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MICROBIOLOGY

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Bacterial infections of the Respiratory Tract 1

Named the other gram-positive cocci because there is Staph aureus. They are catalase-negative, so they are either streptococci or enterococci. Categorized mainly in three categories: the first is pyogenic infection, mainly pharyngitis, or skin infections include cellulitis, erysipelas, necrotizing fasciitis, and impetigo. The second involves toxin-mediated diseases such as scarlet fever and toxic shock syndrome. The third category encompasses immune sequelae like rheumatic fever and glomerulonephritis.

Streptococci are facultative anaerobes, meaning they can grow with or without O2. Catalase-negative, non-motile, non-spore-forming, and non-acid-fast. They deal with O2 using superoxide dismutase, turning it into hydrogen peroxide and aiding in alpha-hemolytic processes that produce a green color as a consequence of converting bilirubin into biliverdin. Streptococci are ovoid in shape, smaller than staph, arranged in chains or pairs, and attach end-to-end because they divide in the same plane.

Concerning classification, no single system can classify streptococci together. Thus, various classification systems are combined. The first one is based on colony morphology and hemolytic reactions: Beta hemolysis represents complete hemolysis by using streptolysins O and S , Alpha hemolysis is partial and appears green due to hydrogen peroxide effect, and Gamma hemolysis shows no hemolysis.

The second system is Lancefield, which explores carbohydrate antigens in cell wall extracts. Medically important groups include A, B (aggalactiae responsible for neonatal sepsis), C (dis-aggalactiae, similar to group A), F, and G. Notably, this system doesn't encompass Strep. Pneumoniae and Viridans group streptococci, but Optochin can differentiate them, as Pneumoniae is sensitive while Viridans is not. Group D (enterococcus) is the only one that can grow in bile esculin.

The last system is based on biochemical reactions and resistance to chemical factors. Strep pyogenes is sensitive to bacitracin, while agalactiae is not.

Up to 30% of children carry strep. viridans and other types in their normal flora, while adults decrease to around 10%, adding complexity to the pathogenesis.

Now, let's discuss Streptococcus Pyogenes. The carriage rate is high, found in health carriers, children, and to a lesser extent, adults, being the only human pathogen. It causes a wide variety of diseases, mainly categorized into:
Pyogenic infections, notably pharyngitis, characterized by the abrupt onset of sore throat, leading to peritonsillar abscess, peripharyngeal abscess, mastoiditis, otitis

media, sinusitis, and meningitis. Additionally, skin infections include cellulitis, erysipelas (well-demarcated erythema), necrotizing fasciitis (flesh-eating disease), and impetigo (honey crusty).

Toxin-mediated diseases such as scarlet fever and toxic shock syndrome, the latter related to erythrogenic toxins acting as superantigens binding to the variable domain for the beta chain of T receptors, causing a cytokine storm. Notably, toxic shock syndrome could be caused by Staph, but it is always non-focal, making it challenging to identify the infection. Furthermore, it gives a negative blood culture, unlike Strep, which is positive and focal.

The most significant category involves immune sequelae, such as rheumatic fever and glomerulonephritis.

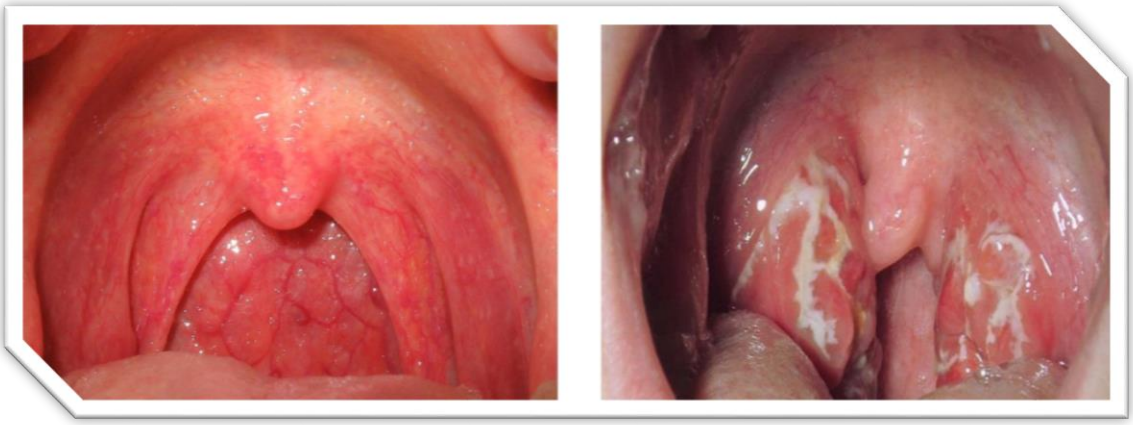
Strep pyogenes could also cause purple fever postpartum.

> Let's delve into the virulence factors of Streptococcus Pyogenes. It's crucial to note that not every bacterial cell contains all these factors, and the presence of genes doesn't guarantee their expression.
> Being Gram-positive, it contains a peptidoglycan layer and group A polysaccharide, earning it the name GAS.
>
> In vitro, young cultures exhibit severe virulence with a hyaluronic acid capsule, considered antiphagocytic. This capsule, similar to the M protein, contributes to molecular mimicry and is not immunogenic, making antibodies non-protective.
>
> M and M-like proteins, immunogenic and antiphagocytic, inhibit the alternative pathway by binding to factor H. They play a pivotal role in immunity against GAS, with a hair-like structure containing a highly variable region. Immunity involves neutralizing antibodies, but it's serotype-specific, lacking cross-reactivity.
>
> The F protein binds fibronectin, and lipoteichoic acid-T protein plays a critical role in attachment and internalization.
>
> Streptolysins O (oxygen labile meaning that it can’t work in presence of O2 and the antibodies generalized against it are protective and antigenic immunogenic and used in searching for past infection by anti streptolysin O) and S (for serum soluble not immunogenic nor antigenic) are involved, along with exotoxins (A, B, and C) inducing fever and producing rash, playing a role in toxic shock syndrome.
>
> Streptokinase converts plasminogen to plasmin.
>
> C5a peptidase cleaves C5a in the complement system, known as a chemoattractant.

Regarding adhesion, the F protein binds fibronectin, facilitating attachment and internalization with assistance from M protein and lipoteichoic acid. For escape or invasion, hyaluronidase degrades ground substance, playing a major role in necrotizing fasciitis. DNAase is highly sensitive in skin infections, breaking nets.

Transmission as upper respiratory tract infection by secretions and droplets and salivary
But as skin infection you need direct contact
Convalescents carriers : after treatment they still have GAS

The most common cause of pharyngitis is viral cause
The most common form of infections with GAS is pharyngitis characterized by abrupt onset of sore throat and dysphageia and odenophageia might accompanied by fever and upper respiratory tract symptoms



Viral	Bacterial
*** Without enlargement of the uvula** ***hoarseness of the voice**	*Grey white patches with yellow lines of exudates
***Oral ulcers**	*Grey furry tongue -If not treated with antibiotics this pharyngitis may be converted into abscess; peritonsillar abscess and retropharyngeal abscess + (cervical lymph node enlargement)
***cough and runny nose**	–Children come with GI symptoms. (enlargements of lymph

	nodes)
***conjunctivitis**	*Enlarged uvula and tonsils

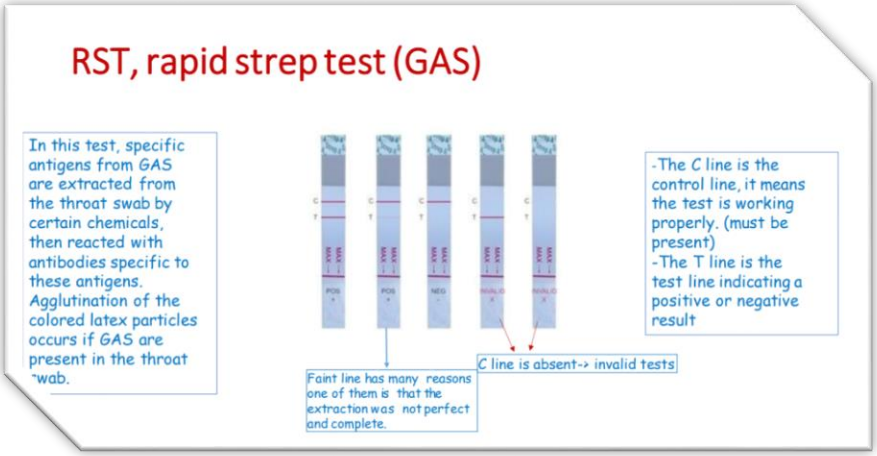
GCS (Group C Streptococcus) has a similar spectrum to GAS (Group A Streptococcus).
If the GAS causing pharyngitis produces exotoxins like SPE-A, SPE-B, and SPE-C, the upper respiratory tract infection (URTI) becomes associated with a diffuse erythematous rash on the skin and mucous membranes, leading to scarlet fever. The rash, characterized as sandpaper-like, emerges 1–2 days after the initial pharyngitis symptoms, starting on the upper chest and extending to the limbs with a maculopapular pattern. Following an initial phase with a yellowish-white coating, the tongue turns red and denuded, known as 'strawberry tongue.' This condition, once a major killer disease, highlights the severity of certain strains of Streptococcus bacteria.

Acute glomerulonephritis (AGN) is characterized by type 3 hypersensitivity reactions and typically occurs 2 to 3 weeks after skin infection by certain group A streptococcal types, with M protein types 47 or 49 causing AGN most frequently in children. It often follows skin infections rather than pharyngitis, presenting with a triad of hypertension, periorbital and ankle edema, and "smoky" urine due to red cells. Although most patients recover completely, some may progress to renal failure. Recurrent infections by Group A Streptococcus (GAS) do not worsen AGN, unlike in rheumatic fever (RF), where recurrent GAS infections exacerbate immunological damage and increase the risk of infective endocarditis. AGN and RF are both systemic diseases stemming from immunological responses to prior group A beta-hemolytic streptococcal infections, with distinct strains contributing to nephrogenic strain causing AGN and rheumatogenic strain causing RF.

On the other hand, acute rheumatic fever (RF) involves type 2 hypersensitivity reactions and typically manifests approximately two weeks after a group A streptococcal infection, often pharyngitis. RF is characterized by fever, migratory polyarthritis, endocarditis, and uncontrollable movements (chorea) indicating brain damage. ASO titers and the erythrocyte sedimentation rate (ESR) are elevated. Penicillin is prescribed not as a therapeutic or prophylactic measure but to ensure the eradication of the microorganism, preventing contagion. RF prognosis is more severe than AGN, and timely treatment of streptococcal infections can prevent RF. In the United States, less than 0.5% of group A streptococcal infections lead to RF, while the rate is higher than 5% in developing tropical countries. Prophylaxis is crucial for individuals suffering from acute RF, involving a single dose of penicillin every four weeks for several years.

In the laboratory diagnosis of streptococcal pharyngitis, Gram-stained smears are ineffective because viridans streptococci, members of the normal flora, cannot be visually distinguished from the pathogenic S. pyogenes. However, stained smears from skin lesions or wounds that reveal streptococci are diagnostically informative.

Cultures from pharyngeal swabs or lesions on blood agar plates exhibit small, translucent β-hemolytic colonies within 18 to 48 hours, requiring at least one day for incubation. If these colonies are sensitive to bacitracin, as determined by inhibition with a bacitracin disk, they are likely to be group A streptococci.



In serologic diagnosis, ASO titers are elevated soon after group A streptococcal infections. Since the bacteria is typically cleared by the time antibodies develop for rheumatic fever (RF), an elevated ASO titer serves as evidence of a previous strep throat infection in patients suspected of having RF. Moreover, high titers of anti-DNase B in group A streptococcal skin infections act as an indicator of previous streptococcal infection in patients suspected of having acute glomerulonephritis (AGN).

Treatment for group A streptococcal infections includes penicillin G or amoxicillin, although it is crucial to note that these antibiotics are not protective against antibody-mediated illnesses like rheumatic fever or AGN if administered after the onset of these diseases. Oral penicillin V is suitable for mild infections, while erythromycin or its long-acting derivatives, such as azithromycin, can be used in penicillin-allergic patients. Clindamycin is an alternative for penicillin-allergic individuals. Importantly, S. pyogenes is not resistant to penicillins. Rheumatic fever prevention involves prompt treatment of group A streptococcal pharyngitis with penicillin. In susceptible individuals, prevention of streptococcal infections, usually with benzathine penicillin once each month for several years, is recommended. There is no evidence supporting penicillin prophylaxis for individuals who have had AGN. Currently, no vaccines are available against streptococci, except for Streptococcus pneumoniae. Healthy carriers of streptococci typically do not require treatment unless they occupy crowded places like prisons, especially for children who are susceptible to group A beta-hemolytic streptococci.