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.

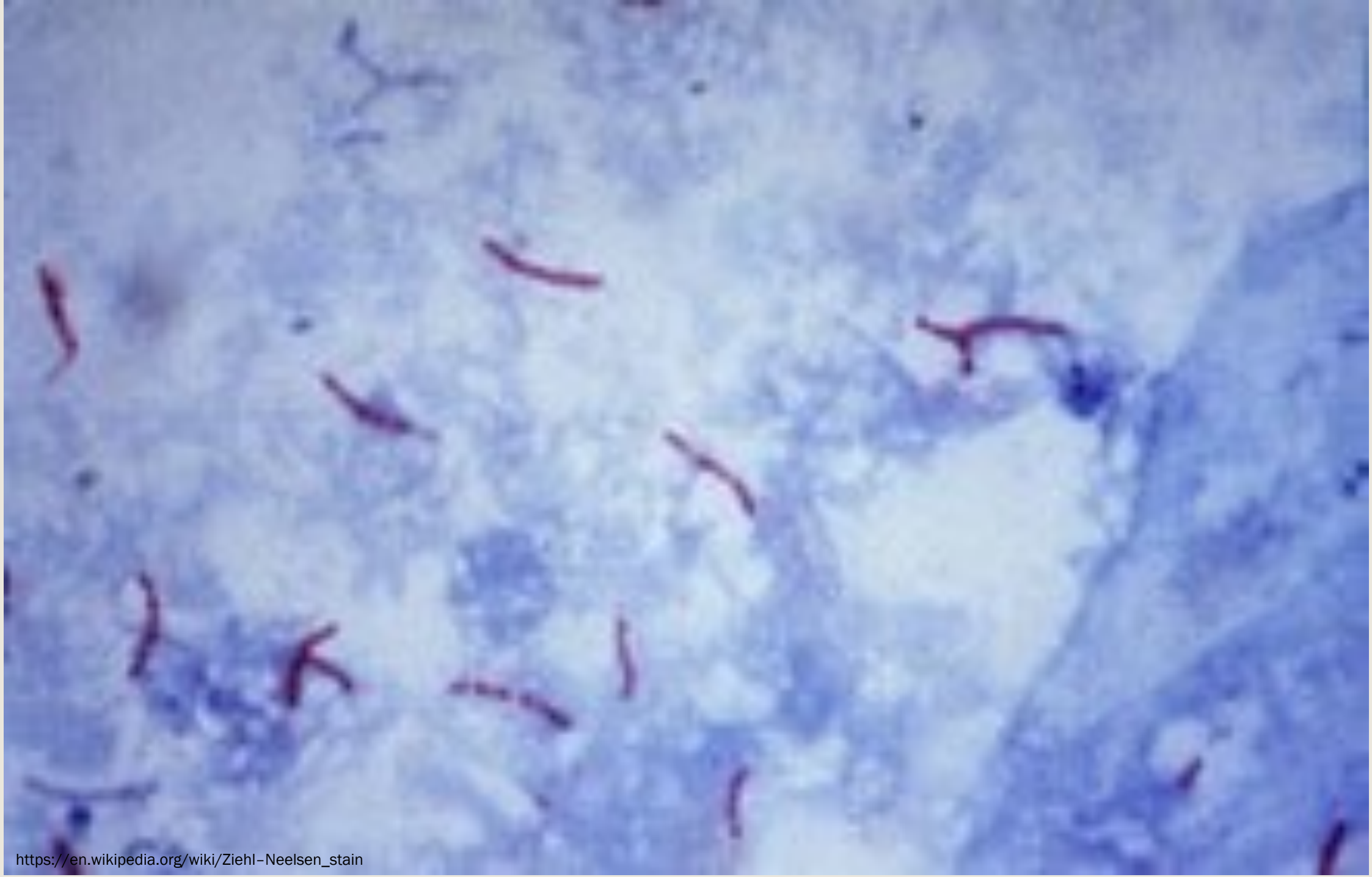
Risk Factors

Poverty, crowding, and chronic debilitating illness.

- **older** adults
- **Poor crowded communities** : Native Americans, African Americans, Hispanics, the Inuit (from Alaska), immigrants from Southeast Asia and members of minority communities
- **Chronic illnesses:** AIDS, diabetes mellitus, Hodgkin lymphoma, Chronic lung disease (silicosis), Malnutrition, Alcoholism, Immunosuppression, and chronic renal failure.

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

- Rare
- contracted by drinking contaminated milk
- Oropharyngeal and intestinal tuberculosis

Mycobacterium avium complex

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

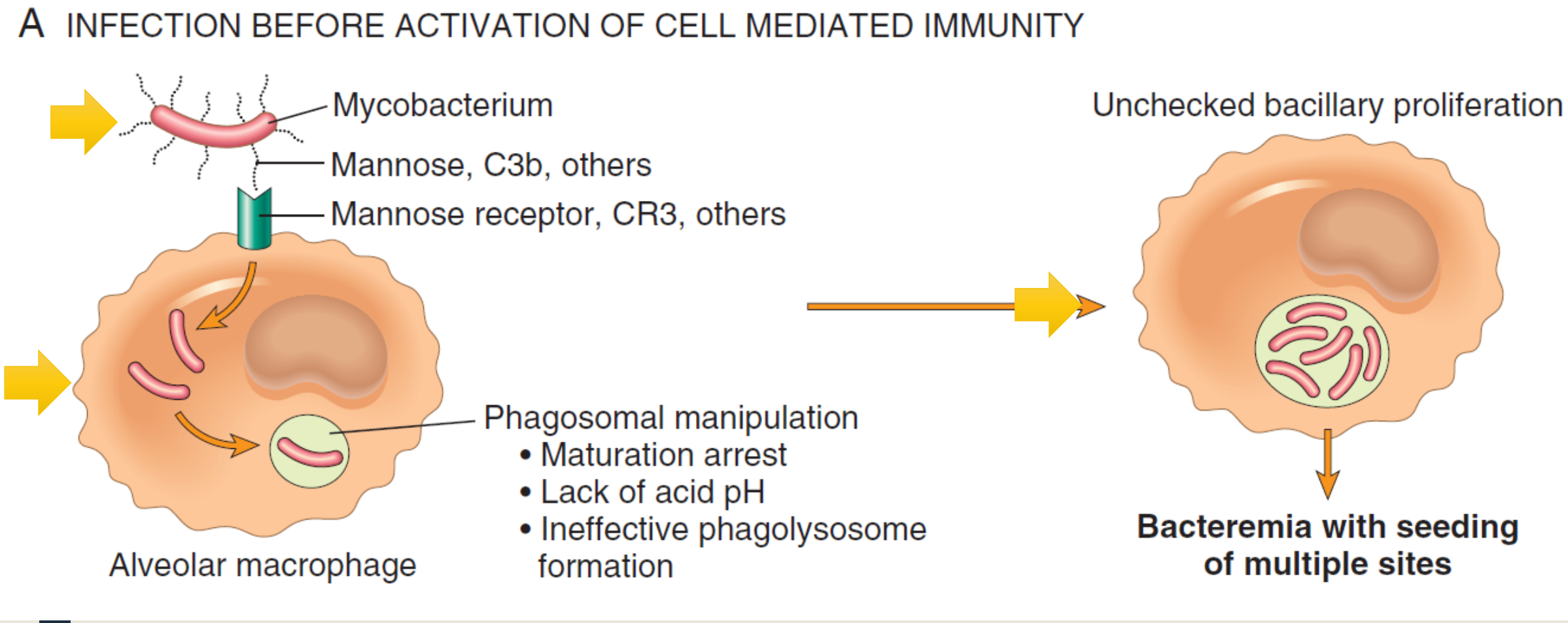
Infection vs. disease

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

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
    - immunity to the organism.

Natural history of primary pulmonary tuberculosis



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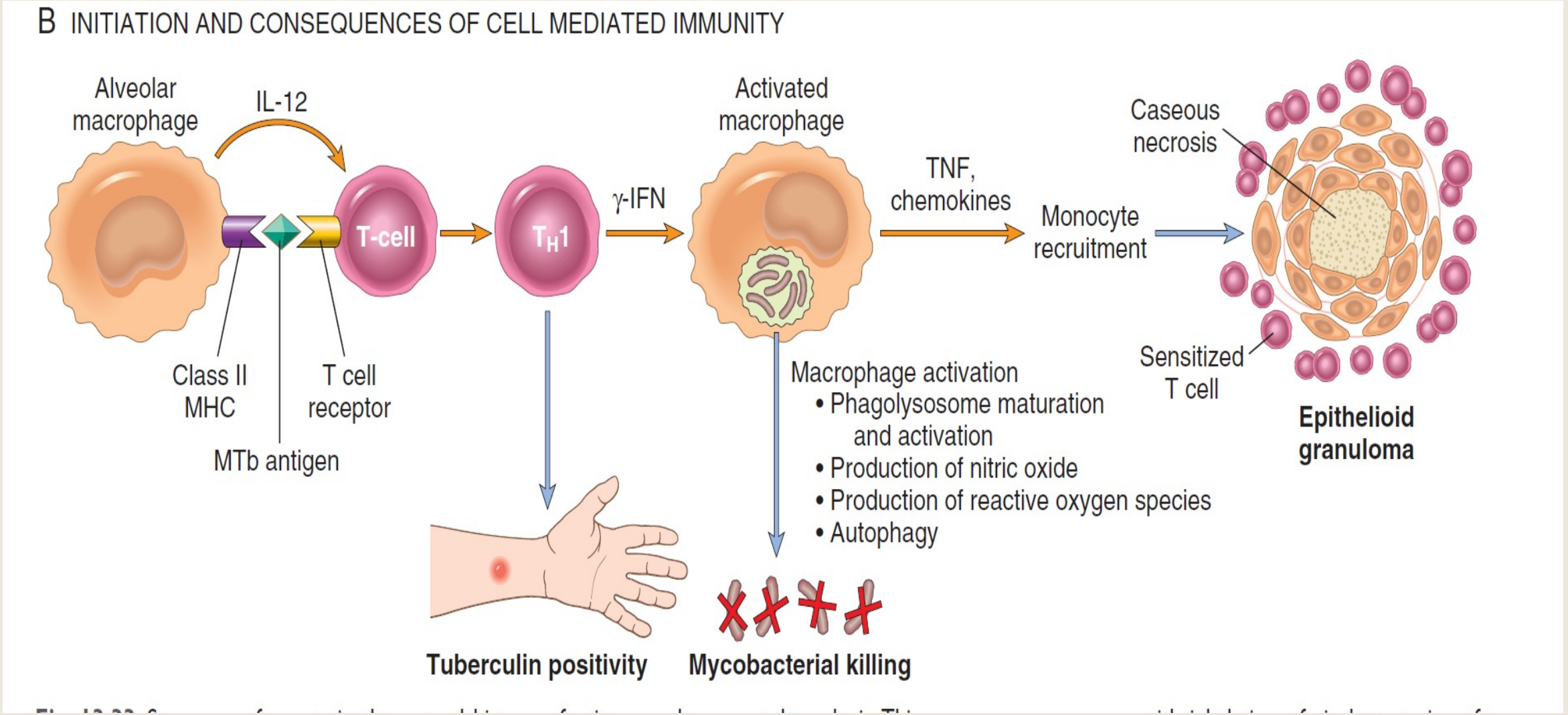
Natural history of primary pulmonary tuberculosis



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Summary:

- Immunity to a tubercular infection is primarily mediated by TH1 cells, which stimulate macrophages to kill mycobacteria.

- 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.

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.

Primary Tuberculosis

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

Primary Tuberculosis

- self-limited ،asymptomatic focus of pulmonary infection
  - *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, presentation:

- In otherwise healthy individuals:
  - Mostly the only consequence are the foci of **scarring**. Which may harbor **viable bacilli a**nd 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

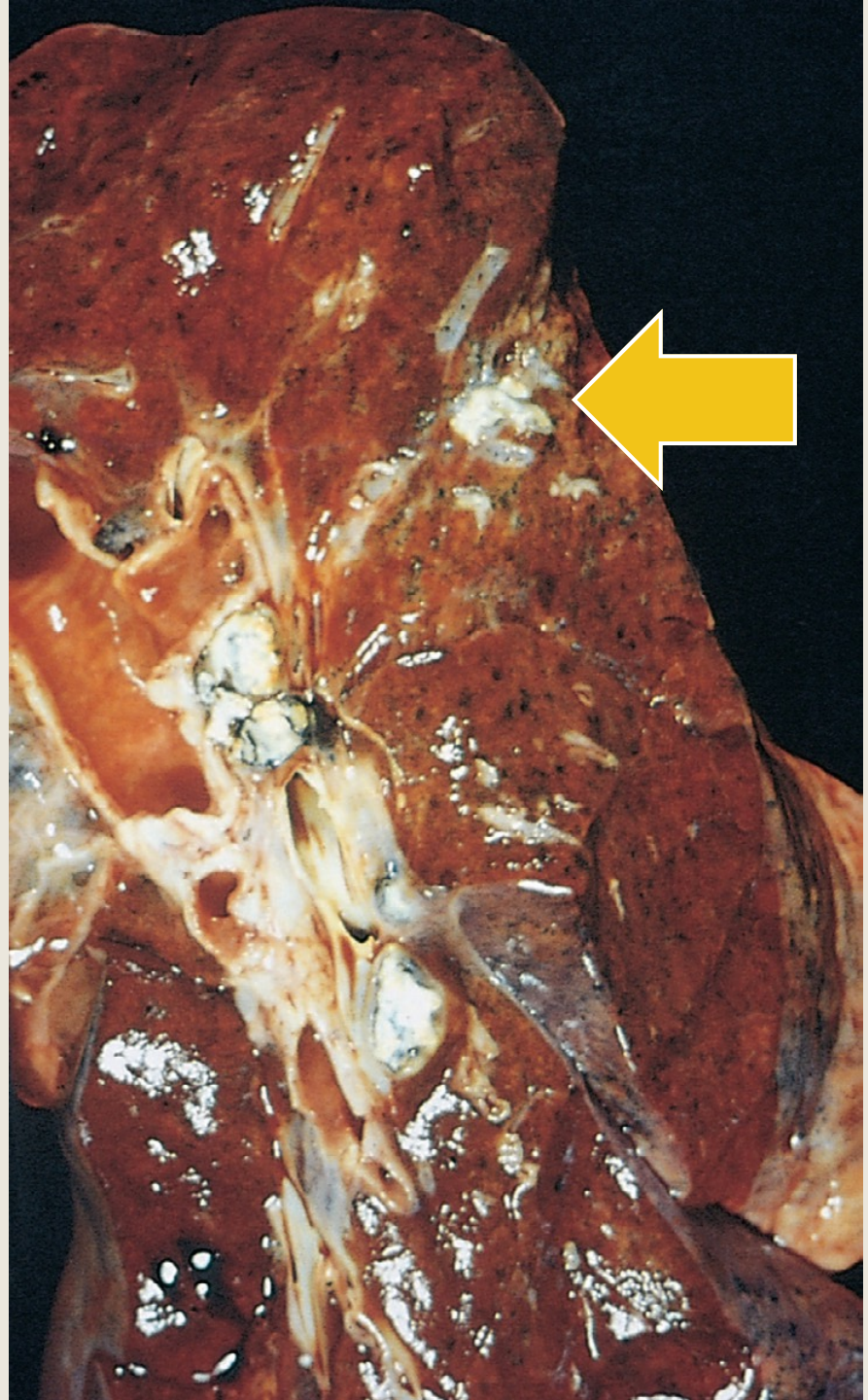
MORPHOLOGY

- 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- 1.5 cm area of gray-white inflammatory consolidation emerges during the development of sensitization
  - ✓ In majority of cases→ central caseous necrosis.



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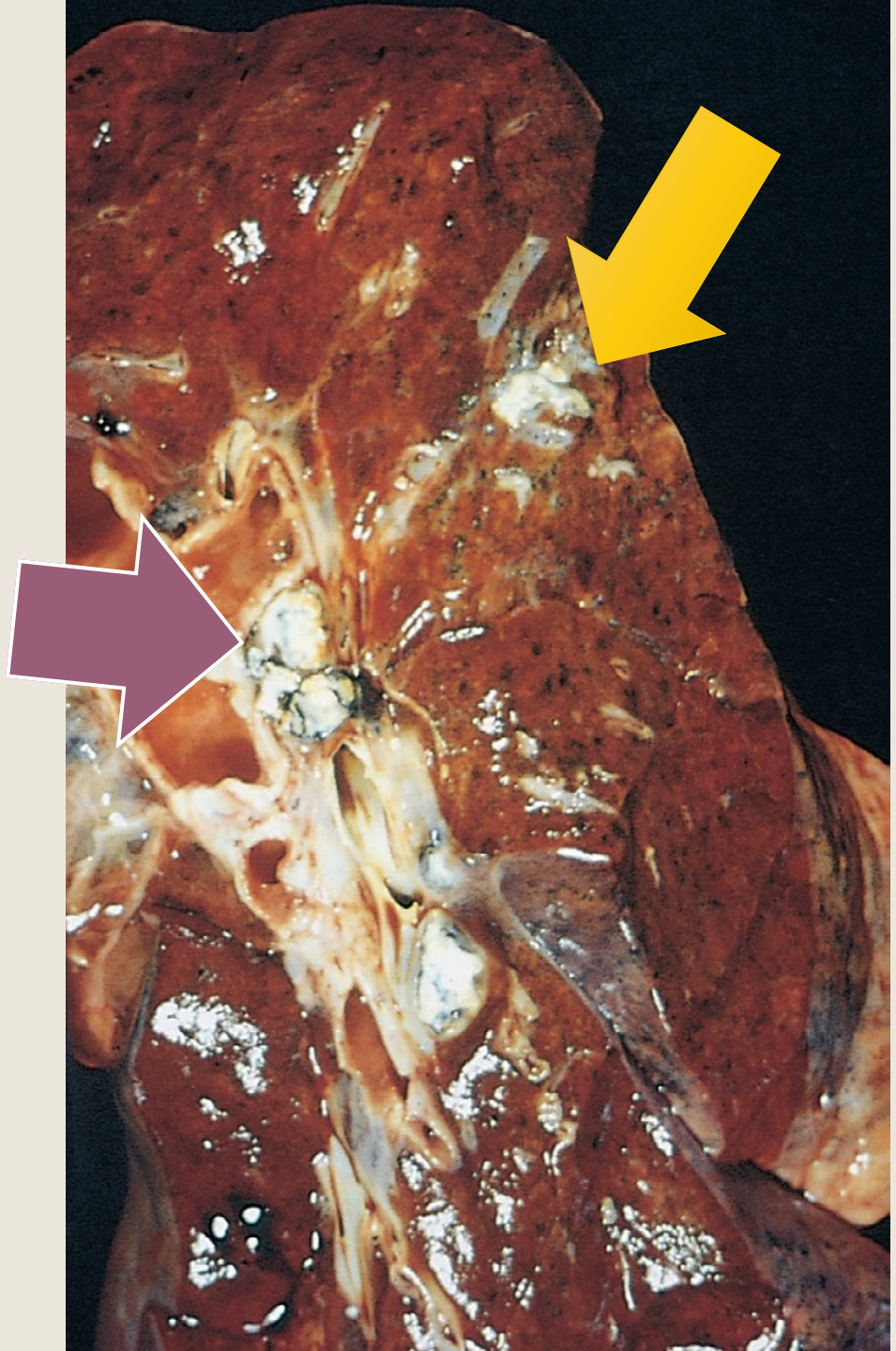
MORPHOLOGY, grossly:

- 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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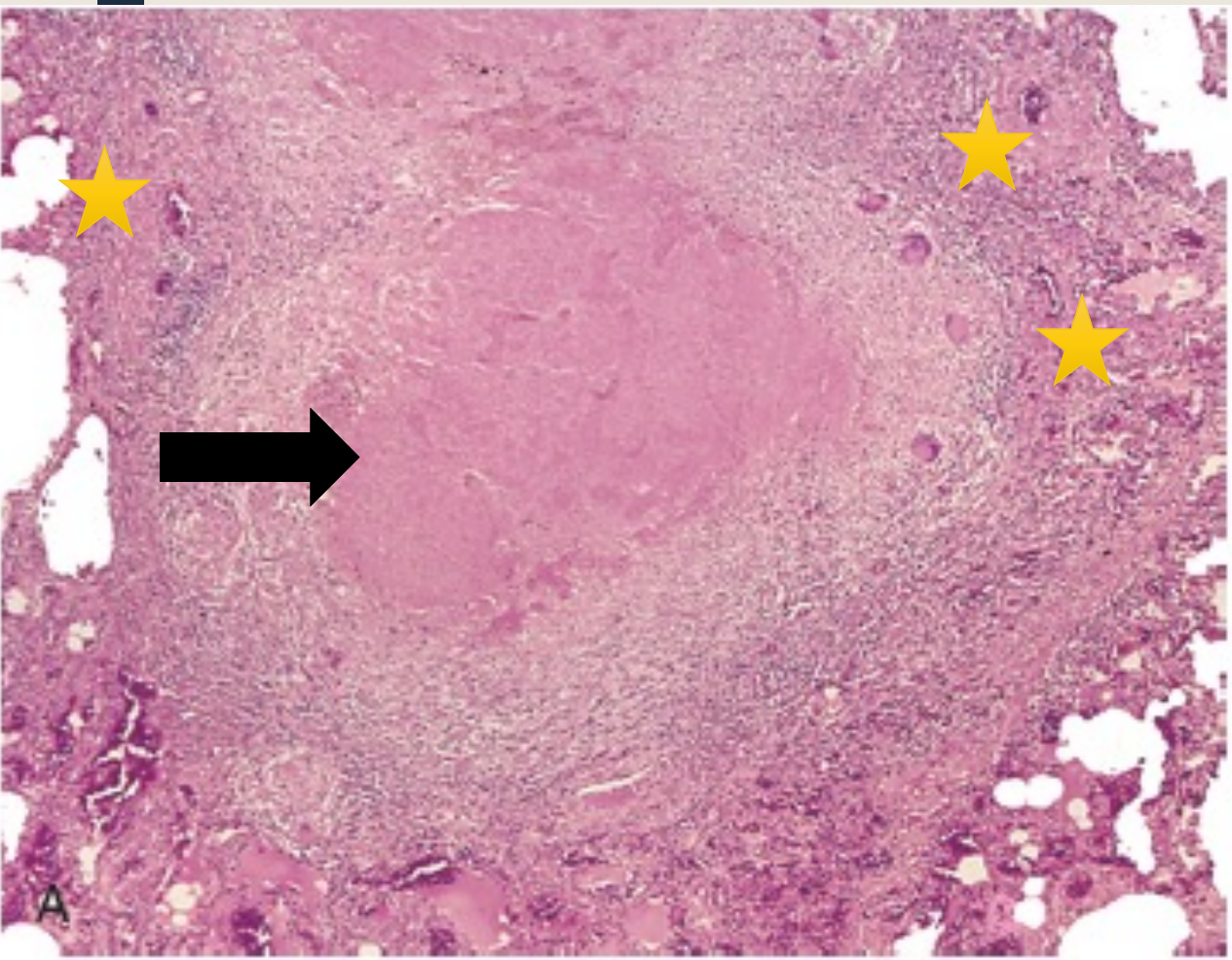
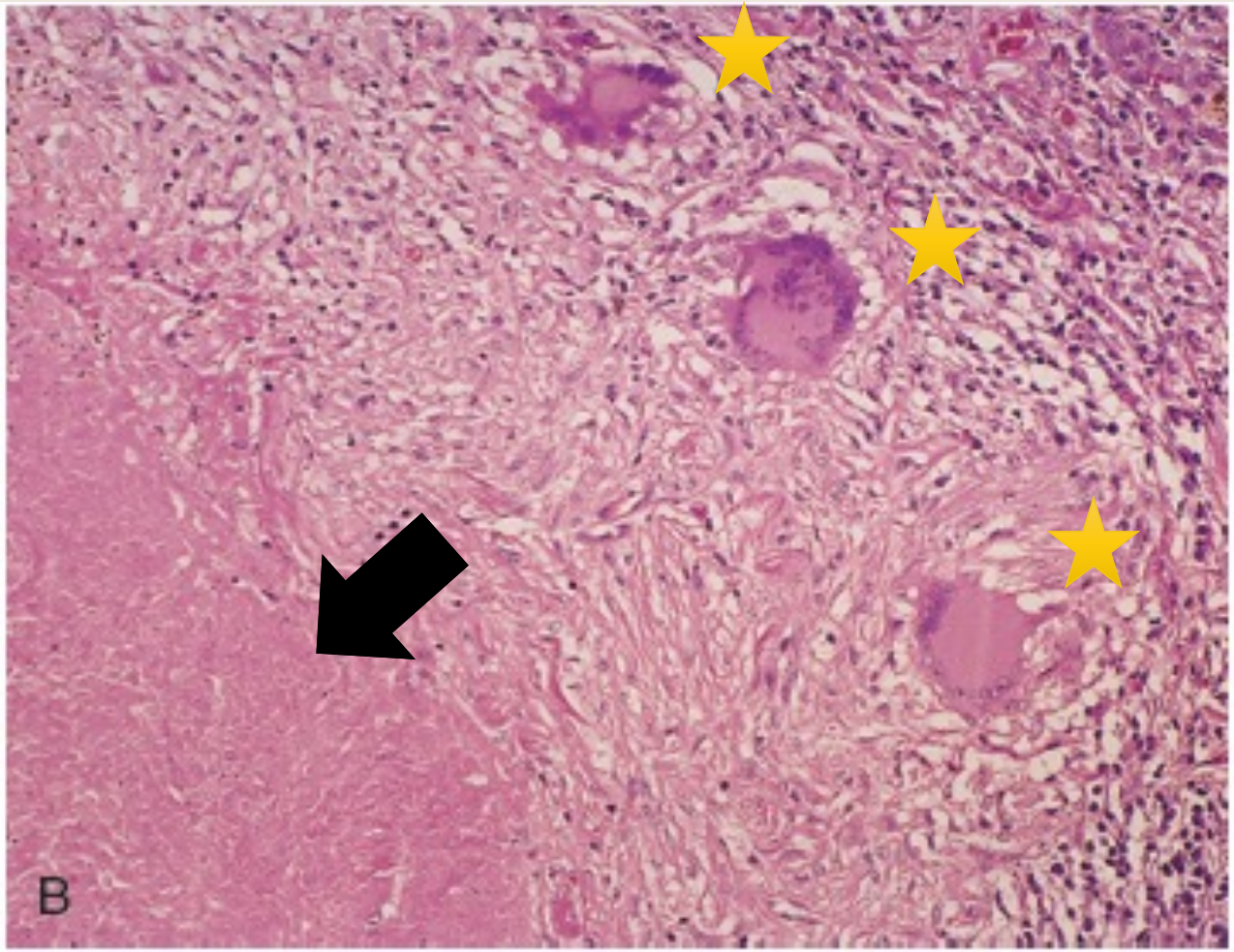
MORPHOLOGY, microscopic:





tubercle

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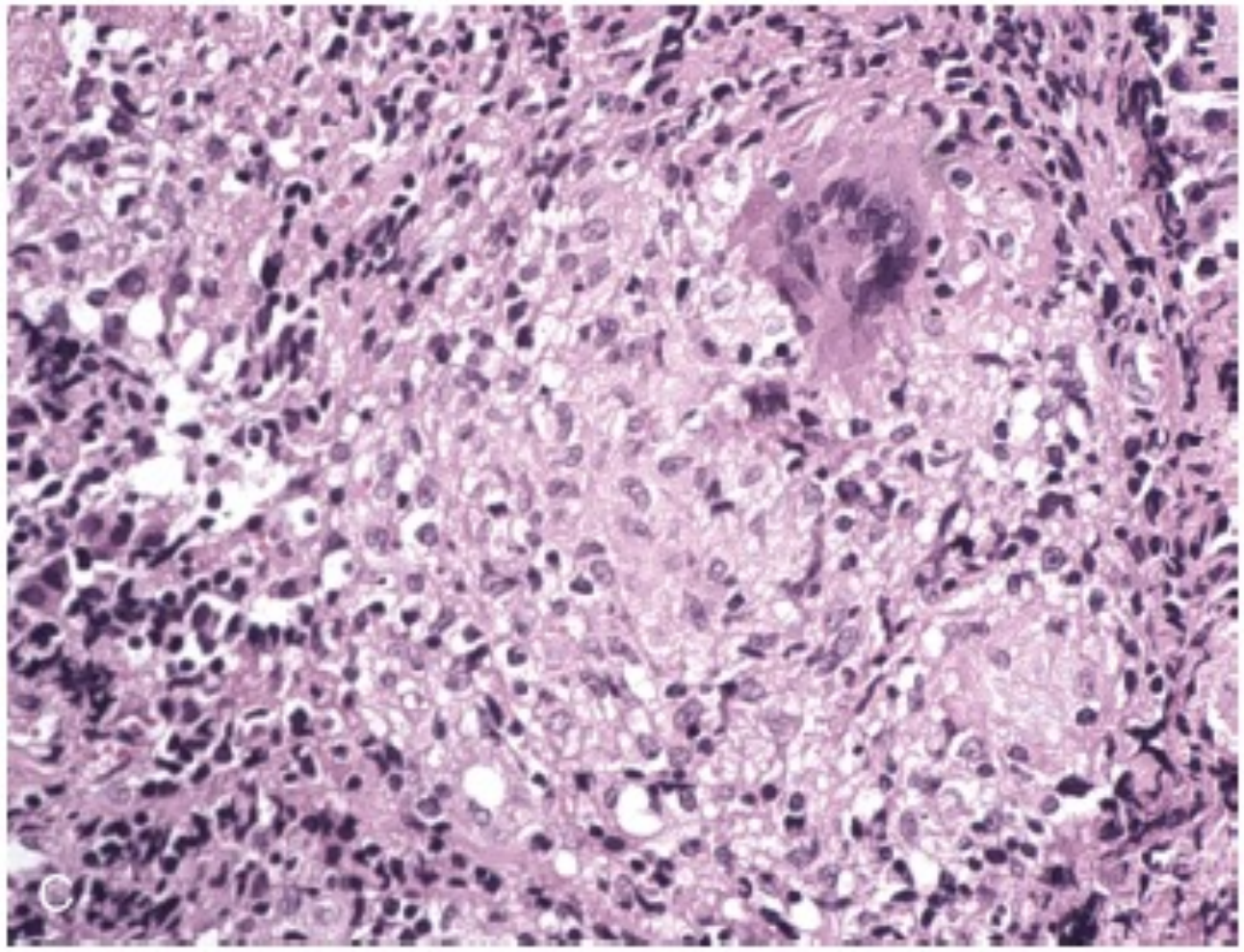

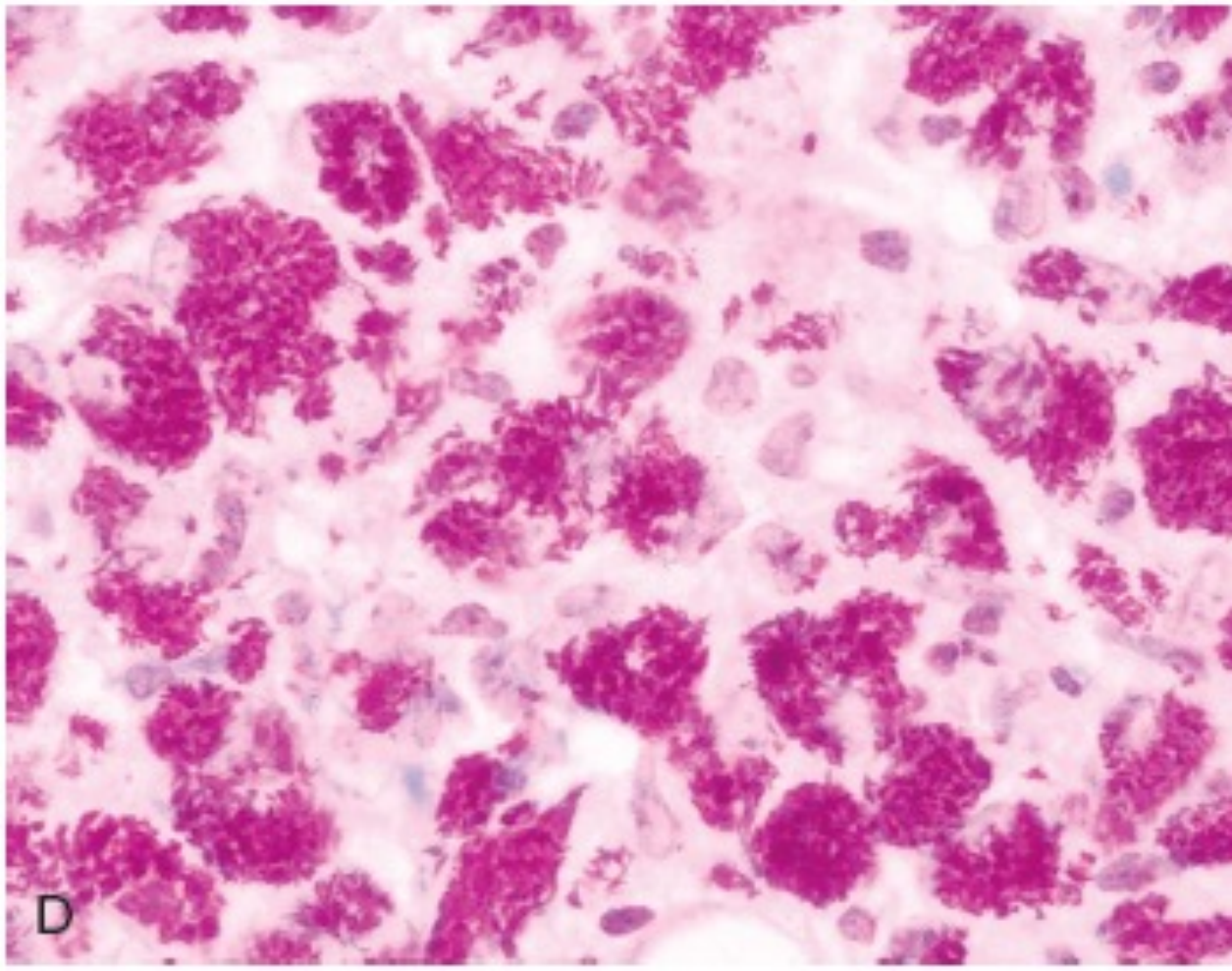

tubercular granulomas without central caseation

ZN stain→ sheets of macrophages packed with mycobacteria

irrespective of the presence or absence of caseous necrosis special stains for acid-fast organism

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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 induce a marked tissue response to wall off the focus (localization)
    - So regional lymph nodes are less involved early in the disease than they are in primary tuberculosis.
  - cavitation
  - erosion 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 near **apical pleura.**
- sharply circumscribed, firm, gray-white to yellow with variable amount of central caseation and peripheral fibrosis

MORPHOLOGY, microscopic:

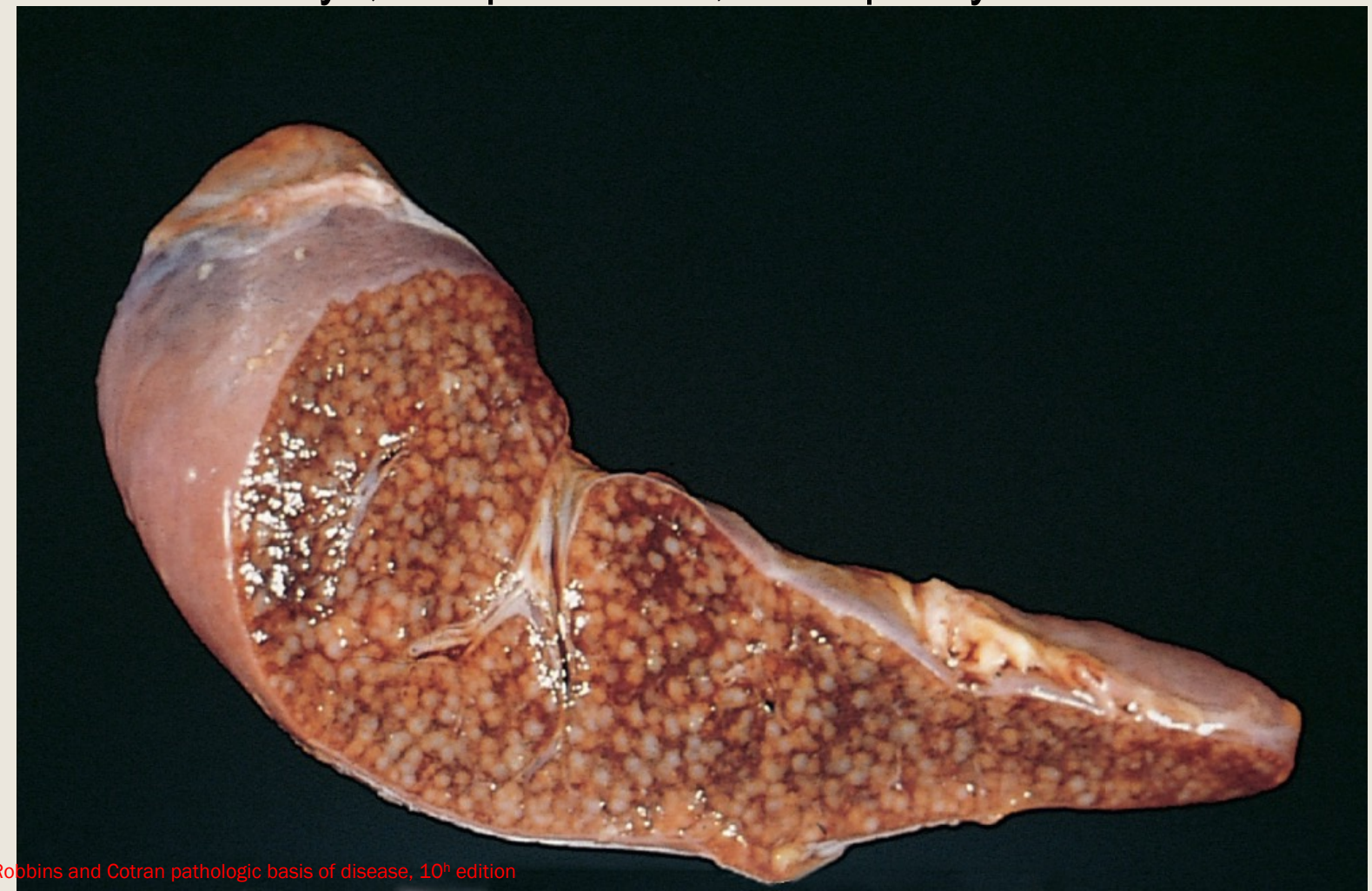
- **active lesions:** coalescent tubercles with central caseation.

- **tubercle bacilli:**
  - can be demonstrated by acid fast stain

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

- **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
  - miliary is derived from the resemblance of these foci to millet seeds.

- **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



Spleen: numerous gray-white granulomas

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Clinical Features

- **Asymptomatic,** especially in Localized secondary tuberculosis

- 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.

Clinical Features of secondary tuberculosis

- **Asymptomatic,** especially in Localized secondary tuberculosis
- **Systemic manifestations**:
  - related TNF and IL-1 released from activated macrophages
  - include malaise, anorexia, weight loss, and fever (low grade +/- 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: from extension of the infection to the pleural surfaces
  - **Extrapulmonary manifestations depend on the organ or system involved**

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**:
  - 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.

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

THANK YOU!