

#Helper-team

## Lec 9

### Granuloma and Tuberculosis

**Granuloma:** is chronic specific inflammation it's collection of macrophages and other inflammatory cells around bacteria or any foreign body. specific (يعنى فيه حاجات معينه تعرفنا على نوع الالتهاب)

ال granuloma دى عبارته عن رد فعل التهابى من الجسم عبارة عن كتلة من macrophages و خلايا التهابية بتحيط الحاجه الى دخلت الجسم

- **Infective granulomas:** such as tuberculosis, leprosy, sarcoidosis, and syphilis

#### Tuberculosis (TB) (السل)

Def: it's chronic **infective granuloma** Caused by bacteria called **tubercle bacilli** (mycobacterium tuberculosis)

يعنى ده نوع من انواع ال granuloma الى تسبب فيه دخول ال tubercle bacilli

#### Method of infection:

1) **inhalation:** of bacteria from a patient with active TB through **coughing** or **sneezing** (human tubercle bacilli)

واحد واصحابه بيخمسوا فى شيشه مثلا ابقو غيرو الى الطبى بقى هه

2) **ingestion:** of contaminated unpasteurized milk (bovine tubercle bacilli (حيوانية

**The primary field of infection:** دي الاماكن الي بيبدأ فيها المرض

1. Lung
2. Intestine
3. Tonsils and lymph nodes

#### Tubercle (tuberculous granuloma)

• It's basic unit of **tuberculosis**. It's microscopic structure contain of collection of **chronic inflammatory** cells, **caseation** necrosis and **fibrosis** around the tubercle bacilli

• it's considered as the **reaction of tissue against T.B bacilli**.

#### Microscopic (mode of formation)

1) Macrophages: are attracted by the lipid part of the bacilli. They engulfed the bacteria and process it and present its antigen (tuberculo-protein) to other immune cells.

2) Epithelioid cell : are altered macrophage . They appear swollen and pink like epithelial cells they are the **essential membrane in tubercle**

3) Langhan's giant cells: are fused epithelioid cell  
They are large cells containing nuclei arranged in horseshoe pattern in the cell periphery

4) T lymphocytes: responsible for **hypersensitivity** and **caseation necrosis** due to reaction of **lymphokines**

5) fibroblasts: causes peripheral fibrosis around tuberculosis lesion

6) central caseation necrosis : combine features

7) neutrophil: are attracted to the polysaccharide part of bacilli (و بتموت)

**Grossly:** fused tubercle form **yellow nodule** .  
They appear soft and cheesy due to caseation

### **Mechanism of caseation** (أسباب حدوثها)

• **Hypersensitivity:** between the **lymphokines** secreted by T lymphocytes and **antigen** of tubercle bacilli (tuberculoprotein)

الى اظهر ال antigen ده ال macrophages

• **Ischemia** (انقطاع الدم): due to **endarteritis obliterans** ( التهاب البطانة الداخليه )  
(للشرايين)

**Fate of tubercle:** مصيره ايه

**A) High immunity:**

1) small tubercle are completely fibrosed بترجع ذى الاول

2) Fused tubercles are capsuled by fibrous tissue and it's central caseation part show dystrophic calcification .living bacteria may remain in the lesion

فالحاله دى لو المناعه ضعفت ال fibrous هيتكسر وهتطلع تانى

**B) Low immunity (lesion spread)**

Methods of spread:

1) **Direct spread** to surrounding

2) **Lymphatic spread** to the regional lymph nodes

3) **Blood spread:**

a) **No effect:** if **small** number of bacteria reach blood

b) **Isolated organ tuberculosis:** if **moderate** number of bacteria reach blood

The bacteria settle in one or few organs causing lesion

C) **Miliary tuberculosis:** if **large** number of bacteria reach blood

4) **Intracanalicular spread:** spread by natural passages or space as trachea and bronchi

5) **Reactivation** of the capsulated fibrosed lesion occurs in person with low immunity leading to **secondary tuberculosis.**

primary tuberculosis	secondary tuberculosis (reinfection)
It occurs when the body is infected for the <b>first time</b>	•it occurs when the body is infected for the <b>second</b> time or <b>vaccinated.</b>
It mainly affects <b>children</b>	•it mainly affects

<ul style="list-style-type: none"> <li>• Spread of infection is <b>more</b> common.</li> <li>•Tissue destruction is <b>less</b> marked.</li> <li>•Caseation is <b>slow</b></li> <li>• It involves: lung, tonsils, lymph nodes, intestine, and skin.</li> </ul>	<p><b>adults</b></p> <ul style="list-style-type: none"> <li>•Spread of infection is <b>less</b> common due to the presence of immunity.</li> </ul> <p>Tissue destruction is <b>more</b> marked due to the presence ,hypersensitivity.</p> <ul style="list-style-type: none"> <li>•Caseation is <b>rapid</b>.</li> </ul> <p>It occurs <b>anywhere</b> in the body.</p>
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## **Pulmonary tuberculosis :**

### **Primary pulmonary tuberculosis:**

Definition: it's follows the **first infection** of the lung with tubercle bacilli. It's called **childhood** type.

Infection is by **inhalation** of the human bacilli.

•Pathological features:

#### **1)Ghon's focus** بؤرة

Grossly:

- Tubercle at the peripheral of the lung under the pleura
- it is usually found in the lower portion of the upper lobe or the upper portion of the lower lobe
- The lesion takes the form of **small focus** about 1cm in diameter which **later caseates**

**Microscopically:** Ghon's focus consists of multiple tubercles macrophages, epithelioid cells, giant cells, peripheral lymphocytes and fibroblasts with central of caseation necrosis

**2 The lymph vessels** show multiple tubercles

### 3- The lymph nodes show many tubercle

**Fate of primary pulmonary tuberculosis same as the fate of Tubercle**

### Secondary pulmonary tuberculosis

Definition: it follows the **second** infection or **reactivation**

It is called **adult** type of tuberculosis.

Infection is exogenous by inhalation or endogenous by reactivation

### Grossly:

1- Apical cavitation: The wall of the cavity is at **first** irregular, and caseating, but **later** on it becomes smooth due to fibrosis.

The blood vessels may be destroyed causing severe **hemoptysis**

هيكح دم

2- Lymph nodes are not involved (عشان المناعة بتوقفها قبل ما توصل للعقد)

### Microscopically

1) multiple tubercles macrophages, epithelioid cells, giant cells, peripheral lymphocytes and fibroblasts with central of caseation necrosis

2) Fibrosis and endarteritis obliterans

### Complications of secondary pulmonary tuberculosis :

1) Hemoptysis due to erosion of blood vessels in the cavity

2) pneumothorax rupture of the cavity into pleura resulting in **pneumothorax** يعني الرئة بتفتح على الكيس الي محاطها و بتتكمش

3) Right sided heart failure may develop due to bilateral lung fibrosis

لما الرئة تتسد نتيجة ال fibrosis فالقلب بببذل مجهود اكبر عشان يعدي الدم للرئة

4) Reactive secondary amyloidosis

5) Fate of tubercle (انتقلت فوق)

## Intestinal tuberculosis

### 1- Primary intestinal tuberculosis:

بتسبب عدوى فمكان الدخول وال lymph nodes و ال lymph vessels

**Causes: ingestion of bovine (من بقرة تعبانة) or human bacilli in milk**

(بينتقل للطفل عن طريق لبن الام اللي بيكون فيه بكتيريا لما تصاب هي بالسل)

#### Pathology:

Primary intestinal complex composed of:

1. **Tubercles in Peyer's patches at terminal ileum.** البكتيريا بتحب تبلطح  
عالحته دي

2. **Ulcers with undermined edges.**

حروف القرخ دي بتبقى متشقلبة لجوه وبيسموها كمان flusk-shaped عكس بتوع ال malignant  
tumors اللي بيبقو لبره (raised everted edges)

3. **Tuberculous lymphangitis.**

4. **Tuberculous lymphadenitis: the mesenteric lymph nodes**  
become enlarged, caseous, and adherent (**Tabes mesenterica**)

الدنيا كلها بتلرزق فبعضها وتعمل كتلة كبيرة اللي هي Tabes mesenterica

#### Complications:

نفس ال general (بتوع ال fate of the tubercle) صفحة 3

### 2- Secondary intestinal tuberculosis

**Cause: ingestion of sputum in patients with chronic fibrocaceous pulmonary tuberculosis.**

نسبة السل الرئوي اكثر من المعوي، ولو المريض ماتعالجش منه كويس ممكن البكتيريا تتبلع مع البلغم  
وتسبب سل معوي.

**Pathology:** (شبه ال primary)

1. **Tubercles in the Peyer's patches at terminal ileum.** بس بيبقو اكثر

2. **Tuberculous ulcers with the following characters:**

a. **Multiple**

- b. Undermined edges
- c. Soft caseous floor
- d. Heals by fibrosis
- e. Transverse

بتكون بالعرض وده اللي بيفرقها عن القرحة بتاعت ال typhoid واللي بتكون بالطول

### 3. No lymphangitis and no lymphadenitis.

#### Complications:

1. Intestinal hemorrhage.
2. Intestinal fistula. ممكن تفتح الامعاء على حاجة تانية.
3. Perforation of the ulcers leading to peritonitis.
4. Reactive secondary amyloid.

#### Fate of the tubercle:

ال general برضو (صفحة 3)

#### Pott's disease:

#### Tuberculosis of the vertebrae (هما الاتنين نفس الحاجة)

**Causes:** secondary tuberculosis. The bacteria reach the vertebrae by blood.

الفقرات مش من ضمن اماكن الدخول عشان كده مافهانش primary lymphatics والعظم مالوش. عشان كده بتوصل للفقرات بالدم بس.

#### Site:

1. Lower thoracic vertebrae. (بتيجي مع ال pulmonary tuberculosis)
2. Upper lumbar vertebrae. (بتيجي مع ال intestinal tuberculosis)
3. Cervical vertebrae. (دي بقى بتيجي مع ال tonsillar tuberculosis)

#### Pathological features:

Two or more adjacent vertebrae as well as the intervertebral disc are destroyed by caseation necrosis.

ال malignant tumor مالوش دعوة بال discs، لكن ال T.B بتاكل كله سواء فقرات او ديسكات.

**Pott's disease is characterized by three main features:**

1. **Kyphosis** (انحناء للخلف), **scoliosis** (انحناء جانبي), **lordosis** (انحناء للأمام) due to collapse of the destroyed vertebrae.
2. **Cold abscess: accumulation of caseous material in a localized area and opening through the skin by sinus tract.**
3. **Paraplegia** (شلل النصف السفلي) in about 10% of cases due to :
  - a. **Spinal cord compression by tuberculous granulation tissue.**
  - b. **Ischemia which is caused by endarteritis obliterans.**  
الشرايين التهابت واتسدت فبالتالي الدم مش هيوصل
  - c. **Traumatic cord injury by fractured vertebrae.**

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## **SYPHILIS**

**Definition:** it's an infectious venereal disease caused by the spirochete **Treponema pallidum**.

الزهري هو مرض تناسلي يحصل بسبب نوع من البكتيريا الحلزونية اسمه بالبرتقالي فوق اهو.

**Mode of infection:**

- a. **Sexual contact with infectious lesions.** The bacteria can penetrate intact mucous membrane.
  - b. **From mother to fetus during pregnancy.**
  - c. **Blood product transfusion.**
  - d. **Occasionally through breaks in the skin that come into contact with infectious lesions.**
- **Syphilis is usually classified into 4 stages: primary, secondary, latent, and tertiary. It can be either acquired or congenital.**

- في ناس بتعتبر ال latent stage او (فترة الراحة) دي مش مرحلة اساساً وان الزهري ليه 3 مراحل بس.
- ال primary وال secondary هدفهم العدوى، بعد كده بقى البكتيريا بتكون دخلت الجسم خلاص وبدأت تتعامل.



## **Acquired syphilis:**

Treponema pallidum rapidly penetrates intact mucous membranes or microscopic dermal abrasions and, within a few hours, enters the lymphatics and blood to produce systemic infection.

### **1- Primary stage (chancre):**

**Onset:** 2-6 weeks after infection.

**Site of chancre:** (site of transmission)

- a. **Genital organs:** penis, vulva, vagina and cervix.
- b. **Extra genital:** lips, tongue, nipple and anus.

**Grossly:**

1. **Chancre begins as a hard, painless, small papule.**
2. **Chancre rapidly becomes an ulcer.**
3. **It is highly infective.** بسبب الافرازات الكثيرة
4. **It heals by minimal fibrosis (thin scar).**
5. **The regional lymph nodes are enlarged.**

**Microscopically:**

1. **Endarteritis obliterans.**
2. **Perivascular plasma cells and lymphocytes.**
3. **Granulation tissue and fibrosis.**

(ال3 دول package واحدة ببيجو مع بعض)

- معلومة مالهائش لازمة بس هحطها بلون فاتح علشان تلفت نظرك برضو: بيقولو ان (chancre) يعني بركان وسموها كده علشان افرازاتها الكثيرة عاملة زي الحمم البركانية كده وهي نفسها عاملة زي البركان.

### **2- Secondary stage:**

During this stage, spirochetes multiply and spread throughout the body.

**Onset:** it starts about 2 months after the primary stage.

**Pathological features:** هنا البكتيريا بقت كتيرة وانتشرت فالجسم وبدأت تطلع سموم

- I. **Systemic manifestations** include malaise (ارق), fever, myalgia (الم عضلات), arthralgia (الم مفاصل) and lymphadenopathy (تضخم ال lymph nodes)
- II. **Skin lesion:**
  - a. **Skin rash:** widespread mucocutaneous lesions involve the palms, soles and oral mucosa. The rash may take the form of macules (بقع حمراء), papules (حبوب) and pustules (اكياس صديدية).
  - b. **Condyloma lata:** raised warty swelling occurring in warm moist sites of the genitals and perineum.
  - c. **Patchy alopecia** (الثعلبة): loss of scalp hair in a moth-eaten pattern.
  - d. **Leucoderma:** oval non scaling papules. ببقى بقع بيضاء عالجلد
- III. **Ulcerative mucous membrane patches.**
- IV. **Generalized lymph nodes enlargement.**
- V. **Periosteal nodules.**

**Microscopically:** (نفسهم برضو)

1. **Endarteritis obliterans.**
2. **Perivascular plasma cells and lymphocytes.**
3. **Granulation tissue and fibrosis.**

### 3- Latent syphilis:

It is a stage at which the features of secondary syphilis have resolved, though patients remain sero-active.

المرحلة دي بيسموها فترة الراحة او الزهري الخفي ال هو يعني المريض لسه عنده زهري وكل حاجة لسه فجسمه بس مايبينش على شكله انه مريض ولا على جسمه. بنعرف بس لو عملنا له مثلاً اختبار مناعة هيطلع positive يعني الزهري لسه موجود. فالمرحلة دي يقدر المريض انه يعدي حد عن طريق الدم بس، لكن مش هيعدي جنسياً.

### 4- Tertiary stage:

It consists of **gummatous syphilis, cardiovascular syphilis and neurosyphilis.**

**Onset:** 2-10 years after healing of secondary stage.

### **A- Gummatous syphilis: (Gumma)**

**Grossly:** Single, soft mass with necrotic centre.

**Sites:** liver, bone, tongue, testis and heart.

**Microscopically:** granulomatous lesion characterized by:

- **Central coagulation necrosis** due to reaction of the immune system against spirochete.
- **Endarteritis obliterans, perivascular plasma cells and lymphocytes, granulation tissue and fibrosis.** لازم يكونو موجودين طبعا

### **Effects of Gumma:**

1. **Gumma of skin or mucous membrane leads to gumma (syphilis) ulcer characterized by:**
  - a. **Punched out edges (sharp and deep) with serpiginous irregular margins (snail tract ulcer).** بتبقى نازلة بشكل مستقيم وعميقة
  - b. **Smooth red floor.**
  - c. **Hard or indurated base (due to fibrosis).**
2. **Gumma of solid organs is destructive due to fibrosis.**

### **B- Cardiovascular syphilis:**

The most common organ affected by tertiary stage syphilis is the cardiovascular system in which **the aorta is the commonest site.**

### **Syphilitic aortitis:**

The lesion commonly affects the ascending thoracic aorta because of its rich lymphatics, then spread in both directions to affect the coronary orifices.

بتصيب اول جزء فال aorta اللي هو ال ascending علشان مليان lymphatics.

## Grossly:

1. **The affected part is dilated.**
2. **The intima** (البطانة الداخلية) **shows raised patches and transverse wrinklings** (تجاعيد).
3. **The media is grayish white, and fibrotic.**
4. **The adventitia** (الغلاف الخارجي) **is also grayish white and fibrotic.**
5. **The coronary orifices are narrowed.**

## Microscopically:

- **Intima:** fibrotic and wrinkled.
- **Media:** endarteritis obliterans, perivascular lymphocytes and plasma cells then granulation tissue and fibrosis. راشقين فأى مرحلة وأي نوع مش فارق معاهم
  - Necrosis of the musculo-elastic tissue then follows.
  - Contraction of the fibrous tissue pulls the intima and causes the intimal wrinklings.
- **Adventitia:** endarteritis obliterans of **vasa vasorum** (اووعية الاوعية), perivascular lymphocytes and plasma cells, later on granulation tissue and fibrosis.

**vaso vasorum** هي الاوعية اللي بتغذي الاوعية الكبيرة، لأن الجدار بتاعهم بيبقى تخين والدم مايبوصلش لكل الاجزاء بتاعت الوعاء، فتيجي الاوعية الصغيرة دي تغذي الحتت اللي مايبوصلهاش دم خصوصاً الاجزاء الخارجية من الوعاء.

## Effects and complications:

1. **Aortic incompetence** (ارتجاع فالصمام الاورطي) **leads to hypertrophy and dilation of the left ventricle then its failure.**
2. **Stenosis of the coronaries** **leads to anginal pain.** (الشرايين التاجية) (هتضيق وهتسبب ذبحة صدرية)
3. **Aortic aneurysm.** (حته زي الجيب كده فجدار الشريان الاورطي)