**Respiratory Block**

# Immunology

## Lecture 4

## Immunology of Tuberculosis

*In this document you will find some main points gathered from the 1st lecture..This document is NOT a replacement for the lecture..If you need additional information go back to the lecture or use a book as a reference so you understand everything correctly.*

*Hopefully all the information is correct and Hope you find them useful.*

*Good Luck to everyone.*


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# Immunology

## Immunology of Tuberculosis

*Some main points you can go through and revise from:*

*T.B. is an example of an infection in which protective immunity & pathologic hypersensitivity coexist, and the lesions are caused mainly by the host response.

#In Tuberculosis both the Pathogen (Bacteria) and our Immune responses cause the diseases progression.

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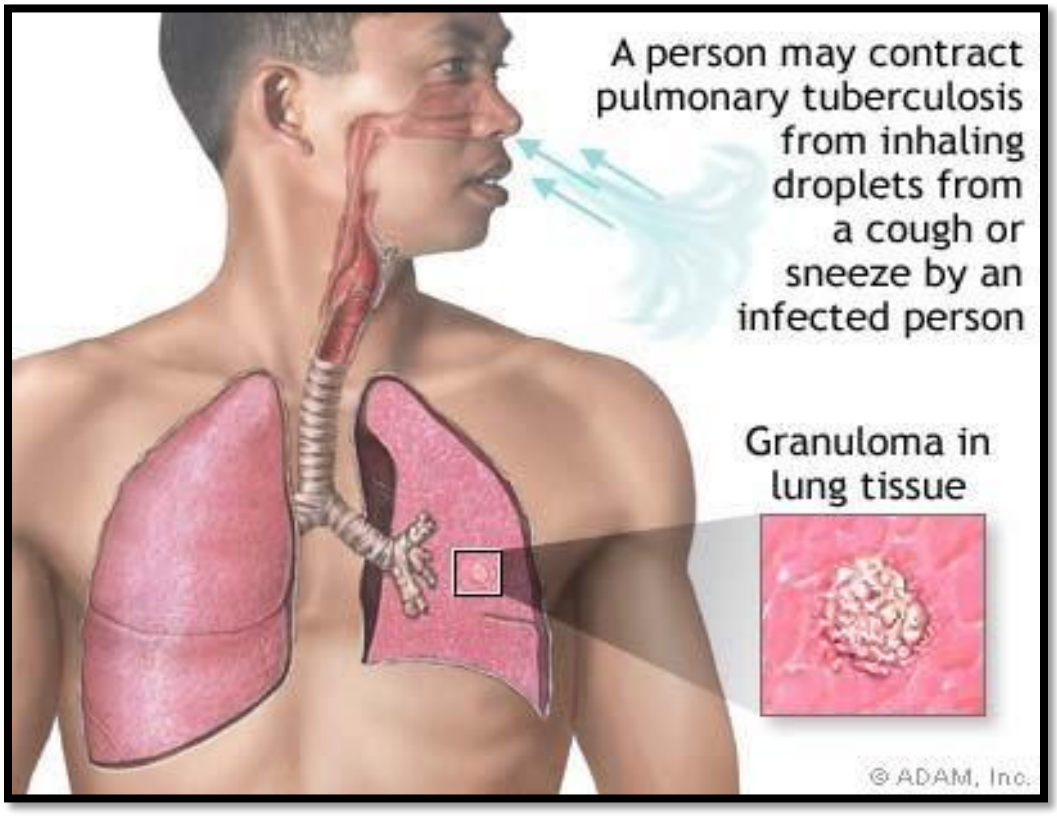
## Definition:

Airborne transmission of tuberculosis → when the infection is acquired by inhalation of M. tuberculosis in aerosols and dust

*Infected people cough up large numbers of mycobacteria

*The mycobacterium is protected by waxy outer coats which will help it to survive for long period. #(The waxy coat prevents its distruction)

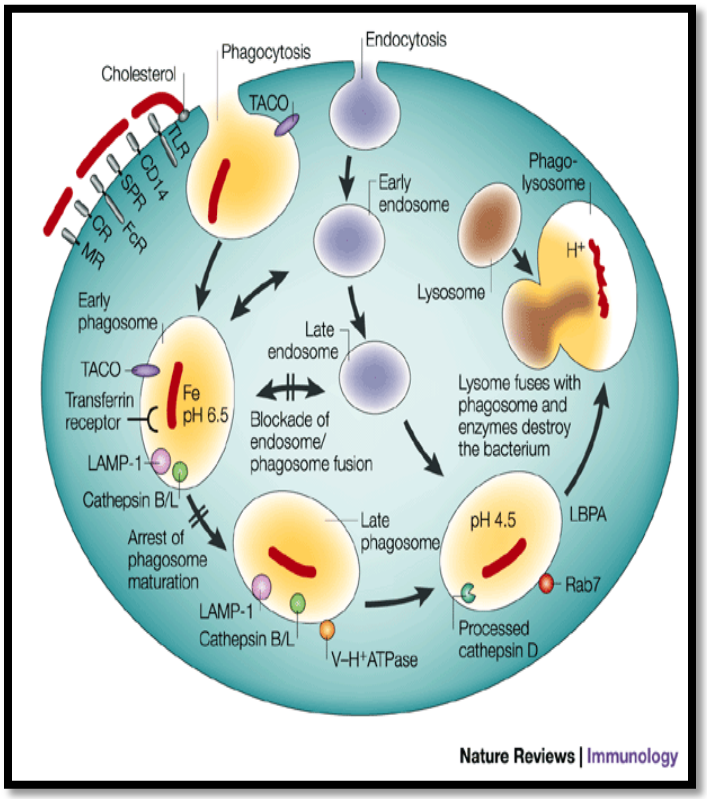



## Primary Infection:

Organisms are inhaled from air or dust →taken up by alveolar macrophages →macrophages travel via lymphatic's to the local (hilar) lymph nodes .

# Mycobacteria persist inside macrophages :

- **Waxy coat** → block phagocyte enzymes.
- **Catalase enzyme**→prevent the respiratory burst.




**Note:**

Respiratory Burst →is the process of taking oxygen in order to kill the organism

**-Mycobacteria**→ Persist (Are sealed) inside macrophages.

**-Waxy coat**→ block phagocyte enzymes .

**-Catalase enzyme** →prevent the respiratory burst .

**-Macrophages** → Present (Produce) Mycobacterial peptide.

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Elicit strong T helper (TH1) response.

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Activated T-cells secrete cytokines.

↓ ↓

Tumor Necrosis Factor (TNF) Interferon-gamma (INF)

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## *By 6-8 weeks after infection :

Macrophages localize in the draining lymph nodes → CD4 T-cells become activated and secrete IFN-gamma #CD8 T-cells become activated later

***(IFN)→**activate ( infected) macrophages

# To enhance their ability to kill phagocytosed (Consumed) bacilli, Because it is hard to kill the mycobacteria as they are sealed in Macrophages.

## *Activated T-cells and activated macrophage→Secrete tumor necrosis factor (TNF).

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## TNF plays a role in :

- Local inflammation.
- Further macrophage activation. #Activation of more macrophages

**The resulting T-cell reaction (CMI)→** is adequate to control bacterial spread . #Cell mediated Immunity controls bacteria and prevents it from spreading

*(Bacilli are contained within tubercles – small granulomas) → #therefore they cannot spread

## DTH Reactions:

**(Delayed type Hypersensitivity Reactions ):-**

Occur as :

- Collateral damage during a protective response to a microbe.
- DTH may be entirely pathologic as in certain autoimmune diseases.

#DTH Reactions are either Protective or Pathologic → meaning they either:

*aim to protect but end up destroying OR aim to destroy from the start

## DTH reactions in tuberculosis :

Chronic DTH reactions develop when the TH 1 response activates macrophages but fails to eradicate phagocytosed microbes . #Macrophages are activated but they do not kill the bacteria

*This will lead to :

- Granulomatous inflammation → which is a form of DTH reactions to the bacilli.

## In chronic DTH reactions macrophages:

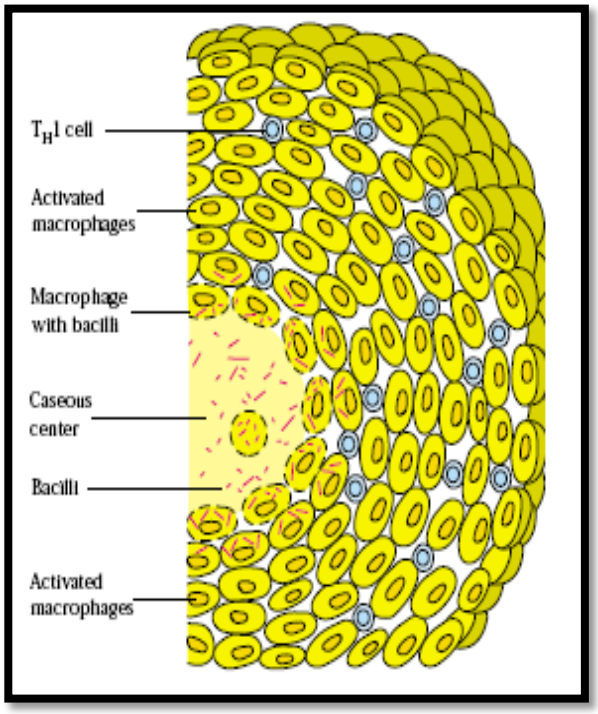
Macrophages change morphology with time → develops increased cytoplasm and become epithelioid cells and fuse to form multinucleated giant cells

*These cells form part of the granuloma in TB

*To help you understand*
The cells are called epithelioid cells because they are similar to epithelial cells.

**Note:**
When granulomas undergo central necrosis it is called caseous necrosis Necrosis result from macrophage products and serve to eliminate infected macrophages. #Necrosis of the infected macrophages is caused by the macrophages products.

*Granulomas may undergo central necrosis (caseous necrosis)
*Necrosis result from macrophage products and serve to eliminate infected macrophages.




***Outcome of primary infection →**depends on the immune state of the individual.

- Most individuals are completely healed by containing the mycobacterium particles in fibrous granuloma. (complete healing )
- Development of a progressive infection.
- Development of Excessive response to primary infection .
- Post primary (Reactivation)

## Outcome of primary infection:

- In most patients (90%) of primary infections heal to leave a small visible scar on radiograph.
- Mycobacteria remain alive inside macrophages

## The Gohn complex consist of :

- Lung lesions (tubercles –small granulomas )+ enlarged lymph nodes .
- Tubercles may heal and become fibrotic or calcified and persist as such for a lifetime.
- Appearance on chest x-ray → as radio-opaque nodules

## In individuals with immunodeficiency:

Mild I.D. → lead to reactivation usually in the apices (top) of the lung .(TB in the lung)

Severe I.D. → leads to more widespread infection beyond the lungs. (TB involving other sites of the body)

In patients with excessive TNF production → lesions break down leading to open T.B.

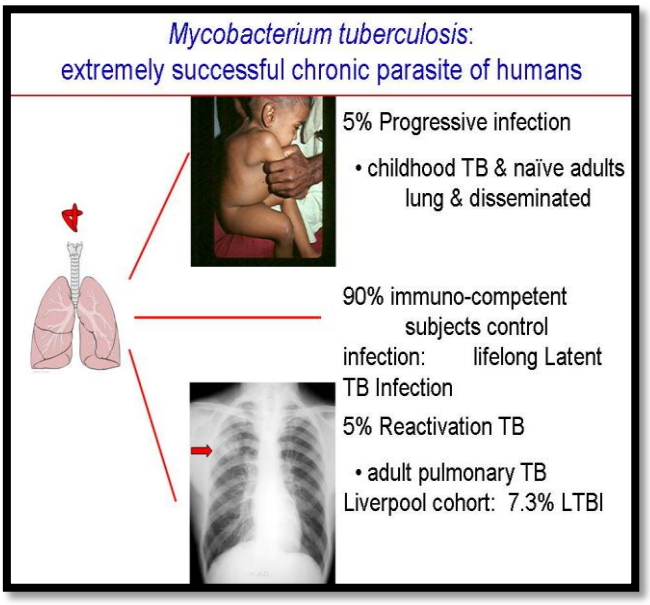
**Note:**
Patients with open TB are infectious, Meaning that they can transmit the disease to other people.

## In a small proportion of young patients,widespread primary T.B. occurs and may present as :

- miliary T.B. (TB spread to other organs)
- tuberculous meningitis .

## Outcome of primary infection:

- 5% → progressive infection.
- 90 % → remain asymptomatic.
- 5% → reactivation.



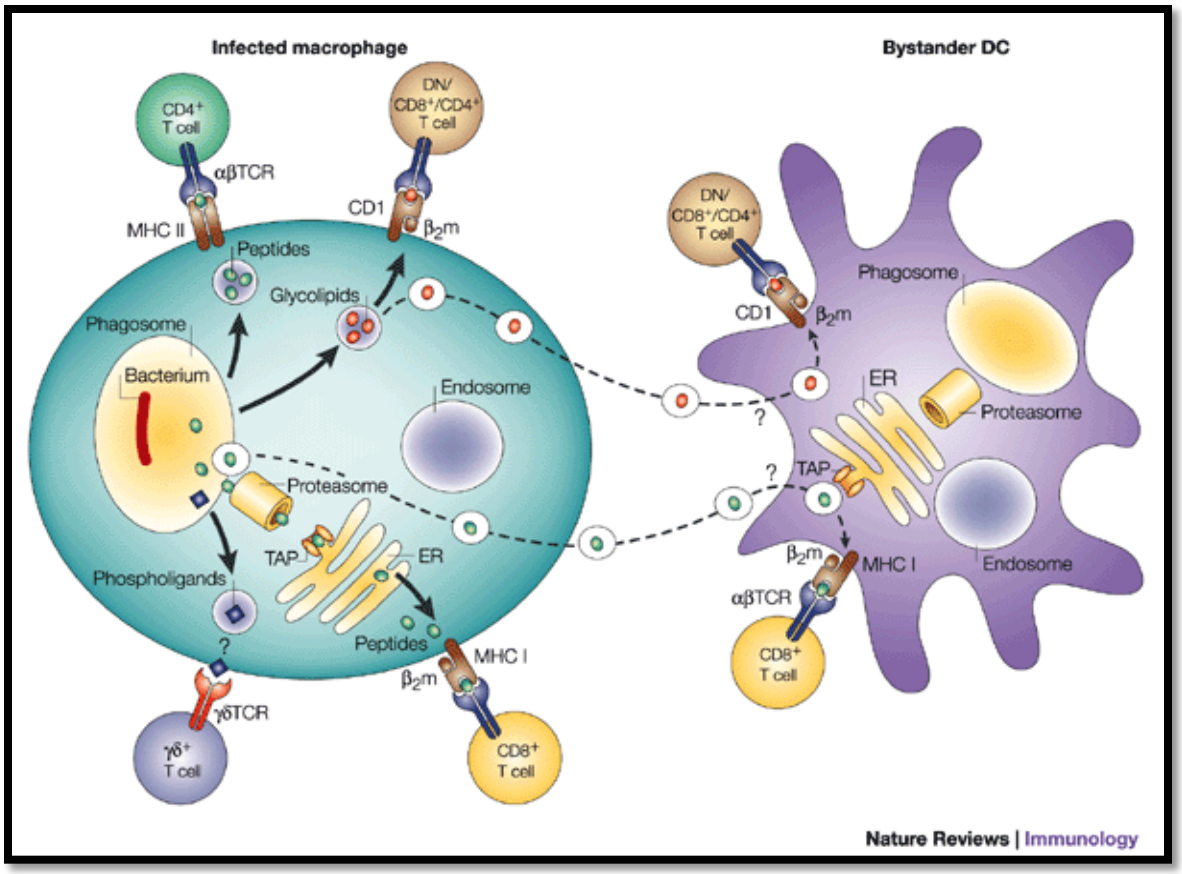

*Reactivation is a consequence of impaired immune function

## Causes for Impaired Immune functions:

- Malnutrition .
- Infection (e.g. AIDS ).
- Chemotherapy.
- Corticosteroids.

## Test for immunity against T.B.

- Delayed Hypersensitivity skin test
- Tuberculin test, or ( Mantoux )
- Intradermal injection of PPD ( purified protein derivative ).




## Tuberculin test reading :

measure diameter of indurations after 48 hours .

## Blood test for T.B. exposure.

1. The test measures interferon – gamma secreted in response to mycobacterial antigen
2. Mycobacterial peptides are added to the patient's blood which is then incubated for 12 hours.
3. The amount of (IFN) produced is then measured by ELISA test .

## Prevention :

- 1. Immunoprophylaxis → vaccination (BCG).
- 2. Chemoprophylaxis → anti- tuberculous drugs .

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