

وَقُلْ رَبِّ زِدْنِي عِلْمًا



# RESPIRATORY SYSTEM

## HAYAT BATCH



SUBJECT : Microbiology

LEC NO. : 3

DONE BY : Ruba Almshaqba



# Respiratory System

\*\*\* ركزت عليه الدكتورة

## IX- Pneumonia

### Community Acquired Pneumonia (CAP):

#### Bacterial causes:

- **Streptococcus pneumoniae** (the commonest cause of lobar pneumonia in young children and elderly).
- Haemophilus influenzae ✓
- Staphylococcus aureus
- Streptococcus pyogenes ✓

#### - Bacillus anthracis (pneumonic anthrax)

- Yersinia pestis (pneumonic plague)

#### - Mycobacterium tuberculosis & Atypical mycobacteria

#### - Atypical pneumonia:

next lectures

(Mycoplasma pneumoniae, Legionella pneumophila, Chlamydia psittaci, Coxiella burnetii).

#### Fungal causes:

- Histoplasma capsulatum, Aspergillus fumigatus, Coccidioides immitis, Blastomyces dermatitis, Cryptococcus neoformans, Pneumocystis jirovecii

#### Viral causes:

Rarely the primary cause of pneumonia and when they cause pneumonia, it is mainly in infants and immuno-compromised patients.

- Influenza
- Respiratory syncytial virus (predominant in infants).
- Para - influenza virus
- Adenoviruses

#### Parasitic causes:

- Paragonimus westermani
- Loeffler's syndrome (Ascaris lumbricoides, Strongyloides stercoralis, Ancylostoma duodenale).

### Hospital Acquired (Nosocomial) Pneumonia (HAP):

(48hs or more after admission)

(**Klebsiella pneumoniae**, **Pseudomonas aeruginosa** and **E. coli**, **Staphylococcus aureus** MRSA).

**Empyema** (a collection of pus in the pleural cavity): Mostly caused by pyogenic G+ve cocci especially **Staphylococcus aureus** and G-ve bacilli especially **Klebsiella pneumoniae**.

**Lung Abscess: Anaerobes** (Peptostreptococcus spp., Prevotella spp. and Fusobacterium), **S. aureus**, **K. pneumoniae**.

## STREPTOCOCCUS PNEUMONIAE

### "PNEUMOCOCCI"



some strains of Streptococcus pneumoniae may lack distinct surface antigens or may possess antigens that are not recognized by the antibodies used in traditional serotyping methods. As a result, these strains cannot be classified into specific serotypes, making them non-typeable

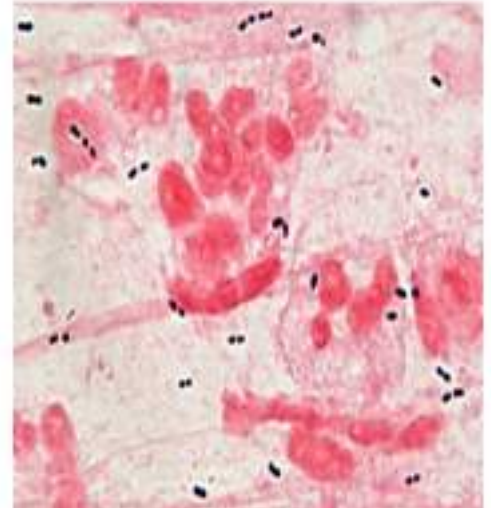
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# Respiratory System

## Morphology

- **Gram-positive, diplococci (arranged in pairs).**
- **Capsulated (Polysaccharide capsule),**  
capsule appears as unstained halo around the organism.



## Culture:

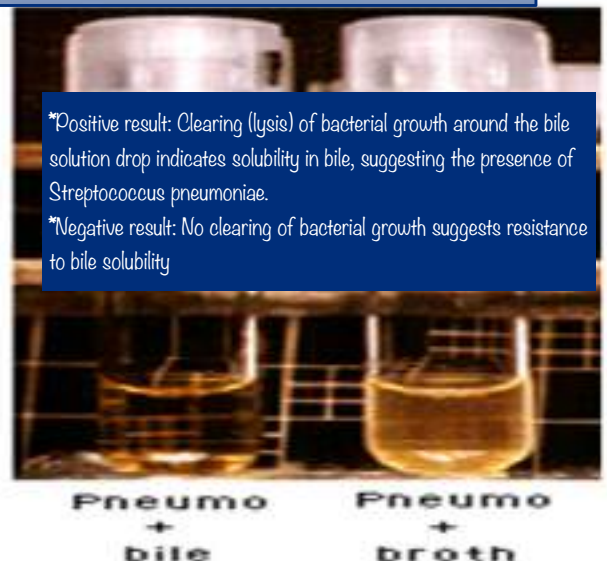
- Aerobic and facultative anaerobe.
- Does not grow on ordinary media. Growth needs an enriched media as blood agar.
- On blood agar, colonies are surrounded by **partial zone of haemolysis with greenish discoloration (Alpha haemolysis).**
- It is **sensitive to optochin (Antibacterial agent).**
- The pneumococcus **dies rapidly in cultures due to natural autolysis.**



These enzymes break down the cell wall components, leading to the rupture of the bacterial cell and subsequent death. In cultures, when the conditions are not optimal or when the bacteria reach a certain density, the autolytic enzymes become activated, causing the bacteria to undergo rapid self-destruction.

## Biochemical reaction:

- **Ferment Inulin.**
- **Soluble in bile.**
- **Catalase-negative.**



\*Positive result: Clearing (lysis) of bacterial growth around the bile solution drop indicates solubility in bile, suggesting the presence of *Streptococcus pneumoniae*.

\*Negative result: No clearing of bacterial growth suggests resistance to bile solubility



# Respiratory System

لأنهم يعملوا Alpha haemolysis

بدي افرق بينهم

Table: Differences between Strept. viridans and Pneumococci

	Pneumococci	Strept viridans
1) Capsule	Capsulated	Non - capsulated
2) Bile solubility	+	-
3) Optochin sensitivity	+	-
4) Inulin fermentation	+	-

## 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  $\alpha$ -hemolysis).
- **Autolysin:** lyse the bacterial wall and release potentially lethal toxins.

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# Respiratory System

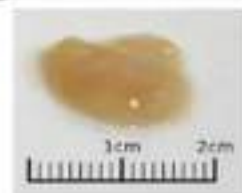
## Pathogenesis & clinical findings:

➤ 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**
- Immunocompromized e.g., HIV, cancers,...
- **Abnormality of the respiratory tract** (viral infections, chronic lung diseases,..)



## Diagnosis:

Specimen: Sputum, CSF, Blood,...

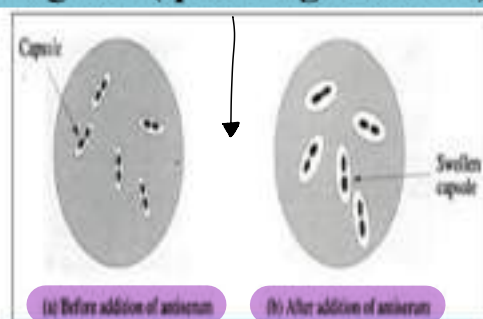
+ كنا نعمله في ال Haemophilus influenzae

1) Gram Stained smears (**Gram-positive diplococci** with unstained halos).

2) Detection & typing of capsule: Capsule swelling test (**quellung reaction**).

3) Culture on blood agar:

- **Alpha haemolysis.**
- **Soluble in bile.**
- **Optochin sensitive.**



4) **Blood cultures** are positive in 15% to 25% of pneumococcal infections.

↪ Associated with bacteremia

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**Prophylaxis:** Two types:

1) **Capsular polysaccharide vaccine**

2) **Pneumococcal conjugate vaccine** (Capsular polysaccharides + protein carrier).

➤ They are **recommended** for:

- **All children less than 2 years of age.**
- **Elderly more than 65 years.**
- Adults with **certain medical conditions** (e.g. immunocompromised, chronic lung disease, **asplenia**,...).

## **KLEBSIELLA PNEUMONIAE** **"FRIEDLANDER'S BACILLUS"**



### **Morphology:**

- It is **Gram-negative bacilli, Non-motile.**
- <sup>Large</sup> **Capsulated** both in tissue and in vitro culture.

### **Culture:**

- **On MacConkey's medium**, it produces **rose pink** colonies due to **lactose fermentation**.
- **Colonies are big, high convex** with a striking characteristic **muroid appearance** due to the production of a **very large polysaccharide capsule**.





# Respiratory System

## Pathogenesis & Clinical findings:

➤ It is **important cause of nosocomial infections:**

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

Sputum characterized by being thick, mucoid, bloody

“**currant jelly sputum**”.

❖ **Urinary tract infections.**

❖ **Bacteremia.**

➤ Infections frequently **have predisposing conditions??**

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

**Hospital Acquired (Nosocomial) Pneumonia (HAP):**  
(48hs or more after admission)  
(*Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *E. coli*, *Staphylococcus aureus* MRSA).

+pneumococcus



**Empyema** (a collection of pus in the pleural cavity): Mostly caused by pyogenic Gram cocci especially *Staphylococcus aureus* and Gram bacilli especially *Klebsiella pneumoniae*.

**Lung Abscess:** Anaerobes (*Peptostreptococcus* spp., *Prevotella* spp. and *Fusobacterium*), *S. aureus*, *K. pneumoniae*.

\* Immunocompromised e.g. HIV, cancer, ...  
\* Abnormality of the respiratory tract (viral infection, chronic lung diseases, ...)

pneumococcus = rusty sputum

*Pseudomonas aeruginosa* = Greenish colour of sputum

## BACILLUS ANTHRACIS

anthracis means coal or coal-like, referring to the coal-like ulcers that form in the skin during anthrax infections.



### Morphology:

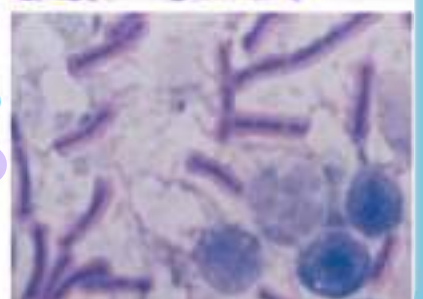
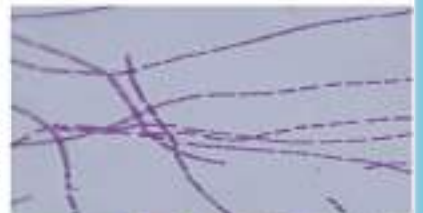
➤ **Gram positive bacilli**, non-motile, **arranged in chains.**

➤ **Sporulated** in vitro. The spores are **oval, central** and **not stained with Gram stain.**

من خلال هاي المعلومة يميزها عن *Corynebacterium diphtheriae*  
لاتها كمان Gram positive bacilli بس هي Non-spore-forming

➤ The organism is capsulated (**Polypeptide capsule**, **“D-Glutamic acid”**) only inside the body, appears as unstained hallow in gram stain).

➤ When the organism is stained with **polychrome methylene blue**, the organism stains blue while the capsule purplish. (**McFadyean’s reaction**)



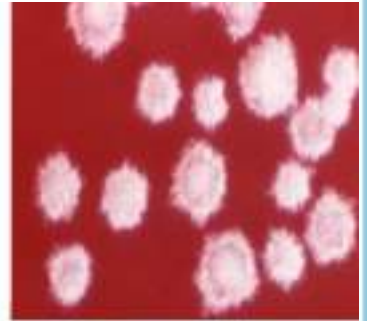


# Respiratory System

## Culture:

- **Aerobes;** grow on **ordinary media.**
- **Colony is large opaque disc** with **rough granular surface** and **irregular fimbriate edge (medusa head colony).**
- Colonies on blood agar are **non-hemolytic**
- It **liquefies gelatin (proteolytic activity)** giving an **inverted fire tree** appearance.

it can break down proteins. Gelatin is a protein commonly used in laboratory settings to create a solid medium for bacterial growth. When *Bacillus anthracis* is cultured on gelatin, it secretes enzymes that break down the gelatin, resulting in liquefaction.



## Virulence factors:

### A) Very powerful exotoxin.

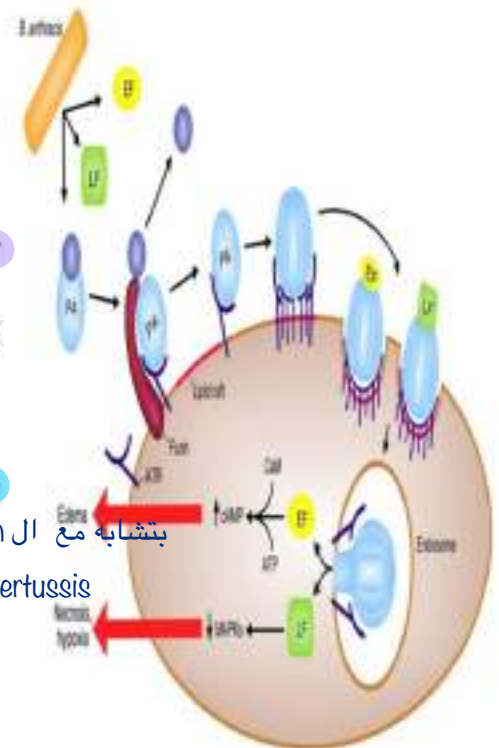
The toxin consists of 3 domains:

**Protective antigen (PA):** binds to specific receptor on host cell with its **proteolytic activity** producing membrane channel and permits entrance of:

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

**Lethal factor (LF)** which cause **tissue necrosis.**

### B) Protein capsule: Antiphagocytic.



بتشابه مع ال Pertussis toxin في

*Bordetella pertussis*

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# Respiratory System

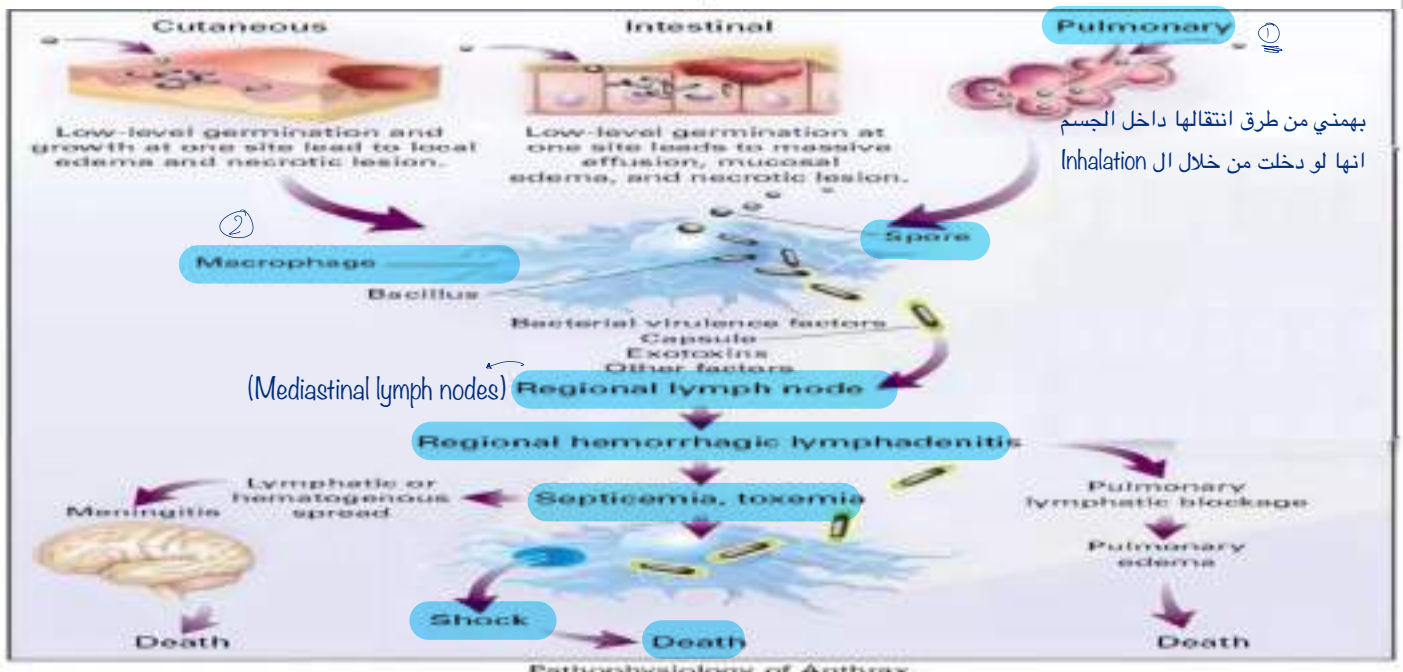
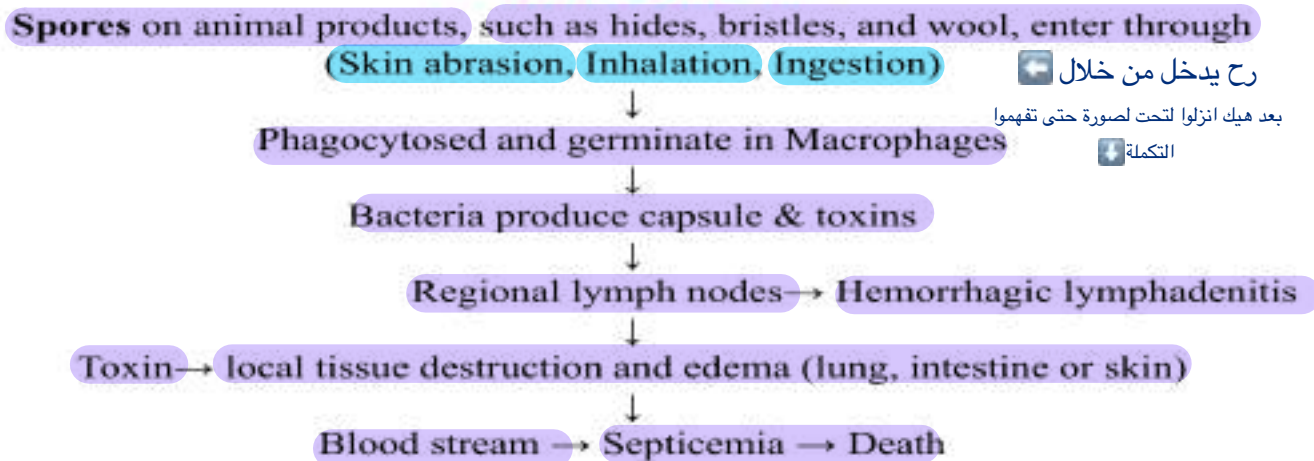
## Anthrax

- It is a disease of farm animals e.g. cattle and sheep (**Zoonotic disease**). ✨
- Man infected by **coming in contact with diseased animals or their dead bodies**.
- Farmers, butchers, wool sorters and veterinarians are more liable to infection.
- Infection could occur in different forms, **the commonest forms are:**

- 1- **Cutaneous anthrax (malignant pustule)**
- 2- **Pulmonary anthrax (wool sorters disease)**
- 3- **Intestinal anthrax**



## Pathogenesis





# Respiratory System

## PULMONARY ANTHRAX "Wool sorters disease"

عمال فرز الصوف



- Pulmonary anthrax occurs when spores are inhaled into the lungs.
- 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**).
- Begins with nonspecific respiratory symptoms resembling influenza.
- This **rapidly progresses to hemorrhagic mediastinitis** (fever, chest pain, RDS and widened mediastinum on chest X-Ray). 🚨🚨🚨
- End by septic shock and death (**Mortality rate is very high > 95%**).



### Diagnosis:

1- **Chest X- Ray or CT scan:** widening of mediastinum or pleural effusion.

2- **Detection of the organism in:**

- **Blood:** blood cultures is positive in most cases. The organism identified by Gram stain, subculture or PCR.

لانه ال organism مش موجود في ال  
air spaces

- **Sputum:** Not useful and seldom yields positive smears or cultures.

3- **Detection of toxin in blood:** (test specific for the PA component of the toxin e.g. ELISA, IF).



# Respiratory System

## 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.

\***Antibiotics** effective only if given before the lymphatic spread or septicemia.



## Anthrax as a Biological Weapon

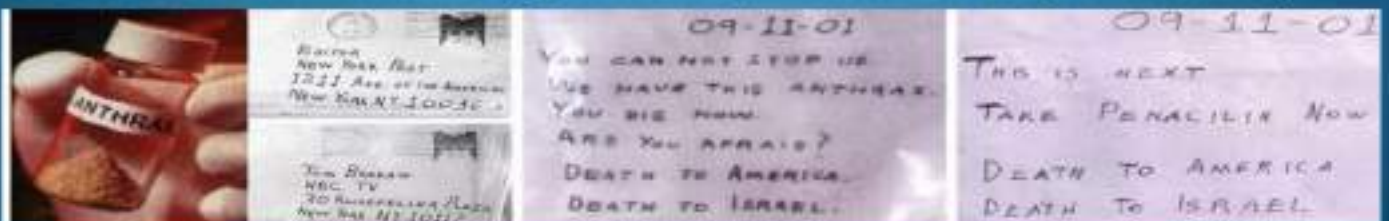


- Biological weapons are germs that can sicken or kill people, livestock, or crops.
- **Anthrax is one of the most likely agents to be used because:**
  - ❖ **Virulent organism with high fatality.** iespecially if not promptly treated.
  - ❖ **Forms spores** which:
    - ✓ Can be produced in lab and put into powders, sprays, food, and water.
    - ✓ Very small so, you may not be able to see, smell, or taste them.
    - ✓ Can last for years in the environment.

مش مطلوبة للامتحان

## BIOTERRORISM-anthrax as a bioweapon

- Anthrax was used by Scandinavian rebels against Russians
- Operation vegetarian by Royal Air Force against Germany in 1944 ,an anti-livestock operation
- In 1997-accidental release of anthrax spores from biological weapons complex in Russia infected 94 people ,68 died
- In Oct.2001 anthrax attacks in USA termed Amerithrax(FBI) 22 cases- 11 inhalation(5 deaths),11 cutaneous(no deaths)





# Respiratory System

Characteristic	<i>Streptococcus pneumoniae</i> (Pneumococci)	<i>Klebsiella pneumoniae</i> (Friedlander's Bacillus)	<i>Bacillus anthracis</i>
Morphology	Gram-positive diplococci	Gram-negative bacilli, Non-motile	Gram-positive bacilli, arranged in chains
	Capsulated (Polysaccharide capsule)	Capsulated both in tissue and culture	Capsulated (Polypeptide capsule)
			Sporulated in vitro
Culture	Aerobic and facultative anaerobe	Lactose fermentation produces rose pink colonies	Aerobes; grow on ordinary media
	Requires enriched media like blood agar	Big, high convex colonies with mucoid appearance	Large opaque disc colonies with irregular fimbriate edge
	Sensitive to optochin		Non-hemolytic colonies on blood agar
Biochemical Reaction	Ferments Inulin, Soluble in bile, Catalase-negative		Liquefies gelatin (proteolytic activity)
Virulence Factors	Polysaccharide capsule, IgA protease, Pneumolysin, Autolysin		Very powerful exotoxin, Protein capsule
Pathogenesis	Common cause of otitis media, sinusitis, pneumonia, bacteremia, meningitis	Nosocomial infections, pneumonia, urinary tract infections, bacteremia	Cutaneous, pulmonary, and intestinal anthrax
Clinical Findings	Fever, chills, cough with "rusty" sputum, dyspnea, tachypnea	Thick, mucoid, bloody "currant jelly" sputum	Widening of mediastinum, pleural effusion
Prevention	Capsular polysaccharide vaccine, Pneumococcal conjugate vaccine		Active immunization with protective antigen vaccine



# Respiratory System

1) A 65-year-old male presents to his family physician with a rapid onset fever, chest pain and cough productive of rusty-yellow sputum. Chest X-ray shows focal lobar infiltrates. A Gram stain of a sputum sample contained many polymorphonuclear leukocytes and extracellular gram-positive diplococci. Capsule-specific antibodies bound to the diplococci resulted in a positive Quellung reaction. Which of the following is the most likely pathogen?

- A. *Streptococcus pneumoniae*
- B. *Enterococcus faecium*
- C. *Streptococcus pyogenes*
- D. *Streptococcus agalactiae*
- E. *Enterococcus faecalis*

Correct answer = A. The most common cause of community acquired pneumonia in this age group is *Streptococcus pneumoniae*. The X-ray and microbiological findings are most consistent with a diagnosis of pneumococcal pneumonia.

2) A 45-year-old cattle rancher presents to his physician with a wound on his forearm that resembles a large scab. Samples collected from the wound were cultured and examined. The bacteria recovered were Gram positive, nonmotile rods with square ends. The cultured bacteria formed irregularly shaped, non-hemolytic colonies on blood agar plates and individual cells from the plates had a centrally located spore. What is the most likely cause of this infection?

- A. *Listeria monocytogenes*
- B. *Staphylococcus aureus*
- C. *Legionella pneumophila*
- D. *Corynebacterium diphtheriae*
- E. *Bacillus anthracis*

Correct answer = E. This cattle rancher is suffering from cutaneous anthrax, which is an occupational hazard. The scab like wound is called an eschar and results from localized edema and tissue destruction caused by the two toxins produced by *Bacillus anthracis*. The microbiological characteristics of the organism are consistent with a diagnosis of *B. anthracis* infection. The other microorganisms do not have the characteristics described.



# Respiratory System

3) A male older adult, hospitalized and recovering from cardiac bypass surgery, develops pneumonia. Sputum culture reveals a gram-negative rod that produces a green pigment but does not ferment carbohydrates.

The most likely organism is:

- A. *Klebsiella pneumoniae*.
- B. *Serratia* species.
- C. *Proteus* species.
- D. *Enterobacter* species.
- E. *Pseudomonas aeruginosa*.

Correct answer = E.. *Pseudomonas aeruginosa* is an obligate aerobe that uses respiratory pathways exclusively. Production of green pyocyanin pigment regularly occurs.

4) An older, alcoholic male develops severe, necrotizing lobar pneumonia. The organism is Lact and produces a luxuriant capsule. The most likely agent is:

- A. *Klebsiella pneumoniae*.
- B. *Serratia* species.
- C. *Yersinia pseudotuberculosis*.
- D. *Pseudomonas aeruginosa*.
- E. *Campylobacter fetus*.

Correct answer =A

5) A 22-year-old Hispanic man worked for a company that processed animal products and provided no medical coverage benefits. One week after working with wool imported from a Caribbean island, he developed a small lesion on his arm resembling an insect bite. One week later, the lesion was 2.5 cm in diameter with a central, black sloughed-skin area. Two weeks later, he presented at an emergency room with early stages of sepsis. Which of the following microbes is responsible for the infection?

- (A) *Bacillus anthracis*
- (B) *Bacteroides melanogenicus*
- (C) *Hemophilus ducreyi*
- (D) *M. scrofulaceum*
- (E) *Treponema pallidum*

Correct answer =A

## Bacteria – Gram Positive Cocci



### Strep Pneumonia “the alpha knight tournament”

1. Purple Background - G+
2.  $\alpha$  knight tournament –  $\alpha$  hemolytic, partial hemolysis where the surrounding zone is a green hue
3. **Strep Pneumonia Knight**
4. Armor – Polysaccharide Capsule is major virulence factor
5. Chin is exposed – Optochin sensitive, optochin inhibits the growth of strep pneumo
6. Double Lance – Lancet shaped diplococci
7. Mud on horses legs - Bile soluble, meaning it does not grow in Bile
8. Rust Colored single lobe on chest – Rust colored sputum and lobar pneumonia
9. Squire mopping up muddy mess MOPS - Meningitides, Otitis Media, Pneumonia, Sinusitis
10. Number 1 sign – number one cause of all these diseases.
11. Cracked Shield with the symbol of IgA dimer molecule - Protease that cleaves IgA that allows invasion of mucosa reducing host defenses
12. Sickle - Removal of spleen leads to susceptibility of infection by encapsulated organisms like in sickle cell anemia.
13. Crows – azithromycin Macrolides
14. 3 Axes - Ceftriaxone
15. **Adults** in the **Mezzanine**, **Children** on the **Ground** - 2 pneumococcal vaccines, adult is a 23 valiant polysaccharide vaccine, children is 7 valent but conjugated to a protein. Adults will have a T-Cell independent response creating IgM that does not last long. Adding the protein adds a more robust antigen response leading to a production of IgG in children.

## Bacteria – Gram Positive Bacilli



### Bacillus Anthracis

### – King Anthra's Axe

- |   |   |
|---|---|
| <ol style="list-style-type: none"> <li>1. Vikings standing around red hot flames and black in the middle – Black Eschar with erythematous ring.</li> <li>2. Viking ships lined up in the background - Large gram pos rods in chains</li> <li>3. Leather armor – encapsulated, this one is made of a protein</li> <li>4. D Belt Buckles - Capsulated with Poly –D glutamate</li> <li>5. Air Bellow - Obligate Aerobe</li> <li>6. walnuts – Bacillus anthracis is a spore forming bacteria allowing them to survive in very poor environments</li> <li>7. Viking Camp Test - EF Toxin <u>increases cAMP intercellularly</u> this will cause fluid to go extracellular space leading to edema inhibiting host defenses and preventing phagocytosis</li> <li>8. MAP with Lethal Factor Viking Burning it - LF (lethal Factor), exotoxin that acts as a protease and <u>cleaves MAP Kinase</u>, this is a signal transduction protein that is responsible for cell growth. This factor will lead to necrosis and black eschar</li> </ol> | <ol style="list-style-type: none"> <li>9. Sheep – pulmonary anthrax, wool sorters disease. Spores can get into wool and hide of animals and persist there. People will inhale the spores when the animal is handled.</li> <li>10. Axe that is dripping blood – represent pulmonary anthrax that can move to mediastinal lymph nodes progressing to hemorrhagic mediastinitis</li> <li>11. Viking ship with a mast supposed to look like a chest xray – widened mediastinum</li> <li>12. Flower and Bicycle wheel on the ship – txt is fluoroquinolone or doxycycline</li> </ol> |
|---|---|



## Bacteria – Gram Negative Bacilli



Klebsiella

9. Klebsiella - Ankylosaurs with club shaped tail - Immotile
  - a. Three A's in the spikes –Alcoholics, Abscesses, Aspiration
  - b. Thick shell like scales is like a polysaccharide capsule
  - c. Knocked over jar of currant jelly, that is sticking him to the table - Current jelly like sputum that is a red color
  - d. Jelly sticking klebsiella to the table - Klebsiella is immotile
  - e. X-Ray - Cavatory lesion on patients right lobe "tb like"
  - f. Ammonia spray bottle - Urease positive