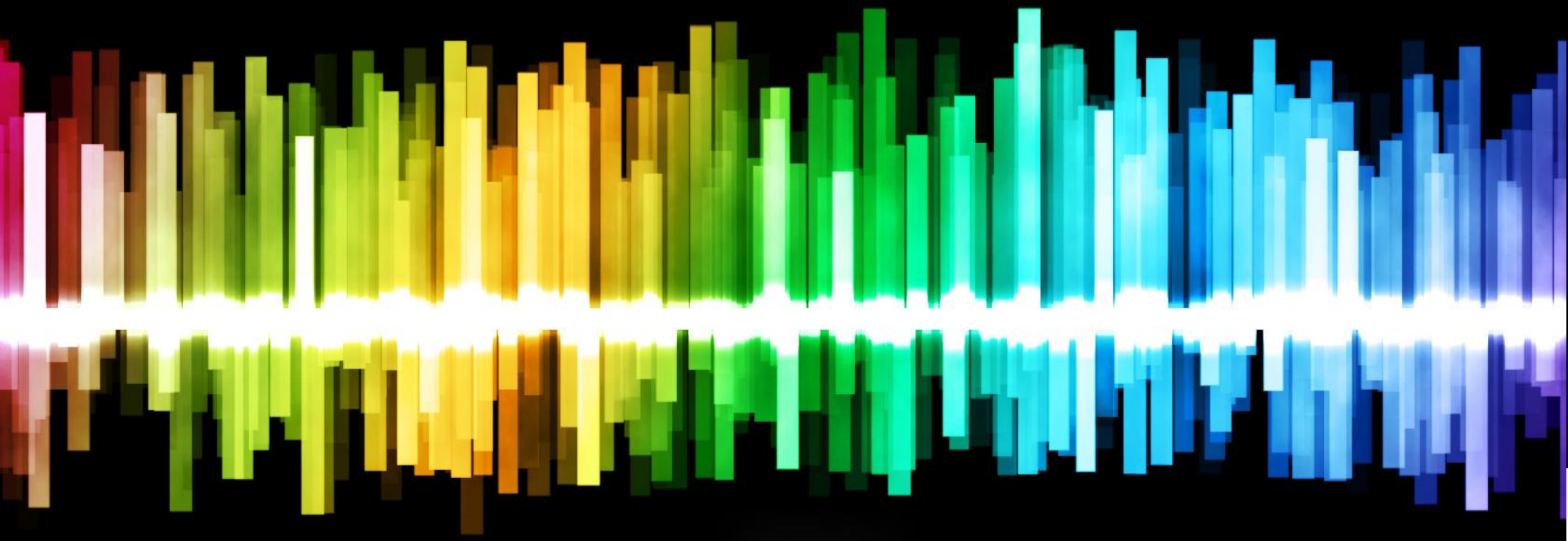
PATHOLOGY
TEAM 433

Pathology of TUBERCULOSIS



Objectives

At the end of this lecture, the student should be able to:

A) define tuberculosis

B)list the disease caused by mycobacteria

C)know the epidemiology of tuberculosis (TB)

D) list the conditions associated with increased risk of Tuberculosis

E)list the factors rep disposing to extension of the infection

F)recognize the morphology of Myobacterai and list spacial stain (the Ziehl-Neeslsen) as well as the morphology of granulomas in TB (tubercles)

Objectives

Continued …

G) in regard to Mycobacterial lung infection : Compare and contras the following in relation to their gross and histologic lung pathology:

1. primary tuberculosis (include a definition of Ghon complex)

2. secondary or reactivation tuberculosis

3. military tuberculosis

H) list organs other than lung that are commonly affected by tuberculosis .

I) know the basis and use of tuberculin skin (Mantoux) test

J) list the common clinical presentation of tuberculosis

k) list the complication and prognosis of tuberculosis

Definition

- TB is a always chronic communicable disease

Epidemic

- Affected by socioeconomic status
- Most common in many country.

Target

- Lungs are the prime target , although any other organ may be infected.

Caused by

- Mycobacterium tuberculosis hominis (Koch bacillus). Occasionally mycobacterium tuberculosis bovis

Reservoir

- Humans

Characteristic lesion

- Epitheloid granuloma with caseous necrosis

Mycobacterium tuberculosis

- Classified as: **acid-fast bacteria + bacilli .**
- **"lipoprotein + glycoprotein" cell wall gives it (resistance) to be killed by macrophages So they are hard to kill.**

- **it other name is called "Acid fast bacilli" . Why ? Because** stained by **Ziehl-Neelsen** stain which stain any organism has ACID

Stains used on the bacilli are

- **Ziehl-Neelsen stain & fluorescent dye auramine O**

Tuberculin test "skin test" +ve

- Presence of purified protein derivative (PPD) which is complex mixture of antigens that found M.tuberculosis

Bacteria cause TB:

People who are at risk of developing TB:

1. Poverty (poor people)
2. Crowding places
3. Malnutrition
4. Elderly
5. Immunocompromised patient " AIDS"
6. Diabetes mellitus
7. Immunosuppression drugs

TB is a granuloma disease

TB has classical caseous granuloma

Granuloma: aggregation of Epitheloid cells, altered & active macrophages

Also seen is langhans-type giant cell. And

Foreign body-type giant cell .

In TB there are areas with caseous necrosis

Leading to calcification (dystropic calcification)

Note: TB granuloma called as TUBERCLES.

Tubercles filled with necrosis becomes very soft & is called SOFT TUBERCLES

Pathogenesis of TB

M.tuberculosis

- **Inhalation**

alveolar macrophages recognize those then phagocyte it

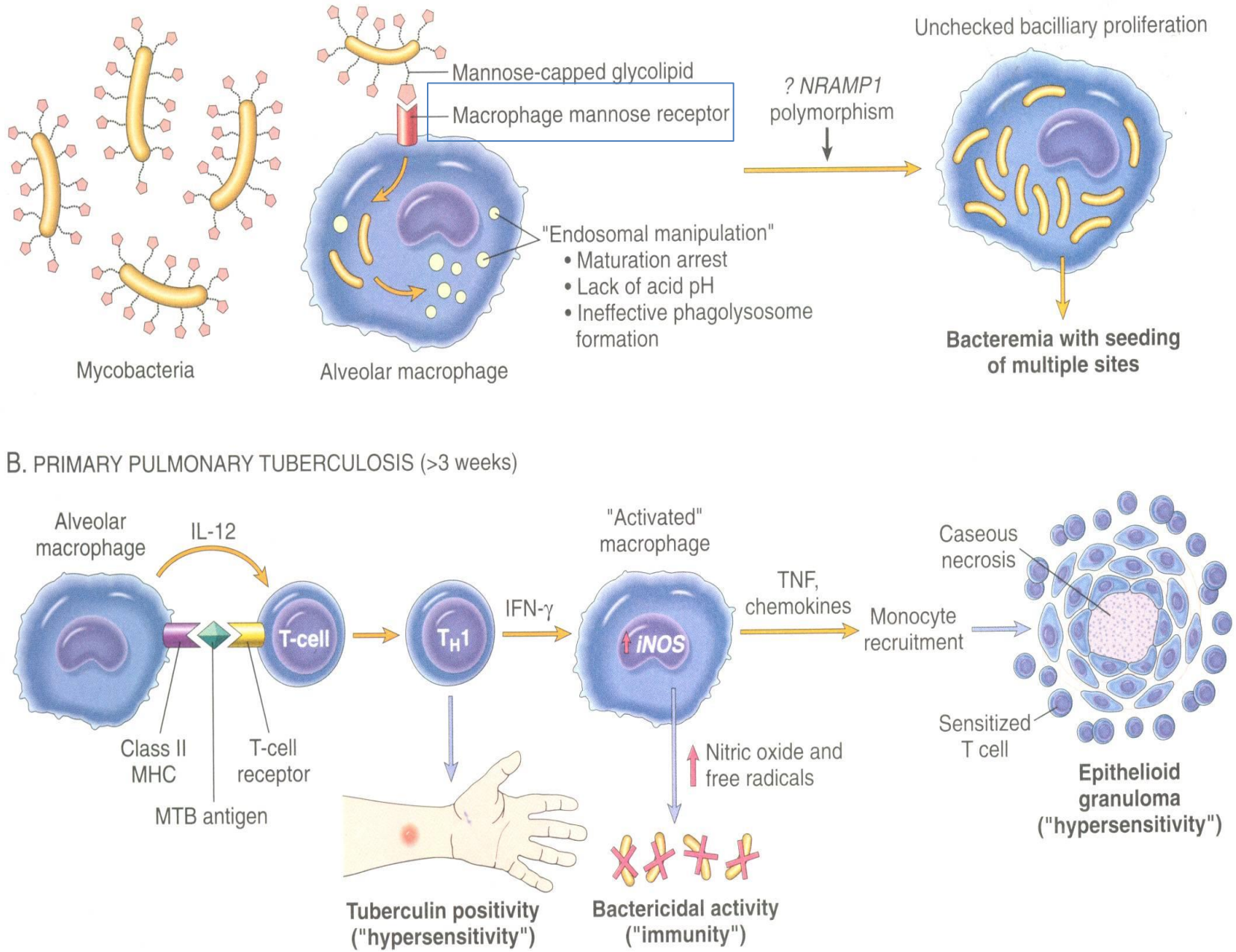
- bacteria by its receptors because the receptors are sensitive for carbohydratic substance is Called **"Mannose"** in outer surface of M.tuberculosis
- macrophages are incapable To kill it

Macrophages secrete IL12 > activate lymphocyte >- transformed into TH1 cells

TH1 cells secret interferon gamma (IFN-γ)

IFN-γ) acts on the macrophage to transfer it into epithelioid macrophages

Epithelioid macrophages (histiocytes/cells) collection is called granuloma which cause granuloma and necrosis


A. PRIMARY PULMONARY TUBERCULOSIS (0-3 weeks)
Mycobacteria
Mannose-capped glycolipid
Macrophage mannose receptor
Alveolar macrophage
"Endosomal manipulation"
• Maturation arrest
• Lack of acid pH
• Ineffective phagolysosome formation
? NRAMP1 polymorphism
Unchecked bacilliary proliferation
Bacteremia with seeding of multiple sites
B. PRIMARY PULMONARY TUBERCULOSIS (>3 weeks)
Alveolar macrophage
IL-12
T-cell
Class II MHC
T-cell receptor
MTB antigen
TH1
IFN-γ
"Activated" macrophage
↑iNOS
TNF, chemokines
Monocyte recruitment
Caseous necrosis
Sensitized T cell
Epithelioid granuloma ("hypersensitivity")
↑Nitric oxide and free radicals
Tuberculin positivity ("hypersensitivity")
Bactericidal activity ("immunity")

Bacilli's fate in the body

- Killed by immune system
- Multiply and cause primary TB
- Become dormant & remain asymptomatic
- Proliferate after period of time
- Immunosuppressed (primary progressive or miliary TB)

The course of TB depends on:
1- immunity of the patient.
2- total burden of organism.

Types of TB

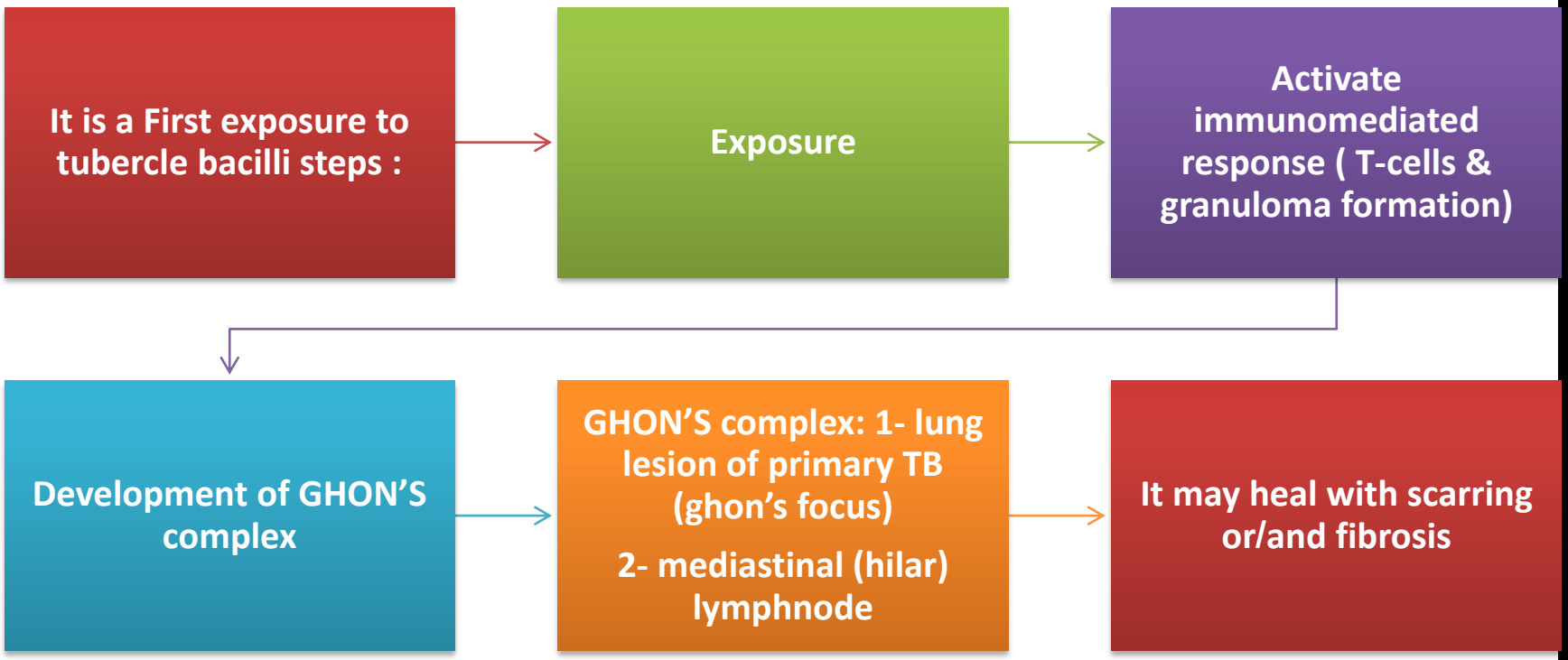
- Primary TB
- Secondary TB
- Miliary TB

TB when enter to lung can cause 2 lesion

- **Ghon focus:** dense lesion in peripheral area of lung **or** lower part of upper lobe **or** upper part of middle lobe.
- **Ghon complex:** Ghon focus + enlargement of lymph node

Primary TB

usually don`t have symptoms



Miliary TB

*TB characterized by milia that resemble seeds مجموعات كبيرة من البكتيريا منتشرة كالحبوب
*occur in primary TB and secondary TB
*Bloodstream spread of organisms produces miliary TB:

If the enlarging caseating erodes blood vessels , or lymph nodes

→

tubercle bacilli

are carried in the bloodstream to many parts of the body,

↓

including the remainder of

the lung, causing miliary tuberculosis

Secondary TB

symptomatic

It is post primary infection in immunized individual

May come from:

1- reactivation of primary TB.

2- New infection

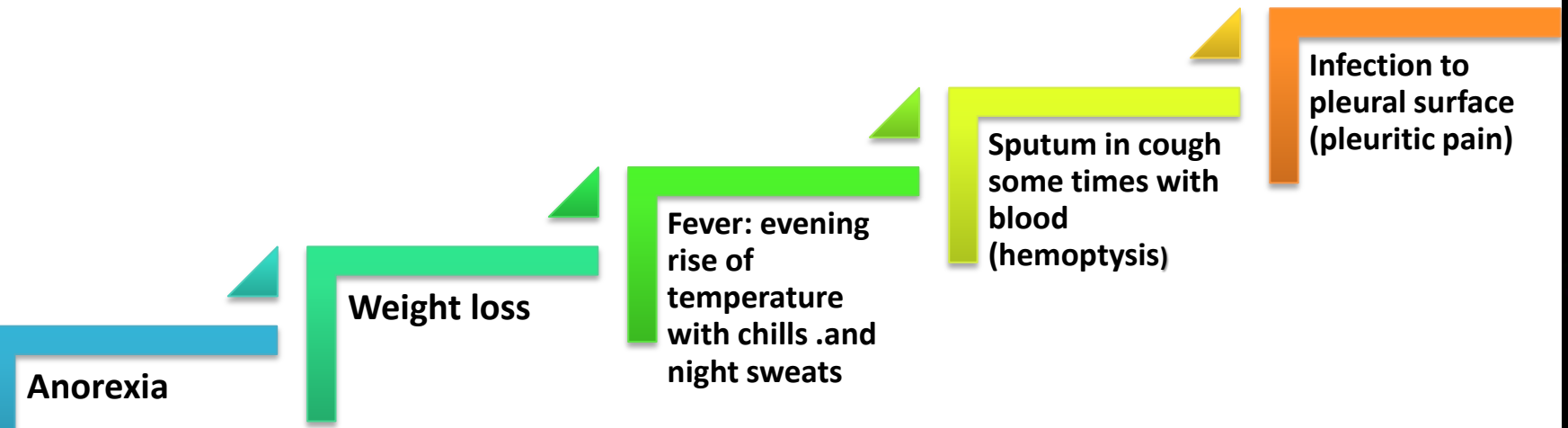
Starts at the apical or sub apical regions of the lungs (loves oxygen)

Patient now coughs sputum that contain active bacilli.

Grossly: big area with central cavitation full of necrosis & free bacilli

Histologically: central caseation & necrosis

Features of TB



Manifestations of TB depend on the organ system involved

Extrapulmonary TB

- Appear in any organ
- Most frequent lymph nodes (tuberculosis lymphadenitis)
- Liver & spleen
- Adrenals , epididymis & prostates , kidney
- Tuberculous meningitis , bone marrow
- Pott's disease
- Intestinal tuberculosis (contaminated milk)

Prognosis depends on:

1. Immunity
2. Kind of drugs the patient have
3. How many & which organs are involved
4. Wither the TB strains are drug resistant or not.

Investigations

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Mantoux test
(tuberculin test)

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Sputum by bronchial wash

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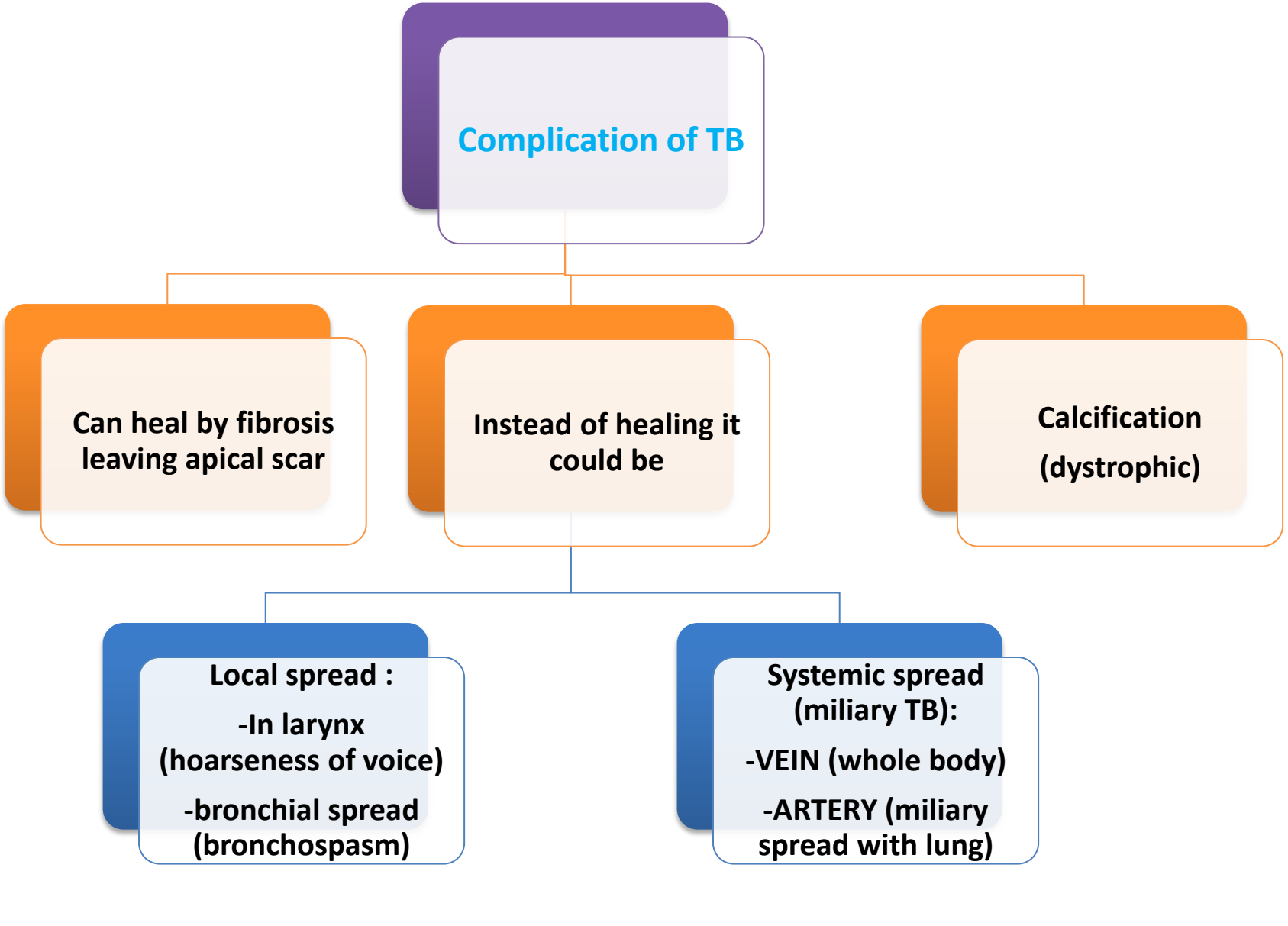
Biopsy

↓

Chest radiographs


Complication of TB
Can heal by fibrosis leaving apical scar
Instead of healing it could be
Calcification (dystrophic)
Local spread :
-In larynx (hoarseness of voice)
-bronchial spread (bronchospasm)
Systemic spread (miliary TB):
-VEIN (whole body)
-ARTERY (miliary spread with lung)

MCQS

1- immunocompromised patient came with TB at which level the pathogenesis stop:

a) TH1 activated.
b) Macrophages
c) Granuloma formation
d) Necrosis formation.

2- the lesion areas of Ghon's focus:

a) Upper part of the lower lobe.
b) Lower part of the upper lobe.
c) Around the main bronchus.
d) Both A+B
e) None of them

MCQS

3- TB test called:

a) Mantoux test.
b) Skin pricke test.
c) Both A+B
d) None of them

4- Result of TB:

a) Ceases necrosis
b) Edema
c) Granuloma formation
d) Both A+C
e) None of them

5- in TB when TH1 get activated it secrets :

a) IL-12
b) INF-**γ**
c) Both A+B
d) None of them

MCQS

6- what is the substances give M.tubeculosis pink colour in Ziehl-Neelsen stain :

a) PPD.
b) Lipoprotein
c) Glycoprotein
d) Both B+C
e) None of them

7- the macrophages can recognize M.tuberculosis by:

a) FAS recptor
b) Mannose receptor.
c) Intracellular receptor.
d) None of them

8- the macrophages can recognize M.tuberculosis because :

a) Has Glycoprotein + lipoprotein on its surface
b) Is parasitic.
c) Lack of Has Glycoprotein + lipoprotein on its surface
d) None of them

Answers: 1- B 2- D 3- A 4- D 5-B 6- A 7- B 8-A

Questions

1- can mycobacterium tuberculosis bovis transmit by inhalation ?

NO , it transmit by drinking unpasteurised milk

2- why mycobacterium tuberculosis is very strong and tough organism ??

because it has **(glycolipoprotein)** in its outer surface which increase resistant to sun , dry atmosphere …ETC ,

3- how do the macrophages engulf the M.TB??

they have a receptor for **mannose** which found in the outer surface of bacteria

4- when the tuberculin test is positive what does that mean ??

than mean the TH1 get activated and that does not mean the patient have the disease , its mean he met the bacteria before (ex: vaccine)

Questions

5- when does the pathogenesis of TB stop in immunocompromised patient ??
it stops at the level of macrophage
ex: HIV patient can't develop granuloma **(why)** because there is no activated T lymphocyte (no cellular immunity)i

6-what is gohn complex ??
enlarge lymph node + gohn focus

7-where dose secondary TB like to effect ??
apical part of the lung (upper part of both lobe (bilateral)

Team's members:

- Maha alzahrani
- Abdulrahman althaqib
- Lulwah alturki
- Zhour alhedgan
- Fahad alotaibi
- Areej alrajeh

http://youtu.be/S0Kak0qQFgM

https://www.khanacademy.org/partner-content/stanford-medicine/tuberculosis

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