TUBERCULOSIS IN THE NORMAL AND COMPROMISED HOSTS

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CME Disclosures:
Planning Committee And Speaker

Speaker: The following speaker has nothing to disclose in relation to this activity: John I. McNeil, MD

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Goulda A. Downer, PHD, RD, LN, CNS – Principal Investigator/Project Director

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AETC-Capitol Region Telehealth Project
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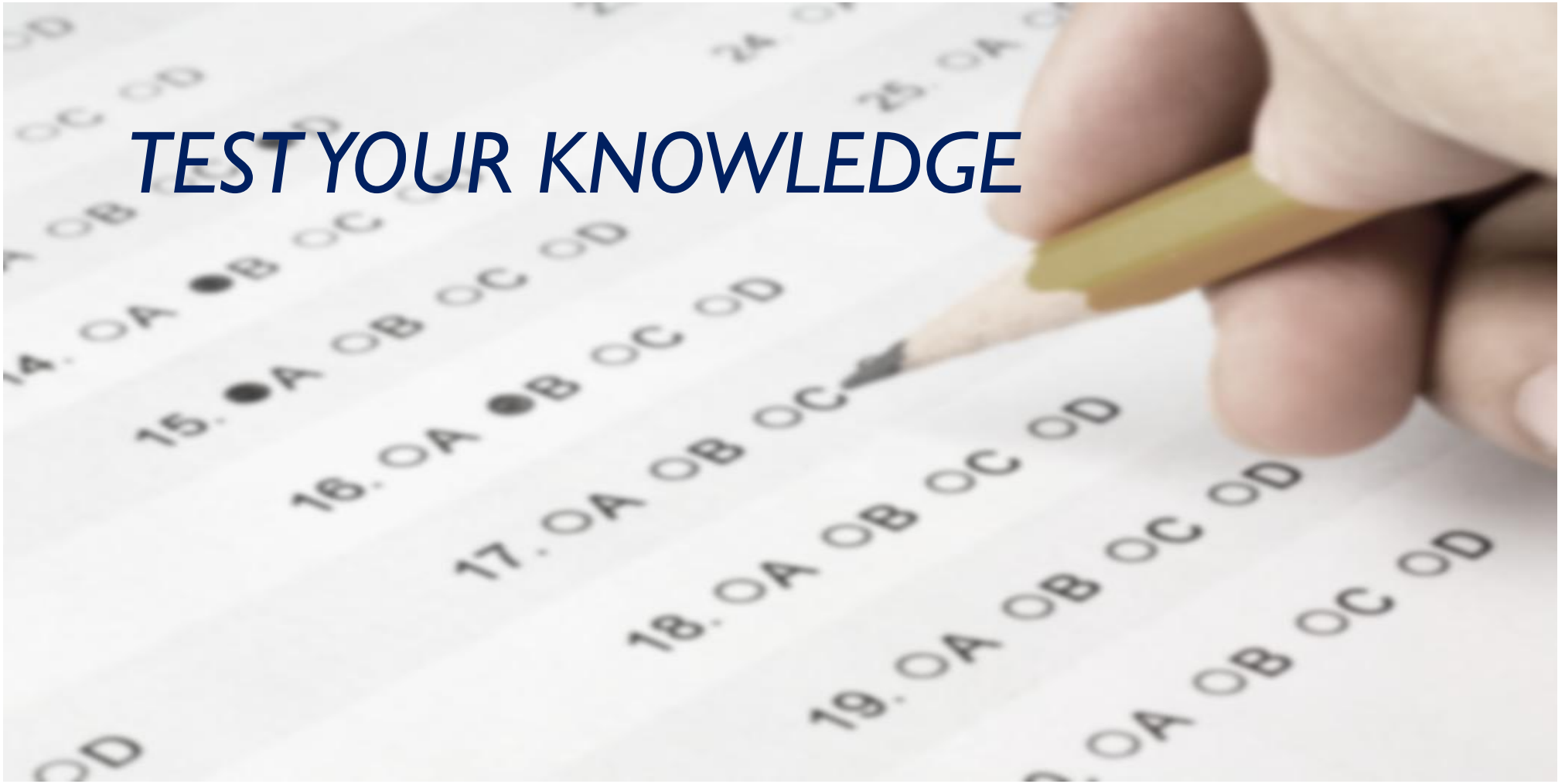
TEST YOUR KNOWLEDGE



Test Your Knowledge
Question #1

All but which of the following are considered risk factors for TB infection?

A. Homelessness
B. Healthcare or Correction Worker
C. Injection drug use
D. Multiple Transfusions

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Test Your Knowledge
Question #2

First line treatment regimen for Active TB disease are:

A. Isoniazid, paritaprevir, capreomycin
B. Rifampin, ledipasvir-sofosbuir, capreomycin
C. Isoniazid, rifampin, amikacin
D. All of the above
E. None of the above

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Test Your Knowledge
Question #3

Some of the most common side effects of treatment for drug-resistant TB include - hearing loss, depression or psychosis, and kidney impairment.

A. True

B. False

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Test Your Knowledge
Question #4

Diagnosis delay and non-completion of treatment are two central behavioral challenges for TB control:

A. True

B. False

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TUBERCULOSIS IN THE NORMAL AND COMPROMISED HOSTS

LEARNING OBJECTIVES

Upon completion of this webinar, participating providers will have the enhanced ability to:

1. Describe the epidemiology of Tuberculosis
2. Describe the epidemiology of TB
3. Discuss risk factors for Infection and Progression to Disease
4. Describe Active TB disease: Clinical Presentations, diagnosis and treatment
5. Identify currently available medications
6. Identify risk factors for Drug resistant TB

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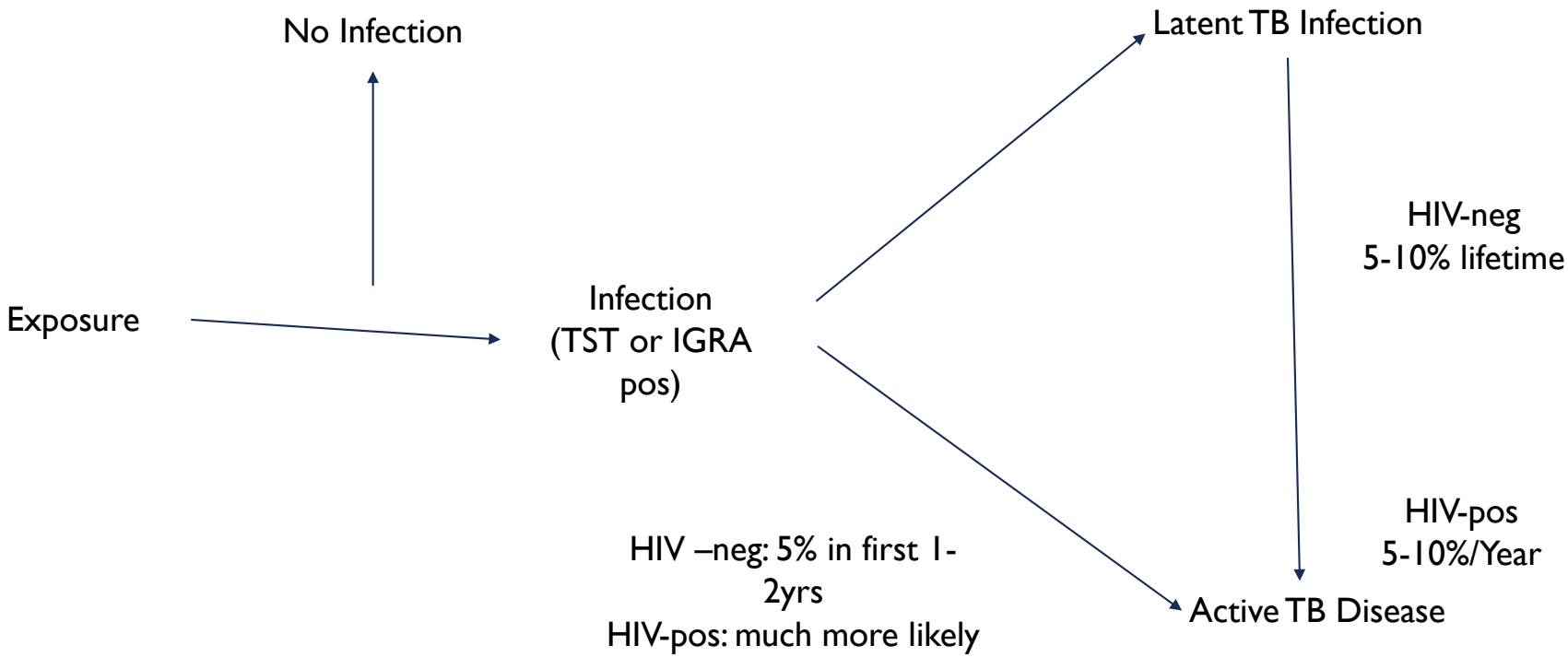
Overview of TB Epidemiology



RISK FACTORS

- For TB Infection
  - Exposure to TB case
  - From TB endemic area
  - Homelessness
  - Works in healthcare or corrections
  - Injection drug use
- For Progression to TB Disease
  - Recent TB infection
  - HIV infection
  - TNF – alpha inhibitors
  - Immunosuppression
  - End stage renal disease
  - Diabetes
  - Silicosis
  - CXR fibrotic lesions c/w prior TB
  - Intestinal bypass
  - CA head or neck, Hodgkin's leukemia

ACTIVE TB DISEASE: CLINICAL PRESENTATIONS

- Fever, sweats, wt. loss
- Cough if pulmonary
- Usually subacute to chronic (wks. to months)
- Can be acute in immunocompromised
- Upper lobe/apical cavity typical
  - With surrounding infiltrates
  - Usually adenopathy

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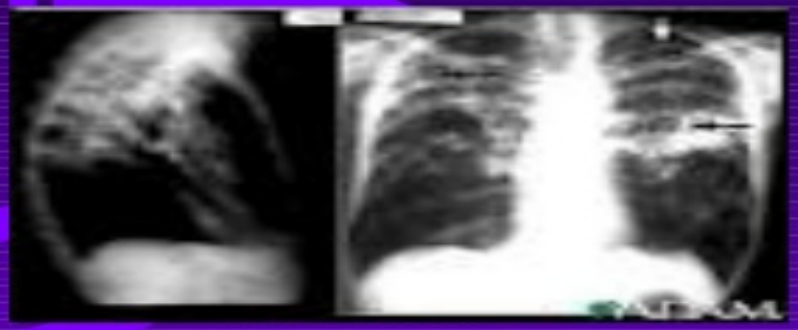
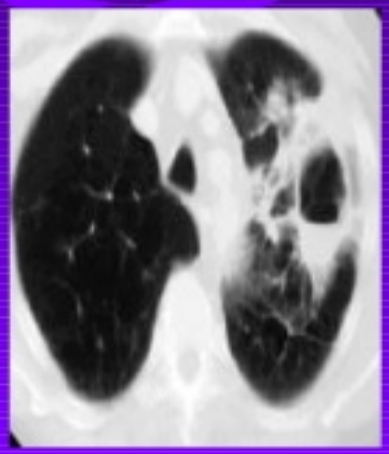
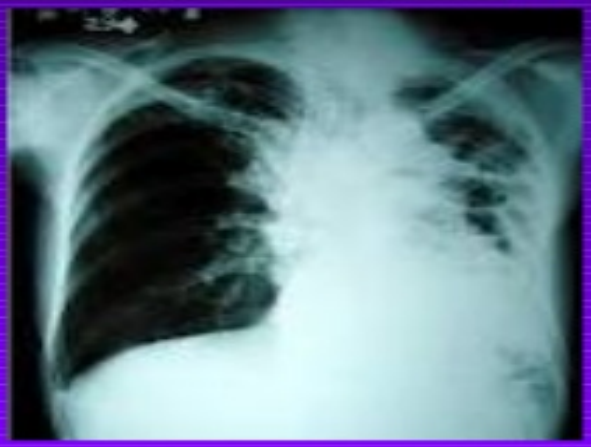
IMAGING CONSIDERATION

- ✓ Chest CT Scan
- ✓ Chest X-ray







ACTIVE TB DISEASE: CLINICAL PRESENTATIONS

Extrapulmonary (dx eval should include biopsy for AFB smear, mycobacterial culture, histopathology)

- CNS (meningitis, focal tuberculomas)
- Lymphadenitis (cervical, thoracic, abdominal)
- Bone and joint
  - Vertebral (thoracic, lumbar, anterior wedging. +/- psoas abscess)
  - Consider TB in DDX of chronic osteomyelitis, arthritis
- Pleural
- Abdominal/Pelvic
  - GU (sterile pyuria, obtain multiple cultures, can be associated with infertility)
  - GI (can mimic inflammatory bowel disease, obtain cultures, histopathology)

Disseminated

- Advanced HIV, significant iatrogenic immunosuppression
- Can present as sepsis
- Mycobacterial blood cultures, obtain respiratory specimens

ACTIVE TB DISEASE: DIAGNOSIS

Smear microscopy for acid fast bacilli

- Low sensitivity takes a lot of bacilli to make a smear positive (sputum 10,000 cfu/ml)
- Overall around 50-60% sensitive for pulmonary TB
- Much less sensitive in advanced HIV (30-50%)
- **IMPORTANT POINT: a negative smear does not exclude dx of active disease**
- In pulmonary TB, the yield of smear microscopy increase4s if multiple specimens are obtained
- Not specific for M. tb (most mycobacteria look alike)
- Good PPV in TB endemic settings

ACTIVE TB DISEASE: DIAGNOSIS

Nucleic Acid Amplification Tests

- E.g. 'Xpert MTB/RIF
- Sensitivity between that of smear and culture
- A negative test does not rule out TB
- High specificity for M. tuberculosis (by design
- Xpert MTB/RIF detects M. tuberculosis and also rifampin resistance (No information about INH)
- Procedures designed for sputum
  - Can be used for other specimens but the test can be false negative due to inhibitors of amplification rxn

ACTIVE TB DISEASE: DIAGNOSIS

Mycobacterial Culture

- **The most sensitive method**
- SLOW (3-6 weeks)
- Once growth observed, the lab performs additional tests to identify species (e.g. M. tuberculosis)
- Considered the gold standard, but not 100% sensitive
  - Pulmonary TB around 90-95% sensitive
  - Extrapulmonary TB much less sensitive

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ACTIVE TB DISEASE: TREATMENT

- First line treatment
  - Rifampin, Isoniazid, Pyrazinamide, Ethambutol x 2 months, then
  - Rifampin plus isoniazid x 4 months (continuation phase)
  - Use pyridoxine (vitamin B6) to prevent neuro toxicity to INH

- Always start with daily treatment
  - Daily more efficacious than intermittent
  - In HIV-positive, intermittent tx associated with emergence of RIF resistance

ACTIVE TB DISEASE: TREATMENT

Extend continuation phase therapy for

- Pulmonary dx if cavitation and cx positive at the end of tx month 2 (9 months total)
- CNS TB (usually 9-12 months total duration)
- Bone and joint TB (6-9 months total duration)

Corticosteroids indicated for TB meningitis

- Pericardial TB: previously universally recommended, but recent placebo controlled randomized trial showed no difference in outcomes overall

ACTIVE TB DISEASE: TREATMENT

Drug adverse effects

- **Hepatotoxicity:** Isoniazid, PZA, rifampin
- **Peripheral neuropathy:** Isoniazid (use pyridoxine)
- **Retrobulbar neuritis:** ethambutol (color vision first affected)
- **Arthralgias:** PZA
- **Vestibular/ototoxicity:** streptomycin>amikacin, kanamycin
- **Nephrotoxicity:** amikacin, kanamycin>streptomycin

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DRUG RESISTANT TB

Risk factors for

- Contact with drug resistant TB case
- From (or prolonged travel to) eastern Europe, former Soviet Union
- Prior h/o TB treatment, especially if non-adherent with hx

MDR=resistance to isoniazid plus rifampin

XDR=MDR plus resistance to fluoroquinolones plus a at least one of the injectable second line drugs (amikacin, kanamycin, capreomycin)

- Treat with multiple agents against which the isolate is susceptible
- Never add a single drug to a failing regimen

ACTIVE TB DISEASE: HIV CONSIDERATIONS

Clinical Presentation

- Lung cavitation may be absent in advanced immunosuppression
- Negative CXR does not exclude TB
- With advancing immunosuppression, risk for
  - Smear-negative pulmonary TB
  - Extrapulmonary TB 9wiith or without pulmonary disease)
  - CNS TB
  - Widely disseminated disease
- Immune reconstitution inflammatory syndromes

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ACTIVE TB DISEASE: TRANSPLANT RECIPIENTS CONSIDERATIONS

- Transplantation associated immunosuppression increases the risk of active TB disease if the person is infected
- Atypical presentations leading to delayed disease
  - 1/3 to ½ is disseminated or extrapulmonary
  - 4% of cases thought to be donor derived
- High mortality
- DDI between rifampin and calcineurin inhibitors (cyclosporine, tacrolimus), mammalian target of rapamycin inhibitors (sirolimus/everolimus:, corticosteroids. At risk for graft rejection
  - Monitor drug levels
  - Use rifabutin

ACTIVE TB DISEASE: TNF-ALPHA INHIBITORS

- TNF-alpha inhibitors markedly increases the risk of active TB if infected
  - Risk greater with anti-TNF antibodies (infliximab) than with TNF receptor fusion protein (etanercept)
  - Can present with atypical TB (non-cavity pulmonary disease, extrapulmonary, disseminated)
  - Increased TB mortality and morbidity
- Test for latent TB infection (TST or IGRA) prior to starting anti-TNF agents
  - If LTBI, then initiate LTBI tx prior to starting anti-TNF
  - Optimal duration of delay between initiating LTBI treatment and initiating anti-TNF treatment not known (some say 2-8 weeks)

LATENT TB INFECTION (LTBI): DIAGNOSIS

Tuberculin skin test

- A mix of antigens; can have false-positive test due to prior BCG vaccination, NTM
- Intradermal inoculation, measure induration at 48-72 hours (a positive reaction lasts a few days)
- Cut-offs based on the likelihood of true exposure, risk of progression to active TB if infected
  - 5 mm
  - 10 mm
  - 15 mm
- Adjunctive in diagnosis eval of active TB

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LATENT TB INFECTION (LTBI): DIAGNOSIS

Interferon gamma release assays

- QFT Gold in-tube: T-SPOT TB
- Blood-based: in vitro stimulation of WBC with protein antigens specific for M.tuberculosis
- SPECIFIC for M. tb infection: no cross-reactivity with BCG
- Sensitivity in approximately the same as TST
- Can be negative immunosuppressed
- Lots of issues around performance in clinical care
- As for TST adjunctive in diagnoses eval for active TB

BACILLE CALMETTE-GUERIN (BCG)

- Attenuated live vaccine (from M. bovis)
- Neonatal vaccination
  - Decreases incidence of severe forms of childhood TB
  - No impact on adult TB
  - Regional lymphadenitis can occur after vaccination: typically no treatment needed
  - Disseminated infection can occur in immunocompromised (treatment indicated)

THANK YOU!


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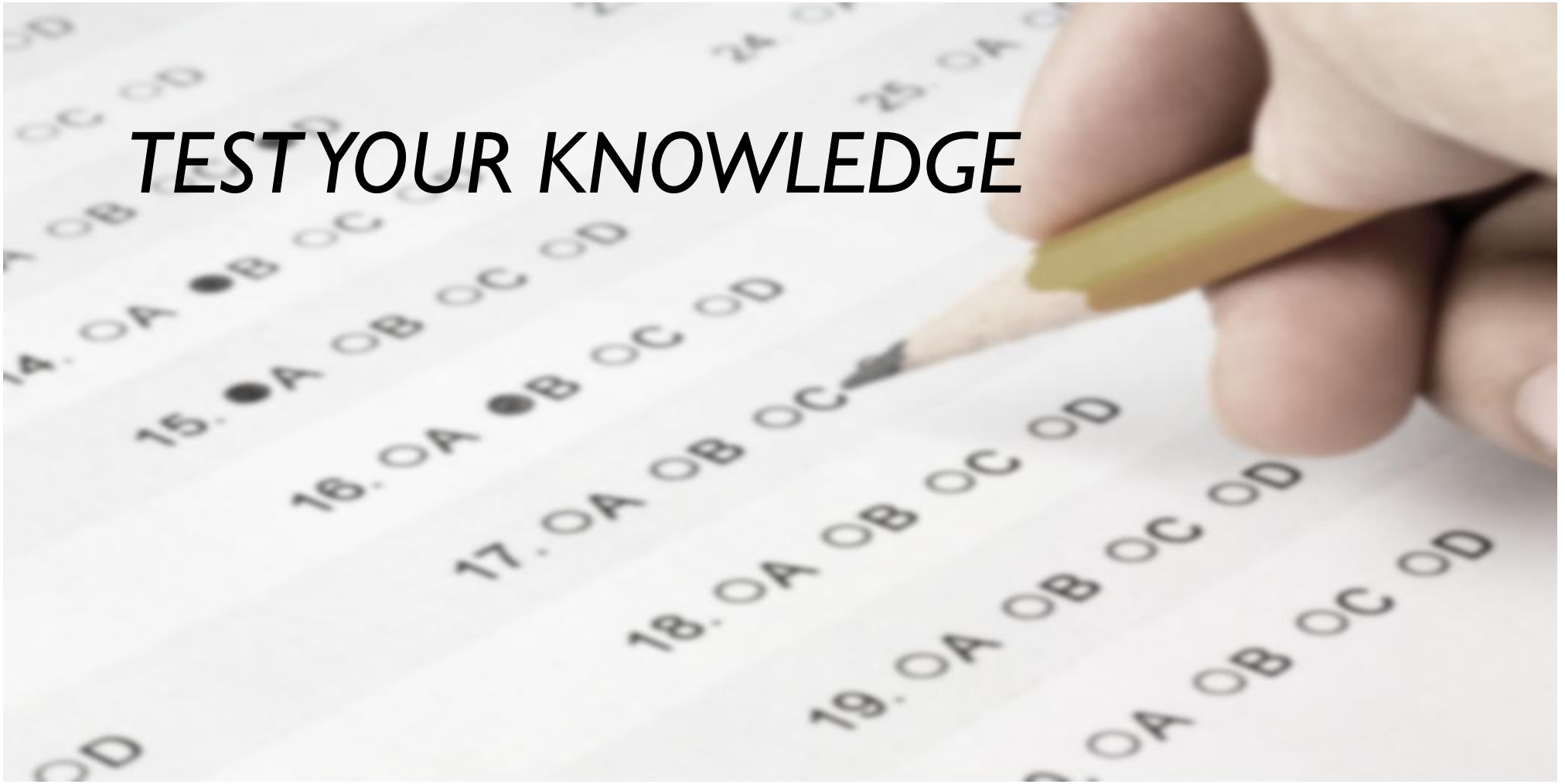
TEST YOUR KNOWLEDGE

Test Your Knowledge
Question #5

All but which of the following are considered risk factors for TB infection?

A. Homelessness
B. Healthcare or Correction Worker
C. Injection drug use
D. Multiple Transfusions

Test Your Knowledge
Question #6

First line treatment regimen for Active TB disease are:

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B. Rifampin, ledipasvir-sofosbuir, capreomycin
C. Isoniazid, rifampin, amikacin
D. All of the above
E. None of the above

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Test Your Knowledge
Question #7

Some of the most common side effects of treatment for drug-resistant TB include - hearing loss, depression or psychosis, and kidney impairment.

A. True

B. False

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Test Your Knowledge
Question #8

Diagnosis delay and non-completion of treatment are two central behavioral challenges for TB control:

A. True

B. False

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