Tuberculosis

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Introduction

- **Tuberculosis is airborne infection caused by the mycobacterium tuberculosis**
- **Pulmonary Tuberculosis is one of the deadliest disease in the world**
- **Wordwide nearly 1billion people will be newly infected with tuberculosis**

Organism

- **Mycobacterium tuberculosis**
- **Slender, rod-shaped, aerobic bacteria that do not form spores.**
- **Similar to other bacterial organisms except for an outer waxy capsule that makes them more resistant to destruction.**

Organism cont…..

- **Organism can persist in old necrotic and calcified lesions and remain capable of reinitiating growth.**
- **The waxy coat also causes the organism to retain red dye when treated with acid in acid-fast staining**
- **Thus, the mycobacteria are often referred to as acid-fast bacilli.**

Organism cont…..

- **The tubercle bacilli are strict aerobes that thrive in an oxygen-rich environment.**

- **This explains their tendency to cause disease in the upper lobe or upper parts of the lower lobe of the lung, where the ventilation and oxygen content are greatest.**

Spread

- **Tuberculosis is an airborne infection spread by minute, invisible particles, called droplet nuclei, that are harbored in the respiratory secretions of persons with active tuberculosis.**
- **Coughing, sneezing, and talking all create respiratory droplets;**
- **These droplets evaporate, leaving the organisms (droplet nuclei), which remain suspended in the air and are circulated by air currents.**

Spread cont…

- **Living under crowded and confined conditions increases the risk for spread of the disease**

Pathogenesis

- **Inhaled droplet nuclei**
- **Deposit in alveoli**
- **Phagocytosed by alveolar macrophages**
- **But bacilli resist killing**
- **Initiate the cell mediated immunity**
- **Though bacilli multiply, macrophages degrade the bacilli and present the antigens to CD4+ T lymphocytes**
- **CD4+ T lymphocytes stimulate macrophages inturn increase the concentration of lytic enzymes and ability to kill bacilli**

Pathophysiology cont….

- **CD4+ T lymphocytes release IL2, INF gamma, recruit more macrophages and develop cell mediated delayed type hypersensitivity reaction**
- **These lytic enzymes also damage lung tissue**
- **In 2-3days macrophages undergo structural changes which resembles epithelial cells called epithelioid cells**
- **Epithelioid cells aggregate in to tight clusters called granulomas (called as Ghon focus)**
- **Single, gray-white, circumscribed granulomatous lesion, called as *Ghon's focus,* that contains the tubercle bacilli, modified macrophages, and other immune cells**

- **Release of cytokines in response to CD4+ T lymphocytes activation play a role in formation of granuloma**

- **Around the mass of epithelioid cells and a few giant cells (macrophages fuse together to form multinucleated giant cells), zone of lymphcytes, plasma cells, further surrounded by fibroblasts (hard granloma/tubercule)**

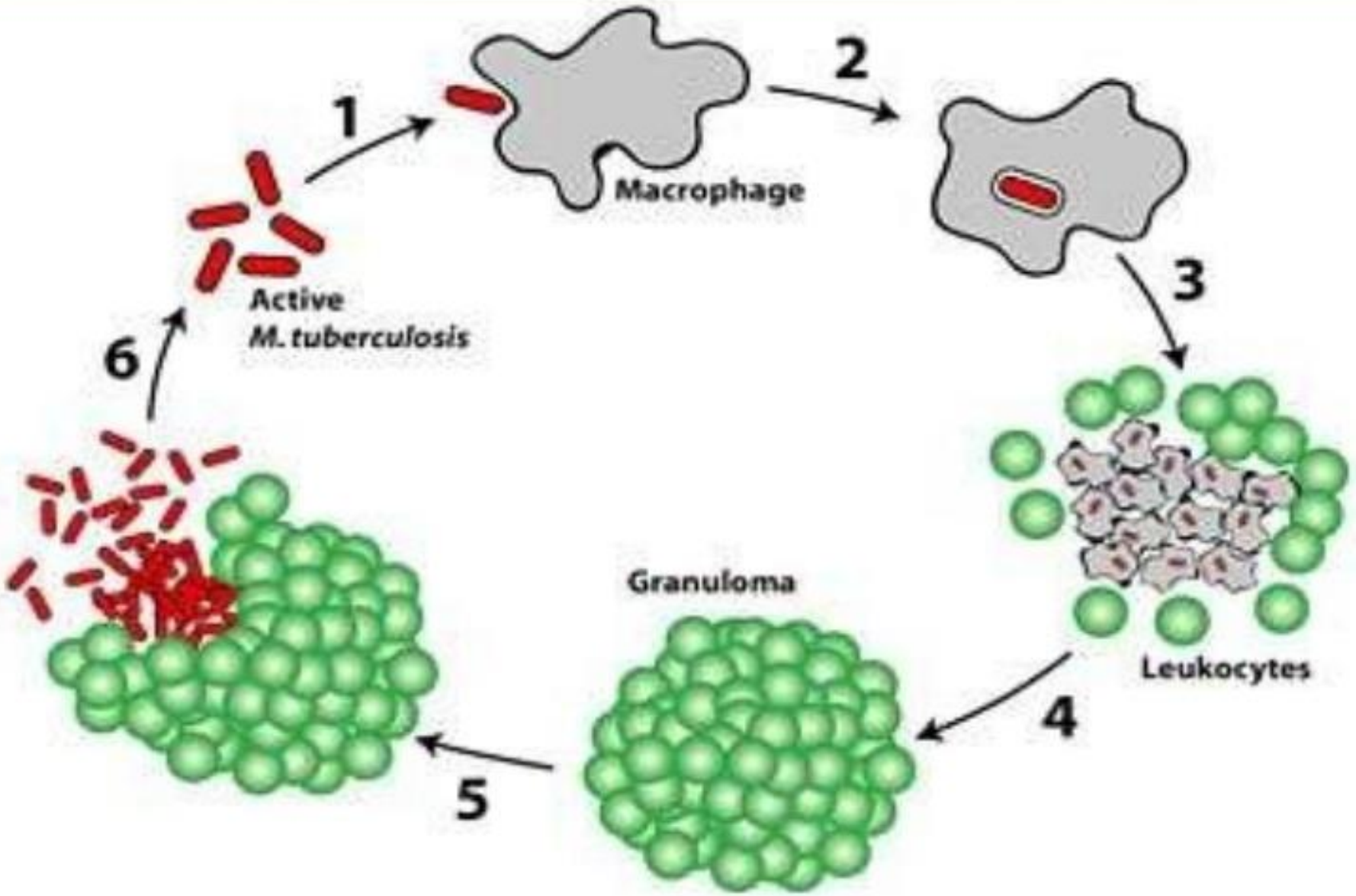
- **Within 10-14 days,the centre of cellular mass begin to undergo caseation necrosis, characterised by cheesy appearance and high lipid content**

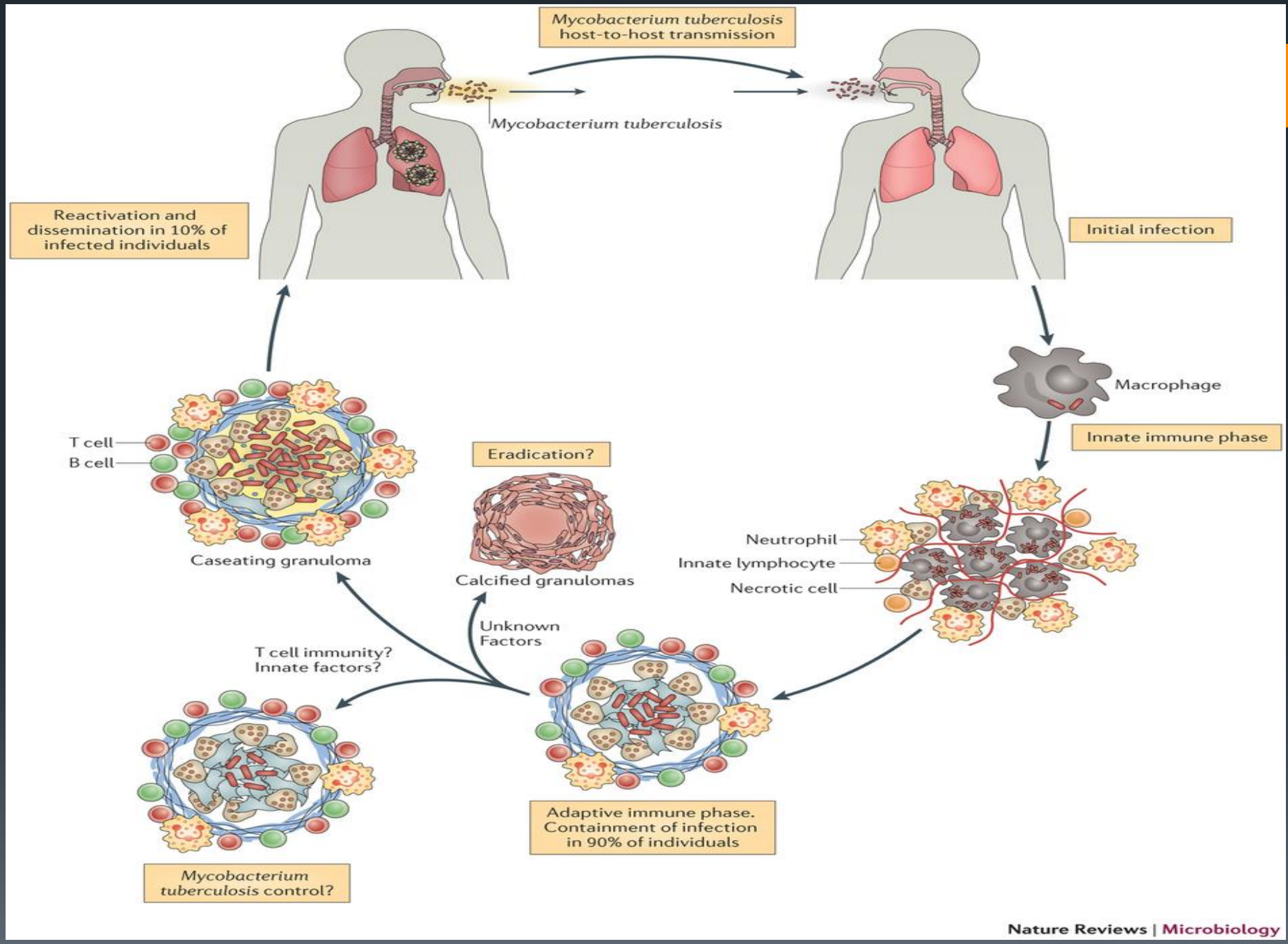
- **This is soft tubercle/granuloma**

- **This caseationis due to**
  - **IFN-gamma released by CD4+**
  - **By Direct CD8+**
  - **Toxicity of mycobacteria on macrophages**

- **Soft tubercle is fully developed granuloma with caseous centre does not allow bacilli to grow**

Pathogenesis of M. tuberculosis




Mycobacterium tuberculosis host-to-host transmission
Mycobacterium tuberculosis
Reactivation and dissemination in 10% of infected individuals
Initial infection
Macrophage
Innate immune phase
T cell
B cell
Caseating granuloma
Eradication?
Calcified granulomas
Neutrophil
Innate lymphocyte
Necrotic cell
Unknown Factors
T cell immunity? Innate factors?
Adaptive immune phase. Containment of infection in 90% of individuals
Mycobacterium tuberculosis control?
Nature Reviews | Microbiology

Fate of granuloma

- **Caseous material may undergo liquification and extend to surrounding tissue, discharge the contents on surface called cold absecss**

- **Free or inside macrophages, drain along the lymph channels to the tracheobronchial lymph nodes of the affected lung and there evoke the formation of caseous granulomas.**

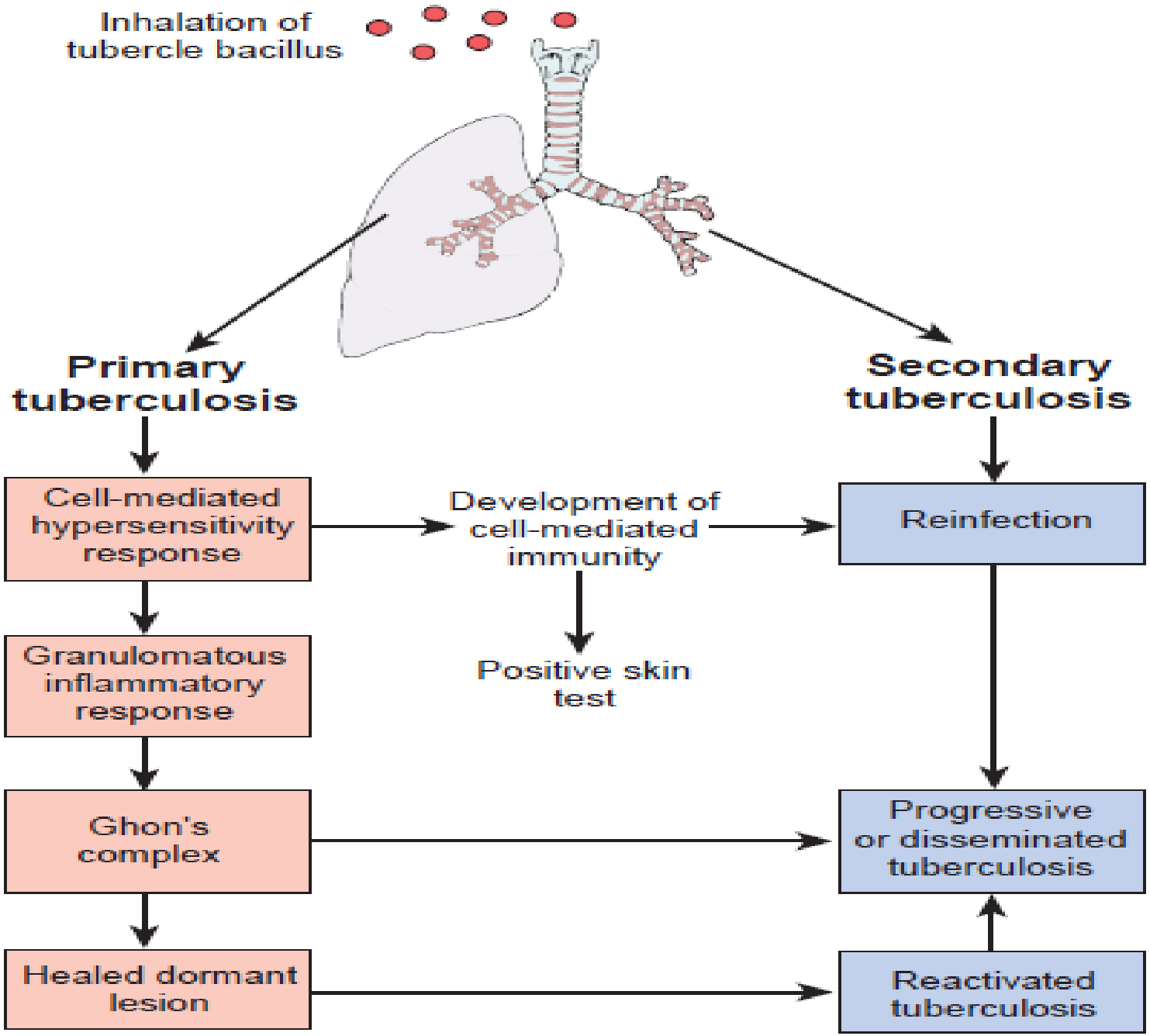
- **The combination of the primary lung lesion and lymph node granulomas is called Ghon's complex**

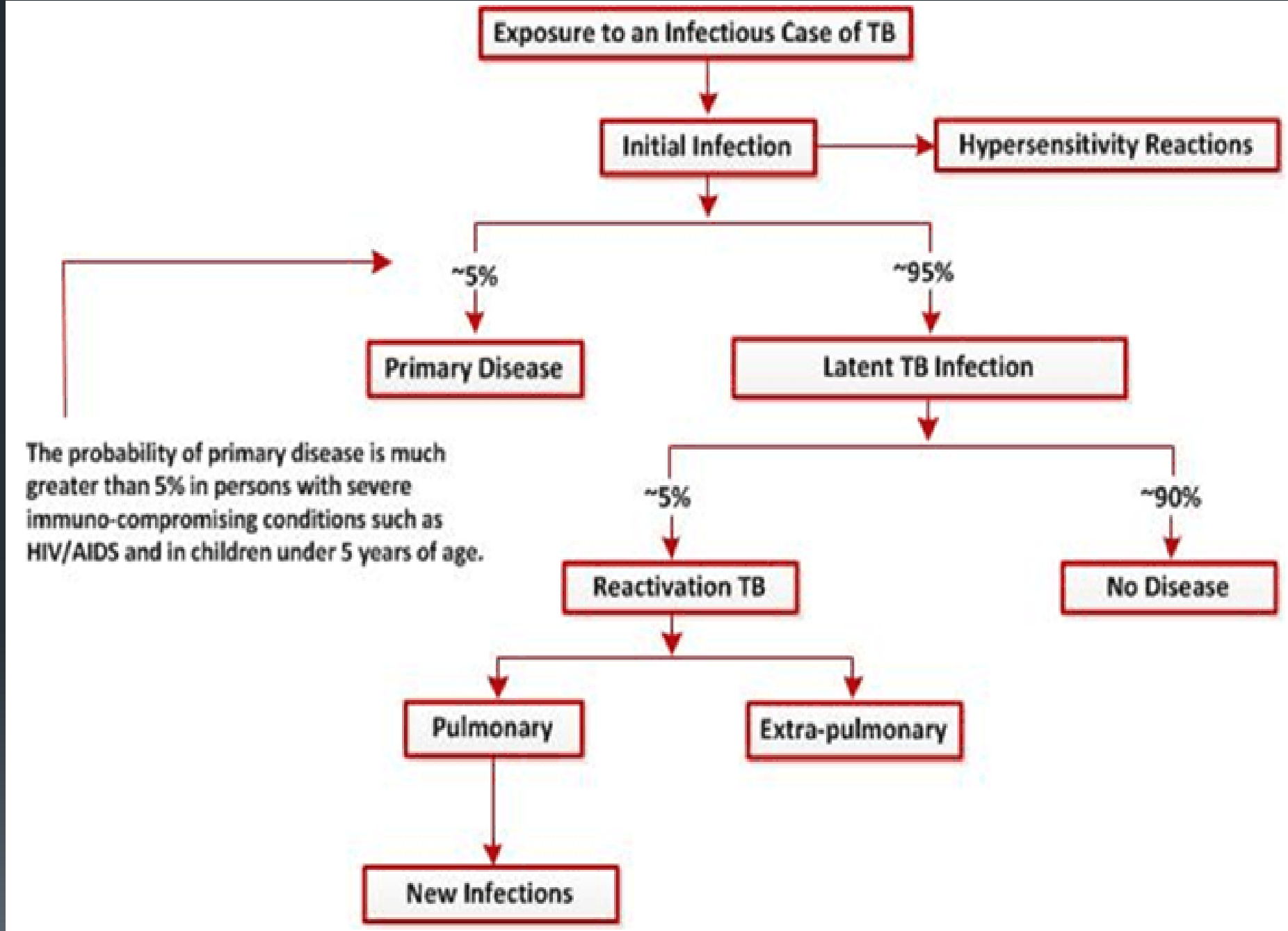
- **Ghon's complex eventually heals, undergoing shrinkage, fibrous scarring, and calcification.**

- **Small number of organisms may remain viable for years**
- **Later, if immune mechanisms decline or fail, latent tuberculosis infection has potential to develop in to secondary tuberculosis.**

Types

- **Primary**
- **secondary**


Inhalation of tubercle bacillus
Primary tuberculosis
Secondary tuberculosis
Cell-mediated hypersensitivity response
Development of cell-mediated immunity
Reinfection
Granulomatous inflammatory response
Positive skin test
Ghon's complex
Progressive or disseminated tuberculosis
Healed dormant lesion
Reactivated tuberculosis


Exposure to an Infectious Case of TB
Initial Infection
Hypersensitivity Reactions
~5%
~95%
Primary Disease
Latent TB Infection
The probability of primary disease is much greater than 5% in persons with severe immuno-compromising conditions such as HIV/AIDS and in children under 5 years of age.
~5%
~90%
Reactivation TB
No Disease
Pulmonary
Extra-pulmonary
New Infections

Primary TB

- **Primary tuberculosis is a form of disease that develops in a previously unexposed & unsensitized persons**
- **Most people with primary tuberculosis are asymptomatic and go on to develop latent tuberculosis infection**
- **Latent tuberculosis do not have active disease and cannot transmit the organism to others.**
- **Approx 5% of newly infected people develop to progressive Primary TB with pulmonary tissue damage especially in young children, hiv patients, immunodeficiency diseases.**

Symptoms of primary progressive TB

- **FEVER**
- **WEIGHT LOSS**
- **FATIGUE**
- **NIGHT SWEATS**
- **PLEURITIS**
- **LYMPHADENITIS**

Secondary Tuberculosis:

- **It arises in a previously sensitised host**
- **Reactivation may be due to exogenous re-infection or**
- **endogenous**
- **5% of the persons with primary tuberculosis get secondary tuberculosis**
- **Secondary tuberculosis is classically localized to the apex of one or both upper lobes**
- **Secondary tuberculosis is always be an important consideration in HIV positive patients**

Symptoms of Secondary TB

- **PLEURAL EFFUSION**
- **TUBERCULOUS EMPYEMA**
- **LOW GRADE FEVER**
- **NIGHT SWEATS**
- **FATIGABILITY**
- **ANOREXIA**
- **WEIGHT LOSS**
- **PRODUCTIVE COUGH (Sometimes Blood Tinged Sputum)**

Miliary/Disseminated TB

- **In rare cases TB may erode in to blood vessels, giving rise to hematogenic dissemination**

- **Dissemination involve any organ, particularly the brain, meninges, liver, kidney and bone marrow.**