Epidemiology of tuberculosis

- Infectious disease – any organ may be affected
- Most frequently: lung

- Incidence in western Europe:

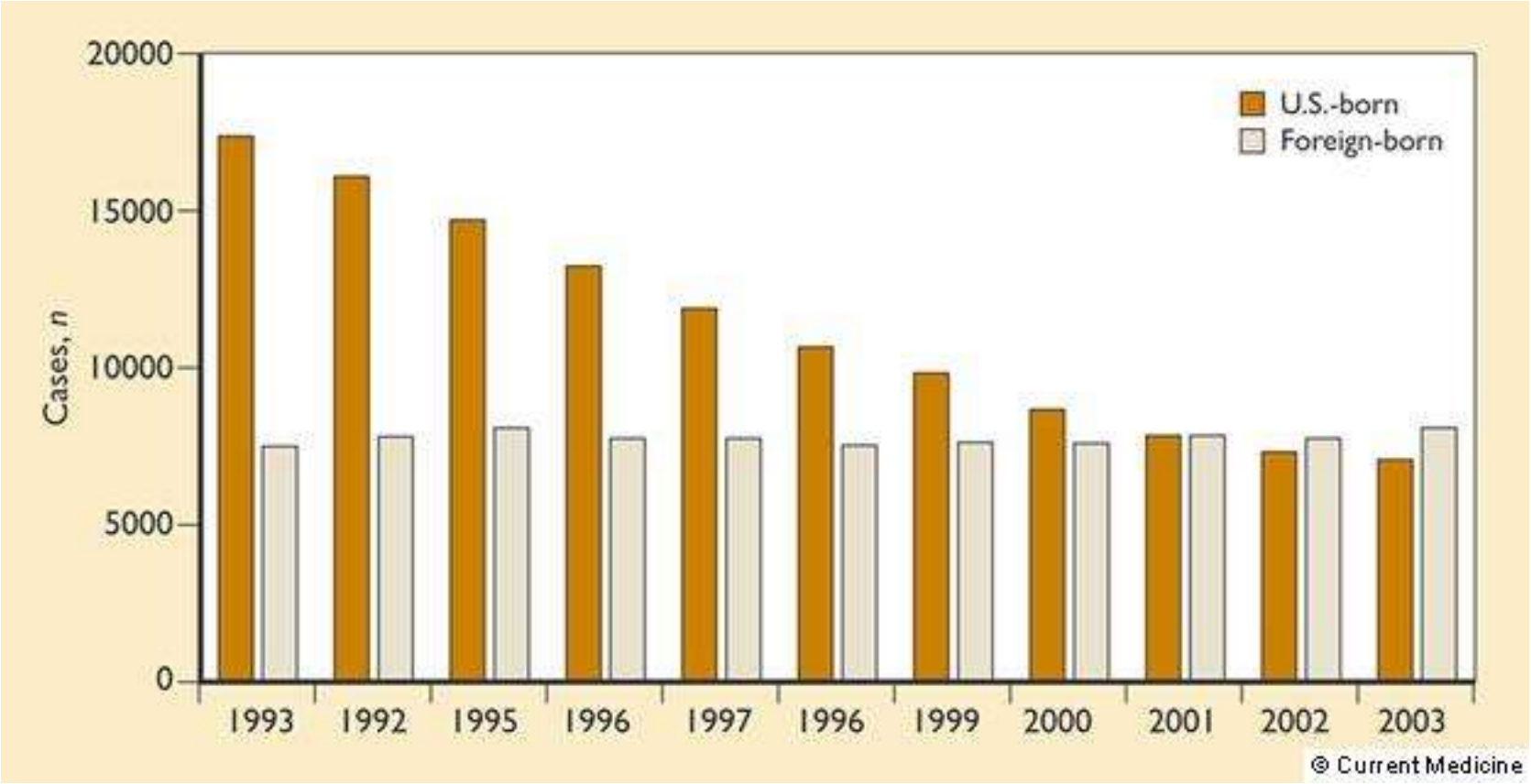
  7-20 per 100 000 inhabitants

  2-4 times higher in people older than 65 years

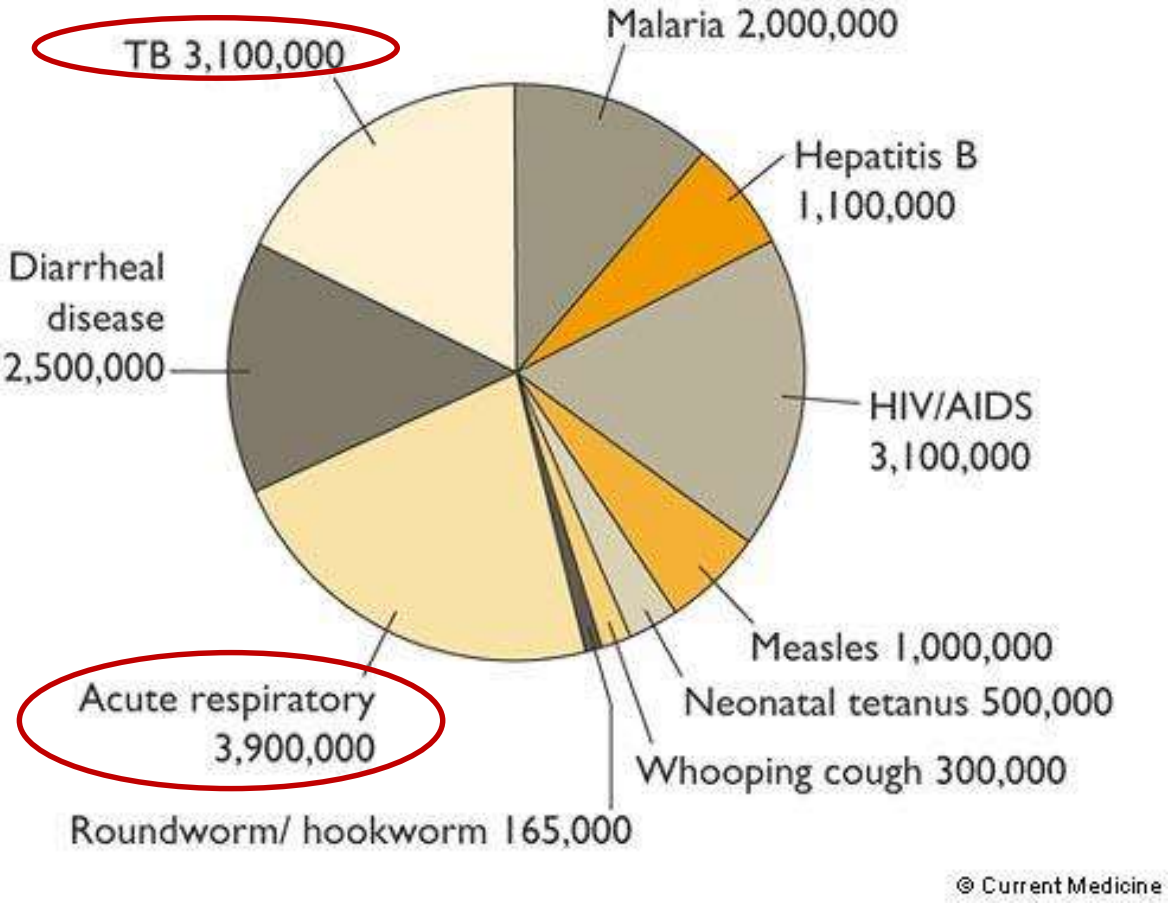
- Incidence in Slovakia since 2009: lower than 10 per 100 000 inhabitants

  (approx 5 in 2018)

Tuberculosis case rates and ethnic influences



Tuberculosis is the second leading cause of death from an infectious disease



Risk groups

- Individuals in contact with active TB
- Low social and hygienic standard
- Immigrants from countries with high prevalence of TB
- Homeless people, malnutrition, alcoholism
- Multimorbidity
- Individuals with impaired immunity:
    - patients with malignancies
    - haematologic malignancies
    - AIDS

Factors that lead to the development of active tuberculosis

- HIV
- Silicosis
- Diabetes mellitus
- Chronic renal failure/hemodialysis
- Malnutrition associated with gastrectomy or jejunoileal bypass
- Solid organ transplantation (renal/cardiac)
- Carcinoma of head or neck
- Prolonged corticosteroids (>15 mg/d) and other immunosuppressive agents

Mycobacterium species

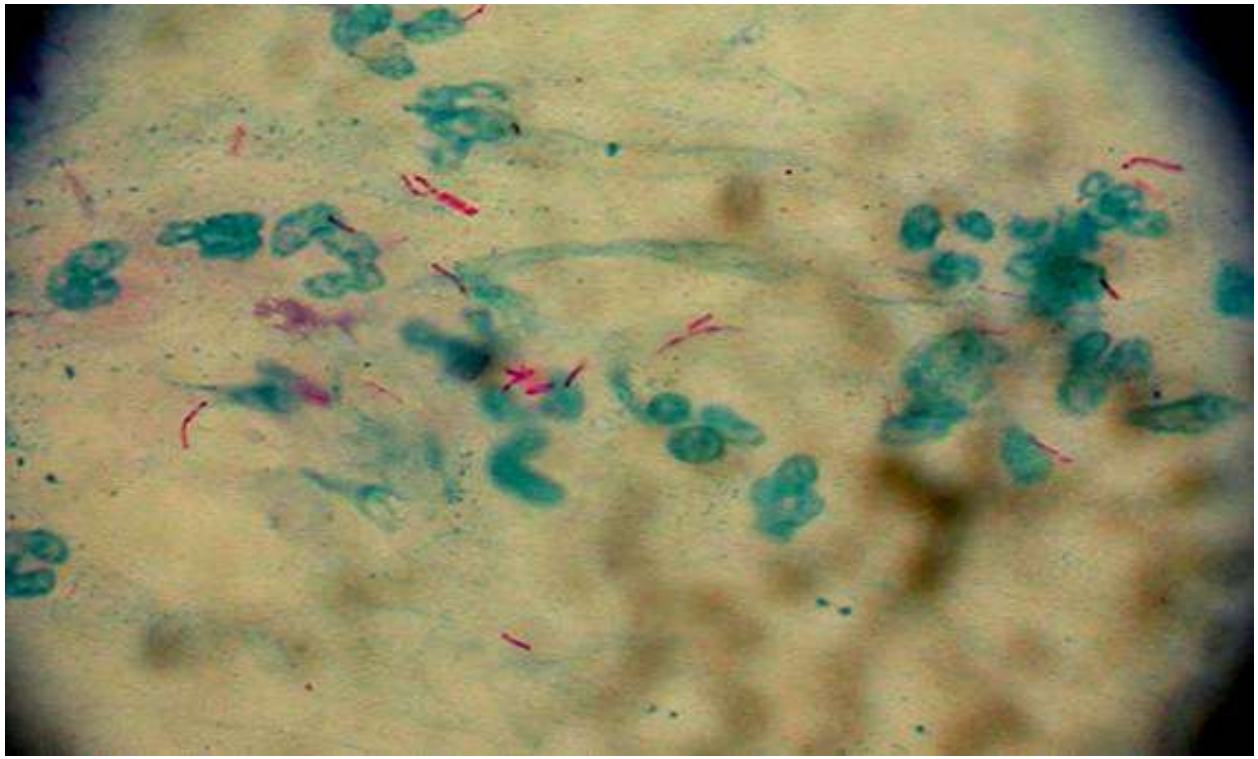
- **Typical:** **Mycobacterium tuberculosis hominis**
  1882 - Koch
  acido-alkali-alcohol-resistant bacillus (species)
  generation time 12-24 hod. – long incubation time

  M. bovis

- **Atypical**: Mycobacterium chelonei
  M. kansasii
  M. avium - intracellulare

Robert Koch

Acid-fast stain (Ziehl-Neelsen)
Mycobacterium tuberculosis



Transmission of tuberculosis

- Organism entry -lung **– 80-90%**

  - innoculation - skin

- Mycobacterium remains alive in the air for 1-2 hours

- Reaction to inhaled mycobacteria :

  a) effective immunological reaction – killing of bacteria

  b) multiplication - primary tbc

  c) dormant bacteria = persistors - latent infection

  d) activation of persistors - postprimary tbc

Forms of tuberculosis

- Pulmonary: I. Primary tbc
  II. Postprimary tbc
  II. A – reactivation
  II. B – reinfection
- Extrapulmonary:
  - pleuritis
  - lymph nodes
  - bones
  - urogenital system
  - meningitis

1. Primary tuberculosis

First contact of a non-immunized subject with M. tuberculosis

a) immunologically competent

b) immunologically not competent

1a) IMMUNOLOGICALLY COMPETENT

- Immunologal mechanisms:

  bacteria in alveoli – nonspecific inflammatory response

  bacteria in lymph nodes

i.e. **lung component + lymph node component**

↓

primary complex (no spread of infection)

1b) IMMUNOLOGICALLY NOT COMPETENT
Progressive primary tuberculosis (rapidly spreading)

- PULMONARY
- PRIMARY GENERALISATION – basilar meningitis, miliar tuberculosis

Primary tuberculosis is a localised (lung) or generalised disorder

- In children (in regions with high prevalence of (TB)
- In adults (in regions with very low prevalence of TB)

2. Postprimary pulmonary tuberculosis

In individuals either infected or immunized (by a vaccine) in their childhood

FORMS:

2a) REINFECTION - further exogenous infection („de novo“) – familiar, professional (low number of cases)

2b) REACTIVATION - progression, reactivation of primary TB (***majority of cases in Europe***)

Postprimary pulmonary tuberculosis
2b REACTIVATION

- Reactivation – replication of previously dormant mycobacteria

- Risk factors: aquired immunodeficiency (diabetes, renal failure, malignancies, AIDS)

- Reactivation of:

  a) pulmonary component of the primary complex

  b) lymph node component of the primary complex

  c) extrapulmonary disseminated mycobacteria

REACTIVATION
REPLICATION of dormant mycobacteria

- Occurs in body regions with the highest O_2 tension
  i.e. – lung apexes
  - long bones: growth regions
  - in kidneys

- This phenomenon is labelled „organ predisposition to TB"

- Reactivation TB is in the vast majority of cases an isolated organ disorder in adults

DIAGNOSTIC PROCEDURES

- Symptoms
- Physical examination
- Chest X-ray (CT)
- Tuberculine test
- Microbiological proof of M. tuberculosis

CLINICAL PICTURE

- No subjective symptoms – accidental rtg finding

OR

- Fatigue, nocturnal sweating, increased temperature
- Weight loss
- Cough with expectoration of mucous or mucous-purulent sputum
- Hemoptysis
- Pleural pain (rarely)
- Dyspnea (rarely)

Physical examination currently adds little to the diagnosis

- Habitus phtisicus
- Scar after tbc vaccination
- Enlargement of lymph nodes
- Chest – deformities after thoracoplasty (50-ties, 20th century)
- In a majority of cases auscultation does not provide diagnostic value

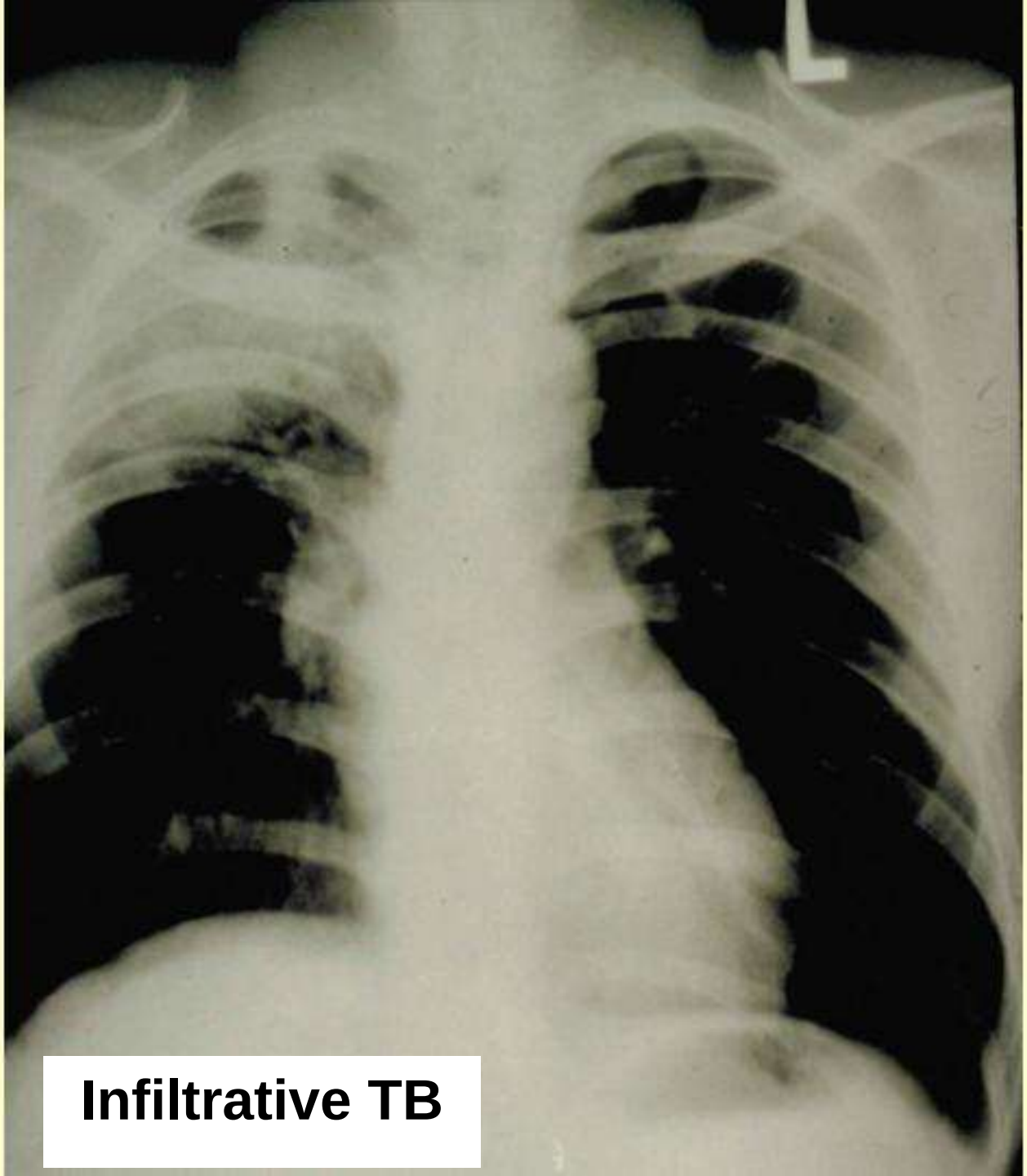
- Percussion: shortened and dull – in TB pleuritis
  hypersonorous in large TB cavern

Chest X-ray

- Infiltrates (frequently infraclavicular)
- Miliar dissemination
- Cavern – thin or thick-wall
- Polycyclic enlergements of hili
- Medium lobe syndrome

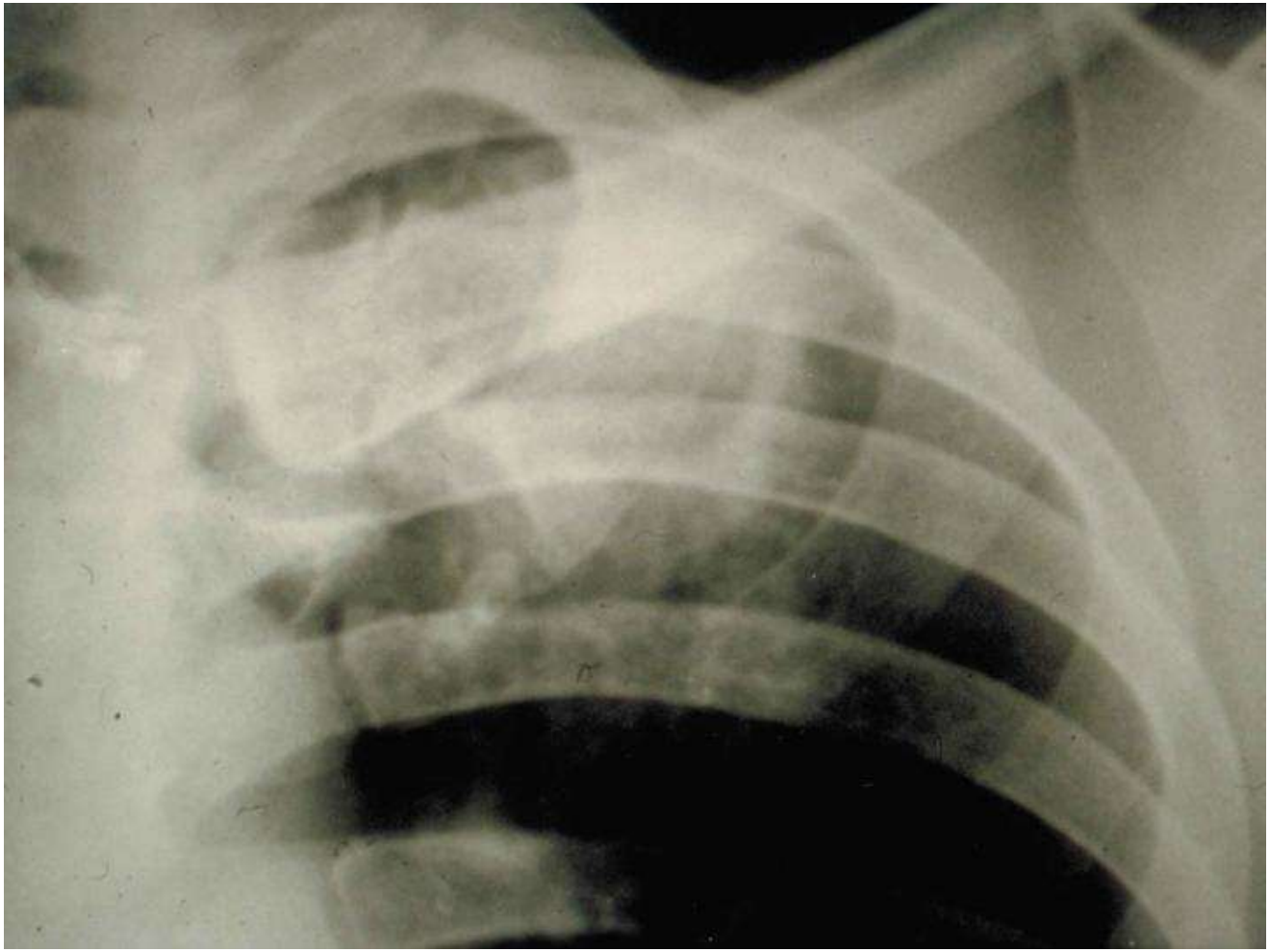
No pathological finding on chest X-ray is exclusive of TB

(i.e. **any finding *may* be TB**)

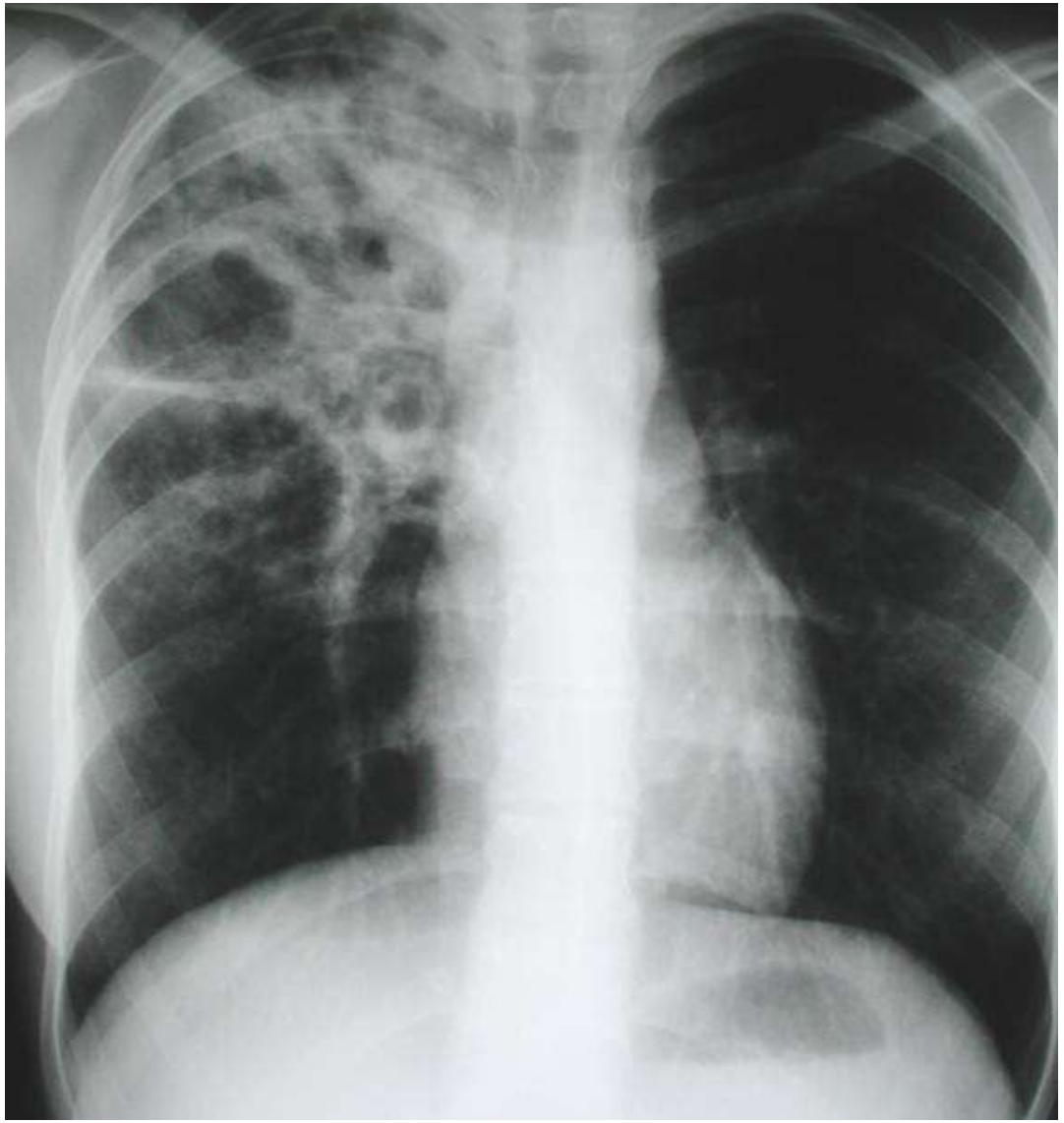


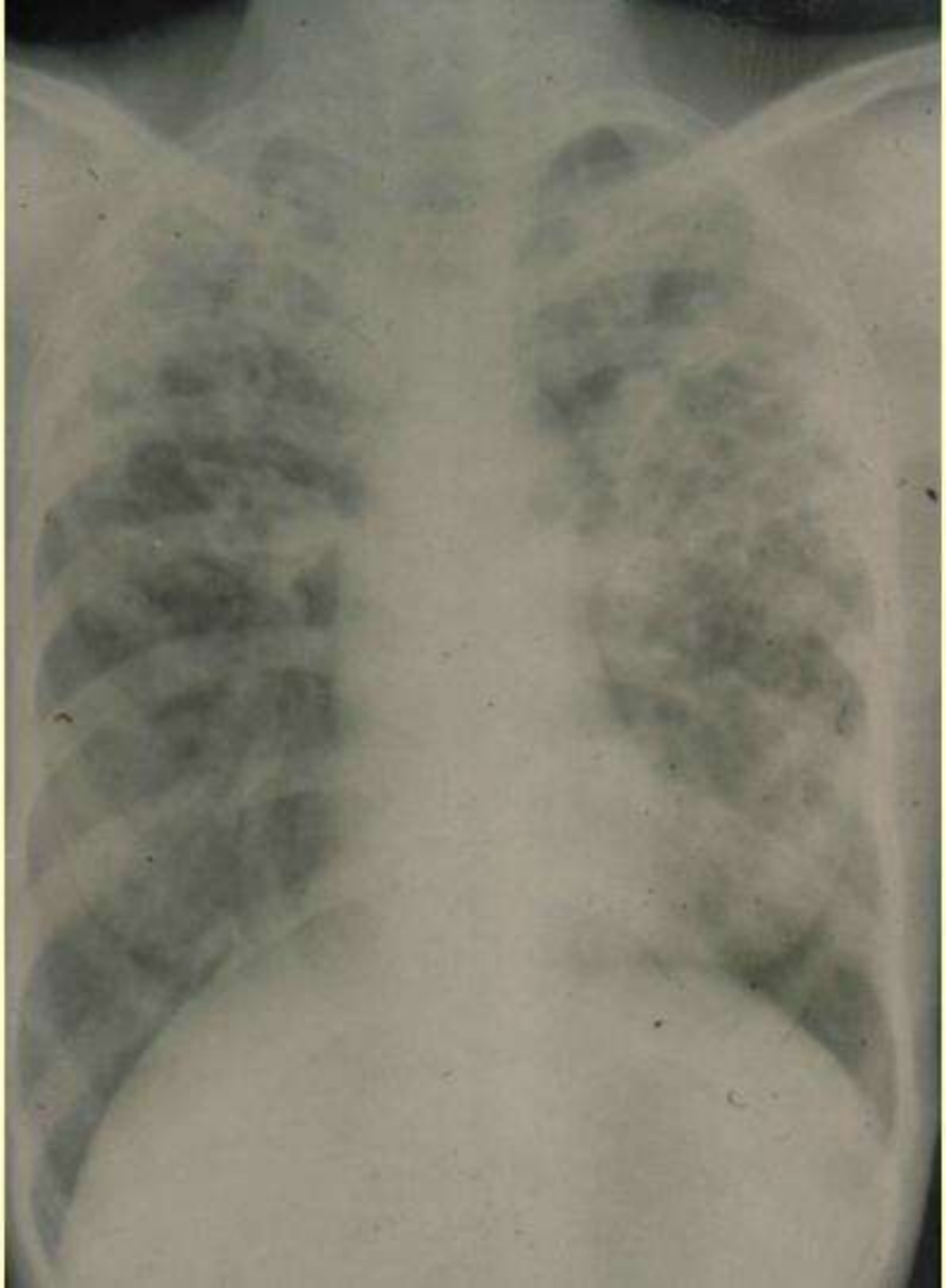
Infiltrative TB

Infiltrative TB



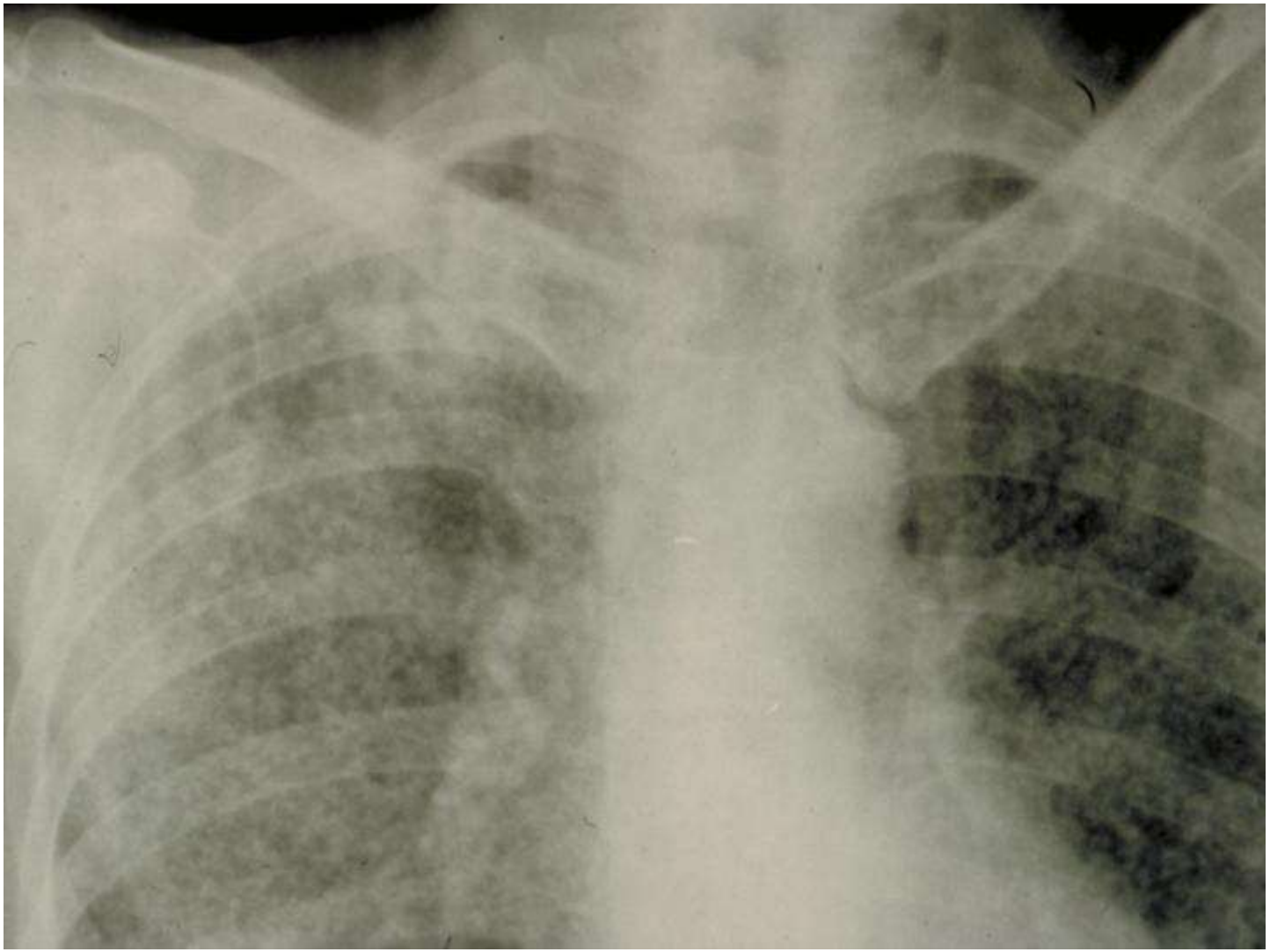
Cavernous TB



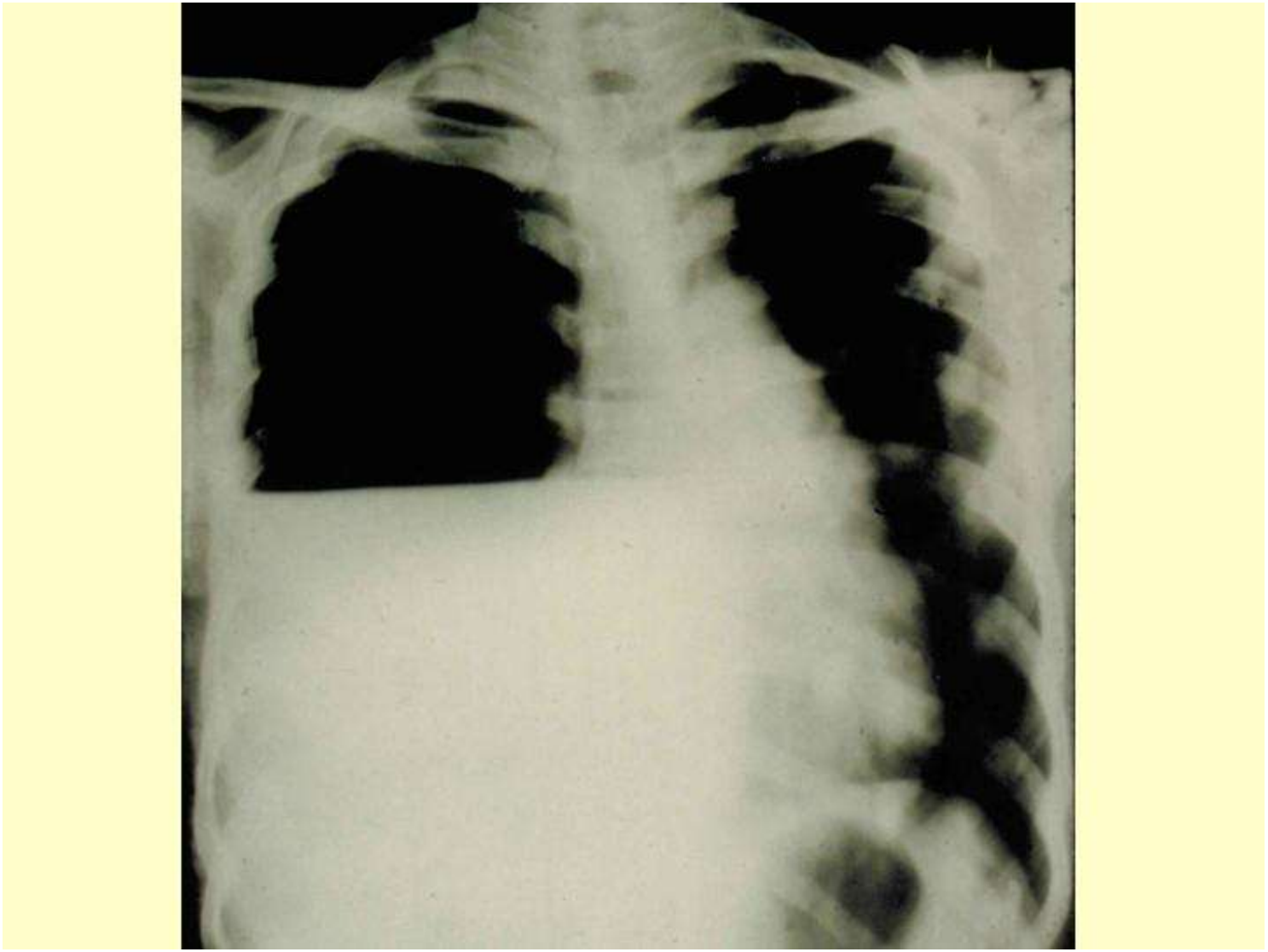


Miliar TB

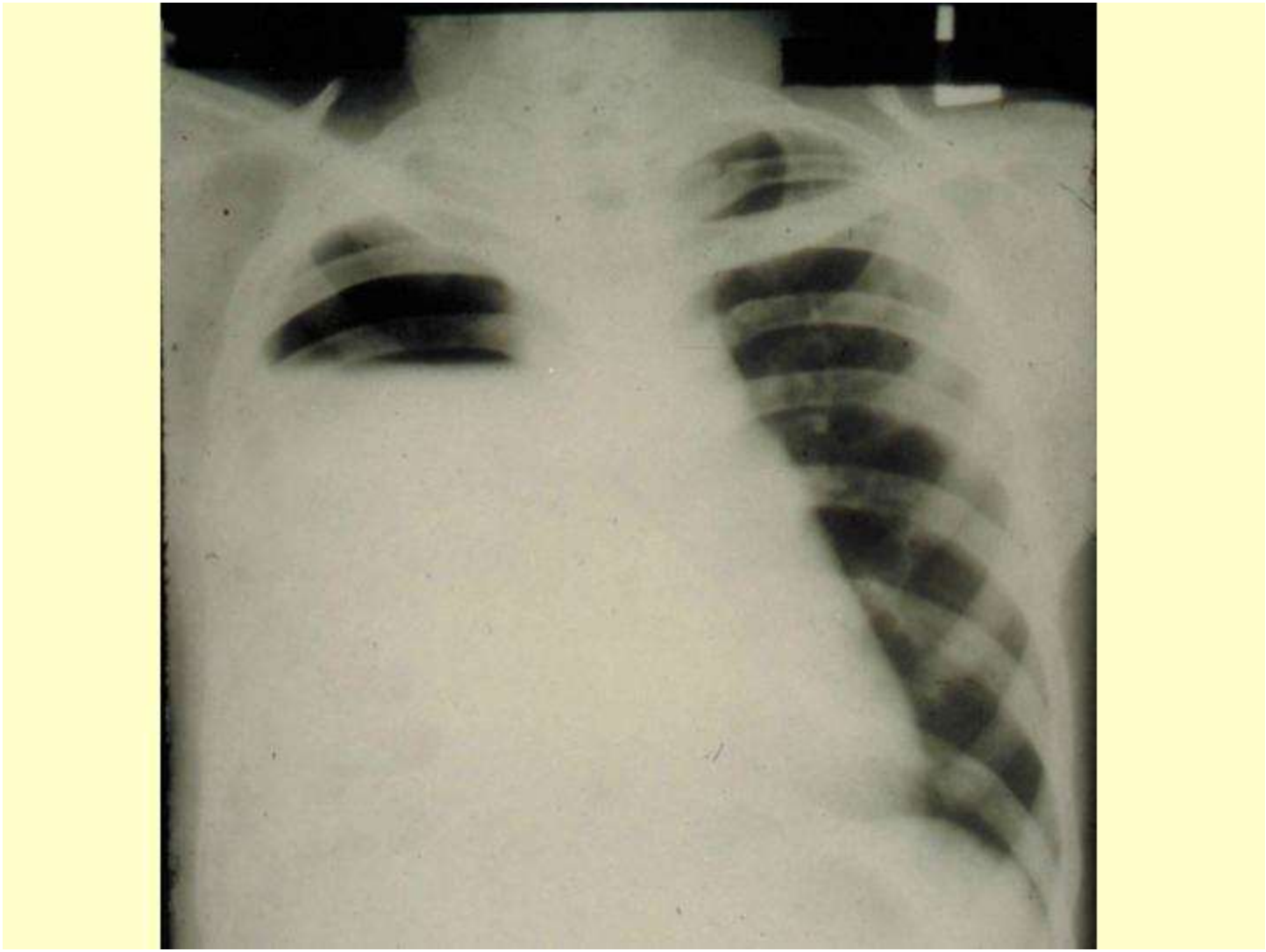
Miliar TB



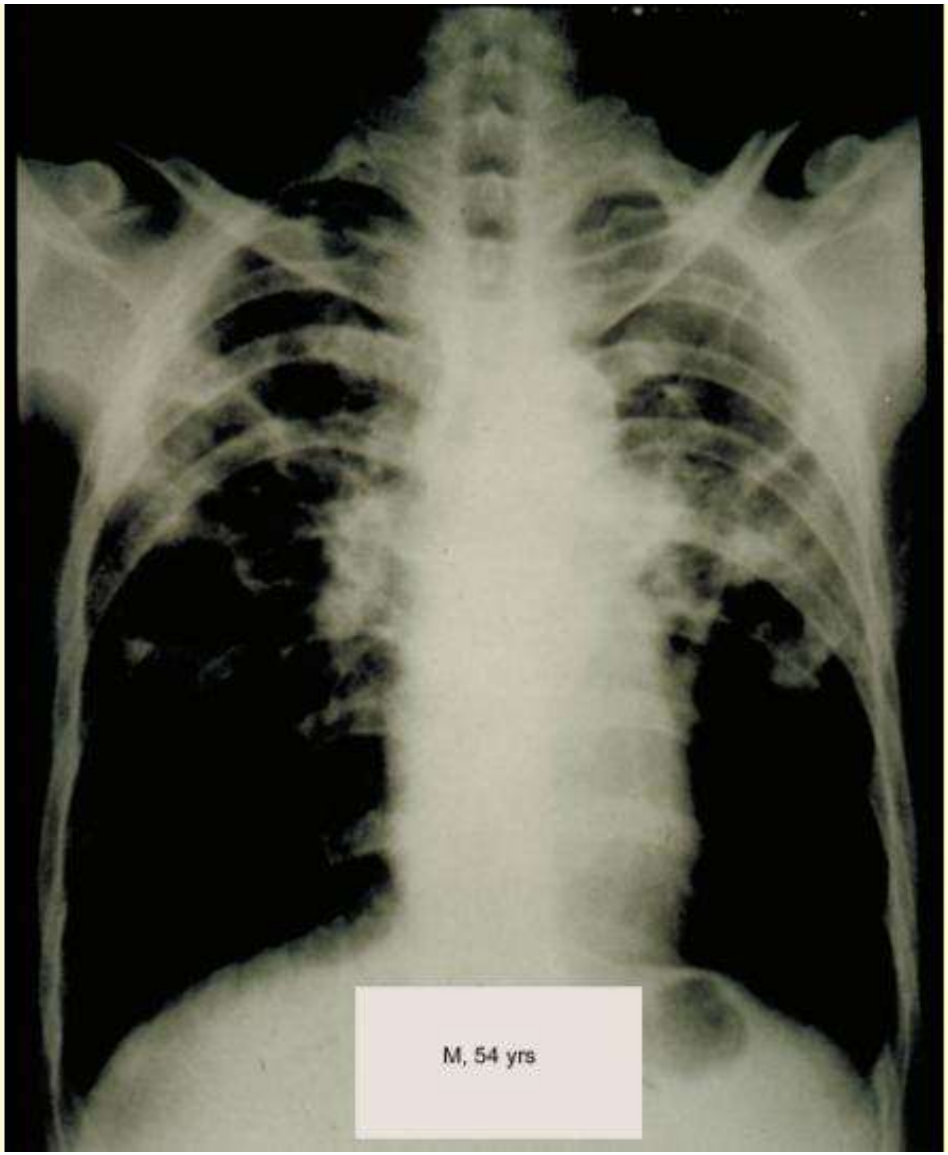
Pleural effusion - TB



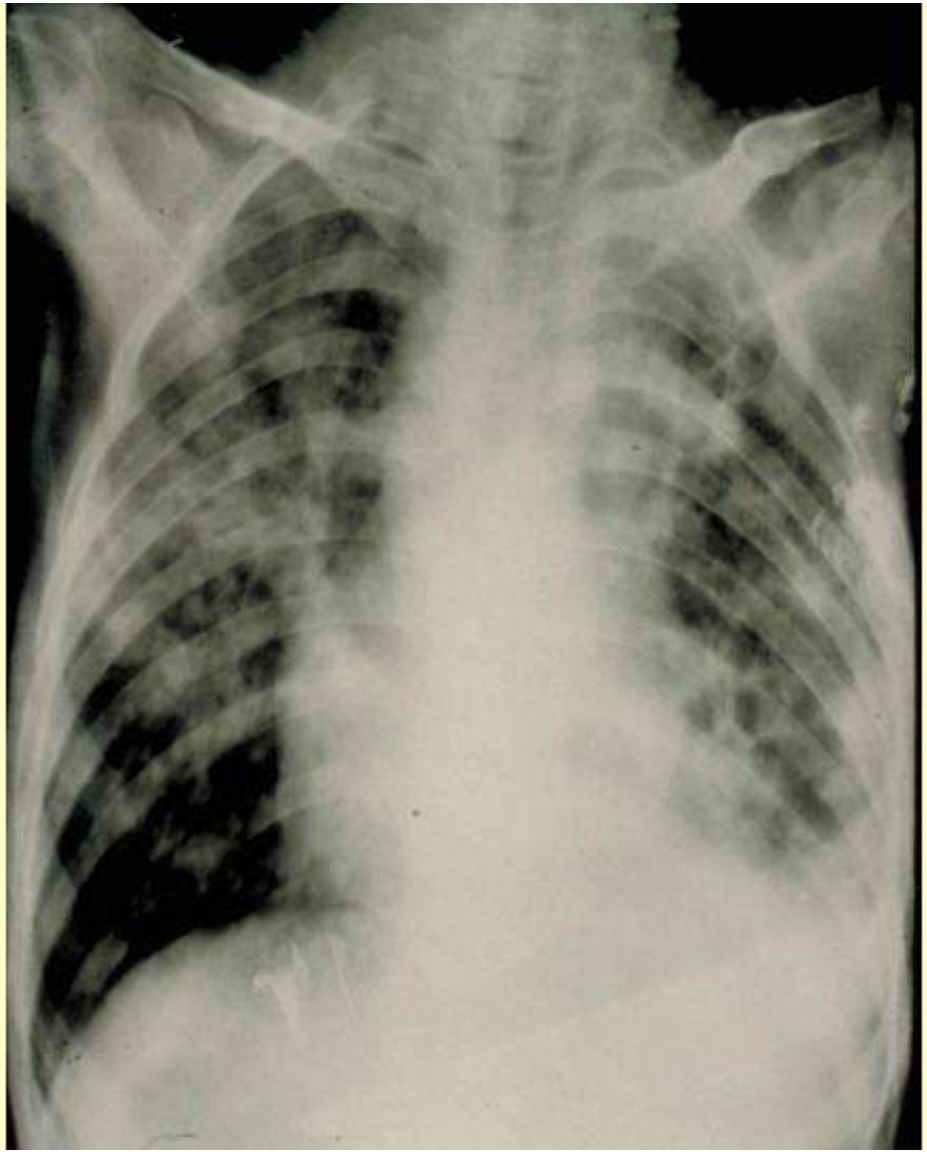
Pleural effusion - TB



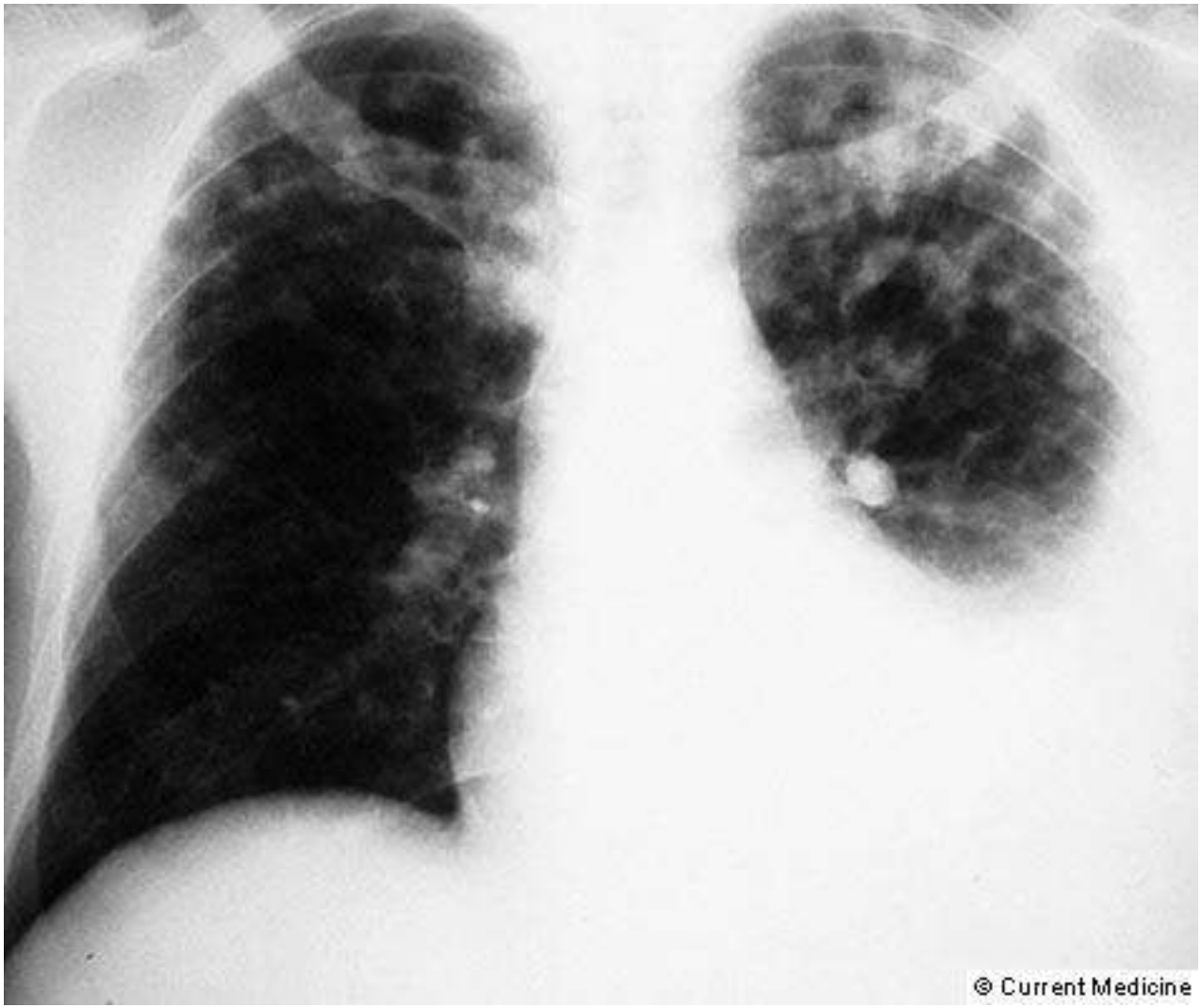
Post-TB Fibrosis



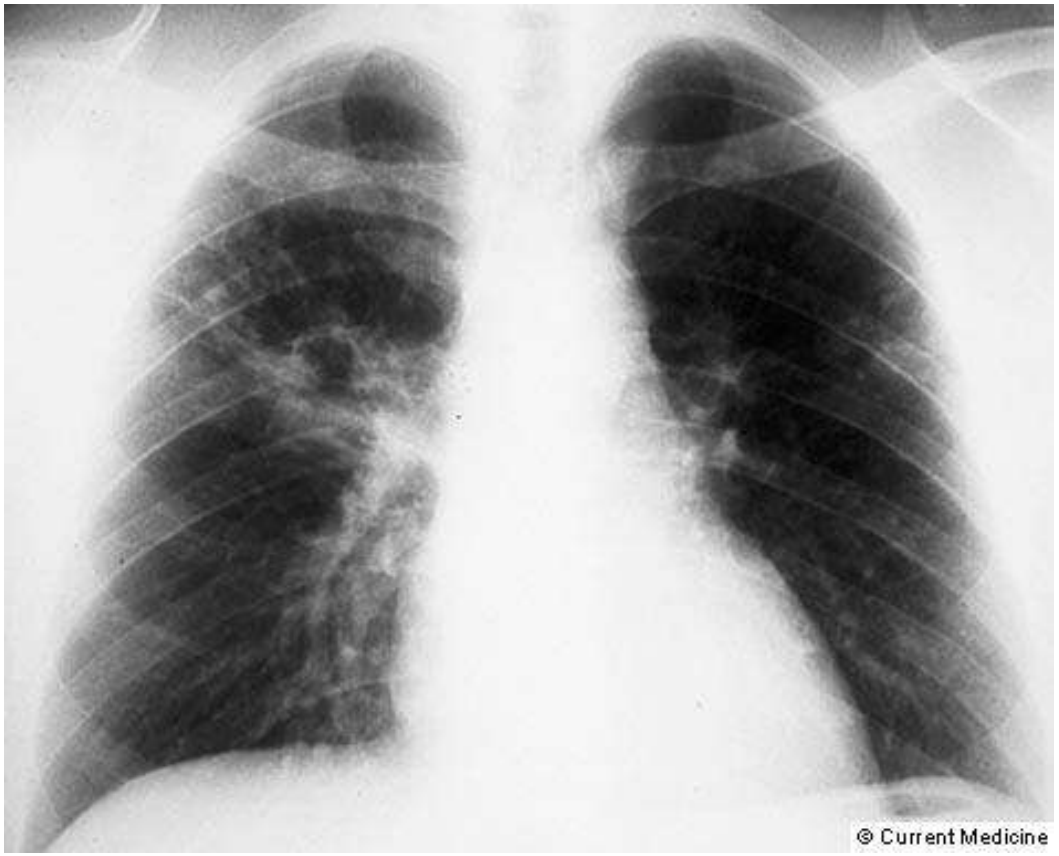
Post-TB Fibrosis



Radiograph of an alcoholic patient aged 53 years, with progressive weigh loss



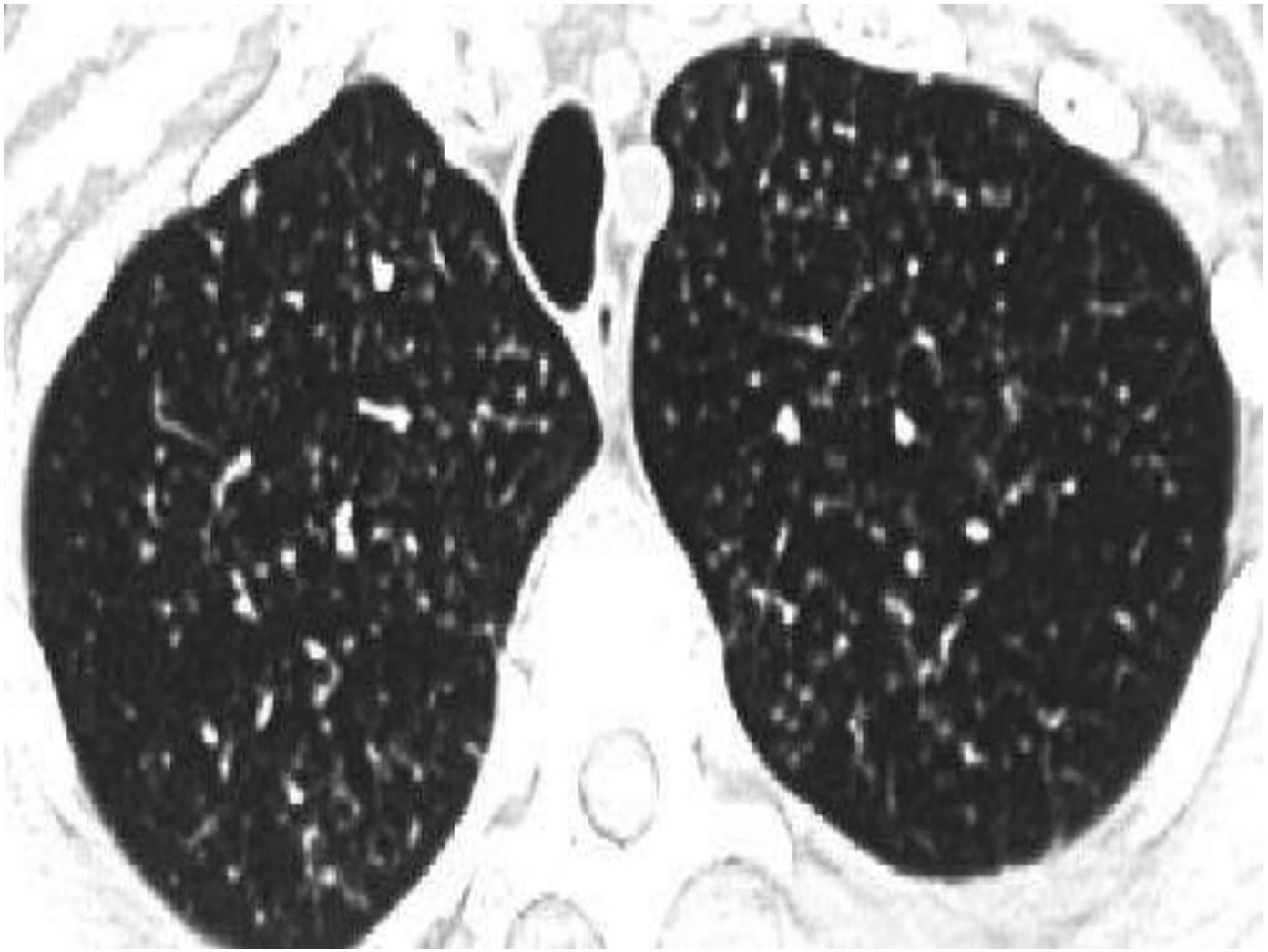
Radiograph of a man aged 49 years with a chronic productive cough and fever



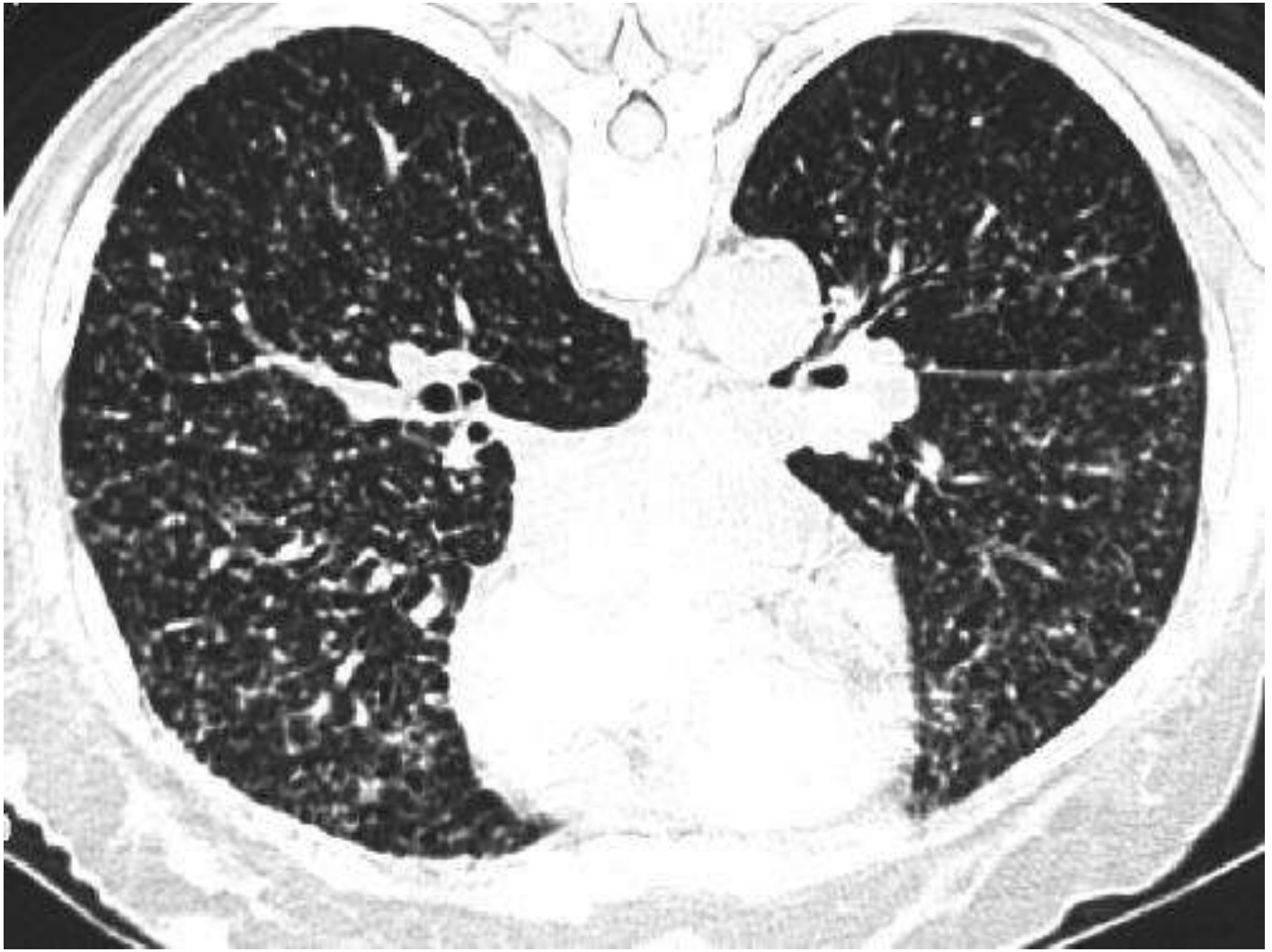
CT in lung TB

- Miliar lung TB
- Mediastinal lymph node involvement
- Pleural involvement
- Vertebrae involvement (MRI)

Miliar TB



Miliar TB



Identification of mycobacteria

- 1. **Microscopic** - sputum, urine, BAL
  - positive if in 100 000 bacilli /ml sputum
  - evaluation: + až +++ depending on the number of bacilli in 50 fields
- 2. **Cultivation** - posit. if 100 bacilli /ml sputum
  - lasts 6-9 weeks
- 3. Proof of BK metabolism (**BACTEC)** (rarely)
- 4. **Molecular – gene probes (PCR)** - 1 bacillus /ml sputum
- 5. **Quantiferon test, TB Spot test – IGRAs**
  (interferon gamma-release assays)

Tuberculine test

- Intradermal tuberculine (PPD-RT)
- After BCG vaccination – postvaccination hypersensitivity, i.e. induration of 6-15mm
- Active infection – more than 15 mm induration

Immunisation

- BCG-attenuated vaccine
- Primovaccinatio of healthy newborn children (SVK – abandoned recently - in 2012)
- Revaccination in tuberculine-negative 11-year old children (abandoned earlier)

Protection induced by BCG vaccination

- Adults:
  Protection against dissemination, meningitis, death
- Newborns – toddlers:
  Protection against any form of TB
- Older children:
  Protection analogical to that achieved in adults

Therapy of TB – antitubercolous drugs

		Side effects
• Isoniaside (INH)	**H**	toxic neuritis, CNS toxicity, hepatitis, fever
• Rifampicine	**R**	toxic hepatitis (worsens toxicity of INH), hemolytic anemia, trombocytopenia, fulminant renal failure
• Pyrazinamide	**Z**	toxic hepatitis, hyperuricaemia, gastrointestinal problems
• Ethambutol	**E**	partially reversible optic neuritis – depending on the dose
• Streptomycine		otovestibular toxicity, exanthema
• Quinolones		

Therapeutical regimens

DOT – directly observed therapy

Minimaly 6 months combination of

four (2 months) and two (4 months)

antituberculous drugs

2HRZE/4HR

Monitoring of therapy

Clinical response: temperature, body weight, hemoptysis

Microbiological response - debacillisation

Chest X-Ray

Monitoring of therapy

Clinical response: temperature, body weight, hemoptysis

Microbiological response - debacillisation

Chest X-Ray

Serious problem in recent years

multidrug resistant TB

prompted research for new anti-TB medication:

e.g. bedaquiline (the most recently approved)

Preventing and controlling tuberculosis in the community

Major priorities

- Promptly **identify and effectively treat all new cases** of tuberculosis with a goal that 95% of patients will be cured by 1 year after diagnosis.

- Promptly **identify all close contacts** of each infectious case, provide tuberculin skin testing with careful clinical evaluation, and offer therapy as indicated

- Provide tuberculin skin testing for groups at high risk for latent tuberculosis infection and treat as indicated

Preventing and controlling tuberculosis in the community

• Provide laboratory and diagnostic service,
including radiograph interpretation to all persons who need it.

Laboratory support should include expert examination of biologic specimens for acid- fast bacilli with reports available within 24 hours.

Culture for mycobacteria and drug susceptibility data should be available for all patients.

• Insure a functioning **central registry** is in place for collecting
and collating data on all new cases of tuberculosis with
epidemiologic, clinical, and laboratory reports tracked to allow monitoring
of treatment outcome, contact investigation,
and treatment of latent infection.

Tuberculosis and HIV

Transmission

1 of 3 TB cases in HIV patients is recently acquired

Immunity is not conferred by previous exposure to TB organisms

Lack of cavitary disease with HIV may render patients less contagious

Spread of TB facilitated by grouping HIV patients together in health care facilities, homeless shelters, and prisons

Clinical manifestations

Positive purified protein derivative with early stages of HIV only

Usual symptoms (fever, sweats, cough, and weight loss) are usually more exaggerated

Rapid progression from exposure to active disease (from loss of cell?mediated immunity)

Higher rate (40%–89%) of extrapulmonary manifestations

Lymphadenitis with fistula formation and abscesses

Radiographic features

Nonapical distribution

Infiltrates in any lung zone

Cavitation rare late in the disease

Intrathoracic adenopathy in 1 of 3 cases

Miliary infiltrates and pleural effusions

Normal chest radiograph in early stages of pulmonary

TB—Tuberculosis

Pulmonary nontuberculous mycobacterial infection

Pulmonary Nontuberculous Mycobacterial Infection

Disease may mimic tuberculosis in that there may be nodules, infiltrates, or cavities.

There is no known human? to? human transmission.

Organisms are ubiquitous in nature, particularly in soil and water.

Diagnosis is currently based on a compatible clinical presentation of cough, fatigue, and radiographic changes, in addition to at least two positive sputum cultures or one positive bronchial wash culture.

Treatment for Mycobacterium avium and Mycobacterium kansasii should generally include rifampin or rifabutin, ethambutol, and either azithromycin or clarithromycin, and should be continued for 12–24 months.

Surgical resection may be considered for large cavitary lesions or localized disease, in conjunction with medical therapy.

Multidrug-resistant tuberculosis (MDRTB)

Multidrug? Resistant Tuberculosis

Description

Resistance to both isoniazid and rifampin

1%–2% of patients with TB are resistant to both isoniazid and rifampin

Contributing factors

HIV

Close contact with patients with MDR TB

Noncompliance with TB therapy and inadequate follow?up

Increased immigration from areas of high prevalence (Asia, Africa, Latin America, the former Soviet Union)

Increased numbers of the homeless, intravenous drug users, and institutionalized patients

Cutbacks in public funding of TB control programs

MDR—multidrug? resistant; TB—tuberculosis.