Bacterial Upper Respiratory Tract Infections

TEAM 439
MICROBIOLOGY

VERSION 1

Objectives

- Discuss the epidemiology and various clinical presentations of URTIs
- Identify the most important etiological agents causing different URTIs, and discuss their virulence factors, laboratory diagnosis and potential preventative strategies
- Determine the antibiotic of choice for the different URTIs
- Discuss complications of GAS and C. diphtheriae infections

Outline

- Pharyngitis, GAS
- Diphtheria
- Epiglottitis
- Whooping cough
- Otitis Media
- Sinusitis
- Deep neck space infections

Colour index:

Red: Important & Doctor's notes.

Grey: Extra info & explanation.

Purple: Only in girl's slides.

Green: Only in boy's slides.

Any future corrections will be in the editing file, so please check it frequently.

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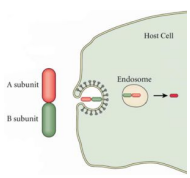
Bacteria (in This Lecture)

- **Gram Positive**
  - GAS (Strept. Pyogenes)
  - Corynebacterium diphetheriae
  - Streptococcus Pneumoniae
- **Gram Negative**
  - Haemophilus Influenzae
  - Bordetella Pertussis
  - Moraxella Catarrhalis

Group A Streptococcus (GAS)

Morphology	Gram +ve cocci in chains, Facultative anaerobe, β haemolytic, Catalase -ve.
Infections	Respiratory infections: • Pharyngitis • Otitis • Sinusitis Other infections: • Skin and soft tissue (Impetigo, Erysipelas, Cellulitis, Necrotizing fasciitis.... Remember???) • Joint and Bone infections (e.g. Acute osteomyelitis in children 2-5 yo) #MSK
Virulence Factor	• Capsule (Antiphagocytic-resist phagocytosis) • M protein in cell wall it helps GAS to **adhere** to epithelial cells of the nasopharynx. Also, plays an essential role in GAS **resistance to phagocytosis**. How? The domains of the molecule will bind to serum factor H, which will lead to to a diminished availability of alternative pathway-generated complement system. • Streptolysin O & S (pore-forming cytotoxin , responsible for the β hemolysis of GAS) التوكسن هذا يثبك على السيل ممبرين لخلية الهوست، الدم مثلا، ويسوي فيه فتحات pores ، ويبطلع كل شي منها وتتحلل الخلية. بالضبط نفس الـhemolysis اللي نشوفه عالبلود اقار. • Streptococcal pyrogenic exotoxins (SPE) (Superantigen, result in excessive activation of the immune system).
Notes (Sherris)	• GAS is the most common bacterial cause of sore throat. • Transmission is person-to-person from the large **droplets** produced by infected persons during coughing, sneezing, or even conversation (Short distances (2-5 feet))

Corynebacterium diphtheriae

Morphology	Gram Positive rod shaped. Dr: the only bacteria that produces black colonies on the blood agar on special media.
Infections	• Diphtheria pharyngitis
Virulence Factor	• **Diphtheria toxin (DT).** A-B toxin that acts in the cytoplasm to inhibits protein synthesis irreversibly in a wide variety of eukaryotic cells. إذا تتذكرون يادكاترة في محاضرة Host-Parasite درسنا A-B Subunit toxin. شرحنا وقلنا B subunit هي اللي ترتبط بالخلية وتضبط الوضع ويدخلون في Vacule لكن A subunit هي اللي بتوقف تصنيع البروتين. Does this picture ring a bell? 
Extra	• It is also known as the Klebs-Löffler bacillus, because it was discovered by German bacteriologists Edwin Klebs Friedrich Löffler. • "They call it Chinese letters under microscope" **Doctor says.**

Haemophilus Influenzae

Morphology

- ❖ Gram Negative pleomorphic, Fastidious. (Coccobacilli)
- ❖ Oxidase AND Catalase Positive.
- ★ Requires X (heme) and V (NAD) factors for growth, used to confirm ID
- ❖ Does NOT grow in regular aggars.
- ❖ It causes periorbital cellulitis in children, remember MSK?

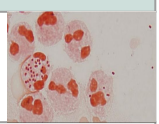
هذي البكتيريا تتغذى على فاكترز X & V سوا اللي موجودين بالدم. ولكن في الـBlood agar العاديةمافيه فاكتر V.
فلذلك لا تنمو إلا في Chocolate agar واللي هي بلود اقار بالأصل، لكن بعد ماتحللت بتعرضها للحرارة وصار لها lysis طلعت انزيم فاكتر V

Types	Encapsulated (Typable)	Non-Encapsulated (Nontypable)
Causes	Cause invasive disease: (invade bloodstream) - Epiglottis - Meningitis - Associated with bacteremia.	Cause local infections: - Sinusitis - Otitis - Pneumonia in elderly
Virulence and Prevention	❖ Capsule is the main virulence factor ❖ A-F, Most important is type B The type B capsule comprises a polymer of ribose, ribitol, and phosphate, called **polyribitol phosphate (PRP).** These surface polysaccharides are strongly associated with virulence, particularly in ***H influenzae* type b (Hib)**. **In short:** Type B is **more virulent** that types A, C,...F because of the composition of its capsule. ❖ Prevention is through a vaccine	-
Treatment	❖ Amoxicillin-Clavulanate ❖ 2nd or 3rd generation Cephalosporin	

Bordetella Pertussis

Morphology	- Gram Negative coccobacilli - Requires a special agar: Charcoal blood (Regan-Lowe) or Bordet-Gengou agar
Infections	● Pertussis (Whooping cough)
Virulence Factor	★ **Pertussis toxin** (Major virulence factor, It is an A-B toxin) ❖ Filamentous hemagglutinin A protein that binds to & agglutinate erythrocytes. Thus, it contributes to strong adherence. ❖ Pertactin (Adhesive structure, just like hemagglutinin).
Notes	● Once attached to mucosa, the bacteria immobilize the cilia and begin to destroy it. بالتالي لو اخذنا Throat swab مارح نلقى شي لأن ماراح يكون فيه cilia أصلًا! فلذلك لازم ناخذ Nasopharyngeal Swab

Moraxella Catarrhalis

Morphology	- Gram negative diplococci. - Catalase and oxidase positive. 
Infections	● Otitis ● Sinusitis ● Pneumonia
Treatment	● Amoxicillin (penicillin binding protein inhibitor) or Amoxicillin + Clavulanic acid (β-lactamase inhibitor)

Bacterial Upper Respiratory Tract Infections

- **Pharyngitis**
  - **GAS**
  - **Diphtheria**
- Epiglottitis
  - Haemophilus Type B
- Pertussis
  - Bordetella Pertussis
- Otitis Media
- Sinusitis
- Deep Neck Space infections

Dr's note: most upper respiratory tract infections are caused by viral infections. Later on, it will be followed by bacterial infection.

Pharyngitis

(Inflammation of pharynx)

Epidemiology	Late fall, winter, early spring, 5 to 15 years "Exposure to infection in school"	
Etiology	**Viral Cause** ❖ (i.e. respiratory viruses) **are the most common cause.** E.g. Corona, H. influenza type A & B **Bacterial causes include:** ❖ Most importantly, Streptococcus pyogenes (i.e. **Group A streptococcus**). ❖ **Corynebacterium diphtheriae** (More serious "Fatal" but less common due to the vaccination) ❖ Fusobacterium necrophorum (Anaerobic bacteria, cause of Lemierre's syndrome) ❖ Neisseria gonorrhoeae (STD)	
Signs and symptoms	**Common Symptoms:**	- Sore Throat - Pharyngeal erythema (redness), edema - Fever
	More consistent with **Viral Cause**	- Coryza (Runny nose) - Cough "if the cough is absent, mostly it's bacteria" - Conjunctivitis "especially if both eyes"
	More consistent with **bacterial Cause** (GAS)	- Tonsillar exudates (Pus collection) - Tender, enlarged >1 cm lymph nodes - Fever 38.4 to 39.4° C (high fever) -Skin rash (scarlet rash)  Scarlet Rash

A- Pharyngitis Caused by GAS

Diagnosis of GAS pharyngitis	❖ **Throat swab:** Take sample of the tonsils from the exudate using tongue depressor then we culture it - Rapid Bacterial antigen detection. Faster results but less sensitive because the antigen might be in low quantity leading to false negative. - Culture on blood agar (β haemolytic) it takes more time but more accurate results. ❖ **Anti-Streptolysin O** (Test mainly used when the patient comes with a complication but undiagnosed infection, to see if the patient previously had GAS pharyngitis by detecting antibodies against Streptolysin O اللي شرحناه فوق - **it is NOT used to diagnose patients IMMEDIATELY after infection**).	
Treatment of GAS pharyngitis	★ **Penicillin for 10 days** GAS almost has zero resistance against Penicillin If the patient is allergic: Clindamycin or macrolide (e.g. Clarithromycin)	
Complications of GAS pharyngitis If GAS pharyngitis is treated it will also **prevent suppurative complications and rheumatic fever**. However, it will **not stop glomerulonephritis**	Suppurative (pus forming)	E.g. Peritonsillar abscess, parapharyngeal space abscess
	Non Suppurative (Non pus forming) More serious (Occurs 1-6 weeks after acute GAS infection)	**1- Rheumatic fever:** - After infection of the respiratory tract only. - Inflammation of heart (pancarditis), joints, blood vessels, & SC tissue. - The patient complains of arthralgia " آلام في المفاصل " - Results from cross reactivity of Anti-M protein Ab and the human heart tissue. (immune system related, NOT direct invasion by the organism) **2- Glomerulonephritis:** In kidney - After infection of the skin or the respiratory tract. - Symptoms: edema, hypertension, hematuria, and proteinuria. - Initiated by Ag-Ab complexes on the glomerular basement membrane. (Also immune system related, NOT direct invasion by the organism)

Note that: Rheumatic fever only occurs post respiratory infections. However, glomerulonephritis occurs post skin **AND** respiratory infections.

B- Diphtheria (الخُنَّاق)

Overview	❖ Rare in developed countries, because it can be prevented by vaccine. ❖ Mainly Presented as Upper respiratory tract infection. ★ Characterized by formation of **pseudomembranes** on the pharynx/throat. ❖ Diphtheria usually manifests as pharyngitis. ❖ It can be severe and cause breath difficulties.
Etiology	❖ Corynebacterium diphtheriae
Virulence	★ **Diphtheria toxin** (DT) (Responsible for the Destructions and Complications.)
Diagnosis	❖ Throat swab. (Mainly) ❖ Culture on special media (Tinsdale media) containing tellurite **to confirm Corynebacterium diphtheriae.** (الـthroat مليان نورمال فلورا وعشان نقدر نميزها نحتاج سبيشل ميديا) .Tellurite enhances the production of black color on the agar ❖ ELEK's test **to confirm the toxin production** Because the disease is caused by DT toxin, not the bacteria itself. (In this test, there is a strip containing antitoxin, when the bacteria interacts with it we know the toxin is there, hence the bacteria).
Treatment	❖ Antitoxin "Antigen attach to the toxin in the blood" **AND** Antibiotic "deal with the organism in the throat" (Penicillin or erythromycin "if the patient has allergy")
Prevention	❖ Vaccination with diphtheria toxoid containing vaccine. الوقاية منه تكون بتطعيمة الثلاثي البكتيري (DPT) وتعطى للأطفال بعمر شهرين * إلزامية بالسعودية وأغلب الدول DTP is a com vaccine for diphtheria, tetanus, and pertussis.
Complications	★ **Myocarditis** Affects the muscles of the heart ends with heart failure. ★ **Neuritis** Inflammation of nerves.

Infection is in the throat. However, the toxin goes everywhere in the body

Epiglottitis

Inflammation of Epiglottis

Overview	❖ Usually affect young **unimmunized** children. ❖ Affecting breathing and sometimes can be a medical emergency.
Signs and symptoms	❖ Dysphagia (Swallowing difficulties) ❖ Drooling (drop saliva uncontrollably from the mouth) ❖ Respiratory distress, hypoxia, cyanosis.
Etiology	★ **Haemophilus Influenzae Type B** ❖ S. pneumoniae ❖ S. aureus ❖ Beta hemolytic streptococci
Diagnosis	❖ Blood cultures Patient will have **bacteremia**, so we can culture the blood itself in a chocolate agar. ❖ Culture of epiglottic surface (under controlled setting) ❖ **Swab is usually not taken**, unless there is airway support ❖ Lateral X-ray
Management Treatment	★ **Maintenance of airway** This infection must be treated as a medical emergency, with primary emphasis on maintenance of an airway (tracheostomy or endotracheal intubation) and antimicrobial therapy. Clinical maneuvers such as direct examination or attempting to take a throat swab may trigger acute obstruction and fatal laryngospasm. ● Empiric treatment: Ceftriaxone + Vancomycin. It means antibiotic therapy before knowing the cause, covering staph, strept, haemophilus, etc..
Prevention	❖ **HiB Vaccination** (Against H.influenzae type B)

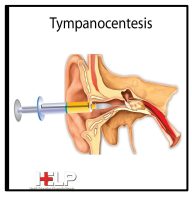
Pertussis (aka. Whooping Cough)

Mainly in children, السعال الديكي

Etiology	Bordetella pertussis (GNB), virulence factor is **Pertussis toxin**
Stages of pertussis	❖ Incubation period 1 to 3 weeks ❖ **1- Catarrhal Stage** 1-2 weeks Symptoms during this phase resemble that of an upper respiratory illness or common cold: runny nose, nasal congestion, sneezing, and occasional cough. ❖ 2- **Paroxysmal Stage** 2-4 weeks Intense and drawn out bouts of coughing characterize this phase. The attacks tend to be more frequent at night, with an average of 15 attacks in a 24-hour period. ❖ 3- **Convalescent Stage** 1-2 weeks a chronic cough that becomes less paroxysmal (fewer sudden outbursts of coughing) in nature characterizes this stage.
Diagnosis	Sample: **Nasopharyngeal (NP) swabs**. (from nasopharynx not nose or nasal cavity, وشرحنا فوق السبب) Special media needed: Charcoal blood (Regan-Lowe) or Bordet-Gengou or PCR
Treatment	● Macrolide (erythromycin).
Prevention	● Acellular pertussis-containing vaccine. Such as DTP There are two main types: whole-cell vaccines and **acellular** vaccines. AND just like we explained before, DTP vaccine is combined against **diphtheria, tetanus, and pertussis**, in which the **pertussis** component is **acellular**.

Acute Otitis Media

Area behind the eardrum called the middle ear becomes inflamed and infected.
Very common infection in the first two years.

Overview	Fluid accumulation + inflammation of the mucosal lining of the middle ear. More common in children.
Etiology	1- S. Pneumoniae 2 - H. influenzae (Non typable) 3- S. aureus 4- Moraxella catarrhalis 5- GAS 6- Viral (alone or with bacteria) Start as viral infection then become bacterial infection
Diagnosis	- Mainly clinical diagnosis - Tympanocentesis sometimes needed The drum is bulging so we need to drain it to take a sample & relieve the patient - Middle ear fluid can be sent for culture. 
Treatment	Amoxicillin or Amoxicillin Clavulanic acid

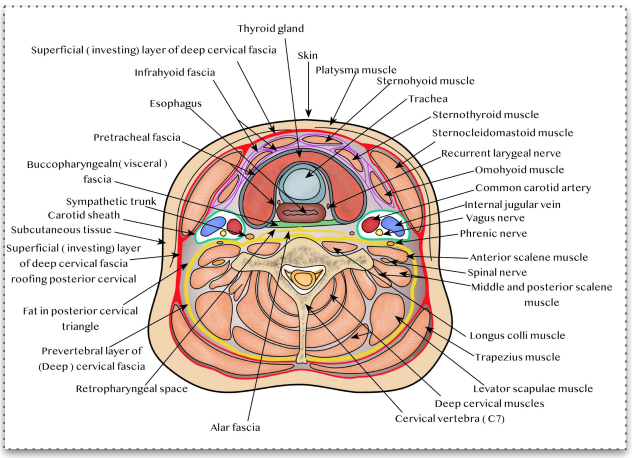
Acute Bacterial Sinusitis

Overview	- More common in children. - Occurs with viral URTI Start as viral infection then become bacterial. 
Etiology	1- S. Pneumoniae 2- H. influenzae (Non typable) 3- Moraxella catarrhalis 4- Anaerobes 5- Viral
Diagnosis	Mainly clinical diagnosis, Imaging **(CT/MRI)** when there is suspension of complications. (لأن المرض خطر ممكن يروح للعين أو المخ لأن مكانها قريب لهم) 
Treatment	- Amoxicillin Clavulanic acid For 1-2 weeks

Dr's Note: Bacteria that causes acute otitis media, acute sinusitis, and pneumoniae are the same

Deep Neck Space Infections

- Lateral pharyngeal, retropharyngeal or prevertebral space.
- Patients are very sick and toxic .
- Neck stiffness can occur with retropharyngeal space infection/abscess .
- Retropharyngeal (danger space) infection may extend to mediastinum and present as mediastinitis.
- **Usually polymicrobial.**
- **Mainly streptococci and oral anaerobes.**
- **Management:**
- **Surgery.**
- **Antibiotics.**
- **Meropenem.**
- **Piperacillin.**
- **Clindamycin.**
- **Duration:**
- **2-3 weeks.**



Last But Not Least

Check Our Summary!

By Clicking here

CASES / SAQ

Case 1: A mother brings her 5 year old unvaccinated son to the emergency department, where he presents with acute dysphagia, respiratory distress & fever. A blood culture was grown on a chocolate agar and showed gram negative coccobacilli.

a) What is the most likely diagnosis b) organism c) treatment d) is it preventable?

Case 2: A 6 year old unvaccinated patient that has recently arrived from India has fever, sore throat, and formation of pseudomembranes on the throat.

a) What is the most likely diagnosis b) organism c) treatment d) how is it diagnosed
e) what is the virulence factor f) What are 2 potential complications?

Case 3: A 3-year-old boy is brought to the hospital because he has been coughing for the past 2 weeks. His mother states that cough seems to come in bouts(phases). The coughing is sometimes severe enough to cause him to vomit.

a) What is the most likely diagnosis b) organism c) treatment d) how is it diagnosed
e) what is the virulence factor f) is it preventable?

Case 4: A 10 year old patient comes to the office complaining from acute pain in his ear. Upon examination a bulging tympanic membrane was found. A tube was inserted into the middle ear and fluid was extracted, it showed gram negative diplococci.

a) What is the most likely diagnosis b) organism c) treatment

Case 5: A teenager comes to the hospital with a fever and sore throat. A throat swab showed a Beta hemolytic colony.

a) What is the most likely diagnosis b) organism c) treatment d) name 4 potential complications?

Answer Key:

1a: epiglottitis
1b:H.influenzae Type B
1c: Ceftriaxone + Vancomycin
1d: yes, by vaccine

2a: Diphtheriae pharyngitis
2b:C.diphtheriae
2c: Antitoxin+penicillin or erythromycin
2d: Throat swab & culture on tinsdale media
2e: Diphtheria toxin
2f: Myocarditis & Neuritis

3a: Pertussis (whooping cough)
3b:B.pertussis
3c: Macrolide (e.g erythromycin)
3d: Nasopharyngeal swab
3e: Pertussis toxin
3f: Yes by vaccine

4a: Otitis media
4b:Moraxella
4c: Amoxicillin & Clavulanic acid

5a: Pharyngitis
5b:S.pyogenes
5c: Penicillin
5d: Rheumatic fever
Glomerulonephritis
Peritonsillar abscess
Parapharyngeal abscess

MCQs

Q1: A patient diagnosed with GAS pharyngitis is treated with penicillin . Which of the following complications does this drug not treat?			
A- Rheumatic fever	B- Post streptococcal glomerulonephritis	C- Peritonsillar abscess	D- Parapharyngeal abscess
Q2: Which of the following is not a virulence factor of GAS?			
A- Capsule	B- Streptolysin O	C- Streptococcal pyrogenic exotoxin	D- Pertactin
Q3: A 26-year-old woman comes to the emergency department because of left-sided redness and swelling of the eyelid with severe pain on eye movement. On physical examination the left eye has decreased vision and reduced movement and is proptotic. The patient is diagnosed with orbital cellulitis and started on aggressive treatment. Which of the following risk factors is most strongly associated with orbital cellulitis?			
A- Hypertension	B- Sinusitis	C- Otitis Media	D- Allergic conjunctivitis
Q4: All the following regarding group A Streptococcus (GAS) pharyngitis are true except:			
A- Diagnosed with throat swab or antistreptolysin O	B- Blood agar will show beta hemolysis.	C- It can predispose to suppurative complications such as rheumatic fever	D- Treatment is 10 days with penicillin.
Q5: All true about epiglottitis expect:			
A- Usually affects children who did not get vaccine.	B- Swab is the preferred way for diagnosis.	C- H. influenzae is the most common cause.	D- Blood culture must be grown on chocolate agar.
Q6: A 2 months old baby has been brought to the hospital with intense cough that gets worse by night. All answers are false expect:			
A- He is in Paroxysmal state of the infection	B- He is in catarrhal stage of the infection	C- Special media such as deoxycholate agar is required for culture.	D- Throat swab is used to diagnose.
Q7: An emergency department physician suspected corynebacterium diphtheriae when examining a patient. What is an appropriate media for the culture of swab obtained from that patient?			
A- Tinsdale media	B- Chocolate agar	C- Neomycin agar	D- Blood agar
83: What is the best TV show in the world?			
A- Brooklyn Ninety Nine	B- Brooklyn 99	C- A and B	D- All are correct

Answer Key:

1)B 2)D 3)B 4)C 5)B 6)A 7)A 8)D

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