
بسم الله الرحمن الرحيم
ذریۃ فاطمۃ

TUBERCULOSIS

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Introduction:

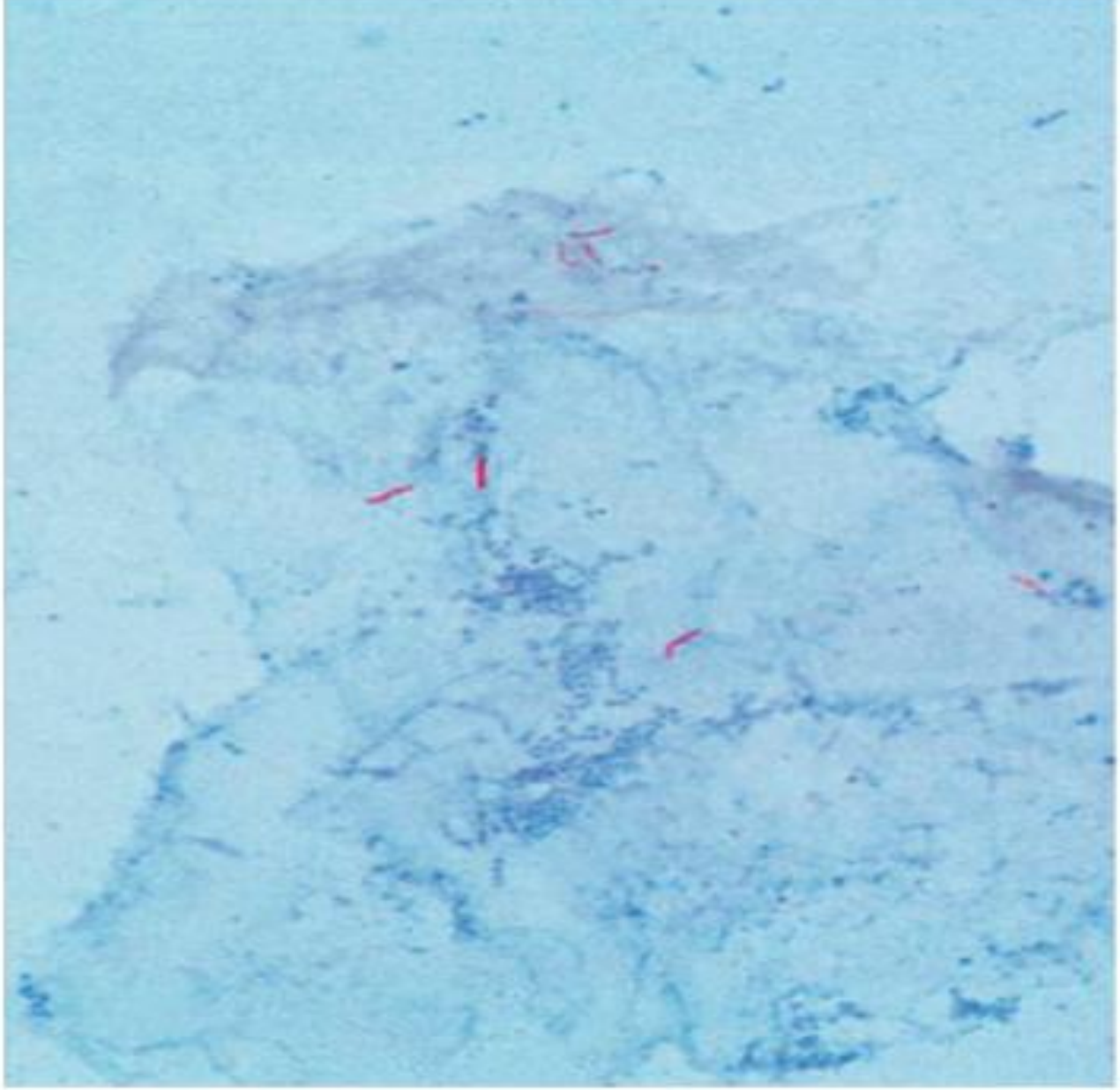
TB: is one of the oldest diseases known to affect humans.

TB: is a major cause of death worldwide.

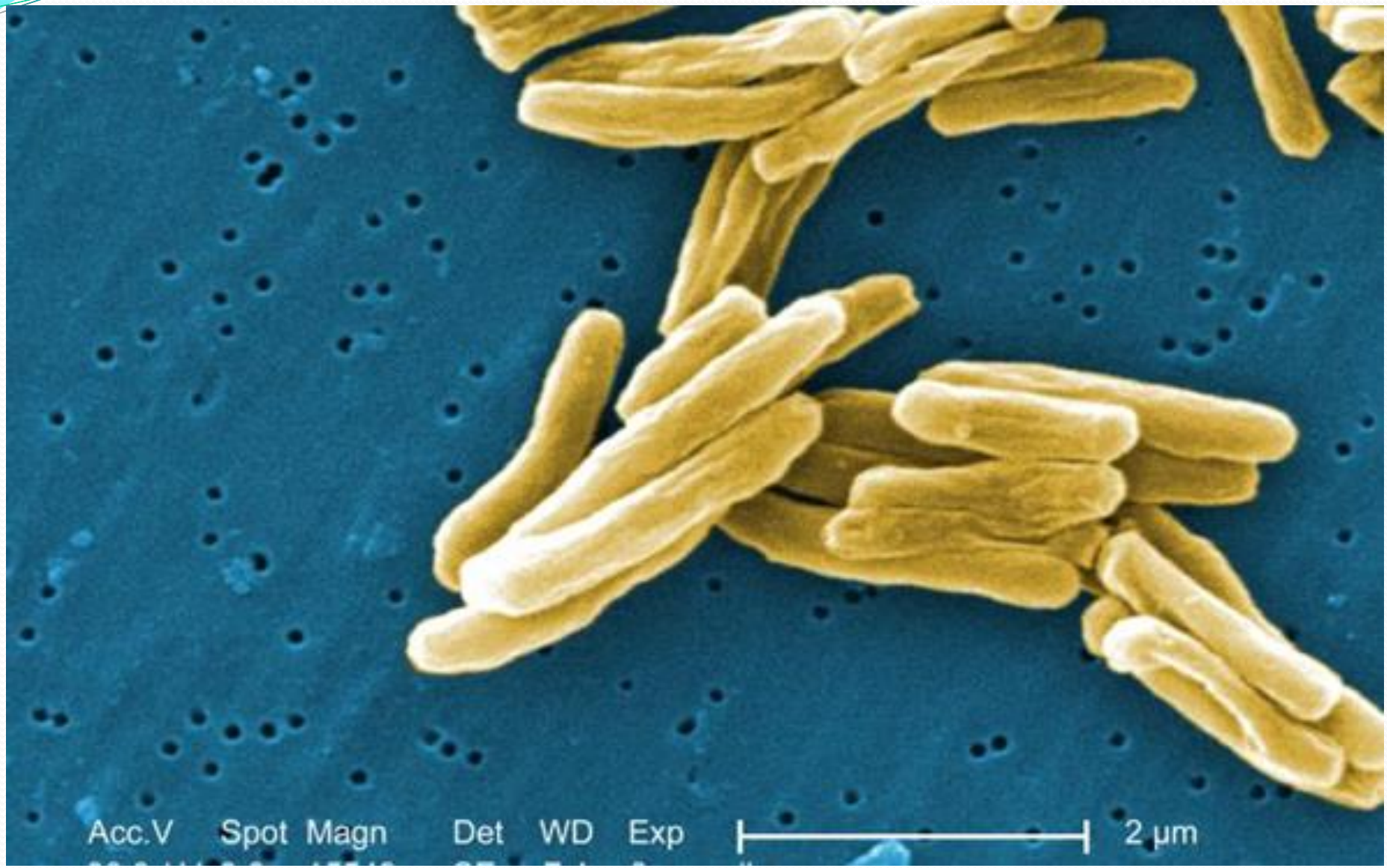
is caused by *Mycobacterium tuberculosis* complex and usually affects the lungs, although other organs are involved in up to one-third of cases.

If properly treated, TB caused by drug-susceptible Strains is curable in virtually all cases.

If untreated, the disease may be fatal within 5 years In 50–65% of cases.



Acid-fast bacillus smear showing *M. tuberculosis* bacilli. *(Courtesy of the CDC, Atlanta.)*


Acc.V Spot Magn Det WD Exp
2 µm

Definition

- Tuberculosis infection means that *Mycobacterium tuberculosis* has infected a host but is not causing disease

- Tuberculosis disease or “tuberculosis” means the disease caused by *M. tuberculosis*

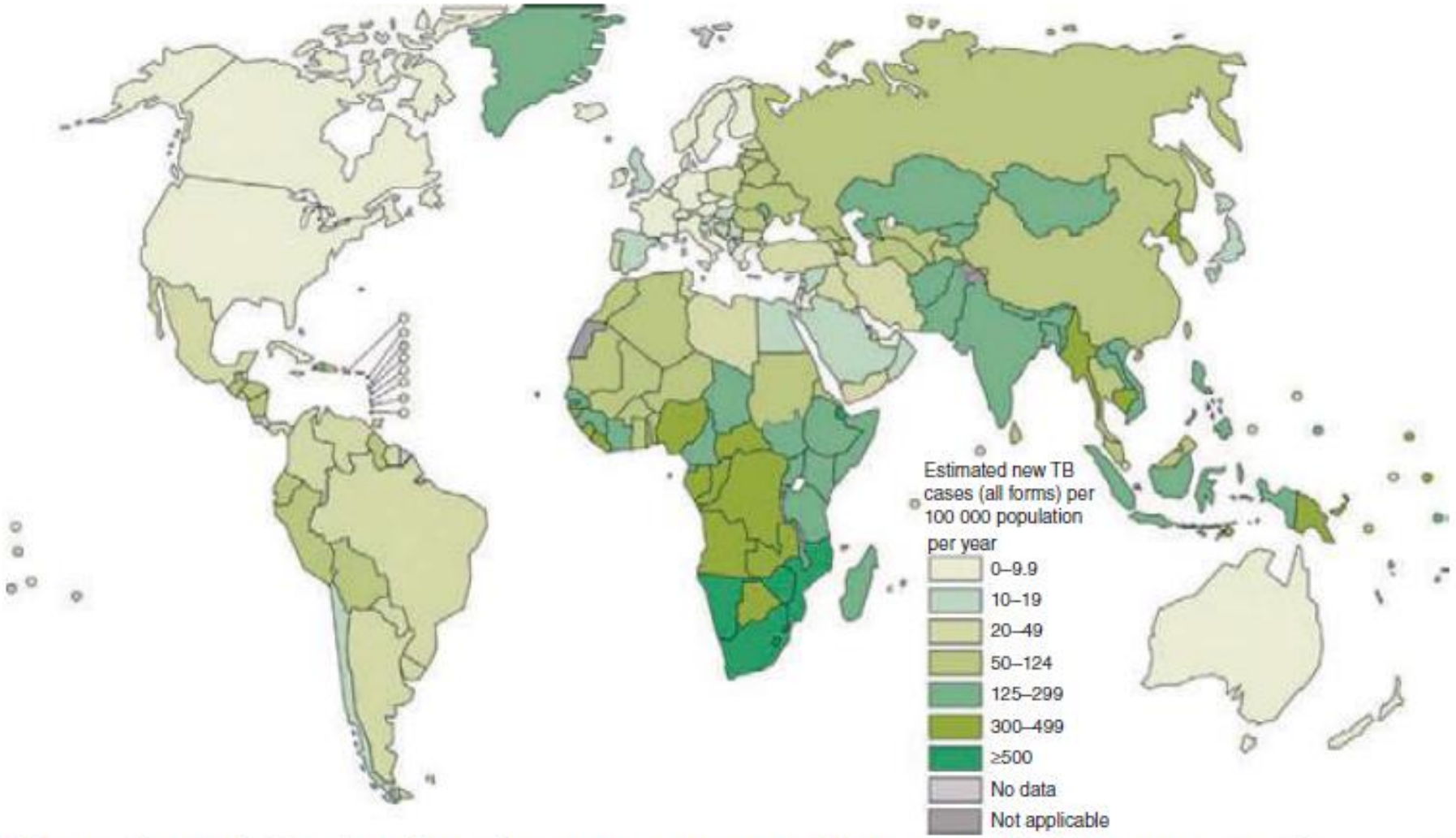


FIGURE 202-2 Estimated tuberculosis (TB) incidence rates (per 100,000 population) in 2013. The designations used and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization (WHO) concerning the legal status of any country, territory, city, or area or of its authorities or concerning the delimitation of its frontiers or boundaries. *Dotted*, *dashed*, and *white lines* represent approximate border lines for which there may not yet be full agreement. *(Courtesy of the Global TB Programme, WHO; with permission.)*

Source Case

Number of organisms:

The number of bacilli in solid nodular lesions ranges from 10^2 to 10^4 organisms

In cavitary lesions, populations are on the order of 10^7 to 10^9 bacilli.

Thus, in tuberculosis control, the contacts of persons with More extensive tuberculosis should be accorded a higher Priority.

Source Case

The most direct means of estimating bacillary population is microscopic examination of properly stained sputum smears.

An average viable bacillary population of 5000 to 10,000 organisms per milliliter of sputum is required for the organisms to be seen in an acid-fast–stained sputum smear.

Contacts of patients who have organisms present in sputum smears have a much higher prevalence of infection than do contacts of patients with negative smears and either positive or negative cultures.

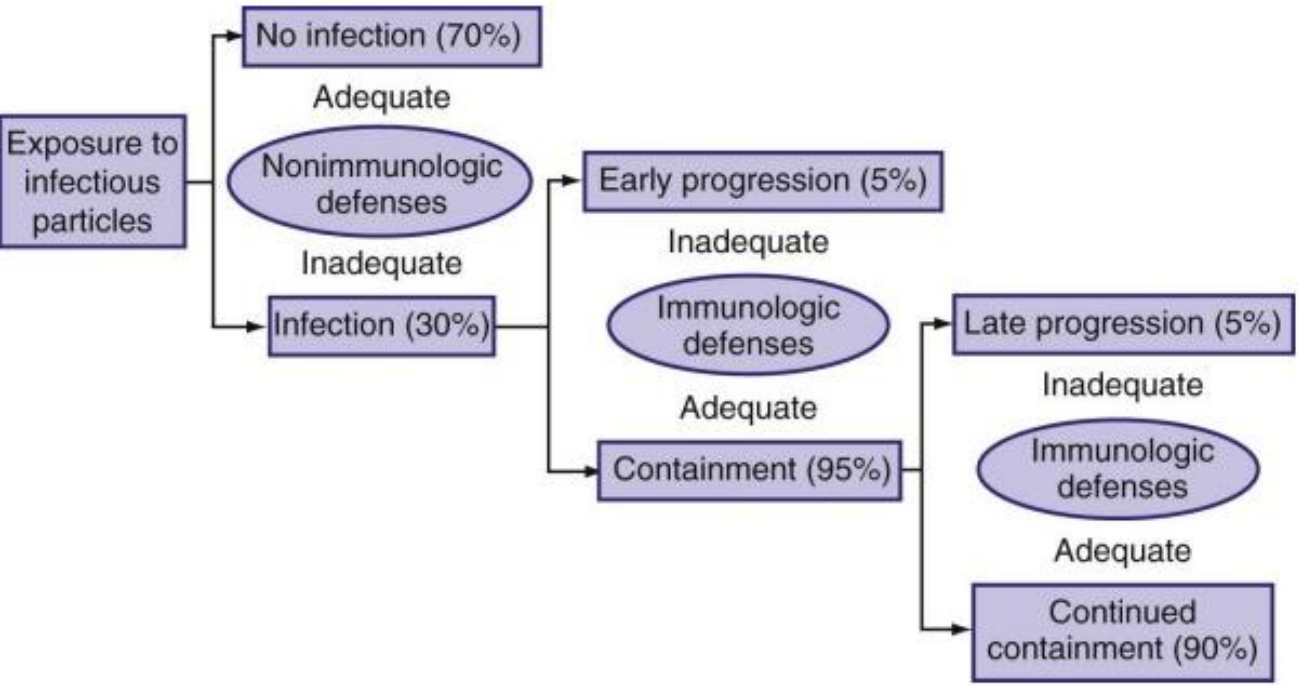
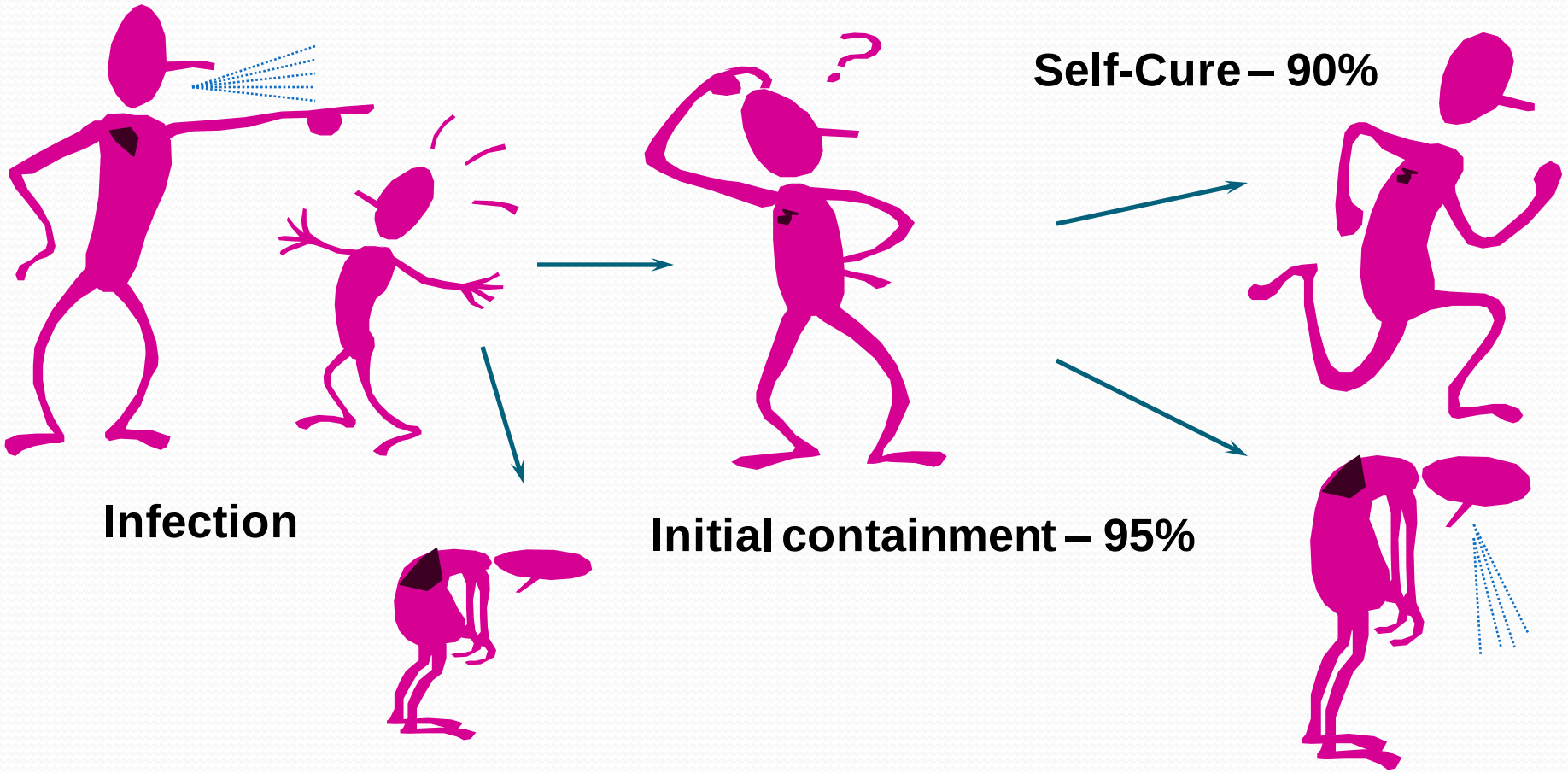
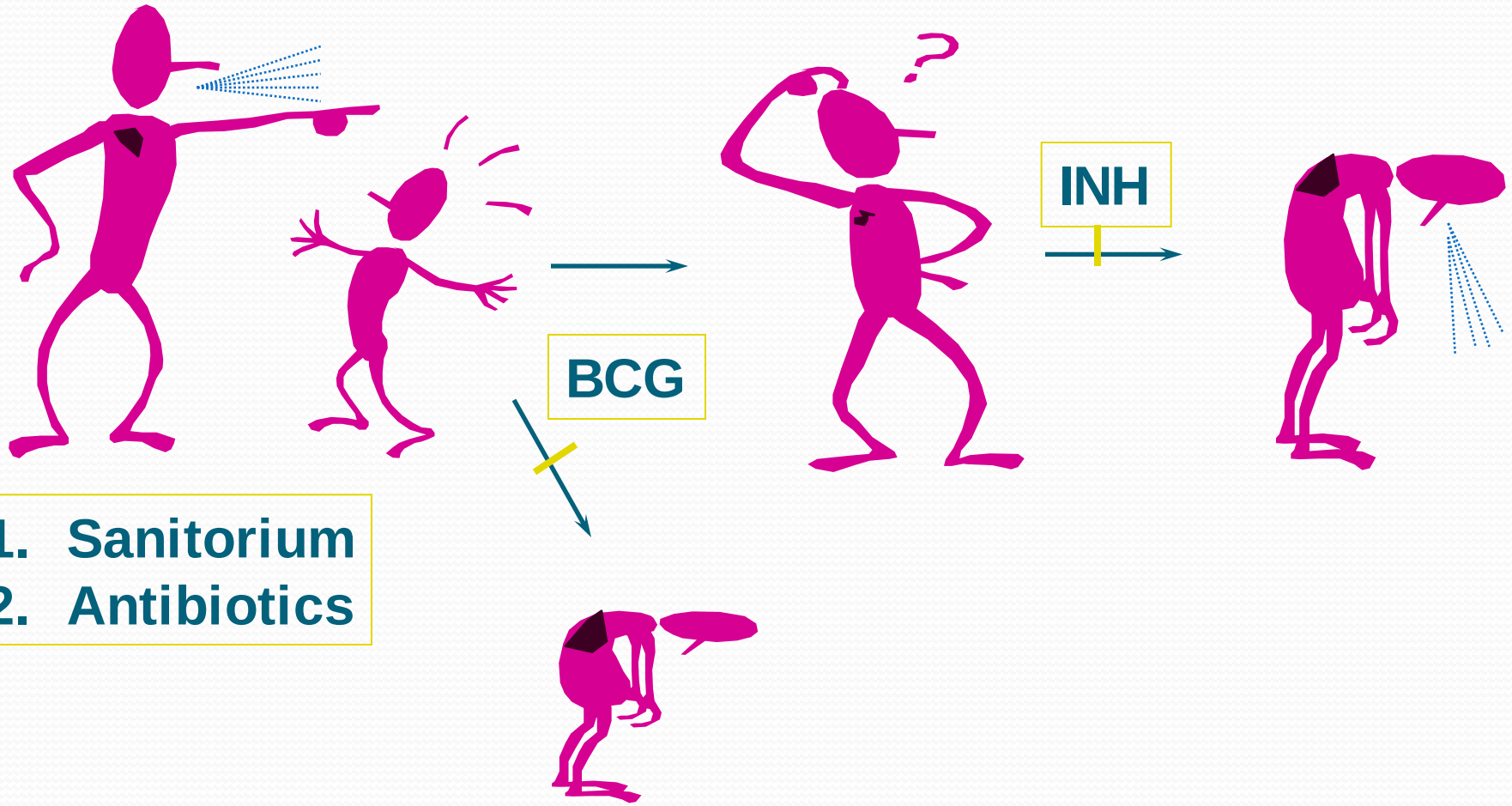


FIGURE 34-3 • Consequences of exposure to an infectious source case of tuberculosis. Exposure to a patient with infectious tuberculosis causes tuberculous infection in approximately 30% of those exposed. Of those who are infected, 3% to 10% develop tuberculosis within 1 year of their becoming infected. Beyond 1 year, an additional 3% to 5% develop tuberculosis during the remainder of their lifetimes.

Tuberculosis: Transmission and Natural History



Role of interventions

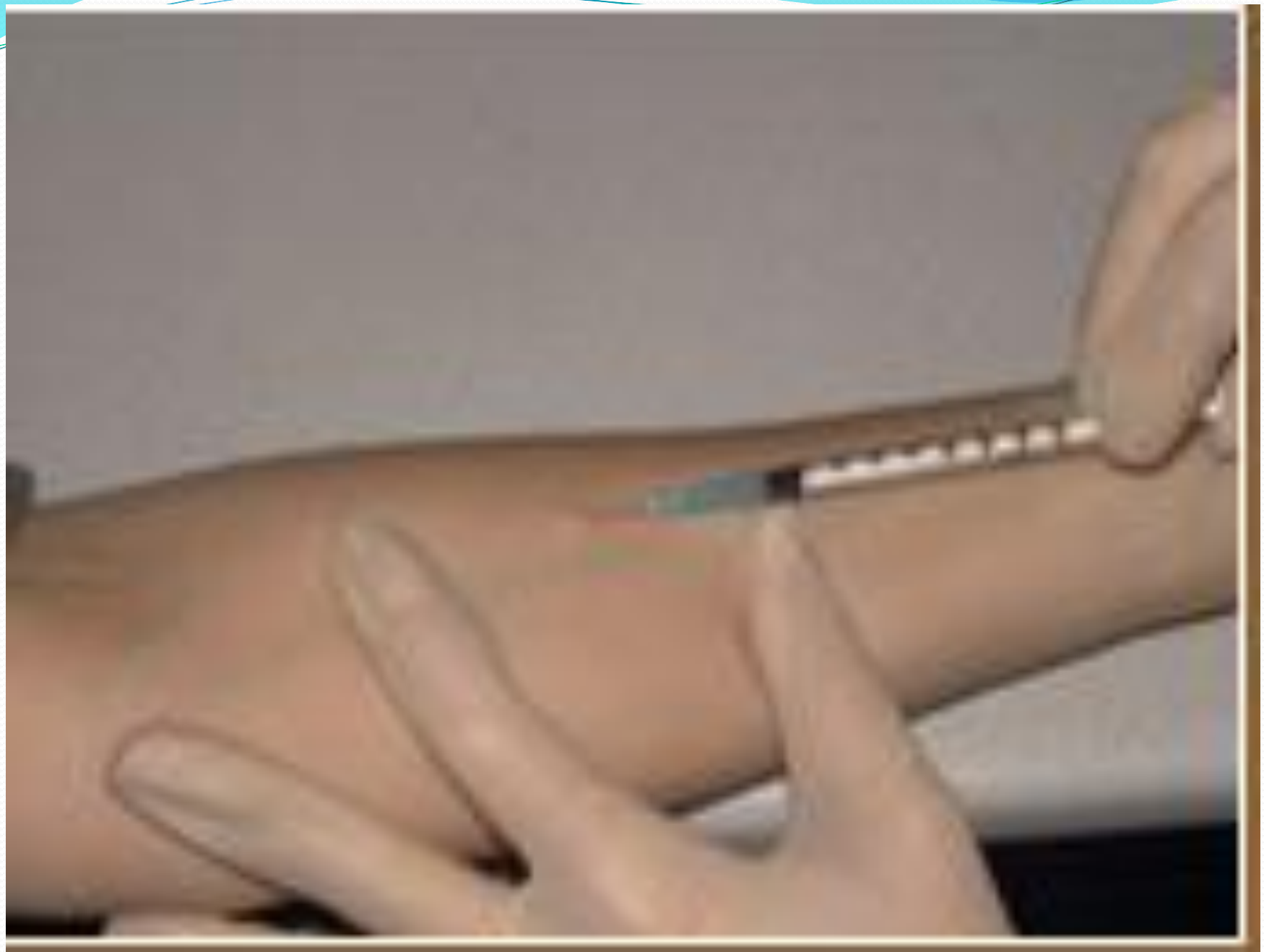


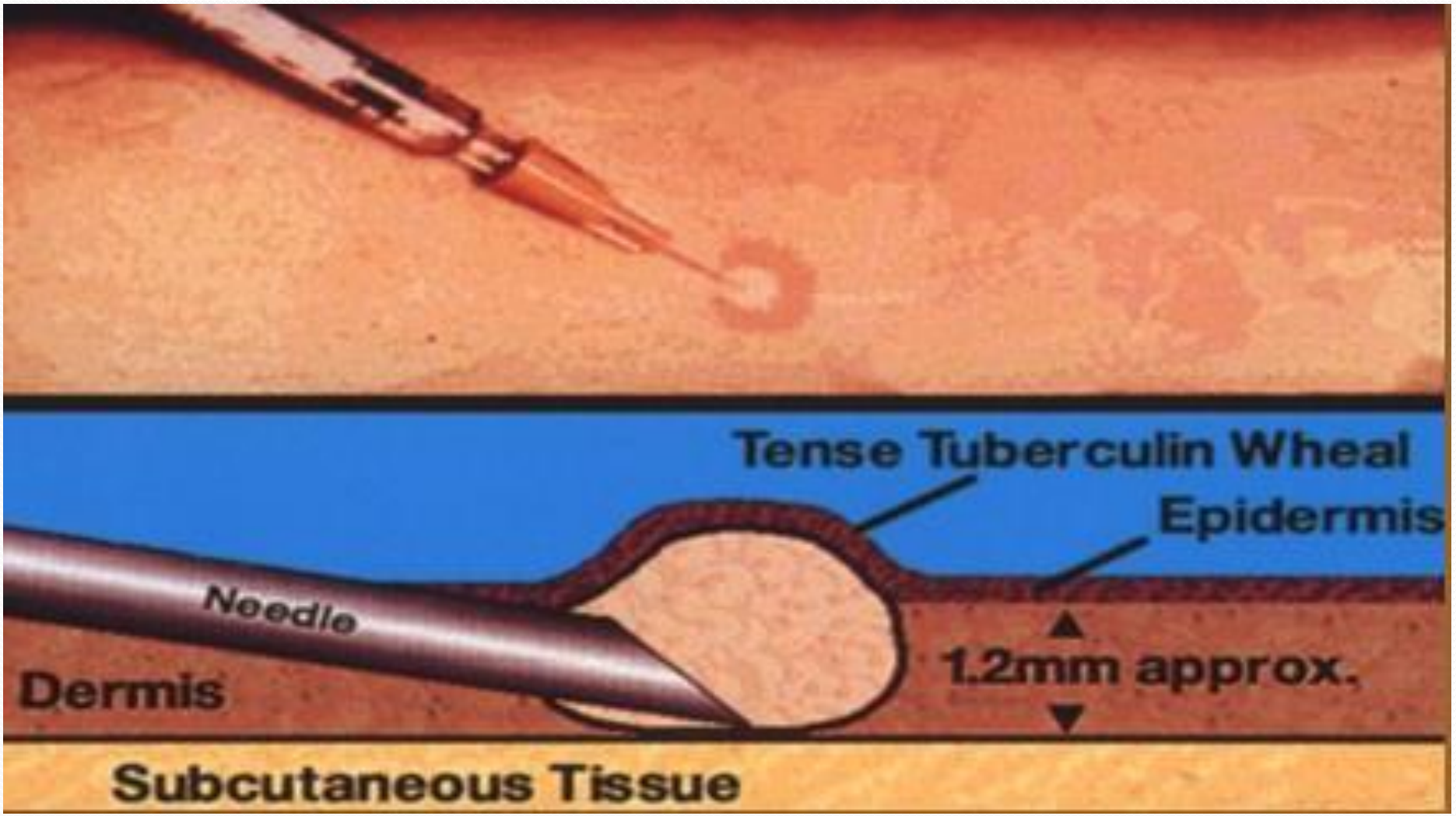
1. Sanitorium
2. Antibiotics

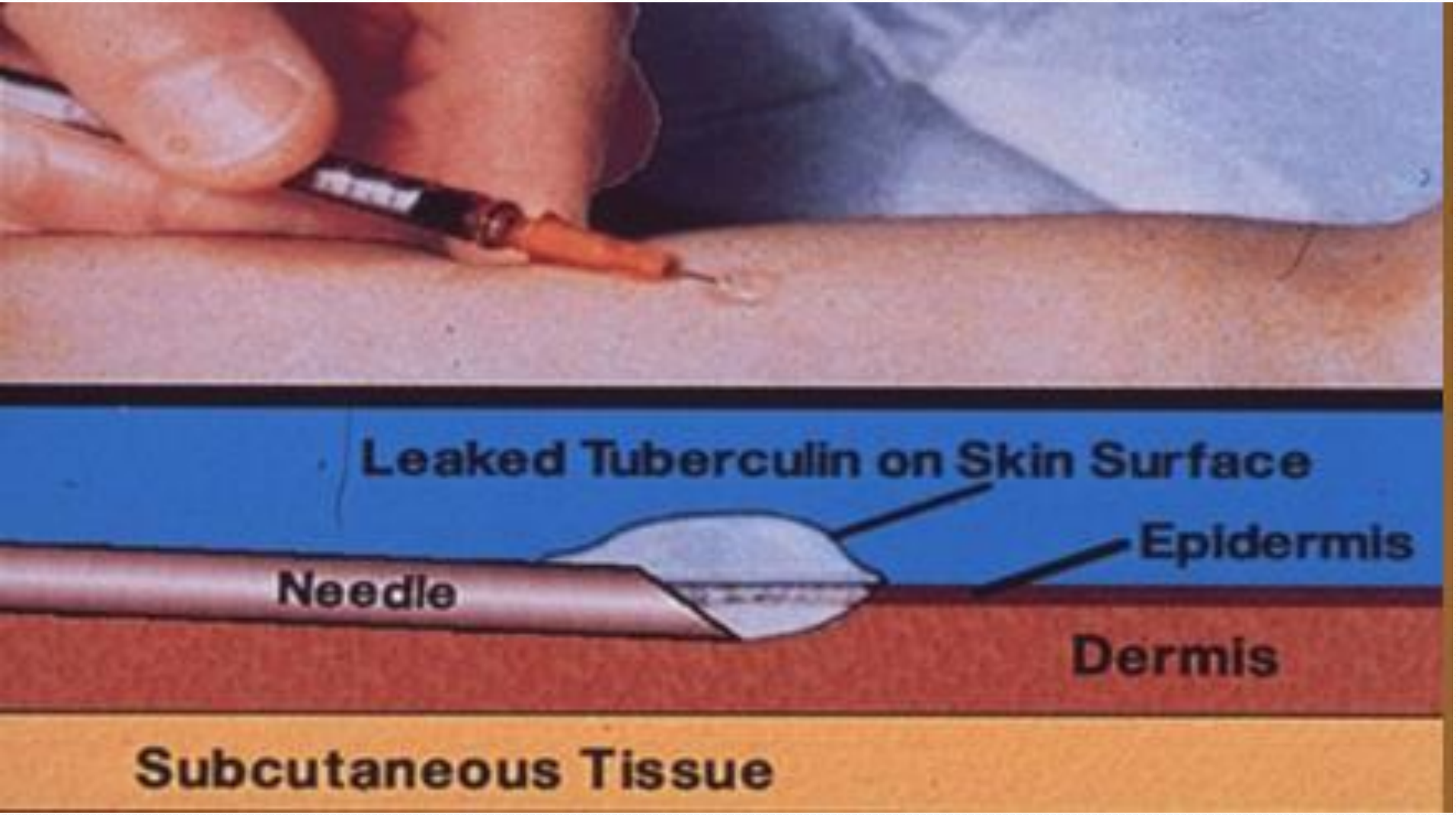
TUBERCULOUS INFECTION

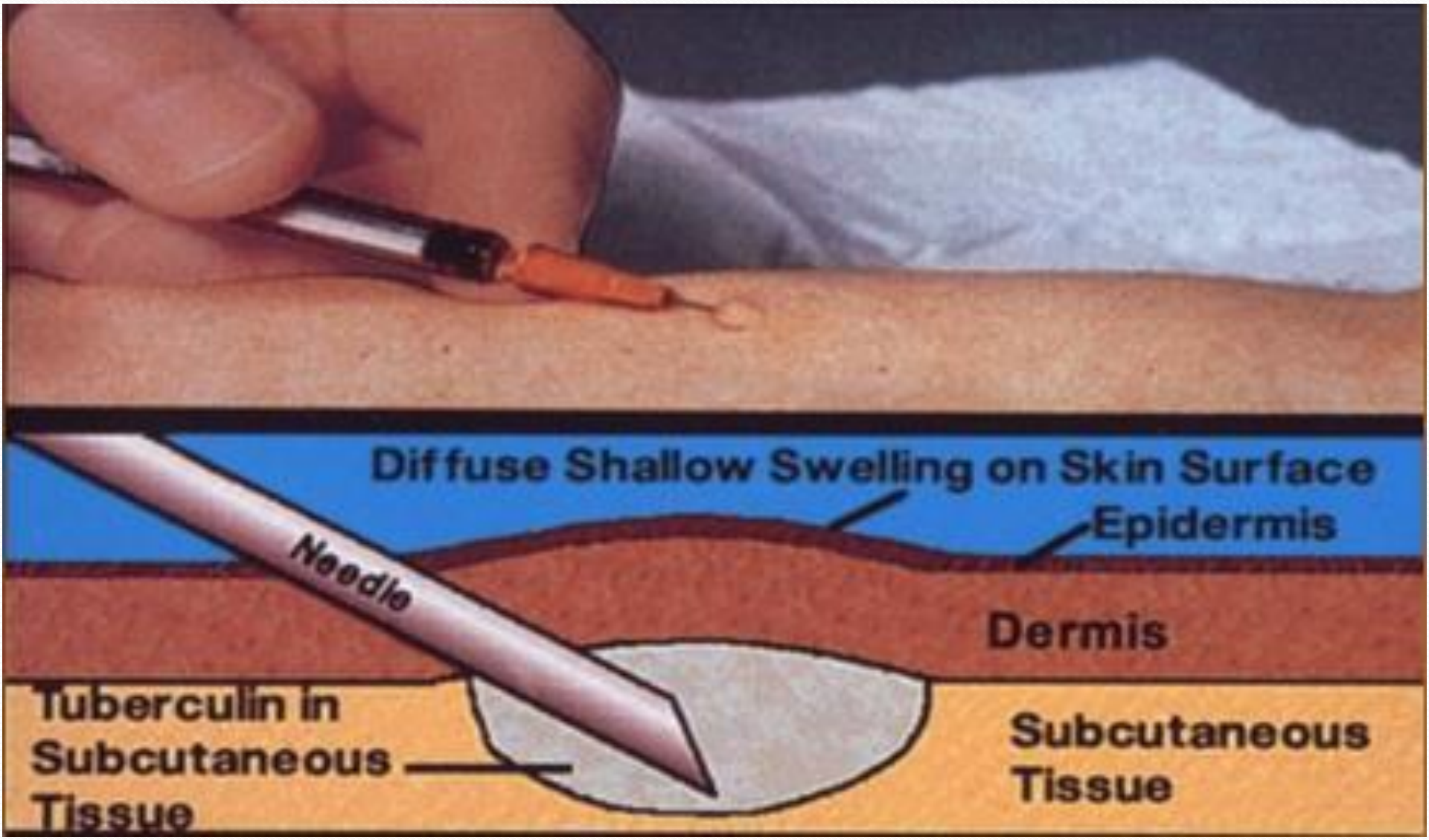
Tuberculin Skin Test (PPD)

Interferon-γ Release Assays




Tense Tuberculin Wheal
Epidermis
Needle
Dermis
1.2mm approx.
Subcutaneous Tissue


Leaked Tuberculin on Skin Surface
Epidermis
Needle
Dermis
Subcutaneous Tissue


Diffuse Shallow Swelling on Skin Surface
Epidermis
Needle
Dermis
Tuberculin in Subcutaneous Tissue
Subcutaneous Tissue

Tuberculin Skin Test (PPD)

The reaction size is determined by measuring the diameter of any Induration with a ruler. The amount of erythema should not be taken into account; only the extent of induration is important. Readings must be recorded accurately in millimeters.

Under most circumstances, a reading of 10 mm or more is considered indicative of infection with *M. tuberculosis*.

In some situations, smaller reactions should be taken to indicate tuberculous infection. Reaction of 5 mm in a child who is a contact of a person with smear-positive tuberculosis indicate tuberculous infection and be considered positive.

5-mm reaction in a person with known HIV infection should be considered positive.

Sensitivity of PPD =80- 85%

There are several reasons why the tuberculin reaction may be interpreted as negative in the presence of tuberculous infection.

Errors in application or reading of the test result,

Improperly handled antigen

HIV infection with CD_4 T LYM less than 400

Lymphoreticular malignancies such as Hodgkin's disease

Corticosteroids and immunosuppressive

Advancing age

Malnutrition

Overwhelming tuberculosis

Sensitivity of PPD =80- 85%

Thus, a negative tuberculin test result cannot be used to exclude tuberculosis as a diagnostic possibility.

Interferon-γ Release Assays

Compared with the tuberculin skin test, the INF-γ release assays have the advantage of being accomplished with one patient visit, being more specific in the presence of BCG vaccination or infection with nontuberculous mycobacteria, having less reader variability

The QuantiFERON-TB Gold test

Interferon-γ Release Assays

usually can be used in place of—and not in addition to—the tuberculin skin test.

Radiographic Features

In developed countries, radiographic examination of the chest is usually the first diagnostic study undertaken, after the history and physical examination

Radiographic Features

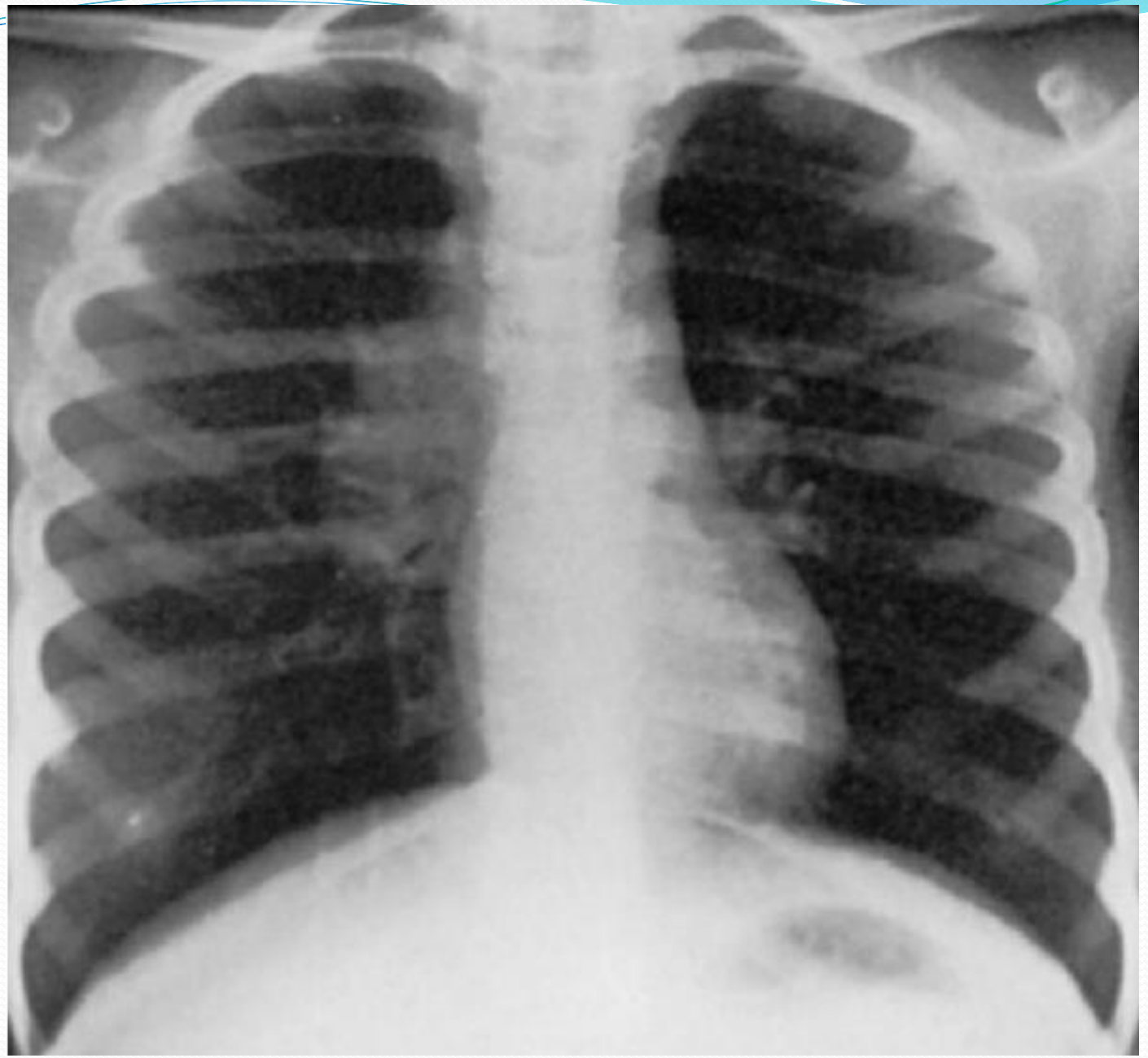
Pulmonary tuberculosis nearly always causes detectable abnormalities on the chest film

although in patients with HIV infection, a normal chest radiograph occurred in as many as 11% of patients with positive sputum cultures.

Radiographic Features

In primary tuberculosis, occurring as a result of recent infection, the process is generally seen as a middle or lower lung zone infiltrate, often associated with Ipsilateral hilar adenopathy

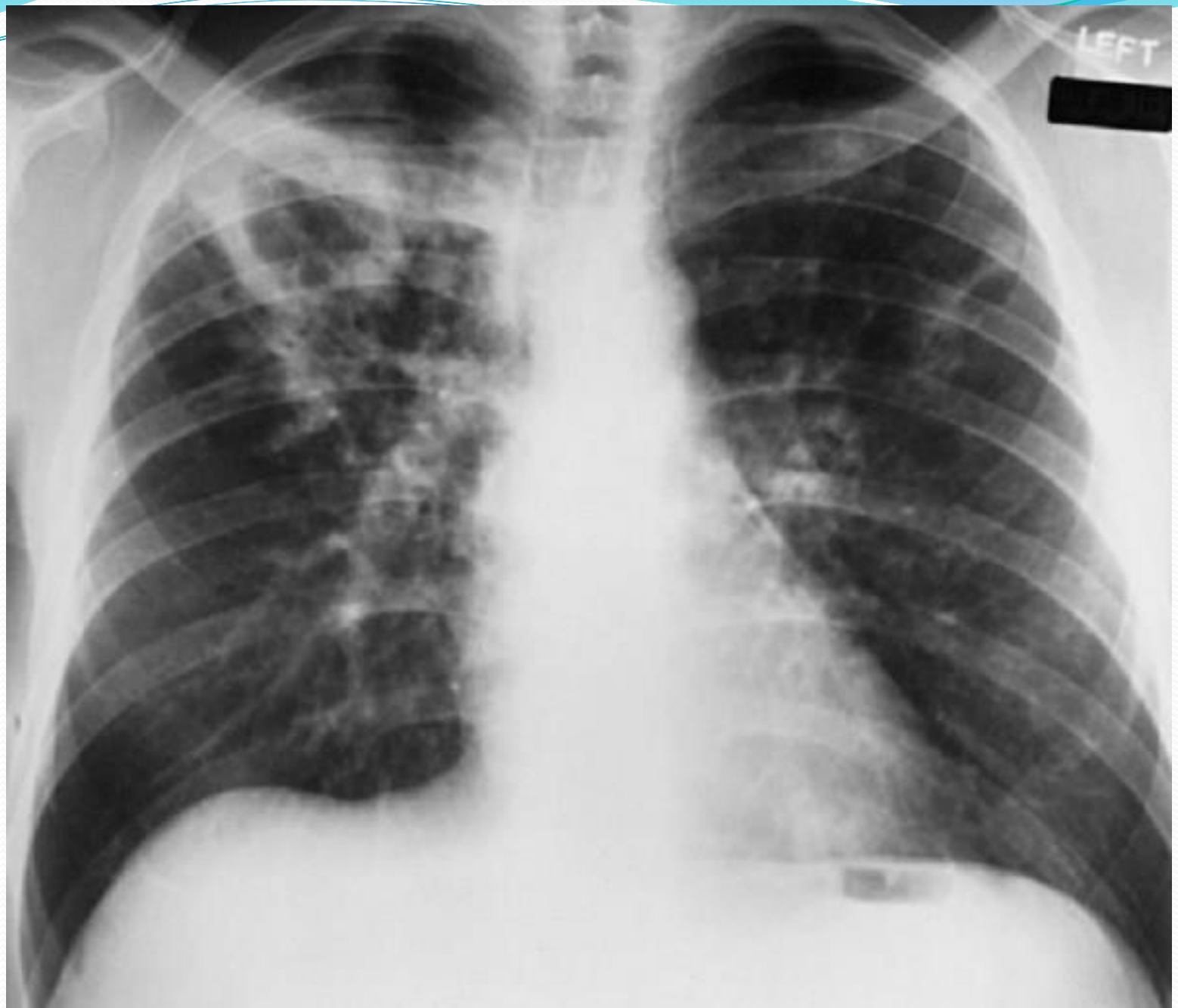
If the primary process persists beyond the time when specific cell-mediated immunity develops, cavitation may occur (so-called progressive primary tuberculosis).



Radiographic Features

Tuberculosis that develops many years after the original infection (endogenous reactivation) usually involves the upper lobes of one or both lungs.

Cavitation is common in this form of tuberculosis.


LEFT

Radiographic Features

The most frequent sites are the apical and posterior segments of the right upper lobe and the apical-posterior segment of the left upper lobe.

Healing of the tuberculous lesions usually results in development of a fibrotic scar with shrinkage of the lung parenchyma and, often, calcification.

Involvement of the anterior segments alone is unusual.

When the disease progresses, infected material may be spread via the airways ("bronchogenic" spread) into the lower portions of the involved lung or to the other lung.

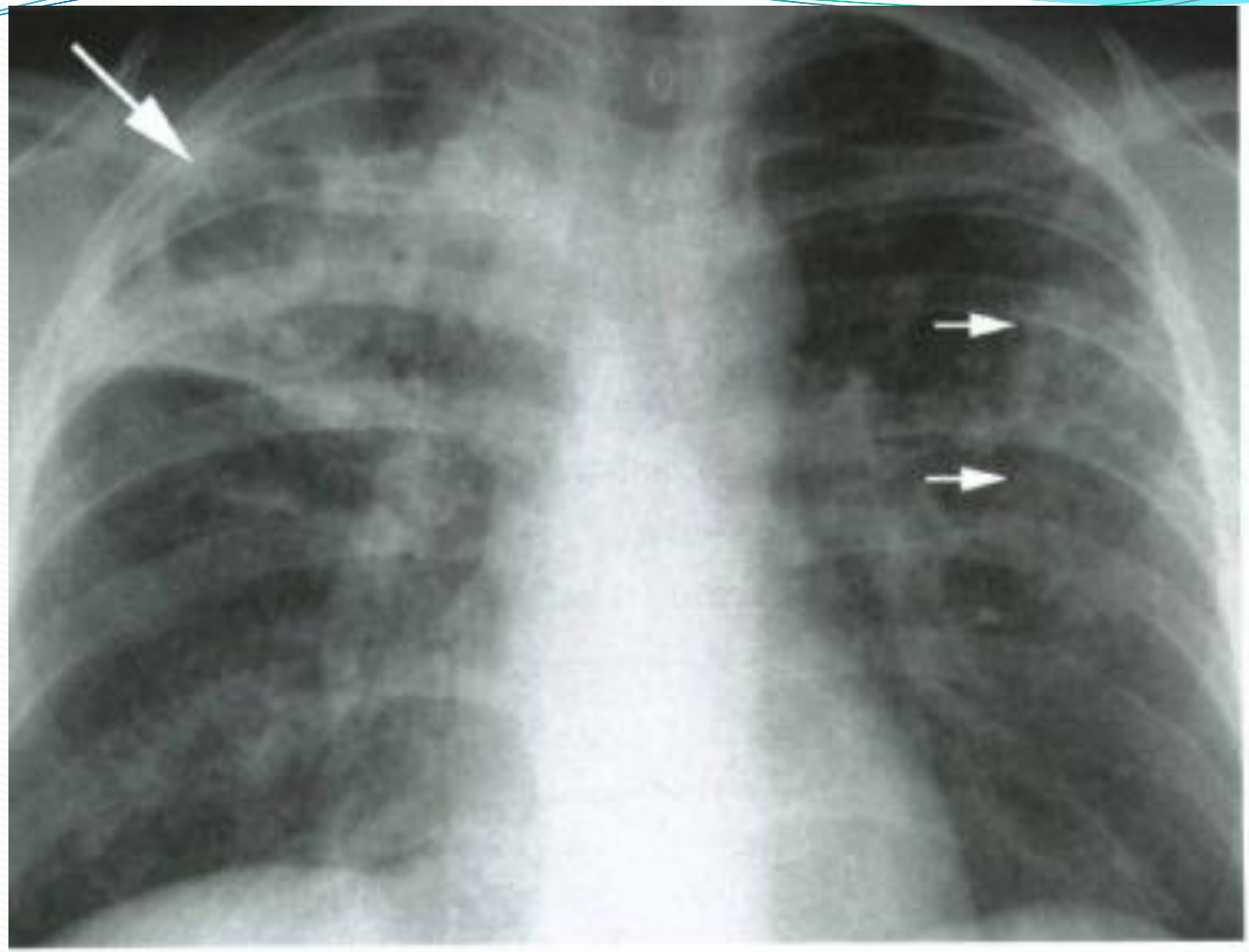
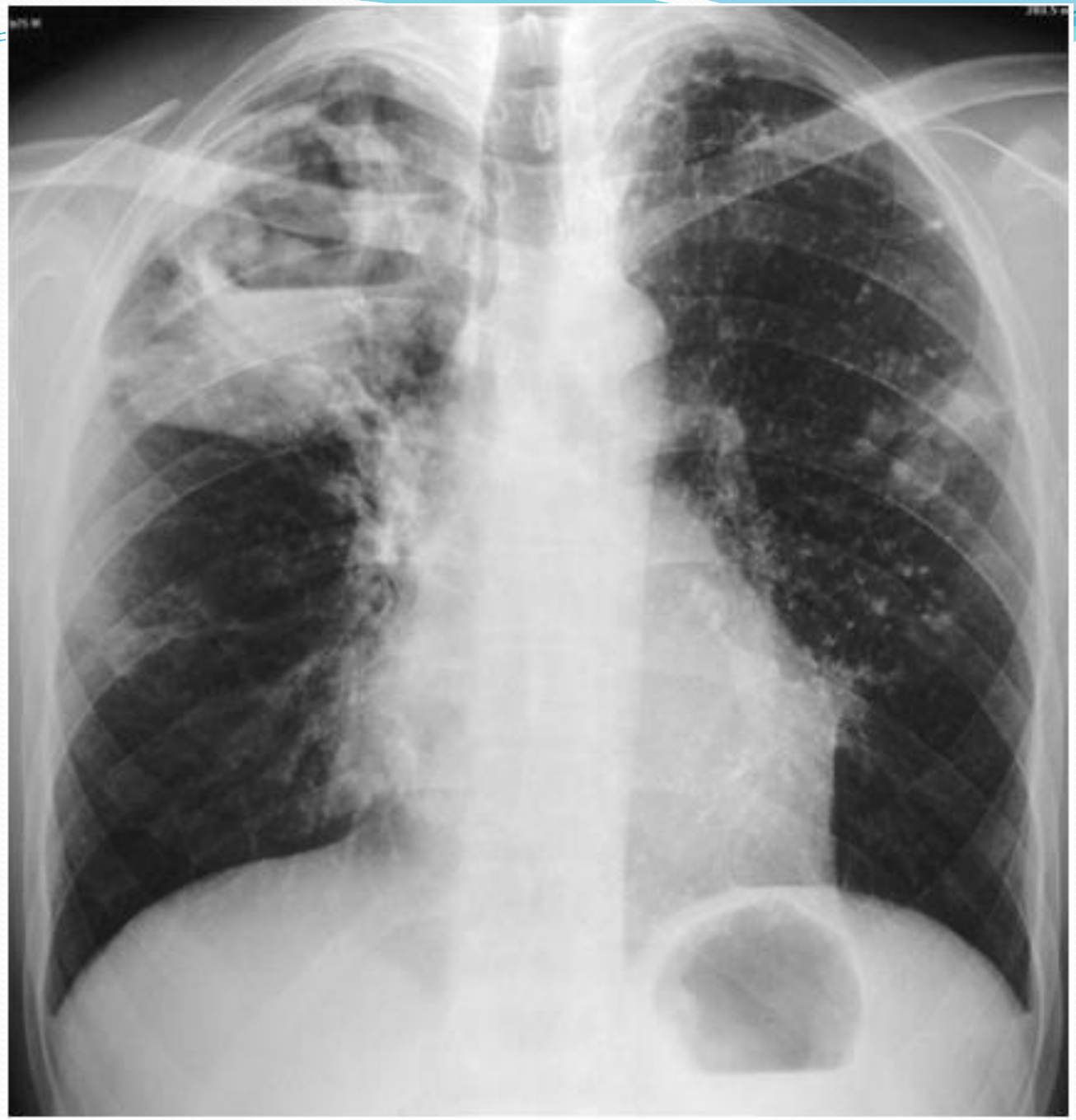
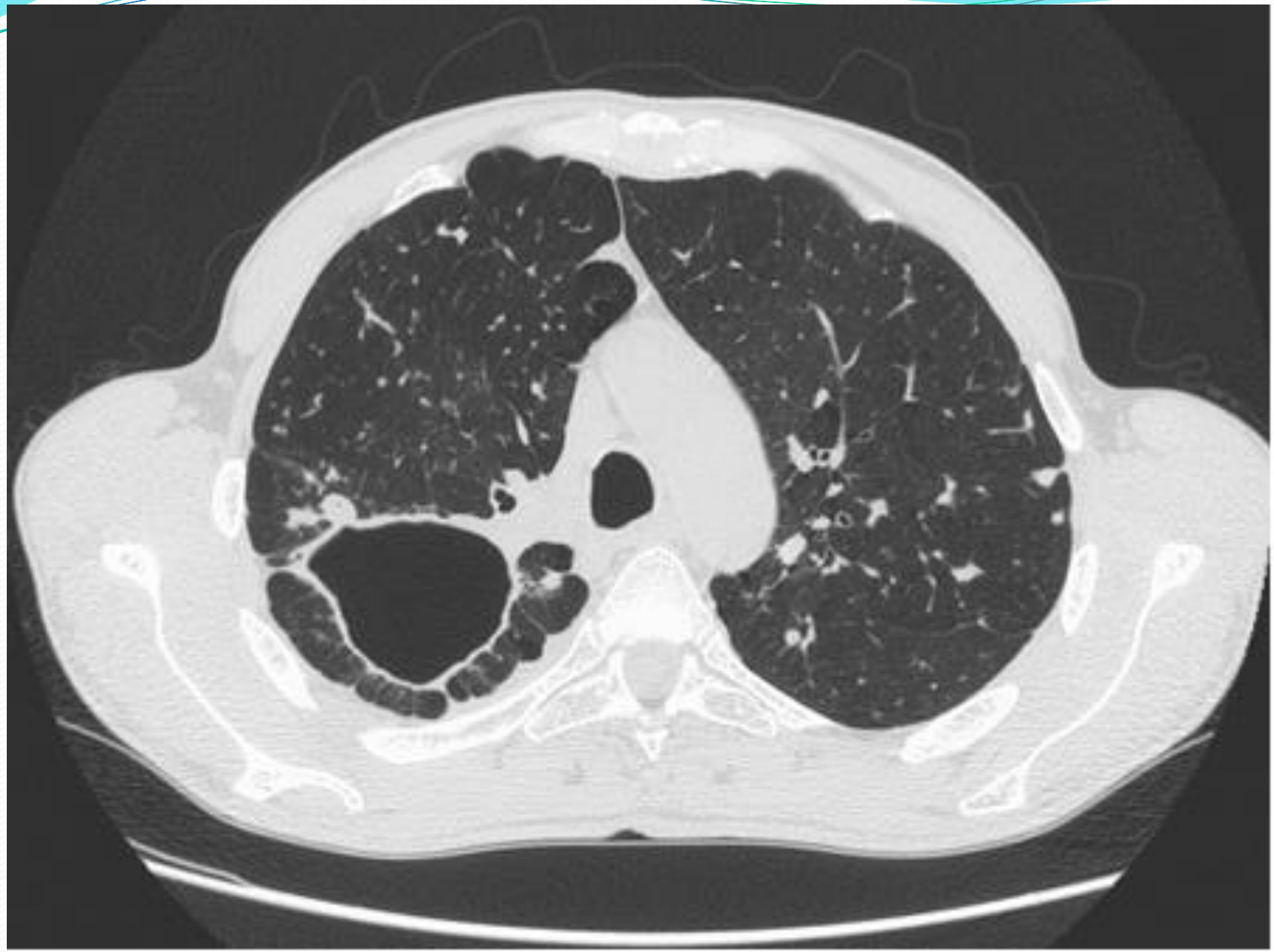


FIG. 12-22. Endobronchial spread of *Mycobacterium tuberculosis* infection. Frontal chest radiograph shows right upper lobe cavitation *(large arrow)* associated with numerous small nodules in the left upper lobe *(small arrows)*, representing airway spread of infectious material.





Erosion of a parenchymal focus of tuberculosis into a blood or lymph vessel may result in dissemination of the organism and **a miliary pattern** on the chest film .

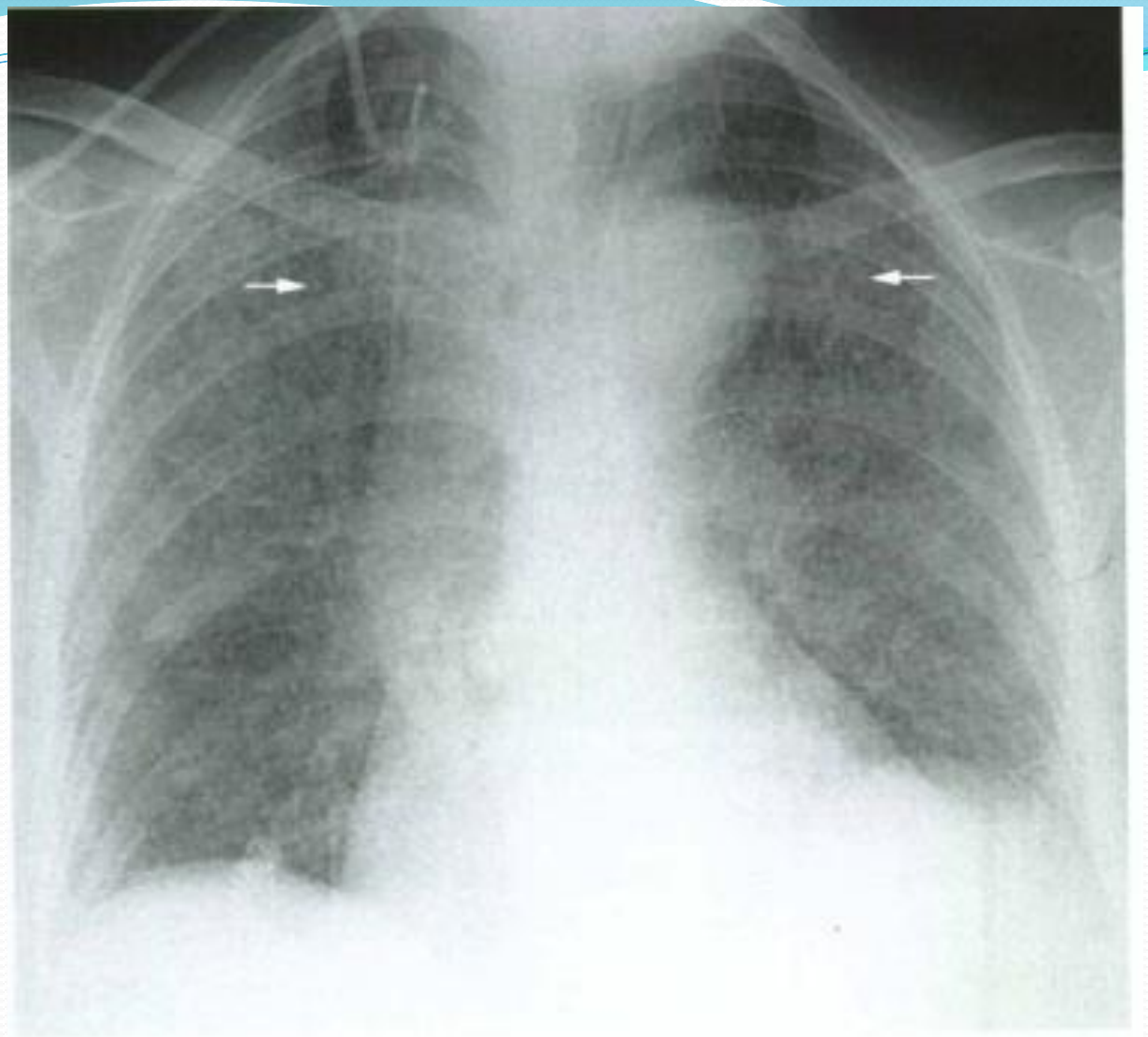
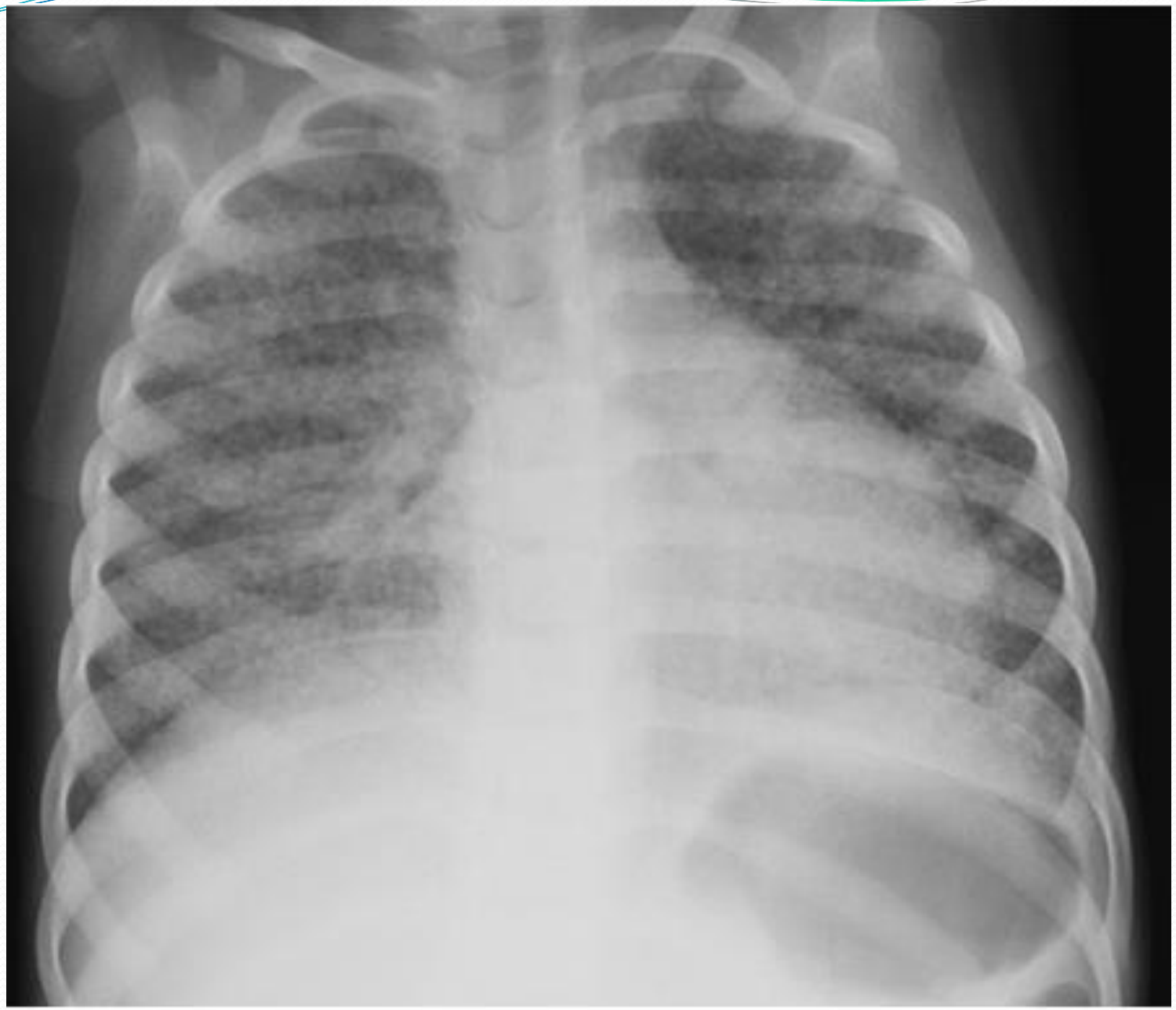


FIG. 12-23. Miliary spread of *Mycobacterium tuberculosis* infection. Frontal chest radiograph shows innumerable, bilateral, diffusely distributed small nodules representing miliary (hematogenous) spread of MTB infection.



Radiographic findings in HIV-infected patients are affected by the degree of immunosuppression. Tuberculosis occurring relatively early in the course of HIV infection tends to produce typical radiographic findings with predominantly upper lobe infiltration and cavitation

With more advanced HIV disease, the radiographic findings become more “atypical”: cavitation is uncommon, and lower lung zone or diffuse infiltrates and intrathoracic adenopathy are frequent

The activity of a presumed tuberculous process cannot be determined simply from a single radiographic examination of the chest.

A cavity might be a sterile residual of an old infection, whereas a fibrotic-appearing lesion may be active.

The chest radiograph, although extremely valuable, cannot provide a definitive diagnosis of tuberculosis.

careful microbiologic evaluation is always indicated.

Bacteriologic Evaluation

A definitive diagnosis of tuberculosis can be established only by isolation of tubercle bacilli in culture or identification of specific nucleic acid sequences.

Obviously, when the lung is involved, sputum is the initial specimen of choice.

Single early-morning specimens have a higher yield and a lower rate of contamination than do pooled specimens

Collecting more than two sputum specimens increases the yield only slightly.

There are several options for obtaining specimens from patients who are not producing sputum.

Inducing sputum

Gastric lavage

If the sputum is negative or cannot be obtained, the next diagnostic step is usually fiberoptic bronchoscopy with bronchoalveolar lavage, and in some instances transbronchial lung biopsy.

The yield of bronchoscopy has been high in miliary tuberculosis and in local disease as well

In some situations, a therapeutic trial of antituberculosis chemotherapy may be indicated before more invasive studies are undertaken.

For example:

In a tuberculin-positive person who is under 40 years of age, is a nonsmoker, and comes from a country where there is a high prevalence of tuberculosis even in the presence of negative smears and cultures of sputum.

Acid-Fast Staining

The first step in the diagnostic sequence is nearly always staining and examining readily available specimens for acid-fast bacilli (AFB).

Finding AFB is very specific

The sensitivity of microscopic examination is relatively low

The level of detection is approximately 10,000 bacilli per milliliter of secretions,

In practice, 40% to 70% of patients with *M. tuberculosis* isolated in culture have positive smears.

Smears generally are interpreted as

Negative

If positive, are reported as

Rare (3 to 9 organisms per slide)

Few (10 or more per slide)

or numerous (1 or more per high-power oil immersion field).

Mycobacterial Culture

Although definitive identification of *M. tuberculosis* can be accomplished by rapid amplification tests, determination of drug susceptibility generally still requires isolation of the organism in culture.

Treatment

Table 165-2 Recommended Dosage[a] for Initial Treatment of Tuberculosis in Adults[b]		
	Dosage	
Drug	Daily Dose	Thrice-Weekly Dose[c]
Isoniazid	5 mg/kg, max 300 mg	10 mg/kg, max 900 mg
Rifampin	10 mg/kg, max 600 mg	10 mg/kg, max 600 mg
Pyrazinamide	25 mg/kg, max 2 g	35 mg/kg, max 3 g
Ethambutol[d]	15 mg/kg	30 mg/kg

Regimens

Standard short-course regimens are divided into an initial, or bactericidal, phase and a continuation, or sterilizing, phase.

During the initial phase, the majority of the tubercle bacilli are killed, symptoms resolve, and usually the patient becomes noninfectious.

The continuation phase is required to eliminate persisting mycobacteria and prevent relapse.

Monitoring Treatment Response and Drug Toxicity

Bacteriologic evaluation is essential in monitoring the response to treatment for TB.

Patients with pulmonary disease should have their sputum examined monthly until cultures become negative.

>80% of patients will have negative sputum cultures at the end of the second month of treatment.

By the end of the third month, virtually all patients should be culture-negative.

patients with cavitary disease in whom sputum culture conversion does not occur by 2 months require extended treatment.

When a patient's sputum cultures remain positive at 3 months

Treatment failure and drug resistance or poor adherence to the regimen should be suspected .

A sputum specimen should be collected by the end of treatment to document cure.

If mycobacterial cultures are not practical, then monitoring by AFB smear examination should be undertaken at 2, 5, and 6 months.

Patients whose smears remain positive at 2 months should undergo a repeat examination at 3 months. Smears that are positive after 3 months of treatment when the patient is known to be adherent are indicative of treatment failure and possible drug resistance.

Monitoring of the response during chemotherapy by serial chest radiographs is not recommended

After the completion of treatment, neither sputum examination nor chest radiography is recommended for routine follow-up purposes.

Drug-Resistant TB

MDR (MULTI DRUG RSISTANT)

XDR (EXTENSIVELY DRUG RESISTANT)

Pregnancy and Breast-feeding

Active untreated tuberculosis represents a far greater hazard to a pregnant woman and her fetus than does treatment for the disease.

Adjuctive Therapy

The adjunctive therapies for pulmonary tuberculosis include **surgery** and corticosteroid treatment

Corticosteroids

The seriously ill patient who had extensive tuberculosis.

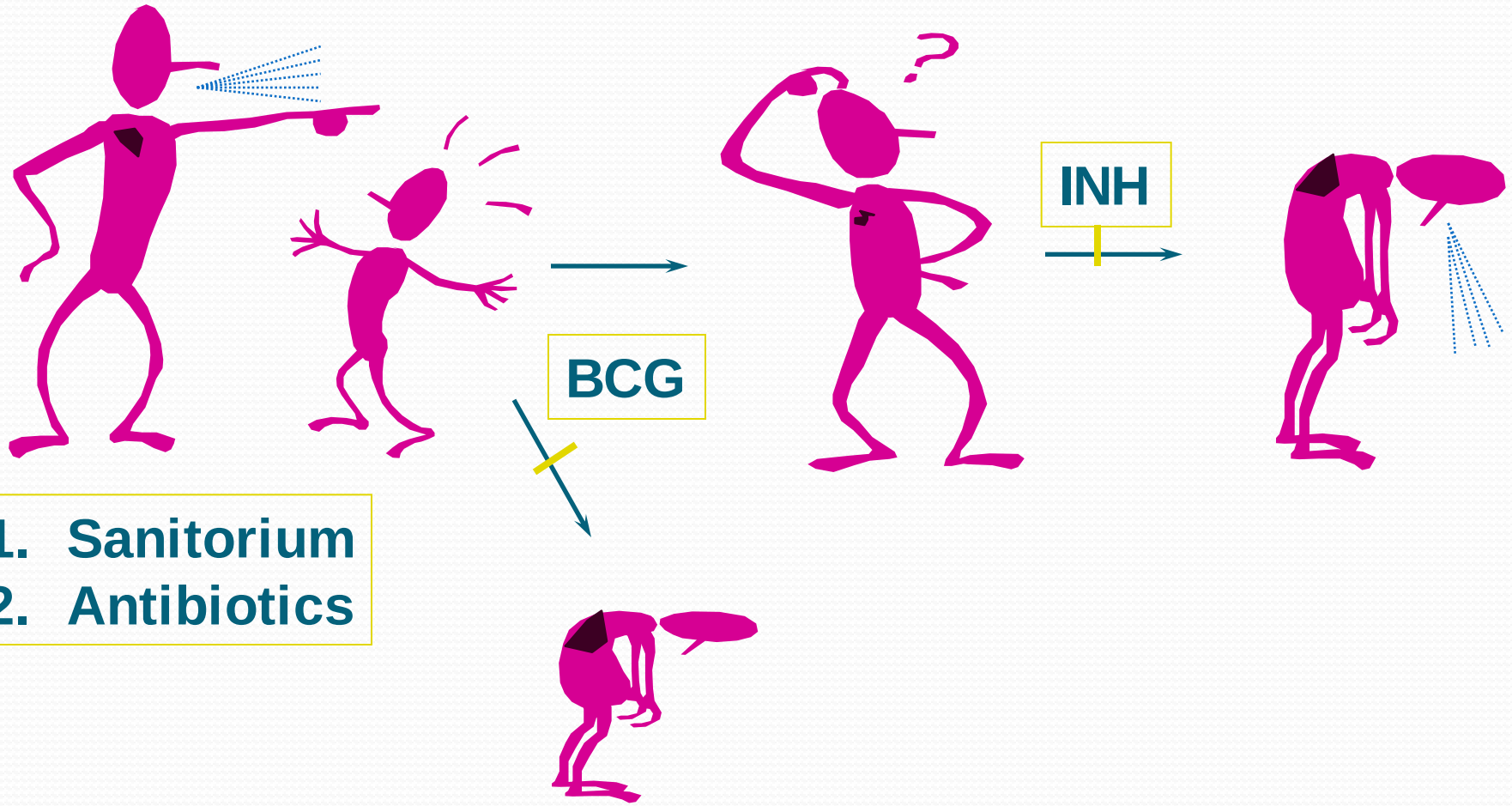
Patients with marked abnormalities of gas exchange and respiratory failure.

Tuberculous meningitis

Tuberculous pericarditis

TREATMENT OF LATENT TB INFECTION

Role of interventions



1. Sanitorium
2. Antibiotics

TREATMENT OF LATENT TB INFECTION

Persons with HIV Infection

Close Contacts of New Cases

Persons with Recent Infection

Persons with Stable Radiographic Findings Consistent with Previous Tuberculosis

Persons with Other Conditions That Increase the Risk of Tuberculosis