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Mayo Clinic Center for Tuberculosis

TB Transmission, Pathogenesis, & Infection Control

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Disclosures

- None

Learning Objectives

- Understand the hematogenous phase of TB infection
- Discuss the pulmonary host defense mechanisms that protect against TB
- Discuss the most common immune suppressive condition in TB patients in the United States

March 11, 2015 Detroit Metro Airport

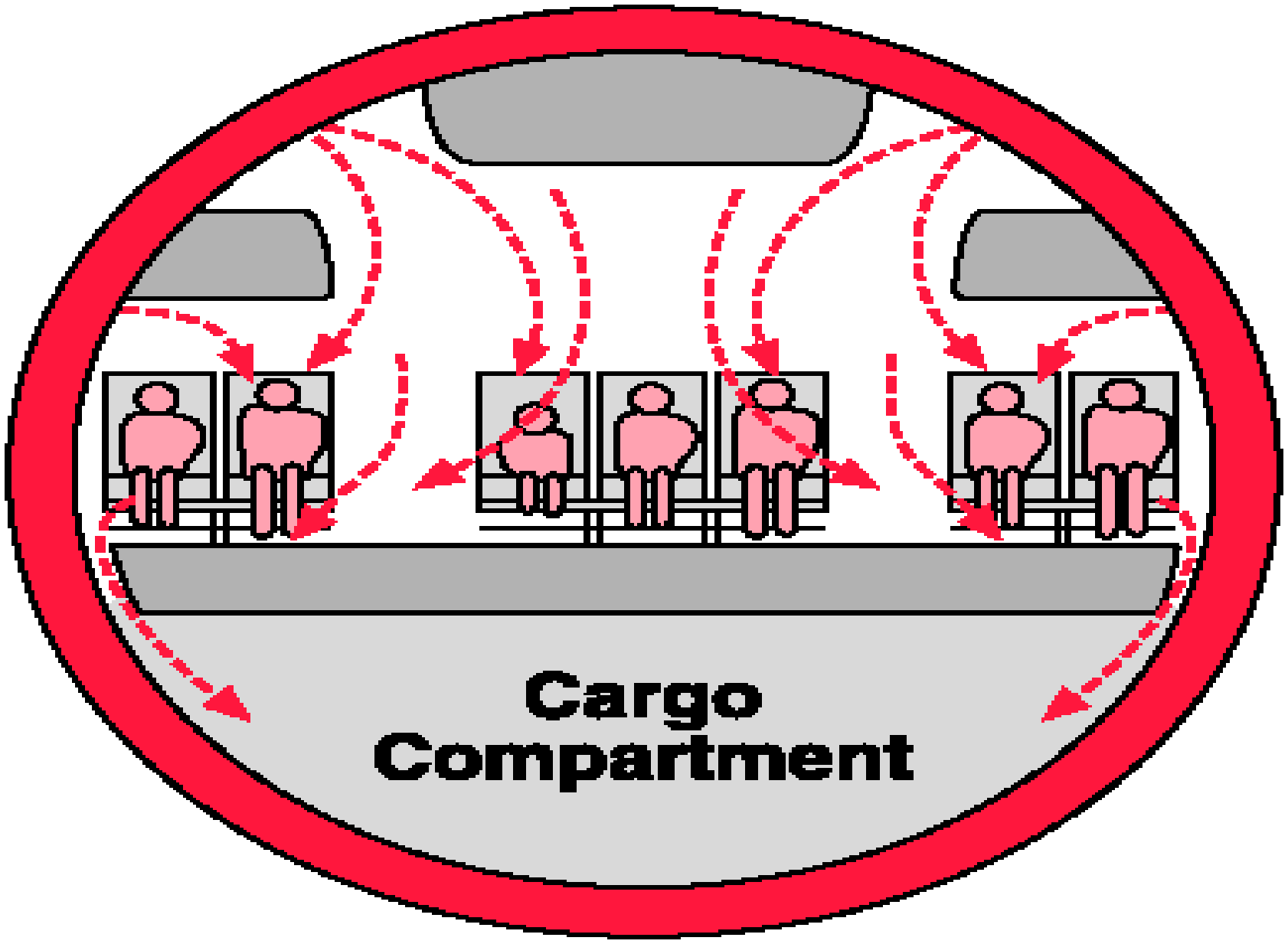
- Flight #456 from Manila
- 60 yr male coughing up blood on flight
- CDC Quarantine Station evaluated traveler
- Sent to our Emergency Room
- Cavitary, smear +, pulmonary TB diagnosed.
- Drug susceptible


Courtesy of www.405themovie.com

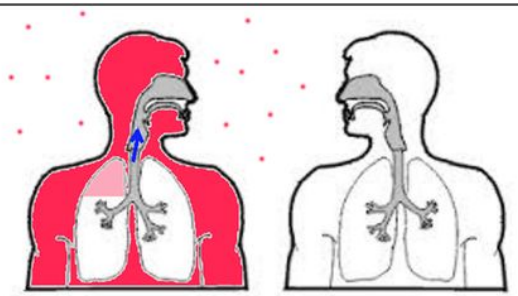
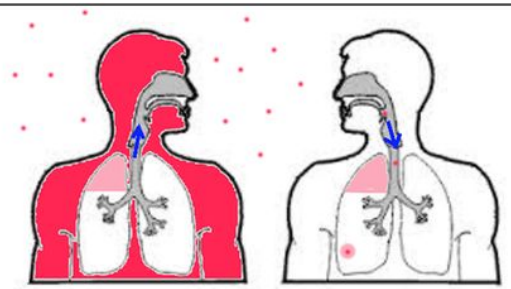
Questions about airplane TB Case

- What is risk of transmission to passengers?
- What predisposed him to get active TB?
- How might have this been prevented?

Figure 1 Cabin Air Flow Patterns

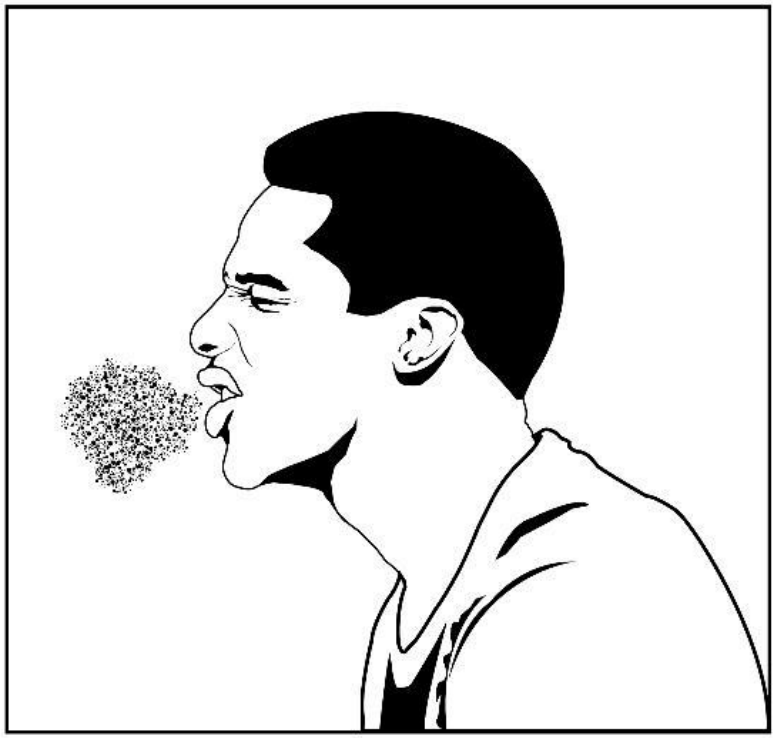


The cascade of tuberculosis (TB) transmission and disease.

		
Step 1: Contact	**Step 2: Generation of Infectious Particles**	**Step 3: Infection and Disease Progression**
A person with active TB and a susceptible person come into sufficiently close contact for airborne transmission of *M. tuberculosis* to occur.	The person with active TB aerosolizes particles of appropriate quality (size, etc.) containing bacilli of sufficient number and virulence to transmit infection.	The susceptible host has an immune background that facilitates initial infection, non-sterilization of the corresponding granuloma, and eventual progression to infectious disease.
Catalyst: Increased contact rates	*Catalyst:* Increased infectiousness	*Catalyst:* Increased susceptibility

TB Transmission (3)

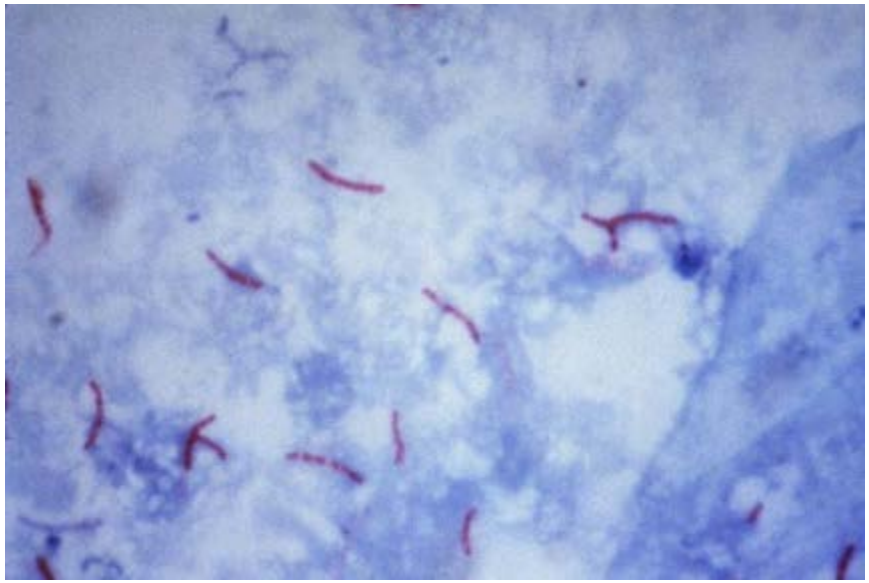
- TB is spread person to person through the air via droplet nuclei
- *M. tuberculosis* may be expelled when an infectious person:
  - Coughs
  - Sneezes
  - Speaks
  - Sings
- Transmission occurs when another person inhales droplet nuclei



TB Transmission (2)
Types of Mycobacteria

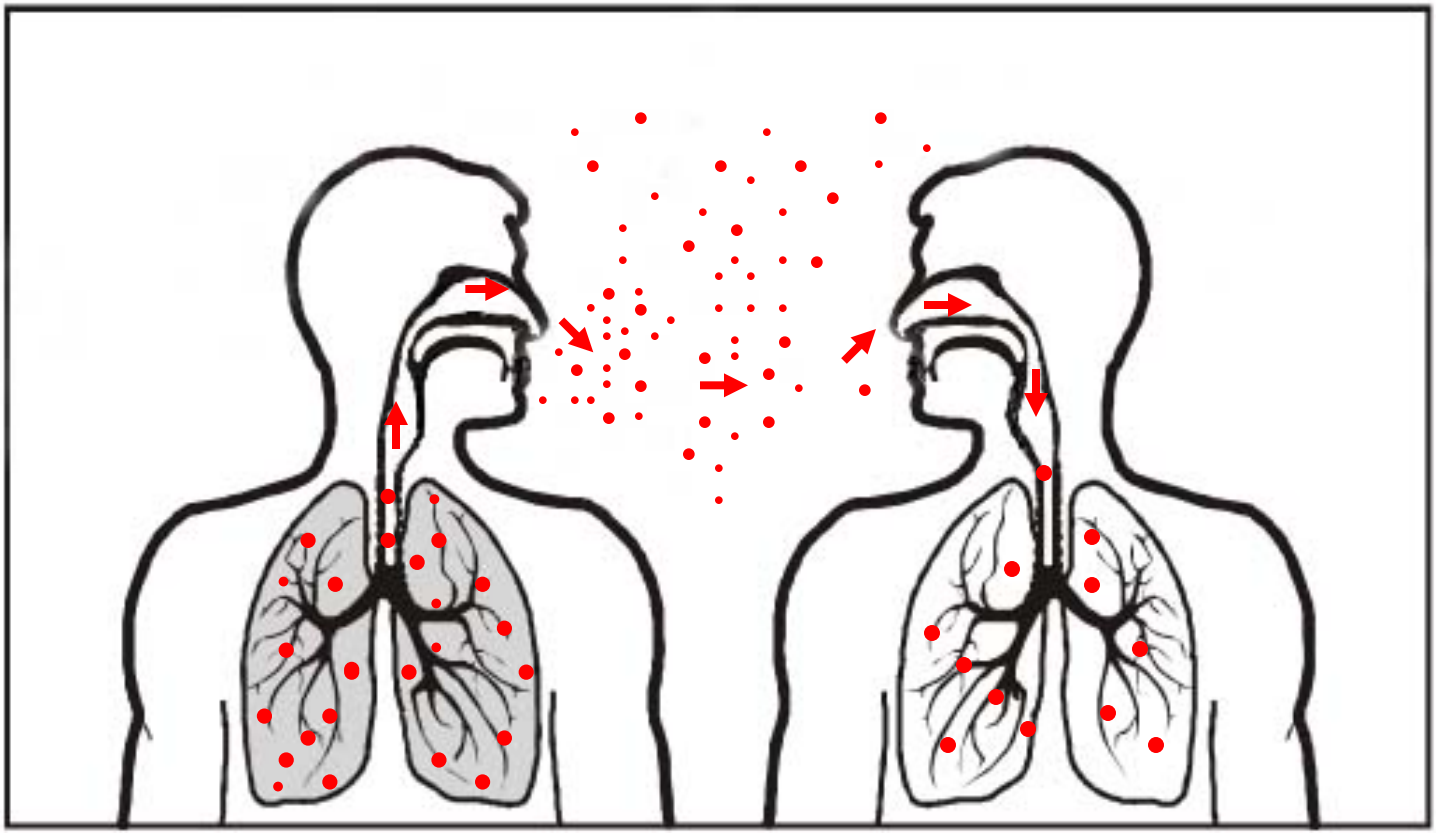
- *M. tuberculosis* causes most TB cases in U.S.

- Mycobacteria that do not cause TB (not airborne person-to-person)
  - e.g., *M. avium* complex
  - *M. kansasii*



M. tuberculosis

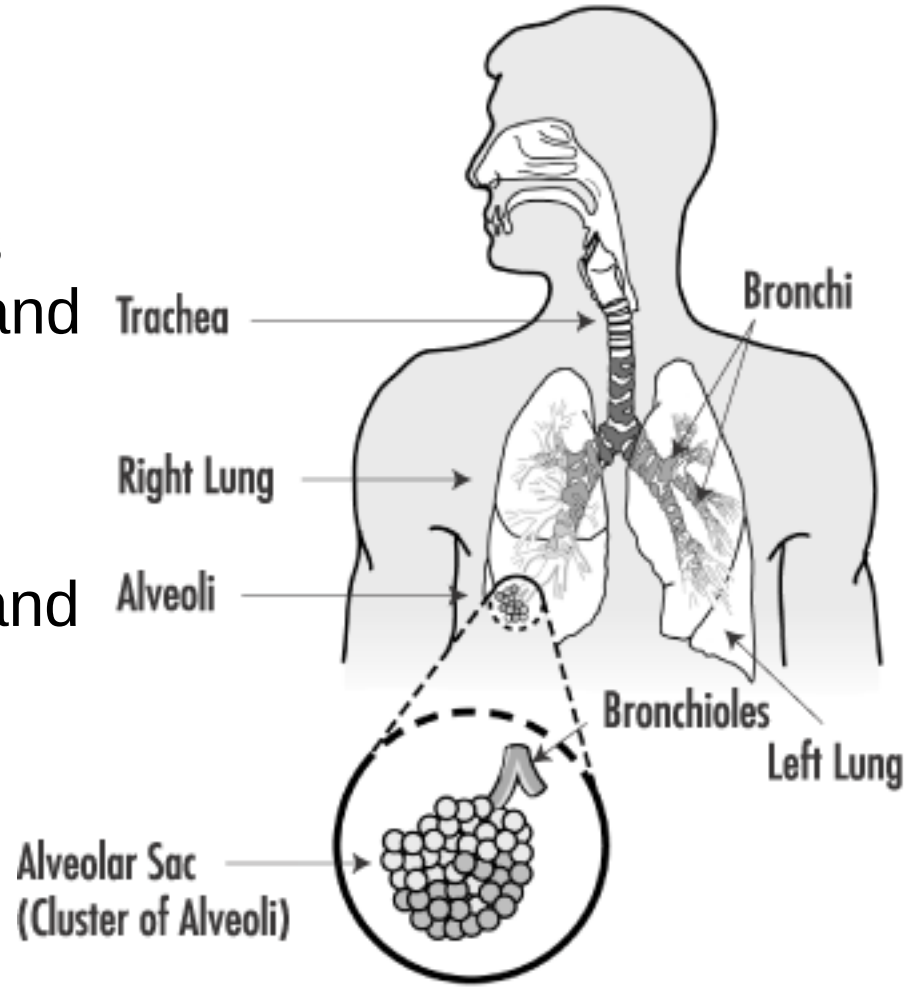
TB Transmission (4)



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

First line of defense – physical & chemical barriers

- Respiratory tract
  - Nose - nasal hair, mucus secretions (phagocytes and antibacterial enzymes), irregular chambers
  - ciliated epithelium (nasal cavity, sinuses, bronchi and trachea)
  - Cough reflexes
  - Alveolar macrophages



TB Pathogenesis
Study Question 1.7

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

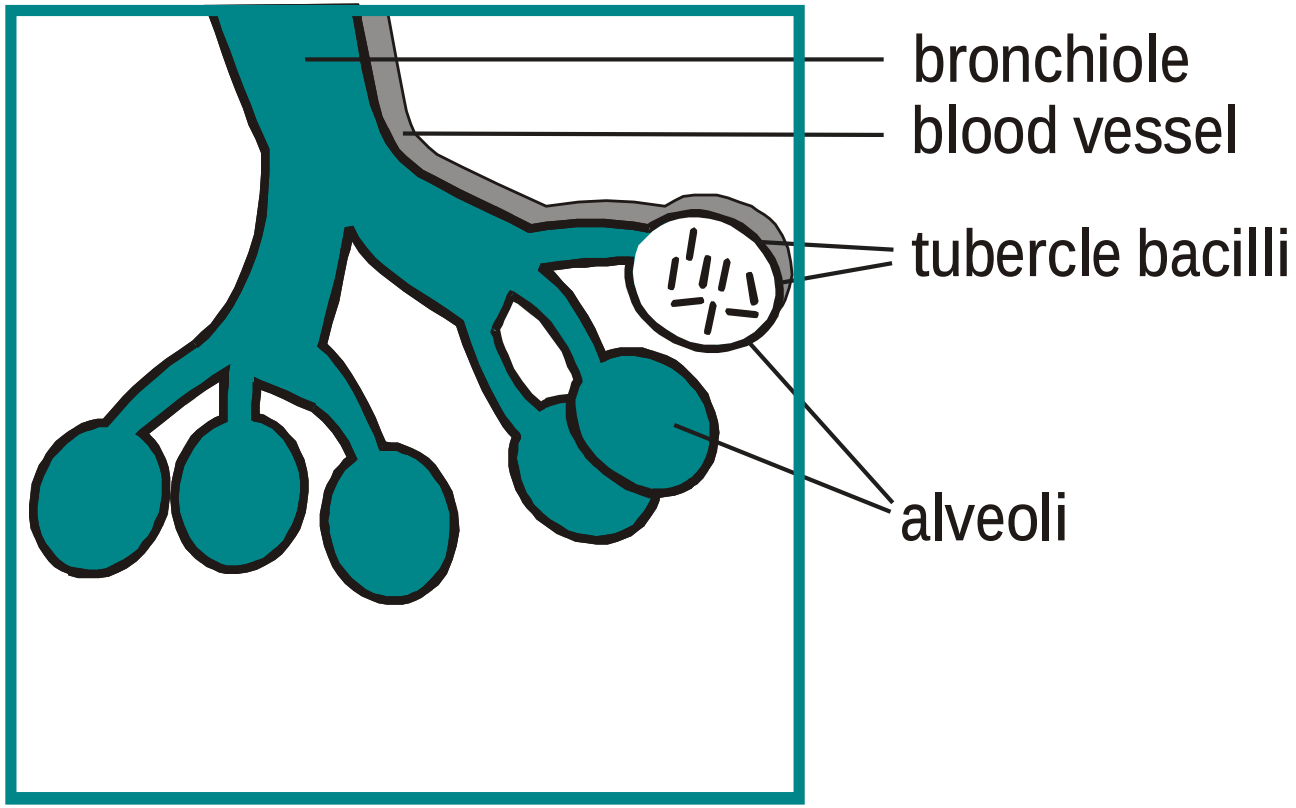
TB Pathogenesis (4)

1

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

TB Pathogenesis (5)

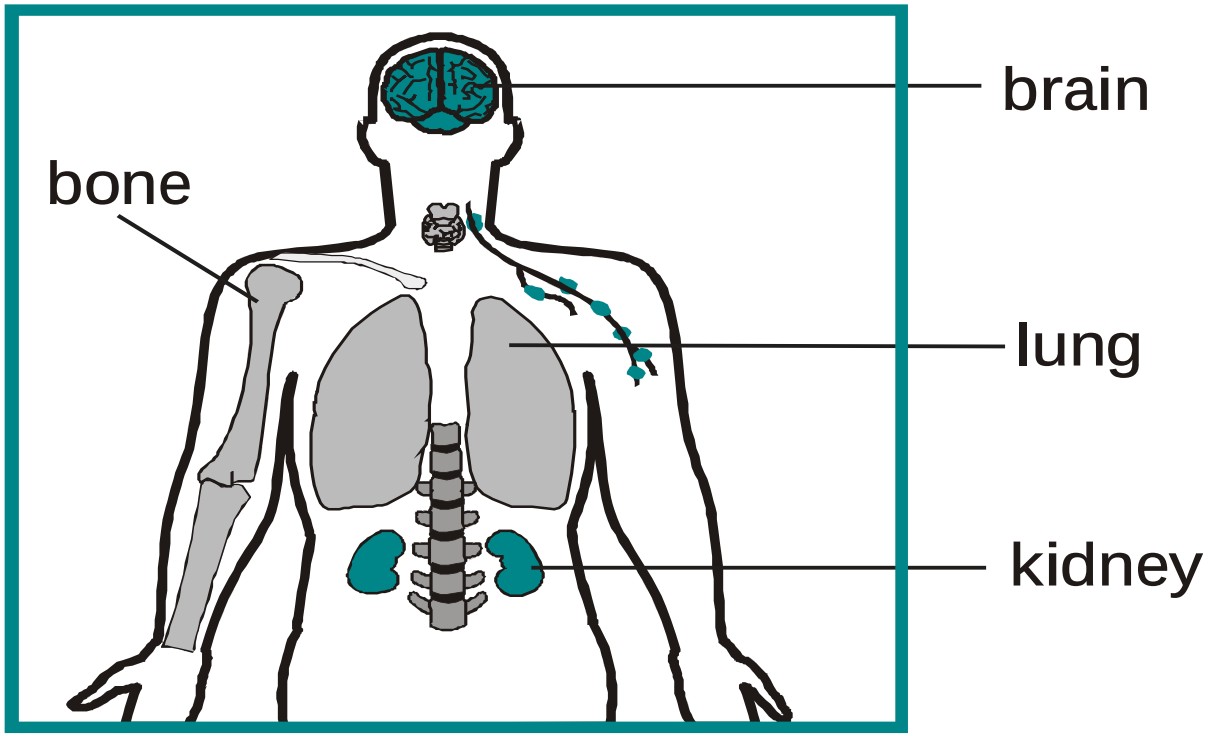
2



Tubercle bacilli multiply in alveoli, where infection begins

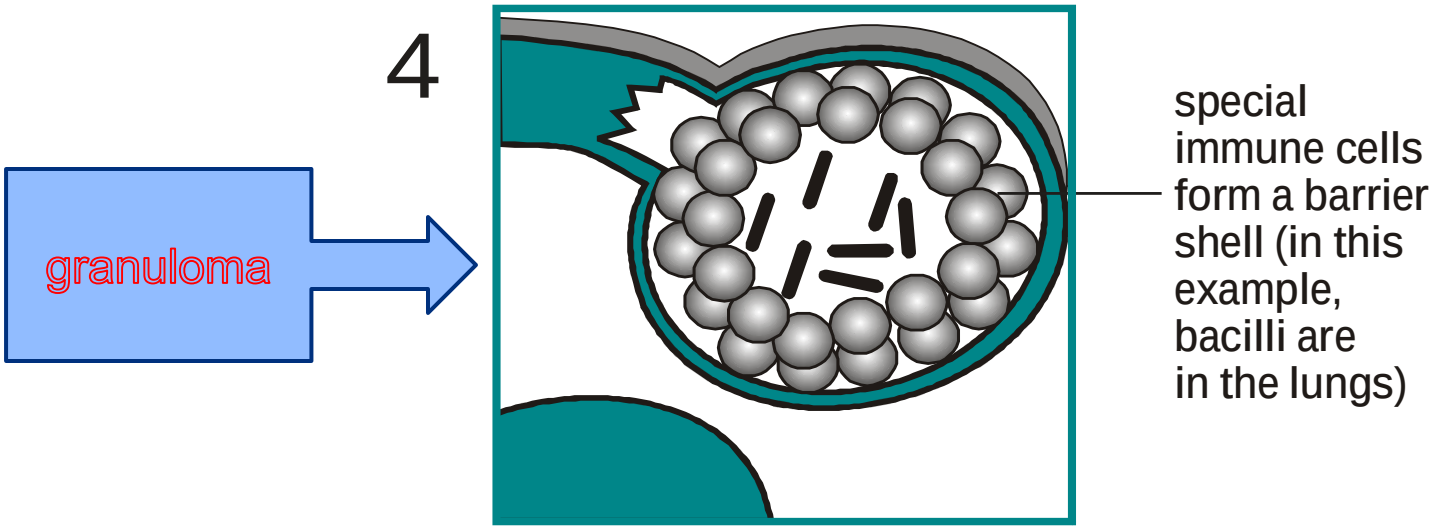
TB Pathogenesis (6)

3



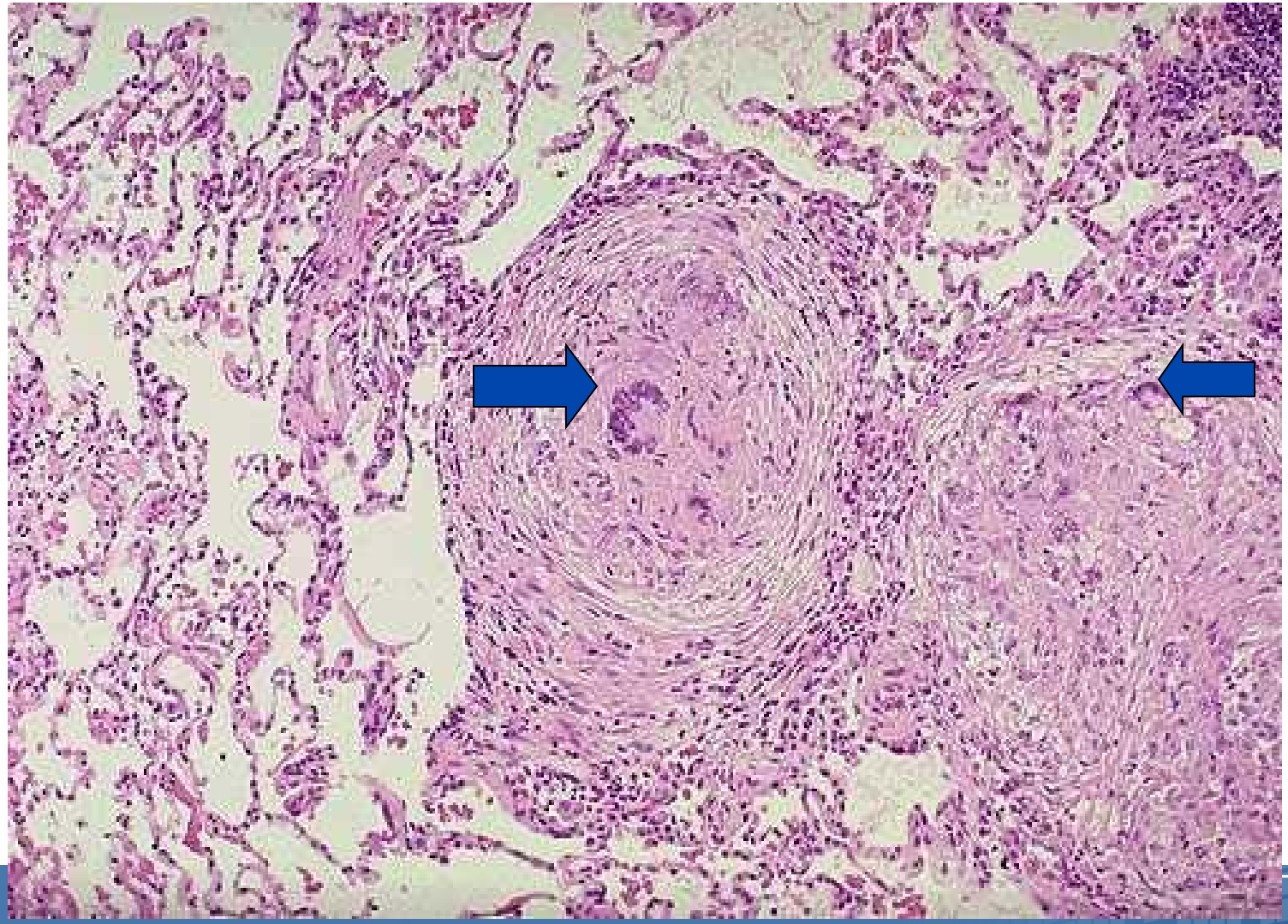
A small number of tubercle bacilli enter <u>bloodstream</u> and spread throughout body

TB Pathogenesis (7)
LTBI

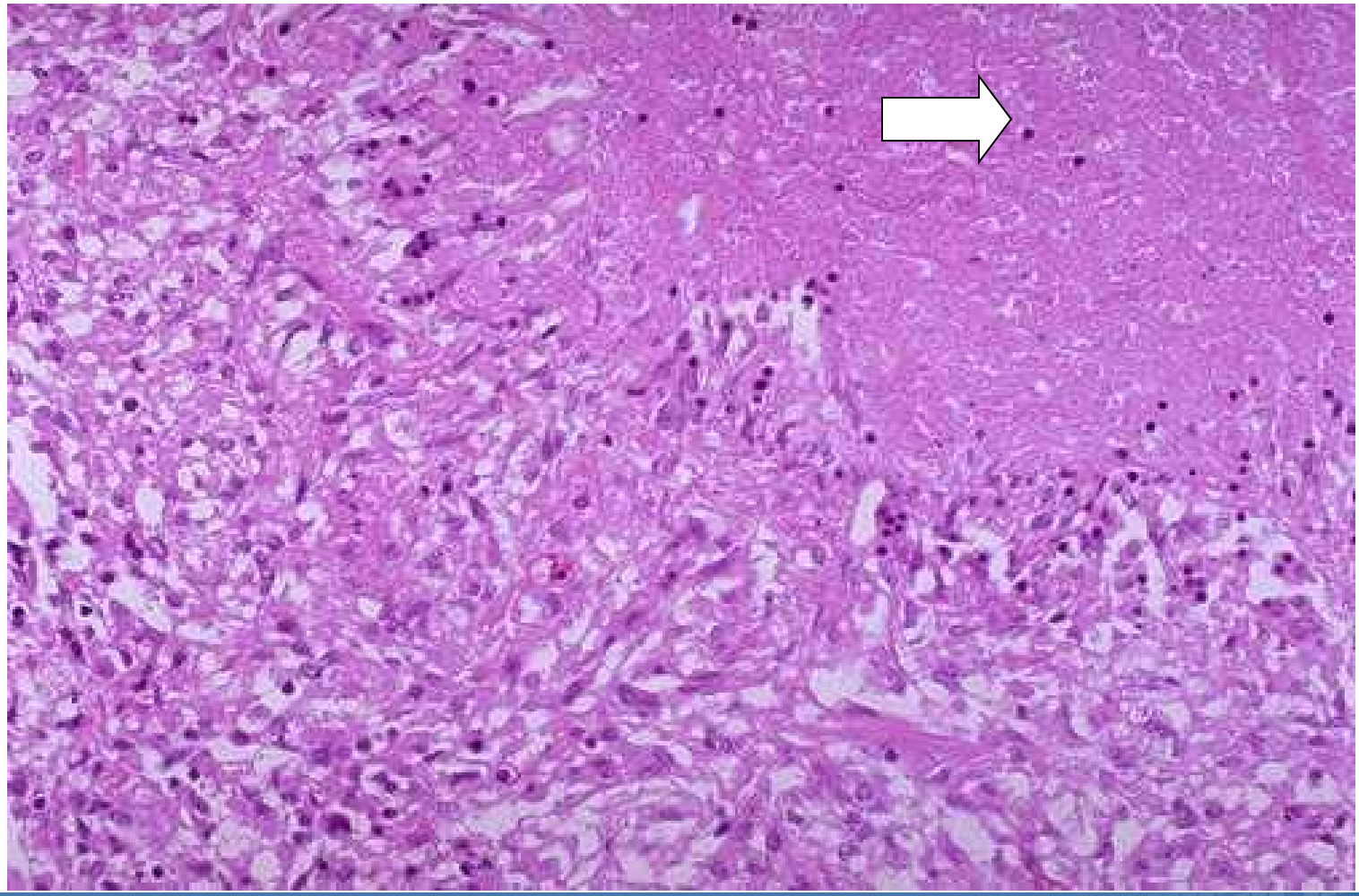


- **Within 2 to 8 weeks the immune system produces special immune cells called macrophages that surround the tubercle bacilli**
- **These cells form a barrier shell that keeps the bacilli contained and under control (LTBI)**

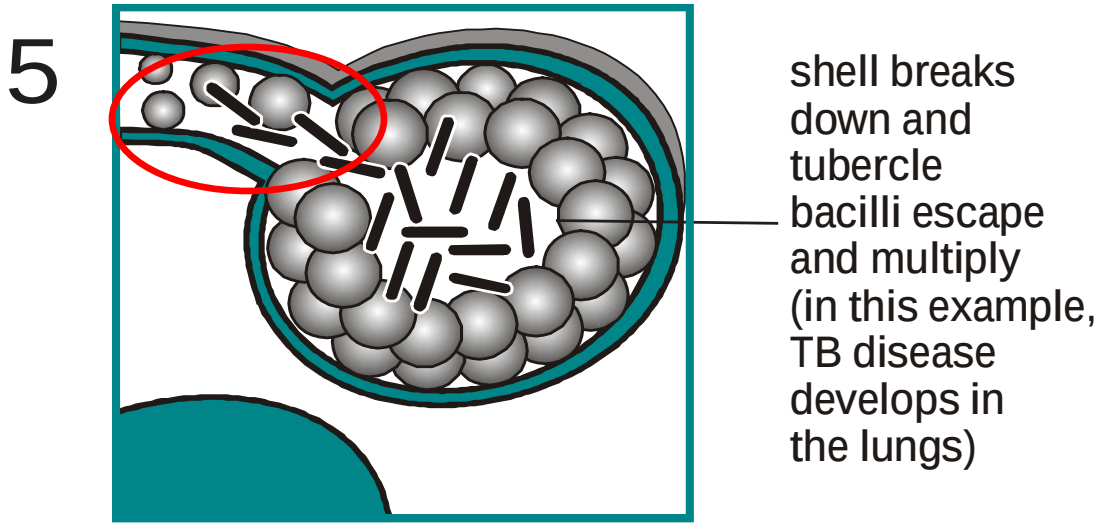
Tuberculous Granuloma



Caseation Necrosis



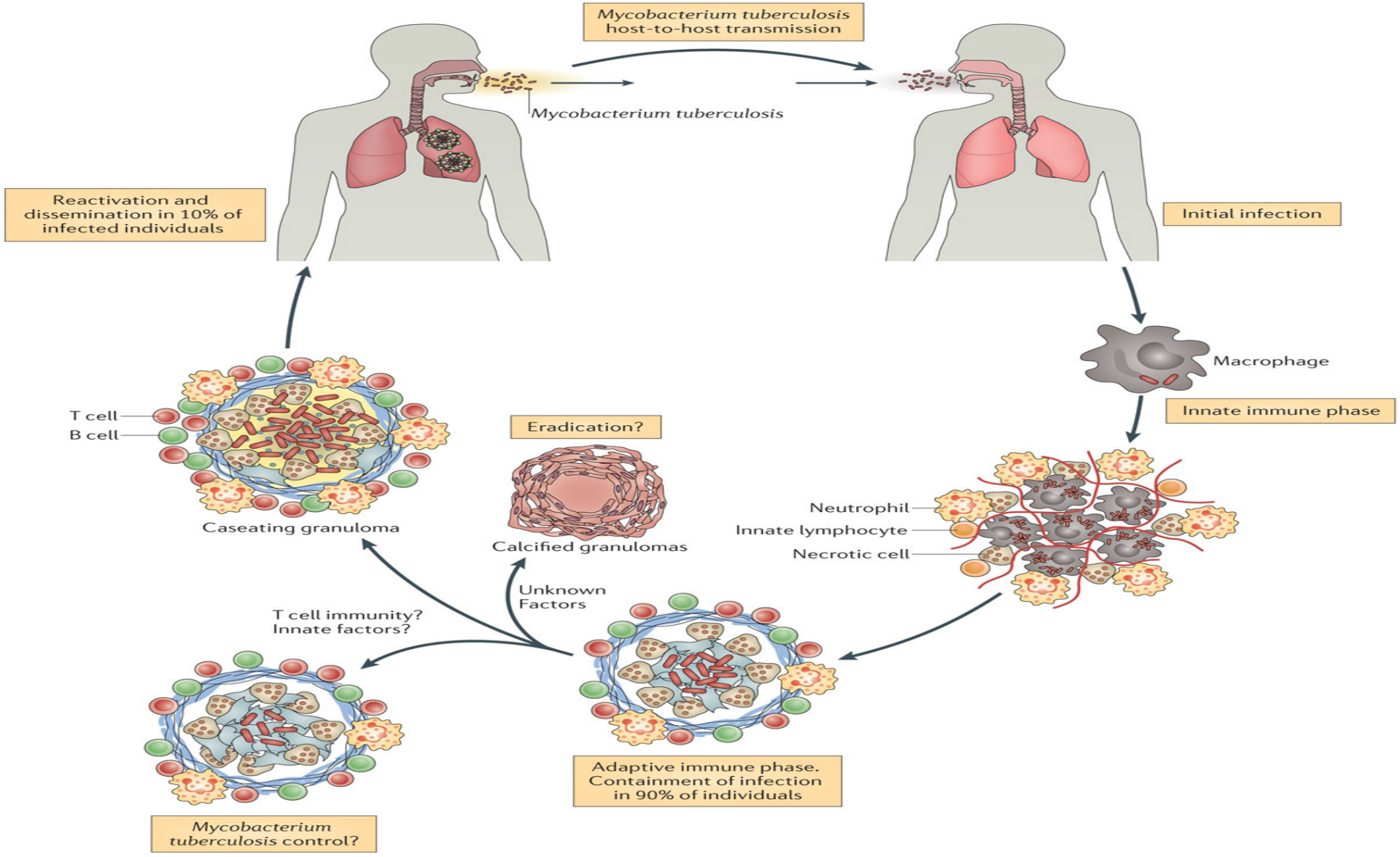
TB Pathogenesis (8)
TB Disease



- **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**

This process can occur in *different* places in the body

- Lungs
- Pleura
- Lymph nodes
- Peritoneum
- Meninges
- Renal
- Fallopian tubes
- Epididymis
- Iritis
- Otitis media
- Synovial fluid
- Skin
- Thyroid
- Adrenal gland
- Liver
- Etc, etc, etc.



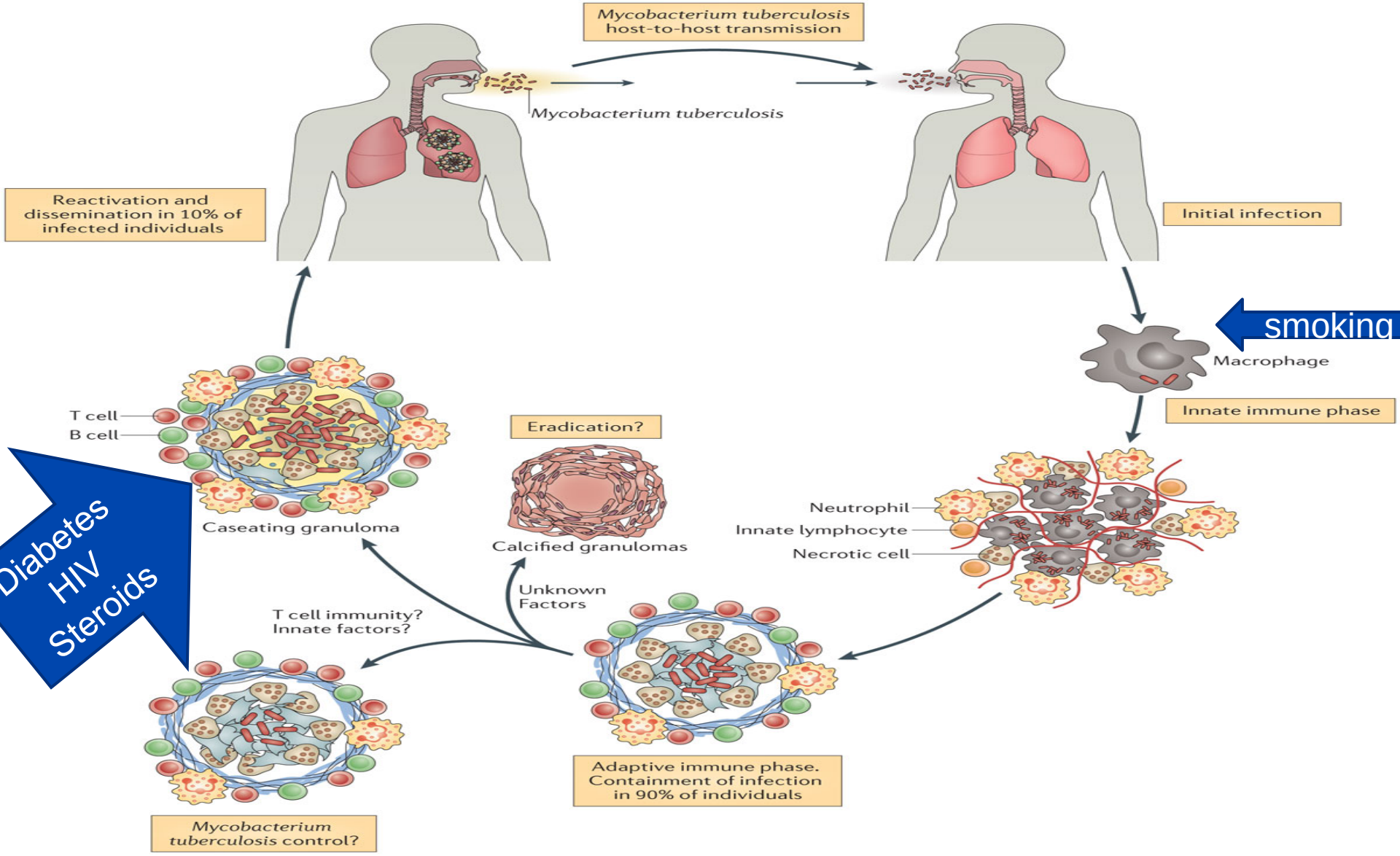
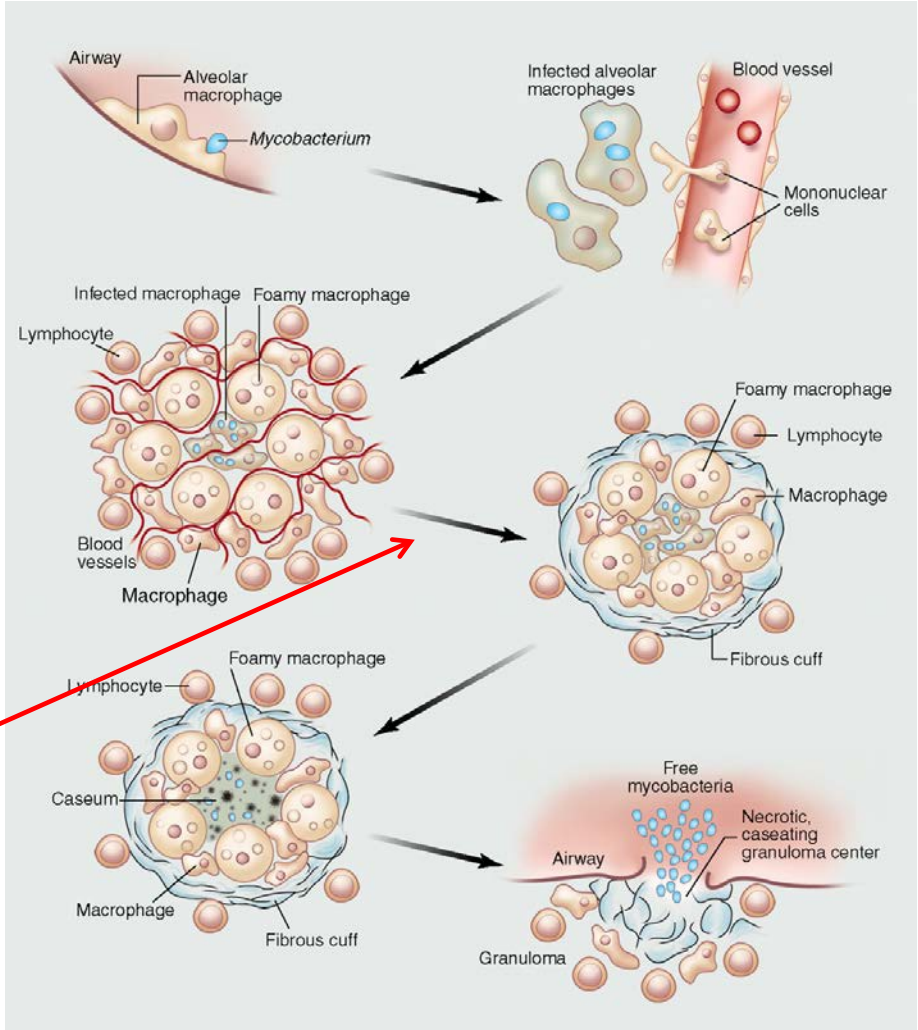


Fig. 1 The life cycle of M. tuberculosis.



2 years

Science
AAAS

David G. Russell et al. Science 2010;328:852-856

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

Conditions with increased probability of LTBI progression to TB disease

- HIV
- Substance abuse
- Chest X-ray findings of previous TB
- Recent TB infection
- Prolonged corticosteroid therapy >30 days
- TNF inhibitors
- Organ transplant
- Silicosis
- Diabetes mellitus
- Severe kidney disease
- Certain types of cancer
- Certain types of intestinal disease
- Low body weight

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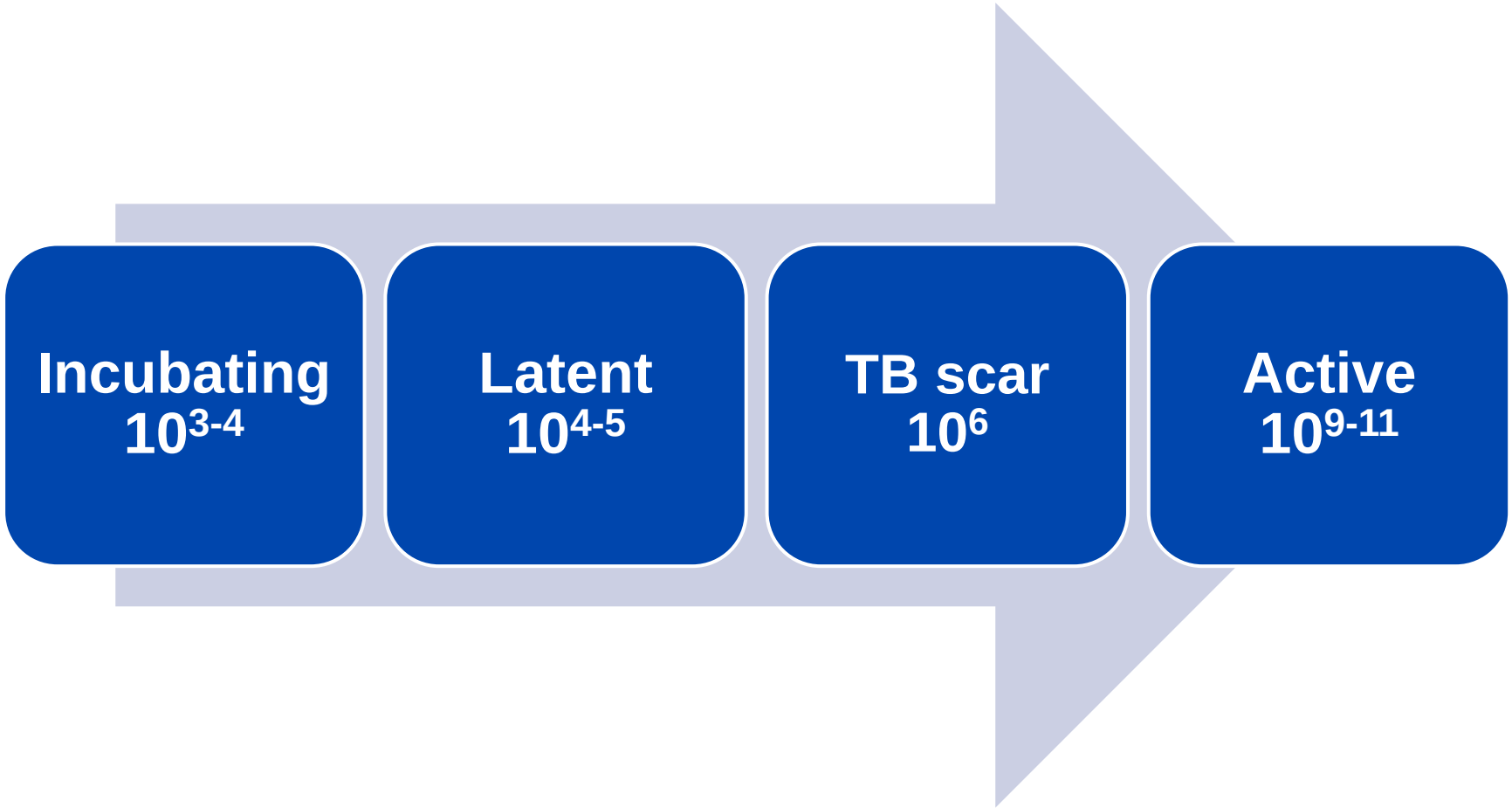
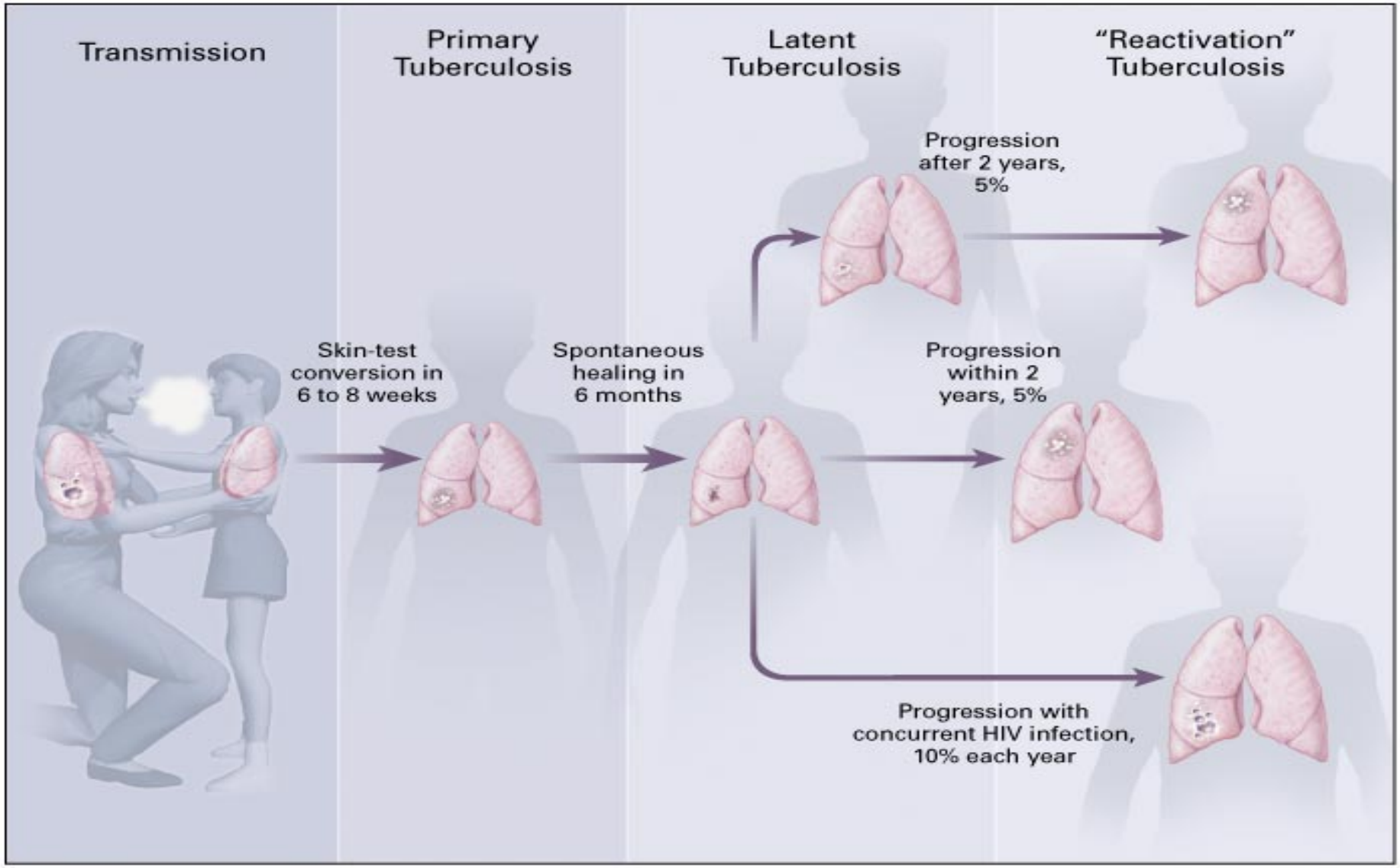
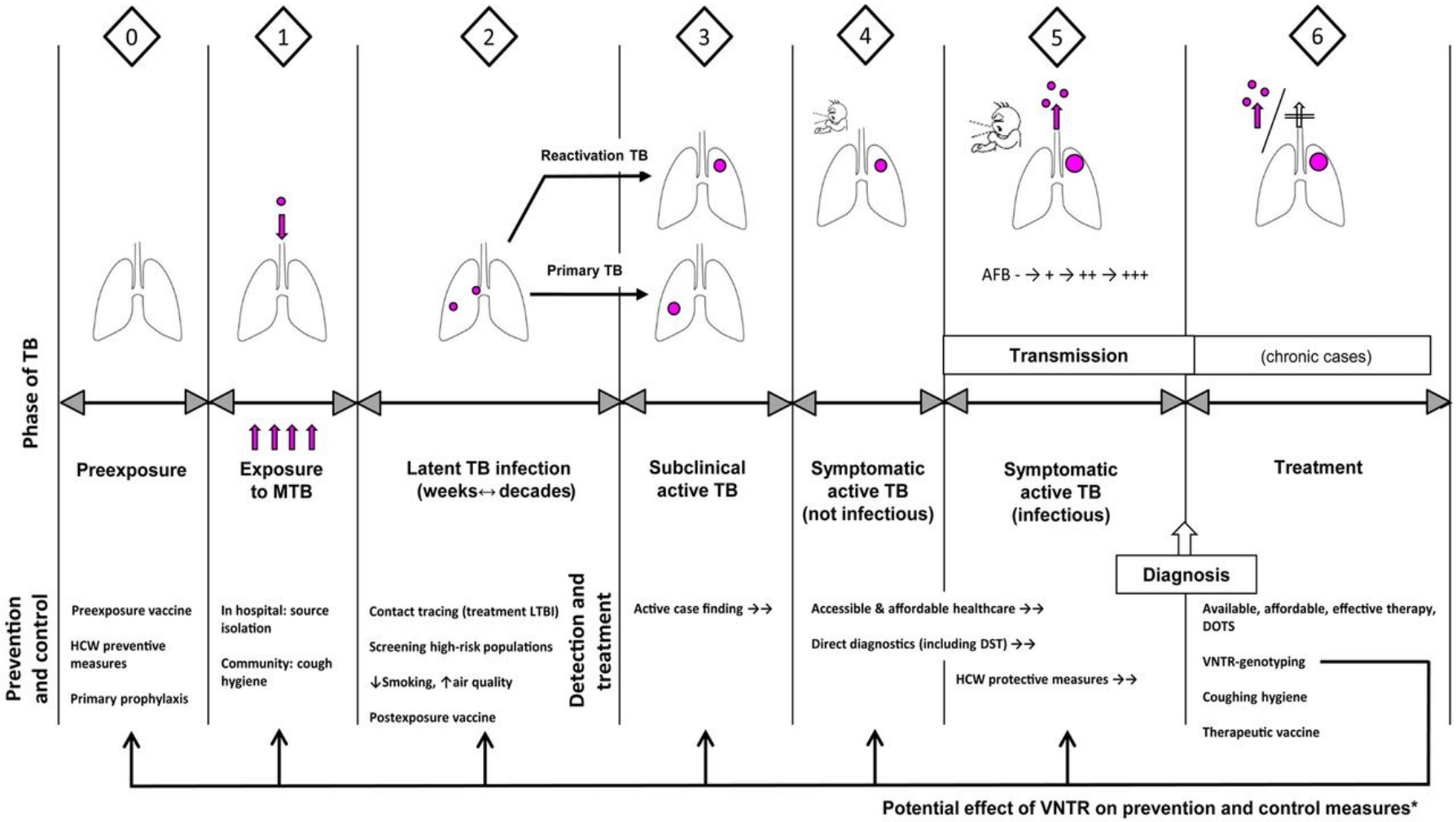
Mycobacterial Burden





Small P and Fujiwara P. N Engl J Med 2001;345:189-200

Overview of the possible phases in the course of pulmonary tuberculosis (TB) and corresponding potential prevention and control measures.



Sandra M. Arend, and Dick van Soolingen Clin Infect Dis. 2015;61:228-232

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
- *Or:*
- Person with HIV infection becomes infected with *M. tuberculosis* and then rapidly develops TB disease

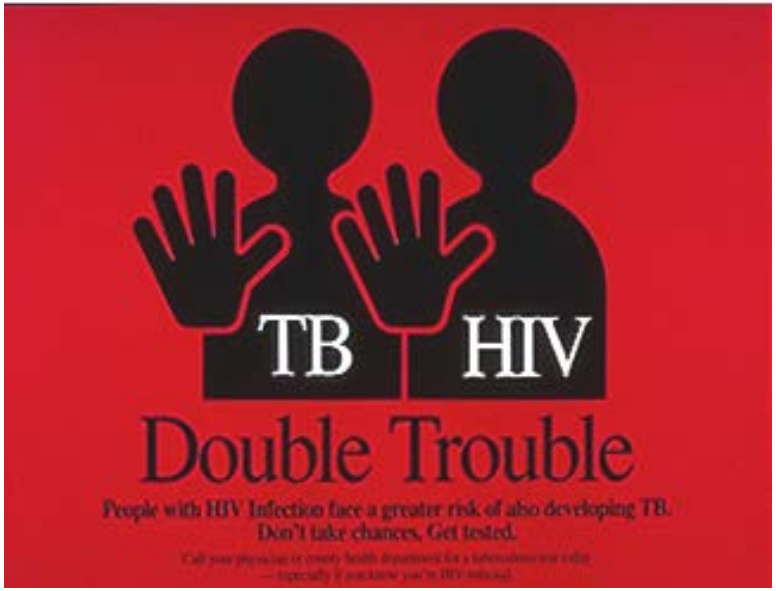
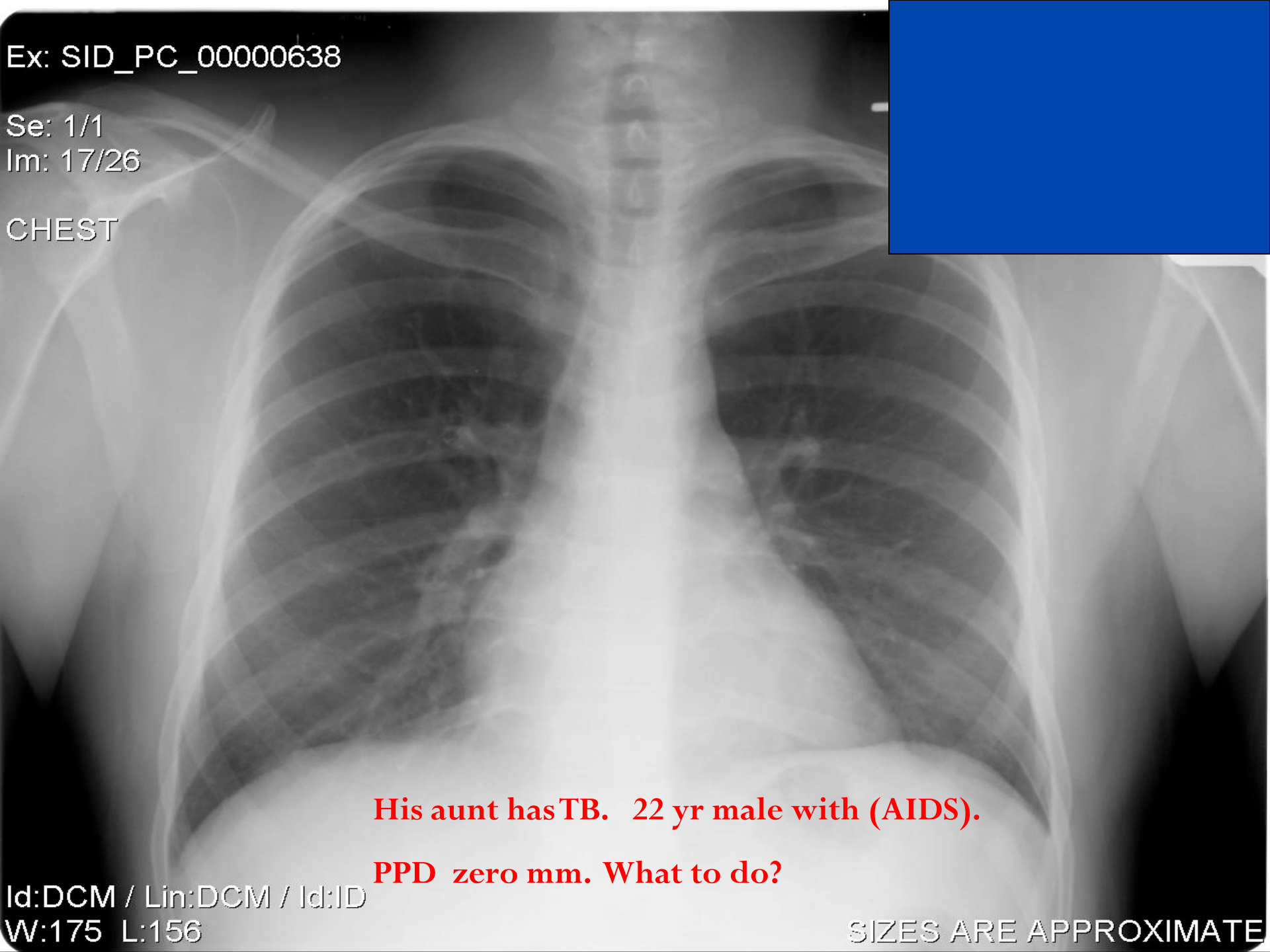
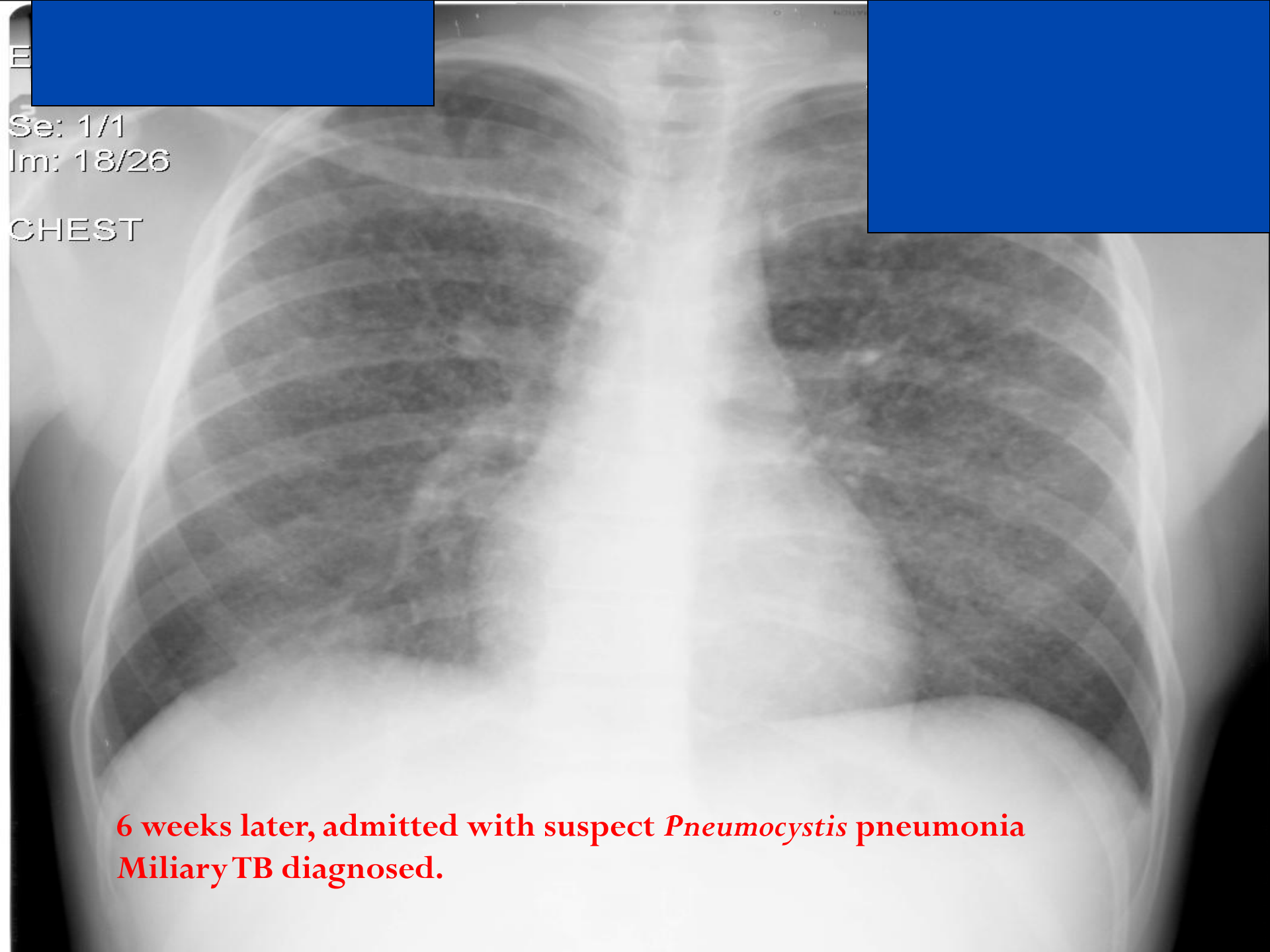


Image credit: Mississippi State Department of Health


Ex: SID_PC_00000638
Se: 1/1
Im: 17/26
CHEST
His aunt has TB. 22 yr male with (AIDS).
PPD zero mm. What to do?
Id:DCM / Lin:DCM / Id:ID
W:175 L:156
SIZES ARE APPROXIMATE



6 weeks later, admitted with suspect *Pneumocystis* pneumonia
Miliary TB diagnosed.

TB Transmission (5)

- 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

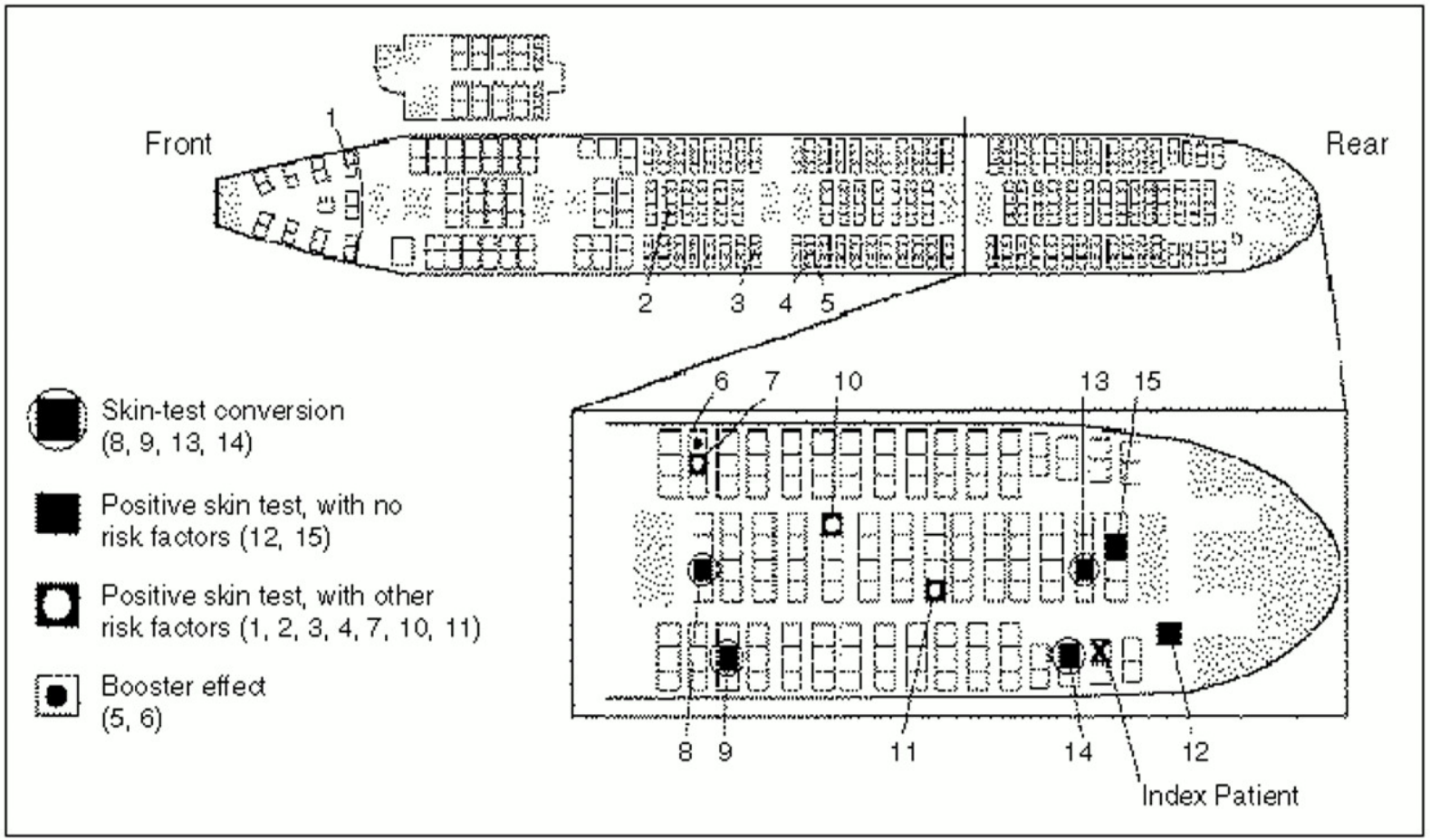
- The best way to stop transmission is to:
  - Isolate infectious persons
  - Provide effective treatment to infectious persons as soon as possible


Courtesy of www.405themovie.com

MDR-TB

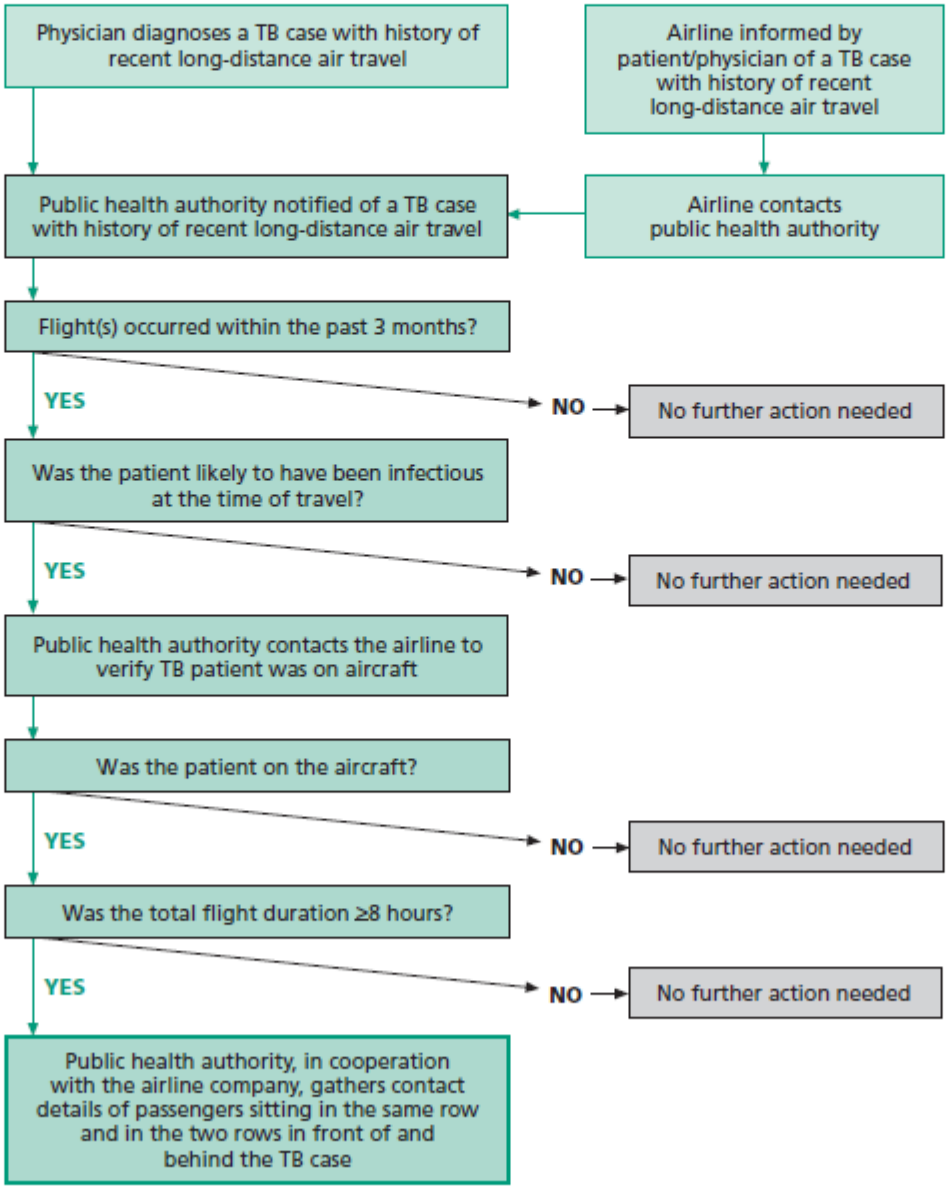
Boeing 747-100

Passengers and Flight Crew on Flight 4 Who Had Positive Tuberculin Skin Tests



Kenyon, T. A. et al. N Engl J Med 1996;334:933-938

Fig. 2 Assessing whether contact-tracing is needed



Major Migration Flows: 1990s

4 x increase in volume as compared to 1960-75

Source: Population Action International 1994

CDC Quarantine Station

- Passengers in adjacent rows notified
- 8 cities across USA.
- No evidence of transmission on flight
- Investigation took ~12 weeks to complete.

- Local Health Dept:
- 3 household contacts IGRA +

What predisposed him to getting active TB?

- Endemic country
- Diabetes mellitus

How might have this been prevented?

- Screen immigrants from endemic countries for latent TB
- IGRA preferable
- Treat latent TB

Chapter 7.
TB Infection Control

Introduction

- ***M. tb* can be transmitted in any setting**
- **Transmission has been documented in health-care settings where there is exposure to persons with infectious TB who**
  - Have unsuspected TB disease,
  - Have not received adequate treatment, or
  - Have not been isolated from others.

Infectiousness

- **Directly related to number of bacilli-laden droplets expelled into the air**
- **Infection occurs when person inhales droplets, which travel to alveoli**
- **Young children with TB less likely to be infectious, but can transmit *M. tb***
- **Infectiousness usually declines rapidly with treatment**
  - However, some remain infectious for weeks or months

Infectiousness (cont.)

Patient factors associated with infectiousness:

- Coughing
- Cavity in the lung
- Sputum smears positive for acid-fast bacilli (AFB)
- TB disease of the lungs, airway, or larynx
- Undergoing cough-inducing or aerosol-generating procedures
- Not receiving adequate therapy
- Culture positive

Criteria to Be Considered Noninfectious

Patients no longer considered infectious if:

- **They have 3 consecutive negative sputum smears,**
- **Their symptoms have improved, and**
- **They are adhering to an adequate treatment regimen for at least 2 weeks**

Environmental Factors that Enhance Risk of Transmission

- High concentration of droplet nuclei in the air
- Exposure in small, enclosed spaces
- Poor ventilation that inadequately dilutes or removes droplet nuclei
- Recirculation of air containing droplets
- Improper specimen handling procedures
- Positive air pressure in patient's room causing flow to other areas

TB Infection Control Measures

- **TB infection control (IC) measures should be based on TB risk assessment for the setting**
- **The goals of IC programs are**
  - Detect TB disease early and promptly
  - Isolate persons with known/suspected TB
  - Start treatment in persons with known/suspected TB

Detection of TB Disease

- Primary risk in health-care settings: unsuspected persons with TB disease
- Protocols for detecting, isolating, and managing TB suspects should be implemented
- Staff admitting patients should be trained to know signs/symptoms of TB

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Airborne Precautions

- **Separate and isolate persons with TB signs/symptoms**
  - Preferably use airborne infection isolation (AII) room
  - Single-patient room with controlled environment to minimize transmission of infection
  - Continue precautions until 3 negative smears, 2 weeks therapy, and improved symptoms
- **Start TB patients/suspects on standard TB therapy**

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Hierarchy of Controls

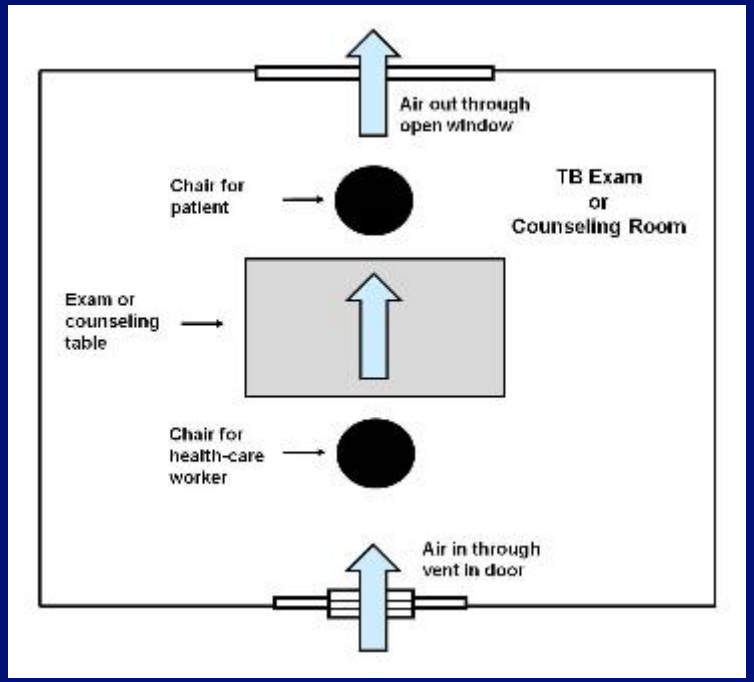
TB IC program should be based on three levels of controls:

- Administrative controls to reduce risk of exposure
- Engineering controls to prevent spread and reduce concentration of droplet nuclei
- Personal respiratory protection to further reduce risk of exposure

Environmental Controls

Prevent spread and reduce concentration of infectious droplet nuclei through

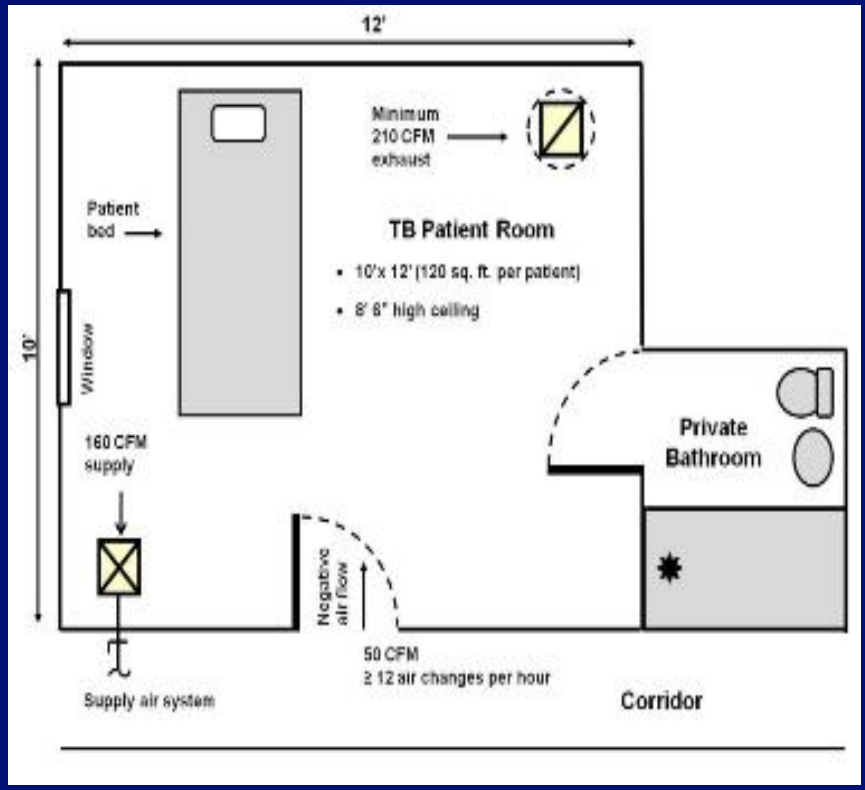
- **Primary controls: ventilation technologies**
  - Natural ventilation: relies on open doors, windows
  - Mechanical ventilation (local exhaust and general): equipment, use of AII room
- **Secondary controls: HEPA filters and ultraviolet germicidal irradiation (UVGI)**



Environmental Controls (cont.)

AII rooms designed to prevent spread of droplet nuclei

- TB suspect/patient should be put in AII room immediately
- Facilities that see TB patients should have at least one AII room



Environmental Controls (cont.)

Characteristics of AII room:

- Single-patient room with private bathroom
- Negative pressure relative to hallway
- Air sent outdoors or through HEPA filter
- Six or more air changes per hour (in some settings 12 or more air changes per hour are recommended)
- Visitors should use N95 respirator

Respiratory Protection Controls

Consists of using personal protective equipment in areas with increased risk of exposure:

- **TB AII rooms**
- **Rooms where cough- or aerosol-producing procedures are done**
- **Vehicles transporting infectious patients**
- **Homes of infectious TB patients**

Respiratory Protection Controls (cont.)

- Settings that use respiratory protection controls should develop, implement, and maintain a respiratory protection program
- Train HCWs on respiratory protection
- Educate patients on respiratory hygiene
- Test HCWs for mask fit and functionality

Respirator for Health-Care Workers

Health-care worker wearing a respirator

- Designed to filter out droplet nuclei from being inhaled by the health-care worker and other individuals.
- Should properly fit different face sizes and features.
- Should NOT be worn by the patient.

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Surgical Mask for Persons with Infectious TB Disease

Infectious TB patient wearing a surgical mask

Surgical masks

- Designed to stop droplet nuclei from being spread (exhaled) by the patient.
- Should NOT be worn by the health-care worker.

Infection Control Programs in Nontraditional Settings

Nontraditional settings seeing TB patients must have an IC program. These include

- Correctional facilities
- Homeless shelters
- Long-term care facilities
- Home-based health-care and outreach settings
- Emergency medical services

TB Infection Control in the Home

Patients can be sent home while still infectious if

- **A follow-up plan has been made**
- **Patient is on standard treatment and DOT arranged**
- **No very young (under 5 years) or immunocompromised persons in household**
- **Patient willing to refrain from travel outside the home except for health-care visits**

TB Infection Control in the Home (cont.)

HCWs visiting patients at home should:

- **Instruct patients to cover mouth/nose when coughing or sneezing**
- **Wear a respirator when visiting or transporting an infectious patient**
- **Collect specimens in well-ventilated area**

HCWs whose responsibilities include visiting patients at

home should participate in an annual TB testing program

Thank You!

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