LECTURE 15

BACTERIA CAUSING UPPER RESPIRATORY TRACT INFECTIONS

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Medical Microbiology and Immunology

OBJECTIVES

- Describe the etiology of the common upper respiratory tract infections caused by bacteria.
- Describe the pathogenesis, lab diagnosis and prevention of infections discussed in the lecture.
- Compare the major characteristics of specific bacterial diseases of the upper respiratory tract

UPPER RESPIRATORY TRACT INFECTIONS

- Common cold (mainly by viruses)
- Pharyngitis
- Tonsillitis
- Epiglottitis
- laryngotracheitis
- Sinusitis
- Otitis Media
- Otitis Externa

Pharyngitis

- Abrupt onset of sore throat, fever, malaise, and headache; tonsillar abscesses and tender anterior cervical lymph nodes .

Common bacterial causes:

- Group A streptococcus *(Strep. pyogenes).*
- Anaerobic bacteria

- *Corynebacterium diphtheriae*
- *Haemophilus infleunzae*

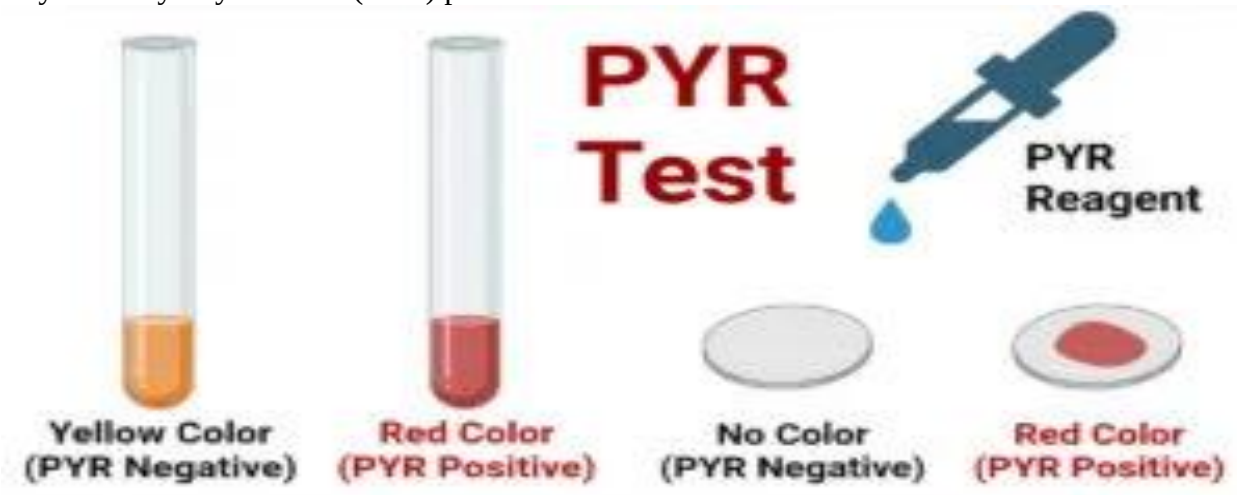
- ***Streptococcus pyogenes* (Group A Streptococcus; GAS)**

Distinguishing Features

• β hemolytic

• Bacitracin sensitive

• Pyrrolidonyl arylamidase (PYR) positive



P**athogenesis**

• Hyaluronic acid: is non-immunogenic.

• M-protein: antiphagocytic, associated with acute glomerulonephritis,

nephritis,rheumatic fever.

• Streptolysin O: immunogenic, hemolysin/cytolysin.

• Streptolysin S: not immunogenic, hemolysin/cytolysin.

Spreading Factors

• Streptokinase: breaks down fibrin clot.

• Streptococcal DNAse: liquefies pus, extension of lesion.

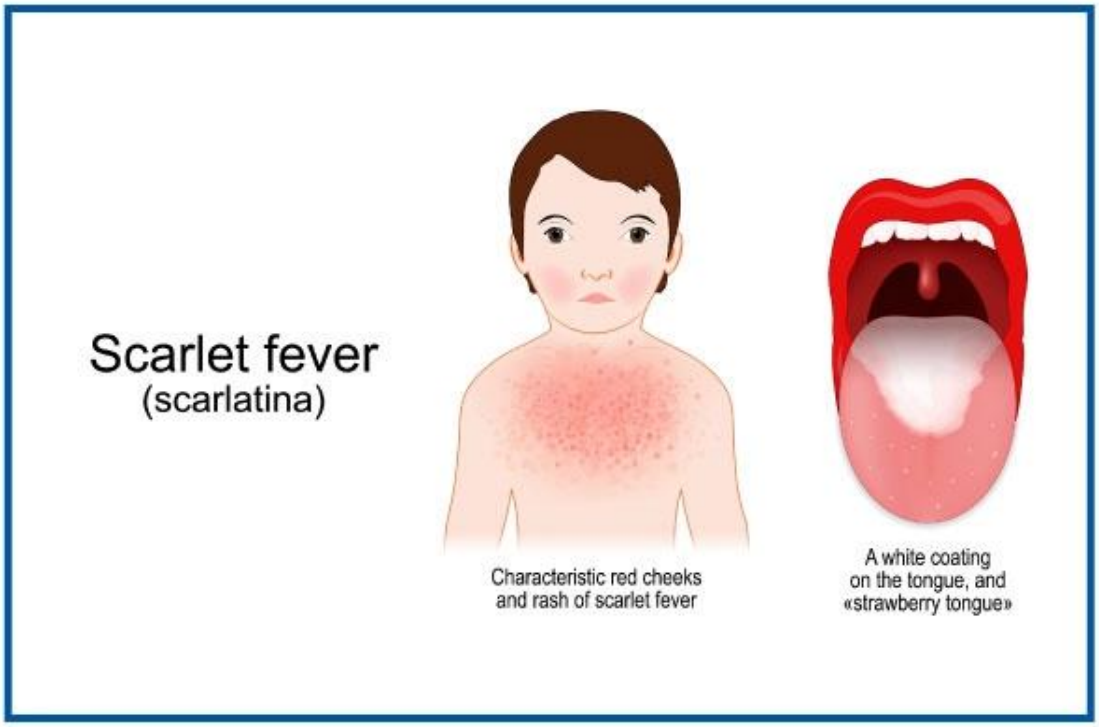
• Hyaluronidase: hydrolyzes the ground substances of the connective

tissues.

• Exotoxins A–C (pyrogenic or erythrogenic exotoxins)

– Phage-coded (i.e., the cells are lysogenized by a phage).

– Cause fever and rash of scarlet fever: superantigens.



Reservoir: human throat; skin

Transmission: direct contact; respiratory droplets.

Diseases

Acute Suppurative Group A Streptococcal Infections*

Diseases	Symptoms
Pharyngitis	Abrupt onset of sore throat, fever, malaise, and headache; tonsillar abscesses and tender anterior cervical lymph nodes
Scarlet fever	Above followed by a blanching **"sandpaper" rash** (palms and soles are usually spared), circumoral pallor, **strawberry tongue**, and nausea/vomiting
Pyoderma/impetigo	Pyogenic skin infection (honey-crusted lesions)

*Also, cellulitis/necrotizing fasciitis, puerperal fever, lymphangitis, erysipelas

Nonsuppurative Sequelae to Group A Streptococcal Infections

Disease	Sequelae of	Mechanisms/Symptoms
Rheumatic fever	Pharyngitis with group A strep	Antibodies to heart tissue/2 weeks post pharyngitis, fever, joint inflammation, carditis, erythema marginatum (chorea later)type II hypersensitivity
Acute glomerulonephritis (AGN)	Pharyngitis or skin infection	Immune complexes bound to glomeruli/pulmonary edema and hypertension, "smoky" urine (type III hypersensitivity)

- ***Corynebacterium diphtheriae***

Distinguishing Features

• Gray-to-black colonies of club-shaped gram-positive rods arranged in

V or L shapes on Gram stain

• Granules (volutin) produced on Loeffler coagulated serum medium

stain metachromatically

• Toxin-producing strains have β-prophage carrying genes for the toxin (lysogeny, β-corynephage). The phage from one person with diphtheria can infect the normal nontoxigenic diphtheroid of another, and thus cause diphtheria.

Reservoir: throat and nasopharynx

Transmission: bacterium or phage via respiratory droplets

Pathogenesis

• Organism **:** not invasive; colonizes epithelium of oropharynx or skin in cutaneous diphtheria

• Diphtheria toxin (A-B component)—inhibits protein synthesis by adding ADP-ribose to eEF-2

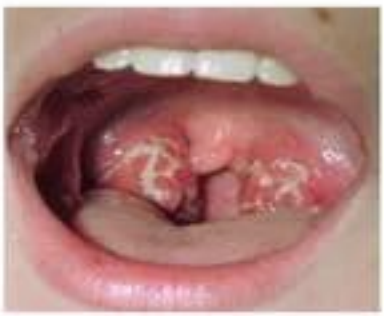
• Effect on oropharynx: Dirty gray pseudomembrane (made up of dead cells and fibrin exudate, bacterial pigment).

• Extension into larynx/trachea (obstruction**).**

• Heart and nerve damage.

Disease: diphtheria (sore throat with **pseudomembrane,** bull neck, potential respiratory obstruction, **myocarditis**, cardiac dysfunction, renal failure.

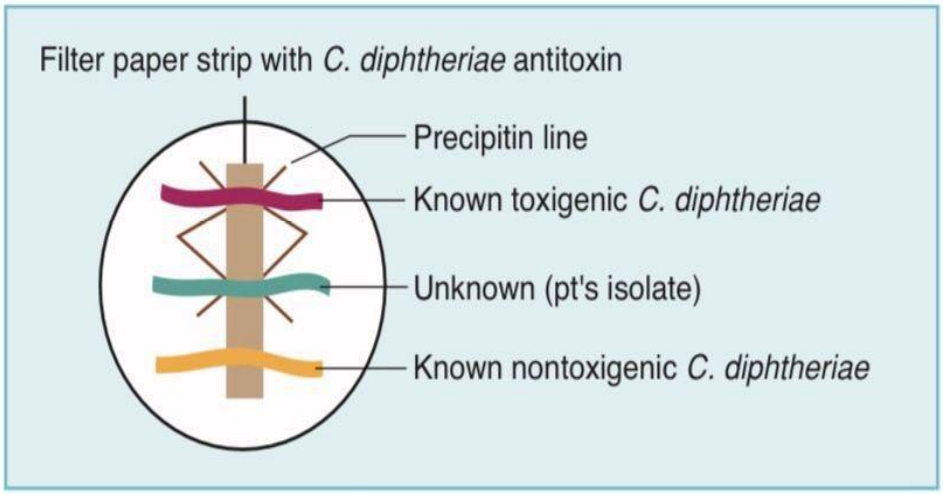
Pharygotonsillar diphtheria:



Bull-neck appearance in diphtheria

Diagnosis

- Elek test to document toxin production (ELISA for toxin is now gold standard)
- Toxin produced by Elek test toxin-producing strains diffuses away from growth
- Antitoxin diffuses away from strip of filter paper.
- Precipitin lines form at zone of equivalence



Elek Test

Prevention: toxoid vaccine (formaldehyde-modified toxin is still immunogenic but with reduced toxicity), part of DTaP, DTP, or Td, boosters 10-year intervals

EPIGLOTTITIS AND LARYNGOTRACHEITIS

- Epiglottitis is an inflammation and swelling of the epiglottis (epiglottis is a flap of tissue that sits beneath the tongue at the back of the throat).
- Uncommon because the *H. influenzae* type B (Hib) vaccine is a routine childhood immunization. *Haemophilus influenzae* type b is the most common cause of epiglottitis, particularly in children age 2 to 5 years. Epiglottitis is less common in adults.
- Usually young unimmunized children presented with severe sore throat, breathing difficulties, drooling and difficulty swallowing, hoarseness, Cherry red

epiglottis.

- Fatal if the throat becomes completely blocked

Haemophilus influenzae

Distinguishing Features

- Encapsulated, gram-negative rod; 95% of invasive disease caused by capsular type b
- Requires growth factors X (hemin) and V (NAD) for growth on nutrient or blood agar (BA)
- Grows near *S. aureus* on blood agar "satellite" phenomenon
- Chocolate agar provides both X and V factors

Reservoir: human nasopharynx

Transmission: respiratory droplet

Pathogenesis

• Polysaccharide capsule (type b capsule is polyribitol phosphate**)** is the most important virulence factor

• Capsule important in diagnosis; antigen screen on CSF (e.g., latex particle agglutination); serotype all isolates by quellung.

• IgA protease is a mucosal colonizing factor.

Diagnosis: blood or throat culture on chocolate agar; PCR; antigen detection of capsule.

Prevention

• Conjugate capsular polysaccharide-protein vaccine

LARYNGO-TRACHEA-BRONCHITIS

- Croup, or laryngotracheobronchitis, may affect people of any age, but it usually occurs in children aged 6 months to 6 years. The peak incidence is in the second year of life. Thereafter, the enlarging caliber of the airway reduces the severity of the manifestations of subglottic inflammation.

B. pertussis causes whooping cough (pertussis).

Bordetella pertussis

Distinguishing Features: small gram-negative, aerobic rods; encapsulated organism

Reservoir: human

Transmission: respiratory droplets

Pathogenesis

B. pertussis is mucosal surface pathogen

• Attachment to nasopharyngeal ciliated epithelial cells is via filamentous hemagglutinin; pertussis toxin (on outer membrane) aids in attachment

• Toxins damage respiratory epithelium.

– Adenylate cyclase toxin: impairs leukocyte chemotaxis ® inhibits phagocytosis and causes local edema

– Tracheal cytotoxin: interferes with ciliary action; kills ciliated cells

– Endotoxin

– Pertussis toxin (A and B component, OM protein toxin): ADP ribosylation of G_i (inhibiting negative regulator of adenylate cyclase) interferes with transfer of signals from cell surface to intracellular mediator system: lymphocytosis; islet-activation leading to hypoglycemia; blocking of immune effector cells (decreased chemotaxis); increased histamine sensitivity

Stages of Whooping Cough (Pertussis) vs. Results of Bacterial Culture

	Incubation	Catarrhal	Paroxysmal	Convalescent
Duration	7–10 days	1–2 weeks	2–4 weeks	3–4 weeks (or longer)
Symptoms	None	Rhinorrhea, malaise, sneezing, anorexia	Repetitive cough with whoops, vomiting, leukocytosis	Diminished paroxysmal cough, development of secondary complications (pneumonia, seizures, encephalopathy)
Bacterial Culture				

Diagnosis

• Fastidious/delicate: Regan-Lowe or Bordet-Gengou media; either direct

cough plates or nasopharyngeal cultures

• Direct immunofluorescence **(DFA)** on nasopharyngeal smear

• PCR and serologic tests available

Prevention: vaccine DTaP (acellular pertussis: filamentous hemagglutinin plus pertussis toxoid); immunity wanes 5–7 years; babies are born with little or no immunity (IgA) from mother

Reference

KAPLAN Medical, USMLE Step 1 Lecture Notes 2021, Immunology and Microbiology,

P:208,209,222,223,236,237,238,239

QUESTION

- **A 6 –year- old girl is brought to a doctor with fever and sore throat. On physical examination the child anxious, ill appearing and reveals a gray pseudo-membrane involving pharyngeal wall. The mother states that the child has not received any immunization. Which one of the following virulence factors is involved in the pathogenesis of this disease?**

  A-Capsule.

  B-Endotoxin

  C-Exotoxin

  D-Hemolysins