

- Upper respiratory tract infections
- Pharyngitis
- Pharyngitis is an acute infection of the oropharynx or nasopharynx
- 60-70% pharyngitis is viral
- Streptococcus sore throat (pharyngitis)
- Streptococcus pyogenes
  - Gram +ve cocci in chains
  - Group A streptococcus in lance field grouping
  - Beta hemolytic on blood agar plate
  - Catalase negative
- Common symptoms include fever, sore throat, and enlarged lymph nodes. It is the cause of 37% of sore throats among children and 5-15% in adults

- Spread by direct person-to-person contact, via droplets of saliva or nasal secretions
- Virulence factors
- Streptococcus pyogenes has number of virulence factors that
  - Evade or overcome the host immune response
    - M-protein (antiphagocytic)
    - Cell wall peptidoglycan and lipoteichoic acid
    - Streptolysin O & S (destroy RBCs and WBCs)
  - Invade or make the organism rapidly tunnel through the host tissue;
    - most important being hyaluronidase also known as spreading factor (destroy hyaluronic acid in tissue)
    - Streptokinase that destroy fibrin
- Toxin

- Certain strains produce pyrogenic toxin seen in scarlet fever
- Streptococcal sore throat complications
- Local complications
  - Acute otitis media
  - Acute mastoiditis
  - Acute peri-tonsillitis (Quinsy)
  - Scarlet fever (Erythrogenic toxin A)
- Scarlet fever
- Scarlet fever – scarlatina – caused by *Streptococcus pyogenes* strains producing pyrogenic (erythrogenic) toxin
- **Common Symptoms of Scarlet Fever**
  - A very red, sore throat
  - A fever (101° F or above)

- A red rash with a sandpaper feel
  - Rash is intensified in underarm, elbow and groin creases forming lines called patia lines
  - A whitish coating on the tongue or back of the throat
  - A "strawberry" tongue
  - Enlarged lymph nodes
  - Circumoral pallor
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- Complications of by streptococcus pyogenes infections
- Immune mediated complications of streptococcal sore throat and skin infections
  - Rheumatic fever
  - Acute glomerulonephritis
- Rheumatic fever
- It occurs as a complication of untreated streptococcus sore throat ( a few weeks later)

- Rheumatic fever is immune mediated ;a phenomenon known as cross reacting antibodies/ molecular mimicry
- M-protein of certain strain of streptococcus pyogenes are similar to the antigens in heart, joints,and brain tissue → antibody produced against these M proteins cross react with self antigens → autoimmunity
- A type II hypersensitivity reaction
- Rheumatic fever
- Six major manifestations of rheumatic fever
  - Fever
  - Carditis (inflammation of heart)
  - Migratory polyarthritits
  - Sydenham's chorea

- A rash known as erythema marginatum
  - Subcutaneous nodules
- Rheumatic fever
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  - Fever
  - Carditis (inflammation of heart) manifest as chest pain, congestive heart failure ,arrhythmias or a new heart murmur.
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  - Fever
  - Carditis (inflammation of heart)
  - Migratory polyarthritits
  - Sydenham's chorea rapid, uncontrolled jerking movements affecting the face, hands and feet
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  - Fever
  - Carditis (inflammation of heart)
  - Migratory polyarthritits
  - Sydenham's chorea
  - A rash known as erythema marginatum
  - Subcutaneous nodules (rubbery nodules just under the skin)
- Post streptococcal glomerulonephritis

- Follows few weeks of a skin infection by certain streptococcus pyogenes strains
- Mechanism:
  - 1.streptococcal antigen and antibody against it combine to form antigen-antibody complex
  - 2.this immune complex is deposited on the glomerular membrane
  - 3.this deposition activates an immune mediated damage to the glomerular membrane
- A type III hypersensitivity reaction
- Post streptococcal glomerulonephritis
- Important clinical features of PSGN
  - Periorbital swelling
  - Swelling of the feet, ankles, hands
  - Hypertension
  - Rust colored urine

- Decreased urine output
- Streptococcus pyogenes lab diagnosis
- Microscopy
- Culture/sensitivity
- Biochemical tests
- Lancefield grouping
- Rapid antigen detection(strep sore throat)
- Serological tests
  
- Specimens
- Depending upon the site of infection
  - Throat swab(sore throat)
  
- Microscopy
- On gram staining they appear as gram +ve cocci in chains

- Culture & sensitivity
- Blood agar is medium of choice
- Colonies are beta hemolytic (clear zone of hemolysis around colonies),
- Bacitracin disc is applied to the media to differentiate between streptococcus pyogenes (group A strep) and streptococcus agalactiae (group B strep) as both are beta hemolytic.
  - Strep pyogenes sensitive
  - Strep agalactiae resistant
- Biochemical tests
- Catalase test:
  - Catalase negative;
  - Mix colony suspension with hydrogen peroxide
    - Bubbles → positive
    - No bubbles → negative

- Lancefield grouping
- Agglutination test
- Based on presence of C carbohydrate in cell wall which is different in different streptococcal species
- Six groups(A,B,C,D,E,F) of streptococcus; Strep pyogenes is group A on lancefield grouping
- Mixing colony suspension with respective antisera(antibodies) result in agglutination
- Presence of agglutination (fine clumps) is positive
- Rapid strep test(strep sore throat)
- *A Rapid strepTest is a rapid chromatographic immunoassay*

- A throat swab is collected
- Placed in a holder on the strip
- If Group A Strep antigen is present in the sample, it will form a colored lines indicating antigen antibody reaction
  
- Serological test
- Anti streptolysin O (ASO) titre is a measure of the serum levels of antistreptolysin O antibodies used for the diagnosis of a streptococcal infection or indicate a past exposure to streptococci.
- The ASOT helps direct antimicrobial treatment and to assist in the diagnosis of scarlet fever,

rheumatic fever, and post infectious glomerulonephritis.

- A positive test usually is  $>200$  units/mL
- It is done by serological methods like latex agglutination or ELISA
- Treatment
- Good news → Penicillins are the main stay of therapy with no resistance
- Therapy may be directed by antibiotic sensitivity report by the lab in penicillin allergic patients
- Other options include macrolides, clindamycin, quinolones, etc.

- Diphtheriae
- Diphtheria is a nasopharyngeal infection caused by *Corynebacterium diphtheriae*
- Gram +ve rods ,
- Nonsporing, aerobe
- *C. diphtheriae* organisms have a characteristic club-shaped bacillary appearance and typically form clusters of parallel rays (palisades) that are referred to as *Chinese letter appearance*
- Epidemiology
- *C. diphtheriae* is transmitted via the aerosol route, primarily during close contact
- Diphtheria once was a major cause of illness and death among children

but widespread vaccination has dramatically reduced its incidence

- Diphtheria is a serious disease
- Virulence factors
- *C. diphtheriae* displays nontoxigenic ( $tox^-$ ) or toxigenic ( $tox^+$ ) types.
- A family of viruses called corynebacteriophages are responsible for toxigenic conversion of  $tox^-$  *C. diphtheriae* to the  $tox^+$  phenotype. A phenomenon known as lysogenic conversion
- Toxigenic strains of *C. diphtheriae* produce a protein toxin that causes formation of pseudomembranes in

the pharynx and systemic toxicity, myocarditis, and polyneuropathy.

- Diphtheria toxin
- The protein exotoxin has two fragments: the A fragment and the B fragment. The B fragment attaches to the cell and A fragment enters into the host cell resulting in irreversible inhibition of protein synthesis by ADP ribosylation of elongation factor 2. The eventual result is the death of the cell.

## –Respiratory Diphtheria

- It is a nasopharyngeal infection by toxigenic strains of *C. diphtheriae*

- Patient presents with fever and sore throat
- Hall mark of infection is the formation of mucosal ulcers with whitish coating called a *pseudomembrane* in the nasopharynx comprising of dead tissue, fibrin, neutrophils etc.
- initially white may turn grey or black
- Tightly adherent (unlike strep sore throat exudate)
  
- Diphtheria pseudomembrane
- Complications of respiratory diphtheria
- Local complications
  - Expanding pseudomembrane may compress the air way

- Bull neck diphtheria
- Systemic complications
  - Occur few weeks into the disease
  - Result from systemic absorption of toxin and manifest as
    - Myocarditis
    - Polyneuropathy

## –Bull neck diphtheria

- A few patients develop "bull-neck" diphtheria, which results from massive edema of the submandibular and paratracheal region and is further characterized by foul breath, thick speech, and stridorous breathing.
- Compromises breathing
- Myocarditis

- It is the inflammation of the heart muscle
- Myocarditis manifests as cardiac arrhythmias or congestive heart failure
- Results from action of toxin on the heart muscle
  
- Polyneuropathy
- Results from action of toxin on the nerves
- Manifests as cranial, peripheral or autonomic nerve involvement
- Symptoms are related to the type of nerves that are involved
  - Diplopia, dysphagia, facial palsy etc (cranial nerves)
  - Sensory motor disturbances (peripheral nerves)

- tachycardia, hypotension, urinary retention(autonomic nerves)
- Respiratory paralysis may occur requiring artificial ventilation
- Recovery is a rule
  
- Lab diagnosis
- Microscopy
- Culture
- Biochemical tests
- Toxin detection
- Skin test
- Microscopy
- Gram staining
- Albert staining
  
- Specimen
- Throat swab
- Gram staining

- Gram staining
  - Gram positive rods
  - Club shaped
- Albert stain
- Albert stain
  - A special stain used to demonstrate the metachromatic granules formed in the polar regions. The granules are called as polar granules, Babes Ernst Granules, Volutin granules, etc
- Culture
- Specimens are inoculated on selective media for *C. diphtheriae*. These media have ingredients to suppress the growth of normal flora and selectively growing *C. diphtheriae*
  - Tellurite blood agar

- gray to black colonies, with dark centers
- Tinsdale agar
  - black colony with halo( because of reduction of cysteine to H<sub>2</sub>S)
- Loefflar serum slant:
  - Enrichment of the organism,
- Toxin detection(Elek's test)
- **Elek's Test:**
  - **Principle:** It is toxin/antitoxin reaction. Toxin production by ***C.diphtheriae*** can be demonstrated by a precipitation between exotoxin and diphtheria antitoxin.
- **Procedure:**
  - A strip of filter paper impregnated with diphtheria antitoxin is placed on the surface of serum agar. The organism is streaked at right angles to the filter paper. Incubate the plate at 37C for 24 hrs

- **Results:**
  - the antitoxin diffusing from filter paper strip and the toxin produced by toxigenic strains produce precipitation lines
- Toxin detection (animal pathogenicity)
- Organism grown in culture is injected subcutaneously in two guinea pigs. One guinea pig is protected by injecting diphtheria antitoxin 24 hrs before.
- If the strain is virulent the unprotected guinea pig dies within 4 days . The protected one remains healthy
- Toxin detection (PCR)

- Toxigenic strains can be detected by polymerase chain reaction which targets the gene encoding the toxin
- Treatment
- Patients in whom diphtheria is suspected should be hospitalized in respiratory isolation rooms.
- Treatment
- Antitoxin
  - Prompt administration of diphtheria antitoxin is critical in the management of respiratory diphtheria. The antitoxin—a horse antiserum—is effective in reducing the complications
- Antibiotic therapy
  - Antibiotics are used to prevent transmission to other susceptible contacts

- Drug of choice is either
  - Penicillins
  - erythromycin
- Prevention of the disease
- Sustained campaigns for vaccination of children is are responsible for the exceedingly low incidence of diphtheria .
- At present, diphtheria toxoid vaccine is coadministered with tetanus and acellular pertussis vaccine. Known as DTaP
- Children should get 5 doses of **DTaP**, one dose at each of the following ages: 2, 4, 6, and 15-18 months and 4-6 years.