TUBERCULOSIS

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Tuberculosis(TB)

Objective of lecture

Definition of tuberculosis-1

. Causative agent -2

Predisposing conditions are related to tuberculosis-3

Classification of tuberculosis-4

Pathogensis of tuberculosis-5

Morphological features and diagnostic criteria of-6 tuberculosis

PBL-3

A 22-year-old man with AIDS (acquired immune deficiency syndrome) complains of persistent cough, night sweats, low-grade fever, and general malaise. A chest X-ray reveals an area of consolidation in the lower part of the left upper lobe and L.N enlargement . Sputum cultures show acid-fast bacilli.

Tuberculosis(TB)

Tuberculosis is an infectious disease that usually affects the lungs and by far the most important of the chronic specific pneumonia .

Tuberculosis is "a communicable chronic granulomatous disease caused by Mycobacterium tuberculosis". It usually involves the lungs but may affect any organ or tissue.

Globally, it is the leading cause of deaths resulting from a single infectious disease .

Tuberculosis thrives wherever there is poverty, crowding, , chronic debilitating illness, elderly, infant and children with their weakened defenses, are also susceptible.

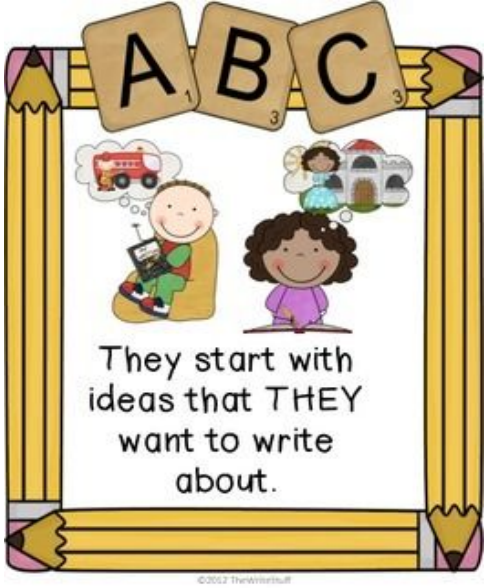
Certain disease states also increase the risk:

1. **Diabetes mellitus**
2. **Hodgkin lymphoma**
3. **Chronic lung disease (particularly silicosis)**
4. **Chronic renal failure**
5. **Malnutrition & Alcoholism**
6. **Immunosuppression including HIV infection.**

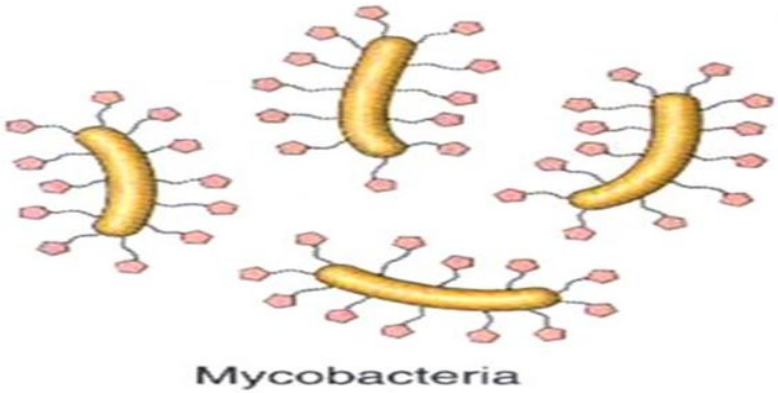
***Most of these predisposing conditions are related to impairment of T cell-mediated immunity against the Mycobacteria.**

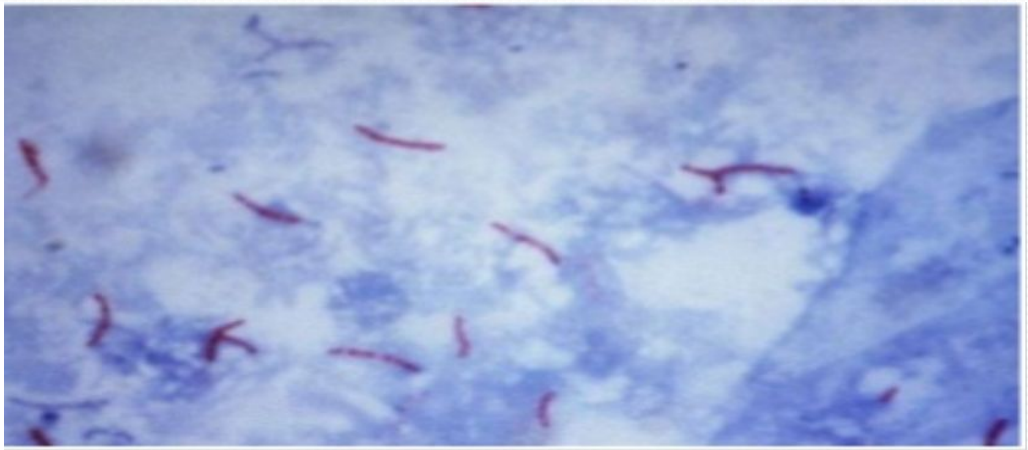
What are Mycobacteria?

- Obligate **aerobes** growing most successfully in tissues with a high oxygen content, such as the lungs.
- Facultative **intracellular pathogens** usually infecting **mononuclear phagocytes** (e.g. macrophages).

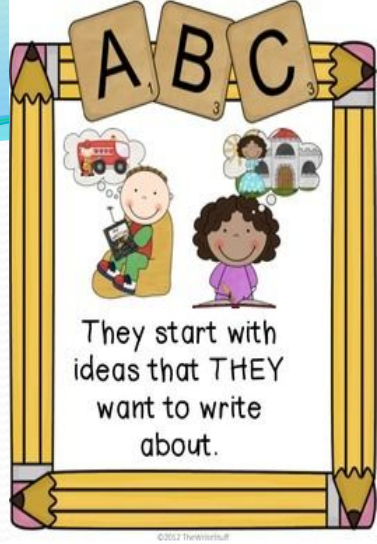


***Mycobacteria TB are slender rods that are acid fast, thus stained positively (red rods in back-ground blue) with Ziehl -Neelson stain(ZN stain) .**


Mycobacteria

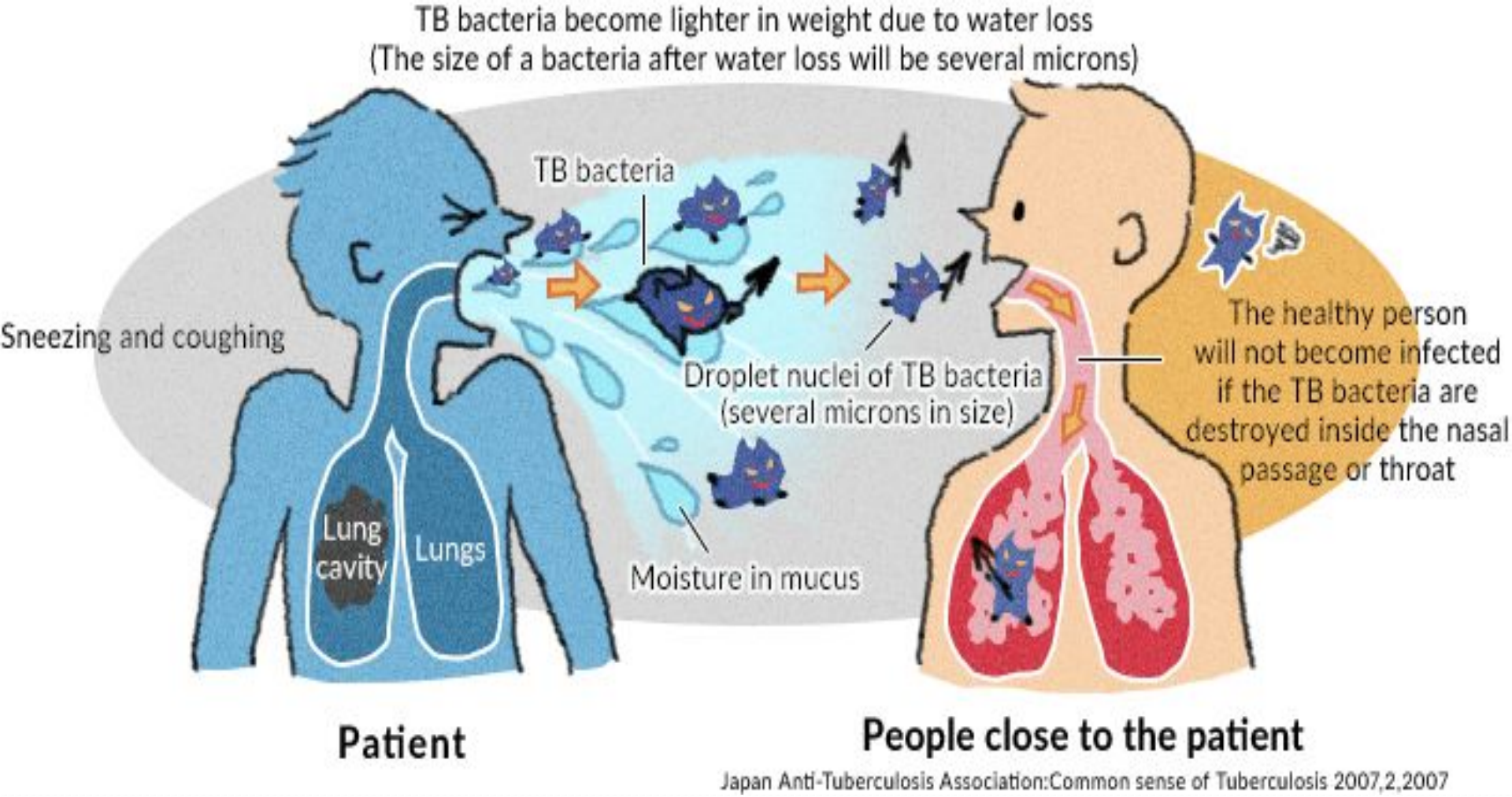


Acid fast organisms like mycobacterium contain large amounts of lipid substances within their cell walls called mycolic acids and because of waxy hard wall of mycobacteria TB ,these resist staining by ordinary methods such as a gram stain .



Mechanisms of Infection

- Mycobacterium do not produce toxins.
- Allergy and Immunity plays the major role.
- Only 1/10 of the infected will get disease.
- Cell Mediated Immunity plays a crucial role.
- Humoral Immunity – not Important.
- CD_4 Cell plays role in Immune Mechanisms.



In patient with (active T.B) , mycobacterium is spread from person to person through the air. The dots in the air represent droplet nuclei containing tubercle bacilli.

TB can classify in to :-

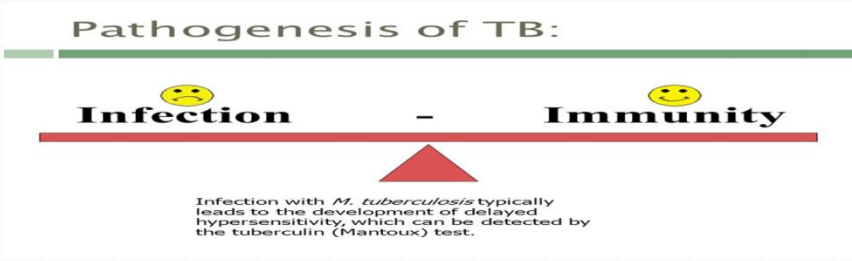
1-primary TB

2- secondary TB

Primary TB

Inhaled bacilli , in the patient previously not infected and the source of the organism is exogenous .

Pathogenesis of primary TB



After inhaled bacilli ,the virulent organisms once inside macrophages will impair effective phago-lysosomal digestion of macrophages by blocking fusion of the phagosome and lysosome inside macrophages , which in turn leads to unrestricted mycobacterial proliferation inside phagosome .

Thus, the earliest phase of primary tuberculosis (less than 3wk) in the non-sensitized person is characterized by bacillary proliferation within alveolar macrophages and air spaces .

Nevertheless, most persons at this stage are asymptomatic

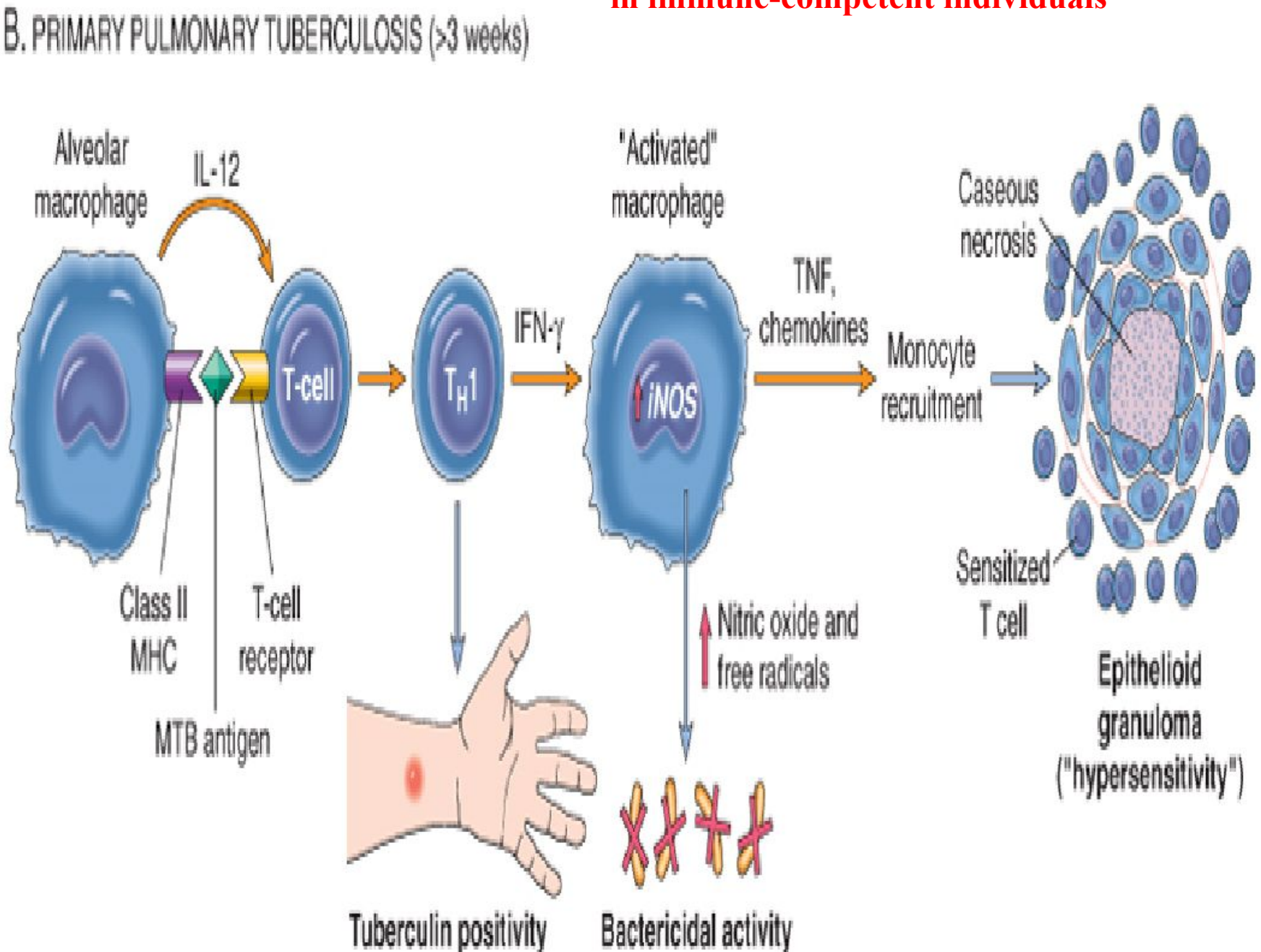
After bacillary proliferation within alveolar macrophages , the alveolar macrophages will stimulate the immuno-system .

The possibility after bacilli proliferation (after 3wk):-

A-If immuno-competent individuals:-

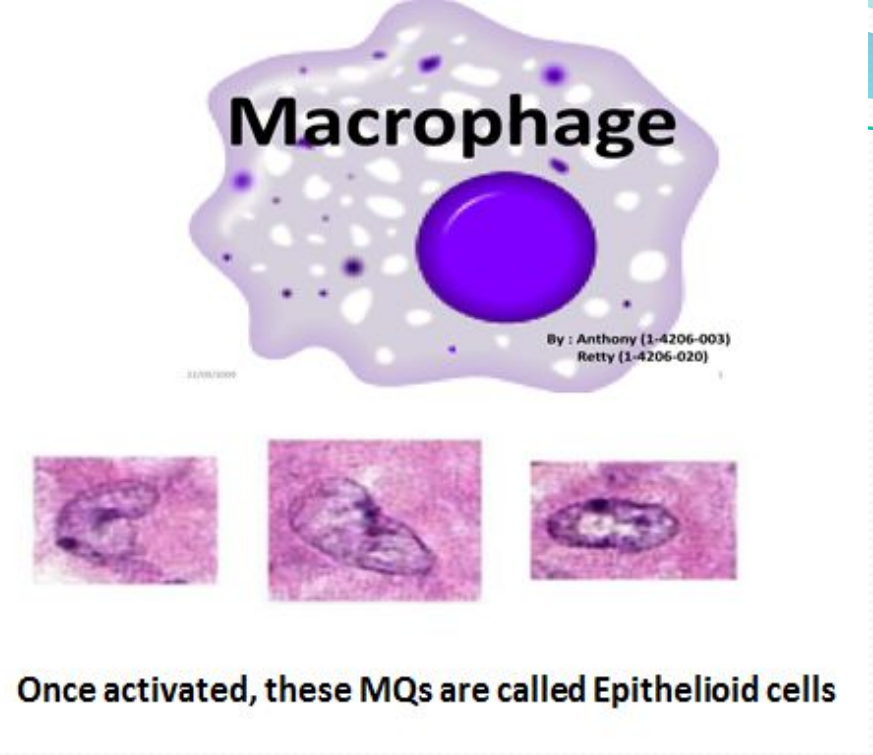
Bacillary proliferation within alveolar macrophages leads to the development of cell mediated immunity through mediator of IL-12 from MQ ; and primarily mediated by TH1 cells(CD4) which give γIFN which stimulate macrophages (activated macrophage) .
The activated macrophages release a variety of mediators including secretion of TNF, which is responsible for recruitment of monocytes, which in turn undergo activation and differentiation into the "epithelioid histiocytes" and these epithelioid cells which joint together to form large cell which is called --- multinucleated giant cells(Langhance giant cells or hoarse show giant cells) and these collection called granulomatous nodule to kill bacteria but this is associated simultaneously with the development of destructive tissue hypersensitivity in the form of caseation necrosis in which healed completely by fibrosis and calcification.

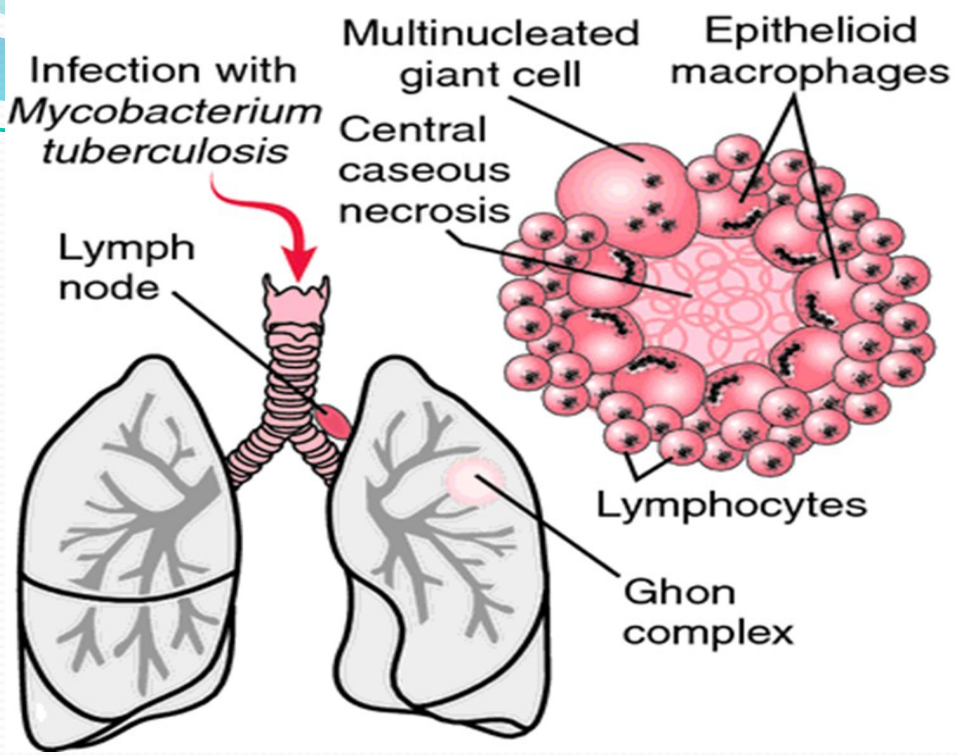
in immune-competent individuals



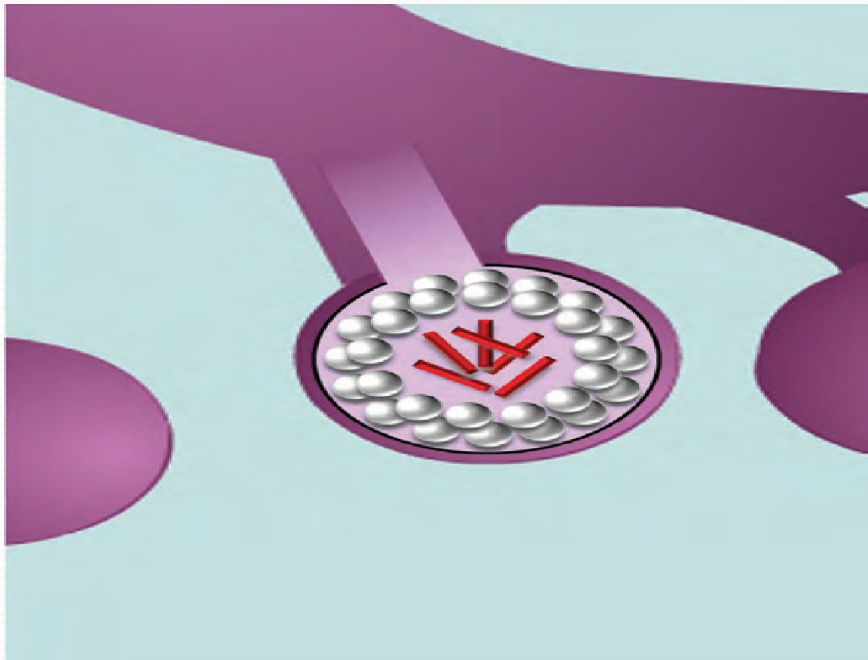
About 3 weeks are needed for the development of the hypersensitivity reaction (so called Delay type hypersensitivity, type IV DHS which is cell mediated immunity) .

DHS is a function of
T- lymphocytes (cellular response) not humeral (no antibody) .



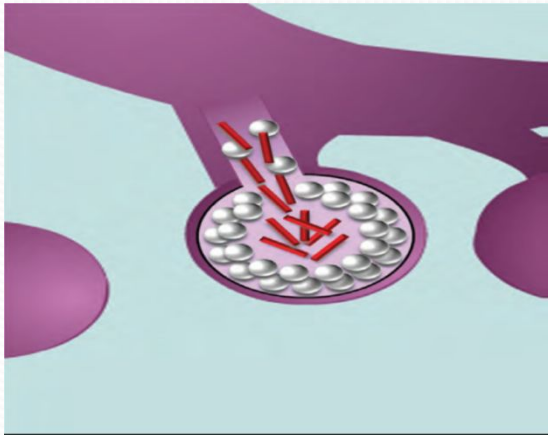


intrapulmonary
Special immune cells
form a barrier shell around
bacilli



B-If immune-competent individuals with mild polymorphism in macrophages or high dose of bacilli :-

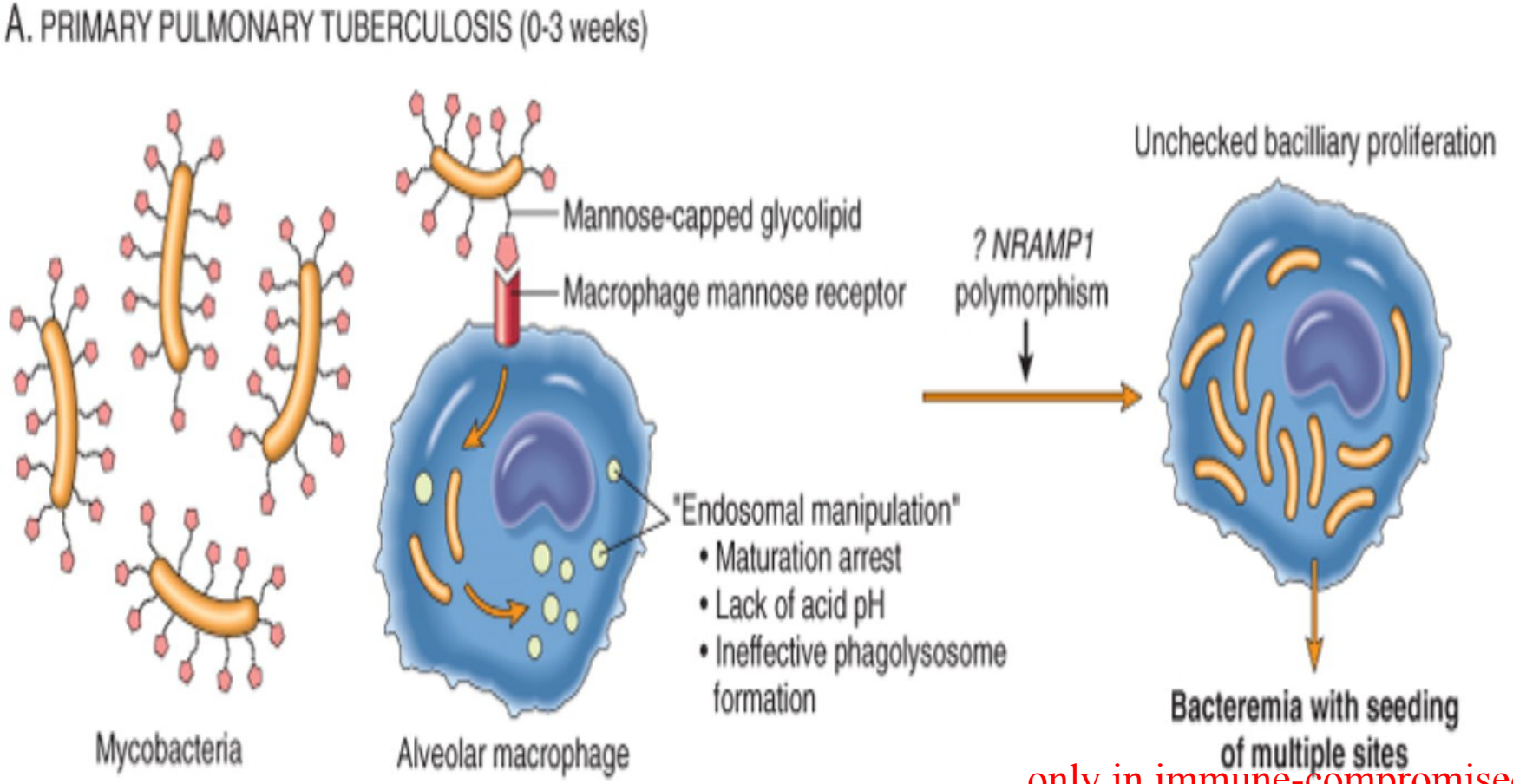
Bacillary proliferation within alveolar macrophages leads to the development of cell mediated immunity granulomatous response without caseaous necrosis and the bacteria still a live in form of dormant bacilli (latent TB) i.e the bacilli still a live but not active in the pulmonary (a symptomatic) and which can be later on reactivate and spread to extra-pulmonary (presented with clinical features) .



***intra- pulmonary bacilli can spread to extra pulmonary because the bacilli can Shell breaks down and tubercle bacilli escape and multiply**

C-if immune-compromised individuals

the end result is bacteremia and seeding of multiple sites with collection of foamy macrophages with bacillary proliferation and patient with prominent clinical features .



only in immune-compromised

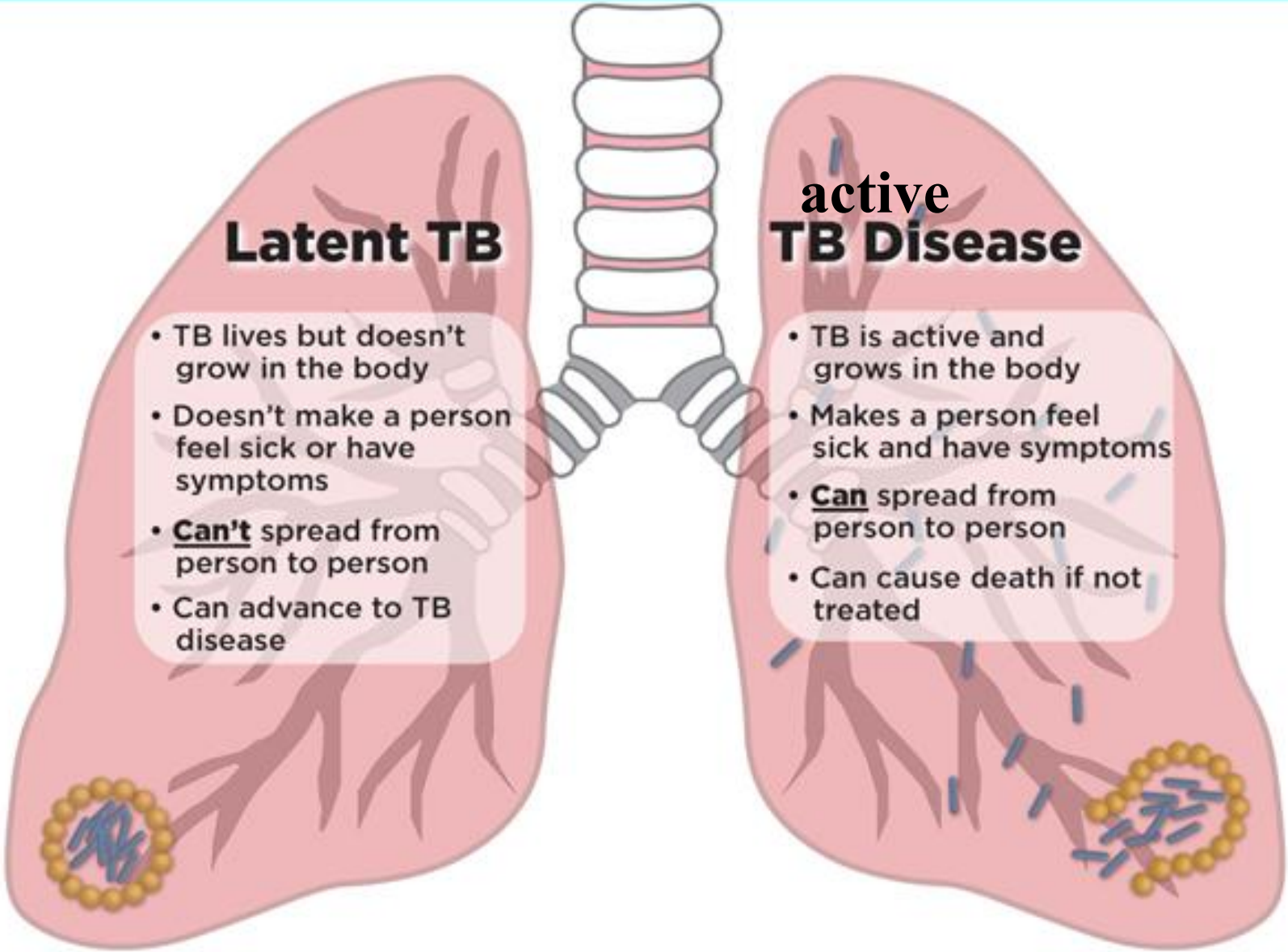
Clinical course of TB

Primary TB with immune-competent individuals are a symptomatic

Latent TB :- The bacteria remain in the body in an inactive state. They cause no symptoms and are not contagious, but they can become active (symptomatic)

Active TB :- The bacteria lead to symptoms and can be transmitted to others. Active disease in adults most commonly represents reactivation of a primary focus and the disease tend to be progressive .

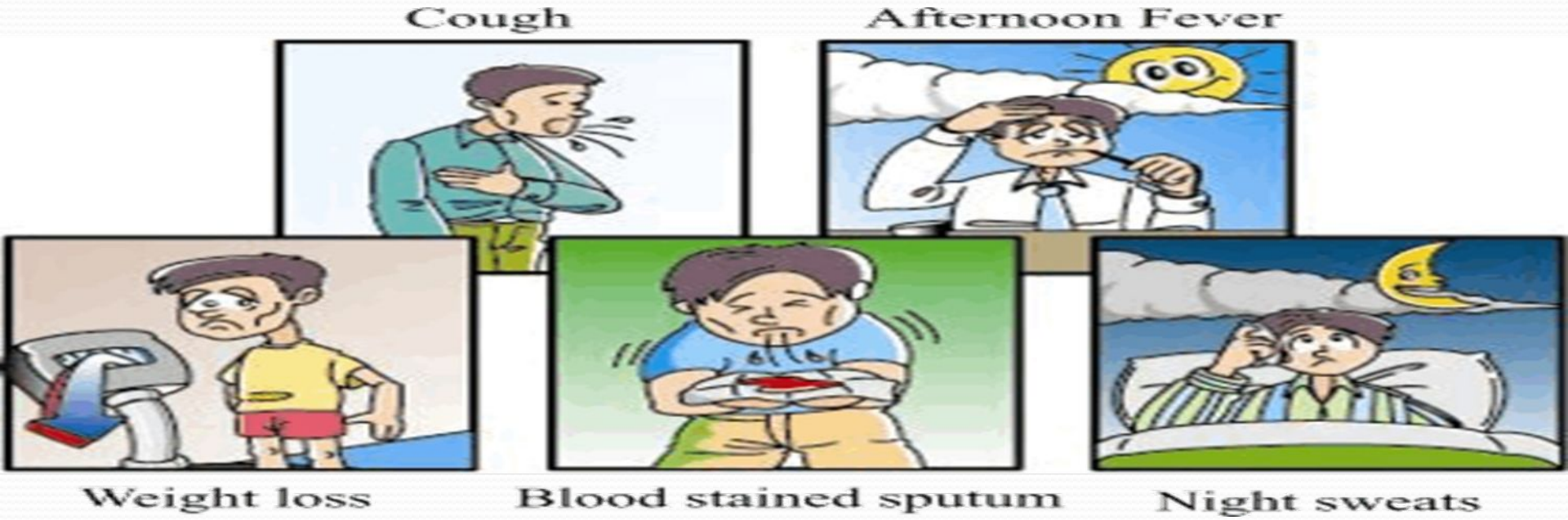
Latent TB versus active TB



Primary TB with immune-competent individuals are asymptomatic

In those who develop progressive primary disease, symptoms are usually insidious and nonspecific .

Clinical features of active TB :-



Clinical features that does not respond to conventional antibiotic therapy.

Pathological features of primary TB

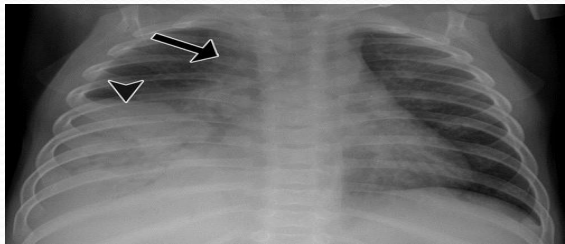
-The inhaled bacilli are embedded in the distal airspaces of the lower part of the upper lobe or the upper part of the lower lobe, usually close to the pleura (sub pleura) .

-As sensitization develops, a bout 1 cm single area of gray-white inflammatory consolidation develops (the Ghon focus).
Primary focus (Ghons focus) at the site of first implantation usually single .
-Tubercle bacilli drain to the regional nodes lead to L.N enlargement .
Complications arise more commonly from regional adenitis than from the primary focus .

If immune-competent individuals lead to granuloma formation with or without caseous necrosis.

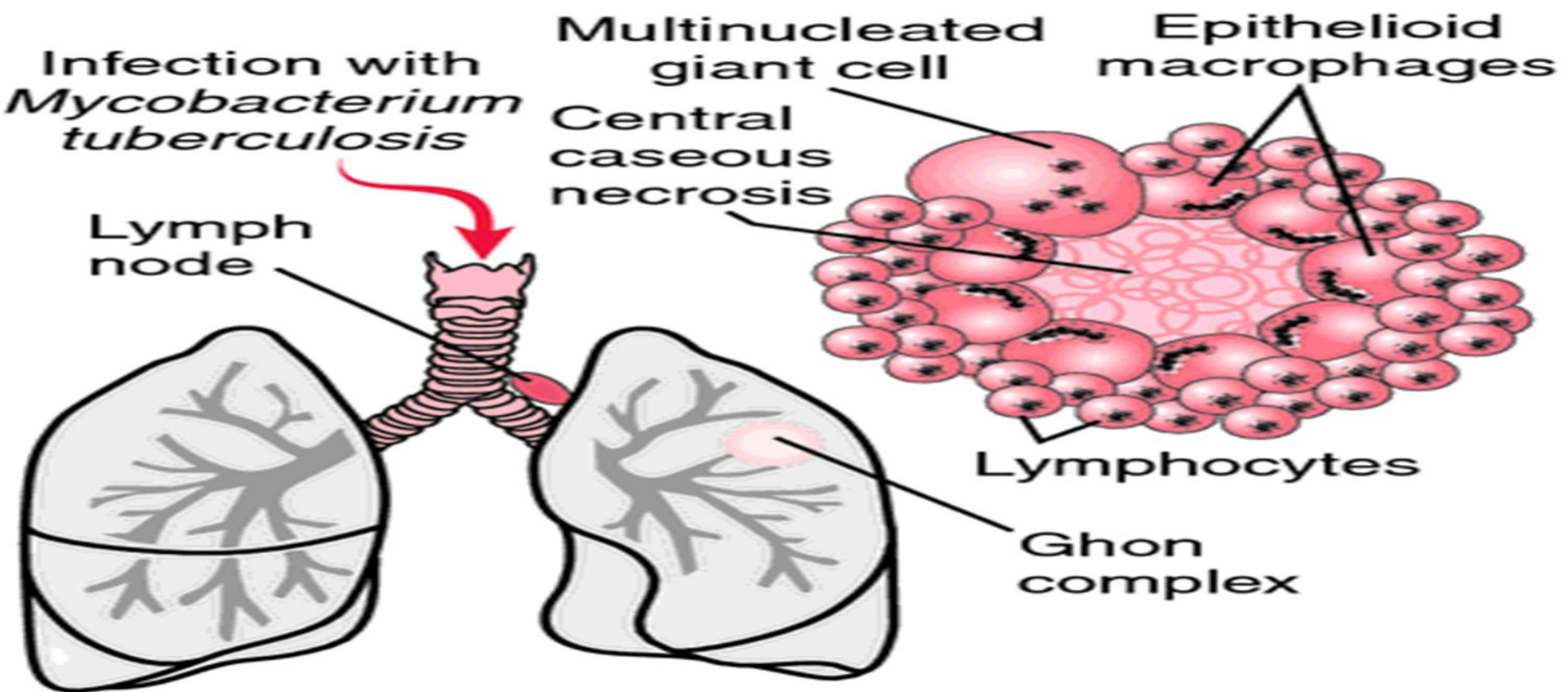
The combination of Ghon focus and nodal involvement is referred to as the Ghon complex .The term caseous is derived from the chessy white gross appeareance of centeral necrotic area which called caseous necrosis which is a combination of coagulative and liquefactive necrosis .

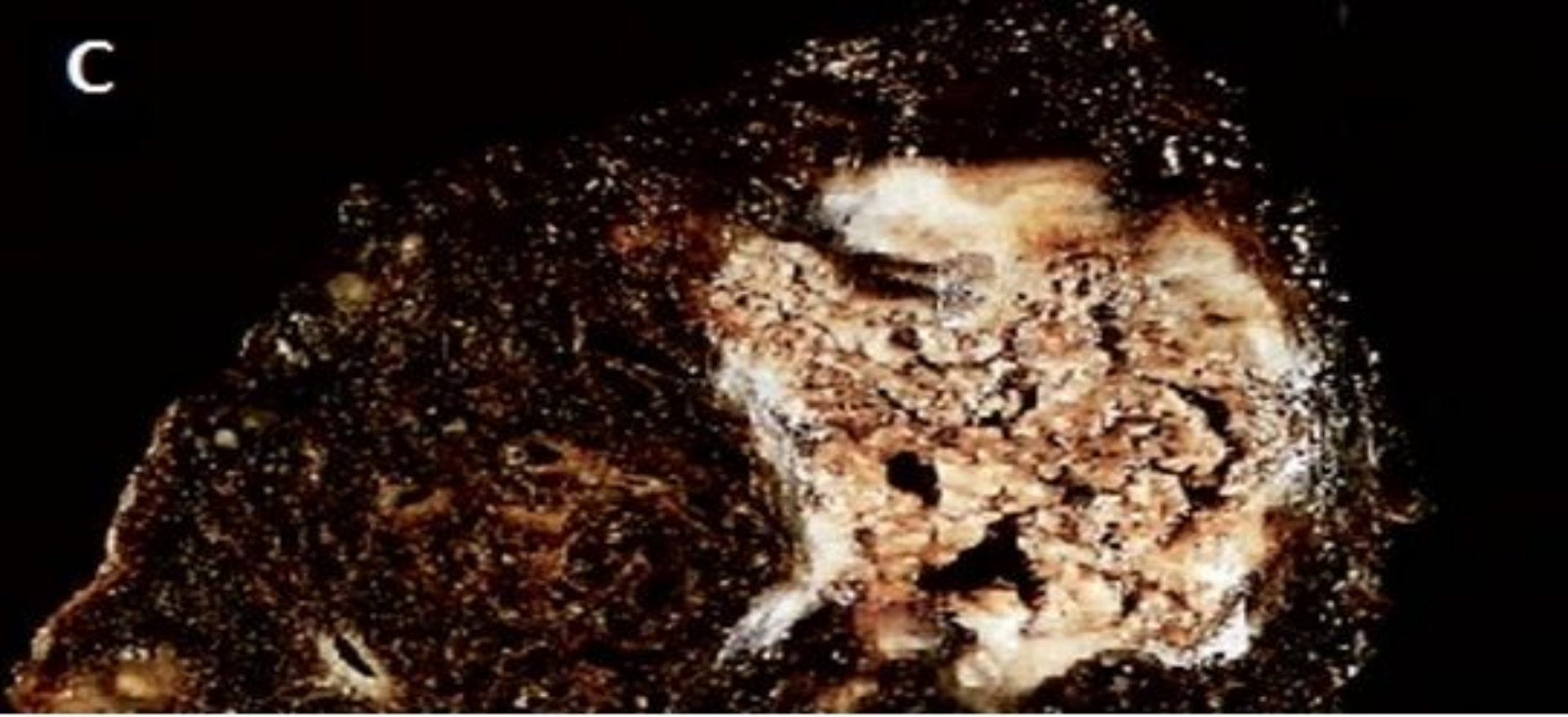
If patient with immune-suppression disease , lead to aggregation of foamy macrophages with bacilli which form the Ghon focus .*after the first few weeks, there is also lymphatic and hematogenous dissemination to other parts of the body .



Microscopically

The granulomas in T.B with or without central granular caseation but are usually central granular caseation that is surrounded by epithelioid and multinucleated giant cells(Langhance giant cells or hoarse show giant cells) enclosed within a fibroblastic rim with lymphocytes.



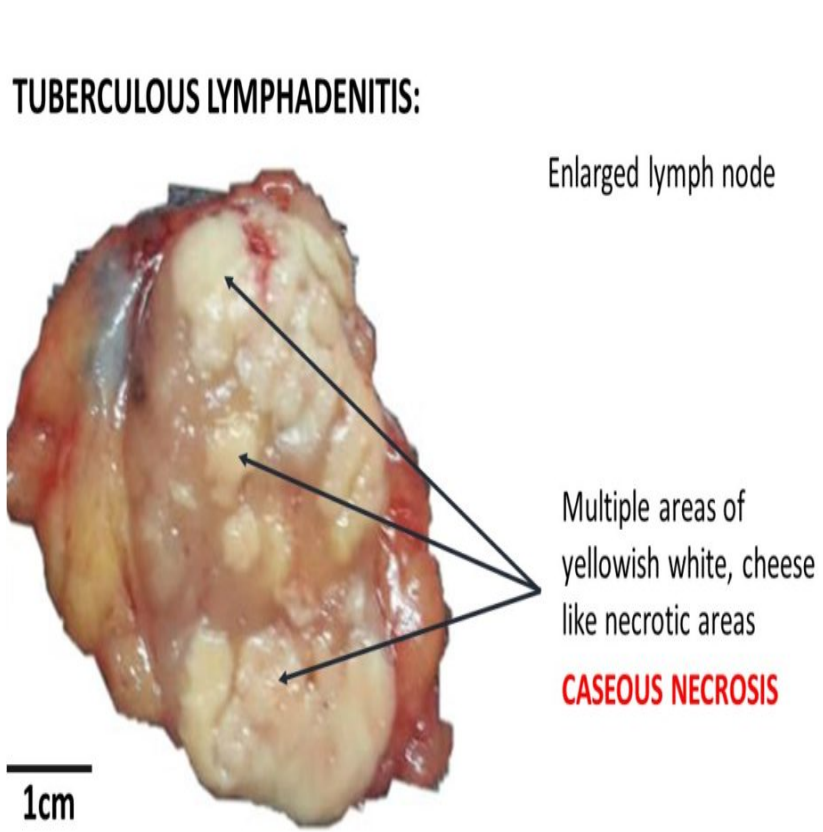


Caseous necrosis in lung tissue

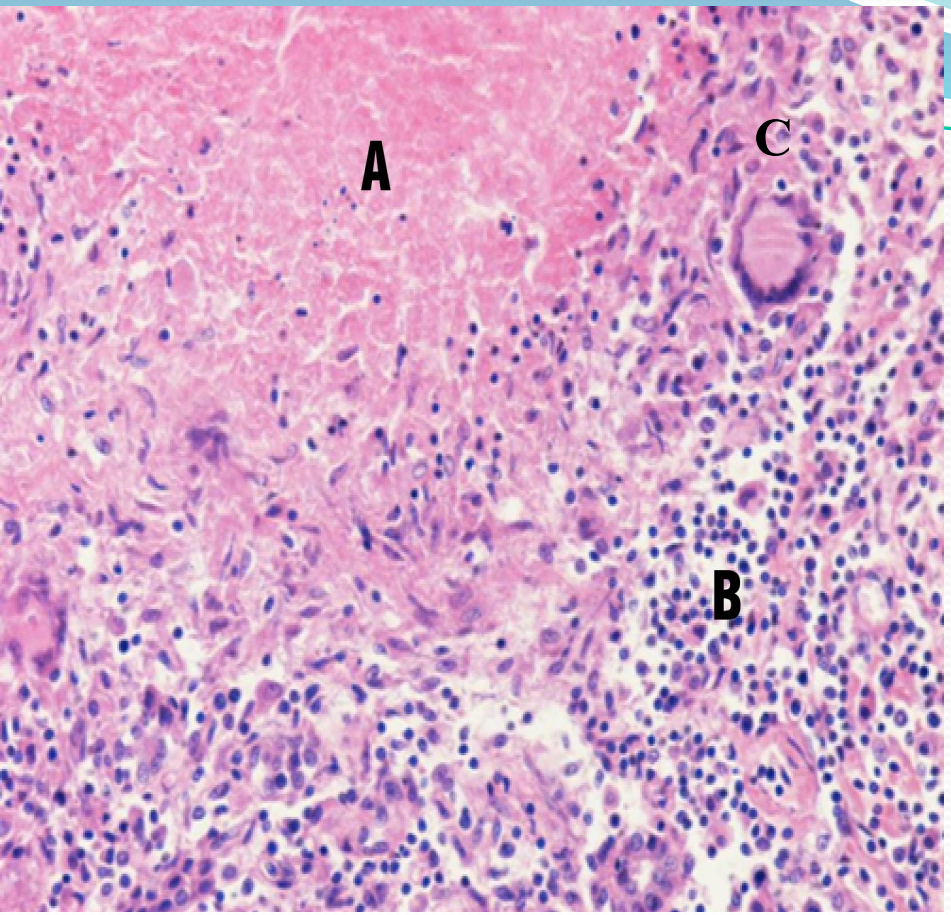
Demonstrates the lung containing caseous necrosis due to tuberculosis which is a combination of coagulative and liquefactive necrosis . Notice the yellow-white and cheesy debris.

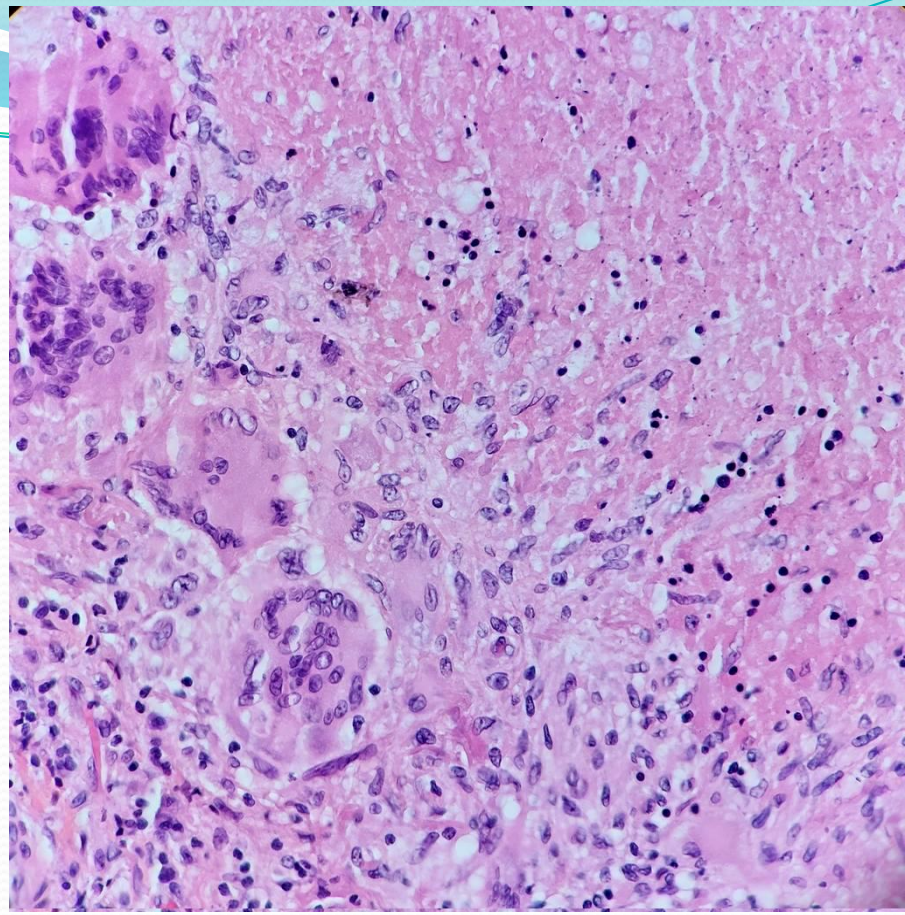
This is the gross appearance of caseous necrosis in a hilar lymphnode infected with tuberculosis. The node has a cheesy tan to white appearance.

Caseous necrosis is really just a combination of coagulative and liquefactive necrosis that is most characteristic of granulomatous inflammation.

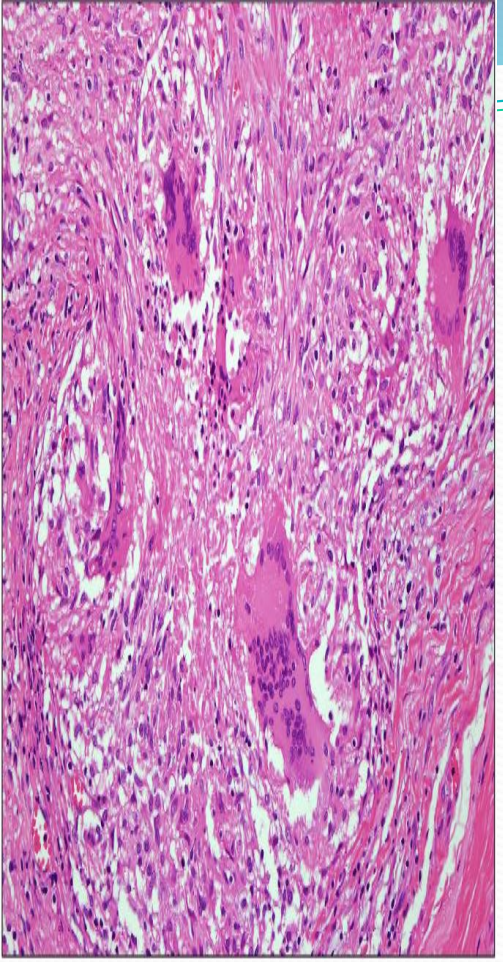
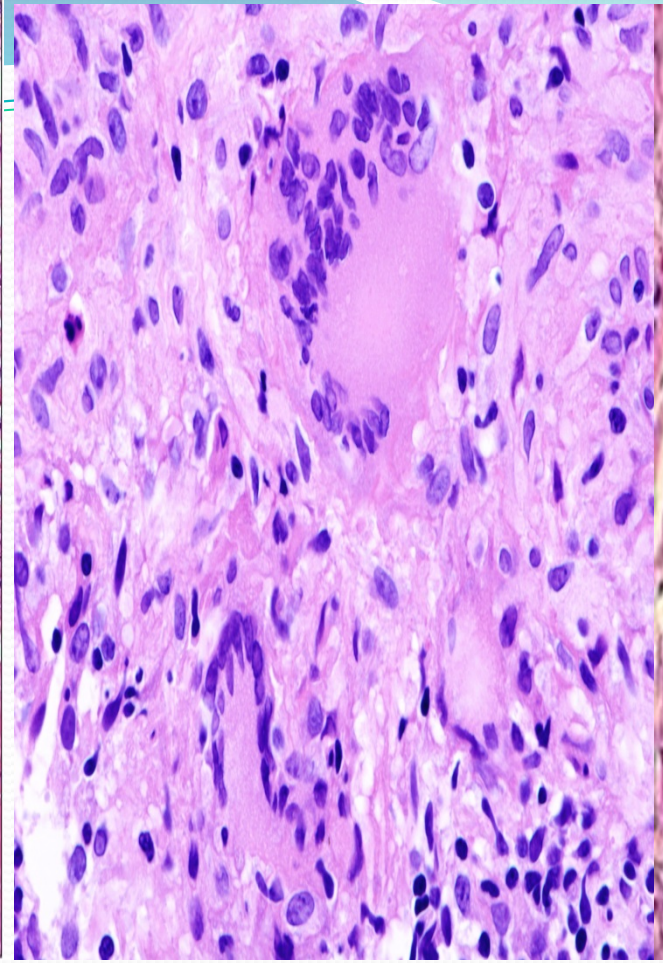
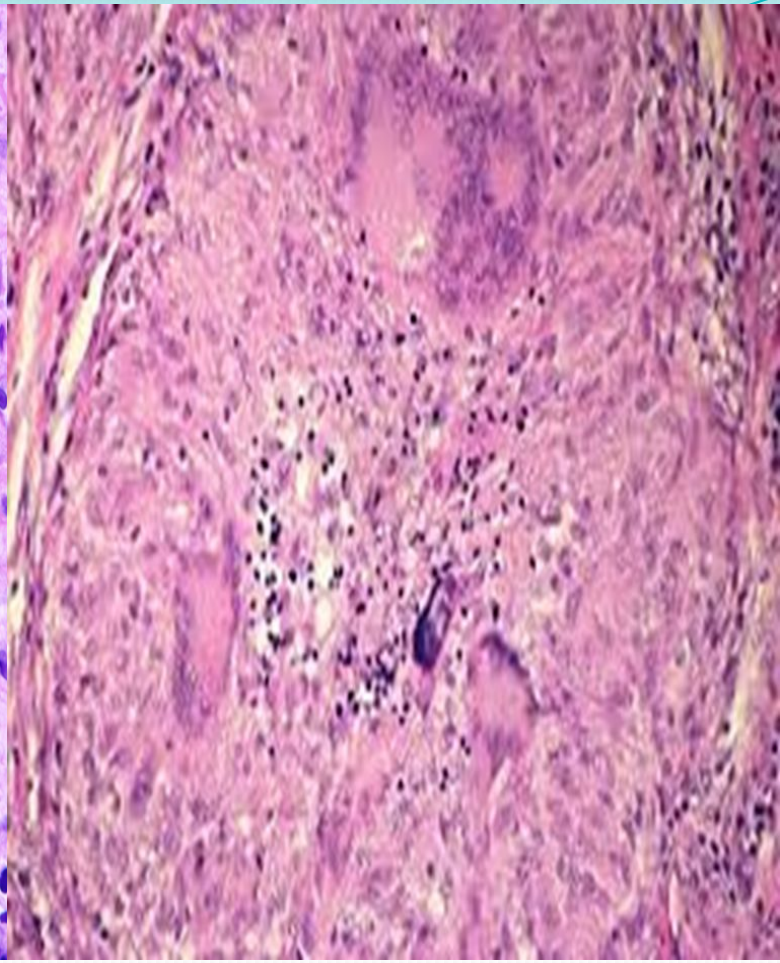


TB Lymphadenitis :- multiple area of cheesy white appearance of central necrotic area which called caseous necrosis .
caseous necrosis is a combination of coagulative and liquefactive necrosis





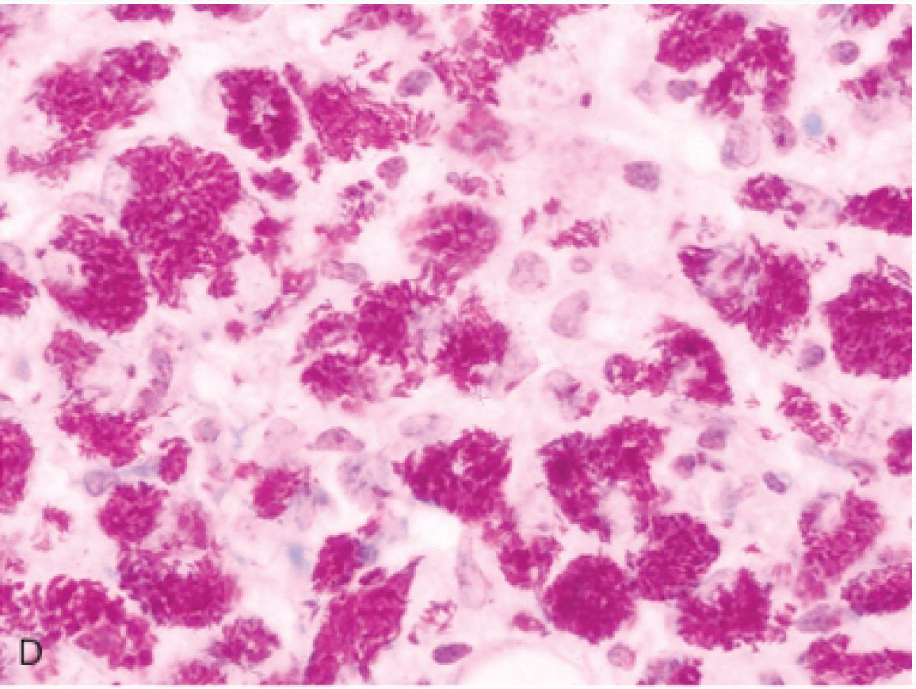
A :- central granular caseation that is surrounded by epithelioid (B) and multinucleated giant cells (Langhance giant cells or hoarse show giant cells) (C) to form tubercular granulomas . caseous necrosis is a combination of coagulative and liquefactive necrosis .(in immune-competent individuals with normal macrophage).

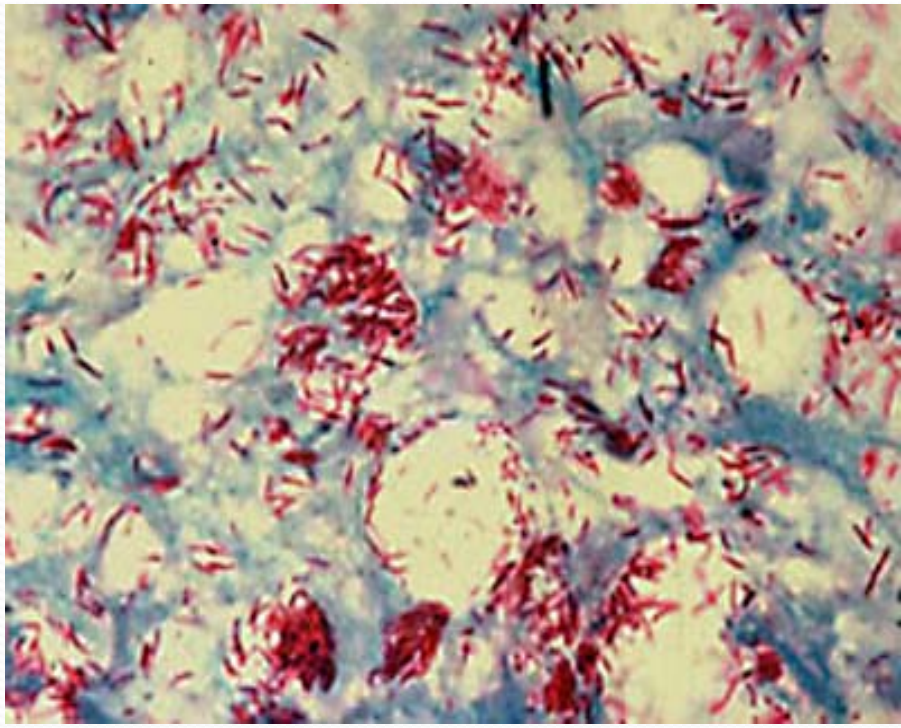




Aggregation of epithelioid and multinucleated giant cells (Langhance giant cells or hoarse show giant cells) to form tubercular granulomas and not show central caseation. (in immune-competent individuals with mild polymorphism of macrophage)

Mycobacteria TB are slender rods that are acid fast, thus stained positively (red rods in back- ground blue) with Ziehl -Neelson stain(ZN stain) .

Immune-suppression results in the absence of a tissue hypersensitivity reaction and thus there are only sheets of foamy histiocytes packed with the bacilli





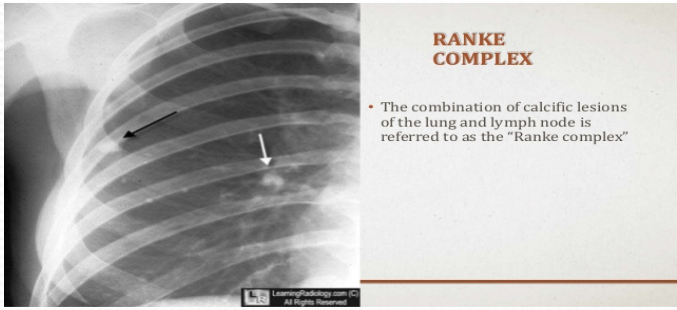
A) sheets of foamy histiocytes packed with the bacilli . Abscent of Aggregation of epithelioid , multinucleated giant cells (Langhance giant cells or hoarse show giant cells) and lymphocyte . AFB organisms are plentiful.

Fate of Primary TB

1-No progression (in immune-competent) .

Complete healing by fibrosis and calcification in complete immune-competent patients (intra-pulmonary) .

***Ghons complex after undergoing progressive fibrosis and produces radiologically detectable calcification called as Ranke complex.**



In immune-competent individuals with mild macrophage polymorphism---- healed with mild fibrosis but with latent T.B (bacilli still a live but not active) in pulmonary /extra-pulmonary .

2-Progressive primary TB

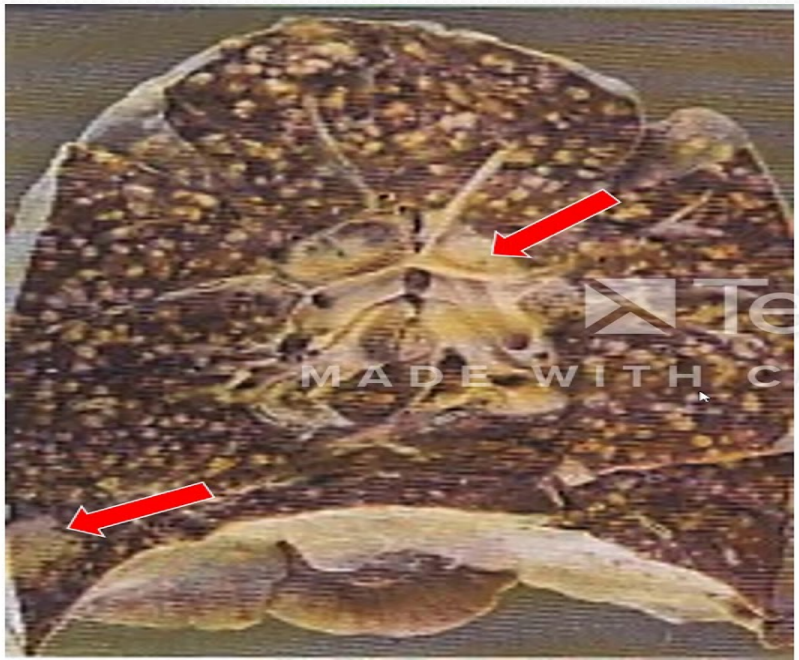
The disease progresses into progressive primary tuberculosis (uncommon) and called miliary TB .

Miliary TB is millet like-grain ,extensive micro-spread through blood , lymphatics and bronchial spread , pulmonary and systemic types present .This occurs in immune-compromised individuals e.g. AIDS patients or in those with nonspecific impairment of host defenses (infant , malnourished children or elderly).
Miliary tuberculosis is a potentially life-threatening type of tuberculosis

miliary tuberculosis

1-Primary pulmonary miliary tuberculosis .

occurs through local spread through pore of kohn and organisms drain through lymphatics into the lymphatic ducts, which empty into the venous return to the (SVC)and then to right side of the heart and then into the pulmonary arteries and from P.A to both lung .

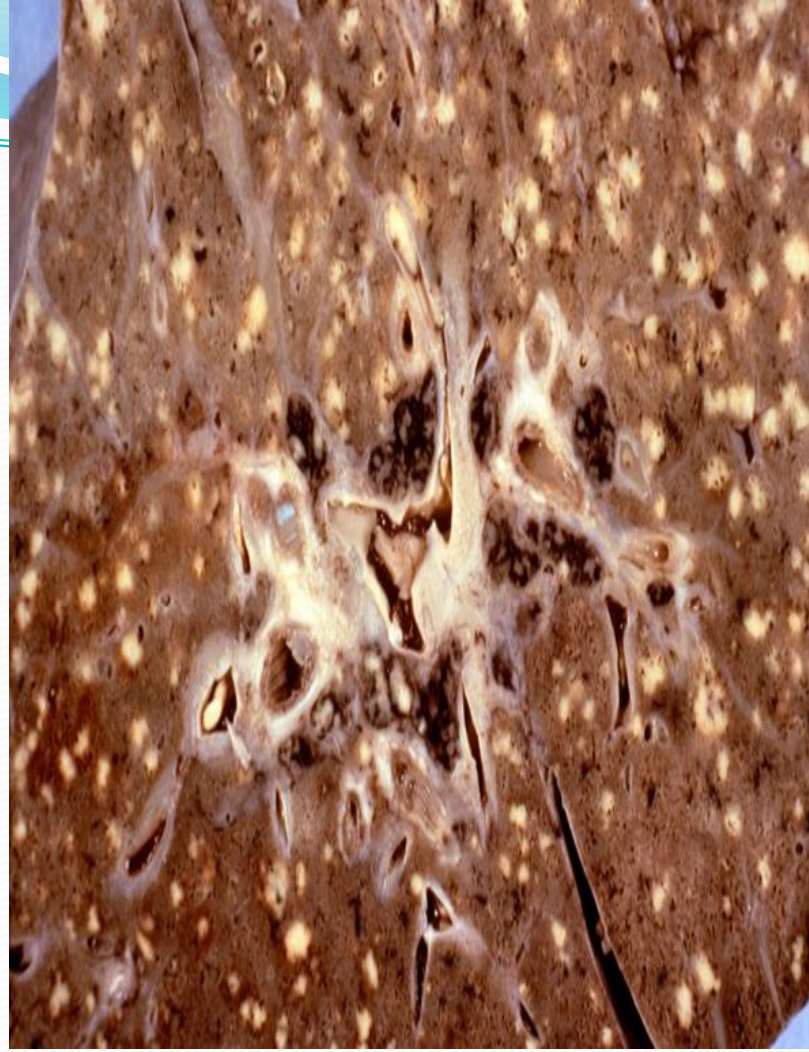


- **Primary Pulmonary tuberculosis**

+ miliary TB

- Multiple small tan granulomas, 2 to 4 m. in size, scattered throughout the lung parenchyma.

cheesy tan white appearance



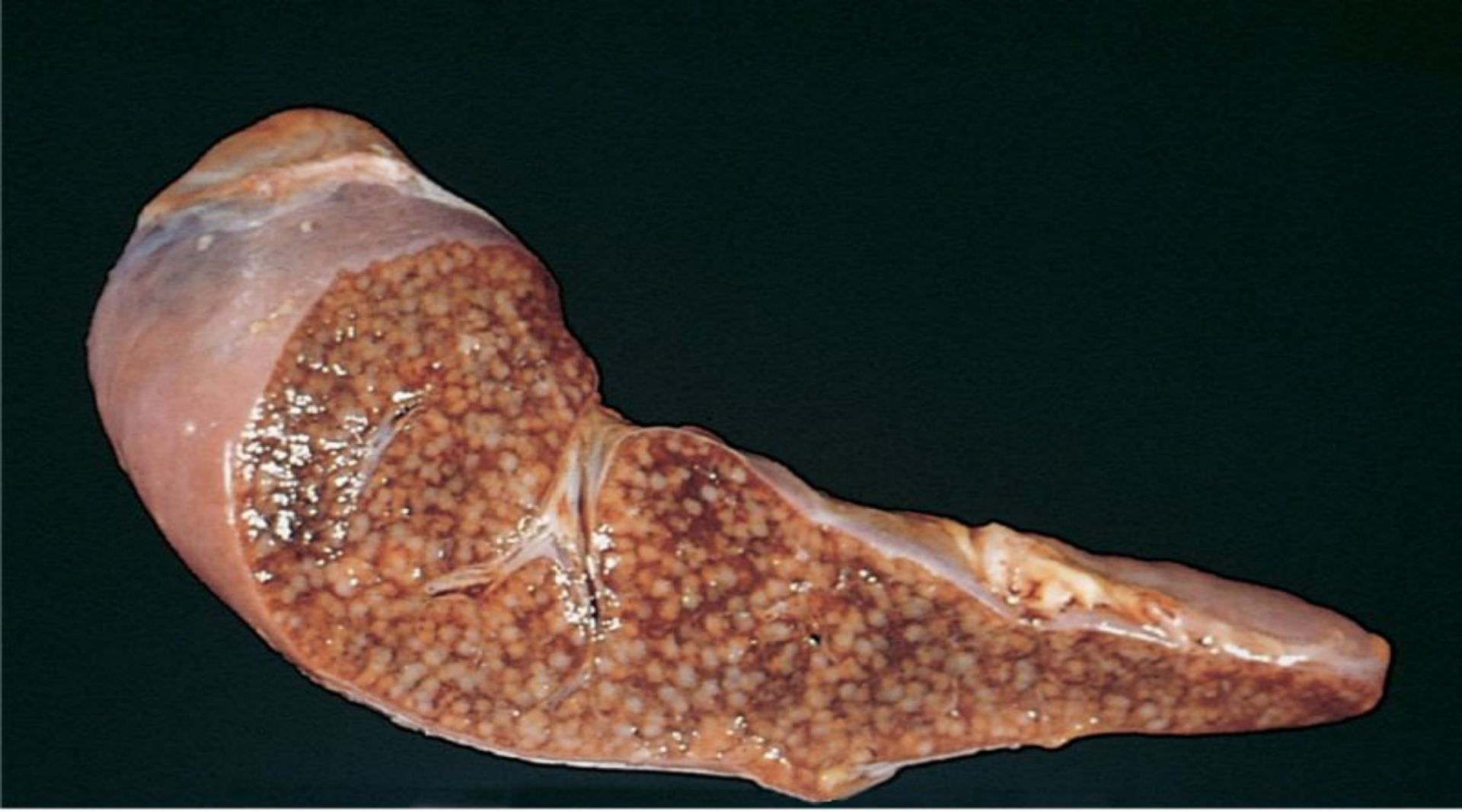
Miliary TB is millet like-grain ,multiple small granulomatus 2-4 mm in size cheesy tan white appearance scattered through out the lung paranchyma

2- Systemic miliary tuberclosis :-

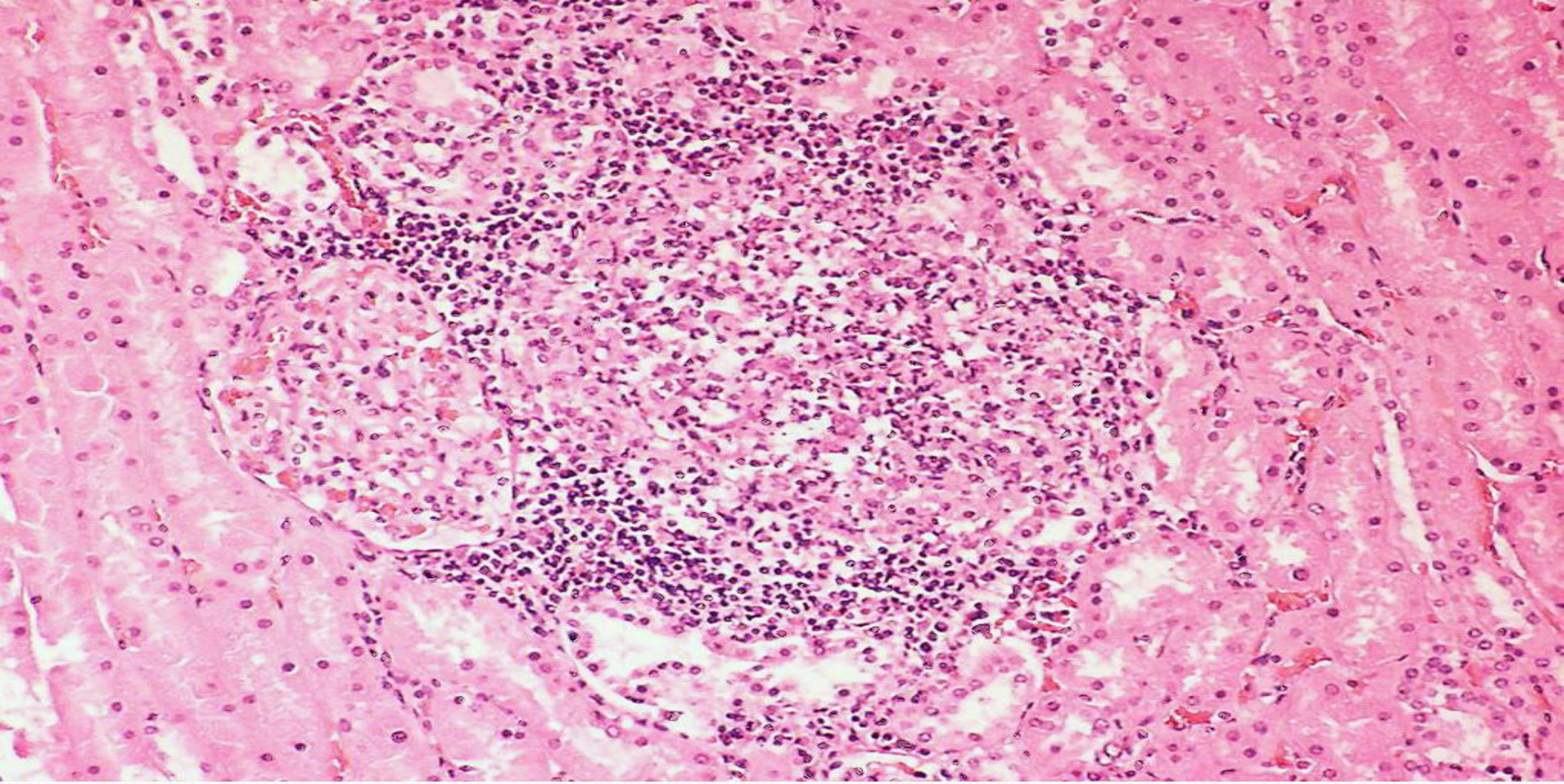
occurs when infective foci in the lungs results in erosion of epithelial layer of alveolar cells and the spread of infection into a pulmonary vein invade the pulmonary vein which return to the heart; the organisms subsequently disseminate through the systemic arterial system , they multiply and infect extrpulmonary organs .

The infected site showed , multiple lesion , each lesion consist of only fomay macrophages ,which form granuloma, giving the typical appearance of miliary TB .

Almost every organ in the body may be seeded like liver , spleen , kidney … ect .



Miliary tuberculosis of the spleen. The cut surface shows , millet like-grain ,multiple small granulomatous 2-4 mm in size cheesy tan white appearance scattered through out the spleen .



miliary TB :- multiple lesion , each lesion consist of only fomay macrophages ,which form granuloma, giving the typical appearance of miliary TB

Thanks

What we learn with pleasure

we never forget