PATHOLOGY TEAM 439

MED439 KING SAUD UNIVERSITY

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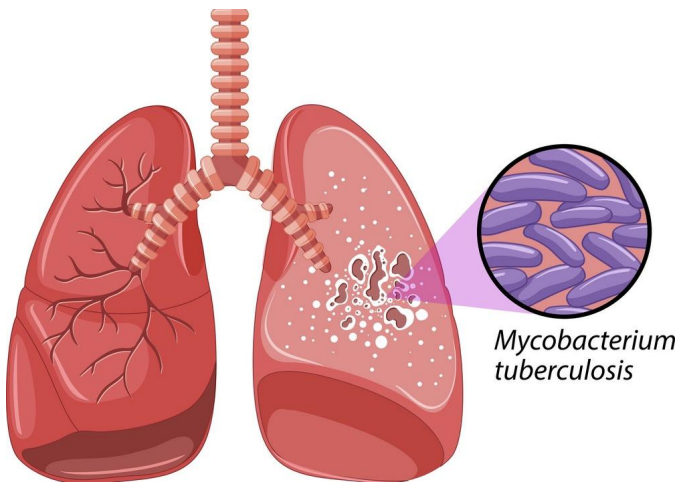


Pathology of TB

Objectives:

- Define tuberculosis
- Know the epidemiology of tuberculosis (TB)
- List conditions associated with increased risk of Tuberculosis
- Recognize the morphology of Mycobacteria and its special stain (the Ziehl-Neelsen) as well as the morphology of granulomas in TB (tubercles).
- Know the Pathogenesis of tuberculosis
- In regards to Mycobacterial lung infection: Compare and contrast the following in relation to their gross and histologic lung pathology:
  - Primary tuberculosis (include a definition of the Ghon complex).
  - Secondary or reactivation tuberculosis.
  - Miliary tuberculosis.
- List organs other than lung that are commonly affected by tuberculosis. Know the basis and use of tuberculin skin (Mantoux) test.
- List the common clinical presentation of tuberculosis.
- List the complication and prognosis of tuberculosis.

Rikabi's content

Index:
Important
NOTES
Extra Information

TUBERCULOSIS

Definition

Tuberculosis is a communicable chronic inflammatory granulomatous disease , that is caused by Mycobacterium tuberculosis.

It usually involves the lungs because it's very aerophilic but may affect any organ or tissue in the body. Typically, the centers of tuberculous granulomas undergo caseous necrosis.

Epidemiology

Contracted by inhalation of Mycobacterium tuberculosis (TB)
TB bacilli are strict aerobe, acid-fast (due to mycolic acid in cell wall)

It is estimated that 1.7 billion individuals are infected by tuberculosis worldwide, with 8 to 10 million new cases and 1.5 million deaths per year

Predisposing Factors

Tuberculosis flourishes wherever there is:

- Poverty
- crowding
- Malnutrition
- chronic debilitating illness

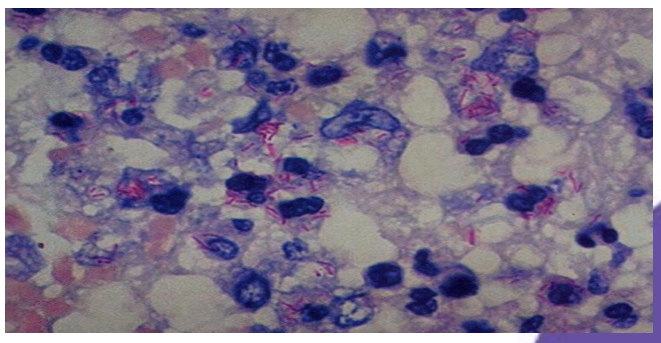
Increased risk factors

- People with AIDS
- Diabetes mellitus
- Hodgkin's lymphoma
- Alcoholism
- Chronic lung disease (particularly silicosis)
- Immunosuppression

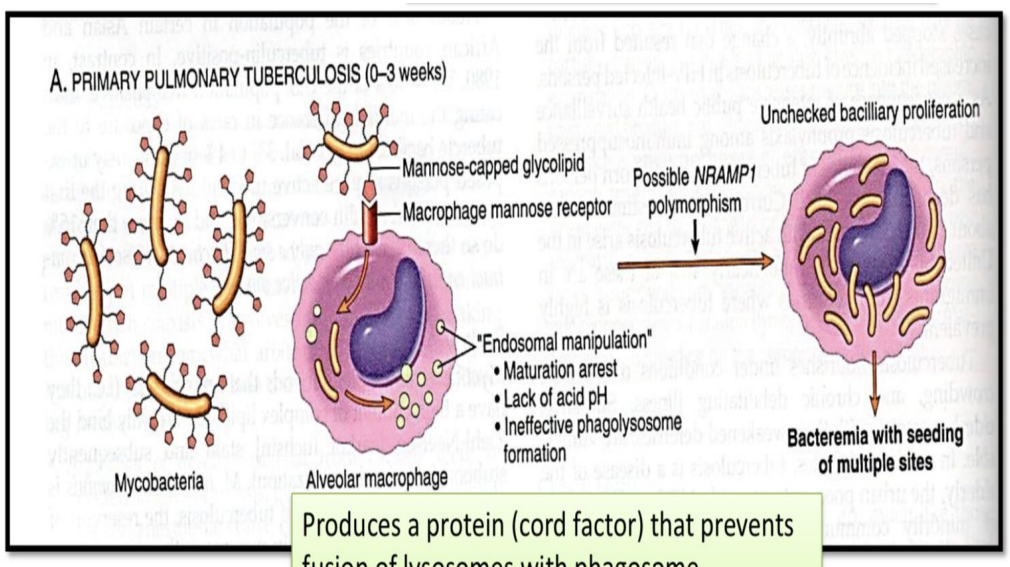
Etiology

- M. Hominus (human—>transmitted via aerial droplets)
- M. Bovis (cows—>transmitted through unpasteurized milk—>goes to lymph node)
- M. Avium (atypical—>only in immunocompromised—>No granulomas)

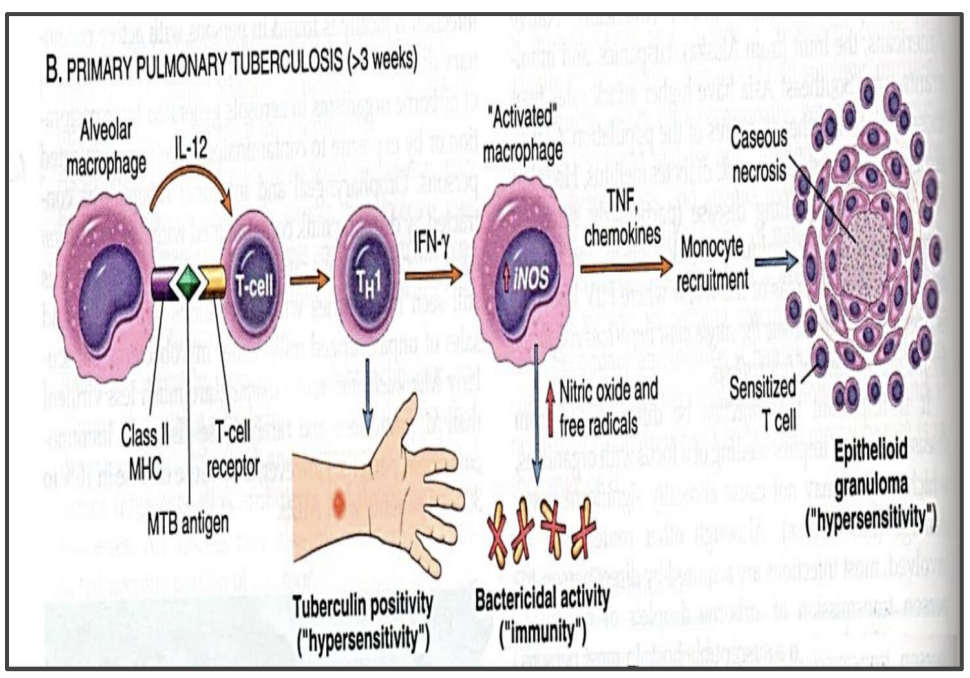
Elongated bacilli stained with ZNS because it's acid fast bacilli that resists the discoloring by alcohol (not stained by gram stain because of the mycolic acid



The pathogenesis of primary TP



Produces a protein (cord factor) that prevents fusion of lysosomes with phagosome



Person is infected by MTB by inspiration,that's goes to lung and meet the alveolar macrophage

(1) in the alveolar macrophage , there's receptor Called (macrophage mannose receptor that bind with a molecule present on the surface of bacteria called mannose capped glycolipid

2. By the receptor macrophage recognize the bacteria and start phagocytosis

3. Bacteria releases cord factor that prevent fusion of lysosomes with phagosome

4. As a result, there's intracytoplasmic proliferation of bacteria within the macrophage

5. After 3 weeks , it goes to lymphatic tissue (lymph node)

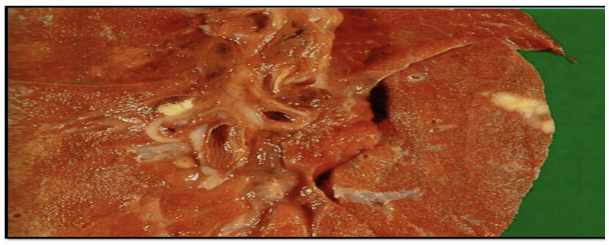
6.As APC that presents the antigen through MHCII that identified by T cell , leading to activate Th1
As result of stimulation of Th1 , there's a releasing of chemokines and IFN-gamma that activates macrophage

7.Activated macrophage becomes large and have abundant NO , free radicals , release TNF that increases the recruitment of monocytes toward the focus of infection.
All that leading to form a
Collection of activated macrophages and lymphocytes (Granuloma)

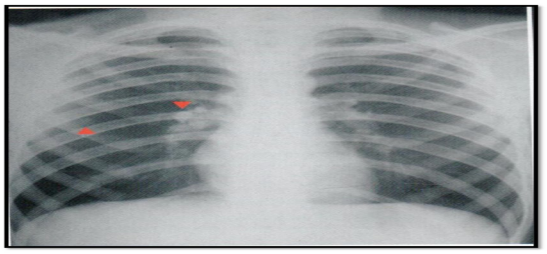
Every single step above will lead to kill many of the bacteria .
some of them remain alive but won't cause disease because it's under CMI controlling

The morphology primary TP

Morphology Of primary TB	-is the first exposure to MTB. The infection occurs in middle lobe, below the pleura (Subpleural location) or (Upper part of the lower lobes or lower part of the upper lobes). -**ghon focus(caseous necrosis) in periphery.** -**Ghon complex (caseous necrosis) in ipsilateral hilar lymph nodes** - Microscopic lesion is granuloma
The outcome	1-Tuberculin test will be converted into +ev after 3 weeks 2- The result of stimulation with good immunity= majority of MTB are died and followed by fibrosis with calcification as healing response lead to form focus (later on rank complex is gunna develop) 3-The infected person is asymptomatic or flu like symptoms 4- 90% will have sero+ev (infected)! and only 2-5 cases will develop a disease .



Primary tuberculosis, microscopic
Ghon complex



Primary tuberculosis, radiograph
Ghon complex with calcification

Secondary Tuberculosis

Definition	the pattern of disease that arises in a previously sensitized host, it arises due to **reactivation** of dormant primary lesions or due to **reinfection**
Site	Classically localized to the apex of one or both upper lobes. Why? The reason is **obscure** but may relate to high oxygen tension in the apices
Complications	Miliary Tuberculosis**(Tertiary TB):** **Haematogenous spread** of TB organism throughout the body ***Usually Occur more in Secondary TB**

From the definition:

secondary TB arises from **reactivation** of latent/ primary TB,
or
could be the result of **new TB infection** added to the old TB
(in immunocompromised)

As a result:

The Immune reaction will be much stronger affecting the upper lobe, uni/ bilateral

And then:

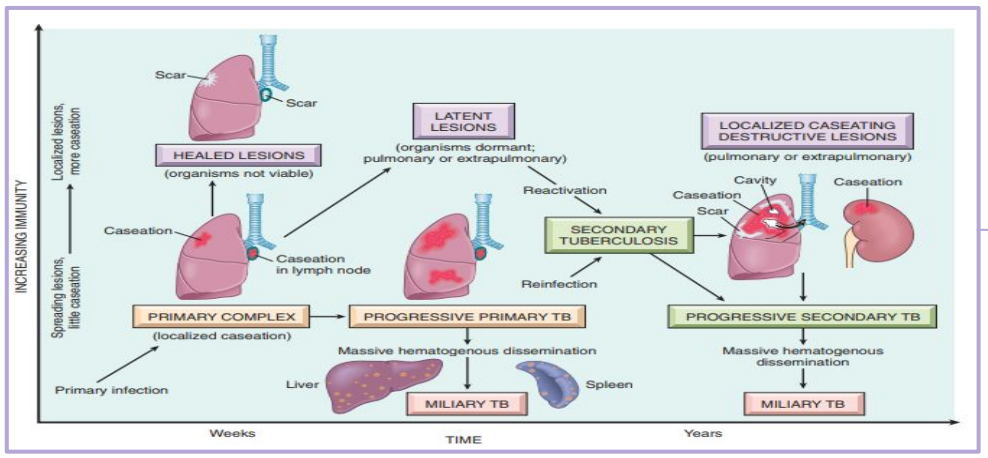
The tissue tends to wall off the focus. resulting in that the regional lymph nodes are less prominently involved early in the disease(in comparison with Primary TB)

Which can lead to:

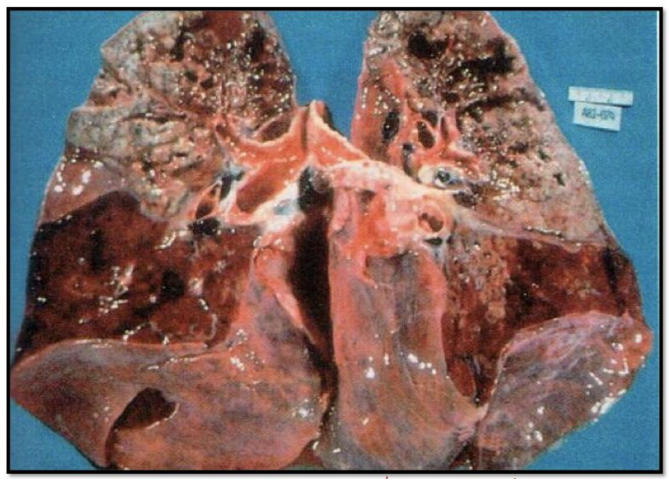
cavitation occurs readily in the secondary form, leading to **erosion** into and dissemination along airways. Such changes become an important source of **infectivity**
(Secondary TB marked by formation of cavitation contains many bacilli that enter the bronchial tree and coughed so that the patient is infectious

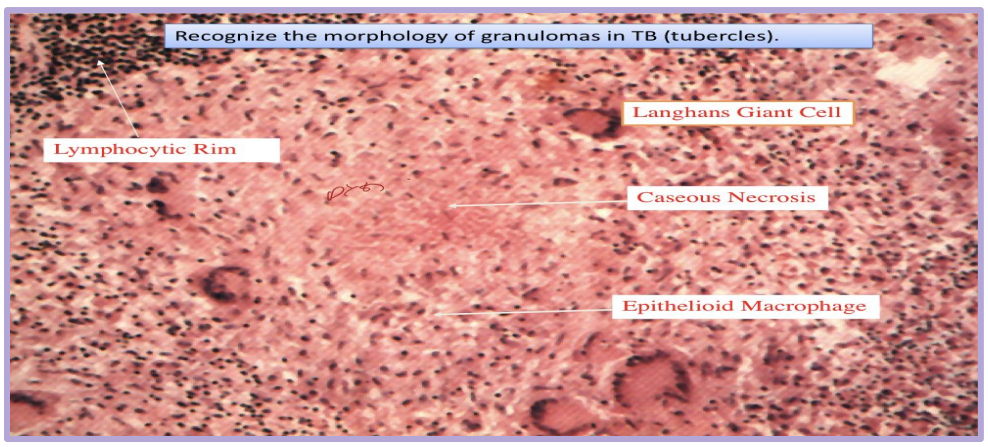
tuberculosis can be acquired through the consumption of Unpasteurized dietary products, (intestinal TB, caused by *Mycobacterium bovis*)

If the erosion happened through a lymph node, it can infect other lymph nodes, and then enter the systemic circulation, it can also erode directly to arteries or veins, to enter the systemic circulation (Which will cause miliary TB)



Secondary Tuberculosis (Reactivation Tuberculosis)





Miliary Tuberculosis

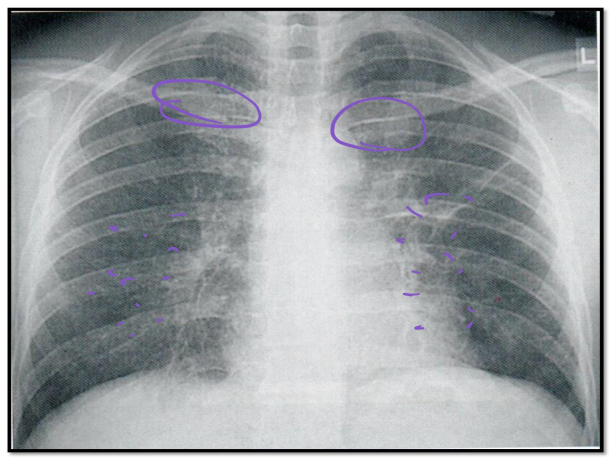
Miliary Tuberculosis**(Tertiary TB): Haematogenous spread** of TB organism throughout the body
***Usually Occur more in Secondary TB**

Pulmonary miliary TB:

Occurs when organisms reach the bloodstream through lymphatic vessels and then re-circulate to the lung via the pulmonary arteries.
The lesions appear as small (2-mm) foci of yellow-white consolidation scattered through the lung parenchyma.

Miliary Tuberculosis:

when bacteria in the lungs ruptures the macrophages and enters the pulmonary venous return to the heart; the organisms subsequently disseminate through the systemic arterial system and the lymphatic channels



Miliary tuberculosis, radiograph

Systemic miliary TB:

is most prominent in the liver, bone marrow, spleen, adrenal glands, meninges, kidneys, fallopian tubes, and epididymis. Multiple small yellow nodular lesions in several organs (Almost every organ in the body may be seeded. Lesions resemble those in the lungs).

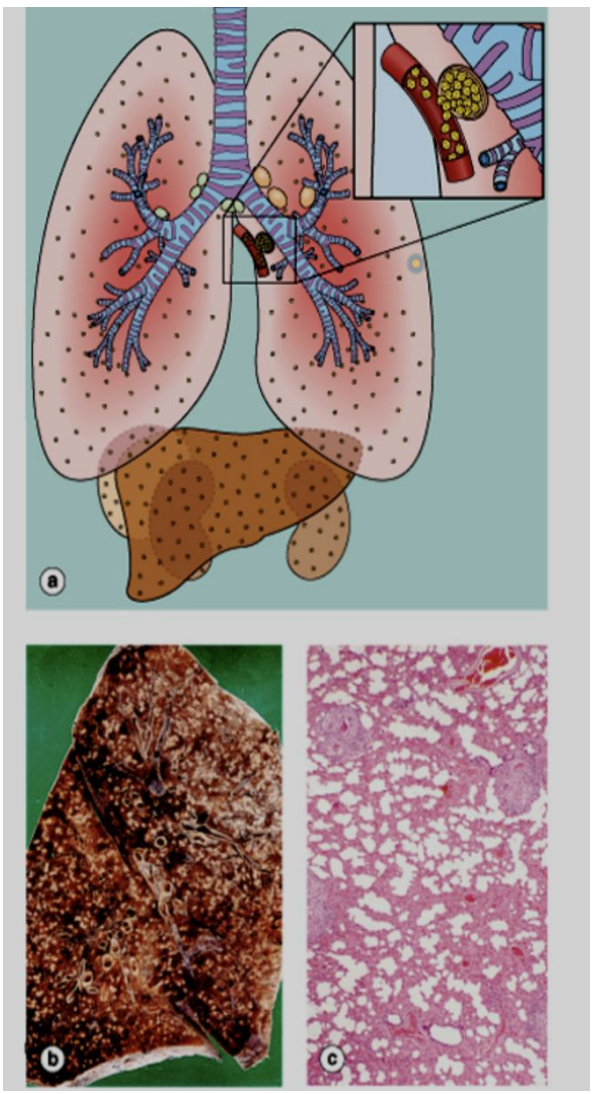
***Granulomas are the same as in the lung**

Isolated-organ TB (Extrapulmonary TB):

(effects all the organs , not imp to know them all just Pott's)

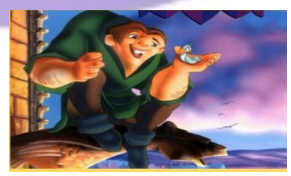
May appear in any **one** of the organs or tissues seeded **hematogenously**, and It Usually effects:

- Lymph nodes (tuberculous lymphadenitis): are the most frequent form of extrapulmonary tuberculosis esp. in the cervical region(Scrofula),
- Pleura with pleural effusion (exudate) Causing severe pain,
- Liver and spleen,
- Adrenals,
- Fallopian tube (**Tuberculous salpingitis**) Causing Infertility and endometrium,
- Epididymis and prostate,
- Kidneys,
- Meninges around the base of the brain (tuberculous meningitis), Brain causing tuberculous encephalitis or some times tuberculoma.
- Bone marrow,
- **Vertebrae (pott's disease)**
- Intestinal TB



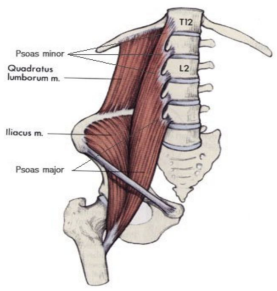
Pott's disease

*destruction of the vertebrae



- It collapses the spine and leads to paraspinal "cold" abscesses.
  why it's cold ?
  usually abscess caused by pyogenic bacteria, they produce large amount of chemical mediators ,eg: prostaglandinE , TNF so the body temperature will be high
  but in cold abscess the amount of chemical mediators not that much so the body temperature will be low.

- in these patients, infected material may track along the tissue planes to present as an abdominal or pelvic mass.



caseous material from the collapsed vertebrae will be pushed to the attached muscle (psoas muscle) then it will accumulate around the hip and cause hip pain and collection of caseous material in the psoas muscle "psoas abscess"

Clinical Features

may be asymptomatic especially in primary TB (only 5% show clinical features)

Systemic manifestations:
1-Weight loss,Night sweats

2-Hemoptysis is present in about half of all cases of pulmonary tuberculosis.

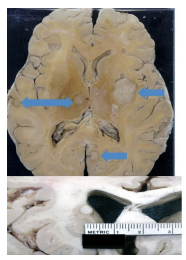
3-Fever (low grade)

4-Anorexia , malaise

5-Extrapulmonary manifestations (if the mycobacterium spreads)of tuberculosis are legion and depend on the organ system involved, For example:

1 Tuberculous salpingitis(1) may present as infertility.

2 Tuberculous meningitis may present as headache and neurologic deficits.



3 Pott disease may present with back pain and paraplegia(2)

(1):inflammation of the fallopian tube
(2):paralysis of the lower limbs,due to injury to the vertebrae

DIAGNOSIS

01

Demonstration of acid-fast organisms in sputum:

1.Sputum analysis

2.Culture (best way, to test susceptibility)

normal culture takes ~ 10 weeks

liquid culture in 2 weeks

3.PCR(detection of bacterial DNA)

02

Chest X-ray:

1.primary TB ; lateral lesions and hilar lymph node

2.secondary TB : apical lesion

3.miliary TB : multiple lesions

03

ziehl-neelsen (AFB) stain

04

auramine stain (immunofluorescence)

05

Mantoux (tuberculin) skin test/PPD:

- SC injection of 0.1ml PPD, then we look for erythema and for the size of induration(redness and swelling) is measured 48– 72 hours later because it's delayed hypersensitivity.
- Positive skin test result(patient has been exposed to bacilli) : signifies cell-mediated hypersensitivity to tubercular antigens ,induces a visible and palpable induration(at least 5 mm in diameter). Helps when patient is not vaccinated or from non-endemic areas
- False-negative : reactions may be produced by certain viral infections, sarcoidosis,malnutrition, Hodgkin lymphoma, immunosuppression and AIDS. يكون عنده تي بي بس تطلع النتيجة نقيتف . Helpful in endemic areas.
- False-positive : reactions may result from infection by atypical mycobacteria.
- does not differentiate between infection and disease

PROGNOSIS

if infections are by drug-resistant strains or occur in aged debilitated, or immunosuppressed persons, they are **at high risk for developing miliary TB**

if infections are localized to the lungs,with proper treatment the prognosis is generally **good**

Qulz

1- 20-year-old man from China is evaluated for persistent cough, night sweats, low-grade fever, and general malaise. A chest X-ray reveals findings "consistent with a Ghon complex." Sputum cultures grow acid-fast bacilli. Examination of hilar lymph nodes in this patient would most likely demonstrate which of the following pathologic changes?			
a- caseous necrosis	b- fat necrosis	c- Fibrinoid necrosis	d- Liquefactive necrosis
2- A 48-year-old man with AIDS is admitted to the hospital with a fever of 38°C (103°F), night sweats, persistent cough, and prolonged diarrhea. His CD4 cell count is less than 300/µL. Stool culture reveals the presence of acid-fast bacilli. Which of the following pathogens is responsible for this patient's respiratory and gastrointestinal disease			
a- Campylobacter jejuni	b- Cryptosporidium	c- Mycobacterium avium-intracellulare	d- Streptococcus pyogenes
3- A 53-year-old man develops weakness, malaise, cough with bloody sputum, and night sweats. A chest X-ray reveals numerous apical densities bilaterally. Exposure to Mycobacterium tuberculosis was documented 20 years ago, and M. tuberculosis is identified in the sputum. The patient subsequently dies of respiratory insufficiency. The lungs are examined at autopsy). Which of the following best characterizes the histopathologic features of this pulmonary lesion?			
a- Acute suppurative inflammation	b-Chronic inflammation	c- Granulomatous inflammation	d- Fibrinoid necrosis
4-:A 22-year-old man with AIDS complains of persistent cough, night sweats, low-grade fever, and general malaise. A chest X-ray reveals an area of consolidation in the periphery of the left upper lobe, as well as hilar lymphadenopathy. Sputum cultures show acid-fast bacilli. Which of the following is the most likely diagnosis?			
a- Bronchopneumonia	b- Pulmonary abscess	c- Sarcoidosis	d- Tuberculosis
5-A 53-year-old man develops weakness, malaise, cough with bloody sputum, and night sweats. A chest X-ray reveals numerous apical densities bilaterally, some of which are cavitary. Exposure to Mycobacterium tuberculosis was documented 20 years ago, and M. tuberculosis is identified in his sputum. Which of the following describes the expected lung pathology in this patient?			
a- Plasma cell infiltration	b- Granulomas	C-Dense fibrosis	d-Interstitial pneumonia

1-A ,2-C , 3-C , 4-D , 5-B

Summary

Tuberculosis

General considerations	• Tuberculosis occurs worldwide, with greatest frequency in disadvantaged groups. • In the pulmonary form, it is spread by inhalation of droplets containing the organism Mycobacterium tuberculosis (also referred to as the tubercle bacillus).
Types of tuberculosis	• **Primary TB:** - It's the initial infection, characterized by the Ghon complex, the combination of a peripheral subpleural parenchymal lesion and involved hilar lymph nodes. - Primary tuberculosis is most often asymptomatic. It usually does not progress to clinically evident disease. • **Secondary TB:** - Usually results from activation of a prior Ghon complex, with spread to a new pulmonary or extrapulmonary site.
Pathologic changes	**A.** Localized lesions: usually in the apical or posterior segments of the upper lobes. Involvement of hilar lymph nodes is also common. **B.** Tubercle formation: The lesions frequently coalesce and rupture into the bronchi. The caseous contents may liquefy and be expelled, resulting in cavitary lesions. Cavitation is a characteristic of secondary, but not primary, tuberculosis; caseation (a manifestation of partial immunity) is seen in both. **C.** Scarring and calcification.
Spread of disease	**A.** Secondary tuberculosis may be complicated by lymphatic and hematogenous spread, resulting in miliary tuberculosis, which is seeding of distal organs with innumerable small millet seed-like lesions. **B.** Hematogenous spread may also result in larger lesions, which may involve almost any organ. **C.** Organs typically involved include: Meninges, fallopian tube" Tuberculous salpingitis", vertebrae"Pott disease", Lymphadenitis in the cervical region "Scrofula".

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