BACTERIAL RESPIRATORY PATHOGENS

DR E. M. MUMBULA

INTRODUCTION

- Classified into four (4) groups

1. Throat / Pharynx
2. Middle ear and sinuses
3. Trachea and bronchi
4. lungs

1. Infections of the Throat and Pharynx

- Sore throat is the commonest symptom accompanied by variable constitutional upsets
- Throat appearance different according to aetiological agent
- Causes may be viral or bacterial

1Streptococcal sore throat

Aetiology: *Streptococcus pyogenes*

- group A Streptococci
- gram + cocci in chains
-

1. Streptococcal sore throat

Clinical symptoms:

- Mild inflamation of the tonsils and pharynx
- oedema of the Fauces
- scarlet fever – children
- headaches
- Malaise
- extension to sinuses and middle ear

1. Streptococcal sore throat

complications:

- Rheumatic fever: fever, painful swelling joints –
- Acute glomerulonephritis: Haematuria, albinuria, oedema

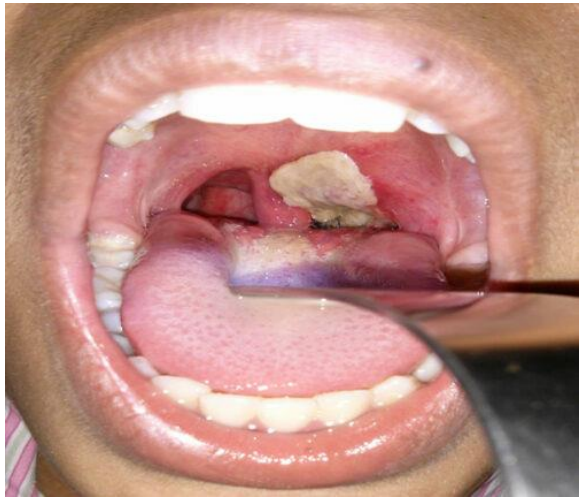
1. Streptococcal sore throat

Laboratory Diagnosis : *Streptococcus pyogenes*

- demonstration of the presence of the pathogen in the site of infection
- Specimen: Throat swab
- Gram stain: G+ Cocci in chains
- Culture: Blood agar & MacConkey = α Haemolytic smooth colonies
- Antigen Detection: Group A antigen

A. Infections of the Throat and Pharynx

2. *Corynebacteria diphtheria*



Charateristics:

- Gram positive rod with tapered ends
- Non-motile
- Non-spore forming
- Produces AB exotoxin
- Significant cause of mortality until 1950s
- Decline due to vaccination with toxoid
- Spread by close contact via droplets from human carriers or humans with active infection
- Common location upper respiratory tract

2. *Corynebacteria diphtheria*

Pathogenesis:

- Invades, coloizes, and proliferates in local mucosal tissue – pseudomembrane
- Elicits an inflamatory exudate and causes necrosis
- Does not cause bacteremia
- Produces toxin which can act on sites beyond the site of infection
- Diphtheria toxin has A and B fragments
- Toxin binds to specific receptor (B subunit)
- A-subunit passes through the membrane and
- Toxin catalyses transfer of ADP-ribose from NAD
- Results: Necrotic and neurotoxic

A. Infections of the Throat and Pharynx

2. *Corynebacteria diphtheria*

Mode of action of toxin:

- A subunit…
  - Enzyme which ADP ribosylates EF-2
  - EF-2 is needed for protein synthesis
  - ADP ribosylation inactivates EF-2
  - One is sufficient to inactivate all EF-2
  - Halts protein synthesis and kills the cell
  - Addition of ADP-ribose inactivates EF2 – Kills cells by irreversible block of protein synthesis
  - EF2 - catalyses hydrolysis of GTP that drives movement of ribosomes on eukaryotic mRNA

A. Infections of the Throat and Pharynx

2. *Corynebacteria diphtheria*

Clinical features:

- Local infection
  - Severe inflammatory reaction
  - Severe swelling in back of neck
  - Sore throat, nausea, vomiting
  - Formation of pseudomembrane
- Systemic
  - Toxaemia as toxin is absorbed from throat and carried by blood to target organs
  - Heart and nervous system

A. Infections of the Throat and Pharynx

2. *Corynebacteria diphtheria*

Diagnosis:

- Made on clinical grounds + history of diphtheria among contacts
- Demonstration of the toxin (Elek – test)
- Microscopy
- Tissue culture cytotoxicity assay
- PCR

A. Infections of the Throat and Pharynx

2. *Corynebacteria diphtheria*

Treatment:

- Anti-toxin, injected on suspicion
- Antibiotics: Penicillin and Erythromycin
- Tracheotomy: necessary to relive obstruction

3. *Haemophilus influenza*

Characteristics:

- Small pleomorphic gram –ve rods or coccobacilli
- Some strains produce polysaccharide capsule
- Six capsular antigens (a-f), demonstratable by PCR; most important type b
- Catalase and oxidase positive
- Ferment glucose
- Reduce nitrate to nitrite

3. *Haemophilus influenza*

Characteristics

- Growth requirements:
  - X factor: Haemin – for synthesis of iron-containing respiratory enzymes
  - V factors: NAD for redox reactions

B. Infections of the Middle Ear and Sinuses

3. *Haemophilus influenza*

Pathogenesis:

- Causes acute epiglottitis
- May also cause; Otitis media, sinusitis, conjunctivitis, exercebate obstructive airway diseases
- Mostly found in children
- Enhanced by the capsular antigen which enables it to evade phagocytosis and complement

B. Infections of the Middle Ear and Sinuses

3. *Haemophilus influenza*

Clinical features:

- Severe croup syndrome in children
- Respiratory obstruction
- Inflamed and oedematous epiglottis

3. *Haemophilus influenza*

Laboratory diagnosis:

- Sputum – gram stain (dilute Carbol-fuchsin better than neutral red)
- Culture – chocolate agar (smooth grey colonies)
- Identification: (Nutrient agar) - growth requires both X and V factors
- PCR
- Slide agglutination with specific anti-sera
- Latex agglutination with rabbit antibody to demonstrate capsular b antigen

3. *Haemophilus influenza*

Treatment:

- Antibiotics: Amoxicillin or ceftriaxone
- Tracheotomy

Prevention:

- vaccination with Hib vaccine in infancy

4. *Streptococcus pneumoniae*

Charateristics:

- Gram +, normally diplococci
- Causes otitis media, sinusitis, pneumonia; also endocarditis, peritonitis, etc

4. *Streptococcus pneumoniae*

Clinical features:

- Pneumonia: due to aspiration of pneumococci in upper airways;
- Fever, rigors, malaise,
- Respiratory symptoms: short breath, cyanosis, cough, pleural pain, rapid shallow breathing
- Purulent sputum

B. Infections of the Middle Ear and Sinuses

4. *Streptococcus pneumoniae*

Pathogenesis:

- Capsule: antiphagocytic, inhibits complement,
- IgA1 protease: cleaves human IgA1
- Pneumolysin: membrane-damaging toxin; inhibits
  - neutrophil chemotaxis,
  - Phagocytosis
  - Lymphocyte proliferation and Ig synthesis
- Autolysin: when activated, break peptidoglycan cross-linkages of the cell wall and allows release of the pneumolysin

4. *Streptococcus pneumoniae*

Laboratory diagnosis:

- Specimen: sputum
- Gram stain
- Culture: Blood agar, α-haemolytic, smooth colonies
- Optochin sensitive
- Bile solubility
- PCR

4. *Streptococcus pneumoniae*

Treatment:

- Penicillin
- Macrolides eg Erythromycin
- Ceftriaxone
- Vancomycin or linezolid

5. *Bordetella pertusis*

characteristics:

- Fastidious
- Strict aerobe
- Grows on nutrien

5. *Bordetella pertussis*

Pathogenesis:

- Non-invasive, infects mucosa
- Colonization of ciliated epithelia of bronchi and trachea
- Produces tracheal toxin – paralyses cilia leading to paroxysms of coughing
- Lymphocytosis due to pertussis toxin
- Rise in neutrophil number

5. *Bordetella pertusis*

Clinical features:

- Severe cough; fluids from nose,eyes, mouth; tongue fully protruding
- Diagnosis can be made on clinical grounds alone

5. *Bordetella pertusis*

Laboratory diagnosis:

- Specimen : swabs and sputum
- Culture:
- PCR
- Serology: detection of antibodies – negative result does not indicate absence of infection

5. *Bordetella pertusis*

Treatment:

- Antibiotics: have little clinical effect when the infection is well established
  - Erythromycin or clarithromycin

- Other measures:
  - Cough suppressants may control the paroxisms

Bacterial Pneumonia

- Inflammation of lung parenchyma

- Stages:
  - Consolidation
  - Red Hepatization
  - Grey Hepatization
  - Resolution

Bacterial Pneumonia

- Symptoms:
  - Cough
  - sputum
  - Chest pain
  - Fever
  - Myalgia
  - Malaise
  - Night sweat +/-

Bacterial Pneumonia

- Signs:
  - Dull percussion note
  - Increase vocal fremitus
  - Reduced air entry
  - Crepitations
  - Pleural rub

Bacterial Pneumonia

- Classification:
  - Aetiology
  - Mode of acquisition
  - Site of infection

Bacterial Pneumonia

- Classification:
  - Aetiology
    - Bacterial
      - *S. pneumoniae*
    - Viral
      - *Influenzae*
    - Fungal
      - *Aspergilus*

Bacterial Pneumonia

- Classification:
  - Mode of acquisition
    - Hospital acquired
      - *S. pneumoniae*
      - *S. aureus*
      - *P. aeruginosa*
    - Community acquired
      - *S. pneumoniae*
      - *H. Influenzae*
      - *Mycoplasma pneumonia*
      - *Legionella*

Bacterial Pneumonia

- Classification:
  - Site of infection
    - Bronchal pneumonia
    - Lobar Pneumonia
    - Interstitial pneumonia

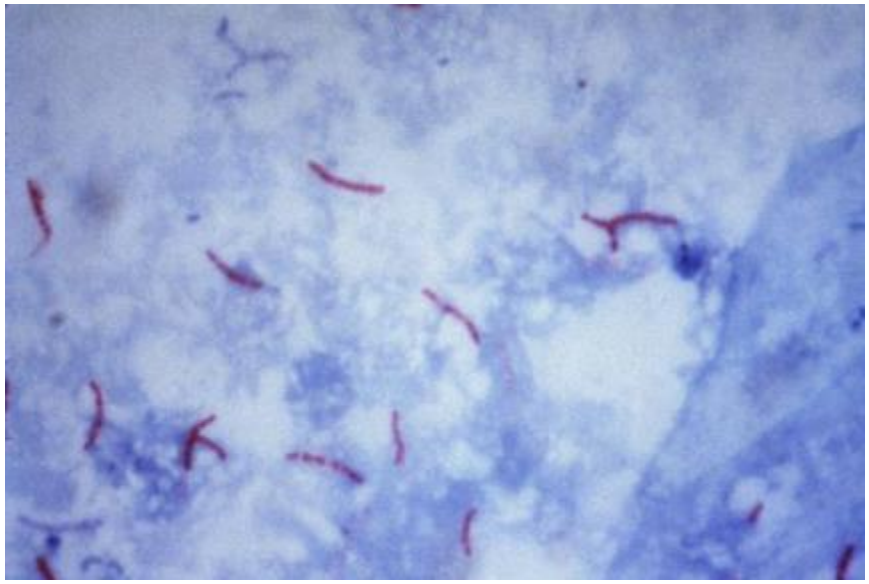
Bacterial Pneumonia

- Diagnosis:
  - Clinical features
  - Laboratory
    - Sputum M/C/S

6. *Mycobaterium tuberculosis*

TB Transmission
Types of Mycobacteria

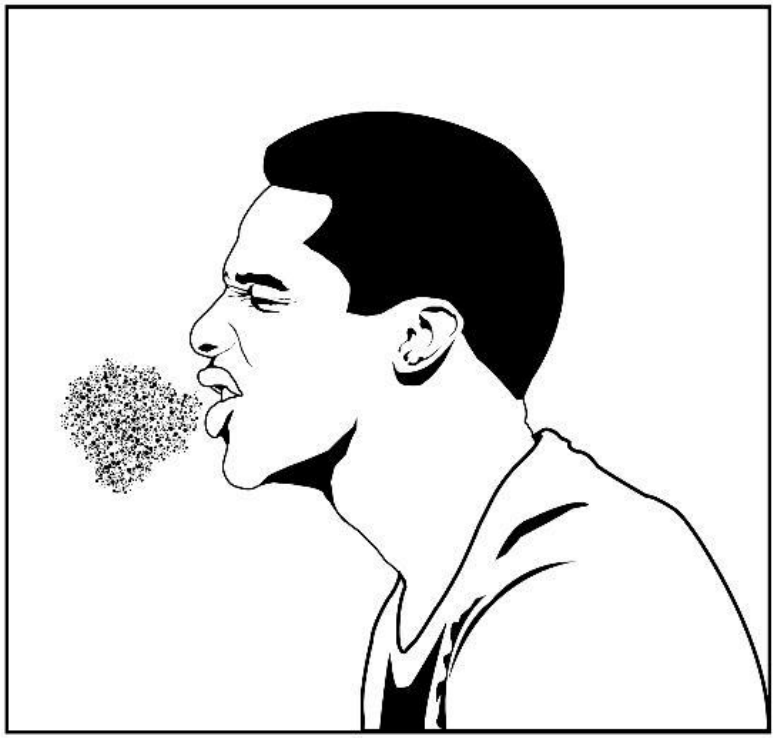
- ***M. tuberculosis* causes most TB cases in U.S.**
- **Mycobacteria that cause TB:**
  - ***M. tuberculosis***
  - ***M. bovis***
  - ***M. africanum***
  - ***M. microti***
  - ***M. canetti***
- **Mycobacteria that do not cause TB**
  - **e.g., *M. avium complex***



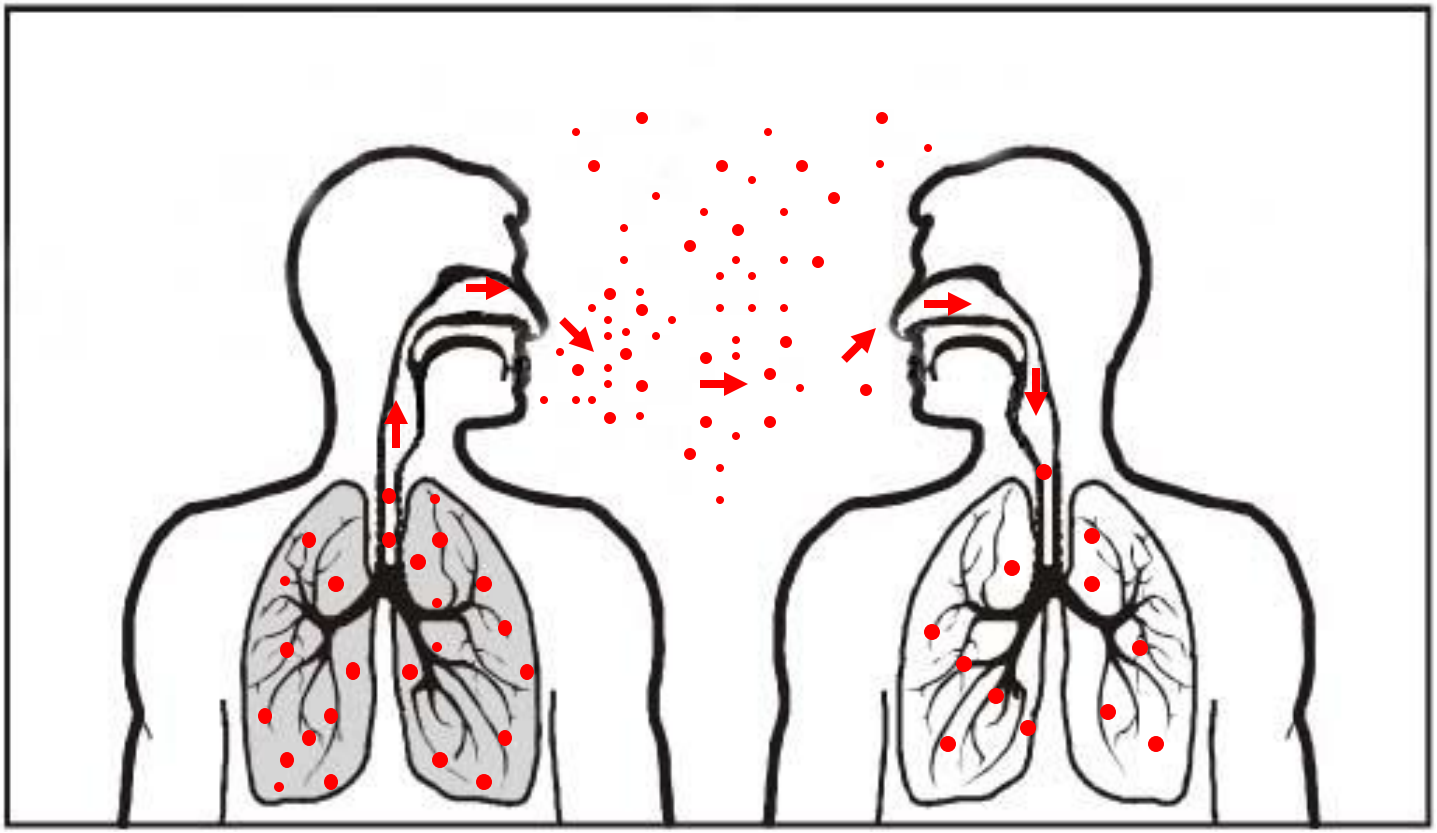
M. tuberculosis

TB Transmission

- **TB is spread person to person through the air via droplet nuclei**
- ***M. tuberculosis* may be expelled when an infectious person:**
  - **Coughs**
  - **Sneezes**
  - **Speaks**
  - **Sings**
- **Transmission occurs when another person inhales droplet nuclei**



TB Transmission



Dots in air represent droplet nuclei containing *M. tuberculosis*

TB Transmission

- **Probability that TB will be transmitted depends on:**
  - **Infectiousness of person with TB disease**
  - **Environment in which exposure occurred**
  - **Length of exposure**
  - **Virulence (strength) of the tubercle bacilli**

- **The best way to stop transmission is to:**
  - **Isolate infectious persons**
  - **Provide effective treatment to infectious persons as soon as possible**

TB Pathogenesis
Latent TB Infection (LTBI)

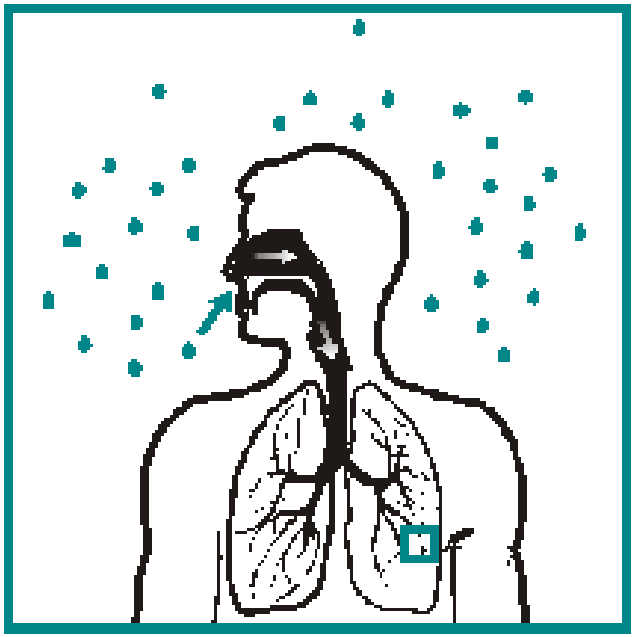
- **Occurs when tubercle bacilli are in the body, but the immune system is keeping them under control**
- **Detected by the Mantoux tuberculin skin test (TST) or by blood tests such as interferon-gamma release assays (IGRAs) which include:**
  - **QuantiFERON®-TB Gold test (QFT-G)**
  - **QuantiFERON®-TB Gold In-Tube (QFT-GIT)**
  - **T-Spot®.*TB* test (T-SPOT)**
- **People with LTBI are NOT infectious**

TB Pathogenesis
TB Disease

- **Develops when immune system cannot keep tubercle bacilli under control**
  - **May develop very soon after infection or many years after infection**
- **About 10% of all people with normal immune systems who have LTBI will develop TB disease at some point in their lives**
- **People with TB disease are often infectious**

TB Pathogenesis

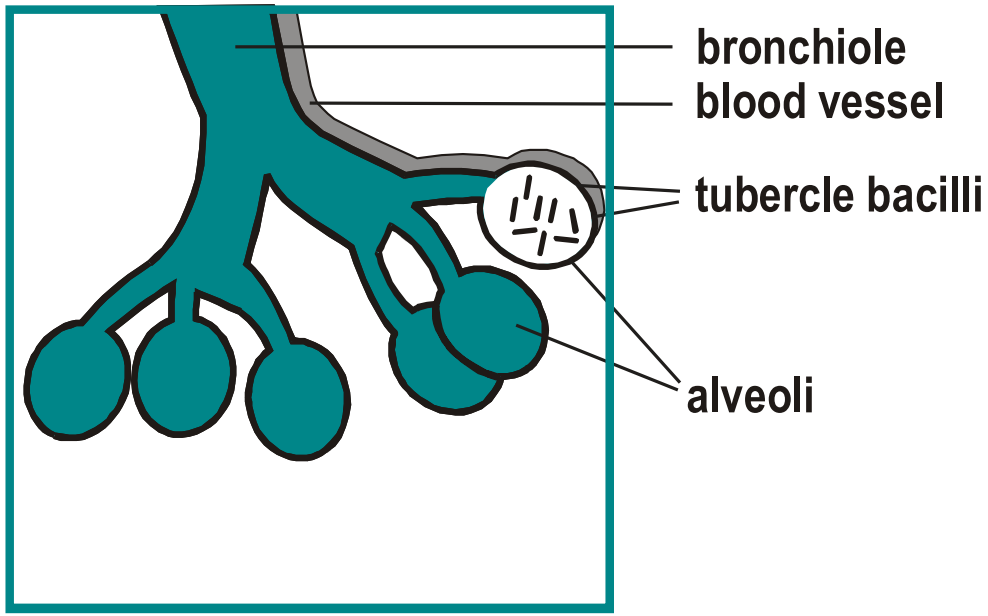
1



Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to small air sacs (alveoli)

TB Pathogenesis

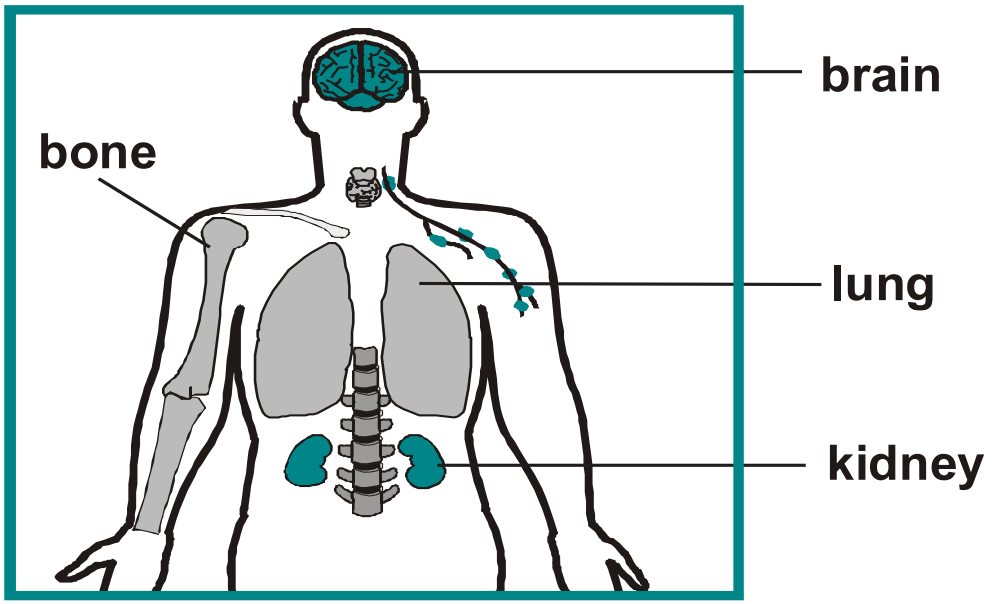
2



Tubercle bacilli multiply in alveoli, where infection begins

TB Pathogenesis

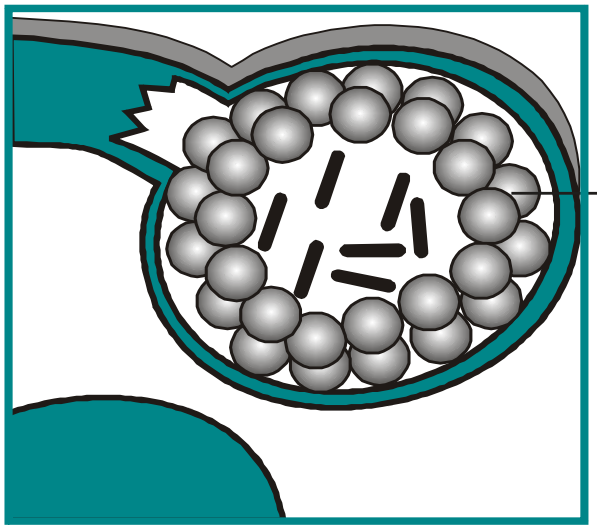
3



A small number of tubercle bacilli enter bloodstream and spread throughout body

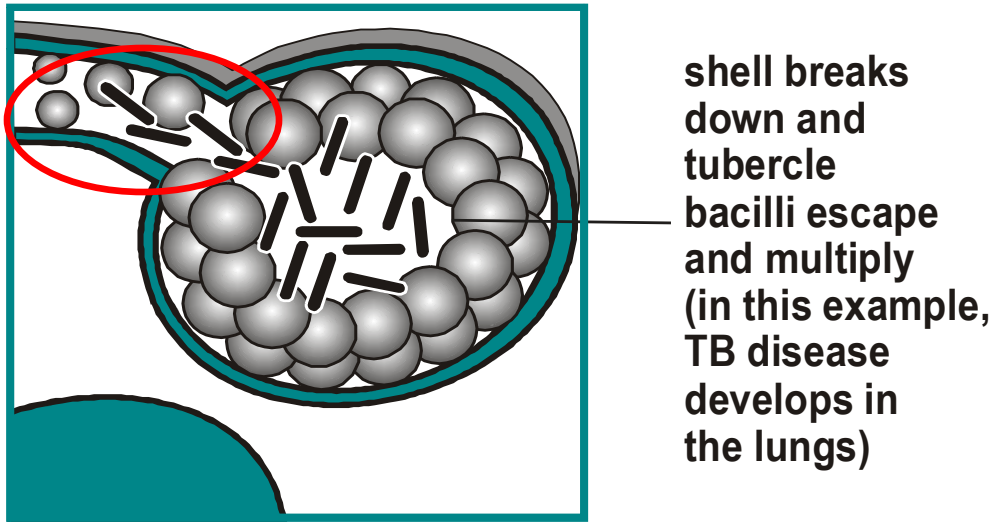
TB Pathogenesis
LTBI

4



- 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)

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

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 blood test results usually positive	TST or 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

TB Pathogenesis

When a person inhales air that contains droplet nuclei containing *M. tuberculosis*, where do the droplet nuclei go? ***(pg. 15)***

- **Most of the larger droplet nuclei become lodged in the upper respiratory tract, where infection is unlikely to develop**
- **However, droplet nuclei may reach the small air sacs of the lung (the alveoli), where infection begins**

TB Pathogenesis

After the tubercle bacilli reach the small air sacs of the lung (the alveoli), what happens to them? ***(pg. 15)***

- **Tubercle bacilli multiply in alveoli and some enter the bloodstream and spread throughout the body**
- **Bacilli may reach any part of the body**
- **Within 2 to 8 weeks, the immune system usually intervenes, halting multiplication and preventing further spread**

TB Pathogenesis

In people with LTBI (but not TB disease), how does the immune system keep the tubercle bacilli under control? ***(pg. 15)***

The immune system produces special immune cells that surround the tubercle bacilli. These cells form a shell that keeps the bacilli contained and under control.

TB Pathogenesis

How is LTBI detected? *(pg. 16)*

LTBI is detected by the Mantoux tuberculin skin test (TST) or blood tests such as interferon-gamma release assays (IGRA), which include the QuantiFERON®-TB test (QFT-G), QuantiFERON®-TB Gold In-tube (QFT-GIT), or T-SPOT.

TB Pathogenesis

What are the major similarities and differences between LTBI and TB disease? List characteristics of each.

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 blood test results usually positive	TST or 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

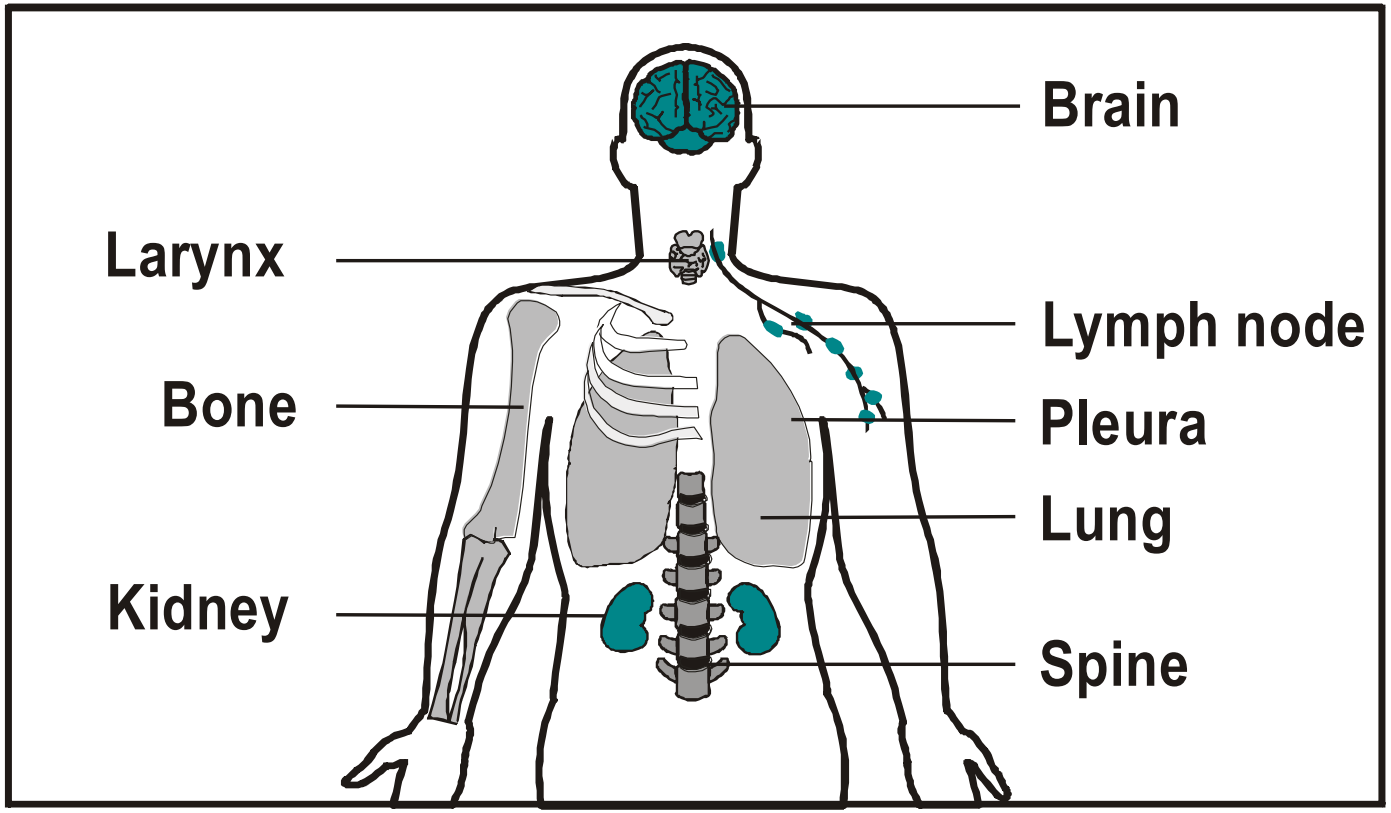
TB Pathogenesis

What happens if the immune system cannot keep the tubercle bacilli under control and the bacilli begin to multiply rapidly? *(pg. 16)*

When this happens, TB disease develops. The risk that TB disease will develop is higher for some people than for others.

Sites of TB Disease (1)

Bacilli may reach any part of the body, but common sites include:



Sites of TB Disease (2)

	Location	Frequency
Pulmonary TB	Lungs	Most TB cases are pulmonary
Extrapulmonary TB	Places other than lungs such as: • Larynx • Lymph nodes • Pleura • Brain • Kidneys • Bones and joints	Found more often in: • HIV-infected or other immunosuppressed persons • Young children
Miliary TB	Carried to all parts of body, through bloodstream	Rare

TB Pathogenesis

Progression from LTBI to TB Disease

Progression to TB Disease (1)

- **Risk of developing TB disease is highest the first 2 years after infection**
- **People with LTBI can be given treatment to prevent them from developing TB disease**
- **Detecting TB infection early and providing treatment helps prevent new cases of TB disease**

Progression to TB Disease (2)

Some conditions increase probability of LTBI progressing to TB disease

- Infection with HIV
- Chest x-ray findings suggestive of previous TB
- Substance abuse
- Recent TB infection
- Prolonged therapy with corticosteroids and other immunosuppressive therapy, such as prednisone and tumor necrosis factor-alpha [TNF-α] antagonists
- Organ transplant
- Silicosis
- Diabetes mellitus
- Severe kidney disease
- Certain types of cancer
- Certain intestinal conditions
- Low body weight

Progression to TB Disease (3)

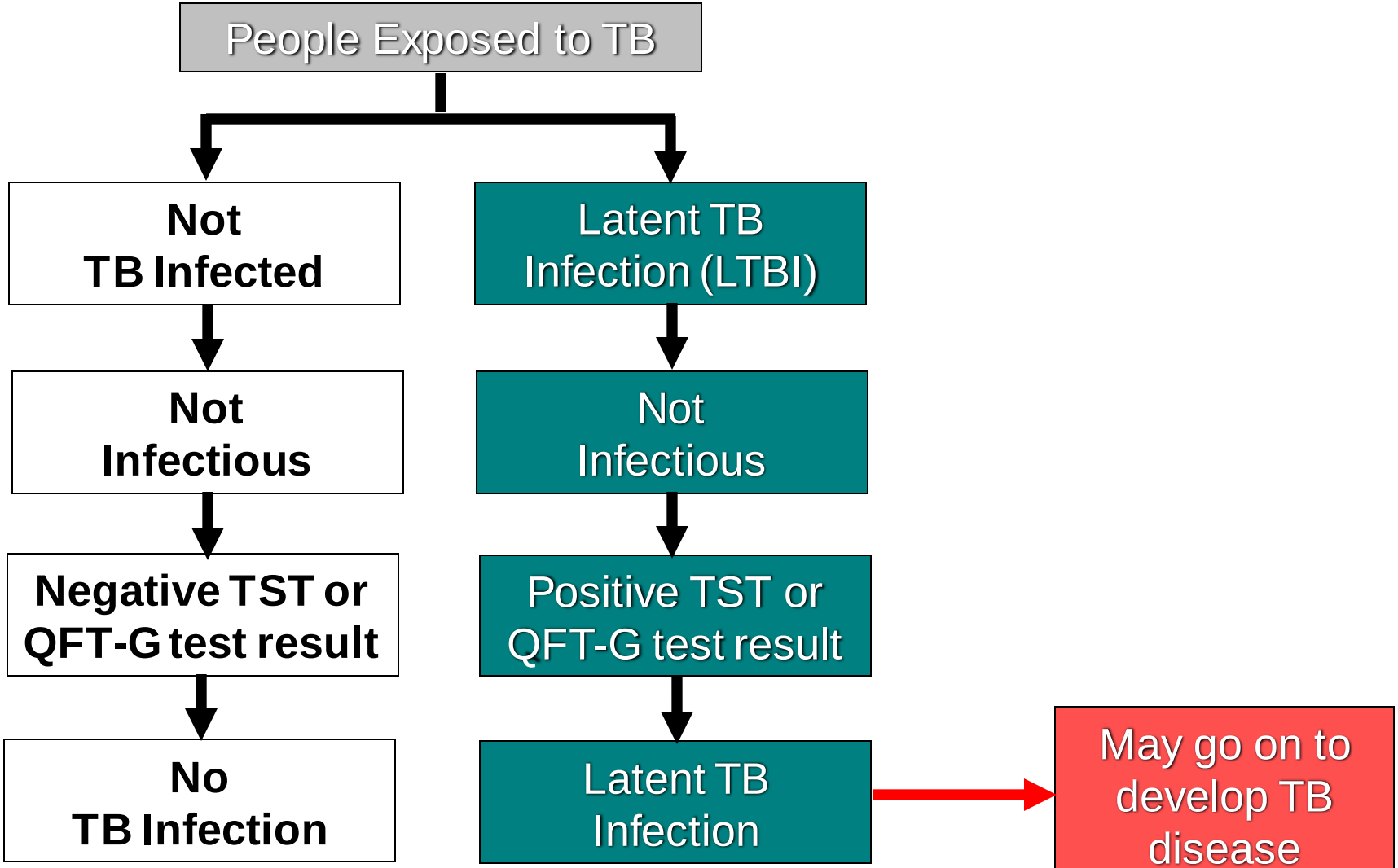


Figure 1.5

Progression to TB Disease (4)
TB and HIV

In an HIV-infected person, TB can develop in one of two ways:

- **Person with LTBI becomes infected with HIV and then develops TB disease as the immune system is weakened**
- **Person with HIV infection becomes infected with *M. tuberculosis* and then rapidly develops TB disease**

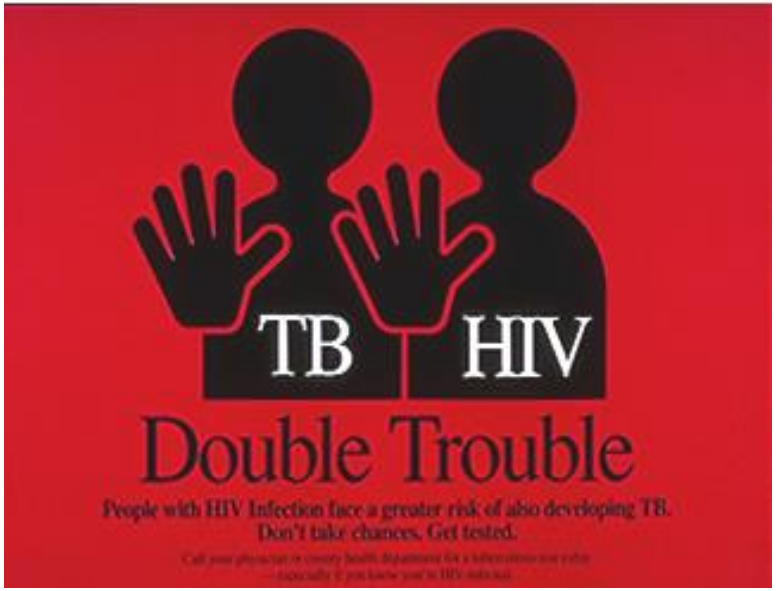


Image credit: Mississippi State Department of Health