TUBERCULOSIS

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Tuberculosis

- Tuberculosis is a communicable chronic granulomatous disease caused by Mycobacterium tuberculosis involving Lungs usually but may affect any organ.

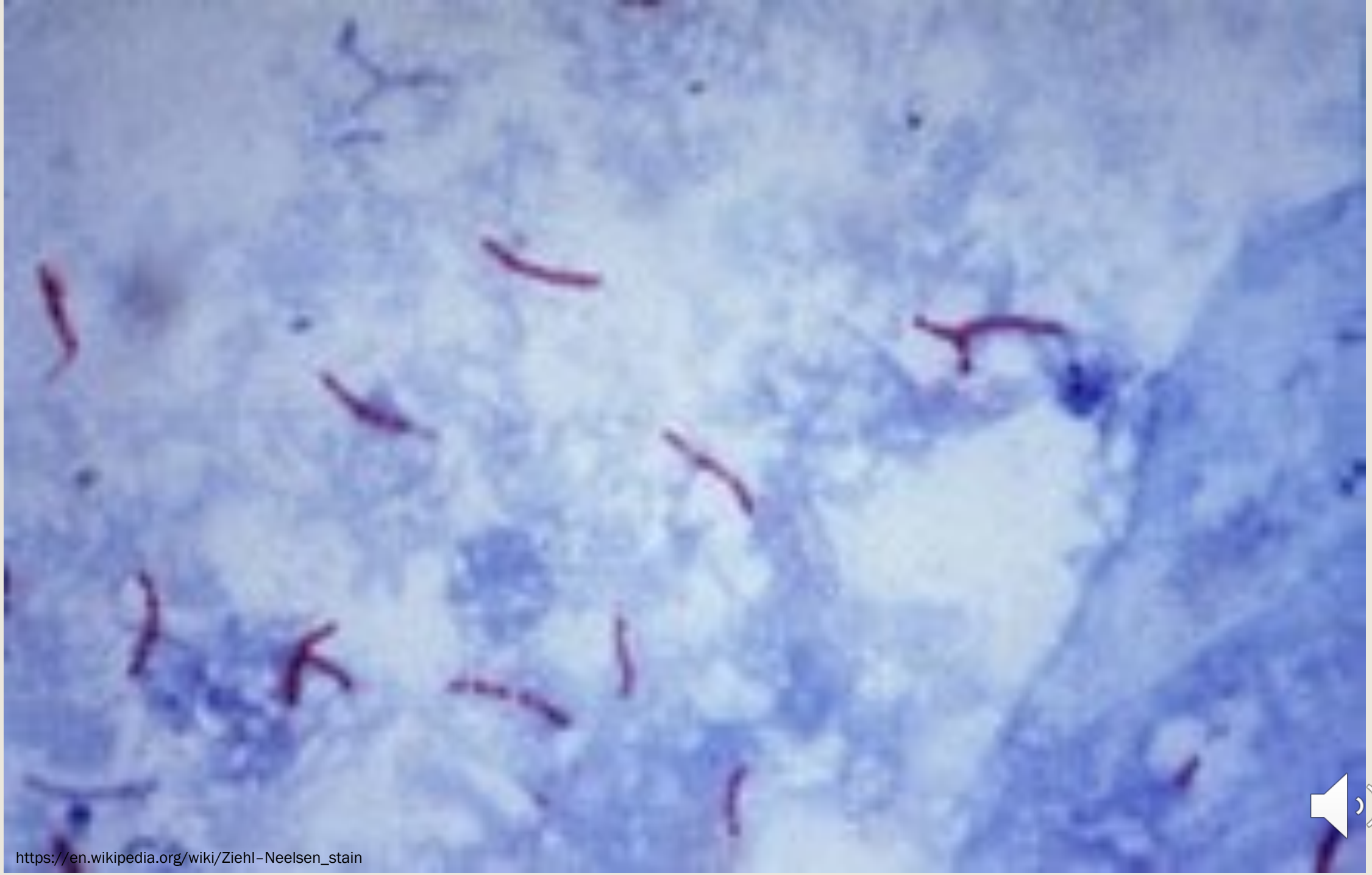
Risk Factors

Poverty, crowding, and chronic debilitating illness.

- older adults
- the urban poor
- patients with AIDS
- and members of minority communities.
- African Americans
- Native Americans
- the Inuit (from Alaska)
- Hispanics
- immigrants from Southeast Asia
- diabetes mellitus
- Hodgkin lymphoma
- Chronic lung disease (particularly silicosis)
- chronic renal failure
- Malnutrition
- Alcoholism
- Immunosuppression
- HIV

Etiology:

- **Mycobacteria:**
  - slender rods
  - acid-fast (i.e., they have a high content of complex lipids that readily bind the Ziehl-Neelsen stain and subsequently stubbornly resist decolorization).



https://en.wikipedia.org/wiki/Ziehl–Neelsen_stain

M. tuberculosis hominis

- Most cases of tuberculosis.
- The reservoir of infection found in individuals with active pulmonary disease.
- Transmission
  - direct, by inhalation of airborne organisms in aerosols generated by expectoration
  - exposure to contaminated secretions of infected individuals.

Mycobacterium bovis

- Oropharyngeal and intestinal tuberculosis
- contracted by drinking contaminated milk

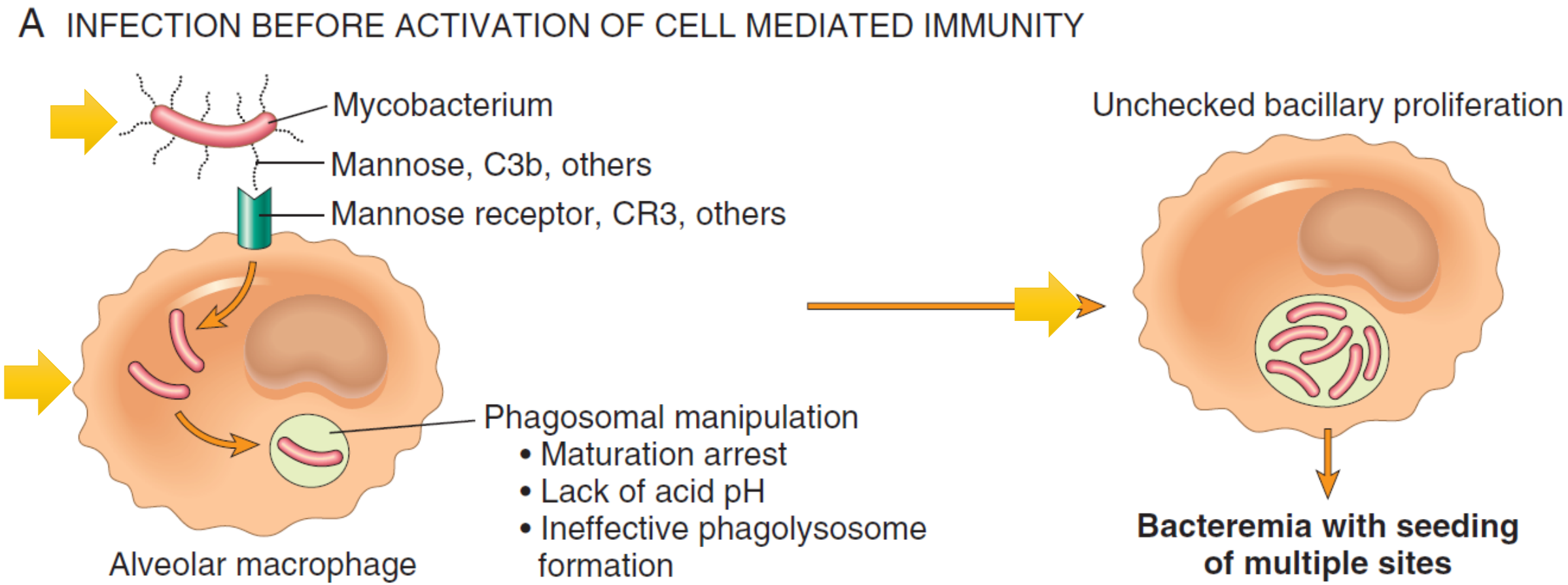
Mycobacterium avium complex

- Less virulent than M. tuberculosis
- Rarely cause disease in immunocompetent individuals.
- Cause disease in 10% to 30% of patients with AIDS.

Pathogenesis

- **In the previously unexposed immunocompetent individual**
  - Development of cell-mediated immunity
    - To resist the organism
    - To develop tissue hypersensitivity to tubercular antigens.
  - Destructive tissue hypersensitivity as a part of the host immune response:
    - Caseating granulomas
    - Cavitation
    - Acquisition of immunity to the organism.

Natural history of primary pulmonary tuberculosis



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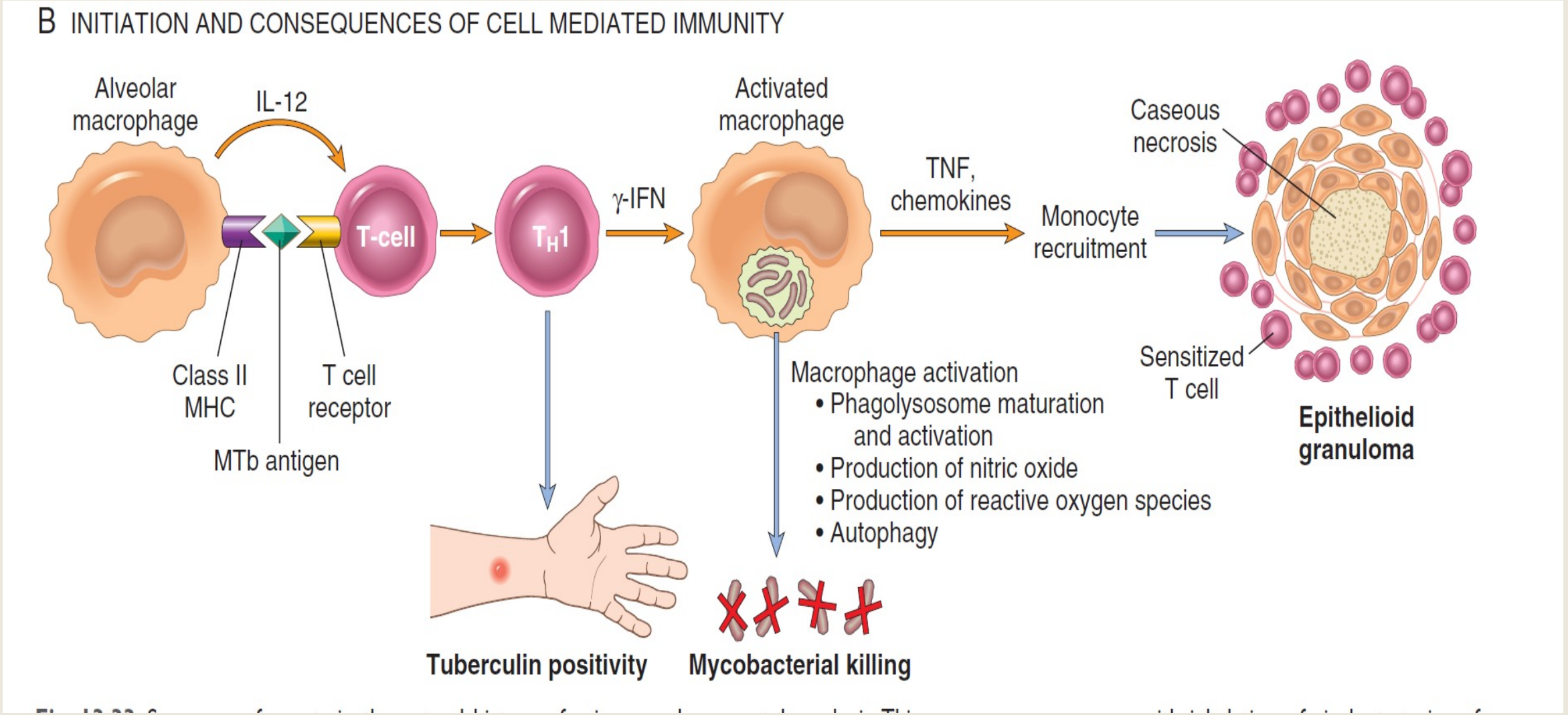

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Activated macrophages

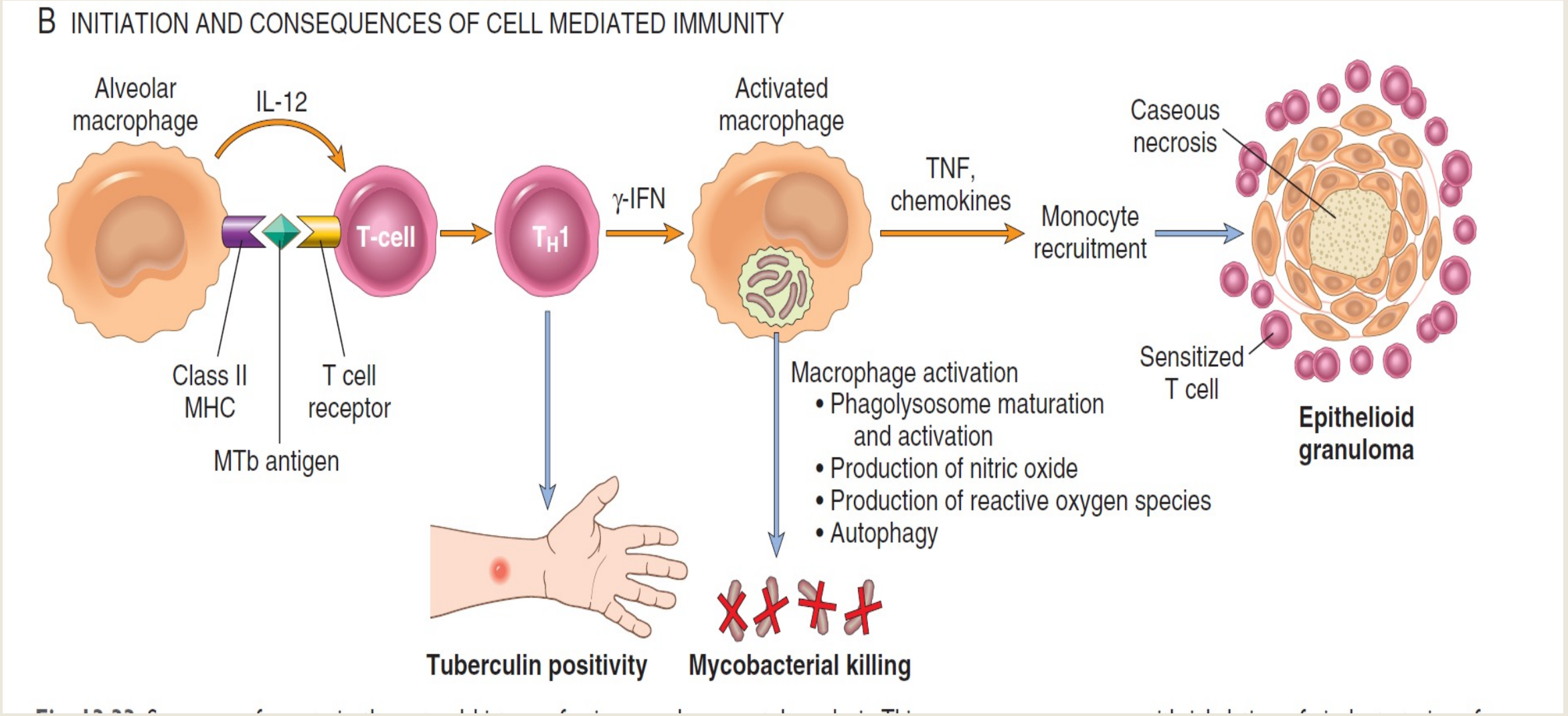
- **TNF**
  - Monocytes recruitment , activation and differentiation into the “epithelioid histiocytes” that characterize the granulomatous response

- **Inducible nitric oxide synthase (iNOS)**
  - raises nitric oxide (NO) levels, helping to create reactive nitrogen intermediates that are important in killing of mycobacteria

- **anti-microbial peptides (defensins)**

  - toxic to mycobacterial organisms.

Natural history of primary pulmonary tuberculosis



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Pathogenesis, Summary:

- Immunity to a tubercular infection is primarily mediated by **TH1 cells**, which stimulate macrophages to kill mycobacteria.
- Immune response, while largely effective, comes at the cost of hypersensitivity and the accompanying tissue destruction
- Defects in any of the steps of a TH1 T cell response (including IL-12, IFN-γ, TNF, or nitric oxide production)
  - poorly formed granulomas
  - absence of resistance
  - disease progression.

- Reactivation of the infection or re-exposure to the bacilli in a **previously sensitized host** results in rapid mobilization of a defensive reaction but also increased tissue necrosis.

- **Hypersensitivity and resistance appear in parallel**
  - The loss of hypersensitivity (indicated by tuberculin negativity in a M.tuberculosis-infected patient) is an ominous sign of fading resistance to the organism.

Tuberculin (Mantoux) test:

- Delayed hypersensitivity
- intracutaneous injection of 0.1 mL of sterile purified protein derivative (PPD)
- A positive tuberculin skin test does not differentiate between infection and disease.

- False-negative reactions or skin test anergy:
  - certain viral infections
  - Sarcoidosis
  - Malnutrition
  - Hodgkin lymphoma
  - immunosuppression
  - overwhelming active tuberculous disease.

- False-positive reactions may result from infection by atypical mycobacteria.

Infection vs. disease

- Infection implies seeding of a focus with organisms.
- Disease is a clinically significant tissue damage
- Routes of transmission
  - Airborne droplets

Primary Tuberculosis

- self-limited
- Uncommonly may result in the development of fever and pleural effusions.
- Viable organisms may remain dormant in a tiny, telltale fibrocalcific nodule at the site of the infection for several years **(infection, not active disease)**
- If immune defenses are lowered, the infection may reactivate a potentially life threatening disease.

Primary Tuberculosis

- The form of disease that develops in a previously unexposed and therefore unsensitized patient.
- 5% of newly infected acquire significant disease.

Primary Tuberculosis, presentation:

- In otherwise healthy individuals:
  - Mostly the only consequence are the foci of scarring. Which may harbor viable bacilli and serve as a nidus for disease reactivation at a later time if host defenses wane.

- Uncommonly, new infection leads to progressive primary tuberculosis:
  - Affected patients are:
    - overtly immunocompromised
    - have subtle defects in host defenses, (malnourished)
    - Certain racial groups, such as the Inuit
    - HIV-positive patients with significant immunosuppression

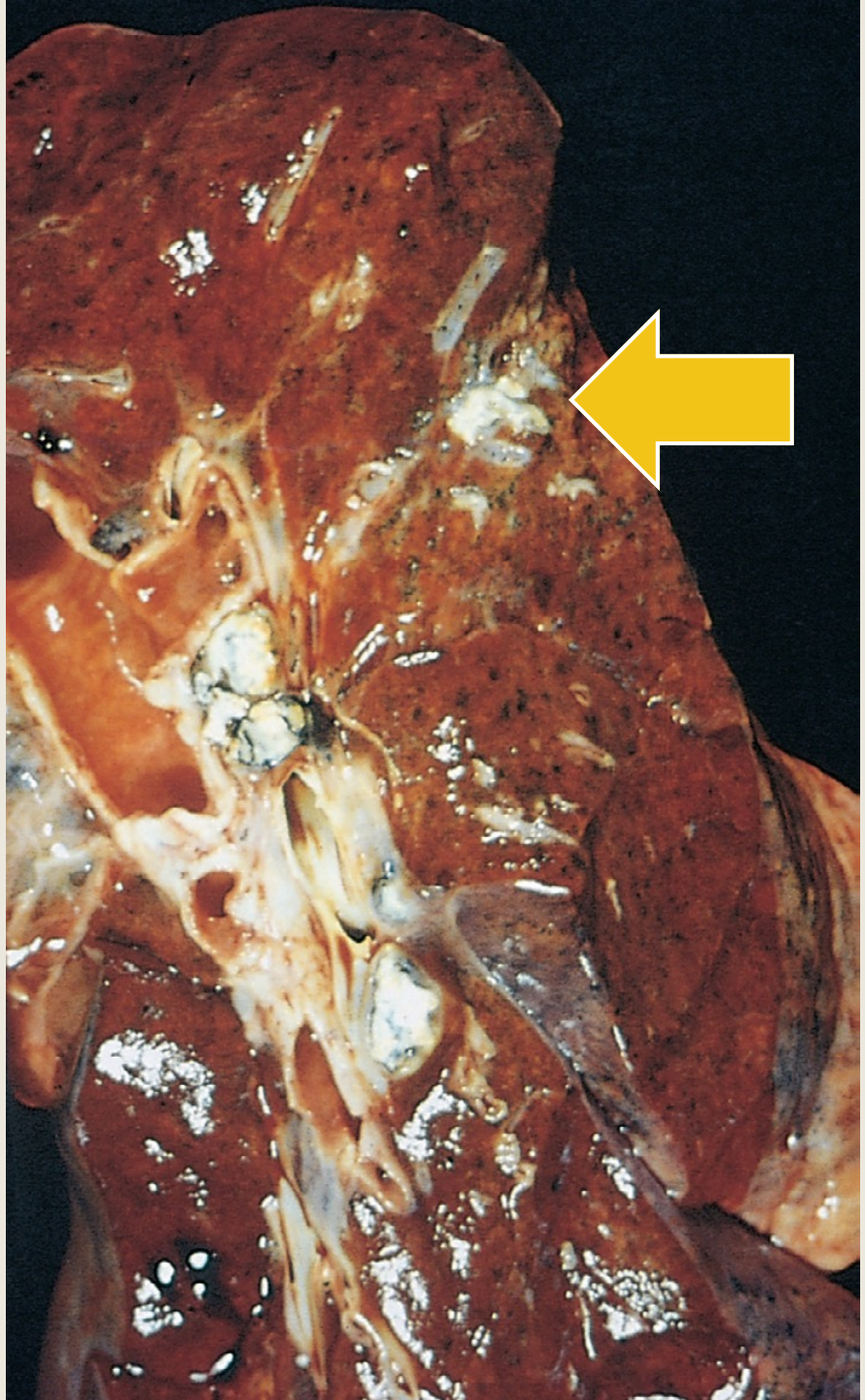
MORPHOLOGY

- Almost always begins in the lungs.

- The inhaled bacilli usually implant close to the pleura in the distal air spaces
  - in the lower part of the upper lobe
  - in the upper part of the lower lobe.

MORPHOLOGY, grossly:

- **Ghon focus.**
  - ✓ a 1-cm to 1.5-cm area of gray-white inflammatory consolidation emerges during the development of sensitization
  - ✓ caseous necrosis.



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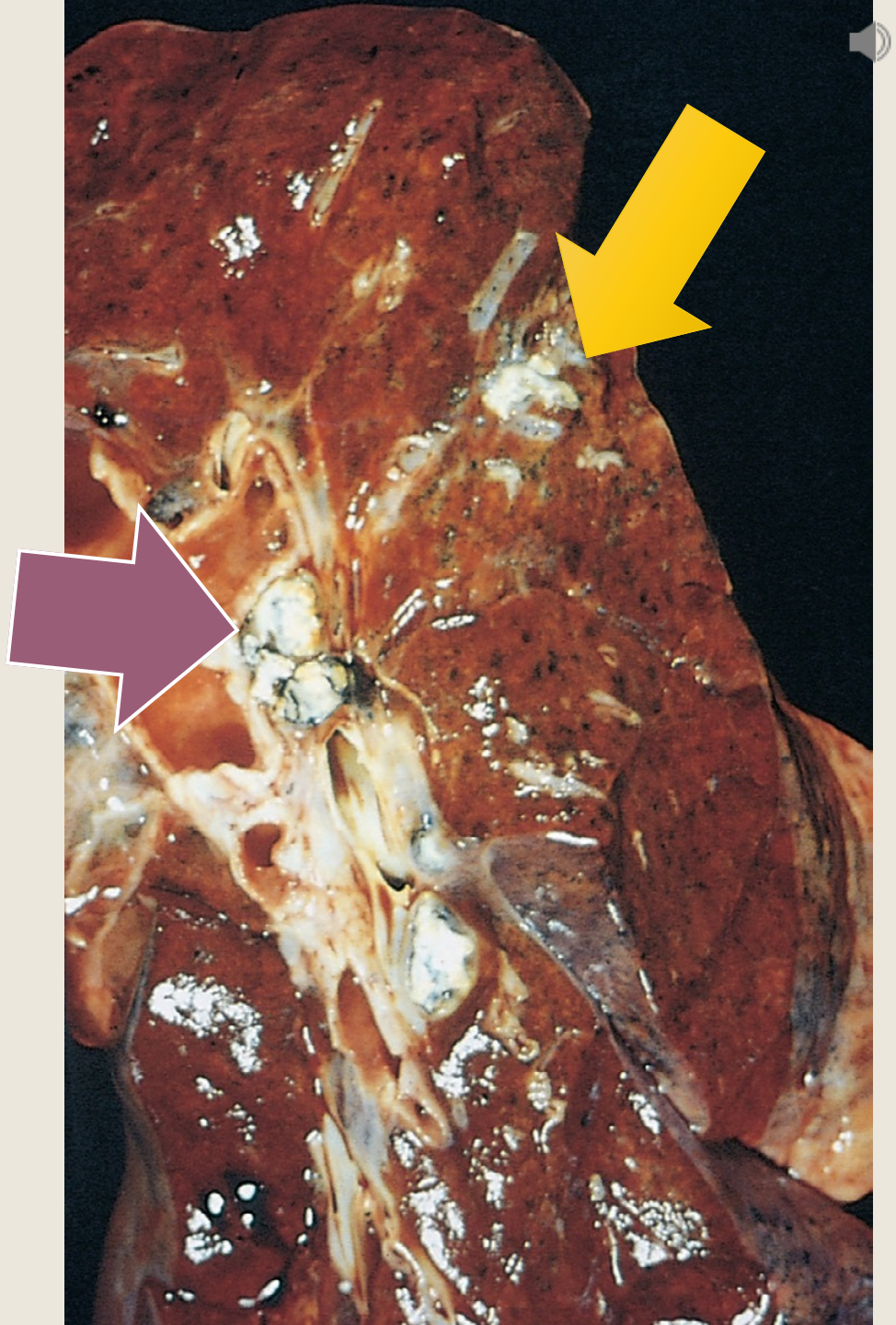
MORPHOLOGY, grossly:

- Tubercle bacilli, free or within phagocytes, travel via the lymphatic vessels to regional lymph nodes.

- **Ghon complex** :This combination of parenchymal and nodal lesions



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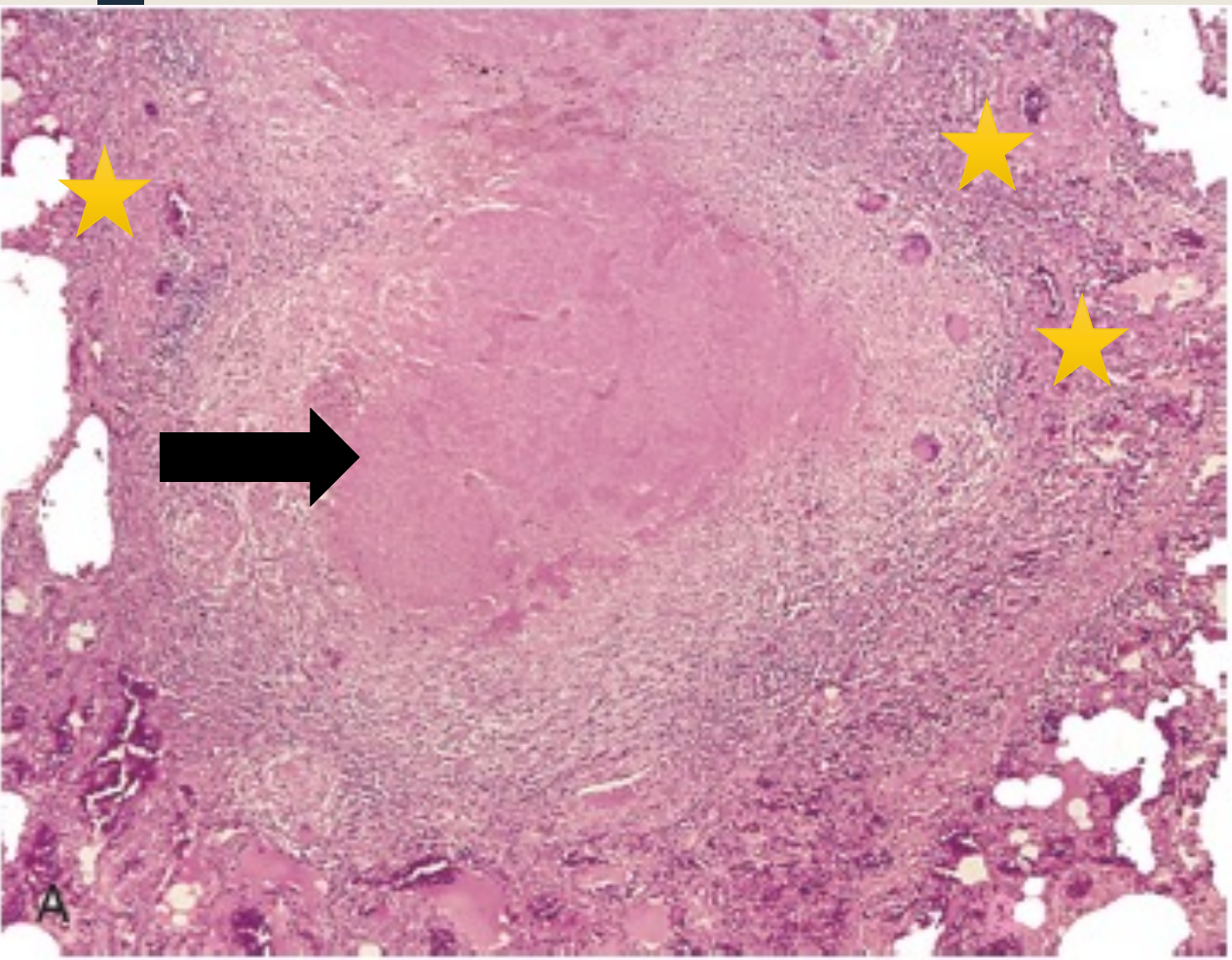
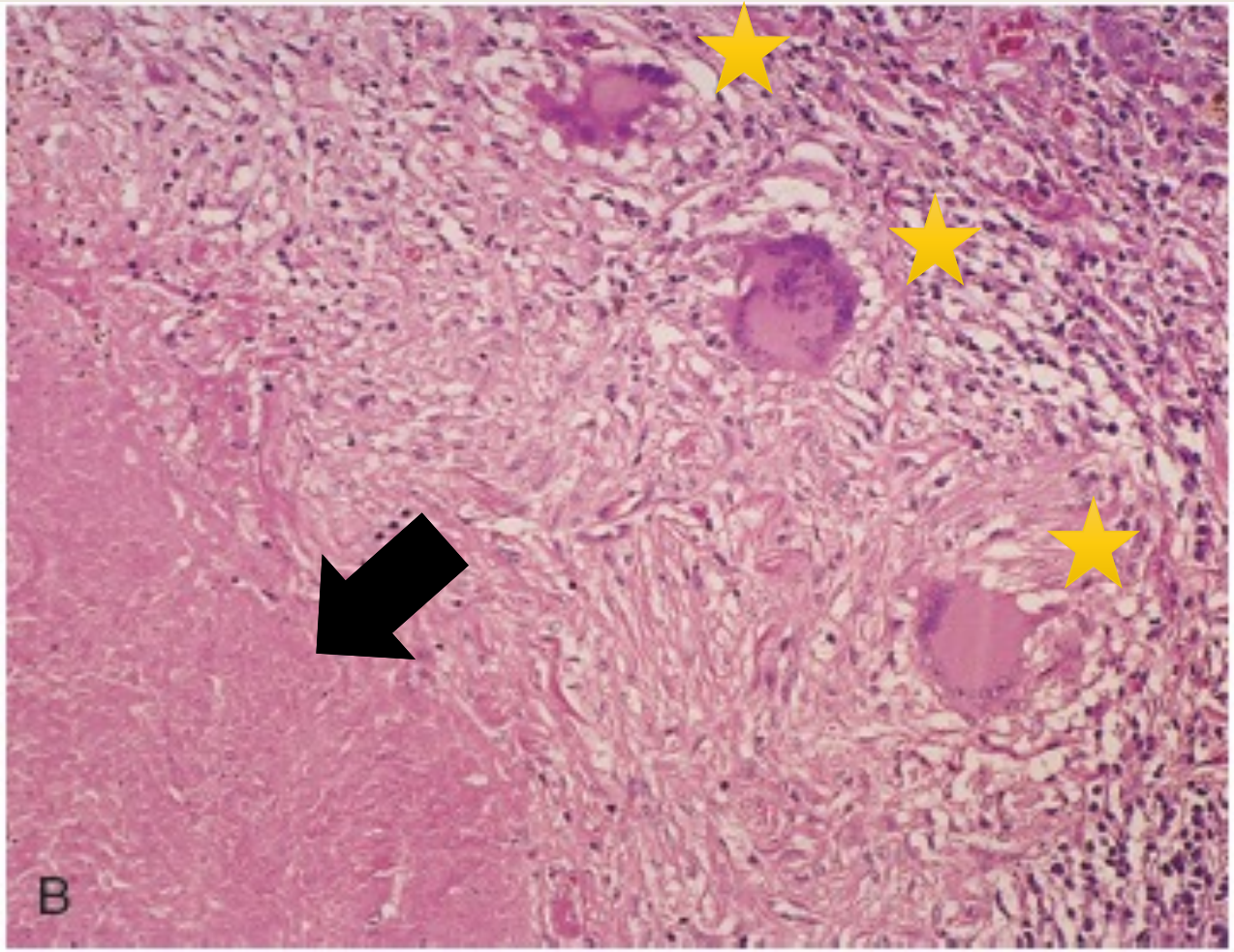
- In the first few weeks, Lymphatic and hematogenous dissemination
- In 95% cell-mediated immunity controls the infection.
- Ghon complex undergoes progressive fibrosis and calcification
- Despite seeding of other organs, no lesions develop.

MORPHOLOGY, microscopic:





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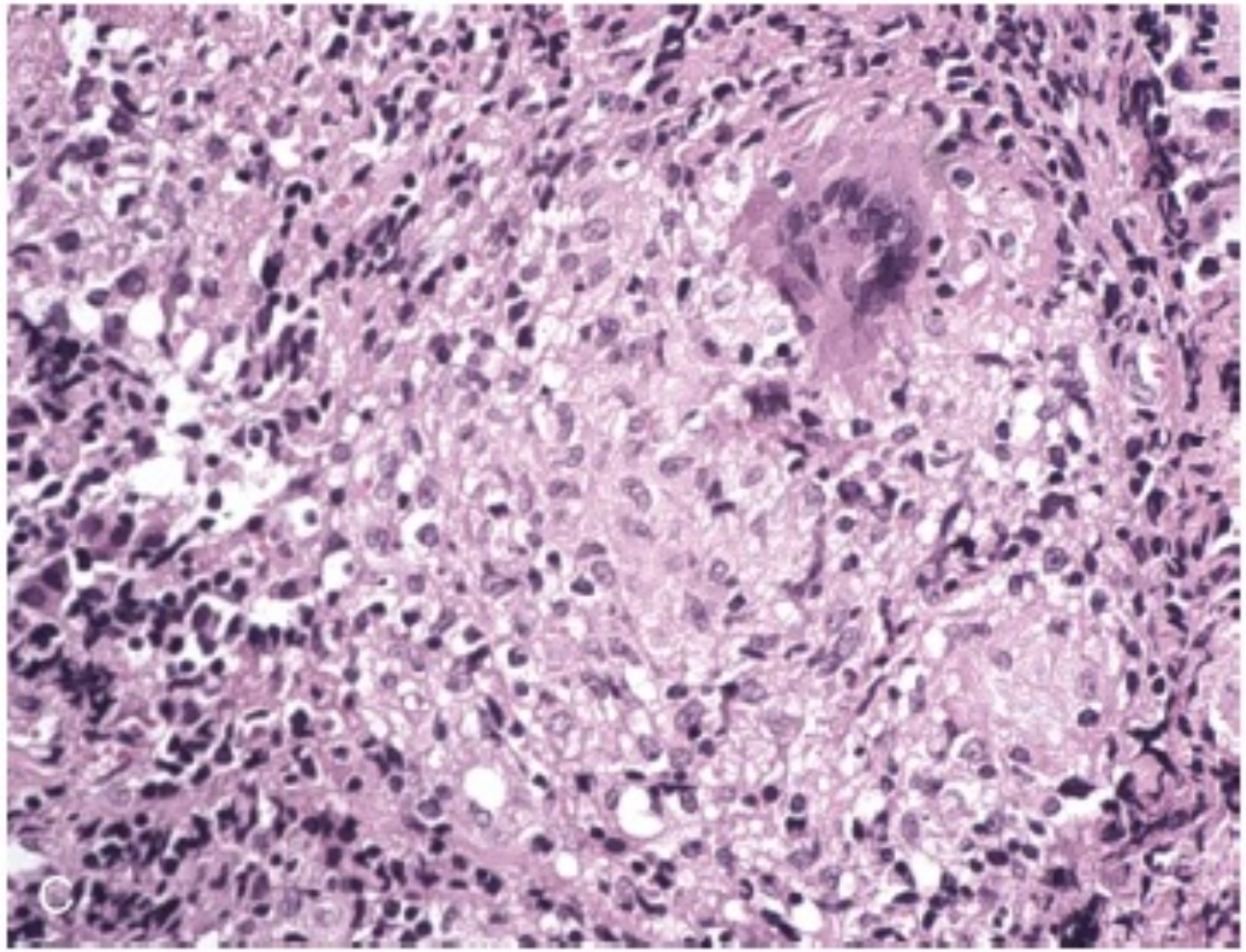

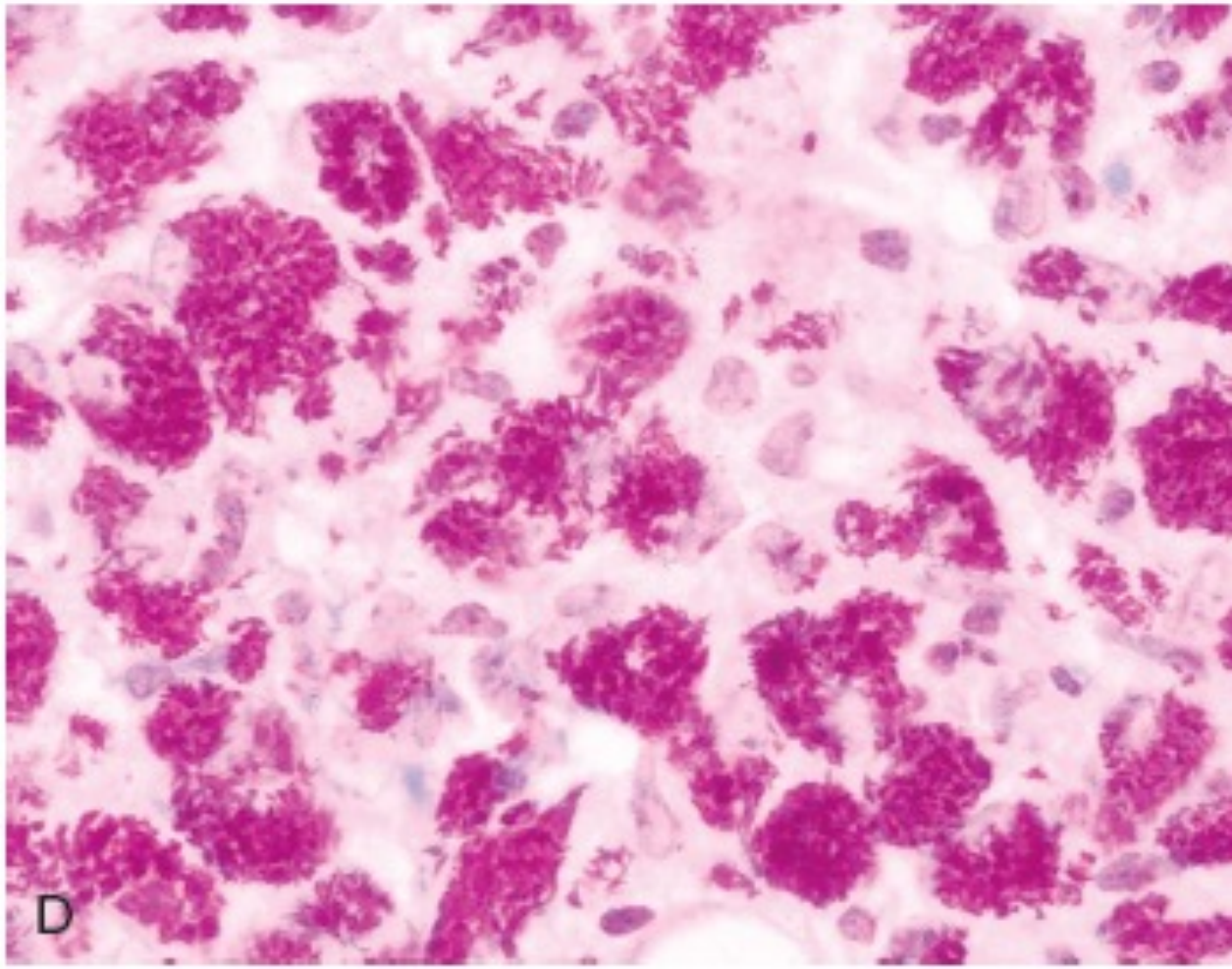

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Secondary Tuberculosis (Reactivation Tuberculosis)

- Arises in a previously sensitized host when host resistance is weakened Or due to reinfection
- <5% with primary disease develop secondary tuberculosis.

- Secondary pulmonary tuberculosis:
  - classically localized to the apex of one or both upper lobes.
  - the bacilli excite a marked tissue response that tends to wall off the focus (localization)
  - regional lymph nodes are less involved early in the disease than they are in primary tuberculosis.
  - cavitation leading to erosion into and dissemination along airways→ important source of infectivity, because the patient now produces sputum containing bacilli.

MORPHOLOGY, grossly:

- initial lesion is a small focus of consolidation, <2 cm, within 1-2 cm of the **apical pleura.**

- sharply circumscribed, firm, gray-white to yellow with variable amount of central caseation and peripheral fibrosis

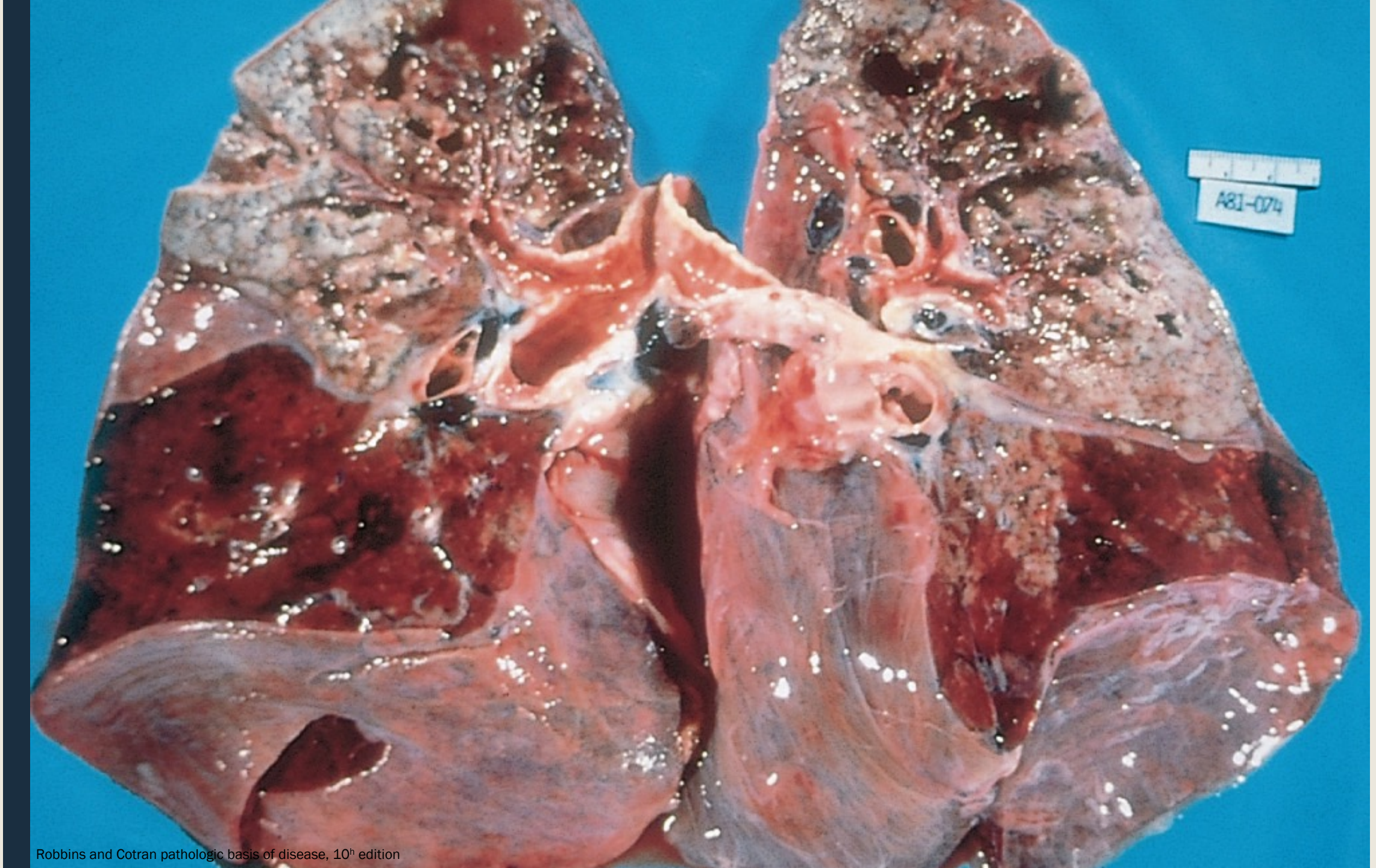
MORPHOLOGY, microscopic:

- **active lesions:** coalescent tubercles with central caseation.

- **tubercle bacilli:**
  - can be demonstrated by appropriate methods in early exudative and caseous phases of granuloma formation
  - Impossible to find them in the late fibrocalcific stages.

- **Localized, apical, secondary pulmonary tuberculosis:**
  - heal with fibrosis either spontaneously or after therapy
  - or may progress and extend along several different pathways.

- **progressive pulmonary tuberculosis:**
  - apical lesion enlarges with expansion of caseation area.
  - Erosion into a bronchus evacuates the caseous center, creating a ragged, **irregular cavity lined by caseous material**
  - Erosion of blood vessels results in hemoptysis.
  - **With adequate treatment**, the process may be arrested
  - **If the treatment is inadequate or host defenses are impaired**, the infection may spread by direct extension and by dissemination through airways, lymphatic channels, and the vascular system.



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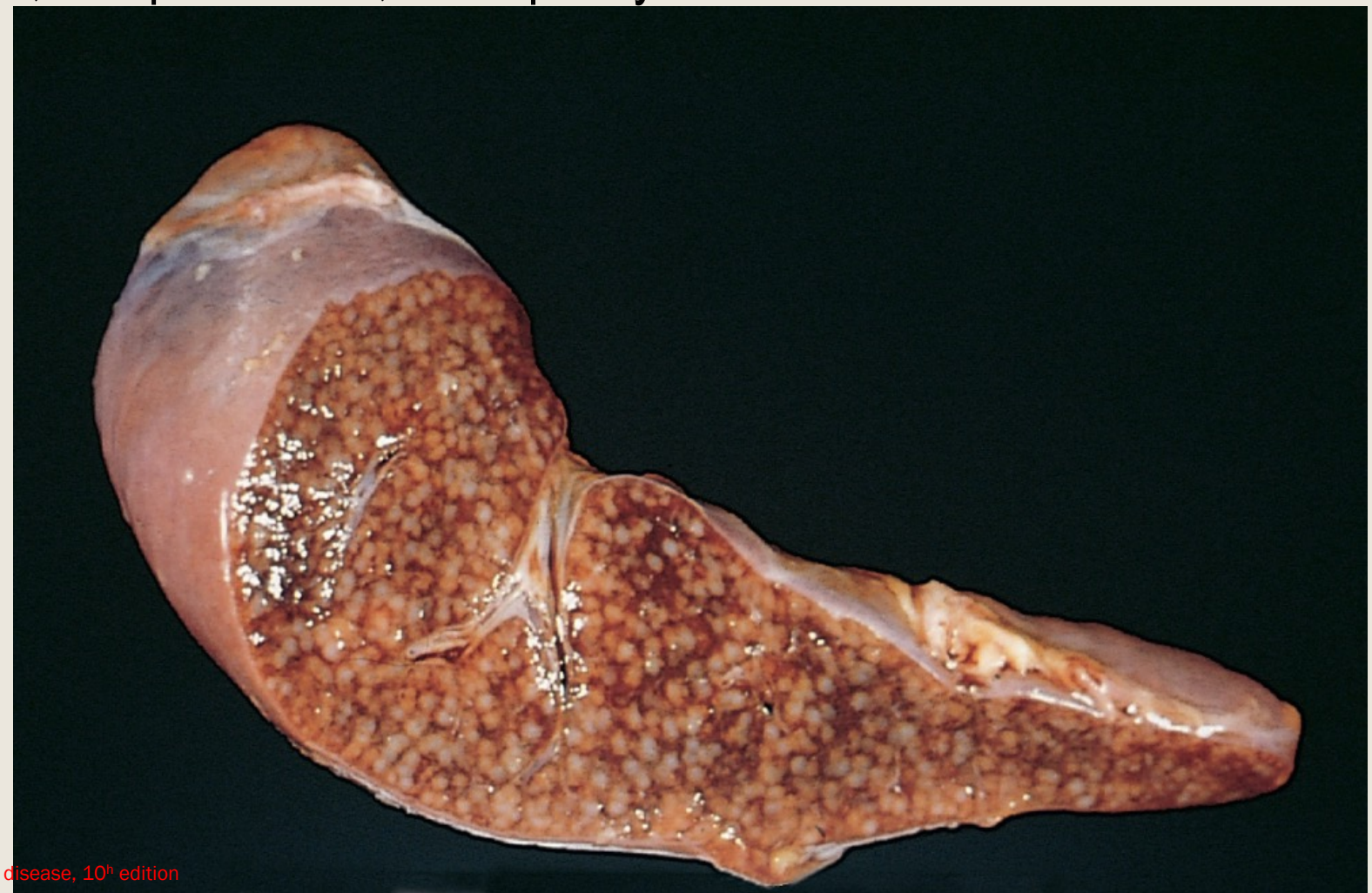
- **Miliary pulmonary disease :**
  - when organisms reach the bloodstream through lymphatic vessels and then recirculate to the lung via the pulmonary arteries.
  - small (2-mm), yellow-white consolidation scattered through the lung parenchyma
  - the word miliary is derived from the resemblance of these foci to millet seeds.
  - With progressive pulmonary tuberculosis, the pleural cavity is invariably involved and serous **pleural effusions, tuberculous empyema,** or **obliterative fibrous pleuritis** develop.
  - **Endobronchial, endotracheal,** and **laryngeal tuberculosis**
  - The mucosal lining may show minute granulomatous lesions

- **Systemic miliary tuberculosis :**
  - when the organisms disseminate hematogenously throughout the body.
  - It is most prominent in the liver, bone marrow, spleen, adrenal glands, meninges, kidneys, fallopian tubes, and epididymis



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- **Isolated-organ tuberculosis:**
  - any organs or tissues seeded hematogenously and may be the presenting manifestation of tuberculosis.
  - meninges (tuberculous meningitis), kidneys (renal tuberculosis), adrenal glands, bones (osteomyelitis), and fallopian tubes (salpingitis),
  - vertebrae (**Pott disease).**

- **Lymphadenitis :**
  - the most frequent form of extrapulmonary tuberculosis
  - cervical region
  - unifocal, and most patients do not have concurrent extranodal disease.
  - HIV-positive patients, have multifocal disease, systemic symptoms, and either pulmonary or other organ involvement by active tuberculosis.

Clinical Features

- **Asymptomatic**

- Insidious onset, with gradual development of both systemic and localizing symptoms and signs.

- **Systemic manifestations**:
  - probably related to the release of cytokines by activated macrophages (TNF and IL-1),
  - appear early in the disease course
  - include malaise, anorexia, weight loss, and fever.
  - Fever: low grade and remittent +/- night sweats.

- **Pulmonary**:
  - increasing amounts of sputum, at first mucoid and later purulent.
  - When cavitation is present, the sputum contains tubercle bacilli.
  - Hemoptysis (50%).
  - Pleuritic pain

- **Extrapulmonary manifestations:**
  - infertility, headache, neurologic deficits, back pain and paraplegia.

Diagnosis:

- based on the **history , physical and radiographic findings** of consolidation or cavitation in the apices of the lungs.

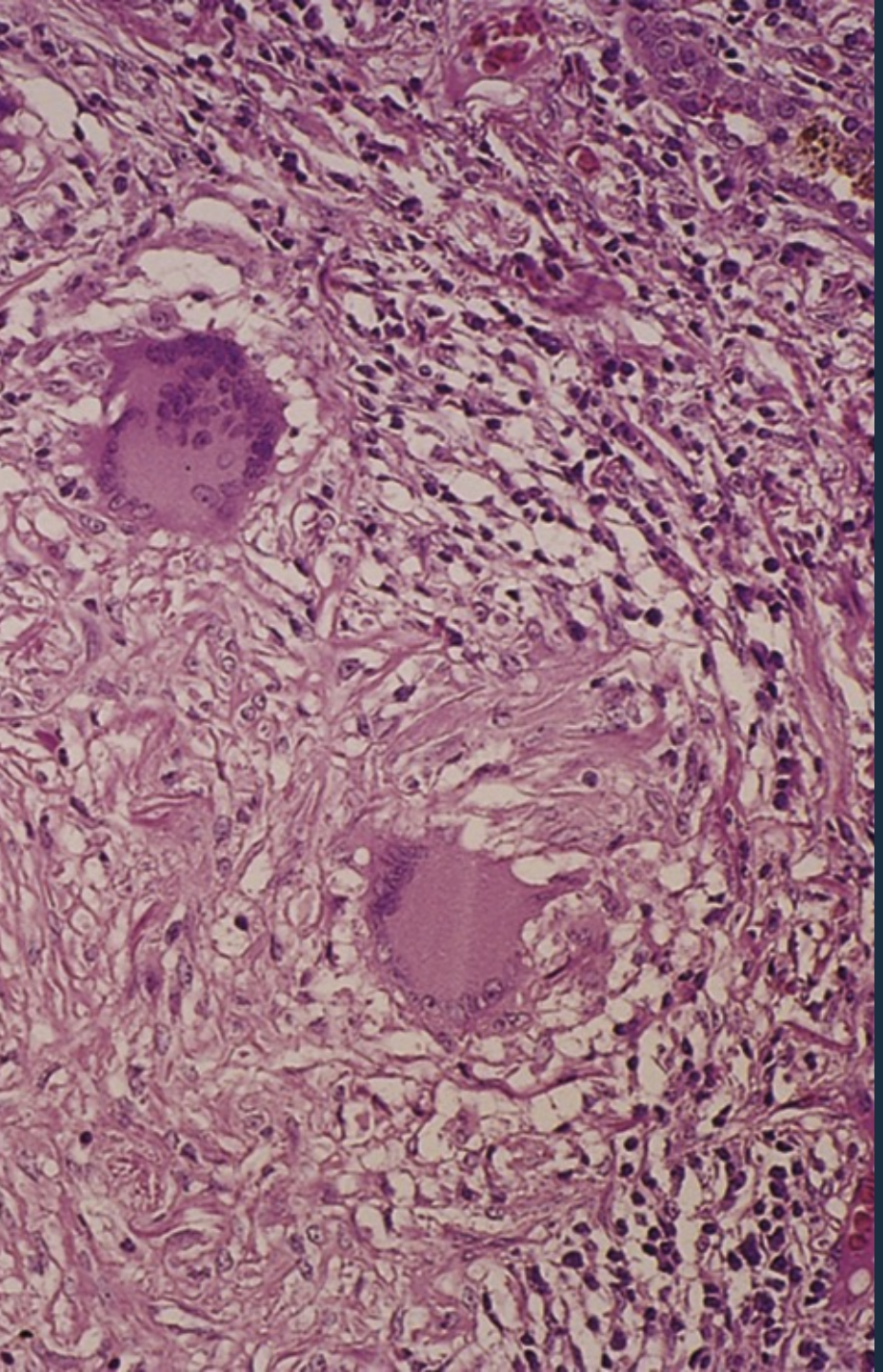
- Ultimately**, tubercle bacilli must be identified**:
  - The most common methodology for diagnosis of tuberculosis remains demonstration of acid-fast organisms in sputum by staining or by use of **fluorescent auramine rhodamine.**
  - **Conventional cultures (10 weeks),**
  - **liquid media–based radiometric assays (2 weeks).**
  - **PCR amplification** on liquid media with growth, as well as on tissue sections, to identify the mycobacterium.

culture remains the standard diagnostic modality

Prognosis :

- determined by :
  - the extent of the infection (localized versus widespread)
  - the immune status of the host
  - the antibiotic sensitivity of the organism

https://baytowncrimestoppers.com/baytowns-most-wanted/unsolved-crimes/



45-year-old lady has a routine health maintenance examination. On physical examination, there are no remarkable findings. Her body mass index is 22. She does not smoke. A tuberculin skin test is positive. A chest radiograph shows a solitary, 3-cm left upper lobe mass without calcifications. The mass is removed at thoracotomy by wedge resection. The microscopic appearance of this lesion is shown in the figure. Which of the following is the most likely diagnosis?

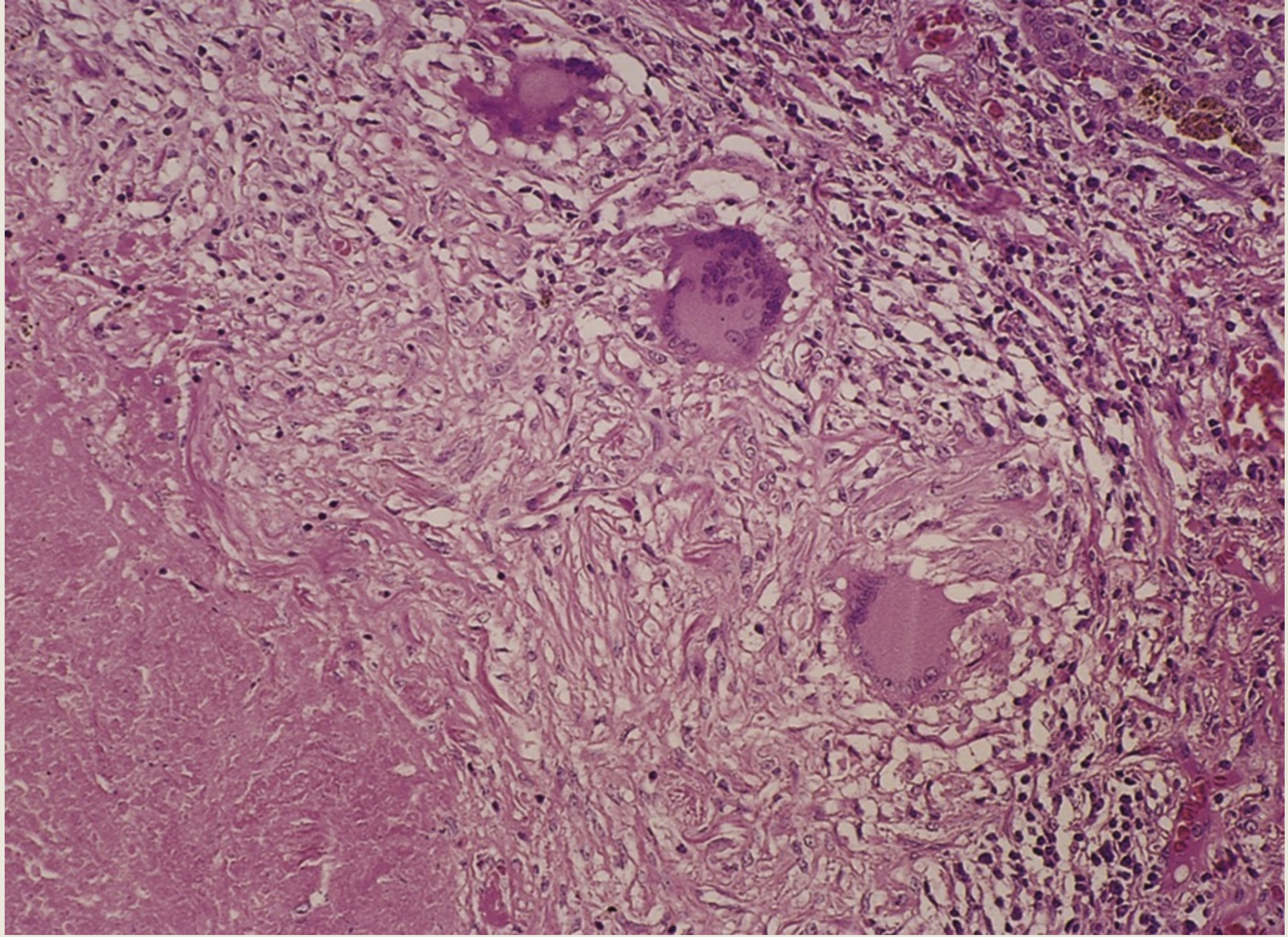
A Mycobacterium tuberculosis infection

B Necrotizing granulomatous vasculitis

C Poorly differentiated adenocarcinoma

D Staphylococcus aureus abscess

E Thromboembolism with infarction



https://exodusescaperoom.com/mysteries-and-solving-clues

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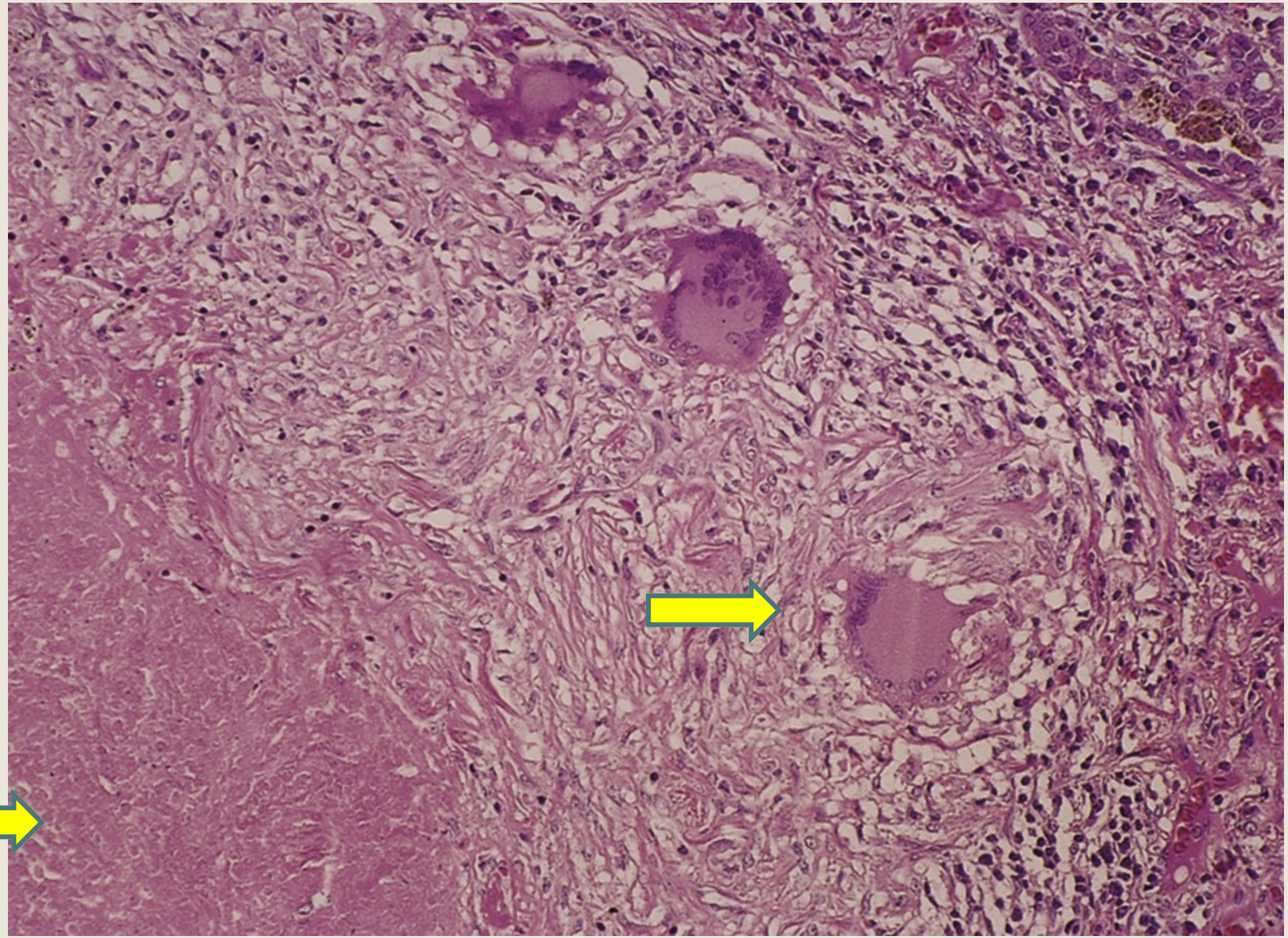

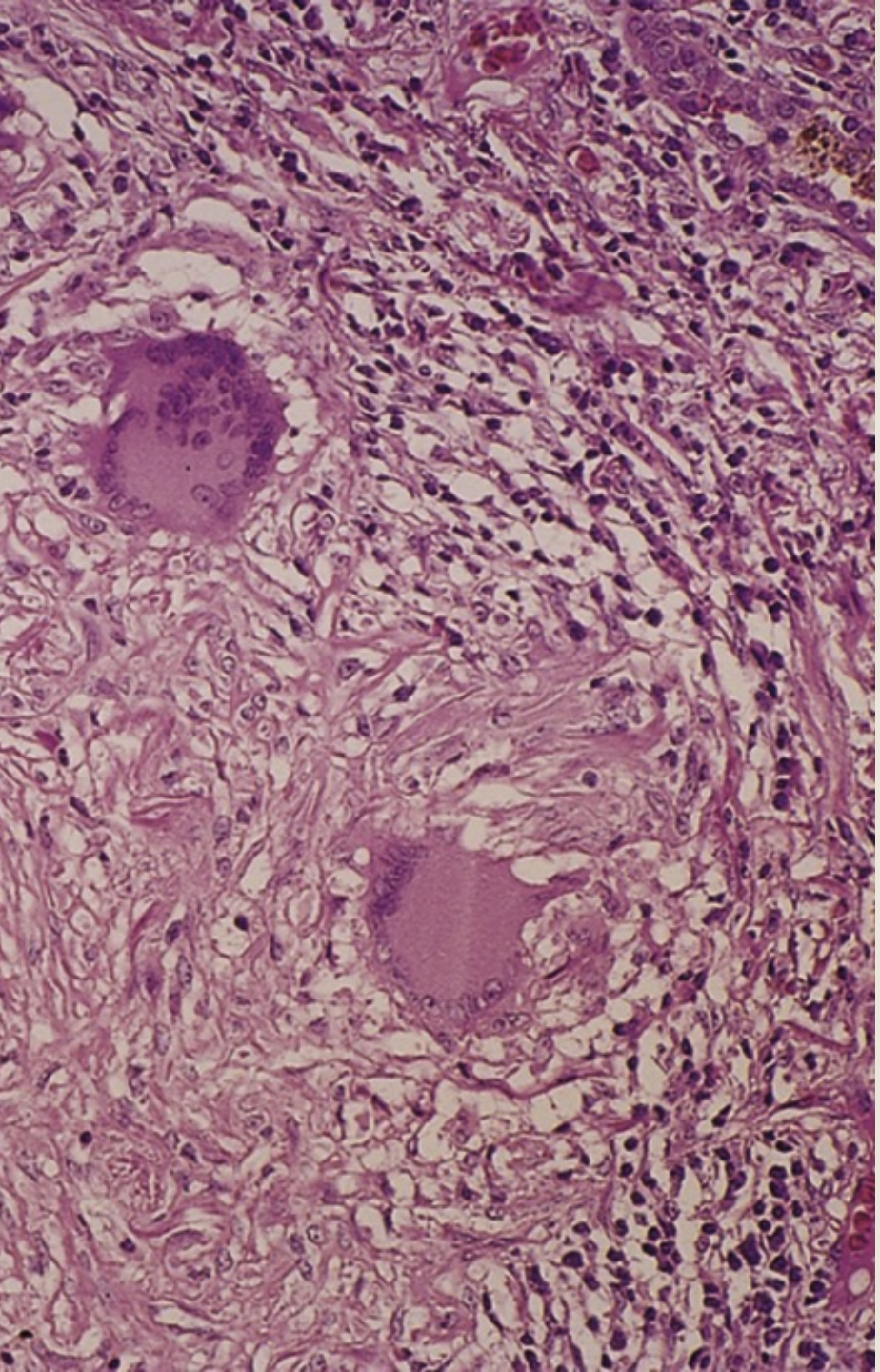

A 46-year-old woman has a routine health maintenance examination. On physical examination, there are no remarkable findings. Her body mass index is 22. She does not smoke. A tuberculin skin test is positive. A chest radiograph shows a solitary, 3-cm left upper lobe mass without calcifications. The mass is removed at thoracotomy by wedge resection. The microscopic appearance of this lesion is shown in the figure. Which of the following is the most likely diagnosis?

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https://www.pennlive.com/news/2019/03/cold-case-findings-generating-news-throughout-pa.html

FOR YOUR QUESTIONS:

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Or E-learning

THANK YOU!