DOCTOR 2020 | JU

MICROBIOLOGY

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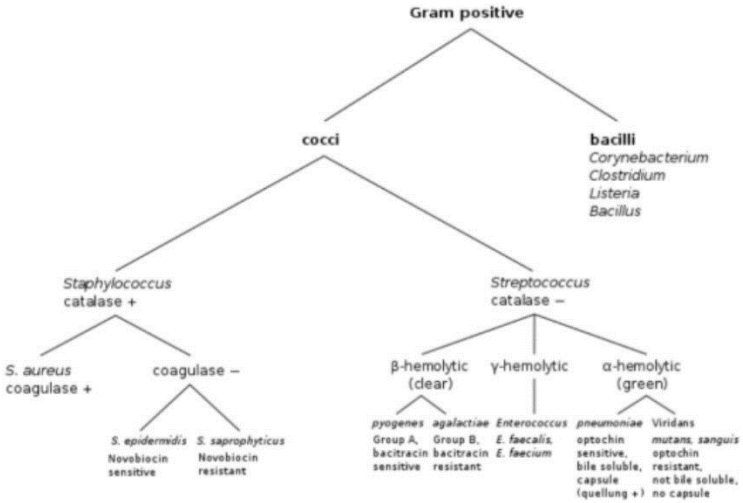
In the coming lectures we will talk about medical pathogens, from all types of bacteria there is a small percentage of them that causes diseases, up to 20-30 types. However, we will talk about the most important medical pathogens.

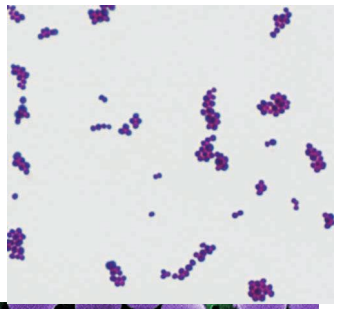
Bacterial genera that will be discussed this lecture are Gram-positive cocci that cause a variety of infections in the skin and mucus membranes, and can secrete a variety of toxins:

1. Staphylococci 2. Streptococci (cocci= spherical)

Remember that cell wall is the main difference between gram positive and gram negative bacteria, exactly peptidoglycan that retain the stain (crystal violet) in g+ bacteria because of thick layers of peptidoglycan and when decolorize it, it still has the stain, g- bacteria don't have the thick stick layer so they lose the stain after washing, And later can be colorized by counter stain.

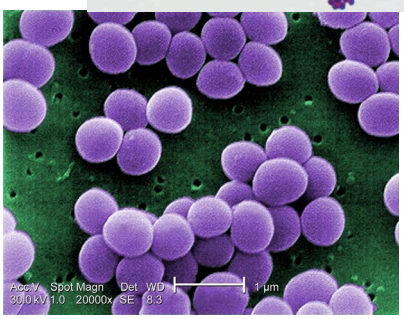


Staphylococci



• The staphylococci are **gram-positive spherical cells**, about 1 µm in diameter usually arranged in grapelike **irregular clusters, it is non-motile**.

• The four most frequently encountered species of clinical importance are
-Staphylococcus aureus, (commonly pathogenic)



-Staphylococcus epidermidis, (non-pathogenic; skin)

-Staphylococcus lugdunensis,

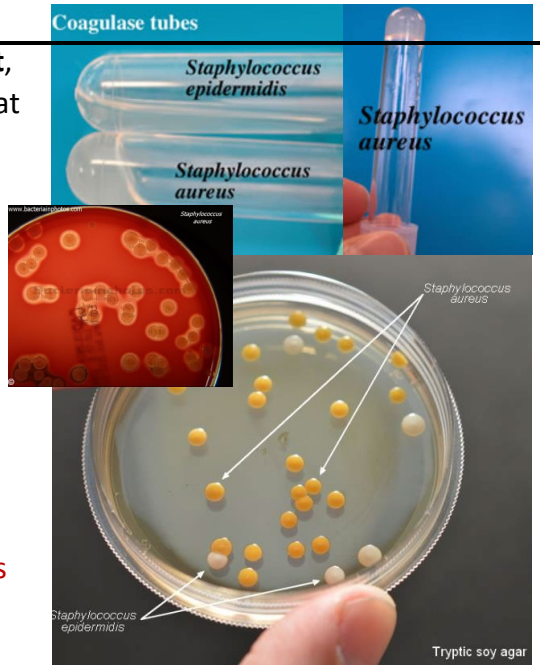
-Staphylococcus saprophyticus. (Non-pathogenic; skin and GI tract)

We have certain biochemical tests to identify bacteria and give proper treatment and diagnosis. The first test we can do is **catalase test**.

Staphylococci produce **catalase**, which converts hydrogen peroxide into water and oxygen (in the form of bubbles). The catalase test differentiates the **staphylococci**, which are **positive**, from the **streptococci**, which are **negative**.

$$2H_2O_2 \xrightarrow{\text{Catalase}} 2H_2O + O_2$$

If we want more detailed identification we do **coagulase test**, that we are testing for the presence of enzyme coagulase that **Causes coagulation of plasma**.



• S aureus is **coagulase positive**, usually **forms gray to deep golden yellow colonies**.

• Various degrees of **hemolysis** are produced by S aureus if we put it in blood agar plate.

• The **coagulase-negative** staphylococci are normal human microbiota. S epidermidis colonies usually are **gray to white on primary isolation.**

Remember: the most important pathogen in Staphylococci is **Staphylococcus aureus**.

Structure and physiology

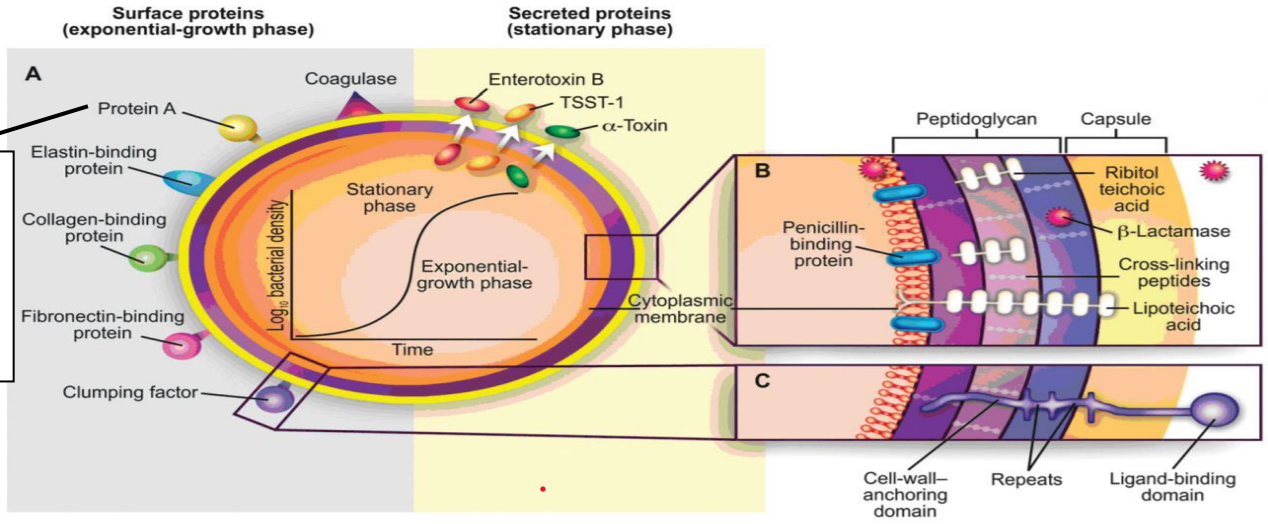
Peptidoglycan in the cell wall activate the immune response (it can be a chemoattractant for polymorphonuclear leukocytes, have endotoxin-like activity, and activate complement sys. and coagulation system and secretion of pro-inflammatory cytokines which may lead to shock and organ failure).

Endotoxin: lipopolysaccharide of g- bacteria

Bacterial attachment to host cells is mediated by **MSCRAMM (microbial surface components recognizing adhesive matrix molecules) proteins**. and these are important virulence factors. (e.g. Protein A, clumping factor)

Clumping factor A is a fibrinogen-binding protein present on the surface of S. aureus that binds to fibrinogen and coats the surface of the bacterial cells with fibrinogen molecules, additionally complicating the recognition process.

Coagulase on the surface is a virulence factor because when **forming a clot around it**, it protects itself from immune cells. So S aureus could have a capsule around it. (Clumping factor A help in the formation of the capsule)

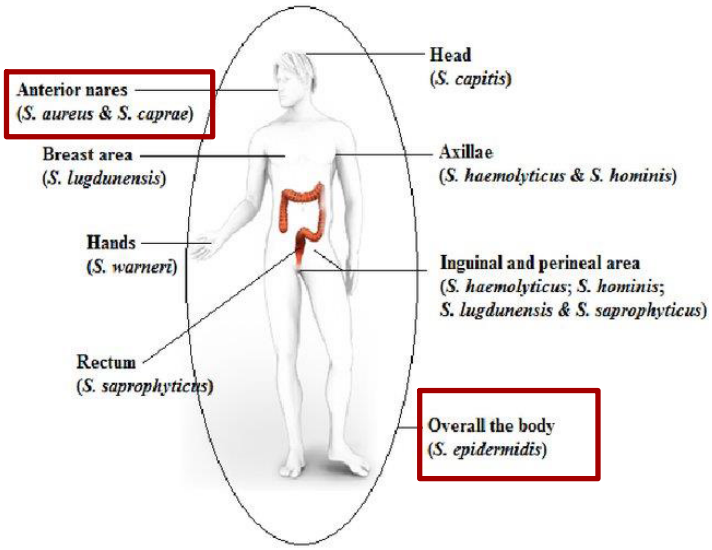


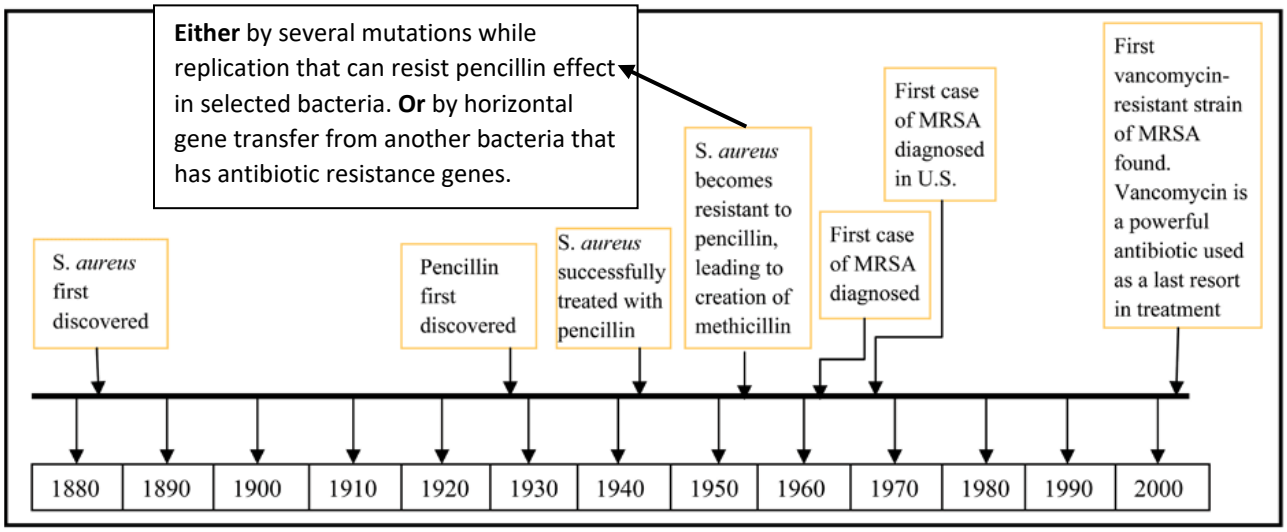
Protein A captures antibodies from fc region neutralizing them (immune evasion)

Epidemiology

Staphylococci, particularly **S epidermidis**, are members of the normal microbiota of the human skin and respiratory and gastrointestinal tracts.

Nasal carriage of **S aureus** occurs in 20–50% of humans, with **a higher incidence** reported for **hospitalized patients**, **medical personnel** (physicians and nurses), persons with **eczematous skin diseases** (tissue disruption causes colonisation of bacteria like; S aureus) . Staphylococci are also found regularly on clothing, bed linens, and other **fomites** in human environments.





Beginning in the 1980s, strains of Methicillin-resistant Staphylococcus aureus **(MRSA) spread rapidly in susceptible hospitalized patients**, dramatically changing the therapy available for preventing and treating staphylococcal infections.

MRSA began as a hospital-acquired infection, but has become **community-acquired** as well as **livestock-acquired.**

People with compromised immune systems (elderly, diabetics, HIV/AIDS), hospitalized patients and children are some of the susceptible groups to MRSA.

This MRSA now is getting resistance to new antibiotics, like **vancomycin**; a strong antibiotic that usually kills MRSA, but after 2000s, the first vancomycin resistant strain of MRSA.

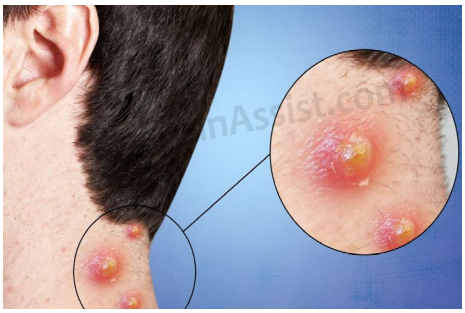
Clinical correlations

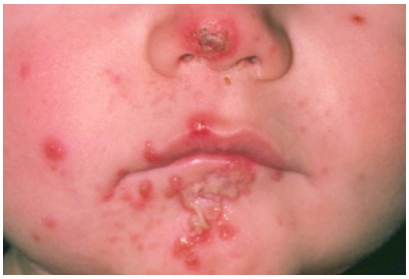
the most common diseases are skin diseases, it has the ability to bind ECM components by **elastin-binding, collagen-binding and fibronectin-binding proteins** very well.

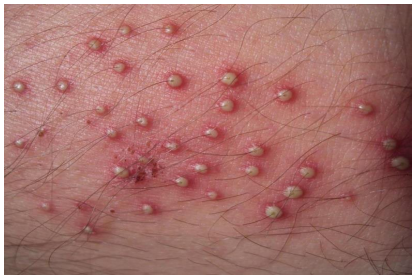
It has also immune evading mechanisms, like **protein A** binds Fc portion of antibodies and **proteases** breaks down complement proteins. It can also evade phagocytosis by its **capsule**, and many other proteins to evade immune system.

A localized staphylococcal infection appears as a **"pimple," hair follicle infection (folliculitis), or abscess**. There is usually an intense, localized, painful inflammatory reaction that undergoes central suppuration and heals quickly when the pus is drained.

Impetigo: localized cutaneous infection characterized by pus-filled vesicle on an erythematous base
Folliculitis: impetigo involving hair follicles
Furuncles or boils: large, painful, pus-filled cutaneous nodules
Carbuncles: Coalescence of furuncles with extension into subcutaneous tissues and evidence of systemic disease (fever, chills, bacteremia)



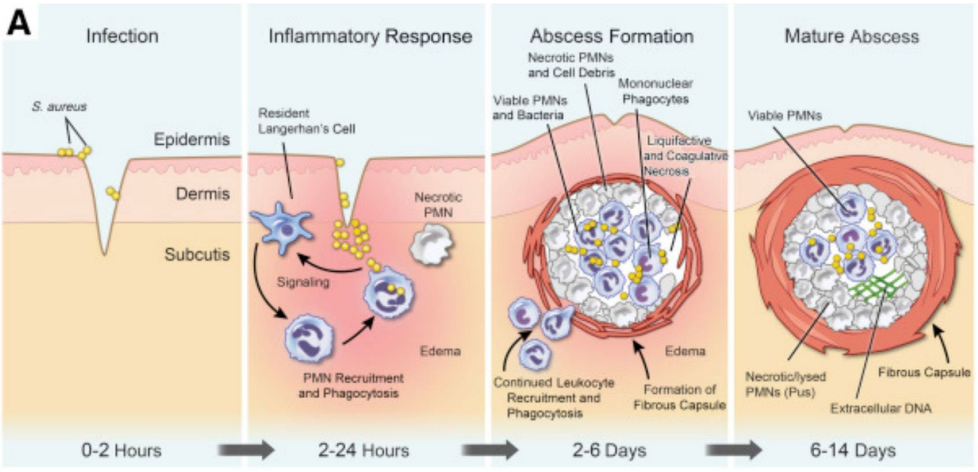




If the epithelial surface broken down, the pathogens like S aureus can enter and induce immune response, PAMPs and DAMPs, TLR, pro-inflammatory cytokines ,recruitment of immune cells such as neutrophils to the site of injury and start release granules that contains digestive enzymes and reactive oxygen species and disrupt the tissue specially when S aureus is resisting killing.

So, tissue disruption and immune evading mechanisms such as forming the capsules by surface enzymes and clumping factor. Altogether, contribute to form a capsule around the infection area. Moreover, the body itself tends to maintain the infection in a certain place and try to form the capsule or lesion.

The new requited immune cells and even antibiotics will find it hard to enter inside it, and we call this lesion an **Abcess**.



This pus contains **dead WBC, PMN cells, tissue debris, dead and live bacteria**. And also we have **extracellular DNA** contributes In the viscosity, that came from NET formation from neutrophils and also from debris.

It is treated by drainage of the contents, and extracting it maybe remove the capsule altogether then give antibiotics. *(This abscess can occur in any other place in the body other than skin with the same mechanism)*

Now, there is another way of S aureus to cause diseases; by toxins especially in the GIT (enterotoxins).

Clinical correlations / Toxin mediated

Staphylococcal food poisoning, one of the most common foodborne illnesses, is an **intoxication** rather than an infection, Disease is caused by **heat stable bacterial toxin** present in food rather than from a direct effect of the organisms on the patient. With **a short incubation period (1–8 hours);** violent nausea, vomiting, and diarrhea; and **rapid convalescence** تعافي (intoxication can occur without the presence of the S aureus itself in the bod, because of hat when we get rid of toxin anyway the symptoms will disappear rapidly).

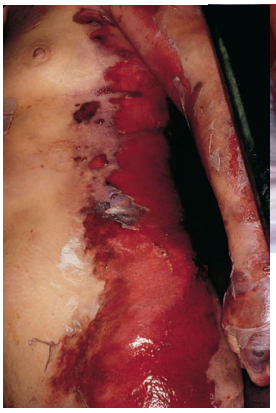
Staphylococcal scalded skin syndrome is a condition which predominantly **affects infants and children** and causes a spectrum of skin lesions.

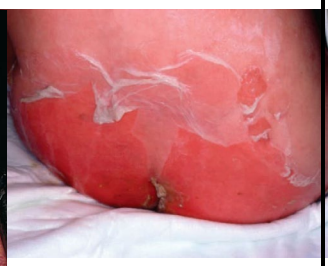
Toxin-Mediated Diseases

Scalded skin syndrome: Disseminated desquamation of epithelium in infants; blisters with no organisms or leukocytes

Food poisoning: After consumption of food contaminated with heat-stable enterotoxin, rapid onset of severe vomiting, diarrhea, and abdominal cramping, with resolution within 24 hours

Toxic shock: multisystem intoxication characterized initially by fever, hypotension, and a diffuse, macular, erythematous rash; high mortality without prompt antibiotic therapy and elimination of the focus of infection





Clinical correlations / Coagulase negative

Those are harmless types of staphylococcus, part of the microbiota can be pathogenic when they **change its original place to another**, but why it becomes pathogenic? Maybe because of the genetic changes according to the new environment.

S epidermidis infections are difficult to cure because they occur in **prosthetic devices** where the bacteria can sequester themselves in **a biofilm**. staphylococci are a major cause of **endocarditis of artificial valves.**

More than 50% of all infections of **catheters and shunts** are caused by **coagulase-negative staphylococci**. These infections have become a major medical problem because long-dwelling catheters and shunts are used commonly for the medical management of critically ill patients.

Catheter surface doesn't have resistance to bacteria or immune responses, so bacteria easily attach to it and form the biofilm.

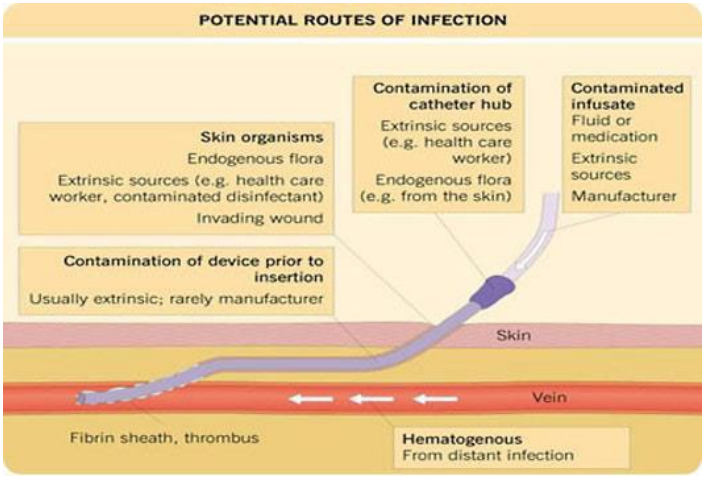
Coagulase-Negative *Staphylococcus* Species

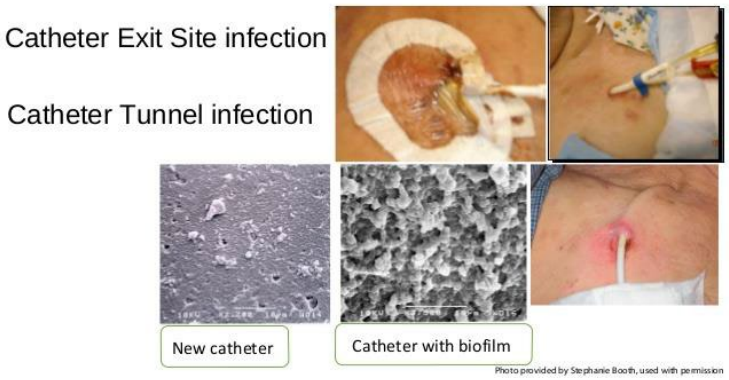
Wound infections: Characterized by erythema and pus at the site of a traumatic or surgical wound; infections with foreign bodies can be caused by *S. aureus* and coagulase-negative staphylococci

Urinary tract infections: Dysuria and pyuria in young sexually active women (*S. saprophyticus*), in patients with urinary catheters (other coagulase-negative staphylococci), or following seeding of the urinary tract by bacteremia (*S. aureus*)

Catheter and shunt infections: Chronic inflammatory response to bacteria coating a catheter or shunt (most commonly with coagulase-negative staphylococci)

Prosthetic device infections: Chronic infection of device characterized by localized pain and mechanical failure of the device (most commonly with coagulase-negative staphylococci)





Streptococci

Streptococci Classification

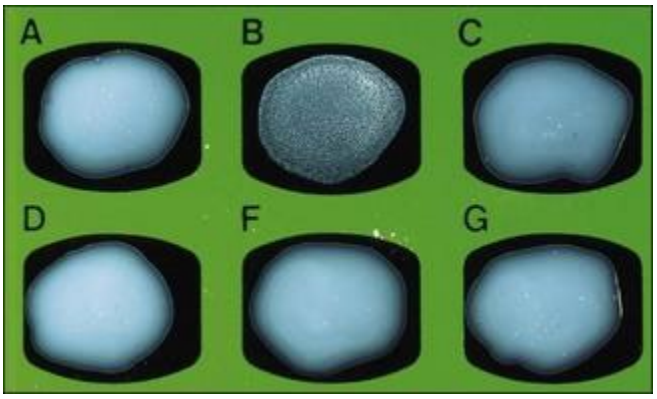
The classification of more than 100 species within the genus Streptococcus is complicated because three different overlapping schemes are used:

(1) serologic properties: Lancefield groupings (originally A to W); The most important pathogenic streptococcal species for humans include Streptococcus pyogenes (group A streptococcus/ GAS) , Streptococcus agalactiae (GBS), group D streptococcus (not really a streptococcus (enterococci), Streptococcus pneumoniae, and Streptococcus viridans.

(2) hemolytic patterns: complete (beta [β]) hemolysis, incomplete (alpha [α]) hemolysis, and no (gamma [γ]) hemolysis;

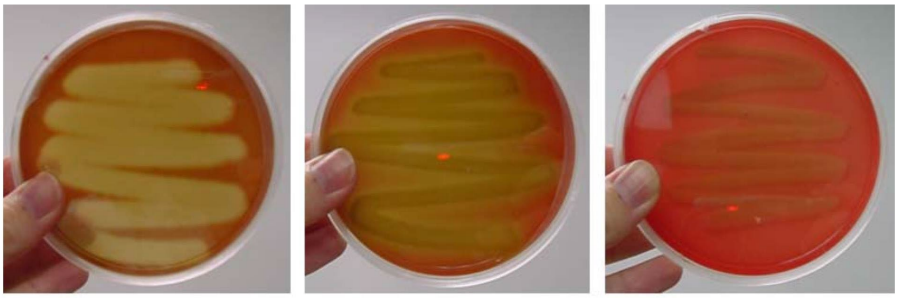
(3) biochemical (physiologic) properties.

Lancefield groupings



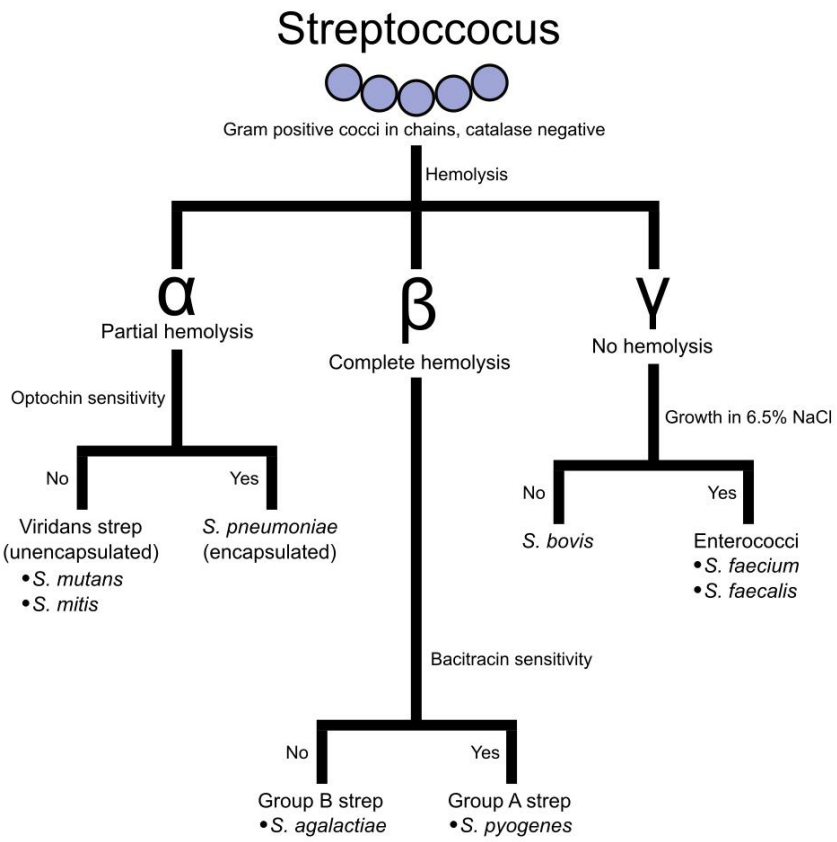
Serological test; we put different antibodies each in different well, then put the colony, and when we see the agglutinations that indicates the attachment of antibodies with the antigen agglutinating them together. (Here the bacteria has the antigen B,so it called **Streptococcus agalactiae** or **group B streptococci (GBS)**)

Hemolytic patterns



Beta Hemolysis **Alpha Hemolysis** **Gamma Hemolysis**

Means break down of RBCs in the blood agar, bacteria gets its nutrients from breaking down RBCs.



Thank you

Moises Dominguez