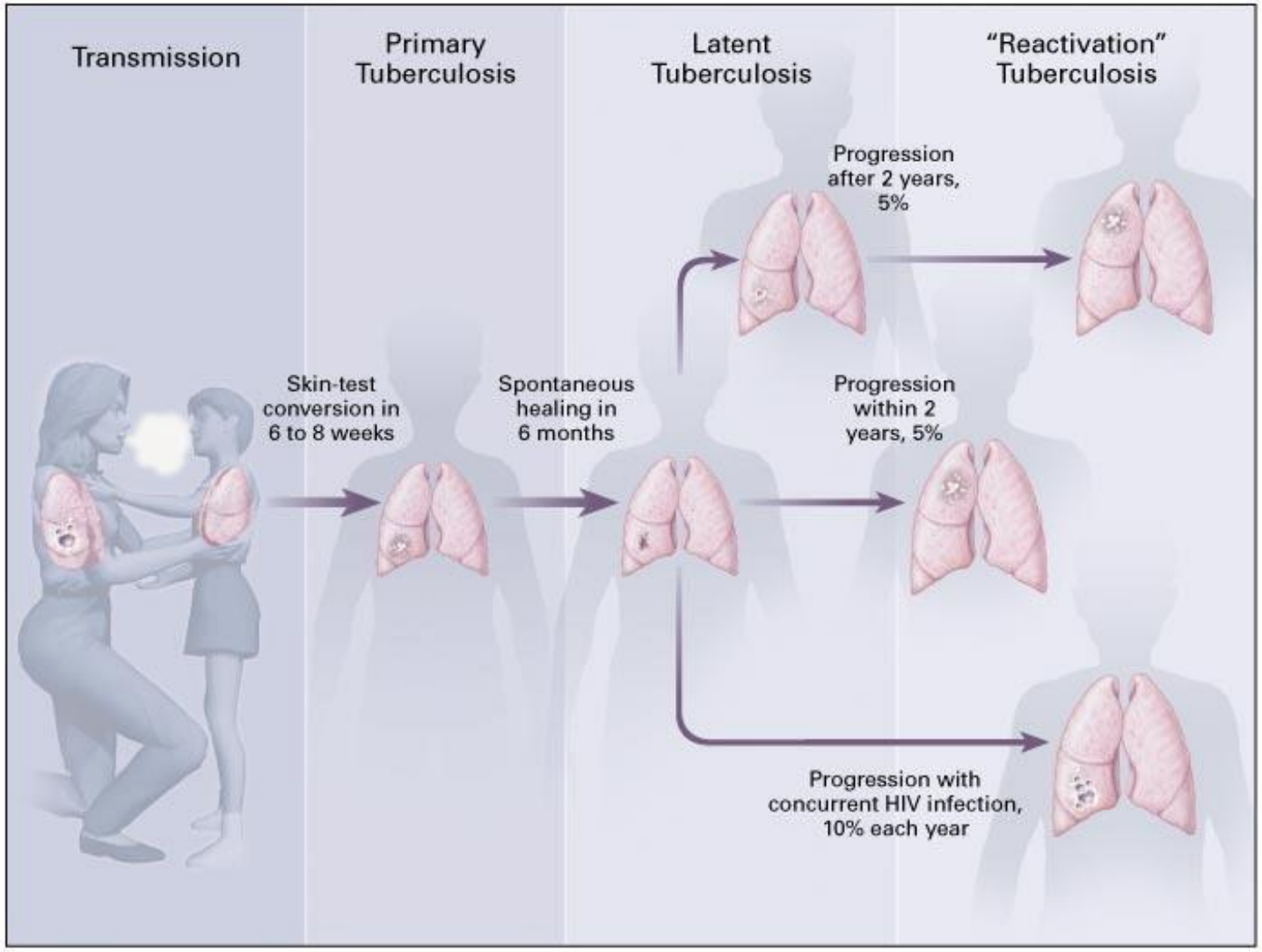
Picture courtesy of Sue Wang & Ian Durrant. Statistics courtesy of CDC.

MICROBIOLOGY

- *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



Small PM, Fujiwara PI, N Engl J Med 2001; 341:189-200

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)

TST

- 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.

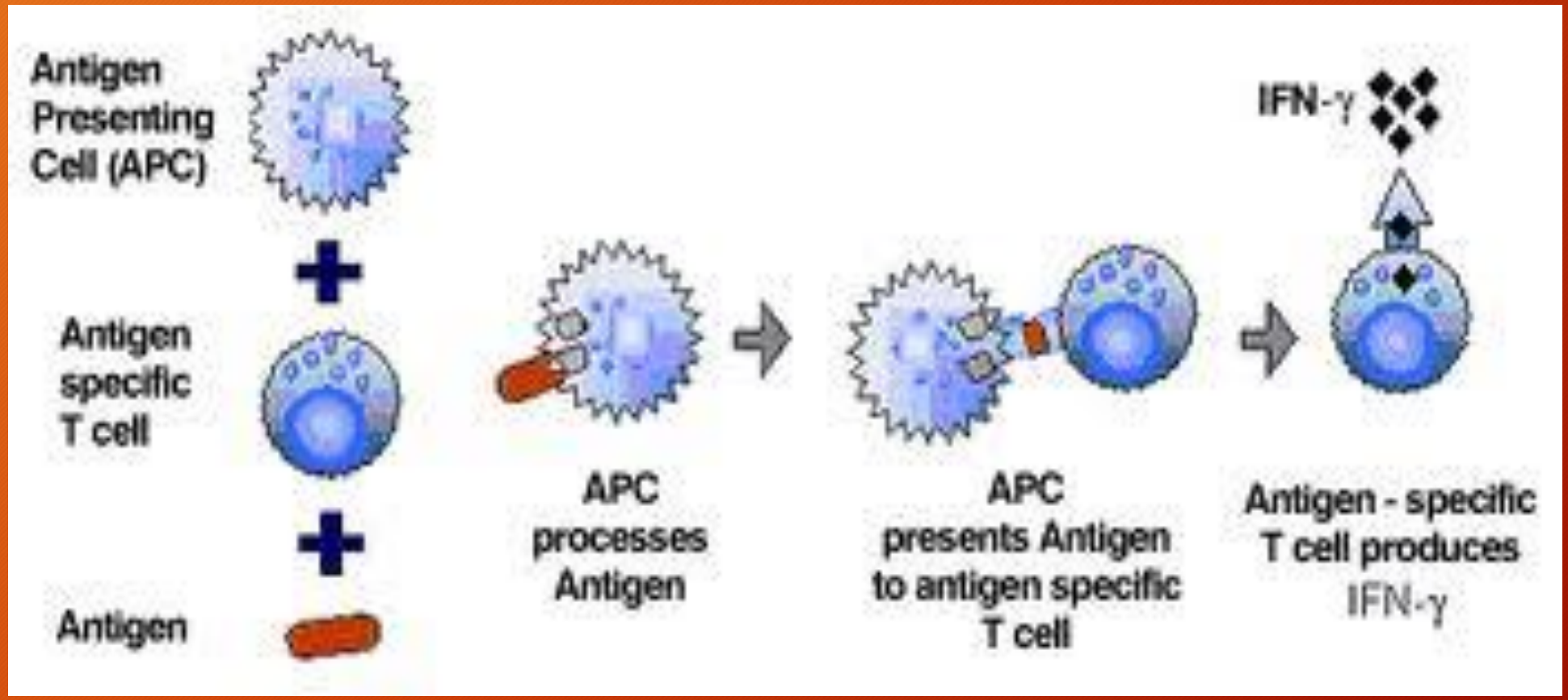
TESTING

- >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 by Jerry Mazurek, Division of TB Elimination, CDC

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).

IGRAs by Jerry Mazurek, Division of TB Elimination, CDC

Use of IGRAs

- History of BCG vaccination
- Contact investigation.
- In all situations where TST can be used.

TREATMENT

- 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