



SHEET NO.



MICROBIOLOGY (Bacteriology)

DOCTOR 2019 | MEDICINE | JU

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bacteria	Identification	Important features	diseases	Treatment
<i>S.pyogenes</i> (group A streptococci)	Bacitracin test -sensitive, unlike other beta hemolytics.	-Beta hemolytic -C carbohydrate -M protein - lipoteichoic acid -five toxins -three invasive enzymes.	pharyngitis and cellulitis (soft tissue infection).Impetigo, necrotizing fasciitis, streptococcal toxic shock syndrome, glomerulonephritis, rheumatic fever scarlet fever.	Penicillin G or amoxicillin. Mild->oral penicillin V. Penicillin-allergic patients 1)erythromycin 2)Clindamycin.
<i>S.agalactiae</i> (group B)	Color detection of Hippurate hydrolytes produced by its hydrolysis	-Beta hemolytic -bacitracin resistant. - M protein -C carbohydrate	neonatal sepsis and meningitis because it abnormally colonizes the birth canal.	Penicillin G Or ampicillin (given orally, it isn't effective in eradicating the organism)
<i>Enterococcus faecalis</i> (group D) (also, <i>enterococcus faecium</i>)	- growth on bile-esculin agar. - resistant to penicillin.	-classical enteric G +ve cocci - can grow in hypertonic 6.5% saline, they survive bile salt. - resistant to penicillin G.	Opportunistically urinary tract infections, biliary infections and endocarditis. Stronger and more infections than <i>S.bovis</i>, because <i>E.faecalis</i> is hardier.	synergistic combination of penicillin and an aminoglycoside (e.g., gentamicin) -vancomycin, but V R Es have emerged.
<i>S.bovis</i> (group D)	-sensitive to penicillin G. -growth on bile esculin.	-not enterococcal - inhibited by 6.5% NaCl	Opportunistically endocarditis	Penicillin G
<i>S.pneumoniae</i> (major alpha hemolytic, no lancefield grouping_	Sensitive to optochin, bile soluble colonies.	Alpha hemolytic	Queen of serious diseases. - 1) pneumonia 2) bacteremia 3) meningitis, and 4) URTI	Penicillin v (mild) penicillin G (severe). Erythromycin, azithromycin (pen. Allergic patients) Vancomycin (pen.resistance)
<i>Viridans group</i> (same as pneumococci) ↑	Opposite of pneumococci.	Alpha hemolytic (viridans=green)	Most common cause of endocarditis	prolonged penicillin treatment (endocarditis)

In the previous lecture we have talked about staphylococci, which are the first gram positive cocci of medical importance. Today, we'll talk about the other gram-positive cocci, **Streptococci**. There **will be** variations in order from the slides.

First, **important properties of streptococci**:

- Streptococci are **Gram positive** cocci arranged in **chains (along the same axis) or pairs (especially pneumococcus)**. They are invaders while Staph. are nesters.
- All streptococci are catalase-negative, unlike staphylococci which are catalase-positive.

(this is *Streptococcus pyogenes*, notice the arrangement)

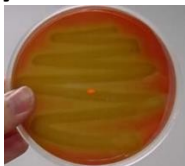
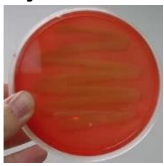


Second, **classification**:

streptococci (especially those of medical importance) are **so many**, that's why we use a **classification system to distinguish between them** and we diagnose disease by classification rather by species. (E.g. we say: a patient is infected with group A streptococcus rather than saying streptococcus pyogenes).

We have two grouping methods:

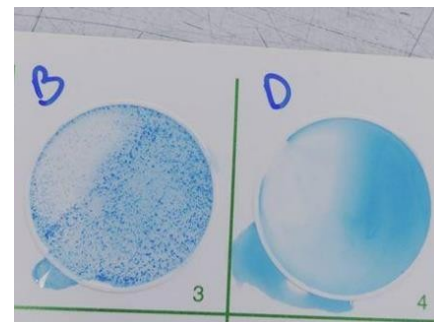
A. mode of hemolysis. According to this we have three types:

Beta hemolytic	Alpha hemolytic	Gamma hemolytic
		
β-Hemolytic streptococci form a clear zone around their colonies because <u>complete lysis</u> of the red cells occurs. β-Hemolysis is due to the production of enzymes (hemolysins) called <u>streptolysin O</u> and <u>streptolysin S</u> (will pass in "Pathogenesis" later).	α-Hemolytic streptococci form a <u>green zone</u> around their colonies as a result of <u>incomplete lysis</u> of red blood cells. The green color is formed when hydrogen peroxide produced by the bacteria <u>oxidizes hemoglobin (red color) to biliverdin (green color)</u> .	Some streptococci are non-hemolytic (γ-hemolysis).

B. Lancefield (a bacteriologist) **grouping (a Serological identification)** by this we classify only beta and mixed hemolytics (can either use α or β hemolysis) to groups from A to U according to a carbohydrate component in their cell wall.

The ones that hold the most medical importance are A, B & D (those are human pathogens). the major alpha hemolytic families are not grouped this way.

Only those which are coagulase negative and catalase negative are grouped



A method used to establish grouping is **latex agglutination test**. On the latex we have wells containing antibodies that can react to the serum or the bacteria we have.

The antibodies are bound on latex, once you pass the serum on the latex (wells) beads (clumps) will form in the well where antibodies react with their antigen (seen in B). If the antigen is not present to that specific antibody on the latex, no beads form (D).

V. Important table:

Species	Lancefield Group	Typical Hemolysis	Diagnostic Features ¹	
<i>S. pyogenes</i>	A	β	Bacitracin-sensitive	
<i>S. agalactiae</i>	B	β	Bacitracin-resistant; hippurate hydrolyzed	
<i>E. faecalis</i>	D	α or β or none	Growth in 6.5% NaCl ²	Resistant to penicillins
<i>S. bovis</i> ³	D	α or none	No growth in 6.5% NaCl	sensitive to penicillins
<i>S. pneumoniae</i>	NA ⁴	α	Bile-soluble; inhibited by optochin	
Viridans group ⁵	NA	α	Not bile-soluble; not inhibited by optochin	

Both utilize bile esculin

Notes on the table:

- ❖ This table gives us all the groups we care about together. The streptococci are grouped according to hemolysis first into alpha, beta and mixed hemolytics, then some are further grouped by Lancefield grouping into A, B and D groups.
- ❖ if we get a beta hemolytic bacteria from the gut it's usually Group D streptococci (gut type streptococci)
- ❖ Viridans group includes many bacteria, like *S.mitis*, *S.mutans*, *S.sanguinis*, *S.salivarius*, *S.gordonii*, *S.anginosus*, *S.milleri*.

- Remember how we said that one would get partial immunity when they meet Staphylococcus? The case with streptococcus is both better and worse. Better because we get full immunity against a strain of strep we met. However, Antibody to M protein provides ONLY type-specific immunity. And There are so many serotypes that we can't possibly be immune to all of them in our life. For example; there are 86 types of pyogenes. Which aids in the occurrence of immunogenic diseases (keep in mind them later).

Unlike staphylococci, where all the fame and fortune were of *S. aureus*, here the fame and fortune are divided to the three most vicious groups:

- 1) **Group A - β hemolytic streptococci (*S. Pyogenes*)** because it has **all the mechanisms of evil action, toxigenic, immunogenic, pyogenic**.
 - 2) **Enteric streptococci (*E. Faecalis*)** because they develop anti-microbial resistance. they inhabit the colon and they are exposed to so many antimicrobials, so they develop resistance eventually.
 - 3) ***S.pneumoniae* (pneumococci)**, because it causes most of the serious diseases which will be discussed separately .
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Details:

Beta hemolytic streptococci:

The first one **group A** known as *Streptococci pyogenes*, the other one is **group B** known as *streptococcus agalactiae*.

Differentiation between the two beta hemolytics: we use **Bacitracin test**, which is an antibiotic, the one sensitive to it is the *pyogenes*, the other one is resistant.

There are **two important antigens** that are most prominent in β -hemolytic streptococci:

- (1) **C carbohydrate** determines the group of β -hemolytic streptococci. (used for **grouping**). It is located in the cell wall, and its specificity is determined by an amino sugar.
- (2) **M protein** is the most important virulence factor and **determines the type** of group A β -hemolytic streptococci. (used for **typing**; further classification of β hemolytic). It protrudes from the outer surface of the cell and interferes with ingestion by phagocytes (i.e. it is **antiphagocytic**).

Streptococcus pyogenes (group A):

Diseases: group A streptococci (*S. pyogenes*) is the leading bacterial cause of **pharyngitis** (presents with exudate on the tonsils) and **cellulitis** (skin/ soft tissue infections), sepsis, endometritis and these are the **pyogenic diseases**, it also causes **impetigo** (characteristic: honey colored crusted lesions on skin) and **lymphangitis** can occur. And Necrotizing fasciitis and streptococcal toxic shock syndrome and scarlet fever which are **toxigenic diseases**. Unlike *Staph. aureus*, which has an association with

Kawasaki disease (but it's not well established). *Streptococcus pyogenes* has well established **immunogenic diseases**, rheumatic fever and acute glomerulonephritis.

- They possess two factors that allow them to adhere to pharyngeal epithelium: pili composed of **lipoteichoic acid** and the **M protein**.
- Many strains have a *hyaluronic acid capsule* that is antiphagocytic

M protein is the main antiphagocytic component of *S. pyogenes* (it prevents complement activation).

M protein is the immunogenic structure that causes the two immunogenic diseases. There are approximately 80 serotypes (bacterial antigens) based on the M protein, hence, you can get multiple infections with *S. pyogenes* from different serotypes.

Imagine that there are few of them that cause **pharyngitis**, antibodies produced against those are cross reactive to the heart, these antibodies end up attacking the heart and joints, causing **Rheumatic fever**, these serotypes are known as Rheumatogenic.

Other serotypes that cause **skin infections**, induce ABs production that are cross reactive to the kidney, these attack the kidney causing a condition called **glomerulonephritis**, these are known as nephritogenic.

Please note that the initial infection did not involve the organs affected later by immunogenic diseases, rather the inflammation induced by the antibodies caused the symptoms in these organs. i.e. the bacteria do not infect the heart or joints in the case of rheumatic fever, it's the antibodies produced against the bacteria in the pharynx that caused the inflammation in the heart and joints.

->It takes two weeks for the titer of antibodies against these bacteria to rise to a level high enough to cause these immunogenic diseases, so we can't detect bacteria in these cases but we **look for the antibodies**. (*post-streptococcal infections*).

->mostly, pediatric patients are affected by these conditions, because **they are more prone to streptococcal infections**.

Transmission: *S. pyogenes* is found on **the skin and in the oropharynx** in small number, that's why we can't differentiate between it and the normal flora by swab under microscope investigation (cannot be visually distinguished).

Transmission by Skin to skin interaction. **However, stained smears from skin lesions or wounds that reveal streptococci are diagnostic**

Pathogenesis:

Very important table

Organism	Type of Pathogenesis	Typical Disease	Main Site of Disease (D), Colonization (C), or Normal Flora (NF)
<i>S. pyogenes</i> (group A)	1. Pyogenic	Impetigo, cellulitis	Skin (D)
		Pharyngitis	Throat (D)
	b. Disseminated	Sepsis	Bloodstream (D)
		Scarlet fever	Skin (D)
	2. Toxigenic	Toxic shock	Many organs (D)
		Rheumatic fever	Heart, joints (D)
	3. Immune-mediated (poststreptococcal, nonsuppurative)		
		Acute glomerulonephritis	Kidney (D)
<i>S. agalactiae</i> (group B)	Pyogenic	Neonatal sepsis and meningitis	Vagina (C)
<i>E. faecalis</i> (group D)	Pyogenic	Urinary tract infection, endocarditis	Colon (NF)
<i>S. bovis</i> (group D)	Pyogenic	Endocarditis	Colon (NF)
<i>S. pneumoniae</i>	Pyogenic	Pneumonia, otitis media, meningitis	Oropharynx (C)
Viridans streptococci	Pyogenic	Endocarditis	Oropharynx (NF)

Notice how all of them have pyogenic features, meaning they cause disease in an area where they infect. However, *pyogenes* has more ways of inducing bad effects.

Note: the table has information about other bacteria, but the one that ate most of the pie here is *S. pyogenes*.

It causes disease by three mechanisms we mentioned before:

1) **pyogenic inflammation**. Induced **locally at the site of the organisms' presence** like in the case of cellulitis or pharyngitis Or **systematically** if the organism reaches the blood like in the case of sepsis.



Both are cases of pharyngitis but the one on the right has exudate and pus - the whitish area - and this is a characteristic of group A strep. Infection. Notice the one on the left is just highly inflamed and reddened (hyperaemia) without the pus, this is most probably a viral infection.

2) **exotoxin production**. Can cause spread systemic conditions, in places far from the organism. Like scarlet fever or toxic shock. Still, in **streptococcal toxic shock bacterial culture is mostly positive** because the organism is present in the blood.

3) **Immunogenic**, which is about the antibodies' cross reaction we discussed before. They might cause inflammation, BUT there are **no organisms found in**

those cases, because mostly they're post infection complications, that we detect by finding antibodies against the bacteria, not the primary bacterial cause.

Apart from its mechanisms *S. pyogenes* produces many enzymes that helps it invade, instead of nesting. These are:

(1) **Hyaluronidase**, this degrades hyaluronic acid, which is the ground substance of subcutaneous tissue (helps with invasion), this is why Hyaluronidase is known as **spreading factor**. (flesh eating bacteria)

(2) **Streptokinase** (fibrinolysin) activates plasminogen to form plasmin, which dissolves fibrin in **clots, thrombi, and emboli**. It can be used to lyse thrombi in the coronary arteries of heart attack patients. (now we use alteplase to dissolve clots)

(3) **DNase** (streptodornase) degrades DNA in exudates or necrotic tissue because there's so much DNA exiting causing DNA hindrance. (anti-DNase is used to detect previous infection with GAS (group A streptococcus)).

To induce the toxigenic effect we discussed, *S. pyogenes* produces **five toxins**:
(refer to slides for pictures)

(1) **Erythrogenic toxin** causes the rash seen in **scarlet fever** (erythema marginatum) which has a characteristic strawberry tongue. Its mechanism of action is similar to that of the TSST (toxic shock syndrome toxin) of *S. aureus* (acts as a superantigen). (skin and tongue are mostly affected).

(2) **Streptolysin O** is a hemolysin – breaks down RBCs for iron. It's Oxygen labile. It is antigenic -important in immunogenic diseases-. Antibody to streptolysin O (anti-ASO) develops after group A streptococcal infections. The titer of these antibodies can be important in the diagnosis of rheumatic fever. (remember we said we use ABs titer for diagnosis).

We know that antibodies titer peaks around two weeks after infection, so if a kid presented with symptoms of rheumatic fever and you do antibodies diagnosis and find the antibodies against streptolysin O, this is an indication of previous infection with GAS e.g. pharyngitis.

(3) **Streptolysin S** is a hemolysin. (oxygen stable).

(4) **Pyrogenic exotoxin A** the toxin responsible for most cases of streptococcal **toxic shock syndrome**. It has the same mode of action as TSST. (invading the blood).

(5) **Exotoxin B** is a protease that rapidly destroys tissue and is produced in large amounts

by some strains of *S. pyogenes*, the so-called “flesh-eating” streptococci that cause necrotizing fasciitis

More about immunogenic post streptococcal non-suppurative diseases:

Acute glomerulonephritis:

It occurs **2-3 weeks after** skin infection, because it requires **antibody production**.

- Occurs mostly in children

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), **puffy kid**
- “smoky” urine (due to red cells, or protein in the urine)
- Most patients **recover completely**, however they are still prone to develop this again if reinfection with streptococci happens, and it gives the same effects.
- 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 the cause of these symptoms isn’t the organism, but the aftermath of it being there, the antibody is already made.

->acute rheumatic fever presents with circles of **erythema with central clearing**.

Acute rheumatic fever:

Approximately 2 weeks after a group A streptococcal infection—usually pharyngitis. characterized by:

- 1- **Fever**,
- 2- **Migratory polyarthrit**is (his knees, or his elbows hurt suddenly)
- 3- **Carditis**, may develop and it’s the most serious, as damage to the myocardial and endocardial tissue, especially the mitral and aortic valves, can result in vegetation (abnormal growth that may contain debris) on the valves.
- 4- **Uncontrollable, spasmodic movements** of the limbs or face (**chorea**) may also occur.

These **complications can be prevented by prompt treatment** (within 8 days) of the organism infecting the patient – **before producing antibodies**.

Each time the patient gets infected, it gets more and more exaggerated, causes more damage to the heart.

to prevent further pain, if the patient is infected again, we **give prophylactics** for the rest of his life. (prophylactics are medications used for preventing a disease or infection, they're given once signs or symptoms of early infection occur).

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.

Treatment:

- Group A streptococcal infections can be treated with either **penicillin G** or **amoxicillin**
- In mild group A streptococcal infections, **oral penicillin V** can be used.
- In penicillin-allergic patients, **erythromycin** or one of its long-acting derivatives (e.g., **azithromycin**) can be used. However, erythromycin resistant strains of *S. pyogenes* have emerged.
- **Clindamycin** can also be used in penicillin-allergic patients.

*Remember: immunogenic diseases (AGN, RF) can't be treated with antibiotics because the antibodies are already produced, the organism is most probably gone.

Prevention : Rheumatic fever can be prevented by prompt treatment of group A streptococcal pharyngitis with penicillin. There is no evidence that patients who have had AGN require similar penicillin prophylaxis.

1) In susceptible people (previous infection) Prevention of streptococcal infections (usually with benzathine penicillin once each month for several years).

2) In patients with damaged heart valves who undergo invasive dental procedures, endocarditis caused by viridans streptococci can be prevented by using amoxicillin PREoperatively. Again PRE OPERATIVELY

Note: To avoid unnecessary use of antibiotics, it is recommended to give amoxicillin prophylaxis **only to those patients who have the highest risk of severe consequences from endocarditis (e.g., those with prosthetic heart valves or with previous infective endocarditis) and who are undergoing high-risk dental procedures, such as manipulation of gingival tissue.**

Streptococcus agalactiae: (group B)

Diseases:

Streptococcus agalactiae (group B streptococcus) is the leading cause of **neonatal sepsis** and **meningitis**; this happens in women who are colonized with GBS -because the first bacteria that a baby gets exposed to are the bacteria in the birth canal- and have had PROM (prolonged rupture of the membrane-the sack of the baby), the delay in birth and the exposure of the fetus predisposes them to the infection. **It causes neonatal pneumonia.**

->GBS is still capable of causing infections in adults (**such as pneumonia, endocarditis, arthritis, cellulitis, and osteomyelitis**)

Diabetes is the main predisposing factor for adult group B streptococcal infections (how come?)- there are theories, the most accepted is that the rise of sugar in blood reduces the function of the immune system, also causes reduction in blood flow (recruitment of WBCs) and nerve damage (also prevents proper immune function)

Testing:

It's bacitracin resistant, so we further confirm it's B by **Hippurate test** (it hydrolyzes it into two molecules (**glycine and benzoic acid**) that can be **color detected**. (it turns blue).

Transmission: It **abnormally colonizes the female genital tract**. (occurs in the vagina and colon) Postpartum endometritis also occurs (infection of the lining of uterus after birth) why after birth? This is a skin pathogen, opening of the usually closed environment of the uterus during birth and manipulation by hospital staff (who are colonized with these bugs).

Pathogenesis:

Group B streptococci have a **polysaccharide capsule** that is **antiphagocytic**, and anticapsular antibody protective. Pathogenesis by group B streptococci (*S. agalactiae*) is based on the ability of the organism to induce an inflammatory response **unlike S. pyogenes**, no cytotoxic enzymes or exotoxins have been described, and there is no evidence for any immunologically induced disease (no toxigenicity **and no immunogenic induced diseases**).

Treatment:

The drug of choice for group B streptococcal infections is either **penicillin G or ampicillin**, Some strains may require penicillin G with aminoglycoside to eradicate the organism.

Prevention:

As for GBS, the incidence of neonatal sepsis can be reduced by a combination of two approaches:

- (1) Screening of ALL pregnant women at 35 to 37 weeks' gestation by doing vaginal and rectal cultures (RST). If cultures are positive, then **penicillin G** (or **ampicillin**) should be administered **intravenously at the time of delivery**.
- (2) If the patient has not had cultures done, then **penicillin G** (or **ampicillin**) should be administered intravenously at the time of delivery to women who experience prolonged (longer than 18 hours) rupture of membranes¹, whose labor begins before 37 weeks' gestation², or who have a fever at the time of labor³. If the patient is allergic to penicillin, either **cefazolin** or **vancomycin** can be used.
- **Oral ampicillin** given to women who are vaginal carriers of group B streptococci does not eradicate the organism.

Mixed hemolytic streptococci (group D):

We are studying two:

a. enterococci -> classical enteric Gram-positive cocci, e.g. *Enterococcus faecalis* & *Enterococcus faecium*.

b. non-enterococci -> e.g., *S. bovis*.

We differentiate between the two by 2 mechanisms:

1st NaCl 6.5% hypertonic saline, *enterococci* can survive it, while *S. bovis* can't.

2nd penicillin, *enterococcus* is resistant while *S. bovis* is sensitive.

They both can grow on bile esculin and turn it black.

🌸 Their hemolysis is variable, some are beta, **most** are alpha and others are non-hemolytic.

Enterococcus Faecalis:

Enterococcus, is a hardy organism, it's the **only gram positive we find in the colon**, because it's the only Gram positive hardy enough to survive the harsh environment of the stomach and the bile.

Enterococcus faecalis is an important cause of **Hospital-Acquired Urinary Tract Infections** (**nosocomial infections**) and **endocarditis**, normally it causes no diseases because it's part of the normal flora. It's an opportunistic bacterium, that gets naughty if it reaches the blood. It causes **urinary, biliary, and cardiovascular infections**. Enterococci also cause **endocarditis**, particularly in patients who have undergone gastrointestinal or urinary tract surgery or instrumentation, this is why they are not common, we do a lot more dental procedures and introduce viridans group that we do GI or UT surgery. They also cause **intra-abdominal and pelvic infections**, typically in combination with anaerobes (the same as other streptococci, if given the access and chance they will cause abscess)

- **HAUTIs** are due to the use of catheters combined with bed pans- contamination
- Thus → Indwelling urinary catheters and urinary tract instrumentation are important predisposing factors.

->About 10% of endocarditis cases are caused by enterococci, but any organism causing bacteremia may settle on already deformed valves.

Transmission:

- enterococci and anaerobic streptococci are located in the colon

Treatment:

since *Enterococci* are tough, we use a synergistic combination of **penicillin and an aminoglycoside** (e.g., **gentamicin**) to kill it.

Vancomycin can also be used, but **vancomycin-resistant enterococci (VRE) have emerged and become an important and much feared cause of life-threatening nosocomial infections.**

- **Enterococcal endocarditis** can be eradicated only by a **penicillin or vancomycin combined with an aminoglycoside**.
- Enterococci resistant to multiple drugs (e.g., penicillins, aminoglycosides, and vancomycin) have emerged.
- Resistance to vancomycin in enterococci is mediated by a **cassette of genes** that encode the enzymes that substitute **D-lactate for D-alanine** in the peptidoglycan. The same set of genes encodes vancomycin resistance in *S. aureus*

- At present, two drugs are being used to treat VRE infections: linezolid (Zyvox) and daptomycin (Cubicin).

Streptococcus bovis:

(Nonenterococci group D) → the classic human pathogen of this group is S. bovis, can cause similar infections to the Enterococci, but they are not strong as Enterococci.

-> S. bovis causes **endocarditis**, especially in patients with carcinoma of the colon. This association is so strong that when we find patients with S. bovis, bacteremia, or endocarditis, these patients should be investigated for the presence of **colonic carcinoma**. Treatment: penicillin G.

Alpha hemolytic streptococci:

These are two, *Streptococcus pneumonia* and the *viridans group*, we differentiate between the two by, 1) **bile solubility**, where pneumococci are bile soluble and viridans aren't 2) **optochin sensitivity**, where pneumococci are sensitive and viridans aren't.

Pathogenesis by S. pneumoniae and the viridans streptococci is uncertain, as no exotoxins or tissue-destructive enzymes have been demonstrated.

Streptococcus pneumonia: lancet-shaped cocci (are oval with somewhat pointed ends rather than being round (نظارات أم كلثوم) : arranged in pairs (diplococci) or short chains

Diseases:

1) **pneumonia** (symptoms: sudden chill, fever, cough, shortness of breath, and pleuritic pain- chest pain that increases with chest movement-breathing).

- Sputum is a red or brown "rusty" color, capsulated bacteria causes sputum coloration. Bacteremia occurs in 15% to 25% of cases.

Spontaneous recovery may begin in 5 to 10 days and is accompanied by development of anticapsular antibodies.

2) **bacteremia** 3) **meningitis**, and 4) **URTI** (upper respiratory tract infections)- such as **otitis media, mastoiditis, and sinusitis** by migration through the blood. 5) **sepsis** in splenectomized individuals (they can't get rid of capsulated bacteria). 6) **conjunctivitis**, especially in children.

Virulence factors:

1) The main virulence factor of S. pneumoniae is its **antiphagocytic polysaccharide capsule** which has 85 antigenically distinct types. (thus splenectomy patients cant clear this organism). With type-specific antiserum, capsules swell (*quellung reaction*), and this can be used to identify the type

This capsule **shields the bacteria as it moves with the blood** to:

the brain causing meningitis, lung causing pneumonia, and the URIs we mentioned.

2) It has an enzyme that helps it break down IgA (**IgA protease**)², that along with capsule and teichoic acid help in its attachment to mucosal surfaces, causing infection.

3) **Teichoic acid**³ in the cell wall is the C-substance (also known as **C-polysaccharide**), to which **CRP (C-reactive protein) reacts**, and this is why we **use these bacteria to measure CRP in diagnosing acute inflammation and heart disease (c-substance holds medical importance) **an elevated CRP appears to be a better predictor of heart attack risk than an elevated cholesterol level.*

4) **Pneumolysin**⁴, the hemolysin that causes α -hemolysis, may contribute to pathogenesis.

5) **Lipoteichoic acid**⁵: complement activator, it induces inflammatory cytokine production which contributes to the inflammatory response and to the septic shock syndrome in some cases

Factors that lower resistance and predispose persons to pneumococcal infection:

• INCLUDE factors that reduce mucus clearing or factors that decrease immune reaction), accumulation of mucus is a happy event, if it happens pneumococci happily cause pneumonia — **THIS IS THE MOST IMPORTANT PIECE OF INFORMATION**

(1) anything that can **depress the cough reflex** : alcohol or drug intoxication or other cerebral impairment (they don't cough, they don't clear mucous, it accumulates and pneumonia happily happens)

(2) **abnormality of the respiratory tract** (e.g., viral infections), pooling of mucus, bronchial obstruction, and respiratory tract injury caused by irritants (which disturb the integrity and movement of the mucociliary blanket) all **prevent clearing of mucus** and predispose to pneumonia caused by pneumococcus.

(3) **abnormal circulatory dynamics** (e.g., pulmonary congestion and heart failure) will congest the blood in the lung, increase pulmonary secretions → pneumococcus comes.

(4) **splenectomy** (capsule, reduces immunity) and certain chronic diseases such as sickle cell anemia and nephrosis, patients with sickle cell anemia auto-

infarct their spleen, become functionally asplenic, and are predisposed to pneumococcal sepsis

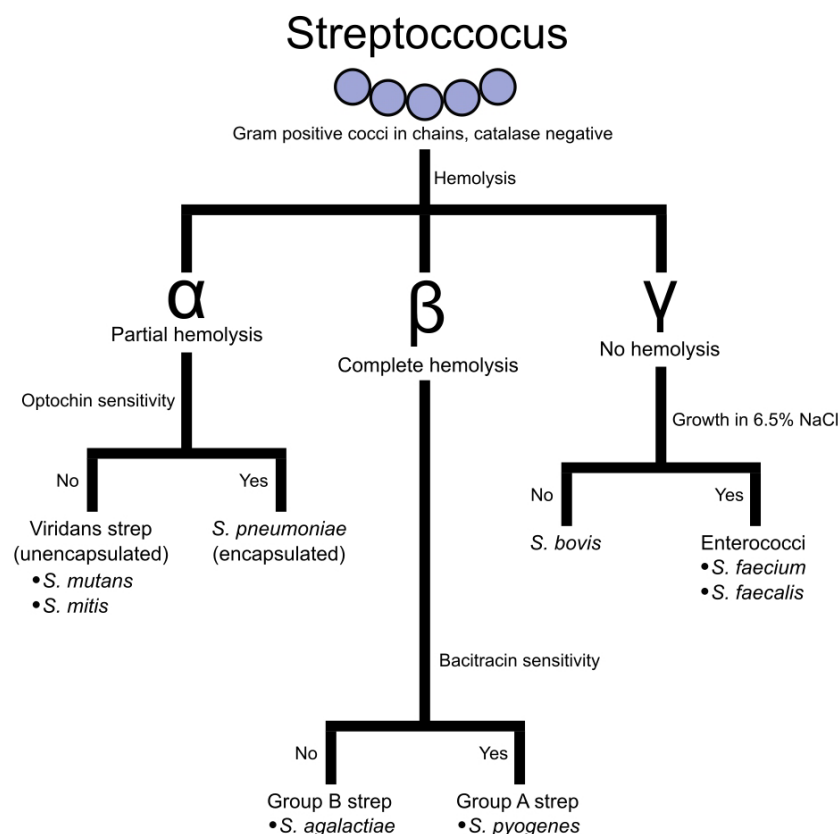
Remember: no spleen, no clearing of capsulated bacteria!

(5) Trauma to the head that causes leakage of spinal fluid through the nose predisposes to **pneumococcal meningitis**

Transmission:

- Humans are the natural hosts for pneumococci; there is no animal reservoir.
- Because a proportion (5%–50%) of the healthy population harbors virulent organisms in the oropharynx, pneumococcal infections are not considered to be communicable (**it happens from your own flora**)

فراغ ما عرفت شو أعمل فيه



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Moises Dominguez



Lab diagnosis:

- Culture of **cerebrospinal fluid** is usually positive in meningitis (by detecting its capsular polysaccharide in spinal fluid using the latex agglutination test).
- A **rapid test** detects urinary antigen (C-carbohydrate not the capsule) for the diagnosis of **pneumococcal pneumonia and bacteremia**.
- Because of the increasing numbers of strains resistant to penicillin, antibiotic sensitivity tests must be done on organisms isolated from serious infections

treatment:

- standard antibiotic: **penicillin (severe infections) and erythromycin** (if sensitive to penicillin), **penicillin V (mild infections)**, although significant resistance to penicillins has emerged
- A fluoroquinolone with good antipneumococcal activity, such as **levofloxacin**, can also be used.
- An increasing percentage of isolates show high-level resistance, which is attributed to multiple changes in penicillin binding proteins (instead of producing β -lactamase)
- **Vancomycin is the drug of choice for the penicillin-resistant pneumococci**, especially for severely ill patients.
- **Ceftriaxone** or **levofloxacin** can be used for less severely ill patients (we use it if we suspect pneumococcal infection, especially in kids (preventive measure)

Prevention:

- **Pneumococci** are the only bacteria of the ones we mentioned that have a vaccine.
- Specific antibody to the capsule forms and **opsonizes the organism, facilitates phagocytosis**, and **promotes resistance**. We use that to give a bacterial polysaccharide vaccine, that gives immunity against *S. pneumoniae*.
- The mortality rate of pneumococcal infections is **high in immunocompromised** (especially splenectomized) patients and **children under the age of 5 years**. Such persons should be immunized with the **13-valent pneumococcal conjugate vaccine (Pneumovax 13)**.
- The immunogen in this vaccine is the pneumococcal polysaccharide of the 13 most

prevalent serotypes **conjugated** (coupled) to a carrier protein (diphtheria toxoid). The **unconjugated 23-valent pneumococcal vaccine (Pneumovax 23)** should be given to healthy individuals age 50 years or older.

- These vaccines are **safe and effective and provide long-lasting** (at least 5 years) protection.

A second “booster” dose is recommended for • **(1) people older than 65 years** who received the vaccine more than 5 years ago and who were younger than 65 years when they received the vaccine, and • **(2) people** between the ages of 2 and 64 years **who are asplenic, infected with (HIV), receiving cancer chemotherapy, or receiving immunosuppressive drugs to prevent transplant rejection**.

Viridans group:

- Several species that are usually **commensal** (non pathogens in immune competent patients) but are **opportunistic** in immune compromised patients.

- Viridans streptococci (e.g., *S. mutans*, *S. sanguinis*, *S. salivarius*, and *S. mitis*) are **part of the normal flora of the human pharynx** and intermittently **reach the bloodstream to cause infective endocarditis** (major cause).

- *S. mutans* (one of the group) synthesizes polysaccharides (dextrans) that are found in dental plaque and lead to dental caries

- Biofilm formation and fermentation of sugars and production of acids is the main mechanism that causes destruction of enamel, means it's infecting deeper.

Poor dental health -> potential heart problem.

Transmission:

Viridans streptococci and *S. pneumoniae* are **found chiefly in the oropharynx**.

- They TYPICALLY enter the bloodstream (bacteremia- bacteria in blood) from the oropharynx after dental surgery, eventually reaching the heart.

Pathogenesis of endocarditis:

Once these bacteria get into the blood, they **hit and stick to the margins of the valves** (in the case of viridans by producing glycocalyx; a sticky sugar coat to form biofilm), in **large numbers** they precipitate on the valves and start eating the valvular tissue around them, thus causes **failing of the valves** -> heart symptoms presentation.

- Signs of endocarditis: are **fever** (teichoic acid induces inflammatory reaction), **heart murmur** (vegetation and destruction of heart valves), **anemia**, and **embolic events** (emboli in the blood. *Emboli are like a ball of bacteria that forms on the margins then dissociates and travels with the blood*) that cause symptoms such as splinter hemorrhages, subconjunctival petechial hemorrhages, and Janeway lesions.
- The vegetation of the heart valves is 100% fatal unless effectively treated with antimicrobial agent (**prolonged penicillin treatment**).

->Viridans streptococci, especially *S. anginosus*, *S. milleri*, and *S. intermedius*, are also a cause of **brain abscesses**. as mentioned before these are usually multi-pathogenic and are seen often in combination with mouth anaerobes (a mixed aerobic–anaerobic infection).

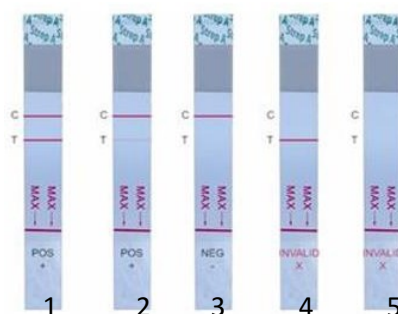
dental surgery provides a portal for the viridans streptococci and the anaerobes in the oropharynx to enter the bloodstream (bacteremia) and spread to the brain.

In summary: these are the general modes of pathogenesis: viridans = biofilm, pneumococcus= capsule, GAS = exotoxins and invasive enzymes, GBS = inflammatory

The rapid step test:

We use it a lot for group A fast identification, to prescribe the appropriate antibiotic fast.

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



->The specificity of these tests is high, but the sensitivity is low (i.e., false-negative results can occur)

->A rapid test is also **available for the detection of group B streptococci** in vaginal & rectal samples. It detects the DNA of the organism, and results can be obtained in approximately 1 hour.

Look at the first three, the first (control) line is present, and it should always be there. It means that it works, if not *like sample 4 and 5*, it's not working.

Even if the second (test) line is faint, it's still considered positive!

Good luck