

وَقُلْ رَبِّ زِدْنِي عِلْمًا



RESPIRATORY SYSTEM

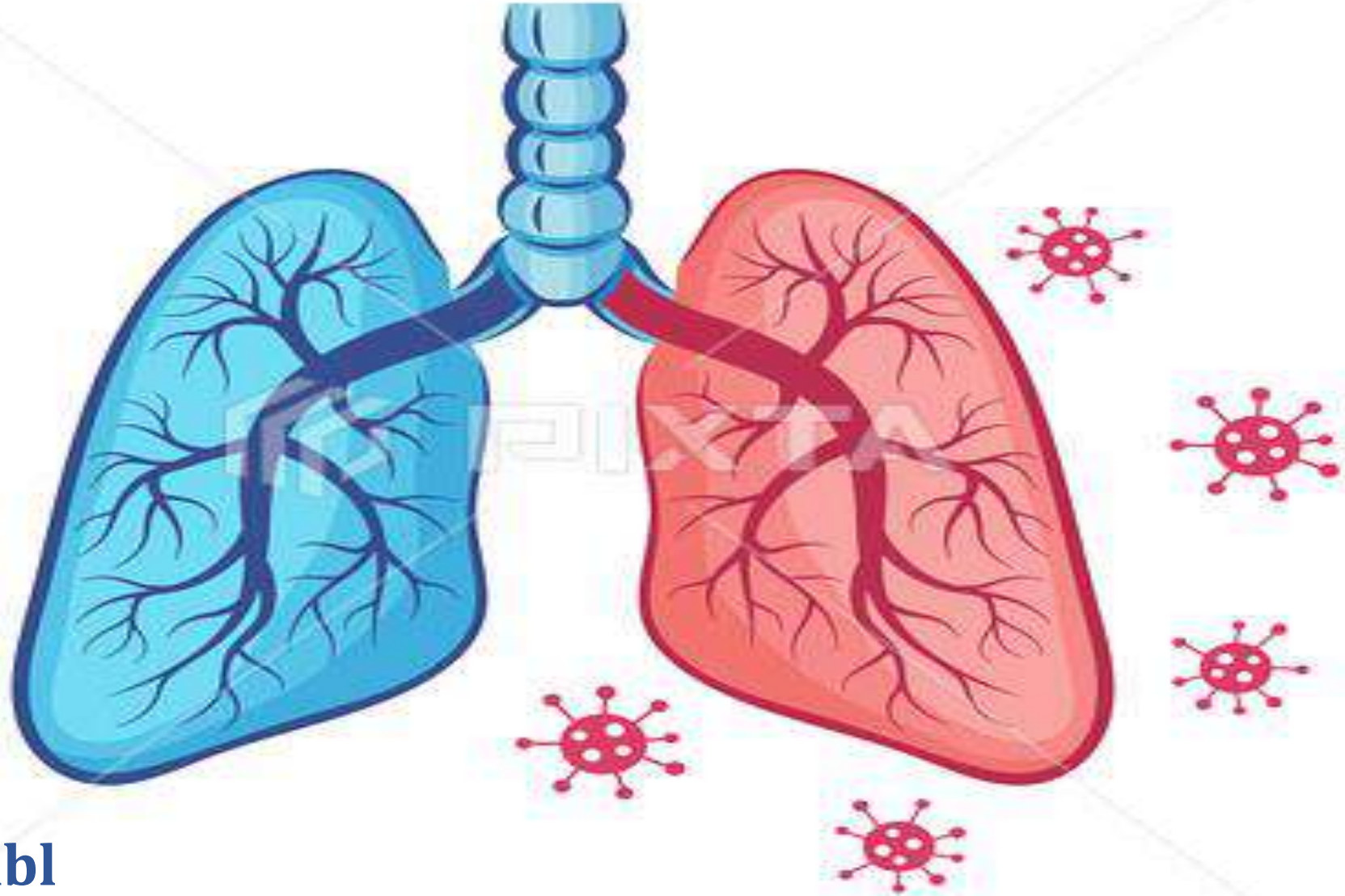
HAYAT BATCH

SUBJECT : The most important

LEC NO. : 1-5

DONE BY : Tabark Aldaboubi

RESPIRATORY TRACT INFECTIONS



By
Prof. Hala Tabl

GROUP A, BETA- HAEMOLYTIC STREPTOCOCCI (STREPTOCOCCUS PYOGENES)

VIRULNCE FACTORS:

Attachment

A) Adherence factors: promotes adherence to epithelial cells.

1- **Fibronectin- binding protein (protein F) and lipoteichoic acids (LTA)**

cell wall *جزء من ال*

2- **M protein:** hair like projections covering the cell wall. *(more than 80 type)*

B) Anti-phagocytic factors:

1- **M protein:** it is a **major virulence factor** that resist phagocytosis.

2- **Hyaluronic acid capsule:** acts as immunological mask

في وجود جسيمنا (بالعدية) يروع يحاوط حاله ب Hyaluronic Acid capsule ال Phagocytic بتتعلق عليها على بالمختص بتقل تقوية وتلبس وشاح الاخفاء وما بصير لها Phagocytosis

3- **C5a peptidase:** breaks down C5a complement

بتكسر

Component in immune system

وظيفة

atraction to phagocytic cell و Phagocytosis لهيلكس بتكسر C5a يبطل بصير Phagocytosis



C) Spreading factors: Group of enzymes that break down the normal host tissues

1- **Streptokinase (Fibrinolysin):** Dissolves fibrin in clots,
يقول لysis لل Fibrin

2- **Streptodornase (Deoxynuclease)(DNase):** - *يكسر ال DNA* degrades DNA.
في خلايا يموت بطلع منها ال DNA يسك بزود ال viscosity تاع ال P45 ، بعيت حركة ال organism فيكسر عشان ينشر بسهولة.

} used in treatment of emboli

3- **Hyaluronidase:**

D) Toxines: *cytotoxin*

1- **Streptolysins (Hemolysins) (pore forming cytotoxin):**

a) Streptolysin O: (oxygen labile).

It is antigenic, and antibody to it (ASO) develops after group A streptococcal infections.
stimuli to immune system → Antibody ASO يكون
Anti strepto lysin O

b) Streptolysin S: (oxygen stable), not antigenic.

It is responsible for β-hemolysis on the surface of a blood agar plate.

2-Pyrogenic (fever inducing) exotoxins:

SPE A (erythrogenic toxin): It causes the **rash** that occurs in scarlet fever.

ال rash المسؤل عن ظهور ال

* *فش كل ال Virulence Factor بتكون موجودة مجتمعة بكل strain من ال Streptococcus pyogenes*

1) Streptococcal pharyngitis (Strep throat) (Acute follicular tonsillitis):-

التصاب اللوز الالتهابي الحاد.

- Affect mainly children (5-15 ys).
- Red swollen tonsils. There is **purulent exudate** (Patches & streaks of pus).
- Enlarged and tender cervical lymph nodes, painful swallowing. *difficult Swallowing*
- High fever, sore throat.



↓
mucus membrane → red و Tonsil ال بتكون ال
Swollen
يكون فيه pus ← ما بتكون ظاهرة عند الأطفال
الي اعراضهم كثير صغيرة

2) Scarlet fever (scarlatina):-

الحمى القرمزية
بتميز بال *Strain* التي قادرة على تصنيع *erythrogenic toxin*

- Caused by streptococci that produce **erythrogenic toxin** (strains of *S. pyogenes* **lysogenized** by a **bacteriophage** carrying the gene for the toxin).

- Affect children < 10 years!

← *bacteriophage* حاملة جين *erythrogenic toxin*

ويتزوج تدخله *Streptococci* التي يتزوج نقلوا *transcription*

ويتحولوا لبروتين ويتفوزوا

- It is characterized by **fever**, **sore throat**, and a **scarlet erythematous rash**.

inflammation

يبدأ على ال *Chest* وينتشر

- A “**strawberry**” **tongue** is a characteristic lesion seen in scarlet fever.



Post-streptococcal diseases : اعراضها بتتميز بعد اسابيع من ال Streptococcal infection بتكون ال Strepto طلعته من الجسم

- These disorders occur **weeks** (time to produce sufficient antibodies) after a local infection with group A streptococci.
- The inflammation is caused by an immunologic (autoantibody) response to streptococcal M proteins that **cross-react** with human tissues. ال Antibody الي بتكونه بروجيها جسم خلايا الجسم نفسه
- **Acute Rheumatic fever:** Follows **pharyngitis (not skin infection)**.
- **Acute Glomerulonephritis (AGN):** Follows **skin infections** rather than pharyngitis.

DIAGNOSTIC LABORATORY TESTS:

b) **Gram stained smears:** are not useful in streptococcal pharyngitis (S. viridans are members of the normal flora). normal flora كونا راج يكون فيه

c) **Culture:** on blood agar show:

translucent β hemolytic colonies which is catalase negative and inhibited by bacitracin (bacitracin sensitive)

d) **Antigen detection tests:** سريعة ELISA or agglutination tests used for **rapid** antigen detection.

e) **Serology (ASO test):** (for diagnosis of **post-streptococcal diseases**) ← وسيلة

ASO titers are high soon after infections.

TREATMENT:

➤ Treatment of scarlet fever:

In addition to penicillin, antitoxin serum is given. It shortens the course of the disease.

Antitoxin to erythrogenic toxin prevents the rash

PREVENTION:

- Rheumatic fever can be **prevented** by adequate treatment of strept. pharyngitis **for 10 days**.
- Prevention of streptococcal infections (usually with long acting penicillin once each month)

in persons who have had rheumatic fever

* Tonsillectomy in frequent tonsillitis

* اهداف ال prevention انه افنع حدوث ال fast disease

* بعطي ال Antibiotic ← 10 ايام ما يوقفوا بعد اتم يوم لما يتحسن

* اي طفل بتكرر عنده يُفضل قبل ال (ASO test) واذا تم تشخيصه بـ rheumatic fever لنتم افضل اعطيه penicillin long acting

CORYNEBACTERIUM DIPHTHERIAE

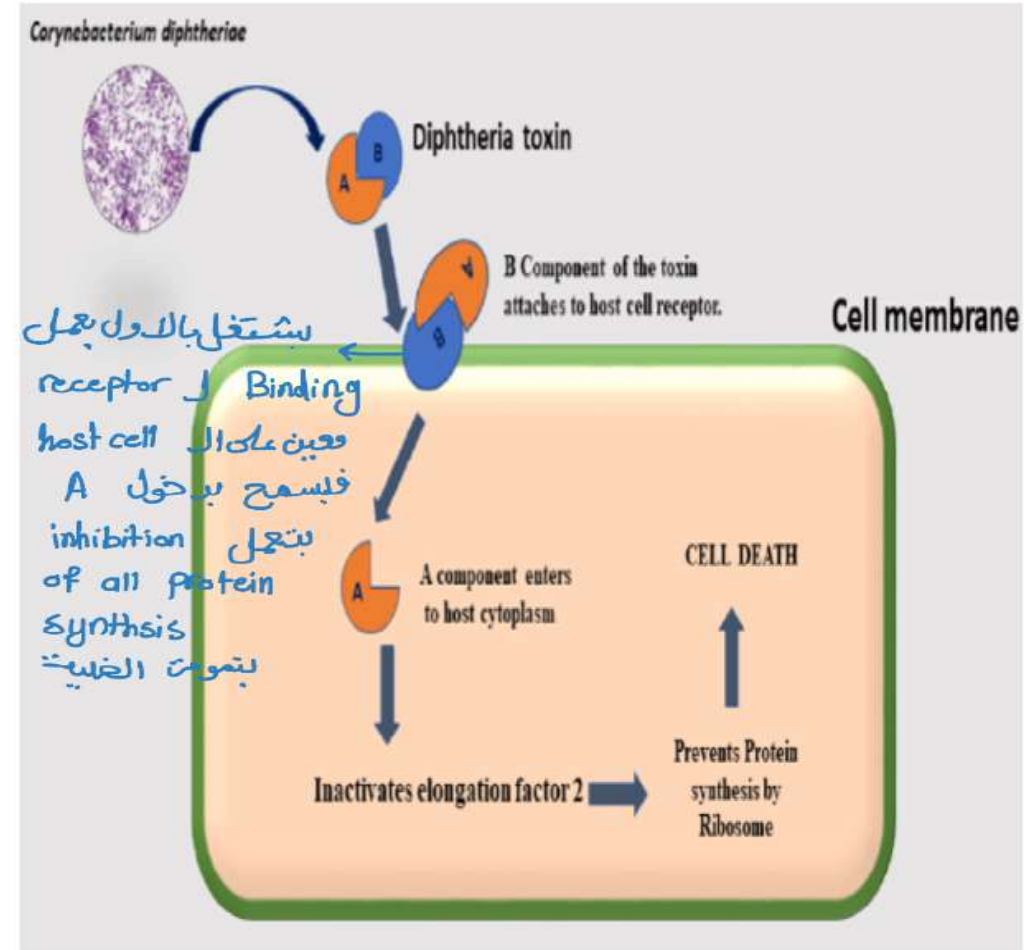
- Gram positive rods, Non-spore-forming.

عش كل ال strain فيها Toxin

VIRULENCE FACTORS:

- Diphtheria toxin is the main virulence factor.
- The toxin is produced **only** by strains of **C. diphtheriae** infected with bacteriophage which carry the gene for toxin production. So, only **lysogenic** strains of C. diphtheriae are **toxigenic** and **virulent**.

- Fragment A is responsible for **inhibition of protein synthesis (Inactivate elongation factor2)**. 23



PATHOGENESIS:

A) Tonsillar diphtheria:

- Is the commonest type and is transmitted by droplets (from **case or carrier**).
- It's a very contagious, life-threatening disease that affect mainly small children but can affect adults.
- The organism **does not invade** the deep tissue and **never** enters the blood stream. The organism **multiply locally**, releasing the toxin causing inflammation of the throat, local necrosis with fibrinous exudate resulting in formation of a spreading grayish white **pseudomembrane**.
- The exotoxin released **diffuses** to the blood stream causing **toxaemia** and affects the **heart, kidneys & nervous tissue**.

حبيبات العنقراض

حامل المرض
ليس ما عنده المرض

فابروج على الدم

عقس بالفibrine

Pharynx

وفظي ال

Trachea
larynx

وممكن ينزل ال

ال Toxin بروج على الدم

CLINICAL PICTURE & COMPLICATIONS:

The patient presents with mild fever and general ill health.

The tonsils are covered with a **grayish pseudomembrane**

which may extend to the larynx



Suffocation may occur due to laryngeal obstruction.

Irregularities of cardiac rhythm indicate damage to the heart.

Nerve involvement may lead to **difficulties in swallowing, speech, vision** or paralysis of limbs.

الـ Toxin توصل للدم ترشح على القلب
وتقول Heart Failure

25

DIAGNOSIS: Mainly clinical diagnosis.

- **Gram stained smears:** seen in a small proportion of cases (**negative result cannot exclude diphtheria**).
- **Cultures:** are made on **Loeffler's serum** and **blood tellurite media**.

بجانب الـ Antitoxin لدرج اعطى Antibiotic بنفس الوقت

TREATMENT:

1- Diphtheriae anti-toxin serum:

- It should be given **without delay**
- It **neutralizes the free toxin** (Not fixed toxin) before it causes irreversible damage.
- It is produced in **animals** (e.g. horse) *may cause allergy*

ما سببت النتائج وسيا العلاج عطلك → started early, without delay
السبب !! انه اعطى neutralization to toxic لصلية عطلك بطيئة - Antitoxin
عشان الحقوا قبل ما يجل irreversible damage

2- Chemotherapy:

Antibiotics are given **in association with anti-toxic serum.**

They inhibit local multiplications of C. diphtheria

PREVENTION.

A- Isolation: Patients with diphtheriae should be isolated.

B- Active immunization (vaccine): → *Toxicity* محمول من الـ Toxin بعد ما عمار لها عليا بت نشالوا منها الـ
Antigenicity بين ضللت محتفظت بالـ

Diphtheriae toxoid (Toxin with removed toxicity but retained antigenicity).

Such toxoid is usually combined with **tetanus toxoid** and **pertussis vaccine** and given as
DPT = الـ 3 سوا بطوا السعك الديكيد

C- Passive immunization:

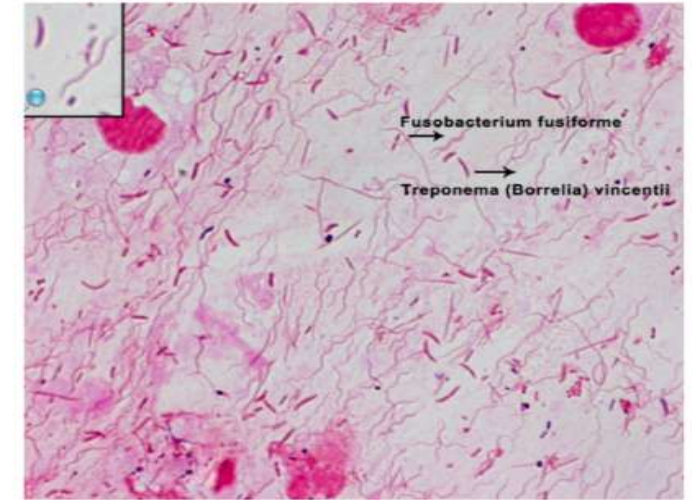
Anti-toxin serum is given to contacts of a case.

A booster dose of toxoid

FUSO-SPIROCHETAL DISEASE (Vincent's angina)

FUSO-SPIROCHETAL DISEASE (Vincent's angina)

- Vincent's angina is **ulcero-membranous** pharyngitis and tonsillitis, caused by infection with two types of bacteria (Normal mouth commensals):
 - Fusiform (^{spindle shap} Fusobacterium) gram -ve **anaerobic** bacilli.
 - Spirochaetes (Borrelia vincenti) gram -ve ^{طوال} spiral bacilli.
- Characterized by unilateral pseud-membrane.
- It is more pronounced in **Immunocompromized** individuals.
rare in healthy people



HAEMOPHILUS INFLUENZA

- Gram negative coccobacilli.
- Requires **X factor (hemin)** and **V factor (Coenzyme e.g. NAD)**.
- Grows **Chocolate agar**.
- Grows Close to colonies of Staph aureus (**Satellitism**).

Virulence factors:

1) **Polysaccharide capsule:** **The major** virulence factor (antiphagocytic activity).
↓
Antiphagocytic Activity لها

- Capsulated strains can be classified into **6 types (a-f)**.
- H. Influenzae **type b (Hib)** is the **most pathogenic** and its capsule composed of (**polyribitol phosphate**) (PRP).
Hib نوع السكر المكون لل capsule تاي

2) **Outer membrane:** ↓↓ mucociliary clearance → colonization.
Colonization حركة ال cilia المسؤولة عن التخلص من اي Foreign body لها تعلق هاي القليات بتساعدنا انها تعلق

3) **IgA protease:** degrades secretory IgA,
Antibody التي موجود بال mucosal surface
المسؤول عن وضع ال organism ادنا قبل Attachment لل الع
فلما يعرفها يصيب سهل على - عليه ال Attachment

Pathogenicity:

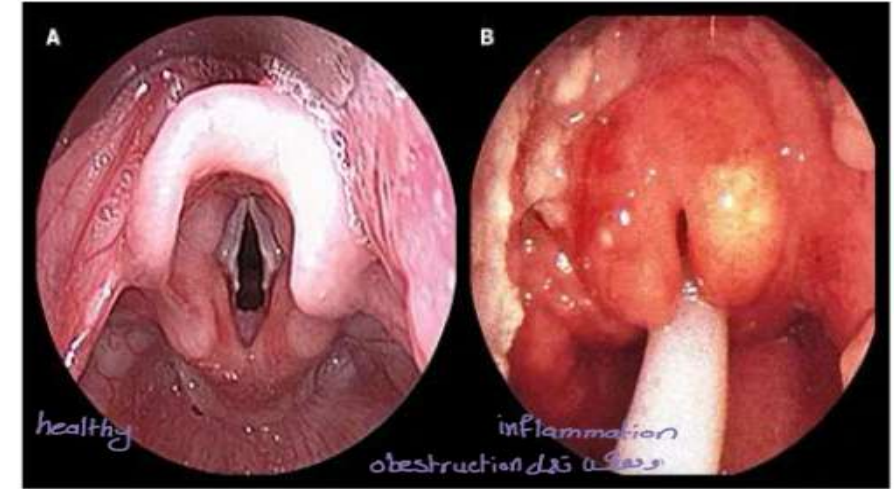
Transmission: droplet infection.

more virulent and more invasive

A. **Capsulated types (invasive) particularly type b (Hib) cause:**

inflammation of epiglott

1- Epiglottitis: This life-threatening disease of young children which can **obstruct the airway (medical emergency)**, is caused almost exclusively by H. influenzae. A swollen “cherry-red” epiglottis is seen. **Tracheostomy or endotracheal intubation is life saving.**



invasive to blood stream

2- Bacteraemia, Meningitis, Septic arthritis.

infection شخصاً شائع ال spleen يكون اكثر عرضة لل

N.B. Asplenia (anatomical or functional) is important risk factor for infection with encapsulated organisms.

*encapsulated organism ال spleen اهم مكان مسؤول عن ال immunity ضد **

ال organism الحي ال لها capsule

B. The non-capsulated (non-typable) (non-invasive) strains cause:

hemophilus influenzae الهمسبي ال Sinusitis and otitis يسبب ربيها

1- Otitis media and sinusitis: (next to *Streptococcus pneumoniae*).

غالبا يتكون عندهم مشاكل اهدل [مأثرة على ال immunity of lung]

2- Tracheobronchitis & Pneumonia: in adults and elderly, in presence of predisposing factors e.g. viral infections, malignancy COPD, cystic fibrosis...

Laboratory diagnosis:

infection حسب المكان تفاعل

A. Specimens: CSF, blood, sputum, ear swab, ...

B. Microscopic examination:

Gram-negative coccobacilli.

C. Detection and typing of capsule: Quellung reaction.

اختبار سريع
or Capsule swelling test

D. Cultivation: on chocolate agar.

E. X&V factor test: (It requires both factors).



Prophylaxis:

➤ **H. influenza type b vaccine (Hib vaccine):**

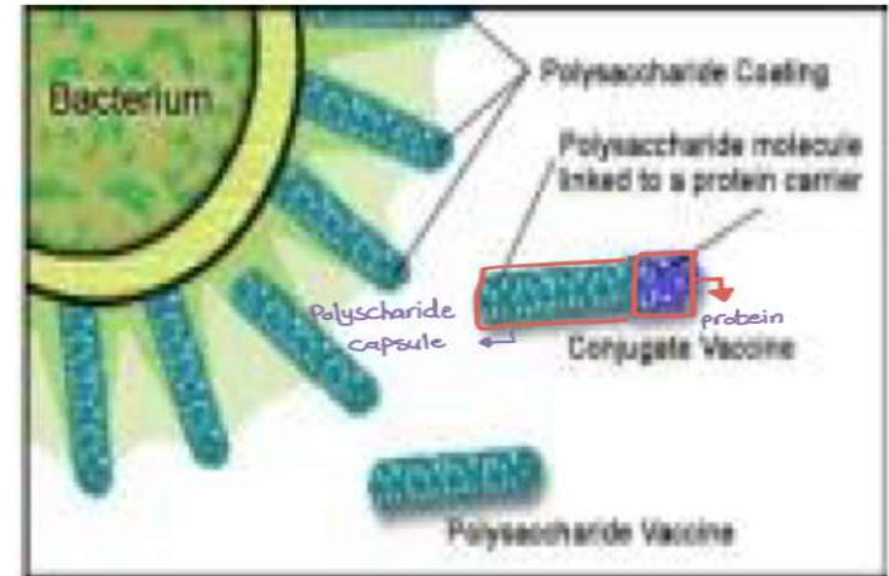
يُحفر من ال polysaccharide capsule

1- Polysaccharide vaccine.

efficacy تلت احسن

2- **Conjugate vaccine (capsule + carrier protein).**

يؤخذ ال polysaccharide capsule مع ال carrier protein وتطيفت انها بتعمل Stimuli immune response against capsule



BORDETELLAE PERTUSSIS

Gram negative coccobacillus.

It does NOT require X and V factors.

Virulence factors:

- **Filamentous hemagglutinin (FHA):**

Attachment فسقول عن ال

- Colonization factor that **promote attachment** of the organism to the cilia of the epithelial cells

- **Pertussis toxin (PTx):**

- Colonization factor.

- It has **adenyl cyclase activity** → ↑↑cAMP → **edema** of the respiratory mucosa.

- **Tracheal cytotoxin (TCT):**

- **Necrosis** (cell death) of ciliated cells of the respiratory mucosa.

Whooping cough (Pertussis)

- It is highly communicable disease that occurs primarily in **infants and young children**.
- Infection transmitted by **droplet** infection.
- Disease occurs in three stages:



1- Catarrhal stage: (1-2 weeks): ^{non specific manifestation} Fever, anorexia, malaise, rhinorrhea, sneezing.

2- Paroxysmal stage: (2-4 weeks): ^{ممكن توصل ل 6 اسابيع} ^{كل attack} **Repetitive cough with explosive character** followed by a high-pitched intake of breath that sounds like **"whoop"**. This may be associated with vomiting, ^{بسبب hypoxia} cyanosis and convulsions. ^{بس يتعرض لنوبات قحة شديده بعدها رح يصطر يومه نفس عيق بطلع معاه صوت high pitched}

3- Convalescent stage: Gradual recovery over weeks (**followed by long lasting immunity**).

- **Complications:** ^{اذا وصل ل lung} (pneumonia, subconjunctival or cerebral haemorrhage, encephalopathy, Rib Fracture).

Prophylaxis: Two types of vaccines:

A- Killed whole cell vaccine.

جاء بالبكتيريا وقتلها وحفظها بال Vaccine

بعد خطر العجز عن الـ encephalopathy اذا استخضع بعد اسبوعين

It is suspected of causing various side effects, including **post-vaccine encephalopathy**

if given

more safe than

B- Acellular vaccine: (fewer side effects than killed vaccine), a combination of:

مجموعة • Pertussis toxoid (genetically inactivated toxin).

Antigen

سوا • Filamentous hemagglutinin.

• Other virulence factors.

DTaP: administered in combination with toxoid of diphtheria and tetanus

PSEUDOMONAS AERUGINOSA

Virulence factors:

- 1- **Pili (fimbriae)**: → Attachment مسؤولية عن ال Attachment
- 2- **Endotoxin (Lipopolysaccharide)**: causes septic shock.
- 3- **Exotoxin A**: Inhibit protein synthesis and causes tissue necrosis. cell death
- 4- **Extracellular enzymes**: e.g., elastases, facilitate invasion into the blood. break down to elastin يساعدها تحلل
- 5- **Pyocyanin**: damages the cilia and cause cell death.
- 6- **Alginate (glycocalyx): (Mucoid strains)** that forms adherent **Biofilm** protecting from antibodies, complement, and antibiotics. فادحة هيمفيا - بفرزها ال organism خمريتها ال mucoid strains يساعدتك Biofilm (تكتل من ال organism) ال medical important لردّها اذا انكونت على medical device بتكون مشكلة لانها بتكون ال (resistance) organism يتمنع ال diffusion تاخ ال Antibody
- 7- **Broad antibiotic resistance**: (intrinsic and acquired).



Medical importance of *P. aeruginosa*:

بعيش لمستوى مختلف من ال nutrient

- It flourishes in wet environments and can grow in **simple aqueous solutions**
- It has a remarkable ability to **withstand disinfectants**, it has been found growing in soap solutions, in antiseptics, and in detergents.

لوقيم
Antiseptic solution

one of the most important cause of

hospital-acquired (nosocomial) infections.

لأنو بعيش بالمعققات

- *P. aeruginosa* is an **opportunistic pathogen** that causes infections in :
 - In whom skin host defenses are destroyed (e.g., **extensive burns**).
 - In those with chronic respiratory disease (e.g., **cystic fibrosis**).
 - In those who are **immunosuppressed**
 - With **medical devices** e.g. catheters, ventilators, I.V line,

غالبًا يكون المريض عنده pathogen زائد

24

→ one of the top antimicrobial resistance threats world wide, multiple drug resistant (MDR)

Clinical findings:

1- Respiratory infections:

Hospital-acquired pneumonia (especially **ventilator-associated pneumonia** and in **cystic fibrosis** patients).

2- External ear infections:

Malignant otitis externa (esp. in diabetics), **swimmer's ear**.

3- Eye infections:

Corneal ulcer (frequently associated with contact lens use).

4- Skin infections: (e.g. **Ecthyma Gangrenosum**).

5- Urinary tract infections: in those with indwelling catheters.

STREPTOCOCCUS PNEUMONIAE

"PNEUMOCOCCI"

- **Gram-positive, diplococci (arranged in pairs).**
- On blood agar, **partial** zone of haemolysis with **greenish** discoloration (**Alpha haemolysis**).
- It is **sensitive to optochin** (Antibacterial agent).

Antigenic structure & virulence factors

➤ **A polysaccharide capsule:**

✓ **The major virulence factor** (Anti-phagocytic).

✓ Permits classification (**Typing**) of pneumococci to more than 90 types.

➤ **IgA protease:** enhances colonization of the respiratory tract.

➤ **Pneumolysin:** Pore forming toxin (the hemolysin that causes α -hemolysis).

rupture *تفتت* *بصير* *pore in cell wall* *ثقب في جدار الخلية*

➤ **Autolysin:** lyse the bacterial wall and release potentially lethal toxins.

Necrotizing *و* *inflammation* *تفتت* *تفتت*

Pathogenesis & clinical findings:

- Pneumococci are **the most common** cause of:
 - **Otitis media and sinusitis.**
 - **Community Acquired Pneumonia.** It is **typical lobar** pneumonia (Fever, chills, cough with red brown “**rusty**” sputum, dyspnea and tachypnea).
 - **Bacteremia.**
 - **Meningitis.**
- **Predisposing factors:**
 - Children < 2 ys and elderly > 65 ys.
 - Smokers and alcoholics (depress the cough reflex)
 - **Asplenia is important risk factor.**
 - Immunocompromized e.g., HIV, cancers,...
 - Abnormality of the respiratory tract (viral infections, chronic lung diseases,..)

Prophylaxis: Two types:

1) **Capsular polysaccharide vaccine**

2) **Pneumococcal conjugate vaccine:** (Capsular polysaccharides + protein
carrier).
Stimuli to immunoreponse against to capsule

KLEBSIELLA PNEUMONIAE “FRIEDLANDER’S BACILLUS”

Pathogenesis & Clinical findings:

➤ It is important cause of nosocomial infections:

❖ **Pneumonia** (sever form of lobar pneumonia which can progress to abscess formation & empyema).

في خطر انه يمسيه
Necrotizing

Sputum characterized by being thick, mucoid, bloody

نوع من انواع العنب الاحمر

“**currant jelly sputum**”.

مهم نفس بين نوع ال sputum لكل organism

❖ **Urinary tract infections.**

❖ **Bacteremia.**



➤ Isolates carry **high degree of antibiotic resistance**.

gen transfer

لانه بيتر المستشفى بسهل عليه ال

↑ resistance

يكون

nosocomial دائما ال

بيتر strain of bacteria

BACILLUS ANTHRACIS

- Gram positive spore forming bacilli
- Capsulated (Polypeptide capsule, “D-Glutamic acid”)
- Medusa head colonies, liquefies gelatin (inverted fire tree appearance).

Virulence factors:

A) Very powerful exotoxin.

The toxin consists of 3 domains:

Protective antigen (PA): binds to specific receptor on host cell with its proteolytic activity producing

المسؤول انه يعلق binding للـ Toxin. Specific receptors. Poor in cell membrane. LF و EF تسمح بدخول الـ

membrane channel and permits entrance of:

Edema factor (EF) with its adenyl cyclase activity → loss of water → → edema.

تخرج المبي من الخلايا

Lethal factor (LF) which cause tissue necrosis.

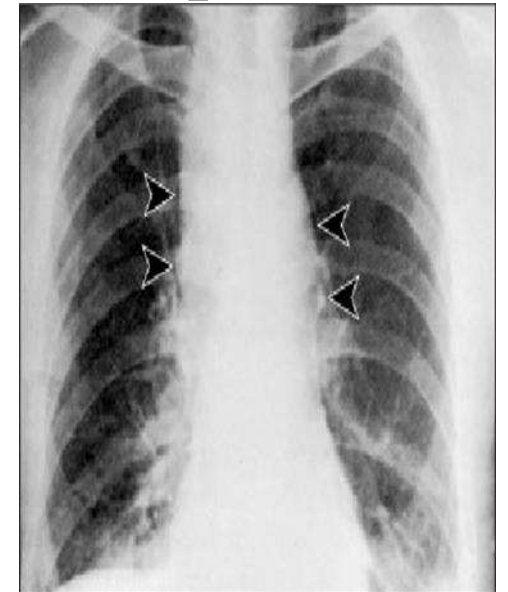
cell death

B) Protein capsule: Antiphagocytic.

PULMONARY ANTHRAX

“Wool sorters disease”

- It is a disease of farm animals e.g. cattle and sheep (**Zoonotic disease**).
- Man infected by Inhalation of spores.
- After inhalation, the organism moves rapidly to the mediastinal lymph nodes.
Because it leaves the lung so rapidly, it is **not transmitted from person to person** by respiratory route (**not contagious**).
- This **rapidly** progresses to **hemorrhagic mediastinitis** (fever, chest pain, respiratory distress and **widened mediastinum on chest X-Ray**).



Treatment & Prevention:

Active immunization:

a) **Pasteur's vaccine** & Live spore vaccine: given only to animals.

b) **Protective antigen vaccine**: It is used for humans. Given to people at high risk.

↓
ما ينعظس للكل .

risk.

MYCOBACTERIUM TUBERCULOSIS

“Tubercle bacillus” “Koch bacillus”

Cultural characters:

➤ They are **obligate aerobe** (upper lobe of the lung).
مناطق الرئتين التي فيها يعيش تتجمل (oxygenated area) infection to upper lobe

➤ They are **slow growers**, growth appears after 4-6 weeks
بدها وقت طويل حتى تنمو بعد زراعتها (تتخذ عكس باقي البكتيريا التي ينمو يوم احاطل !!) 18 ساعة حتى يصير لها تضاعف

Virulence Factors:

1. **High lipid of cell wall (Mycolic acids)**, responsible for:

Resistance to: Antibiotics, acidic and alkaline compounds, Osmotic lysis via complement.
ال lipid يمنع ال diffusion خارج المواد وال Antibiotics

2. **Cord factor:** Virulent strains grow in a characteristic

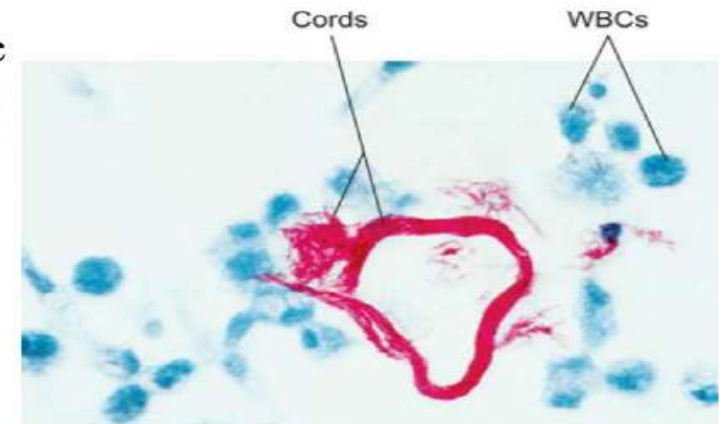
“Serpentine” cordlike pattern.

*يخلي ال organism تنمو في تجمعات و تتكلسبت .
يقوم بنقل ال اهمية و جود ال lipid (يمنع دخول المواد)*

3.

Inhibit phago-lysosomal fusion.

The main pathogenesis of TB



Resistance & Sensitivity:

*They are highly resistant to : ^{للسبب الـ Lipid الـ Cell wall الـ}
الـ diffusion الـ ^{تأخذ المواد}

- Dryness (survives in dried sputum for long periods). ^{لصليق بنلاقي الـ organism بقل survives خارج الجسم متى بعد ما الـ Sputum ينشف لمدة طويلة}
- Chemicals, many acids and alkalis.
- Antibiotics.

*They are killed by:

- Sunlight → ^{لهيئ ان بيين في مويها سئل بنصحوهم بفتحوا الشبايلع ، والتقرض للشمس -الاشعة الـ ينيح}
- U.V. rays
- 5% phenol , Chlorine
- Heat (60°C for 20 min.) (Pasteurization can kill them in milk).

^{خطوة مهمة بـ prevention of these disease حمونيا ان -عنا bovin strain}

Pathogenesis:

➤ Tubercle bacilli do not contain or produce toxins.

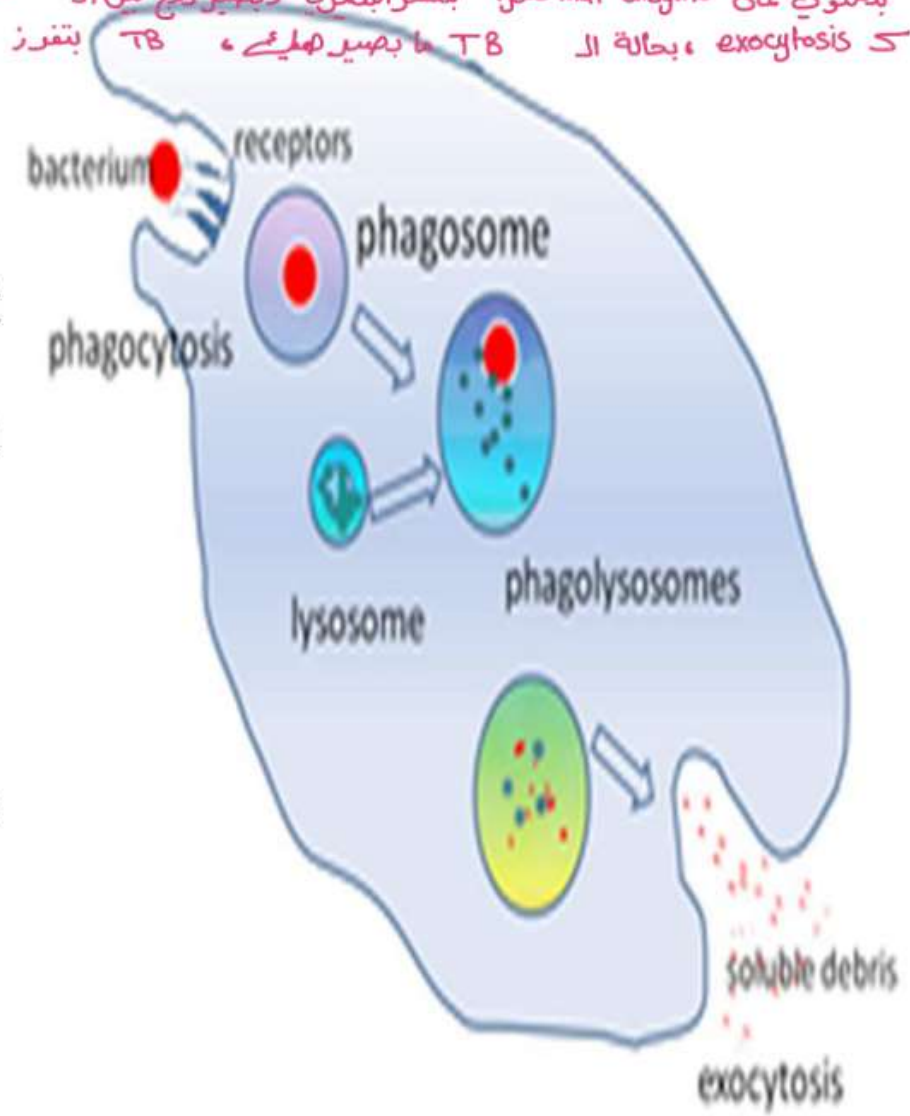
➤ Their pathogenicity **depends** upon the fact that the organism **survives and multiplies in macrophage** and

prevents phago-lysosomal fusion and so, escape the degradation by lysosomal enzymes.

➤ It is an intracellular organism.

بتعمل engelfment للبكتيريا بتدخلها جواتها ب vacule (phagosome) ونتر vacule صغيرة اسمها lysosome
 بتحتوي على lysosomal enzyme بتكسر البكتيريا ويصير دمج بين ال 2 vacule بتسمي phagolysosome بتكسر البكتيريا ويتطلبها
 ك exocytosis ، بحالة ال TB ما بصير لهيمع ، TB بتفرز بروتينان معينات بتمنع انه ال 2 vacule تتجمع بالتالي بتعمل جوال phagosome

فاغندها endotoxin بال cell wall ناعها .

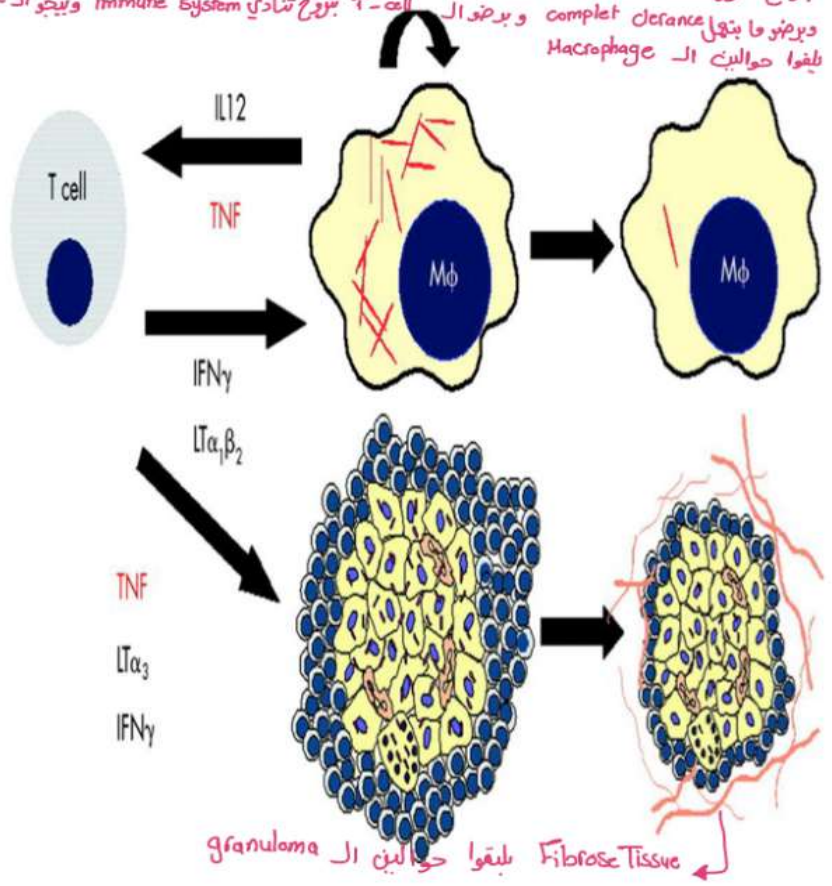


Immunity Against Tuberculosis:

اولما تدخل بكتيريا phagocytic organism لعلها phagocytosis وقتئذ يتقدر عليه
 لما تمسك بالعدوى عليه بترجع تتادى خلية احدى منها (الماستوسيت) T-cell
 بتفرز cytokines بتعمل TNF more activation لل phagocytic cell بيصير زيود ال killing power
 وبتفرز ال T-cell بتفرج تتادى immune system وييجو ال lymphocyte
 بتفوق حواليت ال Macrophage وبتفرز ال complete clearance

انواع ال immunity
1- Cell mediated immunity (CMI) (Delayed-type = type IV hypersensitivity) (Granuloma formation)
 تعتمد على الخلايا تاع ال immune system
 هاي الالهيم بال immunity against to TB
 له بتوخد وقت حتى تتكون
 الاهدق فن هاي العملية :
 that leads to localization of tubercle bacilli, retards their multiplication, limits their spread.

Patients deficient in cellular immunity, such as AIDS patients, are more susceptible to disseminated (miliary) tuberculosis.
 بتعرب خلية ال T cell



Human Tuberculosis (TB)

- **Human** type is transmitted airborne by **inhalation** of respiratory aerosol ($<5\mu\text{m}$).
- **Bovine** type is transmitted by **ingestion** of unpasteurized milk of infected cattle (**zoonosis**).

Primary pulmonary tuberculosis:

- In most cases, it is asymptomatic and tubercles **heal** by fibrosis and calcification, leaving the person immune and hypersensitive (**tuberculin positive**).
90-95%
- Small foci containing **dormant viable** organisms (**Simon foci**) may be formed and often become sites of reactivation (**Latent TB**).
Positive بطلع ← skin test لو غلت Cell mediate immunity عند العريضي
- **Only small % (immunocompromised)** progress into active or disseminated T.B.
*دورمنت ← organism لانه مسنون الحش
بمحل ال
بمرحلة ما يعميروا
reactivate to dormant
بنتشر ب
different system*

Secondary pulmonary tuberculosis:



بتصير نتيجة :

عدوى جديدة

➤ It may be: reactivation of old primary lesion or reinfection.

غالبا يتكون عند الناس :

➤ Occurs mainly in **immunocompromised**, **debilitated** or **diabetic patients**.

بببلش ينتشر بطريقتين

➤ **Spread of the organism occurs by two mechanisms:**

بببلش يعمل infection لبارت ثاني من الlung وغالبا بميل يعمل infection of upper lobe، ليه؟
لأنها more oxygenated

① Local spread: -To other parts of the lungs (**upper lobe**), OR

ⓑ

-A tubercle **cavitate**,

منسي هيا الحالة

(Open TB).

هسا هون بصير عنا necrosis ال tubercle بعمل cavities ، وهاي ال cavity بتروح تفتح على ال bronchus وبتفضي محتوياتها في ال bronchus وبتببلش البكتيريا تنتشر في ال airway، واذا قح المريض او عطس او وهو بحكي وطلع منو sputum (يحتوي على بكتيريا) ينتقل لشخص ثاني

نستدل عن
هل ريف
الرب

② Hematogenous spread: which result in **miliary T.B.**

Laboratory Diagnosis

1- Direct microscopic examination:

صبغة نوع ١

* Z.N stain & Kinyoun:

- Positive film is highly suggestive, **negative film does not exclude T.B.**

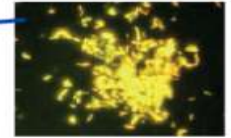
صبغة نوع ٢

* **

* **Flouochrome stain:** More sensitive and allow more rapid screening than Z.N.

2- Culture: مشكلتها بطينة

← هيكل ببتين وضوية



- Culture is the **gold standard and the most conclusive** method.

طريقة اسرع من ال قبل خلال ٣ اسابيع

3- Polymerase Chain Reaction (PCR): Rapid & sensitive.

هاي اسرع ايشي ممكن خلال ساعة تبين النتيجة

Tuberculin Test “Mantoux test”

اختبار حساسية بدني اعمل اختبار للشخص هل هو عندو

Principle: It is skin allergic test used to detect cell mediated immunity to tubercle bacilli which become detectable **few weeks** after natural infection or BCG vaccine.

طب متي جسمي بتعرف على هاي. ال organisms؟ لما يكون شايفها، طب متي بشوفها؟ يا من مطعوم، او يكون انصاب من قبل

Procedure:

Intradermal injection of 0.1ml of **PPD (Purified Protein Derivative)**.

بحقن جزء بسيط 0.1 من T bacilli، بحكي للبيشنت روح وتعال بعد 48-72 ساعة
وبعدھا منحدد، يا رح الاقي صار ريكاشن او ما صار

Read the test **48-72 hours**.

الرياكشن الي بصر الو كراكثير معين، انو يكون بصورة **induration** وهي معناها
granuloma وهي localized hard papule

Measure the diameter of the induration using mm ruler.

“Only the induration”,



Interpretation of Tuberculin test

١٥ → ٥

| <p>An induration of 5 or more mm</p> <p>هون كمان ما يعتبره نيجاتف لانو ممكن يكون بوساتف في حالات الـ high-risk</p> | <p>An induration of 10 or more mm</p> <p>ما بقدر اعتبره نيجاتف لانو يكون بوساتف في هاي الحالات الي منحكيلها moderate risk</p> | <p>An induration of 15 or more mm</p> <p>قولاً واحداً</p> |
|---|--|--|
| <p>Considered positive for:</p> <ol style="list-style-type: none"> 1. People with previous history of TB. 2. Close contacts of TB patients. 3. People with HIV infection. | <p>Considered positive for:</p> <ol style="list-style-type: none"> 1. People in endemic areas where TB is common. 2. Healthcare workers. 3. People with certain medical conditions such as diabetes. 4. Unvaccinated children younger than 4 years old. | <p>considered positive even in absence of any risk factor for TB.</p> |

*** Positive Tuberculin dose not differentiate between active or latent T.B

➤ Negative Test:

A negative test means that there is no infection at all or a very old healed one.

Tuberculin is a good negative test. ✖

➤ False Negative Test: يكون عندو TB بس اعطى نتيجة نيجاتف بشوفها عند مين؟

1. **Anergy:** is the inability to react because of a weakened immune system, e.g.

Severe T.B, HIV infection, Some viral infections or cancer.

2. **Recent T.B:** it takes 2-10 weeks for tuberculin test to become positive. او لسا لقط العدوى جديد، يكون لسا ما تكون antibody له

➤ False Positive Test: ما عندو TB بس (خفه) بين الفحص عند

1- Infection with other non-tuberculous mycobacteria.

2- BCG vaccine (The test reactivity induced by vaccine wanes with time).

أخذ مطعوما

مع الوقت تنقل

Treatment of TB should be: يعتمد على فكرتين رئيسيتين

1-Long Duration: ليه لفترة طويلة؟ شوال بسبب؟

Response of tuberculosis to treatment is slow, this is due to the facts that:

- Intracellular location of the organisms. **antibiotics** في صعوبة بوصول ال
- Caseous material interferes with penetration of the drugs. **المادة هاي بتكون تشيزيبي وبتعمل**
- The slow growth of the organism. **تضاعفه بطيئ والاستجابة بطيئة** **interferes** مع ال **drug** **ال** **تكونت من ال caseous necrosis**
- Metabolically inactive “persisters” within the lesion in chronic cases which may not be eradicated easily by anti-tuberculous drugs (source of reactivation in the future). **ال organism** عندو القدرة على تحول ال **metabolically inactive** يعني بوقف ال **multiplication** بتاعه (بعمل نفسو ميت) وهاي طريقة بتبعها حتى يكتسب **resistant of antibiotic**، وخلينا مفكرين إنه ال **antibiotic** بشتغل على **active metabolic**

2- In Combination: 2-4 drugs simultaneously to:

- ➤ Reduce development of resistance. **لانوكل دوا بشتغل بطريقة مختلفة**
- ➤ Reduce toxicity of the drugs. **بقلل ال side effect**

↓
بستفدم 2 على الاقل
فب نفس التوقيت
- طب شوال الهدف؟

Prevention:

اسماء العلماء الي حضروه

Vaccination: BCG “Bacillus of Calmette-Guérin” vaccine:

بتحضيره

- This is a **living attenuated** vaccine prepared from a **bovine strain**.
- It is given as a **single dose** of 0.1 ml **by** intradermal injection in the left deltoid region.
جرعة واحدة فقط
- It is given to all children during the first month of life. ← اجباري
- It is also given to **adults exposed** to infection e.g. nurses, doctors and **contacts** of the case. ← عن الكنت الشمان معلم مكان التلاميذ
- It should **NOT** be given to **immunocompromised** people. ← منعيه للكبار
- It loses its effectiveness over time, **usually within 5 to 15 years**

ATYPICAL MYCOBACTERIA

Non-tuberculous mycobacteria “NTM”

Mycobacteria other than tuberculosis “MOTT”

- They normally found in soil and water.
- Transmission is from the environment. **NO** person to person transmission.
- They are of **low pathogenicity** for man but occasionally they cause **opportunistic** infections especially in **immunocompromised** persons.
- They cause pulmonary diseases which are **indistinguishable** clinically, radiologically and histologically from that caused by the human tubercle bacilli, but tend to be **more chronic and difficult to be eradicated**.
- e.g. **M. Avium Complex (MAC)** (M. avium, M. intracellulare, M. chimera).

Streptococcus pneumoniae الالتهاب السببي ال

| Typical pneumonia | Atypical pneumonia |
|--|---|
| Sudden onset, severe course commonly require hospitalization | Gradual onset, mild course (do not usually require hospitalization) and self resolution. |
| Lower respiratory tract involvement | Upper and lower respiratory tract involvement |
| High fever, dyspnea, chest pain and productive cough | Mild fever, sore throat, fatigue and dry cough |
| Lobar consolidation on chest radiography | Patchy or interstitial infiltrate ← radiological examination |
| The causative organisms can be isolated on routine media in the diagnostic laboratory | The causative organisms <u>cannot</u> be isolated on routine media in the diagnostic laboratory |
| Respond to B-lactams → Penicillin Cephalosporin تستجيب للـ | Responded differently to antibiotics |
| Streptococcus pneumoniae or other bacteria associated with typical character of pneumonia Hemophilus influenzae Staphylococcus aureus,... | Mycoplasma pneumoniae, Chlamydia psittaci, Legionella pneumophila, Coxiella burnetii |

MYCOPLASMA PNEUMONIA

- **Lack a rigid cell wall** and thus they are: Highly pleomorphic, Can not stained with Gram, Completely **resistant** to penicillins and cephalosporins.
- The only bacterial membrane that contains **Sterol**.
- **Require cholesterol for growth** (medium supplemented with sources of cholesterol e.g. **Eaton's agar**) giving characteristic **“Fried egg”** colonies.

Pathogenesis & Clinical findings:

- Mycoplasma pneumoniae is **the most common cause of atypical pneumonia** and accounts for about 5% to 10% of all community-acquired pneumonia and **the most common cause of pneumonia in people between the ages of 5 to 15 years.**

Atypical pneumonia
بشكل عام
من الممكن استخدامها لـ
“walking pneumonia”.

- During Mycoplasma pneumoniae infection, **autoantibodies** are produced against red cells (**cold agglutinins**).

↓
Causing hemolysis

temperature in the extremities and causes hemolysis.

Laboratory diagnosis:

↓ Gold standard method of diagnosis

Serologic testing: is the **mainstay** of diagnosis.

الدكتور اكتشاف ال infection
العمل detection to Antibody

a) Fourfold or greater rise in **specific IgM** antibody titer.

b) **A cold-agglutinin test:**

• Patient serum + human group “O Rh -ve” RBCs and incubated at 4°C.

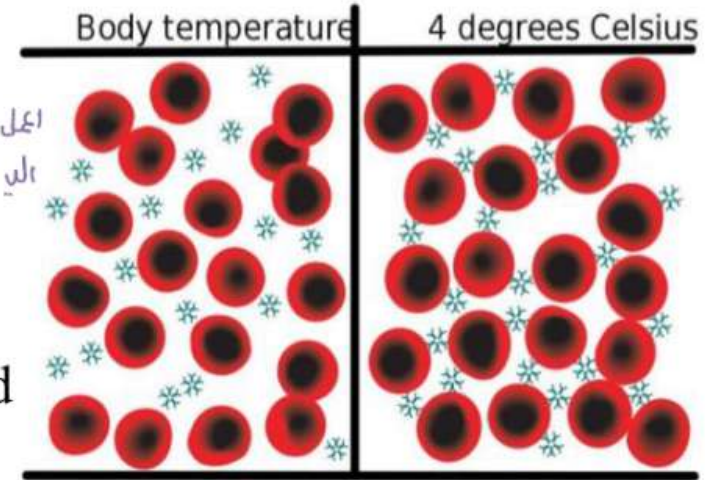
عشان استبعد احتمال ال reaction
Antigen الجي على ال RBC

• Positive result shows clumping of RBCs, which dissociated at 37°C.

لأنه بدرجة الحرارة المنخفضة ال Antibody يتمسك بال RBC ويعطلها clumping

التفكك reversible إذا رفعت الحرارة لـ 37 بطلت ال clumping

- The test is positive in 50-70% of patients.
- The test is **nonspecific** (false-positive results occur in influenza virus and adenovirus infections).



Legend: ● Red blood cell * Antibody



LEGIONELLAE PNEUMOPHILA

- Stain **faintly** with the standard Gram stain, best stained with **silver stains**.
- Grow on **buffered charcoal -yeast extract agar (BCYE)**, special medium supplemented with iron and cysteine.
- Outbreaks of pneumonia in hospitals due to **inhalation** of aerosols of contaminated air-conditioning systems, sinks, water taps and shower heads.
- Despite airborne transmission, **NO person to person spread**.
- The typical candidate for Legionnaires' disease is **an old man who smokes and immunocompromised**.

Clinical findings:

Legionnaire's disease Atypical pneumonia + GIT and Neurological symptoms.

Pontiac fever Mild, flulike illness that does not result in pneumonia.

Laboratory diagnosis:

➤ **Direct fluorescent antibody test (FAT)** of sputum specimen.

➤ **Urinary antigen test:** ^{Test} [↓] ^{جدوا انه هاي البكتيريا بتطلع بال Urine لصيغ ممكنه اعل ما اقل} Enzyme immunoassay for detection of L. pneumophila antigens in the urine is a rapid means of making a diagnosis.

➤ **Polymerase chain Reaction (PCR)**

➤ **Culture:** On BCYE agar
buffered charcoal yeast extract agar

CHLAMYDIA

- Chlamydiae are **obligate intracellular** (i.e., grow only within living cells).
- Can not stained with gram, best stained with **Giemsa**.
- Chlamydiae appear as **intracytoplasmic inclusion body** within the host cell.

Chlamydophila psittaci (Psittacosis)

- Psittacosis is a **disease of birds** (e.g., parrots, pigeons, and poultry).
- Man is infected (**Zoonosis**) usually by **inhaling** dust contaminated by **dry bird feces**.
- In human psittacosis, there is **NO person to person transmission**.

Chlamydophila pneumonia

- C. pneumonia infects **only human** and transmitted **from person to person** by **inhalation**.

Laboratory diagnosis:

➤ **Direct fluorescent antibody test (FAT)** of specimen.

➤ **Culture:** Chlamydiae can be grown in **cell cultures**,

يسن تنمو وتتضاعف بتكون Cytoplasmic inclusion ويصيرها حتى اسشوفها

cytoplasmic inclusions can be seen with special stains

اسم الصبغة

(e.g., **Giemsa stain**).

➤ **Polymerase chain Reaction (PCR)**

➤ **Polymerase chain Reaction (PCR)**



Coxiella Burnetii & Q Fever

- **Obligate intracellular** organisms, therefore, must be grown in **cell culture**.
- They **stain poorly with Gram stain**, best stained with **Giemsa**.
- Two antigenic forms, **phase I (virulent) & phase II (avirulent)**.
- Q fever is a **zoonosis**. Infections transmitted by **inhalation of animal aerosols** (especially urine, feces, placental tissue, and amniotic fluid).
- Q fever is usually an **occupational hazard**. People at high risk include farmers, abattoir workers and veterinarians as well as laboratory personnel.

Clinical findings

➤ **Acute Q fever: (phase II antigen)**

Combination of pneumonia and hepatitis should suggest Q fever.

➤ **Chronic Q fever: (phase I antigen)**

Characterized by chronic cough, intermittent fever, frequent headache and can be complicated with life-threatening **endocarditis**.

Laboratory Diagnosis:

➤ **Serology:** The **mainstay** of diagnosis. Detection of specific antibodies against phase I & II antigens.

➤ **PCR.**

Prevention: vaccination of occupationally exposed (**killed vaccine**).



بالتوفيق