



Mayo Clinic Center for Tuberculosis

Diagnosis & Treatment of Latent TB



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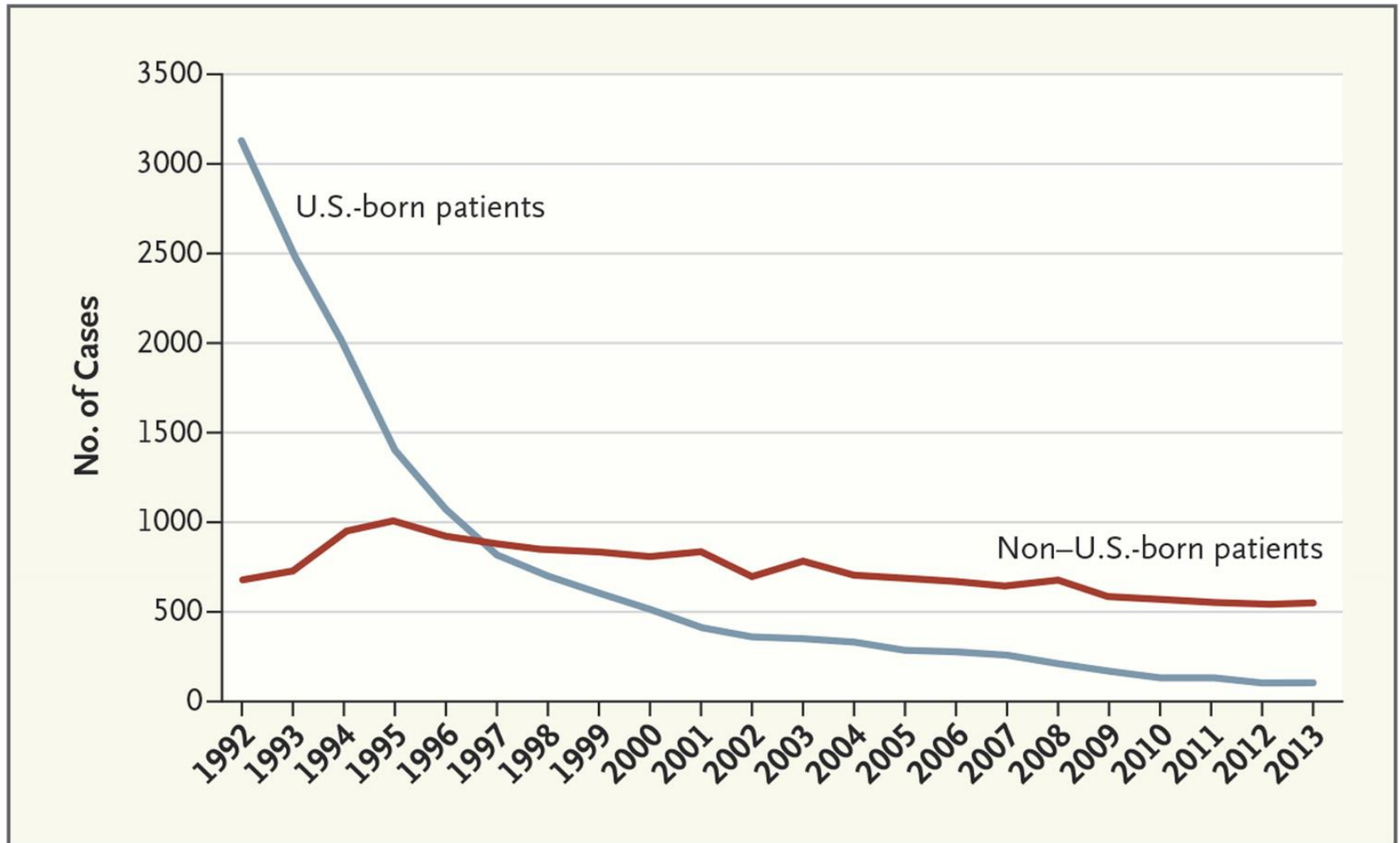
Disclosures

- None

Learning Objectives

- Describe the current guidelines for LTBI treatment
- Describe monitoring recommendations for patients on LTBI treatment

Number of Active Tuberculosis Cases in New York City, According to Birthplace, 1992–2013.

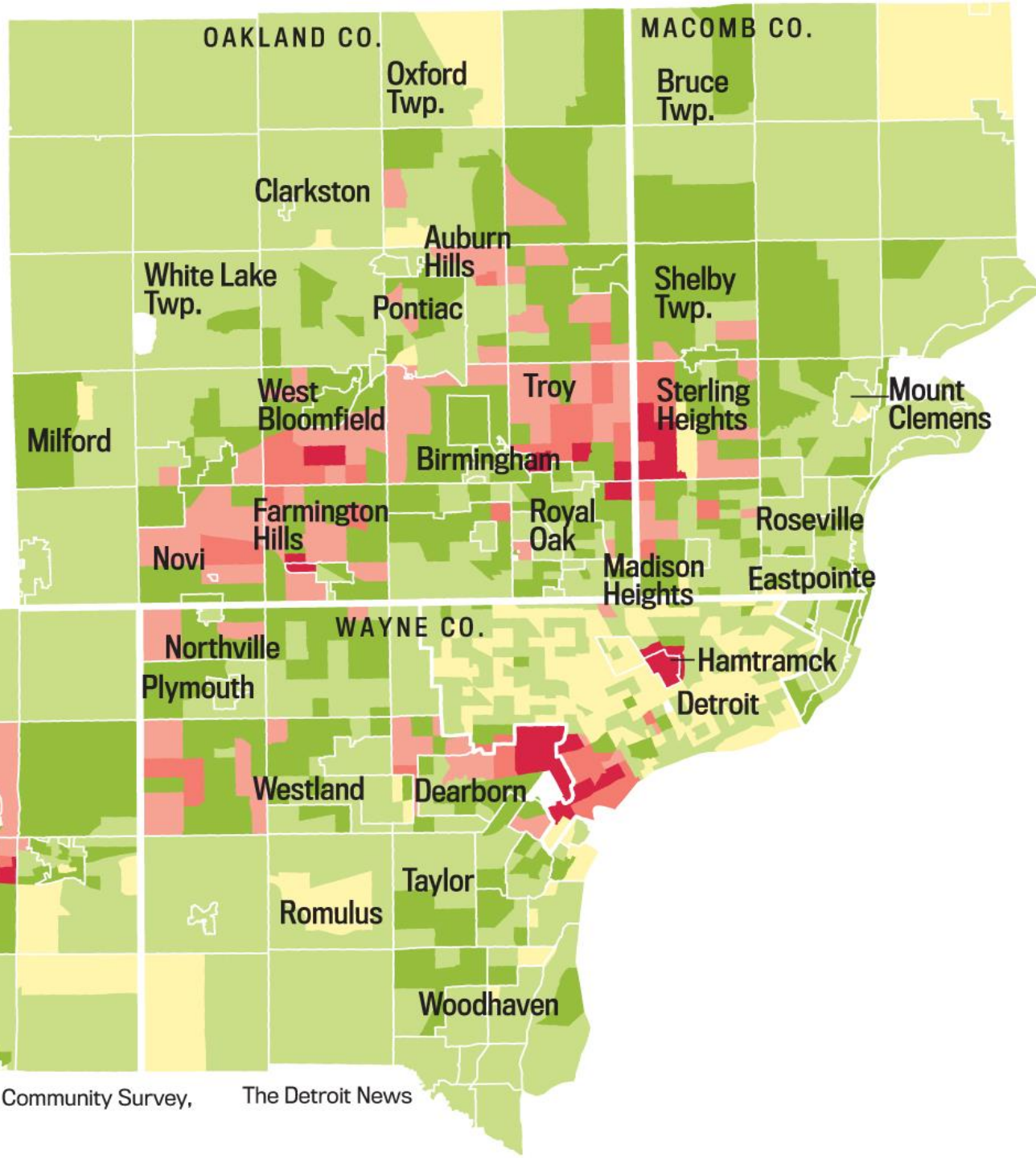
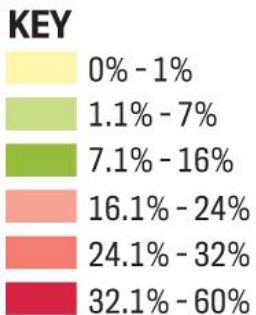


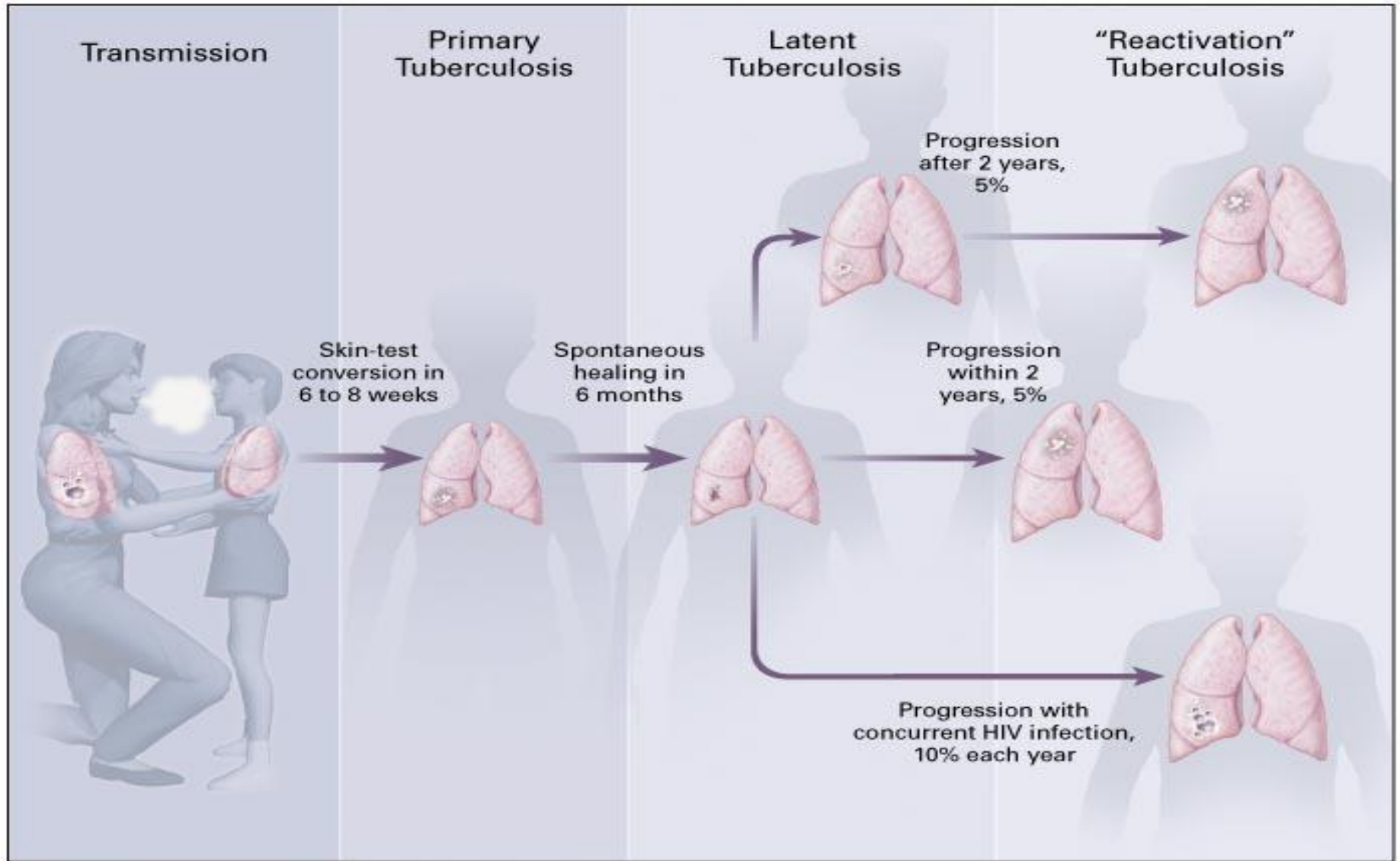
Foreign-born residents

Metro Detroit's foreign-born population helps offset slow growth and increase economic power. Detroit lags, with a foreign-born population under 5 percent and limited to a few small areas of the city.

Metro Detroit's foreign-born population

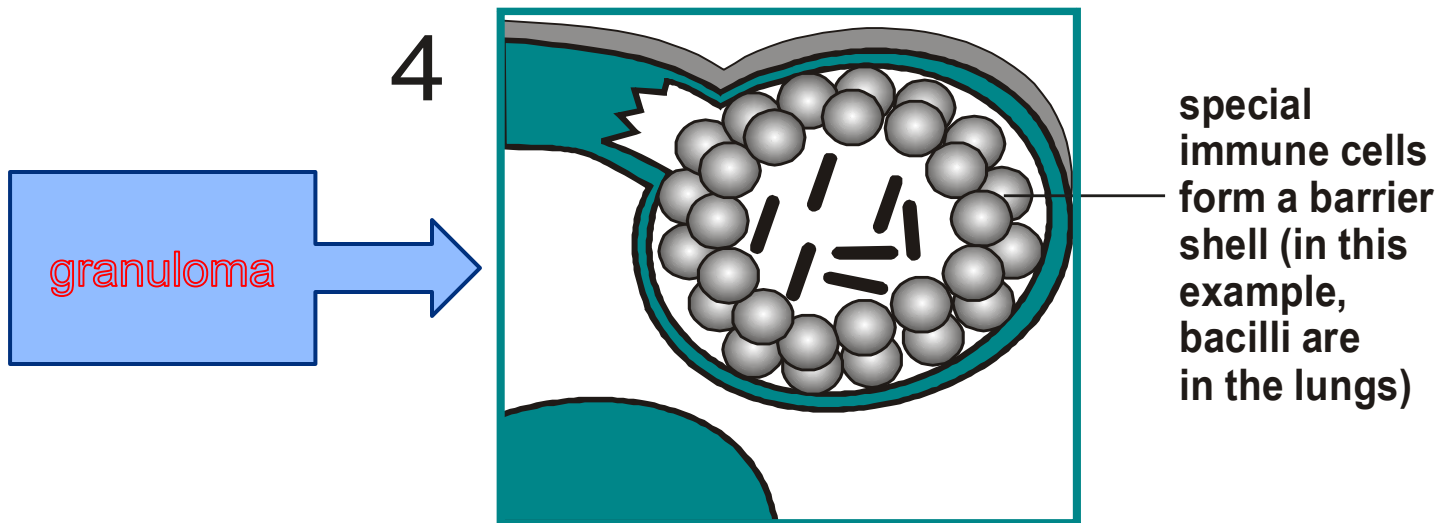
Average: 9.3%





TB Pathogenesis (7)

LTBI



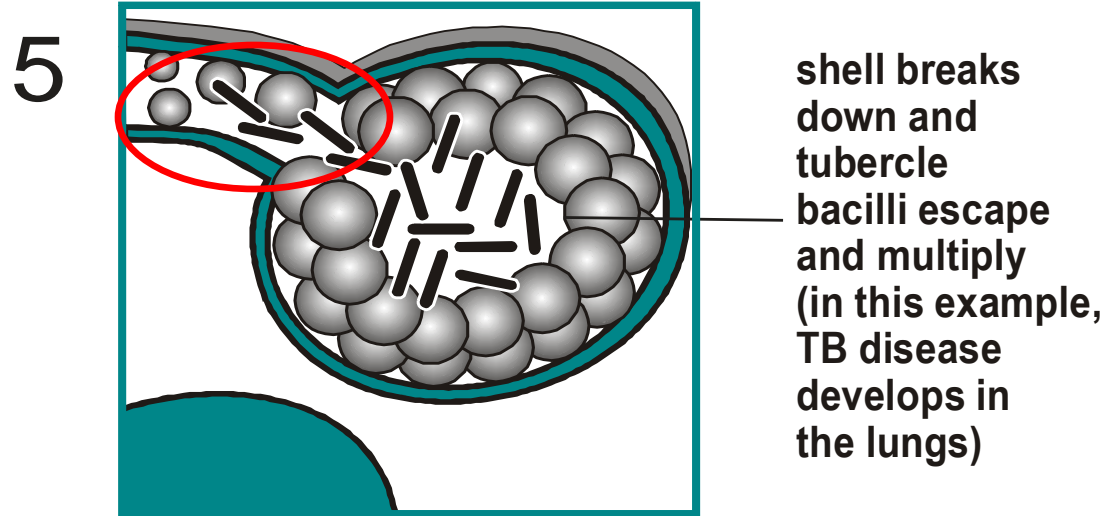
- **Within 2 to 8 weeks the immune system produces special immune cells called macrophages that surround the tubercle bacilli**
- **These cells form a barrier shell that keeps the bacilli contained and under control (LTBI)**

Module 1 – Transmission and Pathogenesis of Tuberculosis

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TB Pathogenesis (8)

TB Disease



- If the immune system **CANNOT** keep tubercle bacilli under control, bacilli begin to multiply rapidly and cause TB disease
- This process can occur in *different* places in the body

Module 1 – Transmission and Pathogenesis of Tuberculosis

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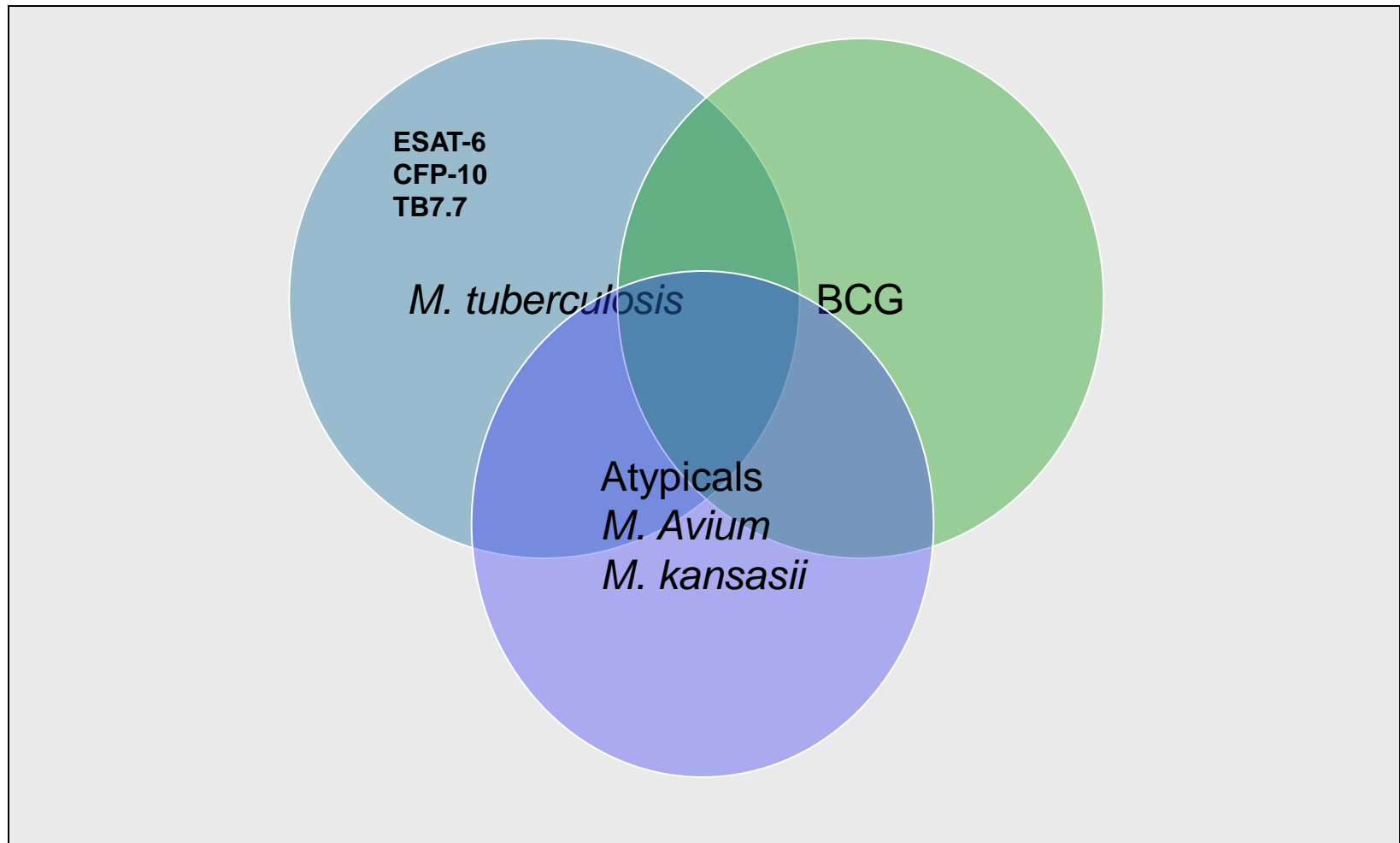
LTBI vs. TB Disease

Latent TB Infection (LTBI)	TB Disease (in the lungs)
Inactive , contained tubercle bacilli in the body	Active , multiplying tubercle bacilli in the body
TST or IGRA blood test results usually positive	TST or IGRA blood test results usually positive
Chest x-ray usually normal	Chest x-ray usually abnormal
Sputum smears and cultures negative	Sputum smears and cultures may be positive
No symptoms	Symptoms such as cough, fever, weight loss
Not infectious	Often infectious before treatment
Not a case of TB	A case of TB

Explaining “Latent” to a Patient

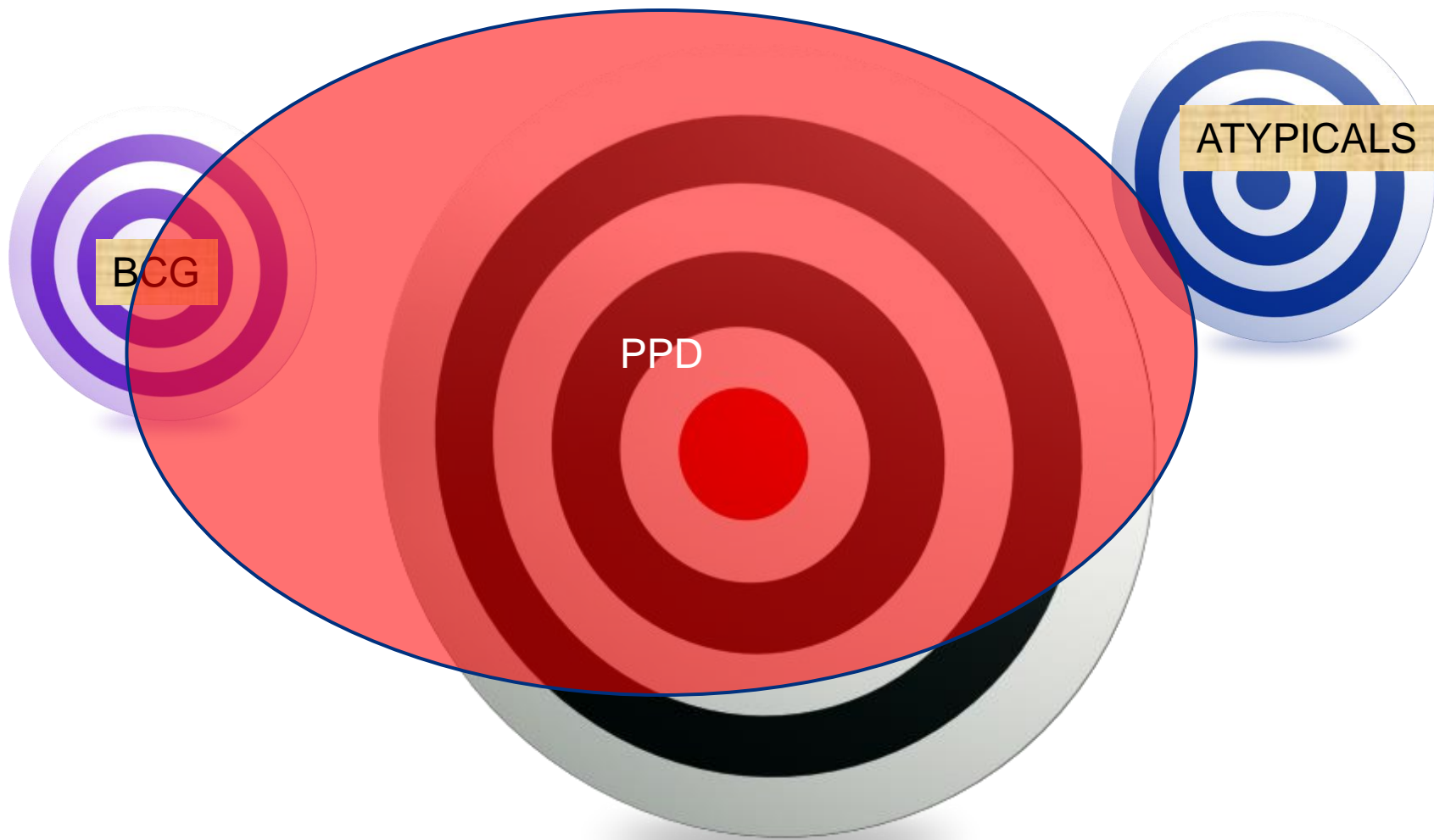
- Dormant
- Trapped or contained
- Not contagious
- Still viable TB bacteria in the body

Alternatives to PPD: Specific Mycobacterial Antigens

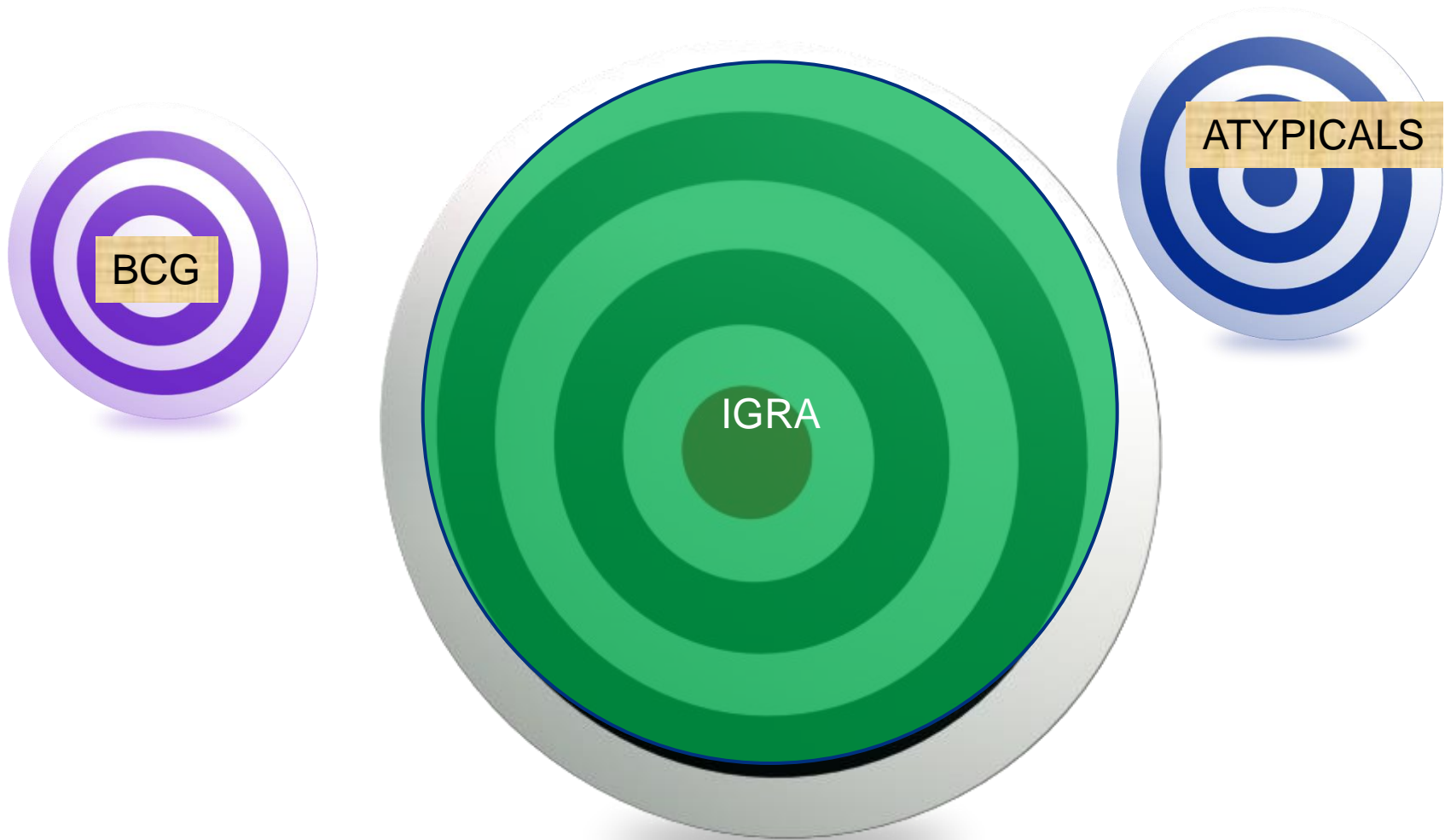




PPD can React with BCG and Atypical AFB



IGRA Tests More Specific Than PPD



Preferred Tests for Latent TB Infection

PPD

- Children <5 years of age

IGRA

- Persons who have received BCG vaccination
- People with poor rates of return to read PPD test

Results of Tests for Latent TB Infection

PPD Result is Positive

- > 5mm: HIV+ or immune suppressed, recent TB contact, fibrotic CXR
- >10mm: all others
- >15mm: no known risk for TB

IGRA

- Negative
- Indeterminate
- Positive

Screening for LTBI

TST or PPD



IGRA



Interferon Gamma Release Assays (IGRAs)

- ❑ IGRAs detect *M. tb* infection by measuring immune response in blood
- ❑ Cannot differentiate between TB and LTBI; other tests needed
- ❑ May be used for surveillance/screening, or to find those who will benefit from treatment
- ❑ FDA-approved IGRAs are QFT Gold In-Tube and T-Spot. *TB* test

General Recommendations for Using IGRAs

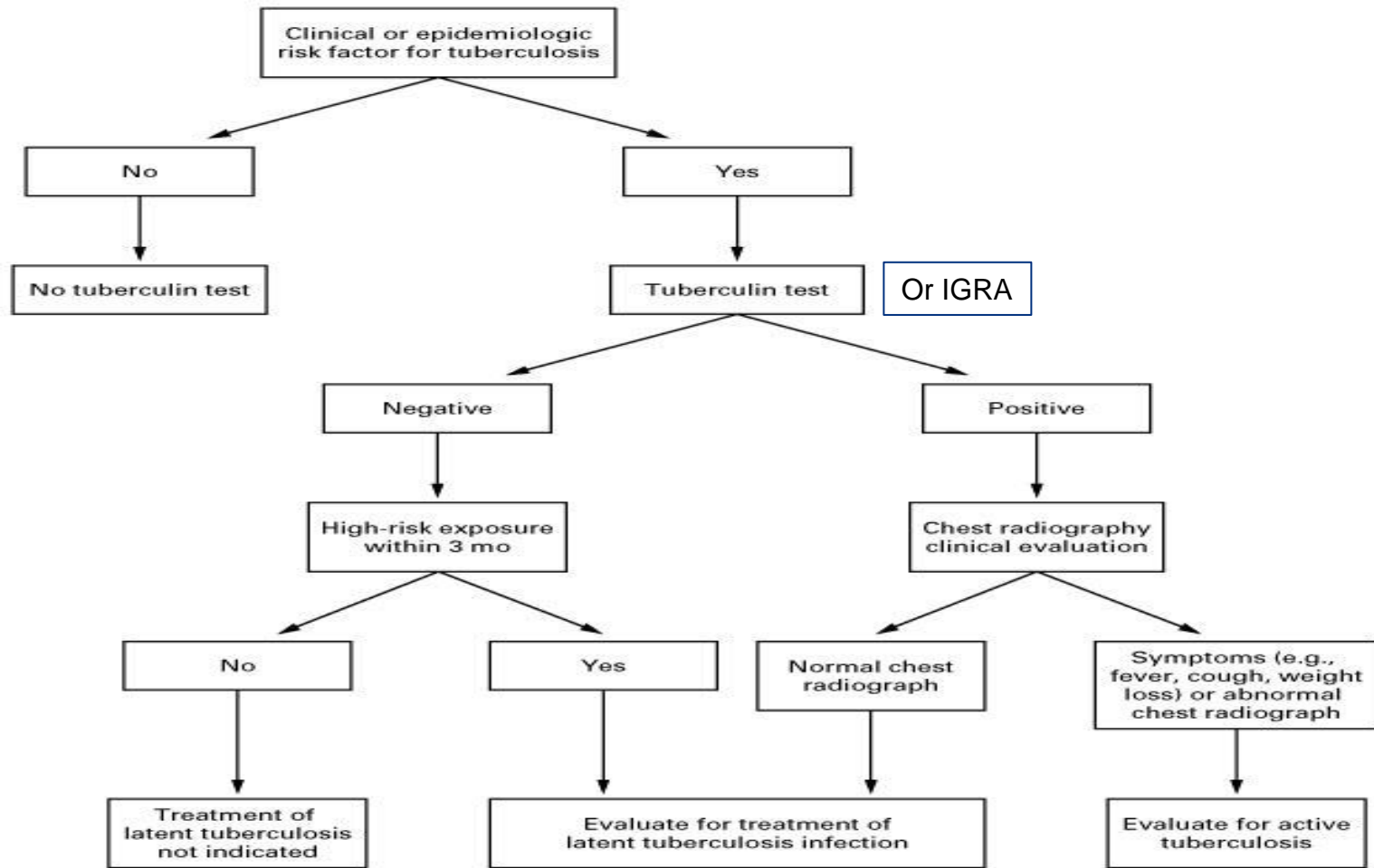
- May be used in place of, but not in addition to, TST
- Preferred when testing persons
 - Who might not return for TST reading
 - Who have received BCG vaccination

- Generally should not be used to test children <5 years of age, unless used in conjunction with TST

General Recommendations for Using IGRAs (cont.)

May be used in place of TST to test recent contacts of infectious TB

- Detect *M. tb* infection with greater specificity than TST
- Data are limited on ability to predict subsequent TB
- In contact investigations, confirm negative via retest 8–10 weeks postexposure
- Use same test for repeat testing to reduce misclassification errors



Chapter 5. Treatment for Latent Tuberculosis Infection

Refer to experienced clinic for LTBI treatment

- Infectious Disease physicians
- Local TB Clinics:
 - Wayne County TB Clinic 734-727-1130
 - City of Detroit TB Clinic 313-577-9827
 - Oakland County Health Dept 248-858-8991

Treatment for Latent TB Infection (LTBI)

- **Over 11 million persons in U.S. estimated to have LTBI (4% of population)**
 - 5%-10% will develop TB disease if untreated
- **Treatment of LTBI essential to controlling and eliminating TB disease**
- **Reduces risk of LTBI to TB disease progression**
- **Use targeted testing to find persons at high risk for TB who would benefit from LTBI treatment**
- **Several treatment regimens available**

LTBI Treatment Regimens

Isoniazid (INH)

- **9-month daily regimen is preferred: 270 doses within 12 months**
 - Effective for HIV-infected as well as HIV-uninfected persons
 - Can be given twice weekly via DOT: 76 doses within 12 months
 - Preferred for children 2–11 years of age

LTBI Treatment Regimens

INH (cont.)

- **6-month regimen also generally acceptable: 180 doses within 9 months**
 - Can be given twice weekly via DOT: 52 doses within 9 months
 - Shorter regimen not recommended for children, immunosuppressed persons, persons whose x-rays suggest previous TB

LTBI Treatment Regimens



NEW

INH-rifapentine (RPT) regimen (12-dose regimen)

- INH and RPT given in 12 once-weekly doses under DOT**

LTBI Treatment Regimens

Dosage for 12-dose INH and RPT:

- Isoniazid: 15 mg/kg rounded up to the nearest 50 or 100 mg, with a 900 mg maximum
- Rifapentine:
 - 10.0-14.0 kg: 300 mg
 - 14.1-25.0 kg: 450 mg
 - 25.1-32.0 kg: 600 mg
 - 32.1-49.9 kg: 750 mg
 - \geq 50.0 kg: 900 mg maximum

Adverse Reactions to INH

Use of INH is associated with some adverse reactions:

- **Peripheral neuropathy** – give vitamin B₆ if patient has risk factors, or if signs/symptoms develop
- **Fatal hepatitis** – pregnant/postpartum women at increased risk; monitor closely
- **Elevated liver enzymes** – discontinue INH if liver enzyme levels exceed 3X normal with symptoms, or 5X upper limit of normal with no symptoms
 - Closely monitor if signs/symptoms of liver injury, or liver enzyme levels are elevated but less than above

Rifampin (RIF)

- **Alternative to INH is 4 months daily RIF: 120 doses within 6 months**
- **Should not be used in HIV-infected persons being treated with some antiretroviral therapy(ART)**

LTBI Treatment Regimens for Specific Situations (cont.)

Pregnancy and Breast-Feeding

- ❑ 9 months of INH daily or twice weekly; give with vitamin B₆
- ❑ If cannot take INH, consult with TB expert
- ❑ 12-dose INH-RPT regimen not recommended for pregnant women; its safety in pregnancy is not known
- ❑ Women at high risk for progression to TB disease, especially HIV infected or diabetic, should not delay LTBI treatment; monitor carefully
- ❑ Breast-feeding not contraindicated

Patient Monitoring

Before starting treatment for LTBI, clinicians should

- Exclude possibility of disease (symptoms, chest radiograph)**
- Determine if patient has history of prior treatment for LTBI or disease**
- Determine if any contraindications to treatment**
- Obtain information about current and previous drug therapy, including adverse reactions**
- Recommend HIV testing, unless the patient declines (opt-out screening)**

Patient Monitoring (cont.)

Establish rapport with patient and emphasize

- Benefits of treatment**
- Importance of adherence to treatment regimen**
- Possible adverse side effects of regimen**
- Establishment of optimal follow-up plan**

Patient Monitoring (cont.)

- Baseline laboratory testing not routinely indicated for all patients**
- Baseline hepatic measurements are indicated for**
 - Patients with a liver disorder or liver disease
 - Patients with HIV infection
 - Pregnant women and those in immediate postpartum period
- Patients with abnormal baseline tests should be monitored regularly**

Patient Monitoring (cont.)

At least monthly, evaluate for

- Adherence to prescribed regimen**
- Signs and symptoms of TB disease**
- Signs and symptoms of adverse effects, especially hepatitis**
 - Jaundice, loss of appetite, fatigue, and/or muscle and joint aches**

Resources

- Mobile App for IOS, Android: CDC LTBI
- www.cdc.gov/tb
- www.michigan.gov/tb



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