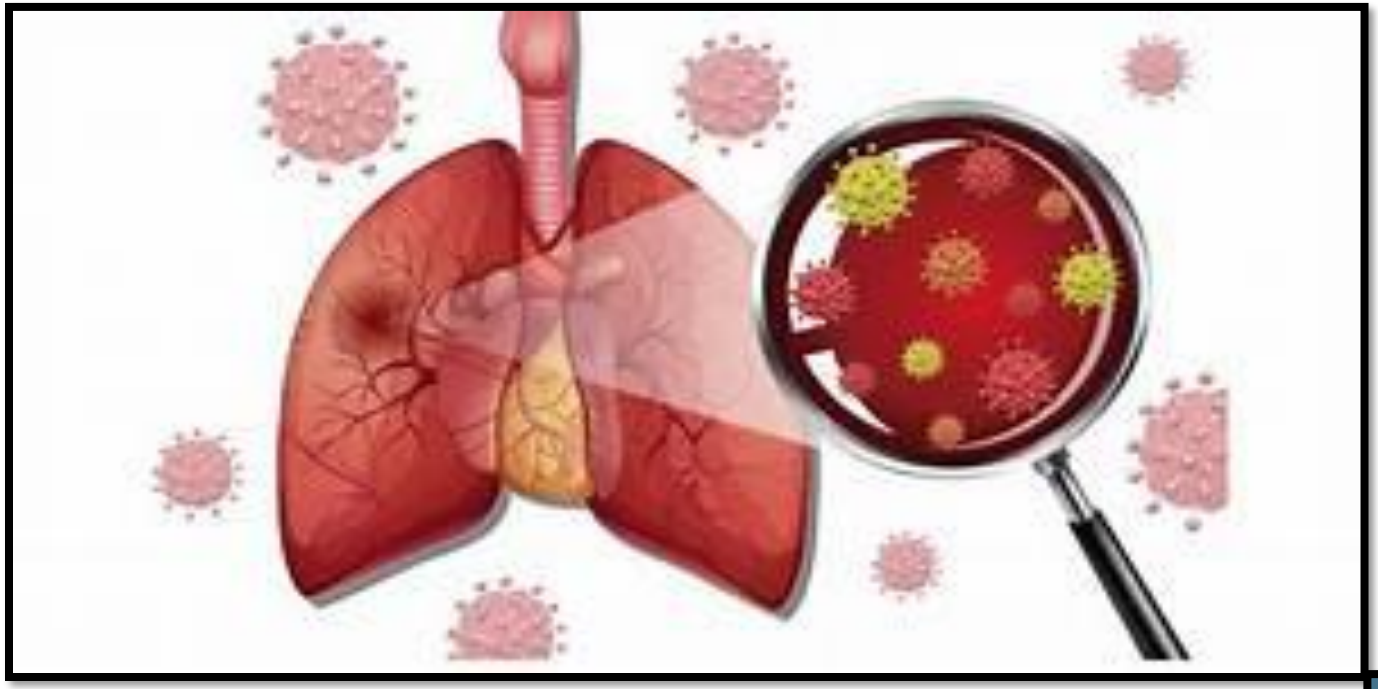


Microbiology : Respiratory System

Writer : Abdelwahab Hamzeh
Corrector : Abood Hamzeh
Doctor : Nader

Streptococcus.

- The “other” Gram positive Coccus
- Some are members of the normal human microbiota; others are associated with important human diseases attributable to the direct effects of infection by streptococci or in other cases to an immunologicresponse to them
- Streptococci (especially those of medical importance) are many, and thus we use a classification system to group and classify them.
- This grouping according to the genetic features of these organisms iswhat we use to diagnose diseases caused by these bugs rather by species.

Important Properties

- Streptococci are Gram positive **cocci arranged in chains or pairs.**
- All streptococci are catalase-negative, whereas staphylococci are catalase-positive
- However, to be able to tolerate oxygen reactive species, they contain superoxide dismutase

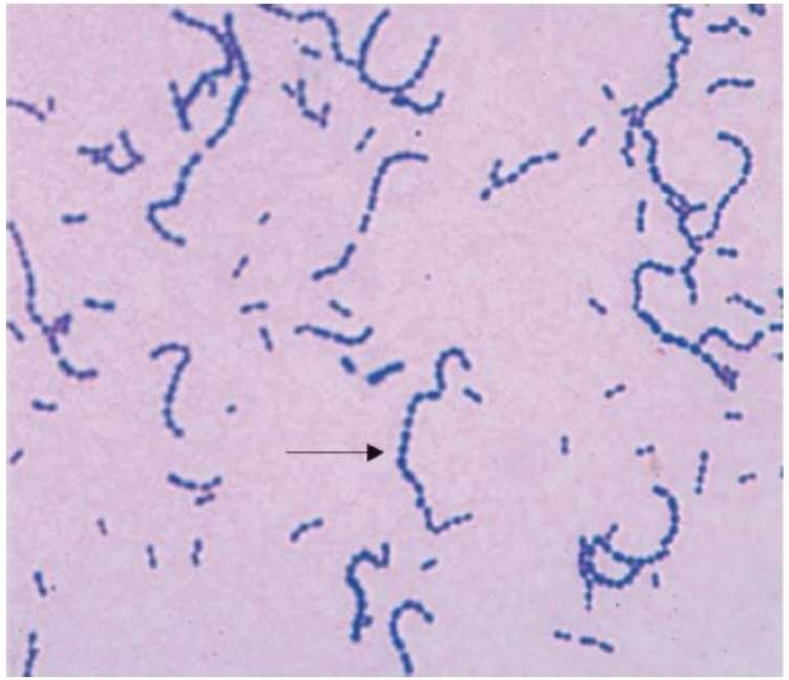


FIGURE 15–11 *Streptococcus pyogenes*—Gram stain. Arrow points to a long chain of gram-positive cocci. (Used with permission from Professor Shirley Lowe, University of California, San Francisco School of Medicine.)

Further Explanation.

- Streptococci are **facultative anaerobes**, (they are aerobes but can grow in the absence of oxygen)
- They are smaller than staphylococcus.
- -They are non-motile, non-spore and not acid fast.

- How does alpha-hemolytic streptococci tolerate oxygen? This bacterium tolerates oxygen through the action of **superoxide dismutase**, which converts superoxide into oxygen peroxide. As an implication, it causes a change in the pattern of hemolysis, resulting in a greasy green color (green sheen) on blood agar plates. This change is caused by the production of hydrogen peroxide (H2O2), which is a byproduct of the oxidation of hemoglobin into **biliverdin i**n alpha-hemolytic streptococci.

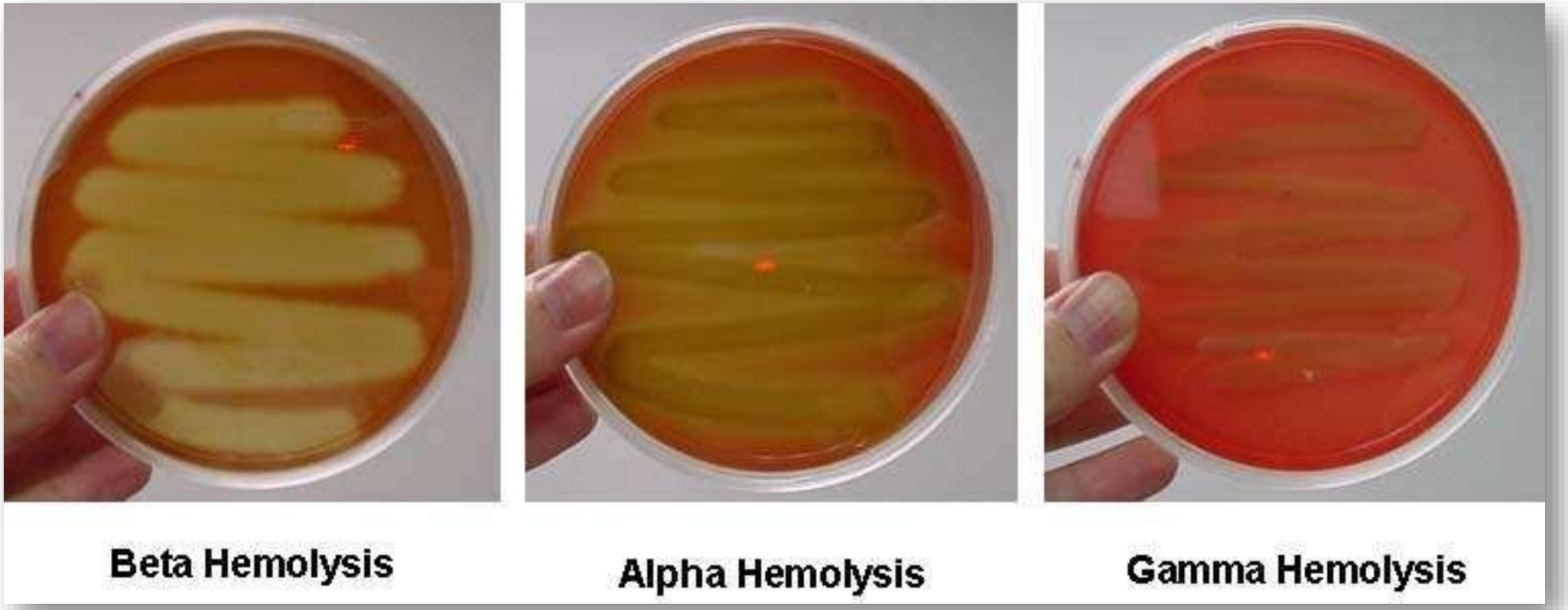
Sorting through the streptococcus.

❖The classification of streptococci into major categories has been based ona series of observations over many years:

- (There is no perfect classification, so we rely on more than one for grouping bacteria)

A. Colony morphology and hemolytic reactions on blood agar.
B. Serologic specificity of the cell wall group-specific substance (Lancefield antigens) and other cell wall or capsular antigens.
C. Biochemical reactions and resistance to physical and chemical factors.

- A- One of the most important characteristics for identification of streptococci is the type of hemolysis



complete hemolysis is caused by streptolysin "O" and "S".

Partial hemolysis Greasy **green** color

No hemolysis

- (1) α-Hemolytic streptococci form a **green** zone around their coloniesas a result of incomplete lysis of red blood cells in the agar. The greencolor is formed when hydrogen peroxide produced by the bacteria oxidizes hemoglobin (red color) **to biliverdin (green color).**

- (2) β-Hemolytic streptococci form a **clear zone around their colonies**because complete lysis of the red cells occurs. β-Hemolysis is due tothe production of enzymes (hemolysins) called **streptolysin O and streptolysin S.**

- (3) Some streptococci are **nonhemolytic** (γ-hemolysis).

- Most disease-causing bacteria are beta hemolytic.

B-Lancefield Grouping

- Lancefield is a bacteriologist
- This **carbohydrate** is contained in the cell wall of many streptococci and forms the basis of serologic grouping into Lancefield groups A – H and K – U.

- Serological identification (based on the presence of polysaccharide and teichoic acid antigens of streptococci), grouped them into groups

- Nowadays **latex agglutination** is used

- Only those that are **Catalase negative and coagulase negative** are grouped
- Groups A, B, C, F, and G are human pathogens. (important in medical field).

B-Lancefield Grouping is based on specific types of antigens and Lipoteichoic acids, it also does not fit all bacteria that affect humans. This includes strep. pneumoniae (the most common cause of community-acquired pneumonia, as well as meningitis, otitis media, and sinusitis) and strep. Viridans (causing endocarditis), which **cannot** be grouped by Lancefield classification.

Species	Lancefield Group	Typical Hemolysis	Diagnostic Features[1]
S. pyogenes	A	β	Bacitracin-sensitive
S. agalactiae	B	β	Bacitracin-resistant; hippurate hydrolyzed
E. faecalis (Enterococci)	D	α or β or none	Growth in 6.5% NaCl[2]
S. bovis[3] (Non-enterococci)	D	α or none	No growth in 6.5% NaCl
S. pneumoniae	NA[4]	α	Bile-soluble; inhibited by optochin
Viridans group[5]	NA	α	Not bile-soluble; not inhibited by optochin

Resistant to penicillin

sensitive to penicillin

[1] All streptococci are catalase-negative.

[2] Both *E. faecalis* and *S. bovis* grow on bile-esculin agar, whereas other streptococci do not. They hydrolyze the esculin, and this results in a characteristic black discoloration of the agar.

[3] *S. bovis* is a nonenterococcal group D organism.

[4] NA, not applicable.

[5] Viridans group streptococci include several species, such as *S. sanguinis*, *S. mutans*, *S. mitis*, *S. gordonii*, *S. salivarius*, *S. anginosus*, *S. milleri*, and *S. intermedius*.

Group C streptococcus (equisimilis) another name dysgalactiae , the spectrum similar to A

Explanation from the previous slide

- Most of the pathogenic bacteria of significant importance are **beta-hemolytic**
- **S.pyogenes** is one of the most prevalent bacterial infections in humans, particularly in pediatrics. It is the most common **bacterial** cause of strep throat and pharyngitis.

- GBS (Group B Streptococcus) like **strep.agalactiae** is the most common cause of neonatal sepsis and meningitis.

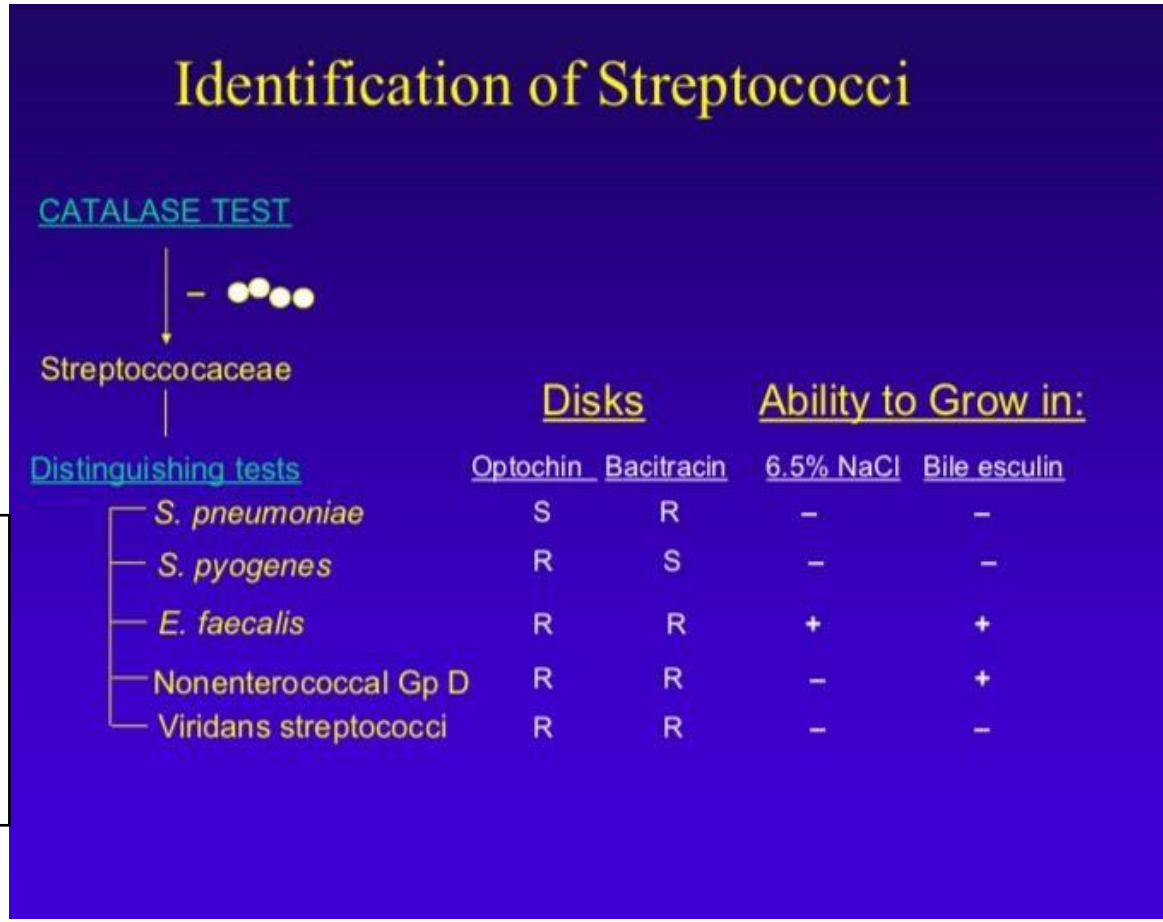
- Lancefield grouping is not applicable to alpha-hemolytic bacteria as they do not have a unique antigen.

- **Streptococcus pyogenes**: group A Lancefield, beta hemolytic, resistant to optochin, does not grow in Bile Esculin.
- Only group D strep (such as enterococci and Streptococcus bovis) can grow in bile esculin.
- Another layer of complexity : they are part of the normal flora, up to 20-30% of children have viridans group in there oral cavity, GAS etc , in adult the percentage is less

C- Biochemical reactions and resistance to physical and chemical factors.

The first test you should do is catalase. If it is negative, they are not Staphylococcus but rather Streptococcus or Enterococci. Then, we use the bacitracin test: Group A beta-hemolytic streptococci are sensitive to bacitracin, while the Viridans group is resistant.

How to differentiate between Streptococcus viridans and Streptococcus pneumoniae?
One way to differentiate them is through their sensitivity to **optochin**.
Streptococcus Pneumonia is sensitive to optochin, while Streptococcus viridans is resistant.



Group A Beta hemolytic streptococci (GAS)

- **STREPTOCOCCUS PYOGENES (GAS)**

Other names for GAS:
Flesh eating bacteria
Pyogenic streptococci
Strep pyogenes

GAS are the most common **bacterial** cause of pharyngitis

- This species consists of Lancefield group A streptococci, is **among the most prevalent of human bacterial pathogens**.
- **GAS are exclusively human pathogens. (important)**
- It causes a wide range of suppurative (pus forming) infections in:

1) the respiratory tract: Pharyngitis which is the abrupt onset of a sore throat is characterized by patients experiencing dysphagia (difficulty in swallowing) and odynophagia (pain when swallowing). These symptoms may be accompanied by fever.

Continued…

2) **skin related diseases**: **Impetigo** is characterized by a honey crust appearance, cellulitis , **erysipelas** present with well-demarcated erythema. Note that the major cause of these diseases is Staphylococcus aureus (staph), although Group A Streptococcus (GAS) can also be a causative agent, but to a lesser extent.

3) **Life-threatening soft tissue infections**, and certain types of **toxin-associated reactions**. Like scarlet fever and TSS (toxic shock)

- Streptococci have serious hallmark POST infective IMMUNOLOGICAL reactions
- A similar spectrum of infections may be caused by the closely related group C and group G streptococci is (*Str. equisimilis,* also known as *Str. dysgalactiae subspecies equisimilis*).

Pathogenesis

- Group A streptococci (*S. pyogenes*) cause disease by three mechanisms :

(1) pyogenic inflammation, which is induced locally at the site of theorganisms in tissue (whether in the pharynx or skin).

(2) exotoxin production, which can cause widespread systemic symptoms inareas of the body where there are no organisms.

(3) immunologic, which occurs when antibody against a component of the organism cross-reacts with normal tissue or forms immune complexes that damage normal tissue (post strep diseases).

- The immunologic reactions cause inflammation (e.g., the inflamed joints of rheumatic fever), but there **are no organisms in the lesions**.

Spectrum of GAS

Upper respiratory tract infection.

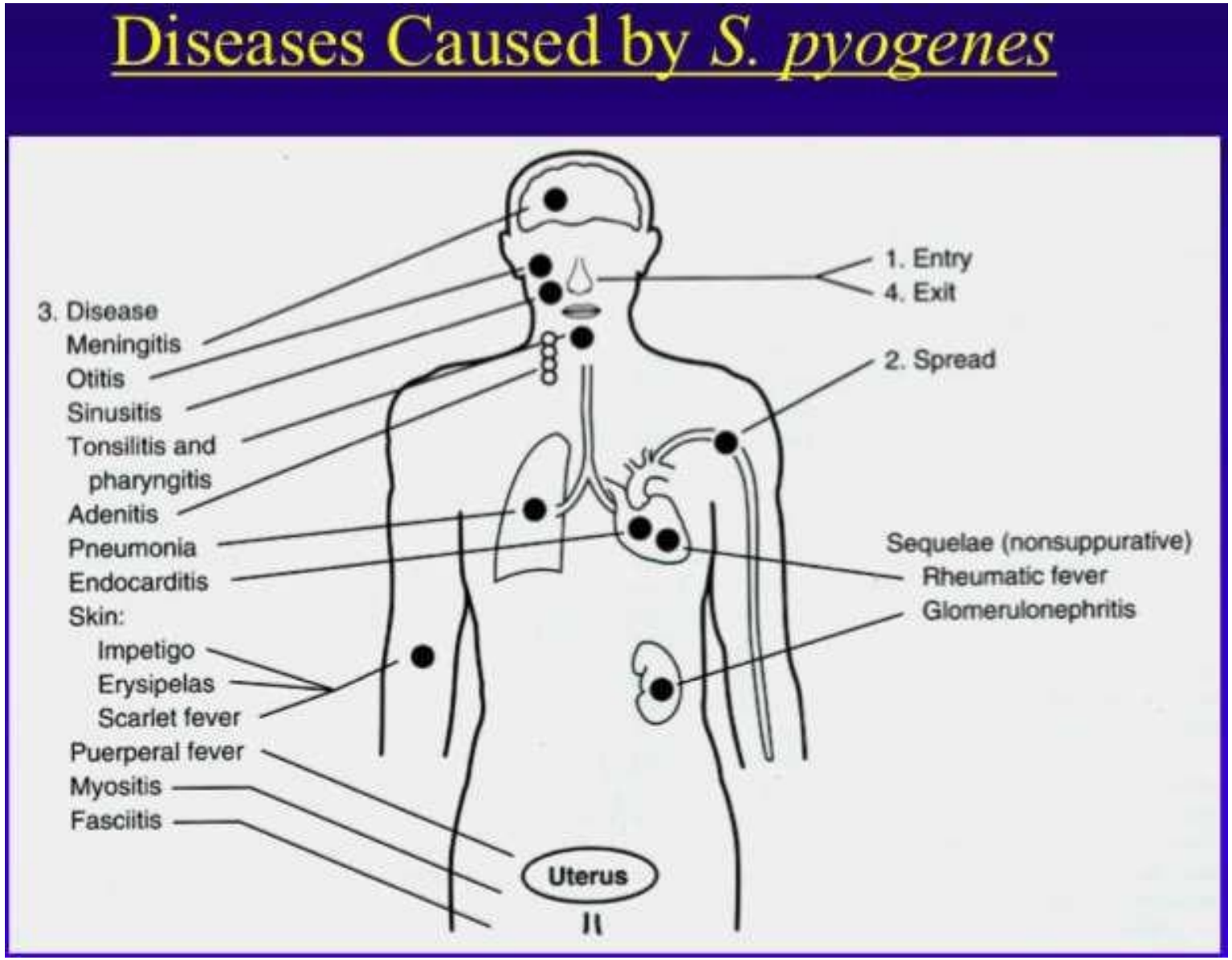
- Pharyngitis and its complications, such as retropharyngeal abscess and peritonsillar abscess, are **highly medical emergencies** because they cause airway obstruction . If left untreated, they can lead to mastoiditis if they spread to the mastoid process, acute otitis media if they reach the middle ear through the Eustachian tube, and meningitis if they affect the meninges.

Skin infections

impetigo, erysipelas, cellulitis ,necrotizing fasciitis and scarlet fever

Immune sequelae (non suppurative)

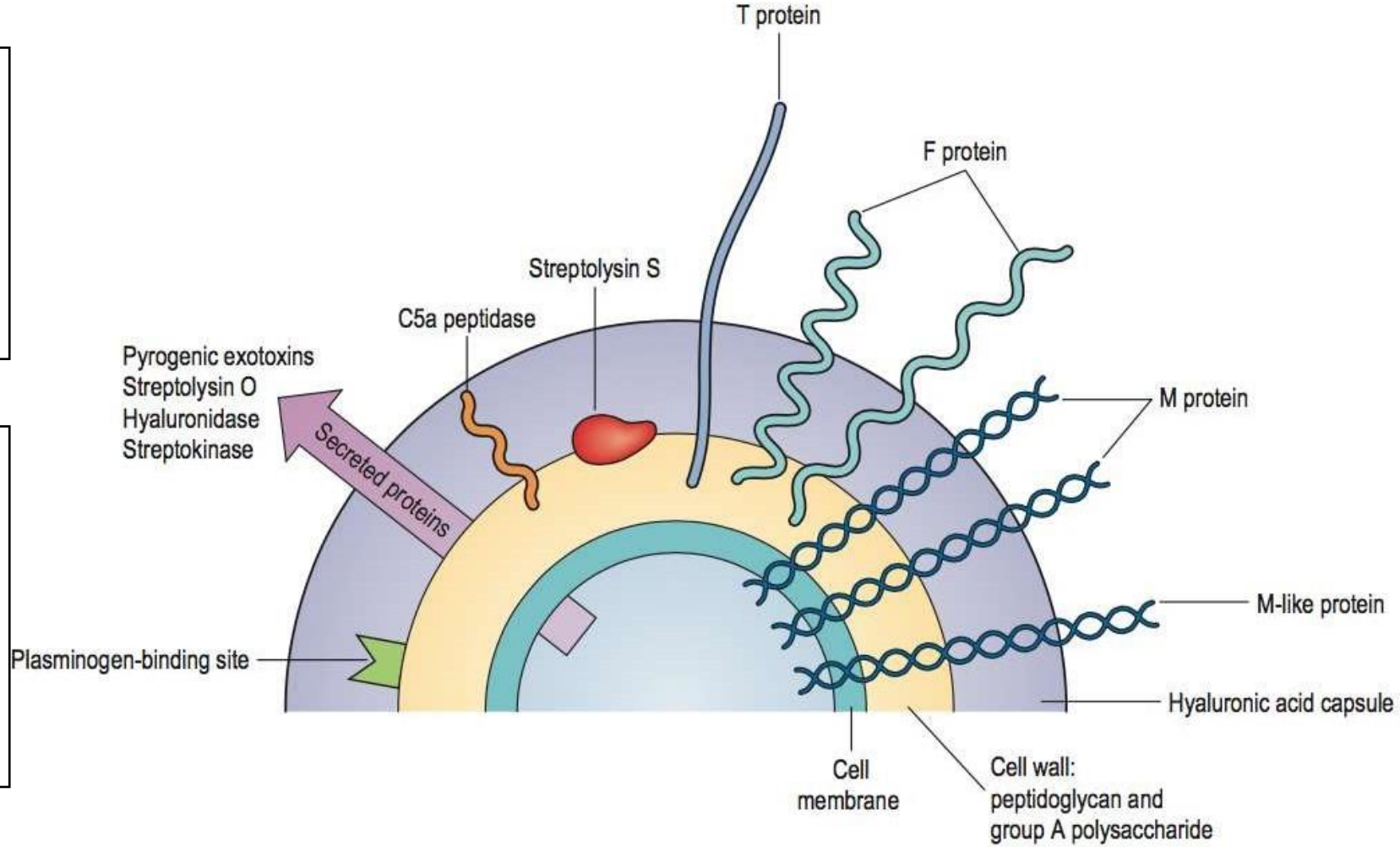
- Rheumatic fever.
- Glomerulonephritis.



Virulence factors

Streptococcus bacteria don't have all these virulence factors for the same bacterium. It could have the gene for a certain virulence factor but not express it. There are different levels of complexity.

They are gram-positive bacteria, meaning they have a peptidoglycan layer. Specifically, they have a polysaccharide called Group A polysaccharide, which is why they are referred to as GAS.



Young culture in vivo and severe cases produced by Streptococci have a **hyaluronic acid capsule**. This capsule is **antiphagocytic** and plays a role in **molecular mimicry** as M protein.

There are M-protein and M-like protein. Both are antiphagocytic, antigenic, and immunogenic. And inhibit the activation of alternative pathway.
F protein : binds to bronectin which is a matrix protein present on eukaryotic cells (pharynx and skin)

Continued …… virulence factors

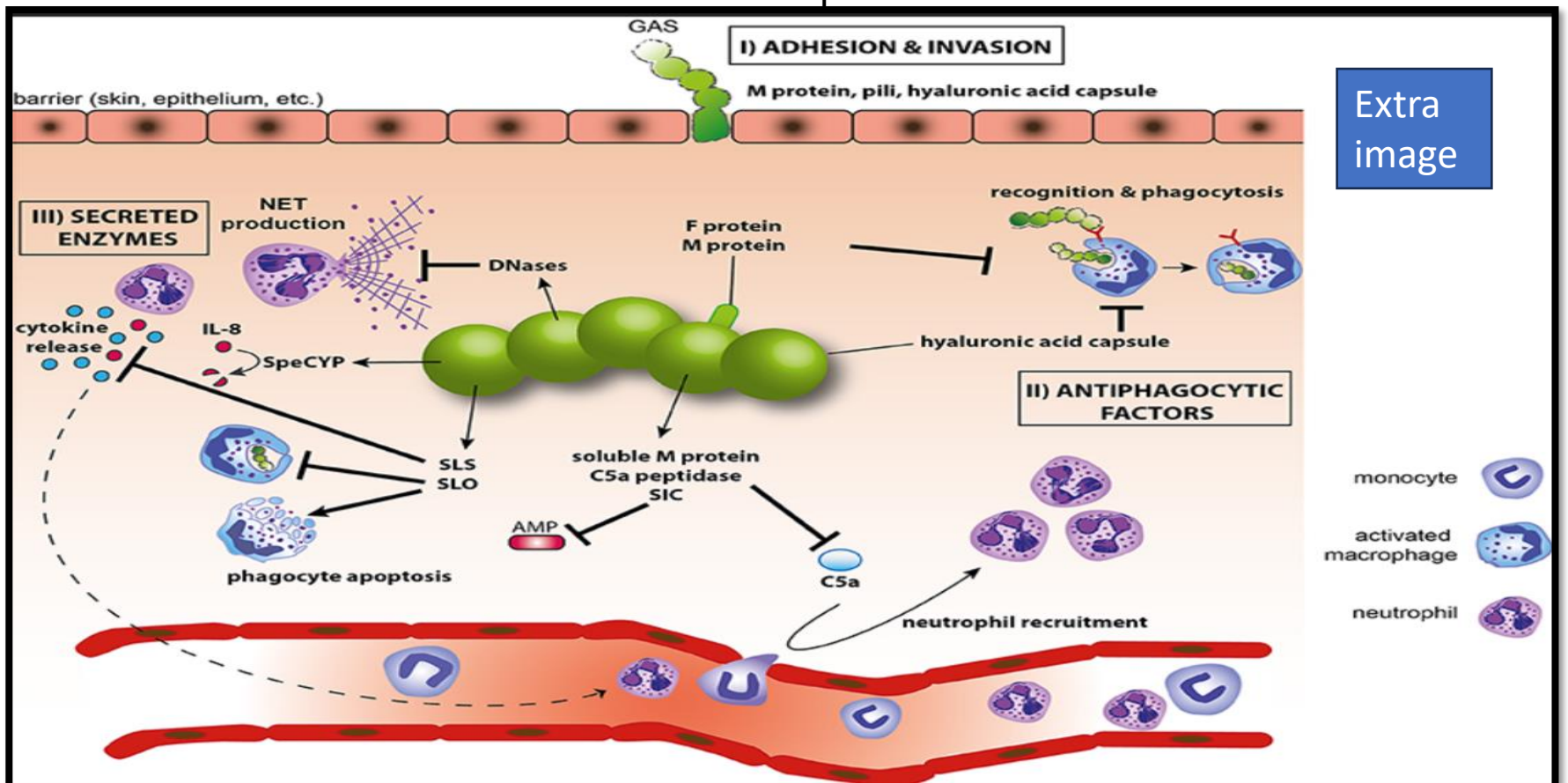
The protein T and lipoteichoic acid play a role in the attachment and internalization of streptococci.

Streptolysin O and streptolysin S are abbreviated: The "S" stands for serum soluble, while the "O" stands for oxygen labile. Can't be functional in the presence of oxygen; must be in the reduced state. The following slides will explain this.

Some bacteria can produce toxins, such as erythrogenic toxins **A, B, and C,** which are associated with toxic shock syndrome and scarlet fever. Other bacteria produce enzymes like hyaluronidase and streptokinase, or have a capsule. The M protein and hyaluronic acid capsule play a role in immune responses and their sequelae.

Adhesion.

- Bronectin, a matrix protein present on eukaryotic cells (pharynx andskin) is recognized by surface F protein on *S. pyogenes*.
- This binding interaction between GAS F protein and bronectin, alsofacilitates internalization of bacteria into host cells.
- Adhesion is also aided by other factors that are common on thesurface of Gram positive bacteria F protein, surface-exposed lipoteichoic acid and M proteins to be involved in adherence tomucosal and skin epithelial cells.



Extra image

F protein: Fibronectin binding protein that binds to the fibronectin on the surface of eukaryotic cells. It facilitates adhesion, attachment, and initiation of infection by S. pyogenes. It also assists M protein and lipoteichoic acid.

M proteins.

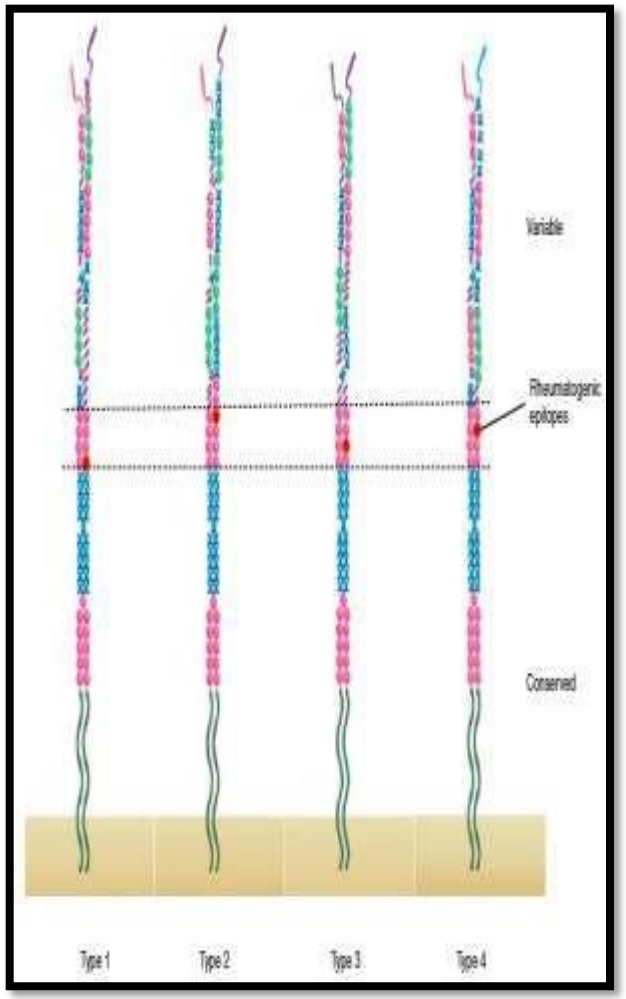
M proteins provide GAS with the ability to resist phagocytosis by host polymorphonuclear leucocytes.

•Some strains produce two different M proteins with antiphagocytic activity, and some an additional structurally related M-like protein.

•What these proteins do is they bind host (self) proteins and coat the bacterial surface with them (host proteins such as fibrinogen, plasminogen, albumin, immunoglobulin (Ig) G, IgA, the proteinase inhibitor α2-macroglobulin.

•They also prevent opsonization of C3b and even some regulatory factors from the complement system.

•Resistance to GAS is formed when antibodies are formed against the M protein, however, the distal part of the protein shows hyper variability and thus recurrent infections



M protein is **the most important virulence factor**, as it exhibits molecular mimicry. It is a hair-like projection that contains more than 100 serotypes. The M protein works as an antiphagocytic agent by preventing the activation of the alternative pathway of the complement system, thus preventing opsonization of C3B. Contains a high variable region, there is no cross reactive immunity between different M proteins

Capsule

- Although rarely seen in UNCOMPLICTAED cases, severe and difficult cases are often found to be capsulated.
- Capsule are anti-phagocytic factors of their own right and have a different mechanism from M proteins, this combined anti-phagocytic effect of M protein and capsule make these strains much harder to clear and thus a lot more
- The capsule is identical to the hyaluronic acid of the connective tissueof the host and **is not immunogenic**. In this way the bacteria can disguise themselves with an immunological 'self' substance

Not all strains have a capsule. It can be observed in young cultures in vitro and in severe complicated cases. The capsule is made of **hyaluronic acid**, not polysaccharide. **Important**

The capsule Plays a role in molecular mimicry, but to a lesser extent than M protein.

The capsule **is not** immunogenic, which means that the antibodies produced against the capsule do not provide protection.

C5a peptidase.

- The C5a peptidase is present on the surface of **ALL strains.**
- *Str. pyogenes*. It specifically cleaves, and thereby inactivates, humanC5a, one of the principal chemo- attractants of phagocytic cells.

C5a is a crucial part of the complement system. **C5a peptidase** breaks down C5a, leading to a decrease in the recruitment of neutrophils (PMN).

Usually, C5a acts as a chemoattractant.

Streptolysins (Important)

- **Streptococcus pyogenes** produces two distinct hemolysins (heme lysing enzymes, they lyse RBCs and some PMNs), Streptolysin O (oxygen labile) and S (serum soluble).
- Streptolysin O belongs to a family of hemolysins found in many pathogenic bacteria. (when injected into experimental animals itcauses death within seconds)
- Significant use for this, is to detect PREVIOUS GAS infections as Streptolysin O is immunogenic

They are responsible for the hemolysis of RBC, streptolysin O cant function if there is oxygen but streptolysin S can.

Streptolysin O

Antibodies that is generated against streptolysin O are **protective** (antigenic and immunogenic).

Can be used as evidence for GAS infection

VS

Streptolysin S

Antibodies that is generated against streptolysin S are **not Protective** (They are neither antigenic nor immunogenic.)

Other virulence factors

- SPE-A, SPE-B and SPE-C are **Pyrogenic (fever inducing)** and **erythrogenic** (rash inducing) exotoxins.
- These function **as super antigens** and cause an **exaggerated** immuneresponse (rash), the cytokines induced by these erythrogenic toxinsare thought to be responsible for the hypotensive shock and organ failure in **severe** GAS infections.
- These exotoxins are implicated in **scarlet fever** and **Toxic shock**

Invasion/escape factor

- GAS secrete hyaluronidase to degrade hyaluronic acid, the groundsubstance of host connective tissue. Usually pathogenic bacteria harbor this enzyme which **facilitates tissue invasion.** Plays a major role in necrotizing fasciitis.

- Streptococci use their streptokinase to stop host build up of serumbarriers, thus facilitating spread .

- DNAase, enzymes to break DNA net that is released from phagocytes('neutrophil extracellular traps' or **NET**) .

DNAase are highly sensitive in GAS skin infection, and they prevent NETs formation.

- the evidence of infection in case of **GAS skin infection** in the presence of **Anti DNAase antibodies**

Clinical features.

Transmission

- **The most common route of entry** of *GAS* is the **upper respiratory tract**, and is usually the primary site of infection and also serves as a focus for other types of infection.
- Spread from person to person is by respiratory droplets or by direct contactwith infected wounds or sores on the skin.
- **Not all individuals** colonized by *Str*. *pyogenes* in the upper respiratory tract **develop clinical signs of infection.**

- After an acute upper respiratory tract infection, the **convalescent patient** may carry the infecting streptococci for some weeks.(Important)

- Only a few healthy adults carry *Str*. *pyogenes* in the respiratory tract, but the carriage rate in young school children is just over 10%. It may be considerably higher before or during an epidemic.

Pharyngitis

- This is the most common infection caused by **Streptococcus pyogenes.**

Clinical signs and symptoms:

- abrupt onset of sore throat. They have dysphagia and adenophagia.
- fever, malaise and headache generally develop 2–4 days after exposure to the pathogen.
- Redness of the posterior Palate.
- **enlarged tonsils** that may show **patches of grey–white exudate** on their surface
- Inflammation causes swelling of cervical lymph nodes.
- tonsillar abscesses may develop, these are very painful and potentially dangerous as the pathogen may spread to neighboring regions and to the bloodstream.

BE CAREFUL!!

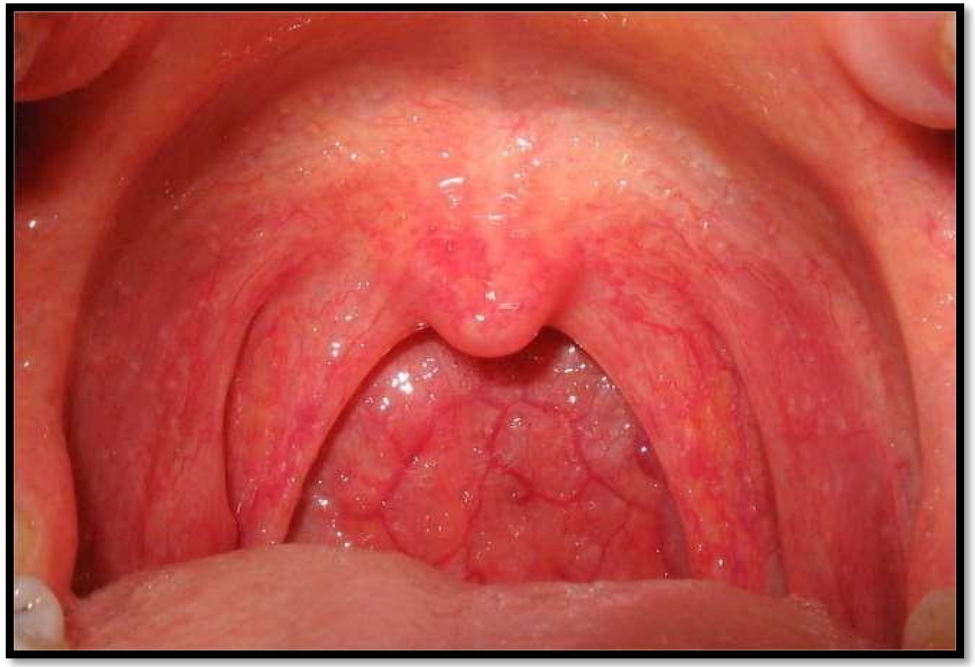
The most common cause of pharyngitis (in general) is viral.

The most common form of disease caused by GAS is pharyngitis.

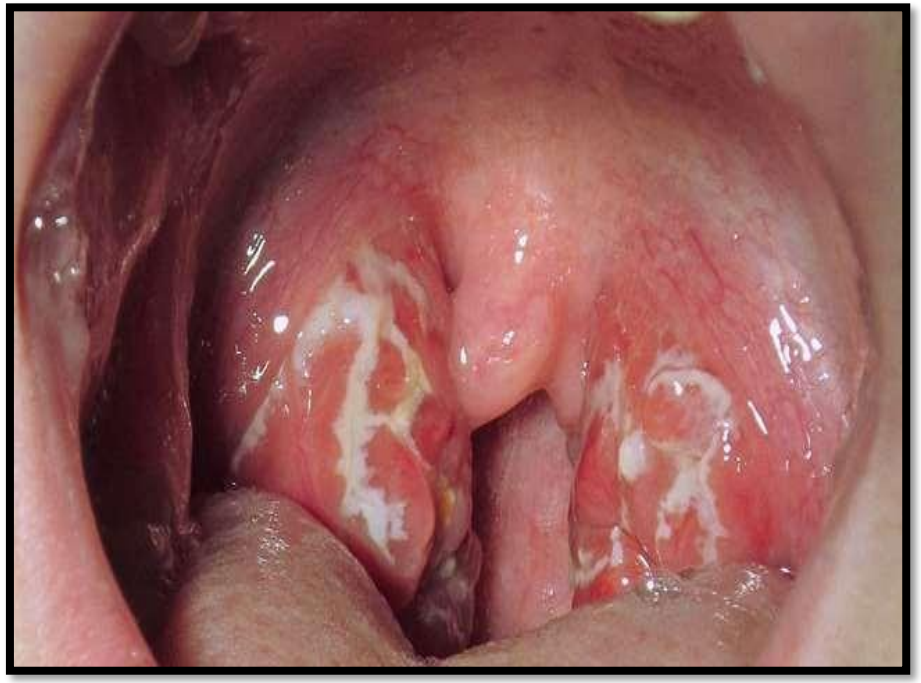
The most commune bacterial cause of pharyngitis is GAS

Important →

- Despite the significant symptoms and clinical signs → differentiating streptococcal pharyngitis (‘*strep throat*’) from viral pharyngitis is impossible without microbiological or serological examination.



VS



Viral

- **redness**.
- Conjunctivitis
- Oral ulcers
- Cough and runny nose
- **Hoarseness** of voice.

Bacterial

- Tonsils with white patches and yellow exudate
- Gray furry tongue
- Petechiae on the palate
- Enlargement of uvula
- Anterior cervical lymph node enlargement (Painful)

- **Despite the significant symptoms and clinical signs → differentiating streptococcal pharyngitis (‘*strep throat*’) from viral pharyngitis is impossible without microbiological or serological examination.**
-
- **Culture studies show that 20–30% of cases of pharyngitis areassociated with *Str. pyogenes* and *Str. Equisimilis (Group C)*.**
-
- **It means we are treating viruses with antibacterial agents! And weare causing positive selection and aiding in the increase of antimicrobial resistance.**

Summary of Clinical Findings

- Streptococcus pyogenes causes three types of diseases:

(1) pyogenic diseases such as **pharyngitis** and **cellulitis**,
(2) toxigenic diseases such as **scarlet fever** and **toxic shock syndrome(TSS)**
(3) immunologic diseases such as **rheumatic fever** and **acute glomerulonephritis (AGN).**

Streptococcus pyogenes (group A streptococcus) is the most common bacterial cause of pharyngitis (sorethroat).

- Streptococcal pharyngitis (strep throat) is characterized **by throat pain and fever**.
- On examination, an inflamed throat and tonsils, often with a yellowish exudate, are found,
- accompanied by tender cervical lymph nodes.
- **If untreated**, spontaneous recovery often occurs in 10 days, but rheumatic fever may occur.
- Untreated pharyngitis may extend to the middle ear (otitis media), the sinuses (sinusitis), the mastoids (mastoiditis), or the meninges (meningitis), Continuing **inability to swallow** may indicate a peritonsillar or retropharyngeal abscess.(Important)

Scarlet fever

- If the GAS causing pharyngitis produces exotoxins mentioned, the upper respiratory tract infection (URTI) will be associated with **a diffuse erythematous rash** of the skin and mucous membranes.

•This condition is called ***scarlet fever***.

•The rash (Sandpaper rash) develops within 1–2 days after the first symptoms of pharyngitis they are first seen on the upper chest, then extremities. After an initial phase with a yellowish-white coating, the tongue becomes red and denuded (’*strawberry tongue*’).

•This used to be a major killer disease. (in the past)

•Scarlet fever develops in patients that are infected with **erythrogenic toxin producing GAS,** in the event that the patient doesn't have the protective antibodies (**antitoxin**). Important

•The “strawberry” tongue is the characteristic lesion seen in scarlet fever. (picture in the next slide)

•*S. pyogenes* also causes another toxin-mediated disease, streptococcal toxic shock syndrome, which has clinical findings similar to those of staphylococcaltoxic shock syndrome.

- Different from Staph Toxic shock, streptococcal toxic shock syndrome usually has a recognizable site of pyogenic inflammation and blood cultures are often positive, whereas staphylococcal toxic shock syndrome typically has neither a site of pyogenic inflammation nor positive blood cultures.
- Group A streptococci cause skin and soft tissue infections, such as cellulitis,erysipelas necrotizing fasciitis (streptococcal gangrene), and impetigo
- Impetigo: superficial skin infection characterized by “honey-colored” crusted lesions, similar to those seen in Staph infections.
- Lymphangitis can occur, especially on the forearm associated with an infection onthe hand.

How to differentiate between Staphylococcus toxic shock syndrome and streptococcus toxic shock syndrome ?

- Streptococcus TSS usually has :
1- Recognizable site of pyogenic inflammation.
2- Blood culture are often positive

- while staphylococcus TSS has not.

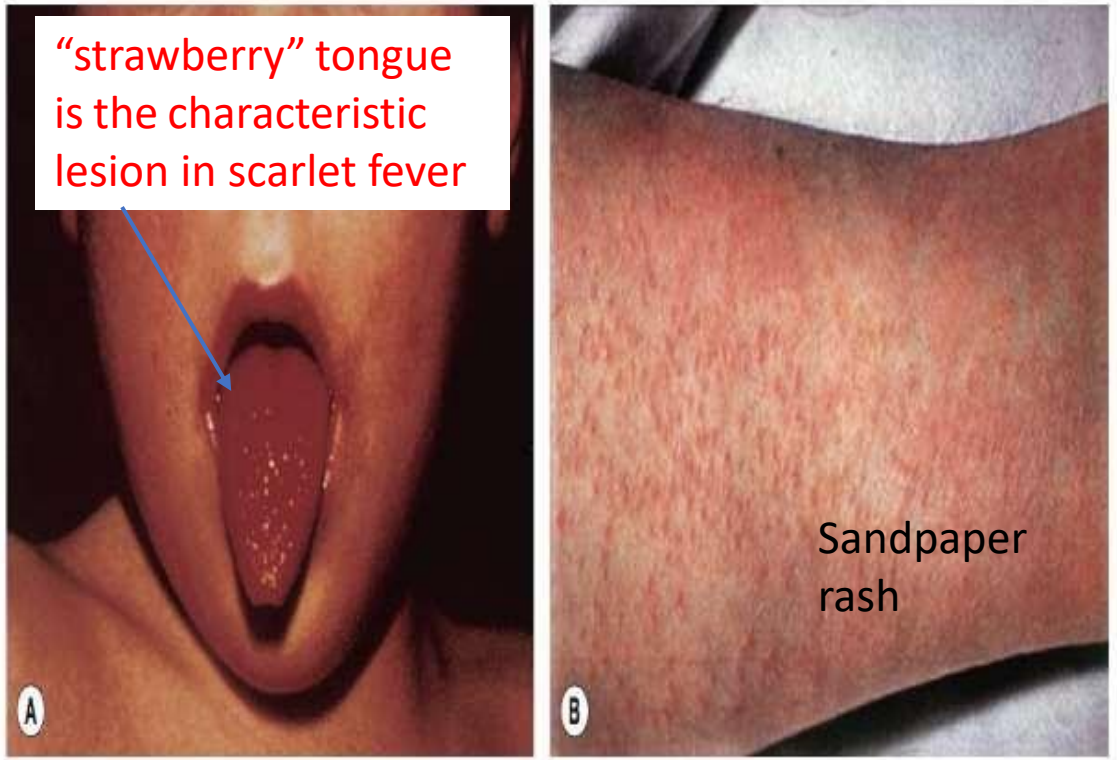


Fig. 16.3 The characteristic erythematous rash on (A) tongue and (B) skin associated with scarlet fever.

Poststreptococcal (Nonsuppurative) Diseases

- These are disorders in which a local infection (in the tissue, not systemin infection) with **GAS** is followed **weeks (it takes that much time for enough cross reacting antibodies to be produced, remember adaptive immunity takes time to develop)** later by inflammation in an organ thatwas **not** infected by the streptococci.
- This is due to the inflammation caused by an immunologic (antibody mediated) response to streptococcal **M proteins** that cross-react withhuman tissues.
- Some strains of *S. pyogenes* bearing certain M proteins (remember thereare 80+ types of this protein) are **nephrogenic** and cause AGN (Type 3 hypersensitivity reactions which is **antigen-antibody deposition**) while other strains bearing different M proteins are **rheumatogenic** and cause acute rheumatic fever. (Type 2 hypersensitivity reactions which is antibody mediated hypersensitivity)

M protein and the **capsule** play a big role in these diseases

Acute Glomerulonephritis

- Typically occurs 2 to 3 weeks after **skin** infection by certain group A streptococcal types in **children** (e.g., M protein type 49 causes AGN most frequently).

- AGN occurs more often following skin infections rather than after pharyngitis.(important)

The most striking clinical features are:

- hypertension (almost always a very odd finding in children)
- edema of the face (especially periorbital edema) and ankles (loss of protein)
- "smoky" urine (due to red cells in the urine). **Hematuria and albuminuria**.

Recurrent episodes of infection with GAS in AGN , don't make the situation worse, unlike rheumatic fever

- Most patients recover completely, however they are still not prone to develop this again if reinfection with streptococci happens.
- The antibodies cross react to a self antigen the glomerular basement membrane, and soluble antigens from streptococcal membranes may be the inciting cross reacting antigen (the antigen- antibody complexes deposit in the glomerular Basement membrane which is **type 3 hypersensitivity reaction**.) **Good prognosis 95%**
- **It can be prevented by early eradication of nephritogenic streptococci from skin colonization sites but not by administration of penicillin after the onset of symptoms. (because it is immunogenic)**

Acute Rheumatic Fever

- Approximately 2 **weeks after a group A streptococcal infection—usually pharyngitis (opposite toAGN) — rheumatic fever can occur.**

RF is characterized by: (from 1-4 are major criteria)

- 1- fever
- 2-migratory polyarthritis
- 3- endocarditis

The carditis (inflammation of heart muscle tissue) **is the most serious**, as damage to the myocardial and endocardial tissue, especially the mitral and aortic valves, can result in vegetationon the valves.

- 4- Uncontrollable, spasmodic movements of the limbs or face **(chorea)** may also occur (braindamage).
- **ASO titers and the erythrocyte sedimentation rate (ESR) are elevated.**
- Note that group A streptococcal **skin** infections do not cause rheumatic fever, most cases of **pharyngitis** caused by group A streptococci occur in children age 5 to 15 years, and hence rheumatic fever occurs in that age group. (Important)

- Modified jones criteria (there are major and minor criteria)
- But first, there must be evidence of GAS infection by detecting either:

1- Anti streptolysin O antibodies
2-Anti DNAase antibodies (in skin GAS infections)

Minor criteria
Fever, arthralgia, elevated ESR and CRP, long PR interval on ECG

Compare this with AGN in the previous slide

Recurrent episodes of infection with GAS in acute rheumatic fever **make the situation worse.**

Important

- Similar to post strep AGN, rheumatic fever is due to an **immunologic reaction** between cross-reacting antibodies to certain streptococcal **M Protein** and antigens of joint (migratory polyarthritis), heart (endocarditis), and brain tissue (chorea).
- It is also an autoimmune disease, however, unlike post strep AGN, it is GREATLY exacerbated(made worse) by **recurrence of streptococcal infections**
- If streptococcal infections are treated **within 8 days** of onset (onset of pharyngitis in this case), rheumatic fever is usually prevented**. (Important)**
- After a heart-damaging attack of rheumatic fever, reinfection must beprevented **by long-term prophylaxis**. **(this is the case that we can give prophylaxis**) we don't give prophylaxis in Acute Glomerulonephritis
- In the United States, fewer than 0.5% of group A streptococcal infections lead to rheumatic fever, but in developing tropical countries, the rate is higher than 5%.

Laboratory Diagnosis Microbiologic

- Gram-stained smears are not useful in diagnosing streptococcal **pharyngitis** because viridans streptococci, which are part of the normal flora, **cannot be visually differentiated from the pathogenic S. pyogenes.**

- However, stained smears from **skin** lesions or wounds that reveal streptococci can be diagnostic. (so a smear from skin can be diagnostic, but a smear from throat is not because the presence of viridans as a normal flora).

- Swabs taken from the pharynx or lesion and cultured on blood agar plates will show small, translucent β-hemolytic colonies within 18 to 48 hours. If these colonies are sensitive to bacitracin (inhibited by bacitracin disk (clear zone)), they are likely to be group A streptococci. (culture is the gold standard of diagnosis)

- Although cultures remain the gold standard for the diagnosis of streptococcal pharyngitis, a **problem exists** because the results of culturingare **not available for at least 18 hours**, and it is beneficial to know while the patient is in the office whether antibiotics should be prescribed**. For this reason**, rapid tests that provide a diagnosis in approximately 10 minutes were developed.

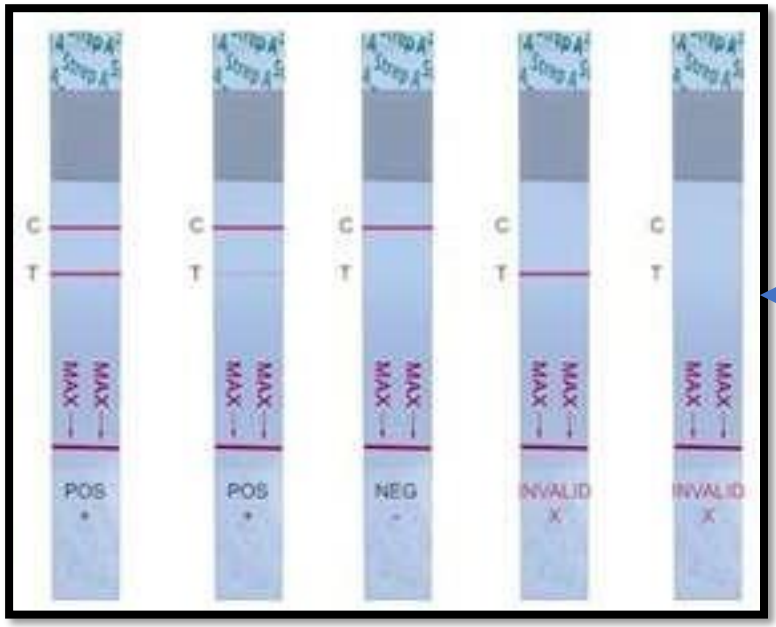
- The rapid test detects bacterial antigens in a throat swab specimen. In the test, specific antigens from the group A streptococci are extracted from the throat swab with certain enzymes and are reacted with antibody to these antigens bound to latex particles.

- **Agglutination** of the colored latex particles occurs if group A streptococci are present in the throat swab. The specificity of these tests is high, but the sensitivity is low (i.e., false-negative results can occur).
- If the test result is negative but the clinical suspicion of streptococcalpharyngitis is high, a culture should be done.

Important →

In rapid test there is

High specificity.
Low sensitivity.
Occurrence of false negative results.



RST, rapid strep test (GAS) ←

Serologic

- **Anti- Streptolysin O** (ASO) titers are high soon after group A streptococcal infections.
- Since the bacteria is usually cleared by the time antibodies develop for RF, patients suspected of having rheumatic fever, an elevated ASO titer is typically used as evidence of **previous strep THROAT infection.**
- Titers of anti-DNase B are high in group A streptococcal **skin infections** and serve as an indicator of previous streptococcalinfection in patients suspected of having AGN.

Treatment

- Group A streptococcal infections can be treated with either penicillin G or amoxicillin (as mentioned this is not protective for antibody mediates illnesses such as rheumatic fever or AGN, these patients do not benefit from penicillin treatment after the onset of the two diseases).
- In mild group A streptococcal infections, oral penicillin V can be used.
- In penicillin-allergic patients, **erythromycin** (which is a macrolide) or one of its long-acting derivatives (e.g., azithromycin) can be used. However, erythromycin-resistant strains of *S. pyogenes* have emerged that may limit the effectiveness of the macrolide class of drugs in the treatment of streptococcal pharyngitis.
- **Clindamycin** can also be used in penicillin-allergic patients.
- *S. pyogenes* is not resistant to penicillin.

Prevention

- **Rheumatic fever** can be prevented by **prompt treatment** of group A streptococcal **pharyngitis** with penicillin.
- In susceptible people (previous infection) Prevention of streptococcal infection(usually with benzathine penicillin once each month for several years).
- There is no evidence that patients who have had AGN require similar penicillin prophylaxis.
- **There are no vaccines available against any of the streptococci except *S.* pneumoniae (Next lecture topic).**

Have fun with the following USMLE question and then study the summary, good luck (:

USMLE Question

A 9-year-old male presents to the emergency department with worsening swelling. His mother reports that he was treated with antibiotics 7 days ago for a sore throat and now believes that he may be having an allergic reaction. She reports that his urine has been a dark brown color for the past 12 hours. Vital signs reveal that the patient is afebrile with a blood pressure of 132/80 mmHg and a heart rate of 94/min. Physical examination reveals 2+ pretibial edema bilaterally with diffuse edema in the periorbital and scrotal regions. Serum laboratory evaluation is shown below. Renal biopsy is planned and reveals polymorphonuclear infiltration within the glomerular basement membrane and approaching the tubulointerstitial area along with mild thickening in the arterial walls. Granular staining of the renal biopsy with C3c was positive on immunofluorescent microscopy. Which of the following features most closely describes the bacteria responsible for this immune-mediated sequela in this patient?

Hemoglobin: 11.3 g/dL
Leukocyte count: 10,500/mm^3
Platelet count: 155,000/mm^3
Serum creatinine: 2.58 mg/dL
Sodium 134 mEq/L
Potassium 4.4 mEq/L
Antistreptolysin-O antibody: Positive titer
C3 22.5 mg/dL (ref: 84-175 mg/dL)

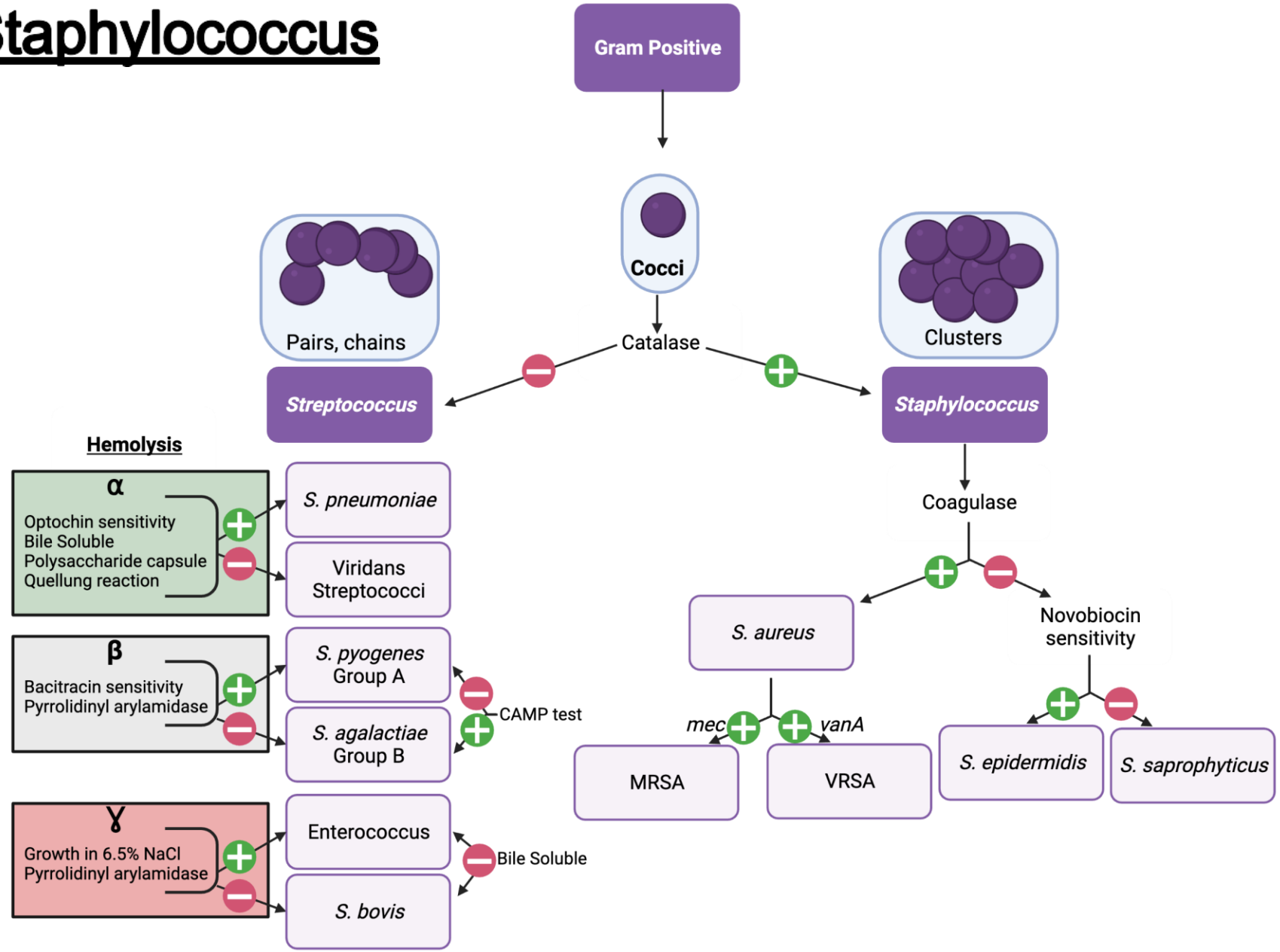
- A.
- B.
- C.
- D.
- E.

	Gram Stain	Catalase	Hemolysis capability	PYR* status
A.	+	+	β	-
B.	+	+	ɣ	-
C.	+	-	β	+
D.	+	-	ɣ	+
E.	+	-	α	-

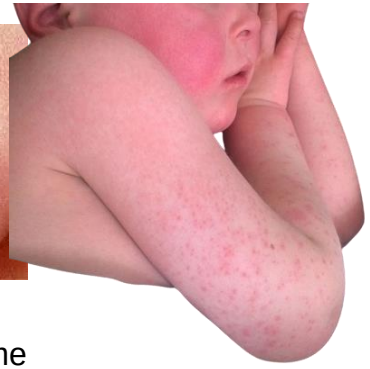
*Pyrrolidinyl arylamidase

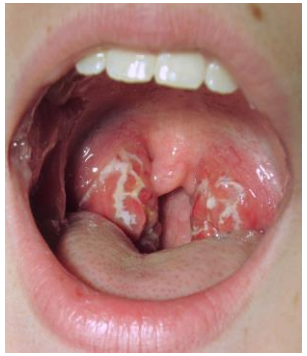
Answer with explanation:
Highly recommended
Click here

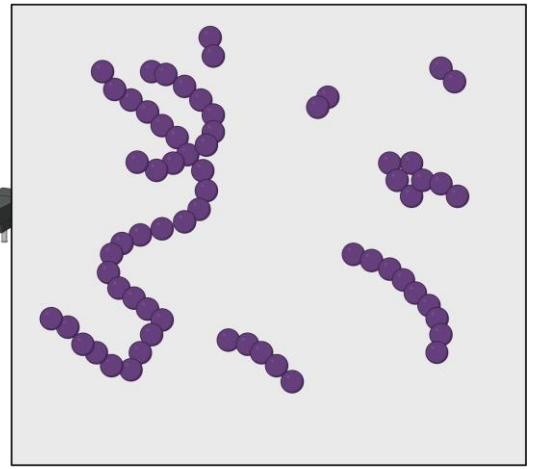
Streptococcus vs Staphylococcus



Streptococcus Pyogenes (Group A)







General Principles:
- Gram positive in pairs and chains
- Catalase negative
- β-hemolytic
- Bacitracin sensitive, facultative anaerobe
- Pyrrolidinyl arylamidase (PYR) positive

Pathogenesis:
- Nasopharynx colonization
- Erythrogenic exotoxin A, B, or C ➔ Scarlett fever
- Streptococcal pyrogenic exotoxins (SPE) ➔ Toxic shock syndrome
- Streptolysin, hyaluronidase ➔ Damages host membranes and cells ➔ Highly antigenic ➔ Anti-streptolysin O Ab produced by host
- Hemolysins
- Hyaluronic acid capsule
- M protein: ↓ Opsonization, phagocytosis ➔ Molecular mimicry ➔ Acute rheumatic fever
- Protein F: Binds fibronectin ➔ ↑ Adherence

Tonsillopharyngitis: Pharyngeal erythema +/- gray-white tonsillar exudates, usually age 5-15 y/o
- Additional: Otitis media, peritonsillar abscess

Scarlett Fever: Mediated by erythrogenic exotoxins, “Scarlet sandpaper” maculopapular rash, “strawberry” tongue

Soft Tissue Infections:
- Erysipelas: Superficial dermis, sharply demarcated
- Cellulitis: Deep dermis and subcutaneous tissue, poorly demarcated, induration
- Impetigo: “Honey-crusted lesions” (Majority caused by *S. aureus)*
- Necrotizing fasciitis: Pain out of proportion to degree of erythema, rapid progression, crepitus, skin necrosis, ↑ risk TSS

Streptococcal Toxic Shock Syndrome: Associated with necrotizing fasciitis and myositis, ↑ mortality rate (vs Staphylococcal TSS)

Acute Rheumatic Fever: Inflammatory sequela to GAS infection, cross reactivity of M protein Ab with host myocardial tissue

Poststreptococcal Glomerulonephritis: Inflammatory sequela to GAS infection, *S. pyogenes* antigen-immune complex deposition in glomerular BM

Diagnostics:
- Throat culture, rapid antigen detection (Rapid Strep Test)
- Serum antistreptolysin O (ASO), anti-deoxyribonuclease B (ADB) titer

Antibiotics:
- Penicillin, Ampicillin, Amoxicillin
- 1st and 2nd generation cephalosporins