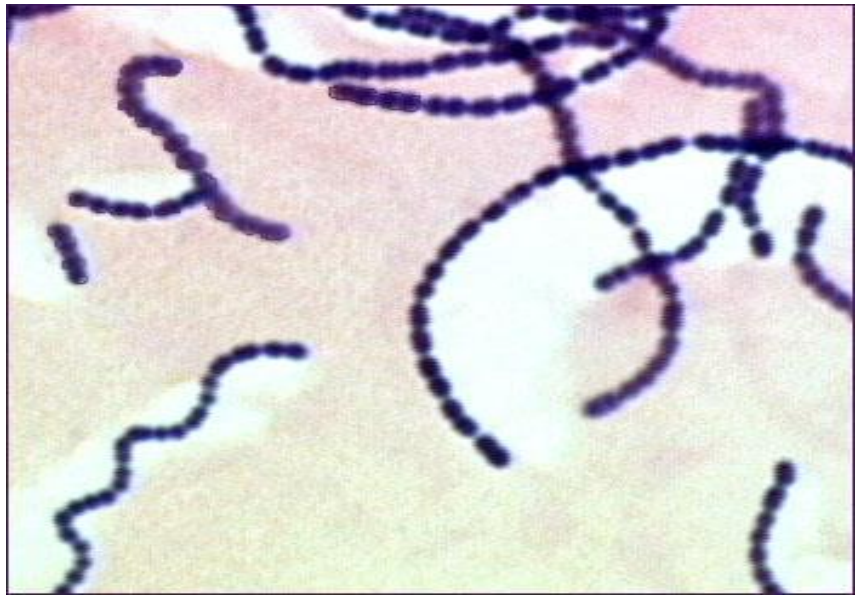
Streptococcus

Learning objectives

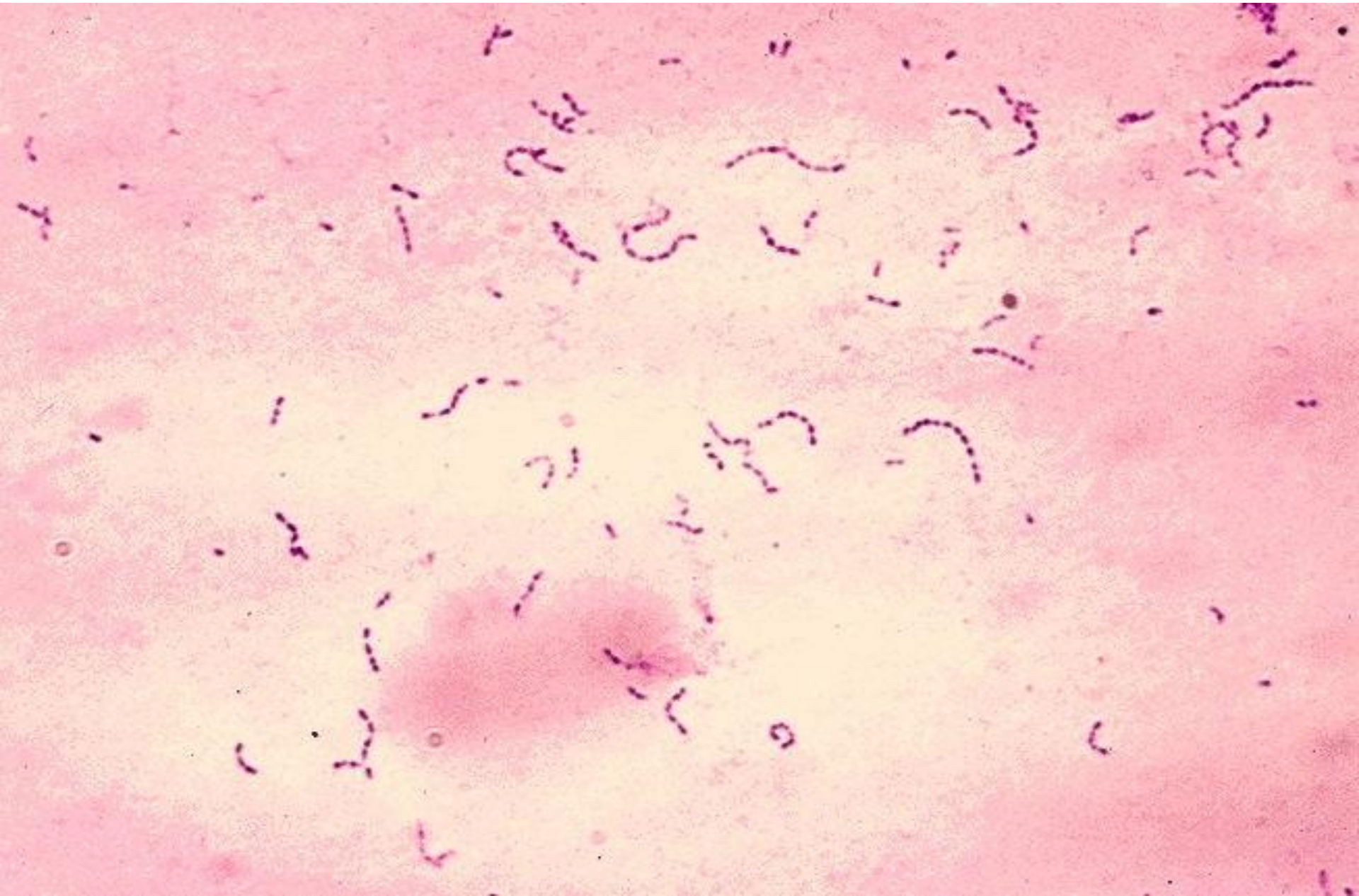
- To know the imp features and classification of Streptococci
- To recognize the virulence factors, pathogenesis, clinical features of diseases caused by Streptococci
- To interpret the lab diagnosis of Streptococci

Streptococci

- Characteristics of Streptococci
  - Gram positive cocci
  - Less then1µm in diameter
  - Chains or pairs
  - Usually capsulated
  - Non motile
  - Non spore forming
  - Facultative anaerobes
  - Fastidious
  - Catalase negative (Staphylococci are catalase positive)



Streptococcus in chains (Gram stain)



Classification of Streptococci

- **Streptococci can be classified according to:**

1) Oxygen requirements

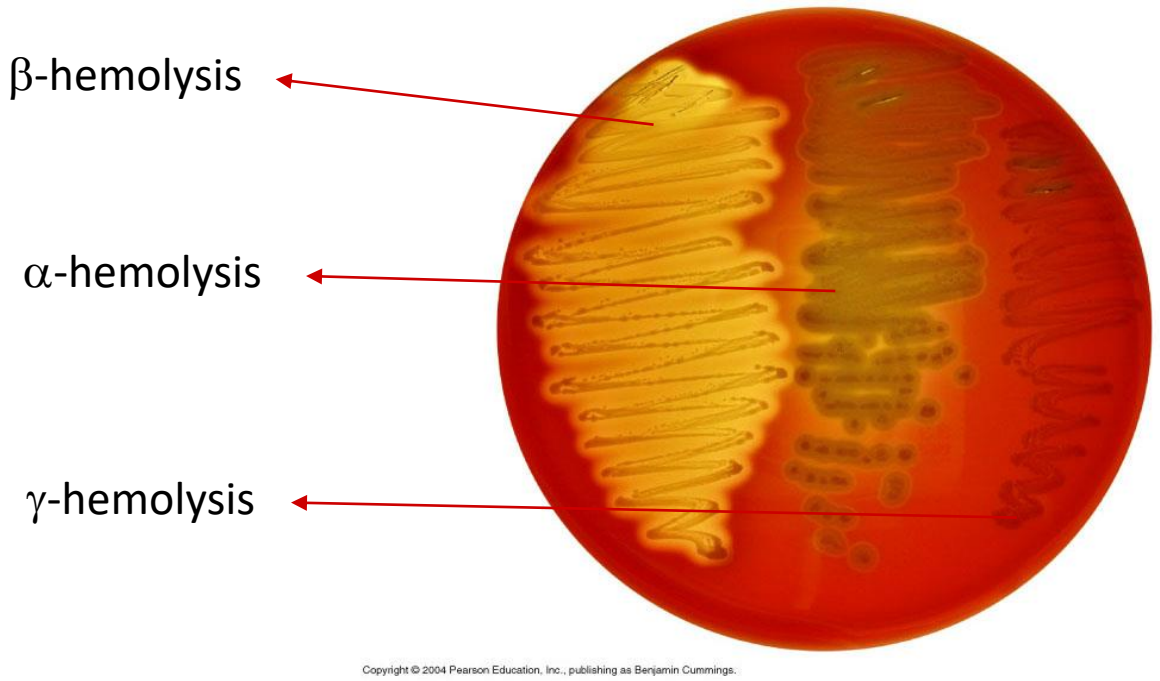
- Aerobic or facultative anaerobic (*Streptococcus*)
- Anaerobic (*Pepto streptococcus*)

2) Hemolysis on Blood Agar (BA)

Classification of Streptococci Based on Hemolysis on Blood Agar

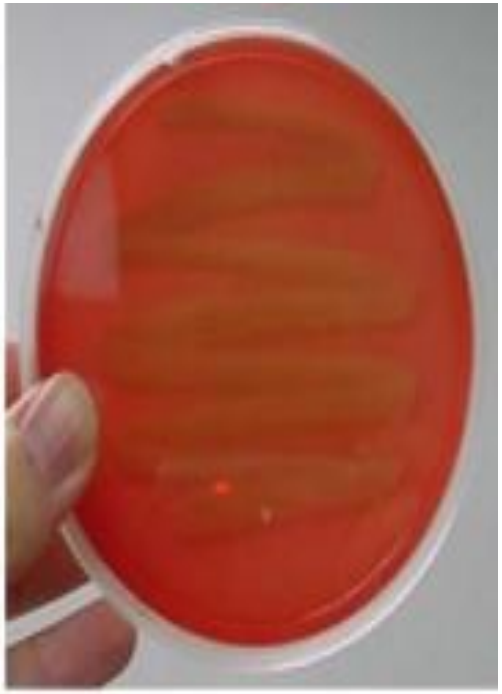
- Hemolysis on BA
  - α-hemolysis
    - Partial hemolysis
    - Green discoloration around the colonies
    - e.g. non-groupable streptococci (*S. pneumoniae* & *S. viridans*)
  - β-hemolysis
    - Complete hemolysis
    - Clear zone of hemolysis around the colonies
    - e.g. Group A & B (*S. pyogenes* & *S. agalactiae*)
  - γ-hemolysis
    - No lysis
    - e.g. Group D (*Enterococcus spp*)

Hemolysis on Blood agar



Beta Hemolysis

Alpha Hemolysis



Gamma Hemolysis

Classification

Based on O_2

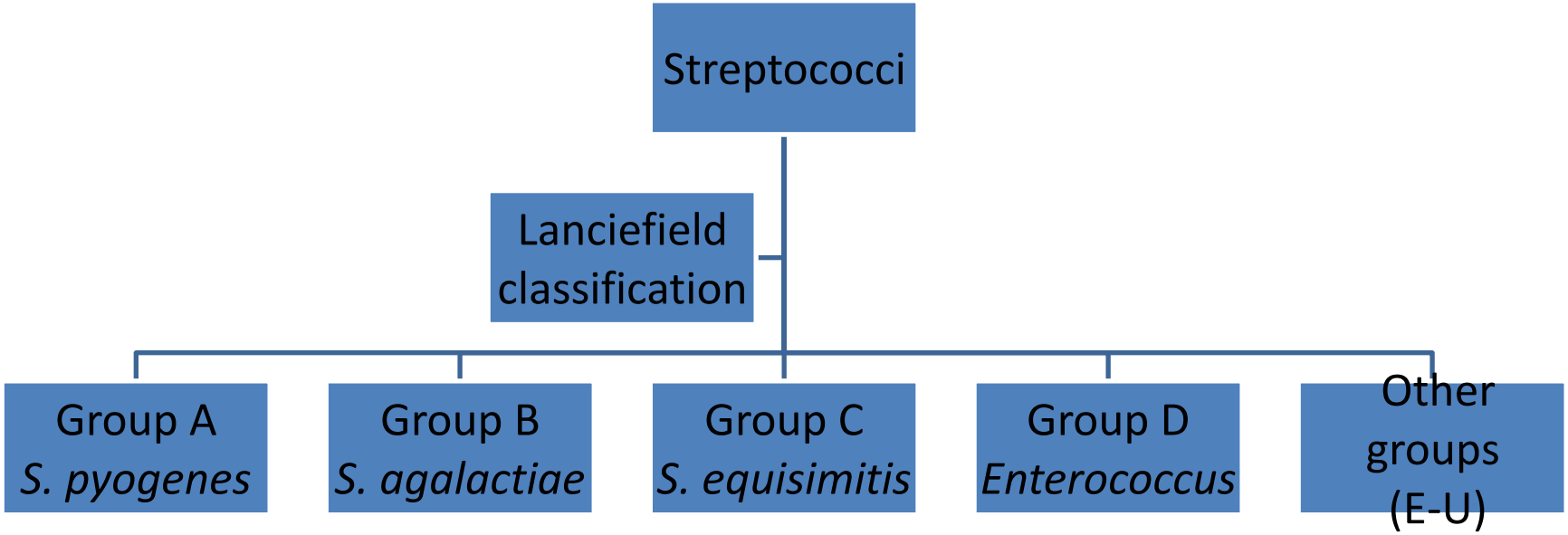
Aerobes ← → **Anaerobes**

Growth on BA — **Peptostreptococci**

α hemolysis	**β hemolysis**	**γ hemolysis**
Incomplete hemolysis (green color)	**Complete hemolysis**	**α / β / no hemolysis**
Strep. viridans ***Strep. pneumoniae***	**Lancefield grouping** specific C carbohydrate Ag on cell wall → **Group A – U (21 groups)**	***Enterococcus fecalis***

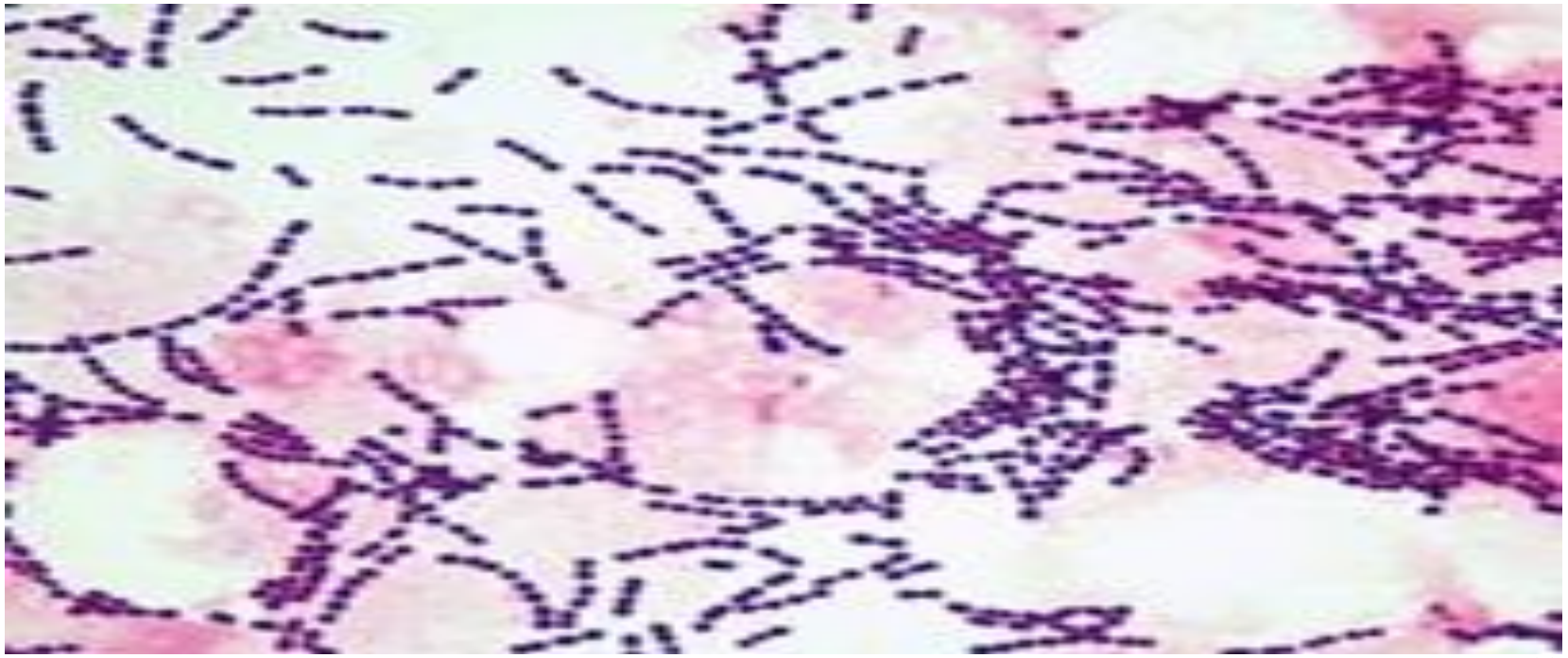
Griffith typing of Group A on MTR proteins into > 100 types

Serology: Lanciefield Classification



- Classification based on C- carbohydrate antigen of cell wall
- Streptococci classified into many groups from A-K & H-V
- One or more species per group

Beta hemolytic Group A Streptococcus
(Streptococcus pyogenes)



Group A Streptococci

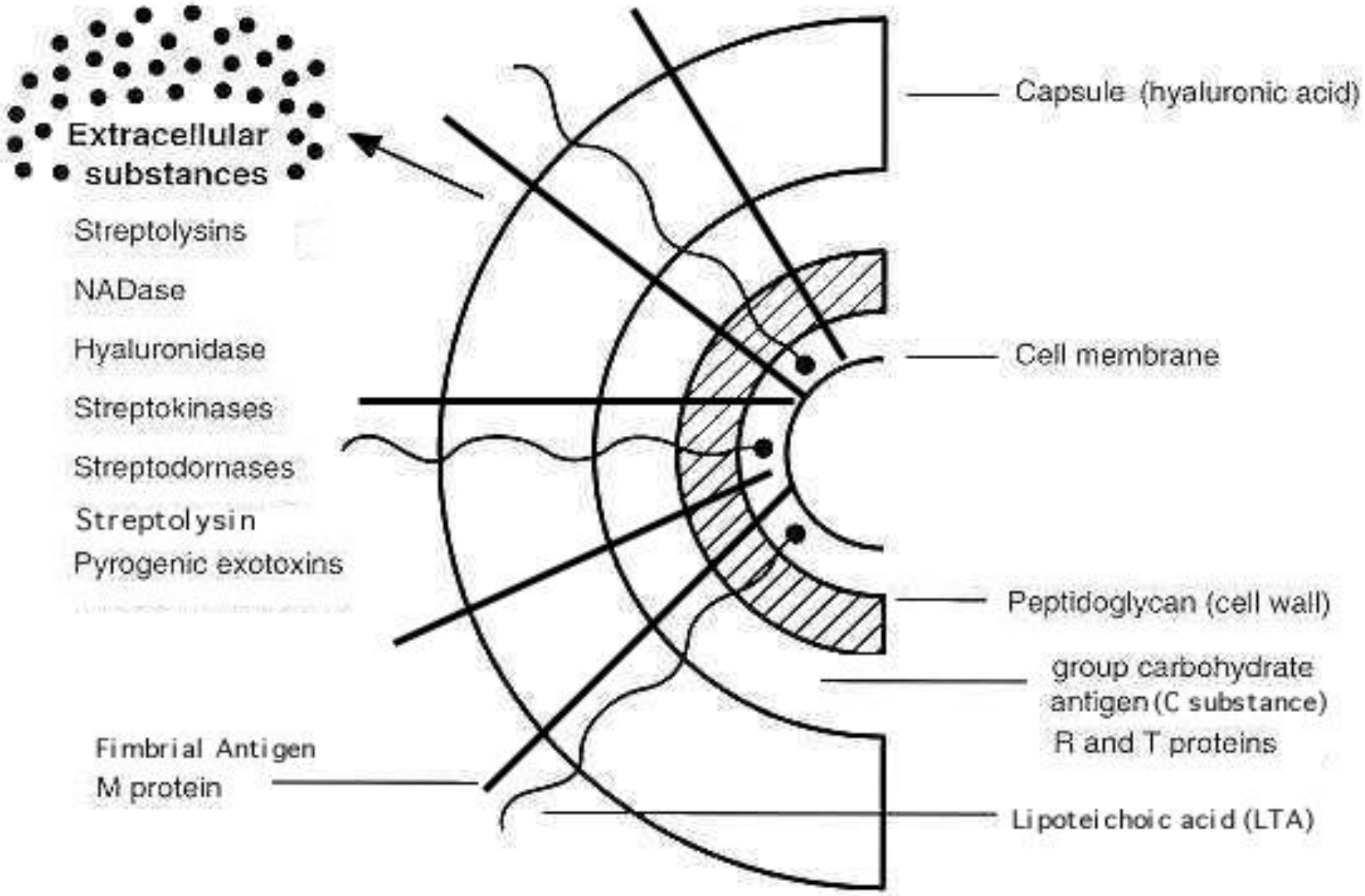
- Include only *S. pyogenes*
- Group A streptococcal infections affect all ages peak incidence at 5-15 years of age.
- 90% of cases of pharyngitis

Pathogenesis and Virulence Factors

1) Cellular or Structural Virulence Factors

2) Extracellellular Virulence Factors

- **Enzymes**
- **Toxins**


Extracellular substances
Streptolysins
NADase
Hyaluronidase
Streptokinases
Streptodornases
Streptolysin
Pyrogenic exotoxins
Capsule (hyaluronic acid)
Cell membrane
Peptidoglycan (cell wall)
group carbohydrate antigen (C substance)
R and T proteins
Fimbrial Antigen
M protein
Lipoteichoic acid (LTA)

Structural components

- **Capsule**: composed of hyaluronic acid identical to that found in connective tissue (non-immunogenic); antiphagocytic .
- Group-specific cell wall antigen C carbohydrate determines the group of β-hemolytic streptococci. Basis of Lancefield gp.
- **M protein** is the most important virulence factor and determines the type of group A β-hemolytic streptococci. Basis of Griffths classification.
- **F protein** - fibronectin-binding protein (the major adhesin for bacterial attachment to the epithelial cells of the pharynx and the skin).

M PROTEIN

- It appears as hair like projection of the cell wall, it help the bacteria to resist phagocytosis.

- Antibody to M protein provides type-specific immunity.

M PROTEIN

- There are approximately 80 serotypes based on the M protein, which explains why multiple infections with *Strep. pyogenes* can occur.
- Strains of *Strep. pyogenes* that produce certain M protein types are rheumatogenic(i.e., cause primarily rheumatic fever),
- Where as strains of *Strep. pyogenes* that produce other M protein types are nephritogenic (i.e., cause primarily acute glomerulonephritis).

Pathogenesis

- 1) Adherence to the epithelial cells;
- 2) Invasion into the epithelial cells;

  Mediated by M protein and protein F.

  Important for persistent infections and invasion into deep tissues
- 3) Avoiding opsonization and phagocytosis;
- M protein, M-like proteins, and C5a peptidase
- 4) Producing enzymes and toxins

Pathogenesis

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

1) Pyogenic inflammation, which is induced locally at the site of the organisms in tissue.

2) Exotoxin production, which can cause widespread systemic symptoms in areas 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

Extracellellular Virulence Factors

Enzymes

- Group A streptococci produce three important inflammation-related enzymes:
- **1) Hyaluronidase**(spreading factor):
- Destroys connective tissue and aids in spreading infecting bacteria.

- **2) Streptokinase(fibrinolysin)** Can lyse blood clots and may be responsible for the rapid spread of the organism. Used (IV injection) for treatment of pulmonary emboli, coronary artery thrombosis and venous thrombosis.

Extracellellular Virulence Factors

Enzymes

- **3) DNase(streptodornase**) degrades DNA in exudates or necrotics. A mixture of this and streptokinase is used in enzymatic debridement and liquifies exudates and facilitates removal of pus and necrotic tissue.

- **4) C5a peptidase**
- Prevents streptococci from C5a-mediated recruitment and activation of phagocytes, and is important for survival of *S. pyogenes* in tissue and blood .

Extracellellular Virulence Factors

Toxins

- **1) Erythrogenic toxins:**
- Erythrogenic toxin causes the rash of scarlet fever.
- Its mechanism of action is similar to that of the toxic shock syndrome toxin (TSST) of *S. aureus.*
- It is produced only by certain strains of *Strep. pyogenes* lysogenized by a bacteriophage carrying the gene for the toxin.
- The injection of a skin test dose of erythrogenic toxin (Dick test) gives a positive result in persons lacking antitoxin (i.e., susceptible persons).

Extracellellular Virulence Factors

Toxins

- **2) Hemolysins**
- **Streptolysin O:** O_2-labile; causes hemolysis deep in blood agar plates. It is antigenic, and antibody to it (ASO) develops after group A streptococcal infections.
- The titer of ASO antibody can be important in the diagnosis of rheumatic fever.
- However, skin infection does not induce ASO.
- **Streptolysin S**: O_2-stable. Causes beta-hemolysis on the surface of blood agar plates. Cell-bound, not antigenic. Produced in the presence of serum. Kills phagocytes by releasing the lysosomal contents after engulfment.

Extracellellular Virulence Factors

Toxins

- **4) Pyrogenic exotoxin A** is the toxin responsible for most cases of streptococcal toxic shock syndrome.

- It has the same mode of action as does staphylococcal TSST (i.e., it is a Super antigen that causes the release of large amounts of cytokines from helper T cells and macrophages).

Extracellellular Virulence Factors

Toxins

- **5) Exotoxin B** is a protease that rapidly destroys tissue and is produced in large amounts by the strains of *Strep. pyogenes*, the so-called “flesh-eating” streptococci that cause necrotizing fasciitis.

Disease caused by streptococcus pyogenes:

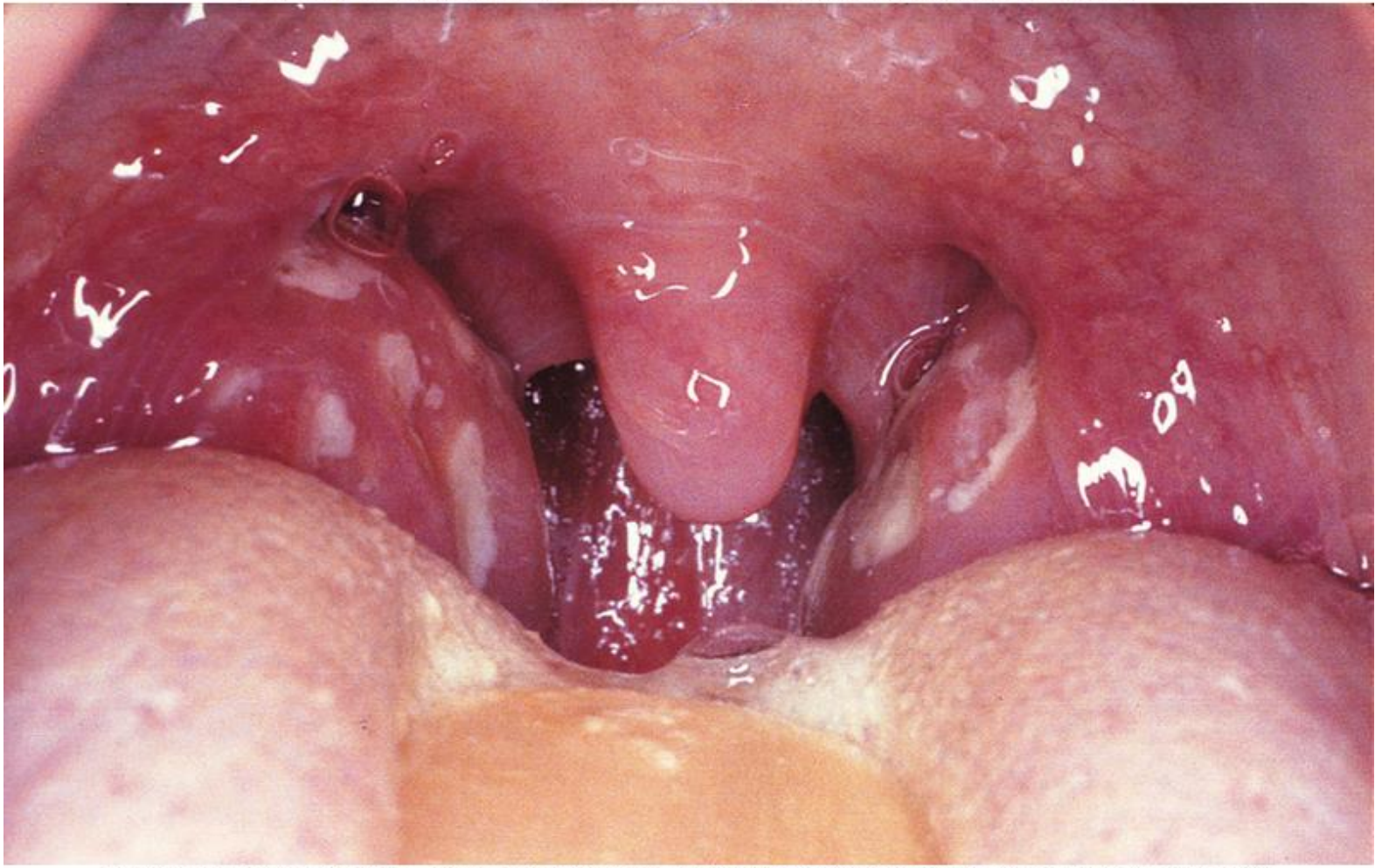
- Can be divided into two groups:
- 1) Suppurative infection (pus forming).
- Non invasive
- Invasive
- 2) Non suppurative sequelae.

Group A Streptococcal Diseases (cont.)

- **Streptococcal Pharyngitis:**
  Infection of the throat; it is characterized by a reddened, highly inflamed, swollen area with a fever of 103˚F.
- In itself, streptococcal sore throat is not life threatening.

  Dangerous aspect of the disease is the possibility of it spreading and causing other sequel clinical forms. That is why sore throat is closely monitored

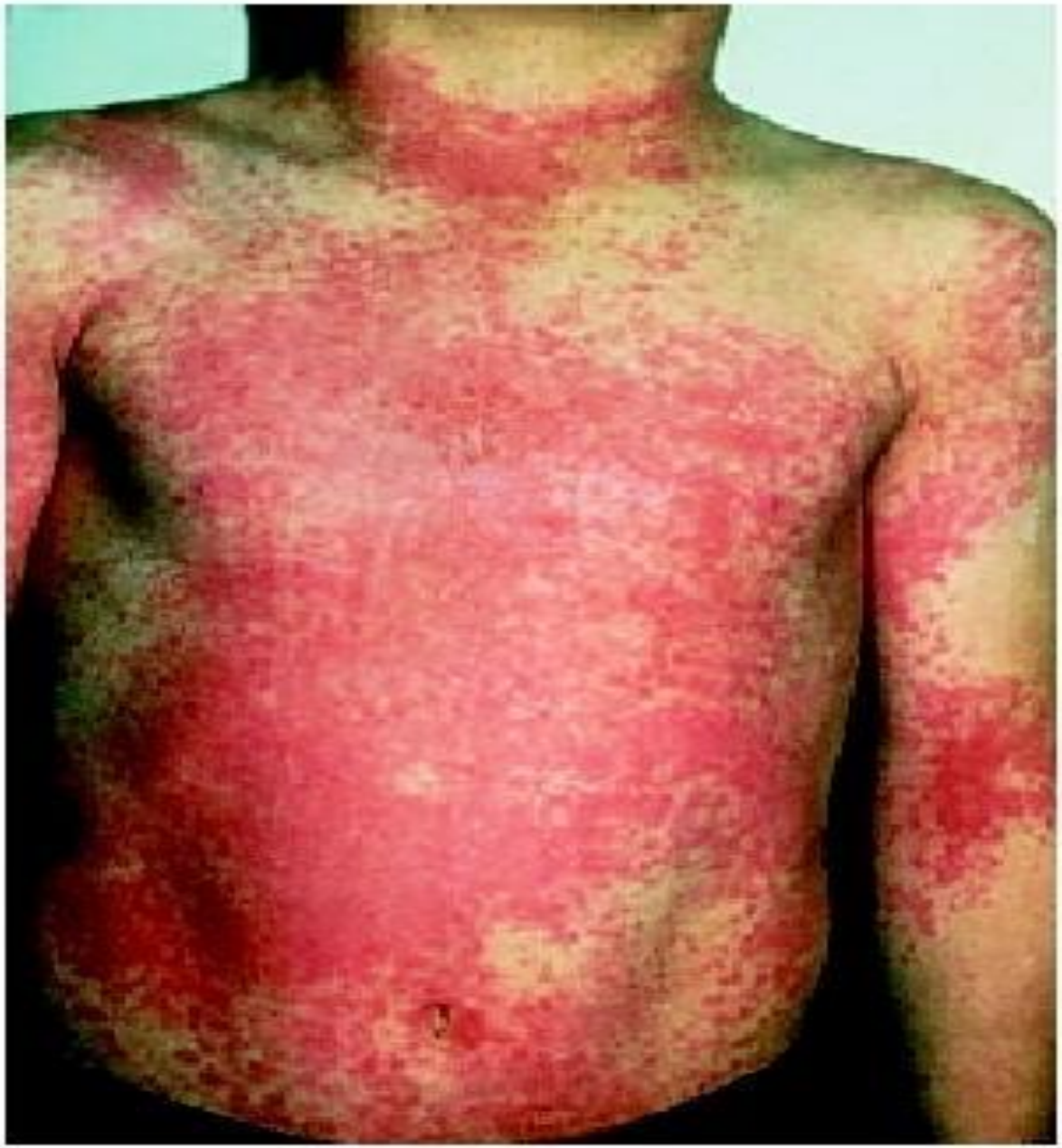
Pharyngitis and tonsillitis



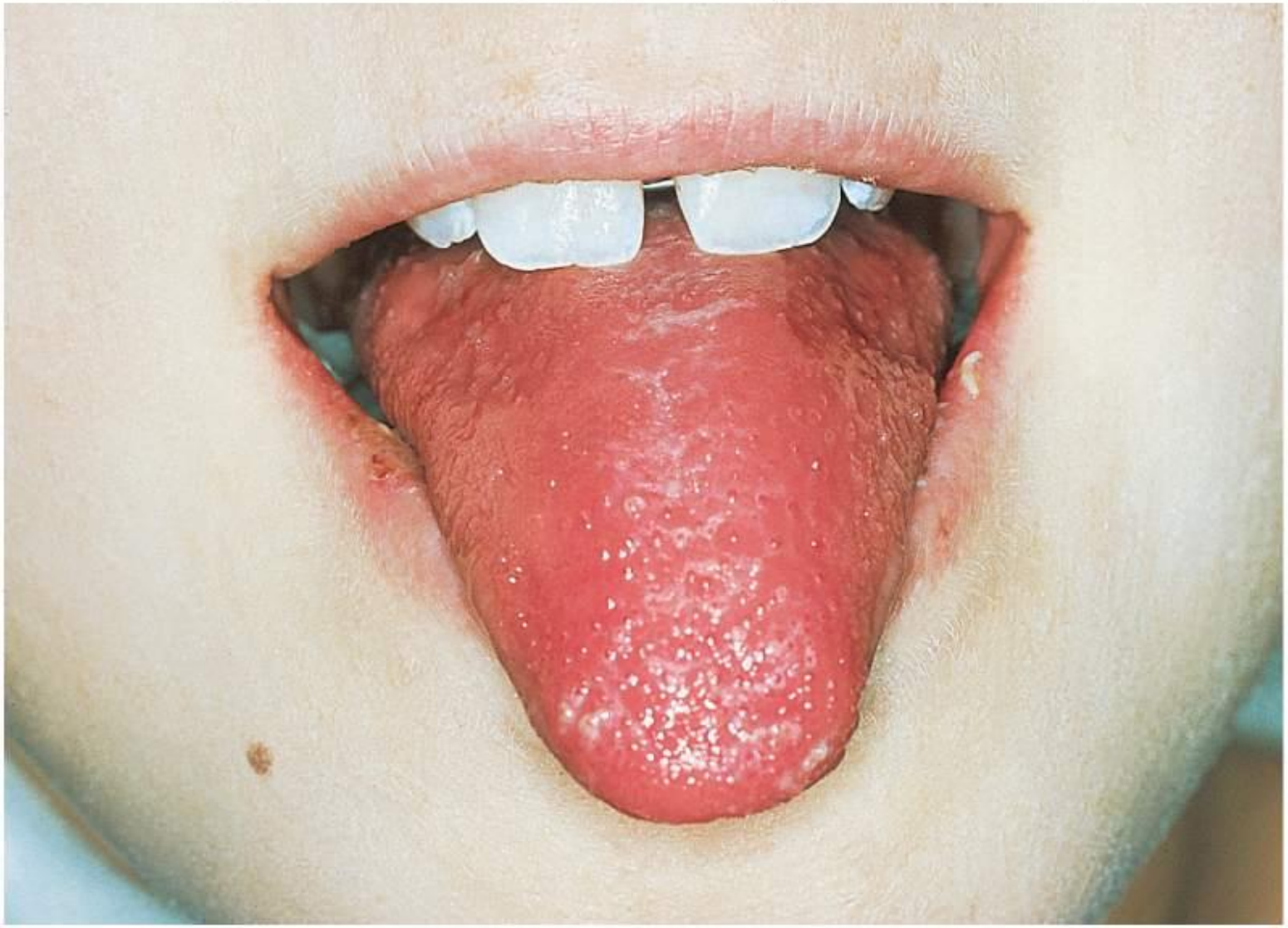
© From Farrar W.E., Woods M.J., Innes J.A.: Infectious Diseases; Text and Color Atlas, ed 2. London, Mosby Europe, 1992.

Group A Streptococcal Diseases (cont.)

- **Scarlet fever.**
- **Scarlet fever is a complication of streptococcal pharyngitis**
- If the strain of *S. pyogenes* is lysogenic for a particular phage which expresses an erythrogenic toxin the result is Scarlet fever
- Rash appears and characteristic is the strawberry colored tongue.

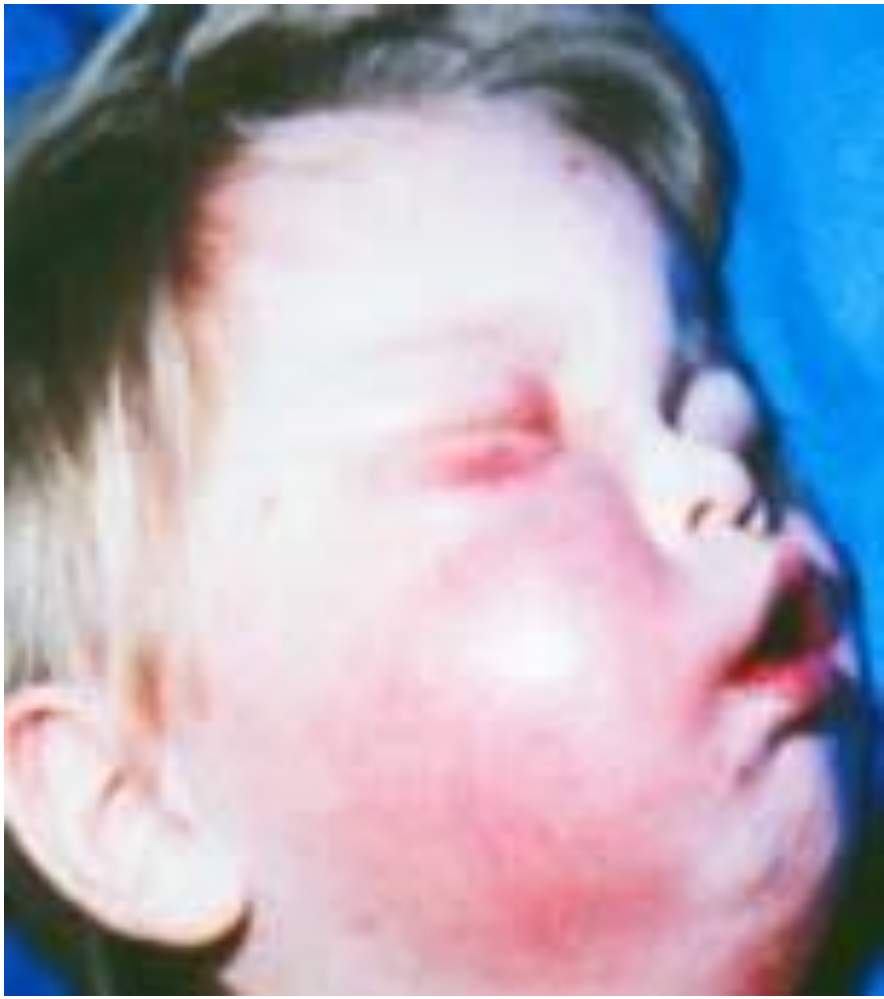


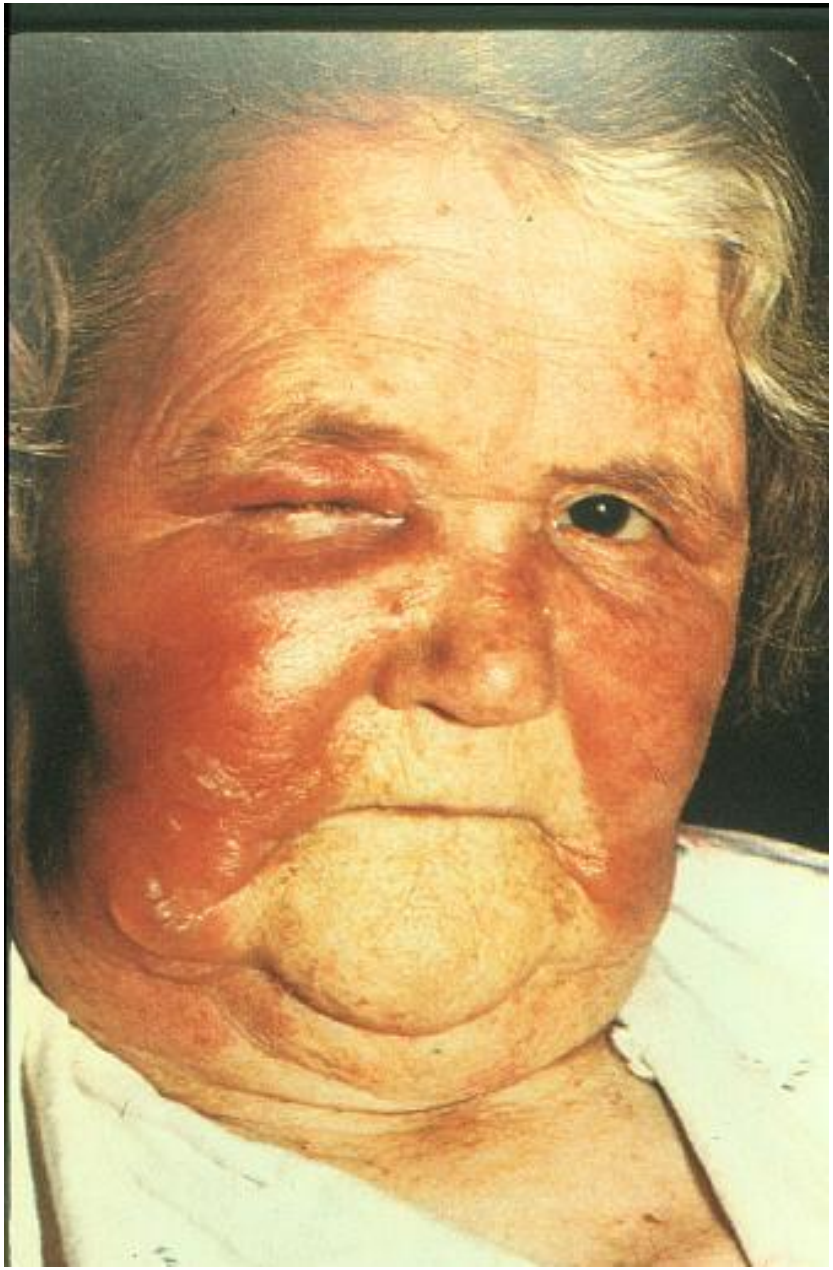
Strawberry Tongue



Group A Streptococcal Diseases (cont.)

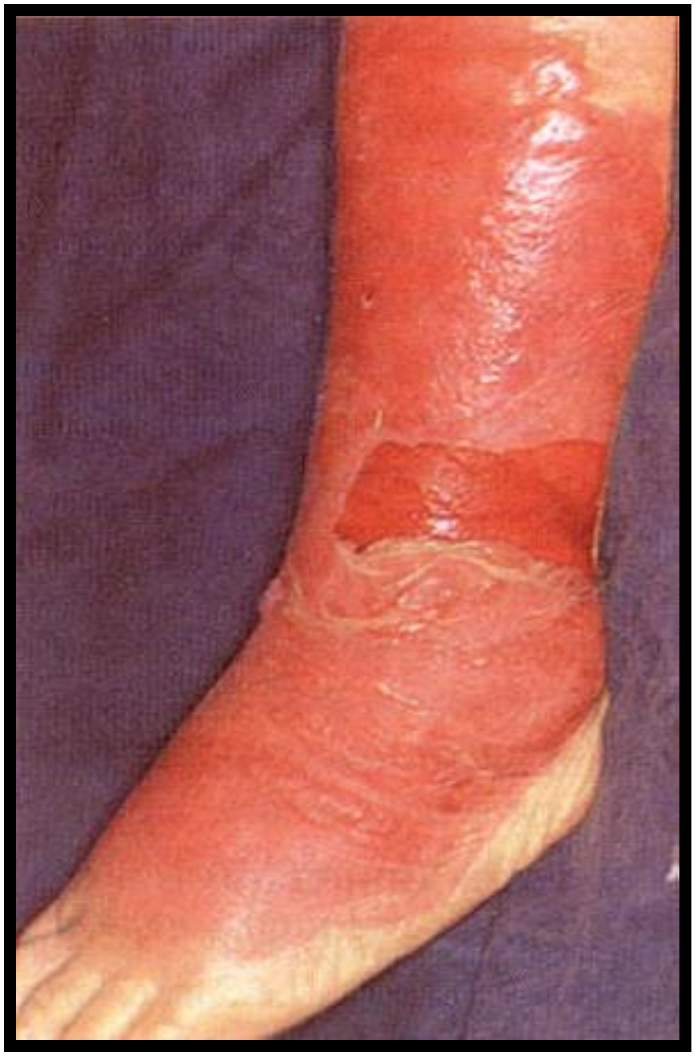
- **Erysipelas** – a diffuse, erythematous skin infection that is most often on the face and and lower extremities, skin and subcutaneous tissues.





Erysipelas

Erysipelas



NOTE:

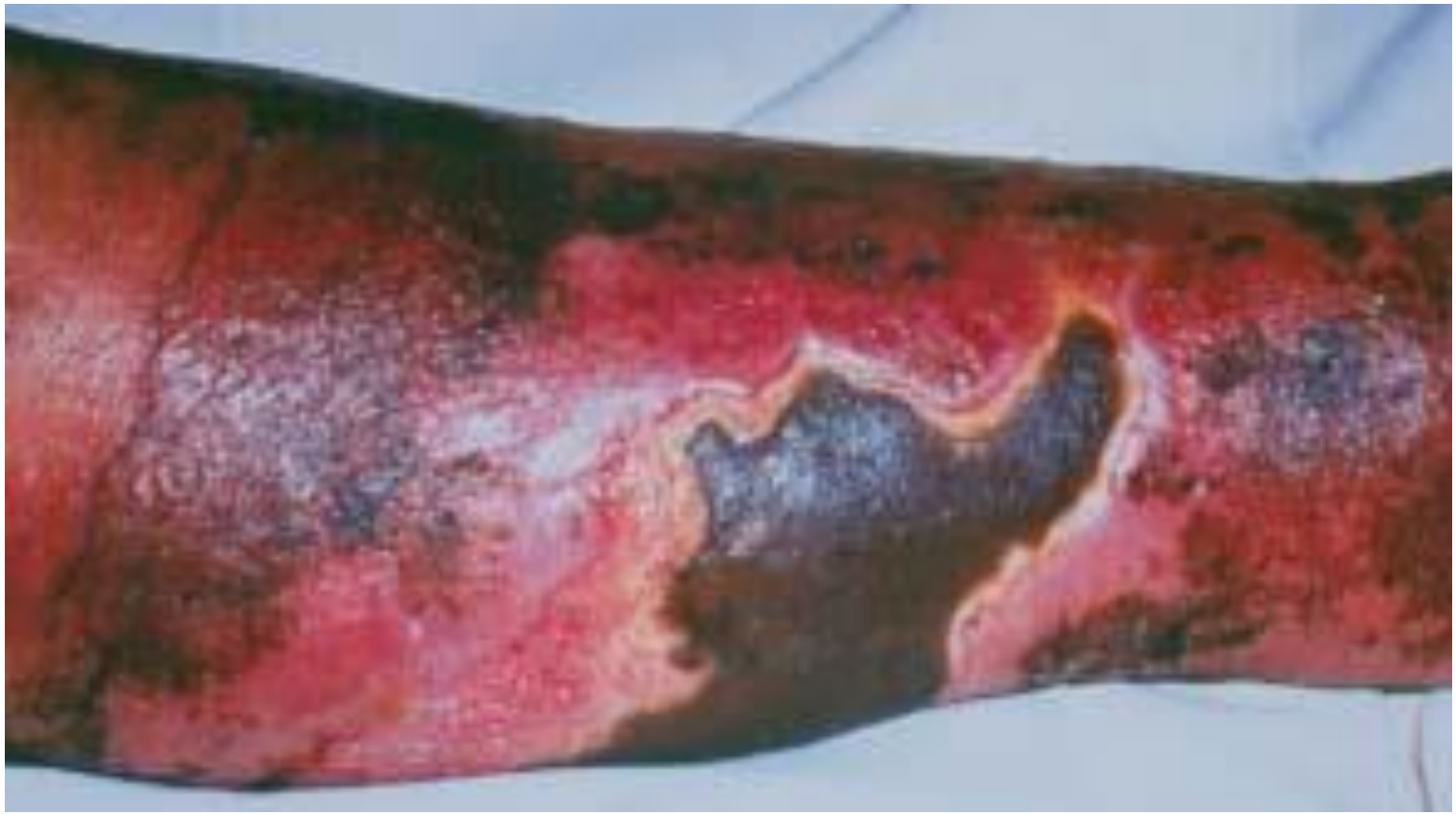
√ erythema

√ bullae

Group A Streptococcal Diseases (cont.)

- **Invasive lesions by *S. pyogenes***
  - **Cellulitis**: Involvement of deeper subcutaneous tissues; Deeper invasion with systemic symptoms
  - **Necrotizing fasciitis:** ("flesh-eating bacteria"): Infection deep in subcutaneous tissues that spreads along fascial planes, destroying muscle and fat; Initially cellulitis followed by bullae (fluid filled blisters; bulla is singular), gangrene, systemic toxicity, multiorgan failure and mortality in more than 50% of patients
  - **Wound Infections**

Necrotizing fasciitis



Necrotizing fasciitis

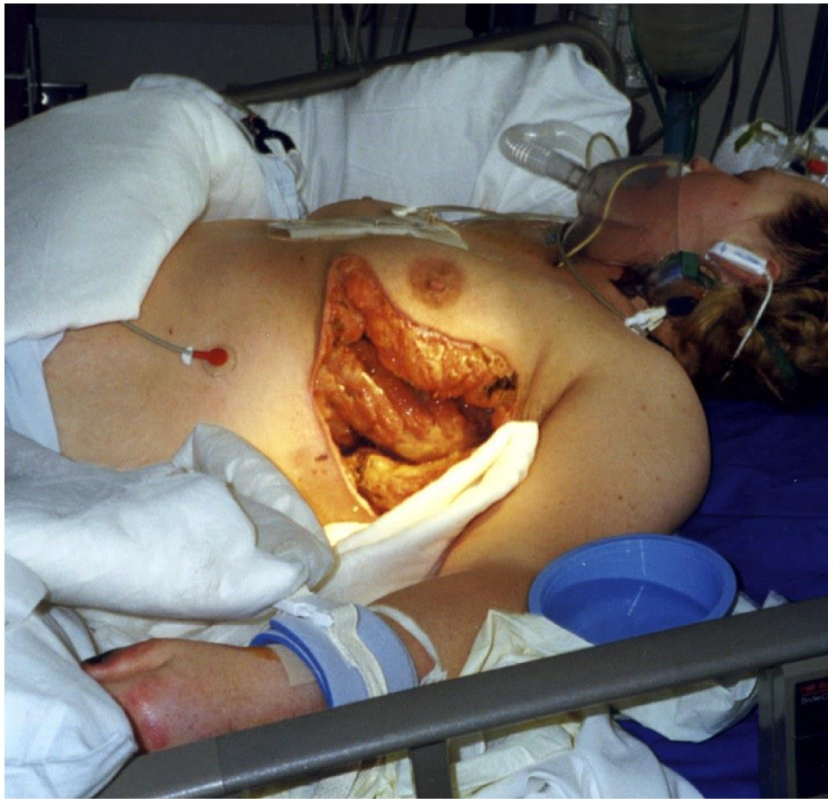


Figure 26.3a Microbiology: An Evolving Science
Courtesy Cassi Moore

Flesh removed to stop spread

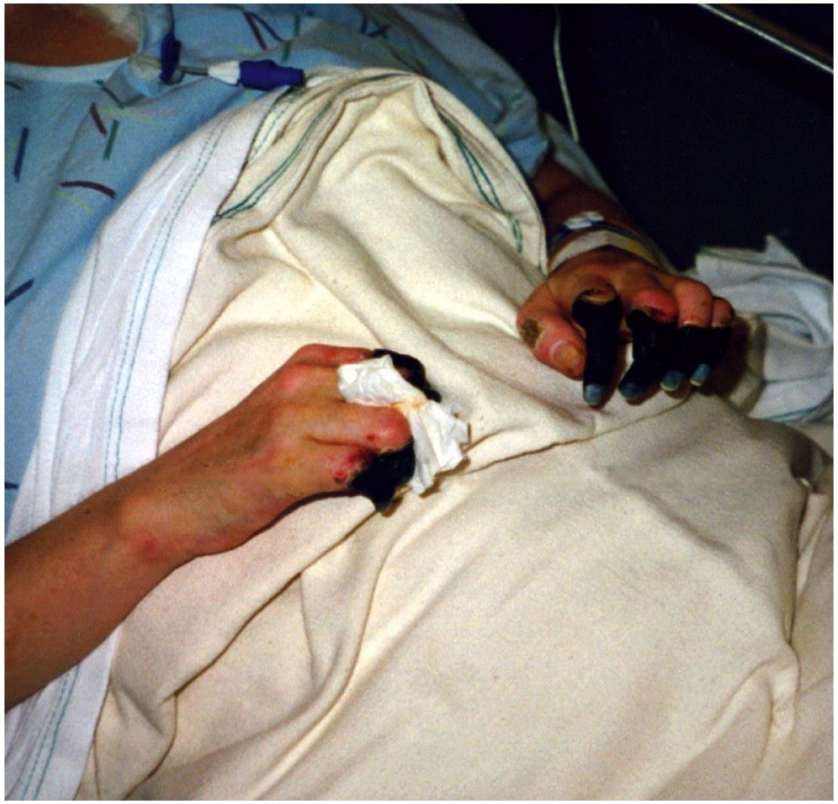
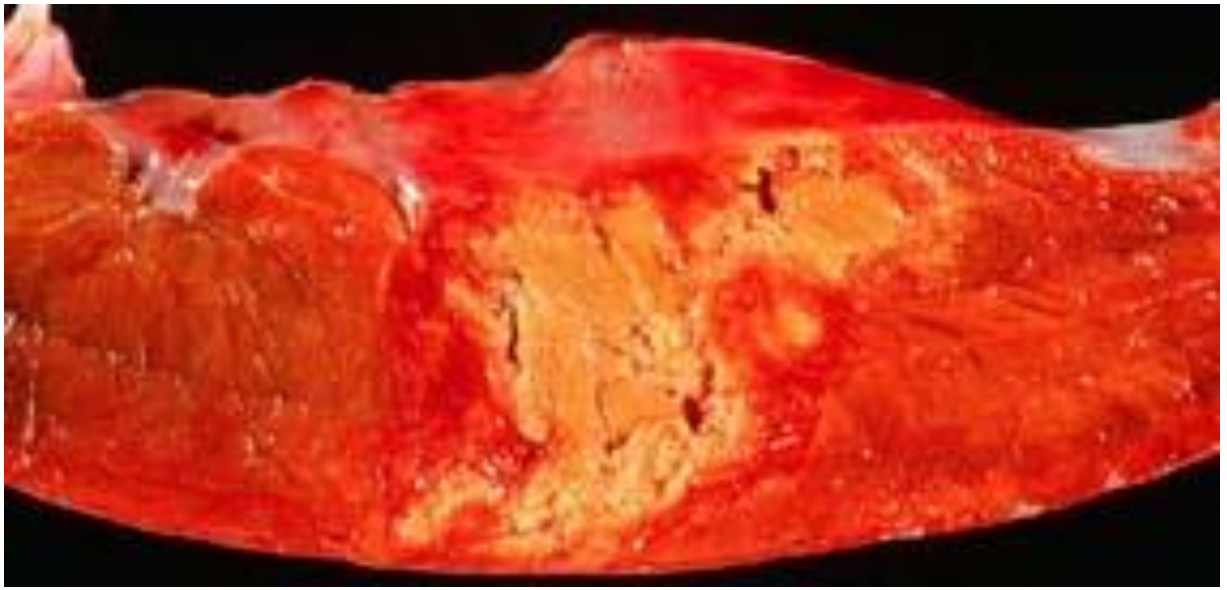


Figure 26.3b Microbiology: An Evolving Science
Courtesy Cassi Moore

Gangrene

Group A Streptococcal Diseases (cont.)

- **Myositis** – is a result of *Strep* invasion of muscle tissue resulting in extensive muscle necrosis and overwhelming sepsis. This condition is usually fatal.



Group A Streptococcal Diseases (cont.)

- **Systemic Disease**
  - **Streptococcal Toxic Shock Syndrome (TSS)**: **Multisystem toxicity** following soft tissue infection progressing to shock and organ failure (not to be confused with **Staphylococcal Toxic Shock Syndrome**)

Group A Streptococcal Diseases (cont.)

Non suppurative Sequelae

Post-infection complications of Group A streptococcal disease; Serious complications in **pre-antibiotic era**; still important in developing countries

Acute rheumatic fever (ARF):

Inflammation of heart, joints, blood vessels, sub-cutaneous tissues

Rheumatic heart disease (RHD):

Chronic, progressive heart valve damage

Acute glomerulonephritis (AG):

Acute inflammation of renal (kidney) glomeruli

Rheumatic fever-etiology

- Rheumatic fever is due to an immunologic reaction between cross-reacting antibodies to certain streptococcal M proteins and antigens of joint, heart, and brain tissue.
- If Streptococcal infections are treated within 8 days of onset, rheumatic fever is usually prevented.
- After a heart-damaging attack of rheumatic fever, reinfection must be prevented by long-term prophylaxis.
- 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%.

Rheumatic fever

Approximately 2 weeks after a group A streptococcal infection—usually pharyngitis—rheumatic fever, characterized by fever, migratory polyarthritis, and carditis, may develop.

The carditis damages myocardial and endocardial tissue, especially the mitral and aortic valves, resulting in vegetations on the valves.

Rheumatic fever

ASO titers and the erythrocyte sedimentation rate (ESR) are elevated.

A streptococcal skin infections do not cause rheumatic fever.

Most cases of pharyngitis caused by group A streptococci occur in children aged 5 to 15 years,

Acute glomerulonephritis (AGN)

- AGN 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).
- **immune complex disease of kidney**
  - Antigen-antibody complexes deposit in the glomerulus
  - Inflammatory response causes damage to the glomerulus and impairs the kidneys
- The most striking clinical features are hypertension, edema of the face (especially periorbital edema) and ankles, and “smoky” urine (due to red cells in the urine).

Lab Identification of *S. pyogenes* (Group A)

- Specimens: throat swab, pus, blood
- Microscopy :Gram stain - GPC in chains
- Culture: BA - beta hemolytic colonies

  Zone several times greater than diameter of colony
- **Identification tests -**
  - **Catalase Negative**
  - **Bacitracin sensitive**
  - **Penicillin sensitive**
  - **PYR-positive**

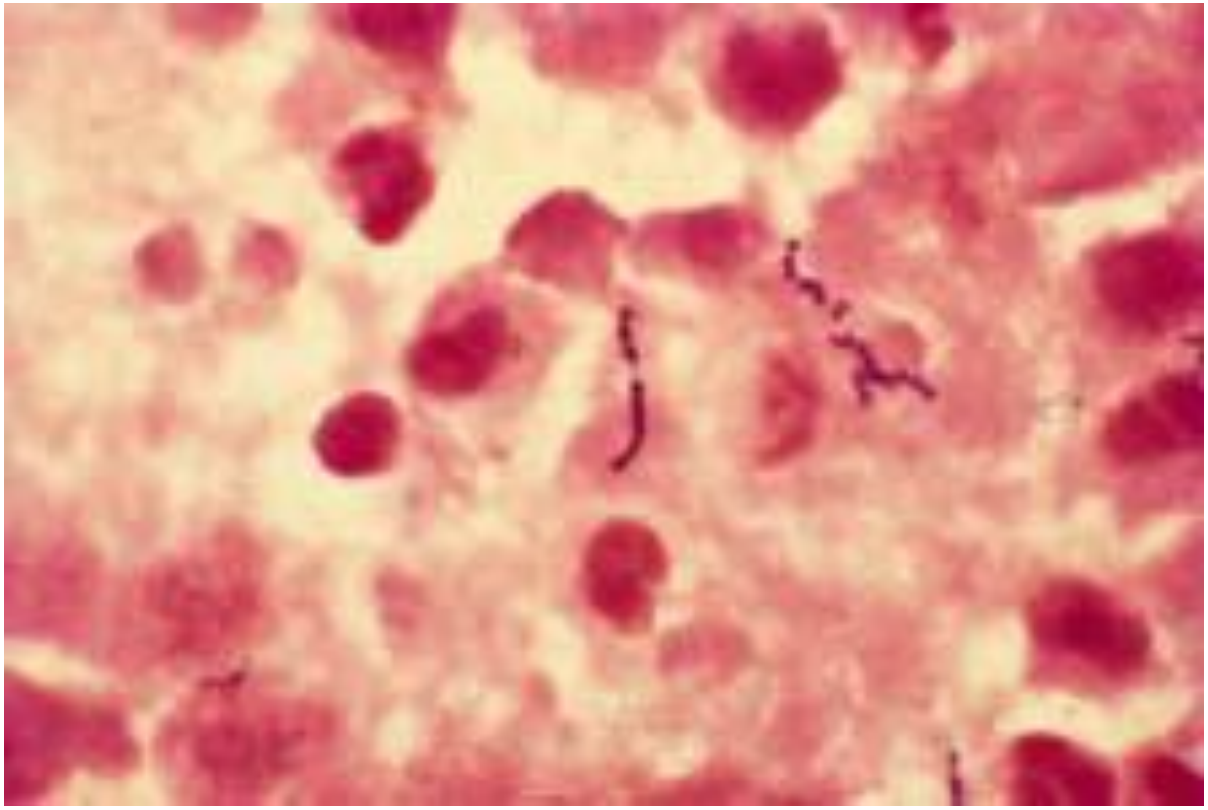
Laboratory Diagnosis: Group A Streptococcus

- Antigen detection tests: commercial kits for rapid detection of group A streptococcal antigen from throat swabs.
- Detection of group A streptococci by molecular methods: PCR assay from pharyngeal specimens.

Laboratory Diagnosis: Group A Streptococcus

- Antibody detection
- ASO titration for respiratory infections.
- Anti-DNase B and anti hyaluronidase titration for skin infections.
- Anti streptokinase; anti-M type-specific antibodies.

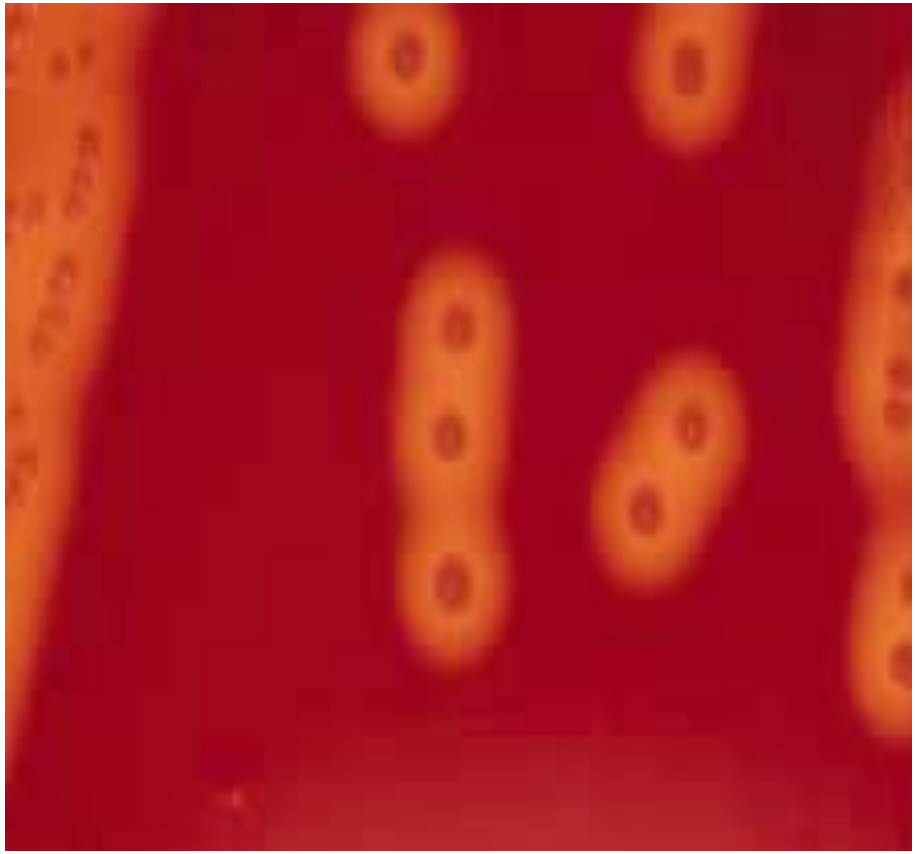
Laboratory Diagnosis: Group A Streptococcus



Grams stained wound smear showing gram-positive cocci in chains with numerous “polys”

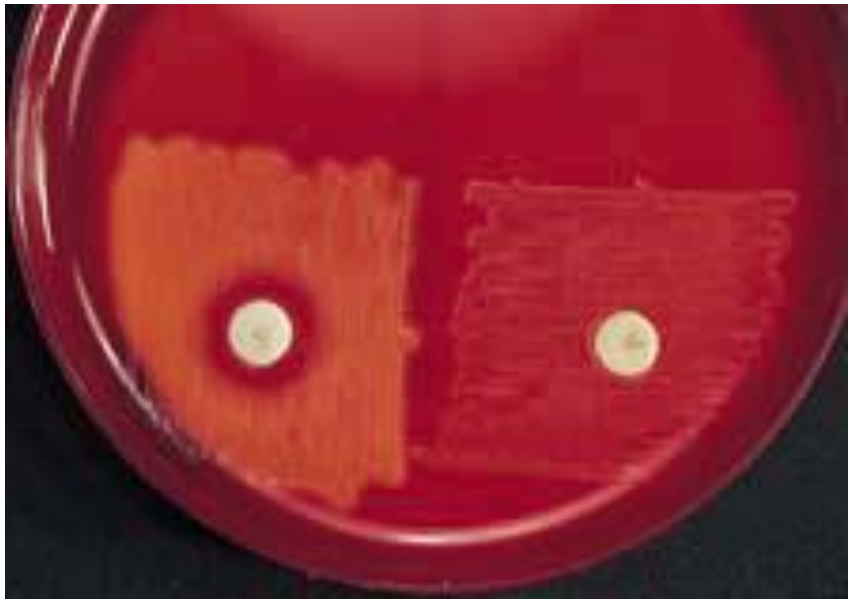
Laboratory Diagnosis: Group A Streptococcus

- Colony morphology
  - **Transparent, smooth, and well-defined zone of complete or β-hemolysis**



Biochemical Identification

- Susceptibility tests
  - **Bacitracin (0.04 units) or "A" disk**
    - **Identifies Group A streptococci**



Group A *streptococcus* is susceptible to "A" disk (left)

Biochemical Identification

- **PYR hydrolysis**
  - Substrate L-pyrrolidonyl-β–napthlyamide (PYR) is hydrolyzed by Group A Streptococci and *Enterococcus* sp.
  - More specific than Bacitracin for Group A streptococci

PYR test for Group A streptococci and enterococci. Both are positive for this test (right); left is a negative result

Treatment

- 1) Pencillin G
- 2) Erythromycin.

Treatment

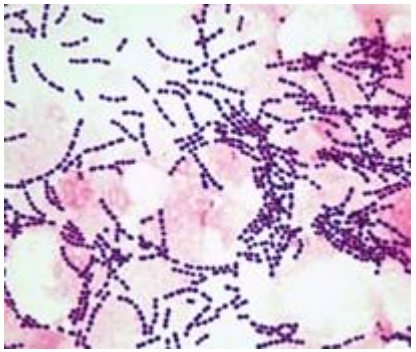
- Rheumatic fever can be prevented by prompt treatment of group A streptococcal pharyngitis with penicillin.
- Prevention of streptococcal infections (usually with benzathine penicillin once each month for several years) in persons who have had rheumatic fever is important to prevent recurrence of the disease.

Group B *Streptococcus*

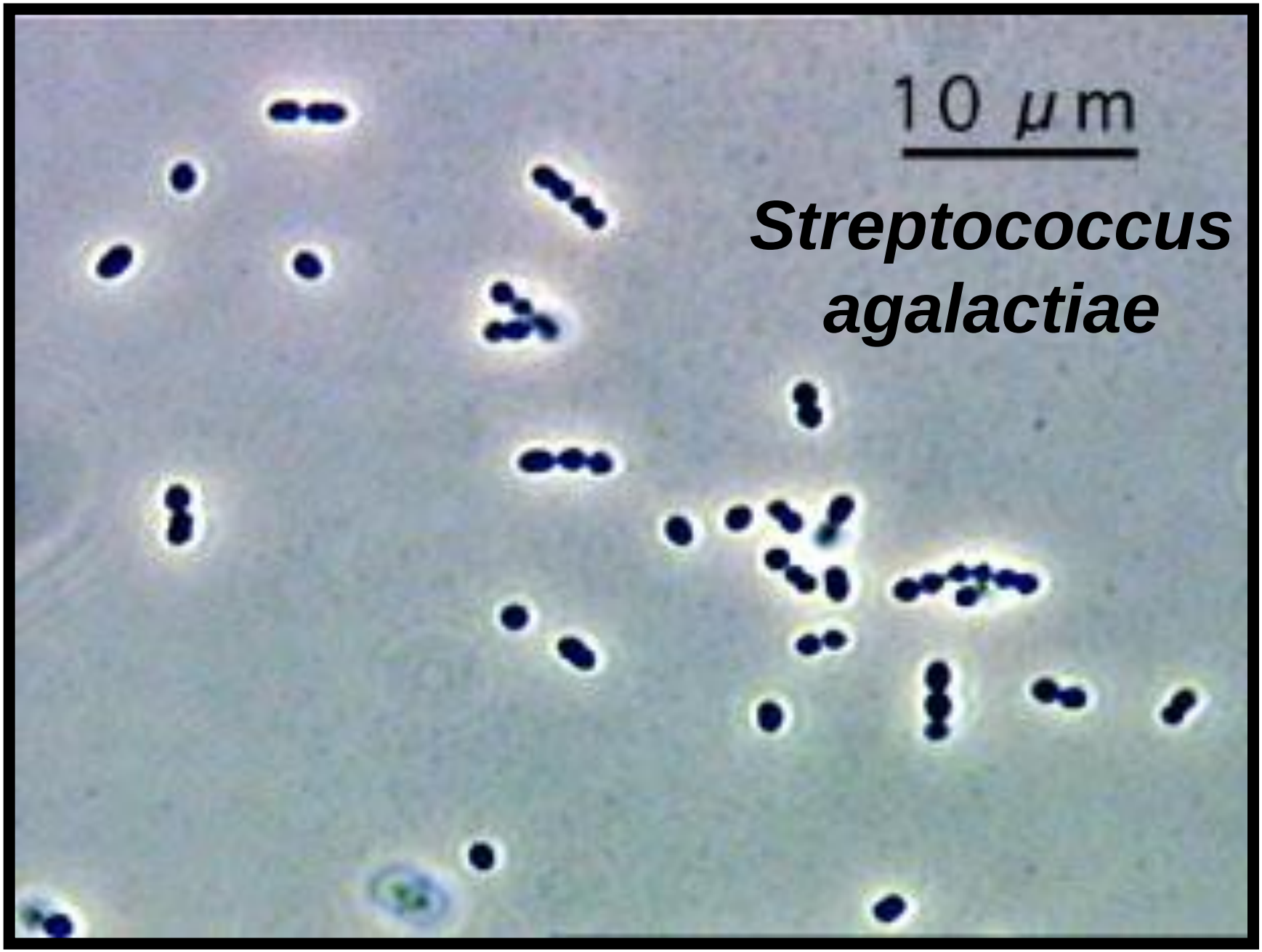
Streptococcus agalactiae

Beta hemolytic Group B Streptococcus

- Normal flora in lower GIT, female genital tract



- Pathogenicity
  - Neonatal meningitis
  - Puerperal sepsis
  - Pneumonia

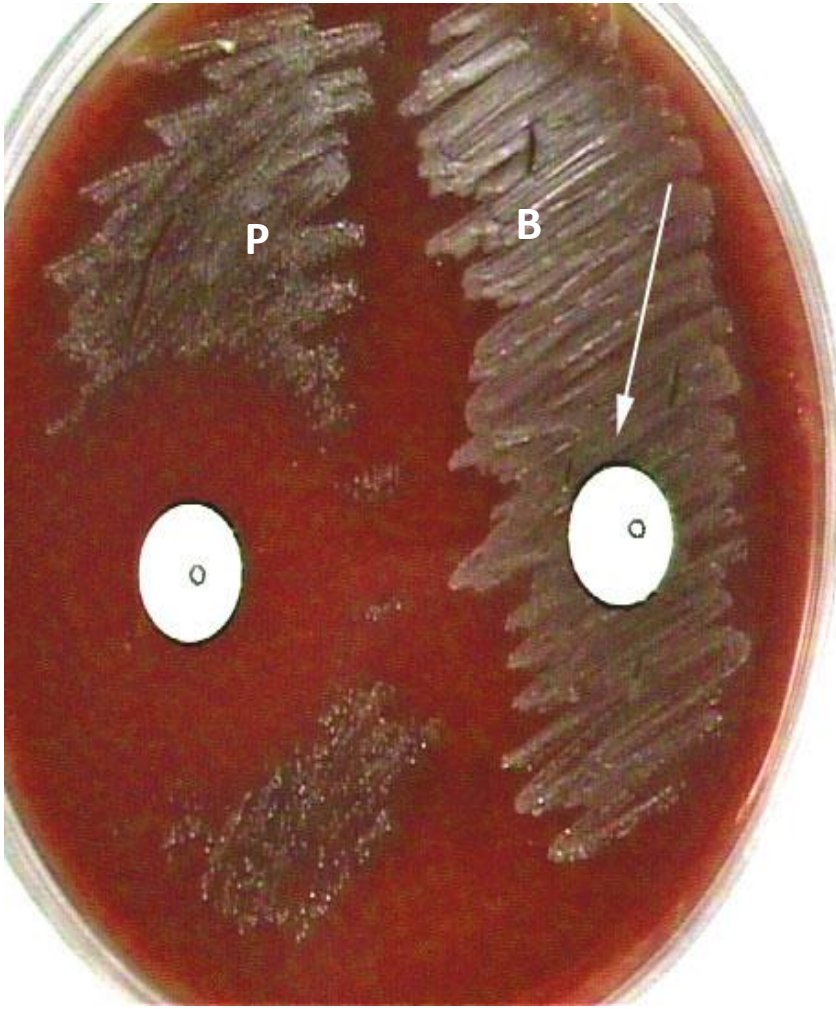

10 μm
Streptococcus agalactiae

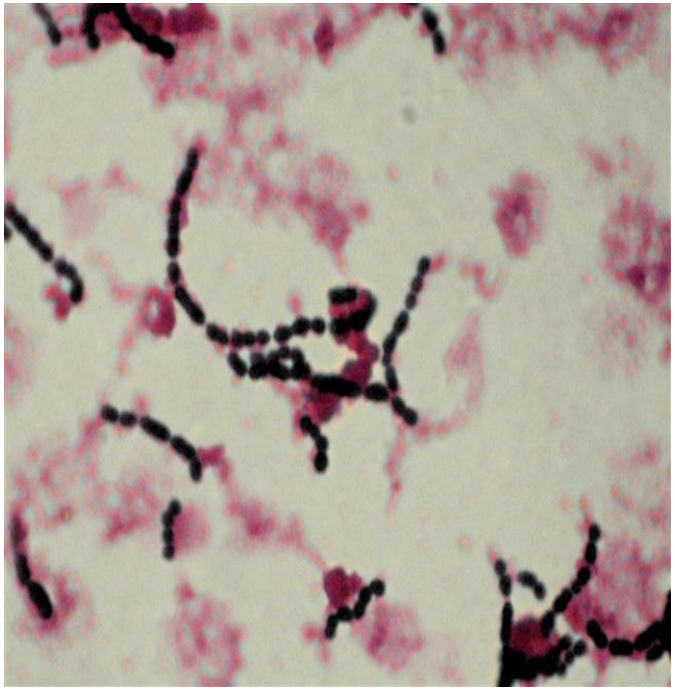
Streptococcus agalactiae

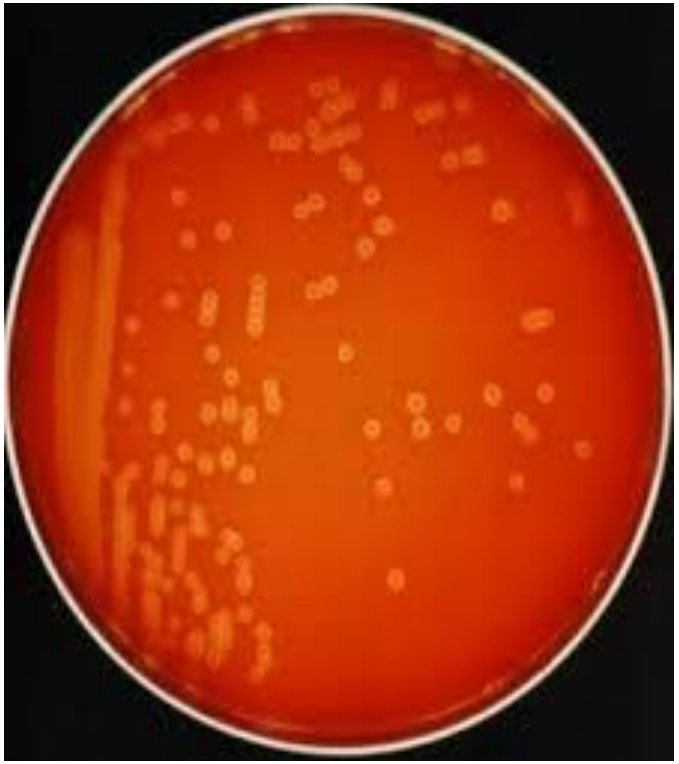
- The drug of choice for group B streptococcal infections is either penicillin G or ampicillin.
- Some strains may require higher doses of penicillin G or a combination of penicillin G and an aminoglycoside to eradicate the organism.
- If the patient is allergic to penicillin, either cefazolin or vancomycin can be used.
- Oral ampicillin given to women who are vaginal carriers of group B streptococci does not eradicate the organism.

Lab diagnosis – Group B Streptococci

- Specimens: CSF, blood, vaginal smears, urine
- Microscopy :Gram stain - GPC in chains
- Culture: BA - beta hemolytic colonies
- Identification tests
  - Catalase negative
  - Bacitracin resistance
  - CAMP Test +
  - Penicillin sensitive



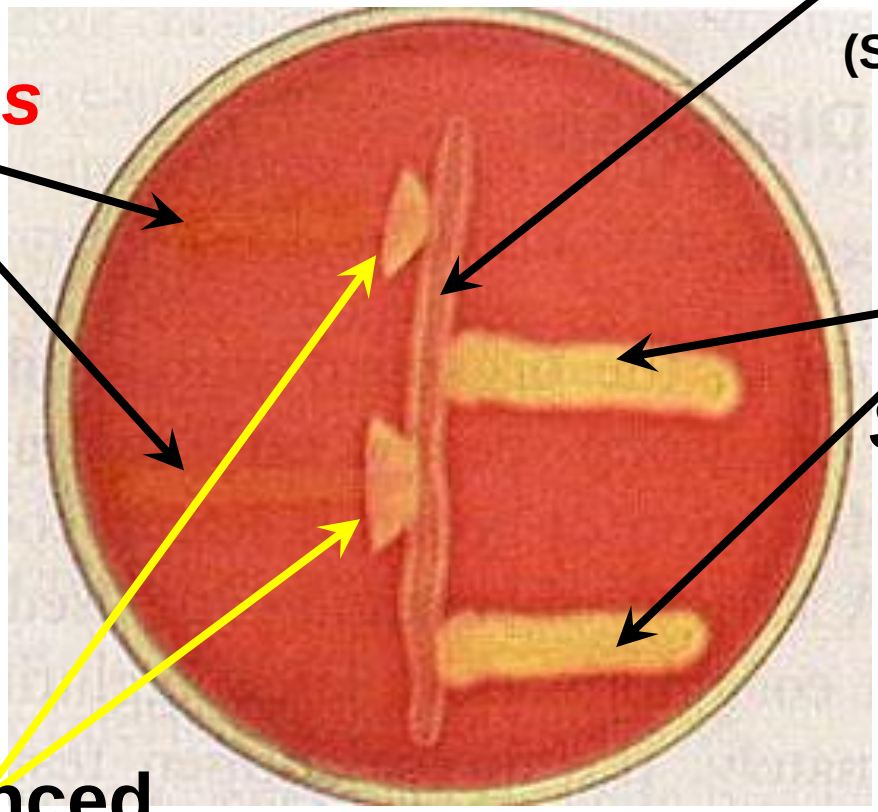




Biochemical Identification

- Christie-Atkins, Munch-Petersen (CAMP) test
  - **Detects the production of enhanced hemolysis that occurs when β-lysin of staph and the hemolysins of Group B streptococci come in contact**
  - Group B streptococci showing the classical “arrow-shaped hemolysis near the staphylococcus streak

CAMP Factor Test



S. aureus

(Spingomyelinase C)

Group B
Streptococcus

(CAMP Factor)

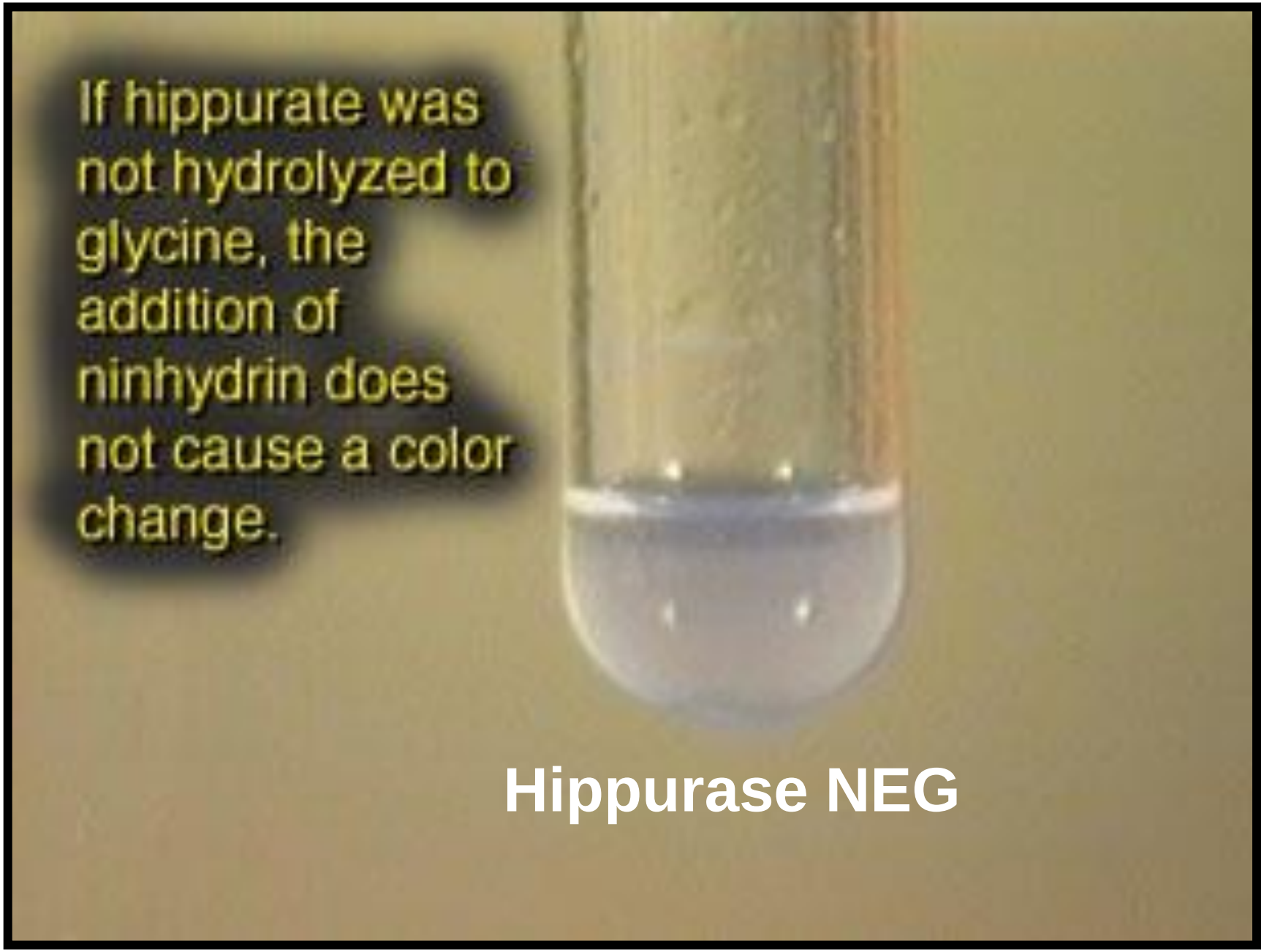
Group A
Streptococcus

Enhanced Zone of Hemolysis

Biochemical Identification

- **Hippurate hydrolysis**
  - Differentiates Group B streptococci from other beta hemolytic streptococci Group B streptococci hydrolyzes sodium hippurate .

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


If hippurate was not hydrolyzed to glycine, the addition of ninhydrin does not cause a color change.
Hippurase NEG

Prevention

- The incidence of neonatal sepsis caused by group B streptococci can be reduced by a two-pronged approach:
- 1- All pregnant women at 35 to 37 weeks' gestation should be screened by doing vaginal and rectal cultures.

  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 membranes, whose labor begins before 37 weeks' gestation, or who have a fever at the time of labor.

Streptococcus *pneumoniae*

- **INTRODUCTION:**

Genus → Streptococcus

Species → *Pneumoniae*

They are :

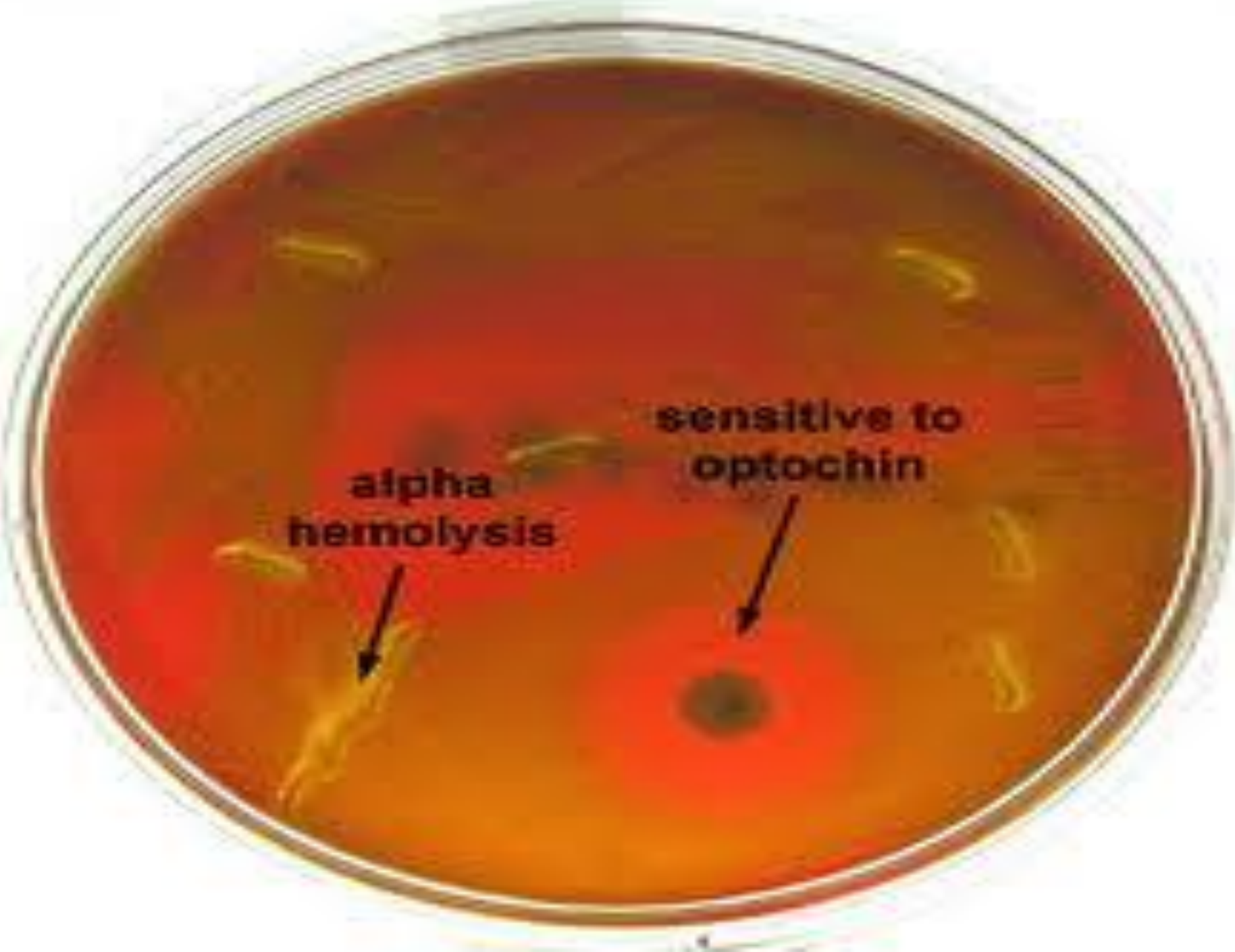
- Gram positive
- Diplococci
- Catalase negative
- Alpha hemolytic
- Aerobic or Facultative anaerobes
- Normal inhabitants of upper respiratory tract of human 5_40%

- **MORPHOLOGY:**

- Gram positive cocci occur in Pairs (diplococci)
- Short chains
- Diplococci are ovoid or lanceolate in shape with distal ends narrowed.
- Non motile
- Non spore forming
- Fresh isolated strains are capsulated

- **GROWTH CHARACTERS:**

- Grow on ordinary media but better on media containing 5- 10% serum, blood or heated blood.
- Alpha hemolytic colonies on blood agar.
- Growth is inhibited by optochin.
- Colonies are soluble in bile.


sensitive to
optochin
alpha
hemolysis

- ANTIGENIC CHARACTERS:

- The capsular polysaccharide is immunologically distinct for each 91 serotypes.
- The capsular polysaccharides is covalently bond with peptidoglycan and to cell wall polysaccharide.
- Capsule may be present as loose slime or ‘specific soluble substance’ SSS.
- Immunity to infection depends on antibody to specific capsular antigens

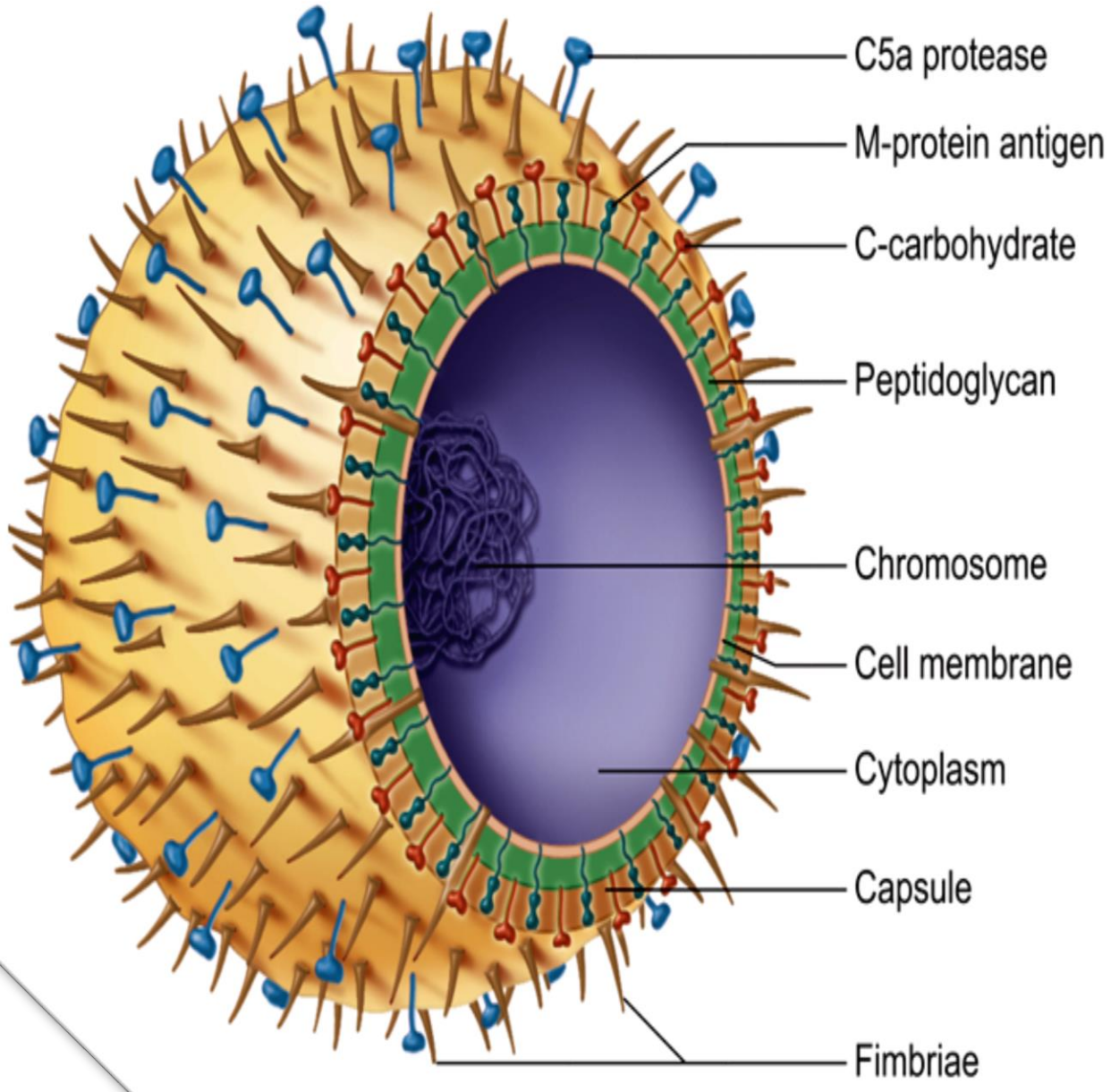
- **ANTIGENIC STRUCTURES:**

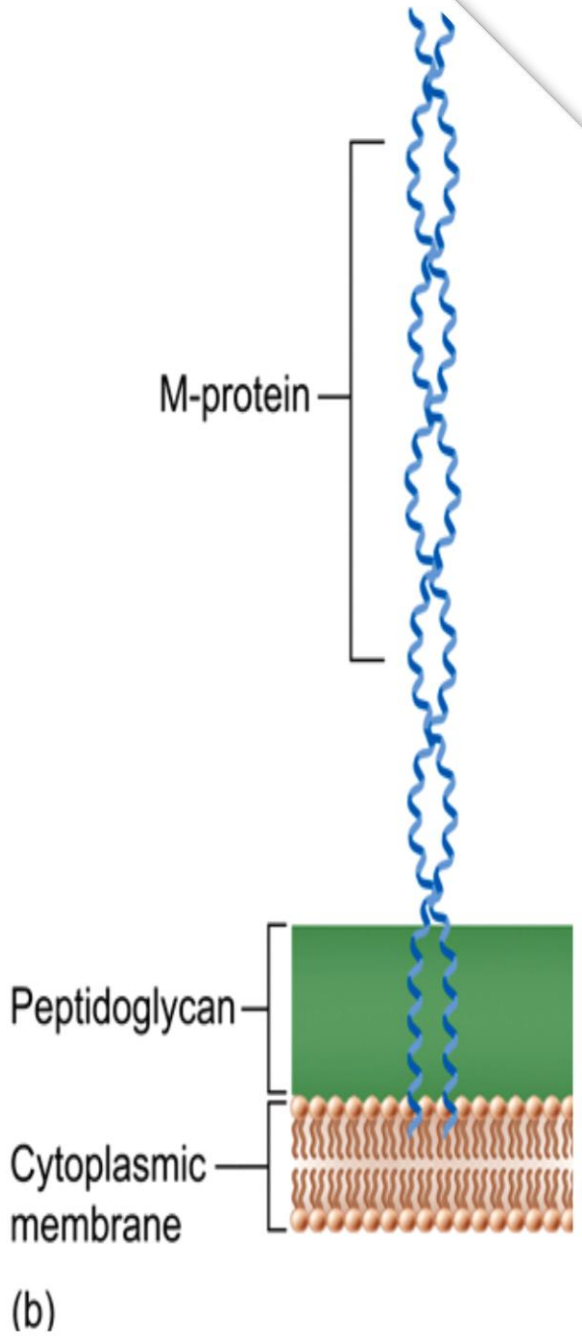
- **CELLULAR COMPONENTS:**

  - **C-POLYSACCHARIDE:**
    - It is found in cell wall and specific to species.
    - They are found in urine and CSF and diagnostic.

- **PROTEINS:**
  - **T-antigen:** They adjunct with M protein, so marker for routine surveillance of isolates.
  - **SOF (serum opacity factor):** It is associated with M protein. Has ability to opacify horse serum.

- **M-antigen :**
  - Appear as hair like projection on cell wall in electron microscope. Most virulent factor of streptococcus.
    - M protein persist in infected person until antibodies appear. Antiphagocytic activity of M protein is attributed to an interference with deposition of complement C3b on streptococcal cell surface.


C5a protease
M-protein antigen
C-carbohydrate
Peptidoglycan
Chromosome
Cell membrane
Cytoplasm
Capsule
Fimbriae


M-protein
Peptidoglycan
Cytoplasmic membrane
(b)

- **EXTRACELLULAR COMPONENTS:**

Pneumolysin O:

- Is a pore-forming toxin that is inhibited by cholesterol. It is common to all serotypes of *S. pneumoniae*.
- Multi-effective factor for virulence following pneumococcal infection.
- The toxin cause induction of apoptosis.
- Activation of host complement.
- Induce proinflammatory reactions in immune cells.
- The toxin may cause widespread direct cellular and tissue damage by virtue of its membrane pore forming properties.

– **NUCLEASES:**

- These enzymes having DNase and RNase activity. Antibody titers to these enzymes are of great value in serodiagnosis of pharyngeal or skin infection.

– **STREPTOCOCCAL HYALURONIDASE:**

- They are present in streptococcal capsule are antigenic and important in serodiagnosis. And spreading factor.

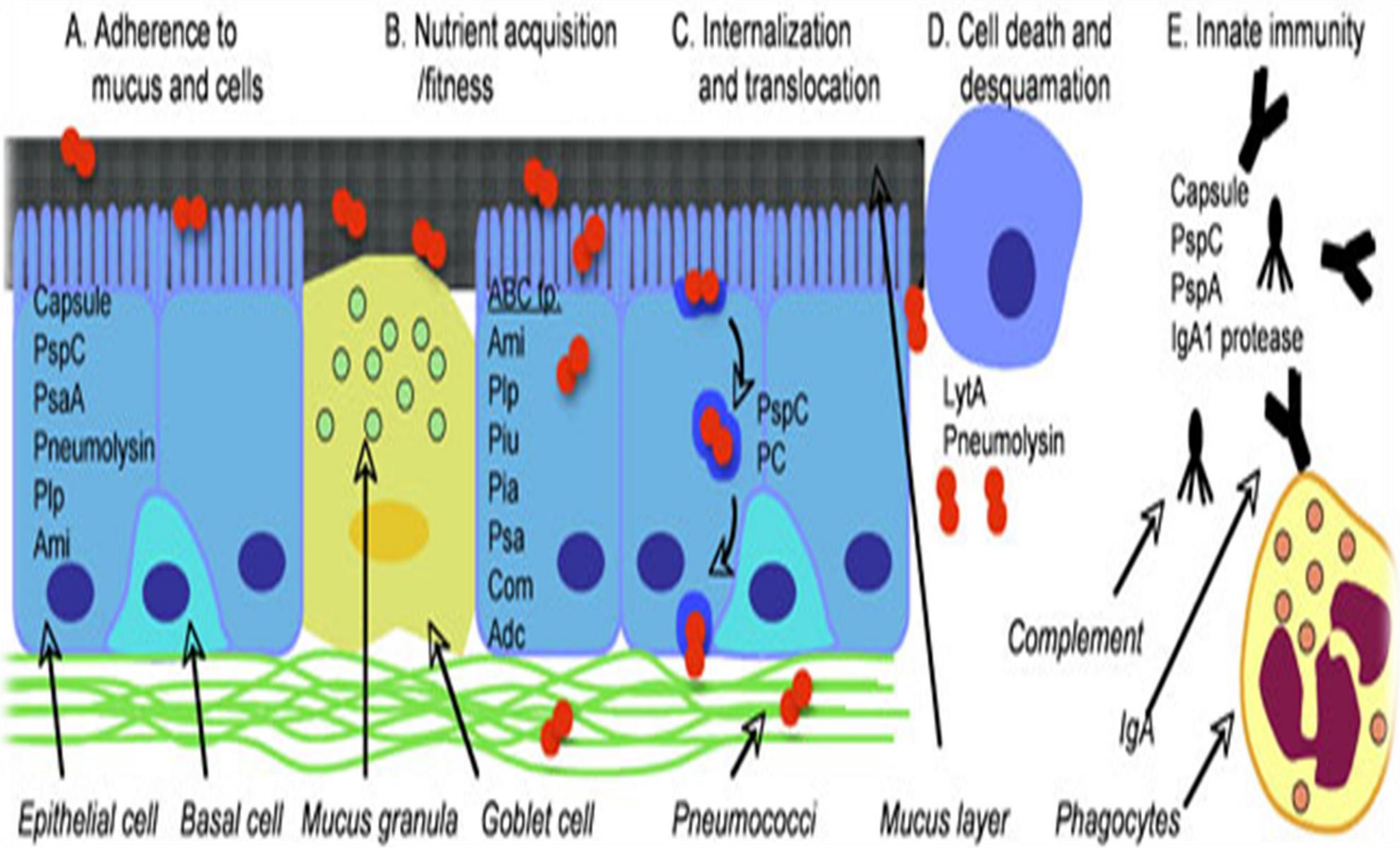
– **STREPTOKINASE:**

- Activates plasminogen to form plasmin. Dissolves fibrin in clots, thrombi, and emboli. Can be used in lysis of thrombi in CHDs.

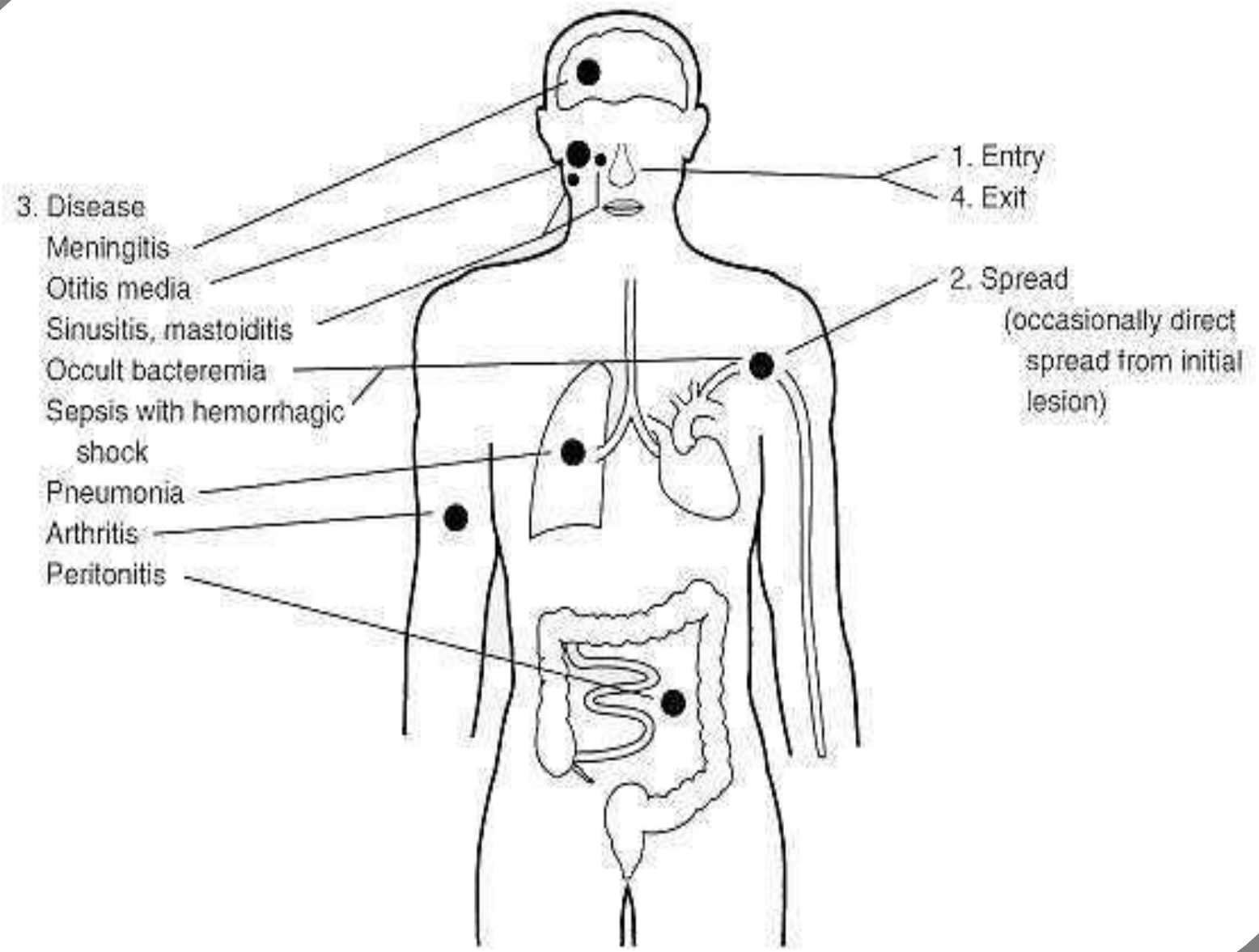
- **PATHOGENESIS:**
- **ADHERENCE:**
- Pneumococci can adhere to respiratory epithelium and mucus.
- Phospho-choline of the cell wall are known to interact with the platelet-activating factor receptor on activated epithelial and endothelial cells.
- IgA1 protease inactivates human IgA and mediate increased pneumococcal adherence to the epithelium.
- Capsule, pneumolysin, also help in adherence.

HOST EVASION:

- Capsule is important for protection against phagocytosis and absolutely required for virulence of pneumococci .
- IgA1 protease inactivates human IgA and mediate increased pneumococcal adherence to the epithelium.


A. Adherence to mucus and cells
B. Nutrient acquisition /fitness
C. Internalization and translocation
D. Cell death and desquamation
E. Innate immunity
Capsule
PspC
PsaA
Pneumolysin
Plp
Ami
ABC tp.
Ami
Plp
Piu
Pia
Psa
Com
Adc
PspC
PC
LytA
Pneumolysin
Capsule
PspC
PspA
IgA1 protease
Complement
IgA
Epithelial cell
Basal cell
Mucus granula
Goblet cell
Pneumococci
Mucus layer
Phagocytes

- **<u>CLINICAL FINDINGS:</u>**
- Types 1_8 are responsible for 75% cases of pneumonia and bacteremia.
- In children type 6, 14, 19, 23 are frequently causing infections.
- Causing lobar and bronchopneumonia.
- Pneumonia is associated with fever, chills, sharp pleural pain, bloody sputum.
- Empyema is complication.
- Involved sinuses and middle ear.
- Meningitis
- Endocarditis
- Septic arthritis


1. Entry
4. Exit
2. Spread
(occasionally direct spread from initial lesion)
3. Disease
Meningitis
Otitis media
Sinusitis, mastoiditis
Occult bacteremia
Sepsis with hemorrhagic shock
Pneumonia
Arthritis
Peritonitis

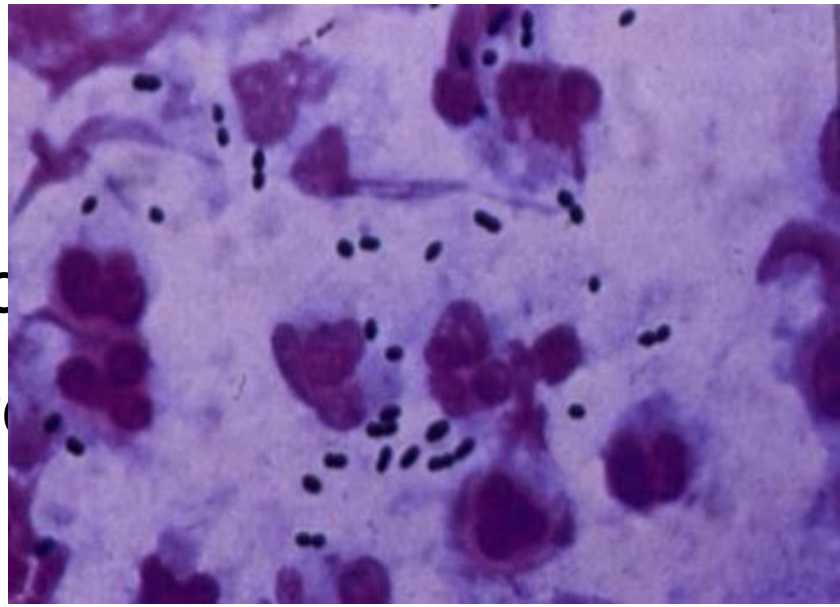
- **LABORATORY DIAGONOSIS:**

- **1. SPECIMENS:**

- Blood for culture
- CSF and sputum for smear and culture
- CSF and urine for C-polysaccharide by immune chromatographic membrane assays.
- The specimen should be sent as soon as possible as pneumococci tend to autolyse.

2. GRAM STAINING:

- Gram positive diplococc
  when taken from cultur



3. CULTURE:

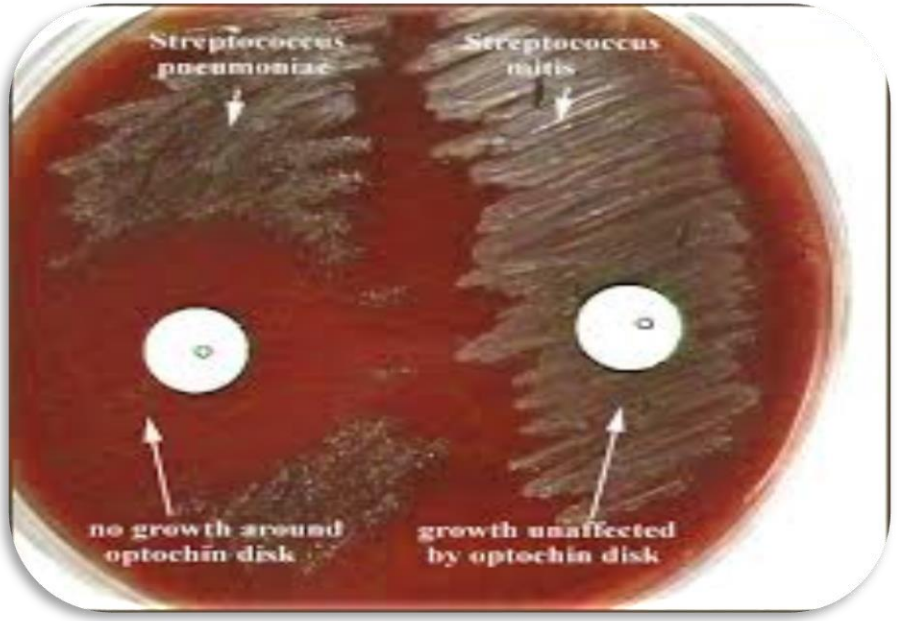
Blood Agar:

- small, round, low convex , may depressed from center, glistening colonies appear on blood agar with zone of alpha hemolytic greening of agar.
- On repeating subculture smooth colony forming pneumococci may give rise to few non capsulate, rough mutant organism.

4. BIOCHEMICAL TESTS:

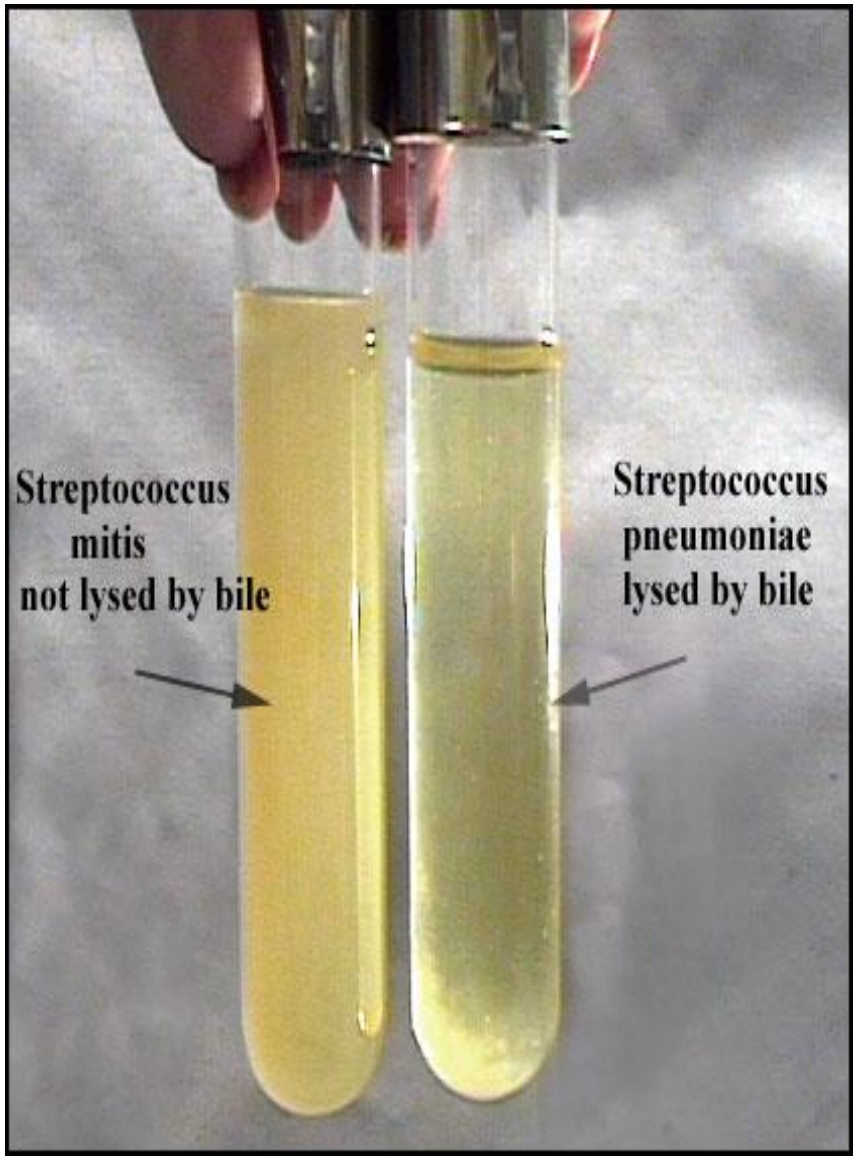
OPTOCHIN SENSITIVITY TEST:

- This test is used to distinguishes pneumococcus from viridans.
- Place a paper disc of 5 micro gram of optochin (ethyl hydrocuprein) on blood agar plate on which pneumococcus inoculated. Incubate at 37˚ C in 5-10% CO_2. Pnemococcal growth is inhibited in a zone of about 5mm from margin of disc. Whereas viridans grow up to disc.



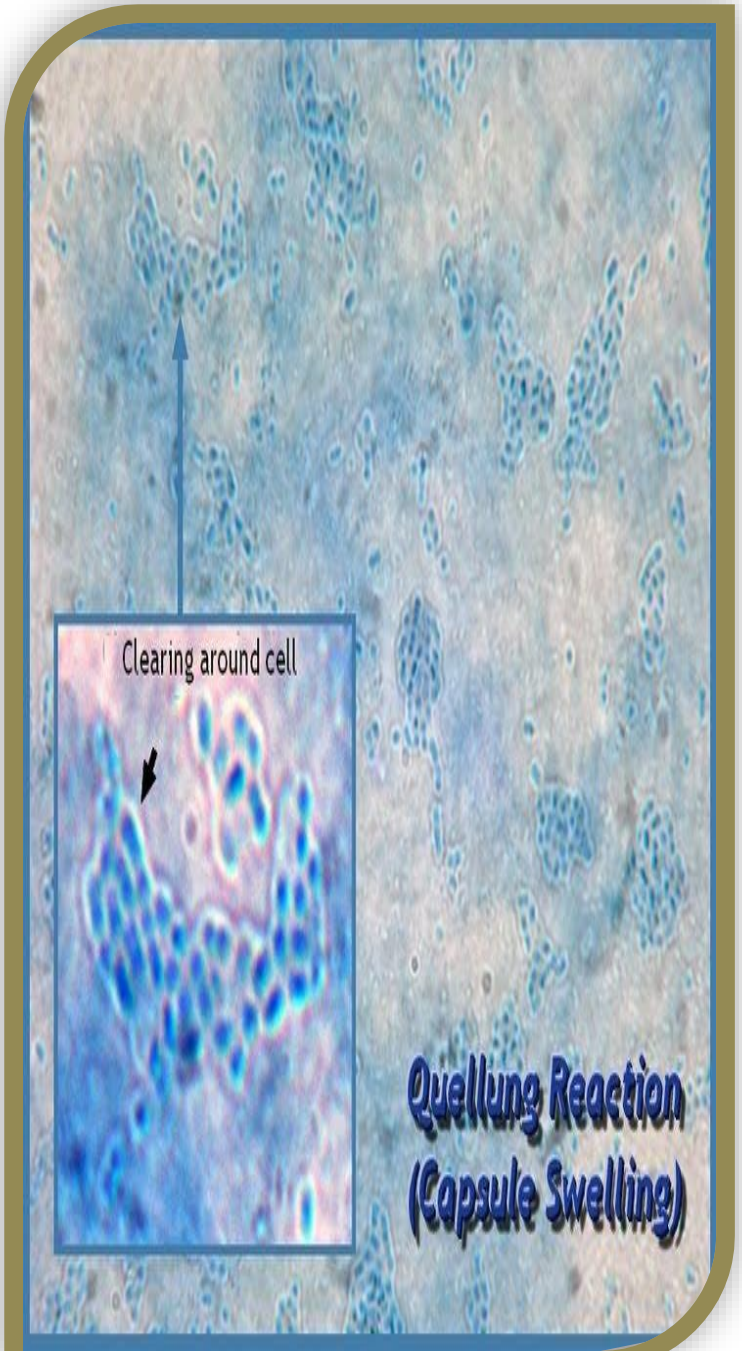
– BILE SOLUBILITY TEST:

- » Pneumococci are soluble in bile whereas viridans are not.
- » Rapid presumptive test is performed on primary culture plate. Touch 2% sodium deoxycholate solution on blood agar pneumococcal colony after 20min at room temp colony will disappear leaving an alpha hemolytic area.



– **QUELLUNG OR SWELLING REACTION:**

» When pneumococci of certain type mixed with specific antipolysaccharide serum of same type or with polyvalent antiserum on a microscope slide , the capsule swells markedly and organism agglutinate by cross linking of antibodies.



- 5. **PNEUMOCOCCAL ANTIGEN DETECTION TEST:**
  - »Counter Immunoelectrophoresis (CIE)
  - »Coagglutination test (COA)
  - »Latex agglutination (LA)
  - »Enzyme-linked immunosorbent assays (ELISA)

- **IMMUNITY:**
  - Type specific
  - Depends on antibodies to capsular polysaccharide
  - Intact phagocytic function
  - Vaccine induce antibodies production.
- **Factors lower the immunity:**
  - Viral infections >damage to surface cells
  - Alcohol > depress cough reflex > stasis of secretions
  - Abnormal circulatory dynamics
  - Malnutrition
  - Sickel cell anemia > auto splenic infarct >pneumococcal sepsis
  - Hyposplenism
  - Nephrosis
  - Complement deficency
  - Trauma to nose > pneumococcal meningitis

- **TREATMENT:**
  - » Penicillin G is drug of choice.
  - » In mild pneumococcal infection oral penicillin
  - » In penicillin allergic patient erythromycin or azithromycin can be used
  - » Floroquinolones levofloxacin also used
  - » Vancomycin used in penicillin resistant strains.
- **Pneumococcal vaccines:**
  - » **PPSV-23:** For 23 serotypes . Recommended for 19 to 64 years of age, For immunocompromised patients , for asthmatic patients, for above 65 years age group.
  - » **PCV-7:** conjugated to diphtheria . Recommended for 2 -23 months, selected children of 24- 59 months.
  - » **PCV-13:** Four doses at 2, 4, 6, and 12-15 months.

STREPTOCOCCUS *viridans*

- **INTRODUCTION:**

They are:

- Gram positive cocci
- Round appear in short chains
- Alpha or non hemolytic
- Normal microbiota of Upper Respiratory Tract and GIT

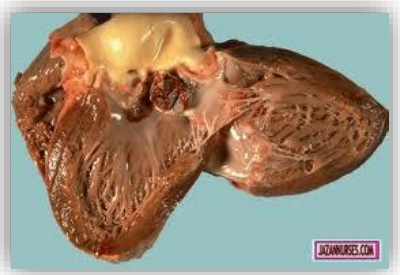
- **MORPHOLOGY:**
  - Gram positive cocci
  - More ovoid in shape
  - Occurs in short chains
  - Non motile
  - Non spore forming
  - Anerobic or facultative anerobes

*CULTURAL CHARACTERS:

- *Small
- *Low convex
- *Colorless colonies
- *Round in shape
- *Having zone of alpha hemolysis and produce green color around their colonies

- **GROWTH CHARACTERS:**
  - Grow well on nutrient or blood agar
  - Fails to grow on MacConkey bile-salt agar
  - Better seen on heated blood agar
  - Growth enhanced by 5-10% CO_2 to air in which culture incubated.
  - Growth is not inhibited by optochin
  - Colonies are not soluble in bile.
  - Sensitive to penicillin
  - Resistant to gentamicin so placing of these antibiotics discs on primary culture help to identify them.

- **PATHOGENESIS:**
  - They are prevalent normal microbiota of URT .
  - Important for healthy state of mucous membrane
  - They may reach in bloodstream as a result of trauma
  - Some of viridans synthesize large polysaccharides such as dextrans or levans and contribute to the gensis of dental caries.



- **CLINICAL FEATURES:**

ACUTE ENDOCARDITIS:

- Streptococcus viridans settle on normal or deformed heart valves and produce acute endocarditis.
- Rapid valve destruction causes cardiac failure in days or weeks.

SUBACUTE ENDOCARDITIS:

- Involved abnormal ,congenital deformed , rheumatic or atherosclerotic lesions of valve
- **Endocarditis** is associated with fever ,heart murmurs, embolic events like splinter hemorrhages, sub conjunctival hemorrhages.

- **DENTAL BACTEREMIA:**

  - 30% of patients developed viridans bacteremia after tooth extraction.
  - They may also developed brain abscess.
  - They may cause abdominal abscesses after entering in a bloodstream.

- **LAB DIAGNOSIS:**

SPECIMEN:

- **Blood**
- **CSF**
- **Abscess**

GRAM STAINING :

- shows gram positive cocci. Both from specimen and from culture.

CULTURE ON BLOOD AGAR:

- **Well grow on blood agar. Producing small round colonies, low convex and having green zone of alpha hemolysis.**

BIOCHEMICAL TESTS:

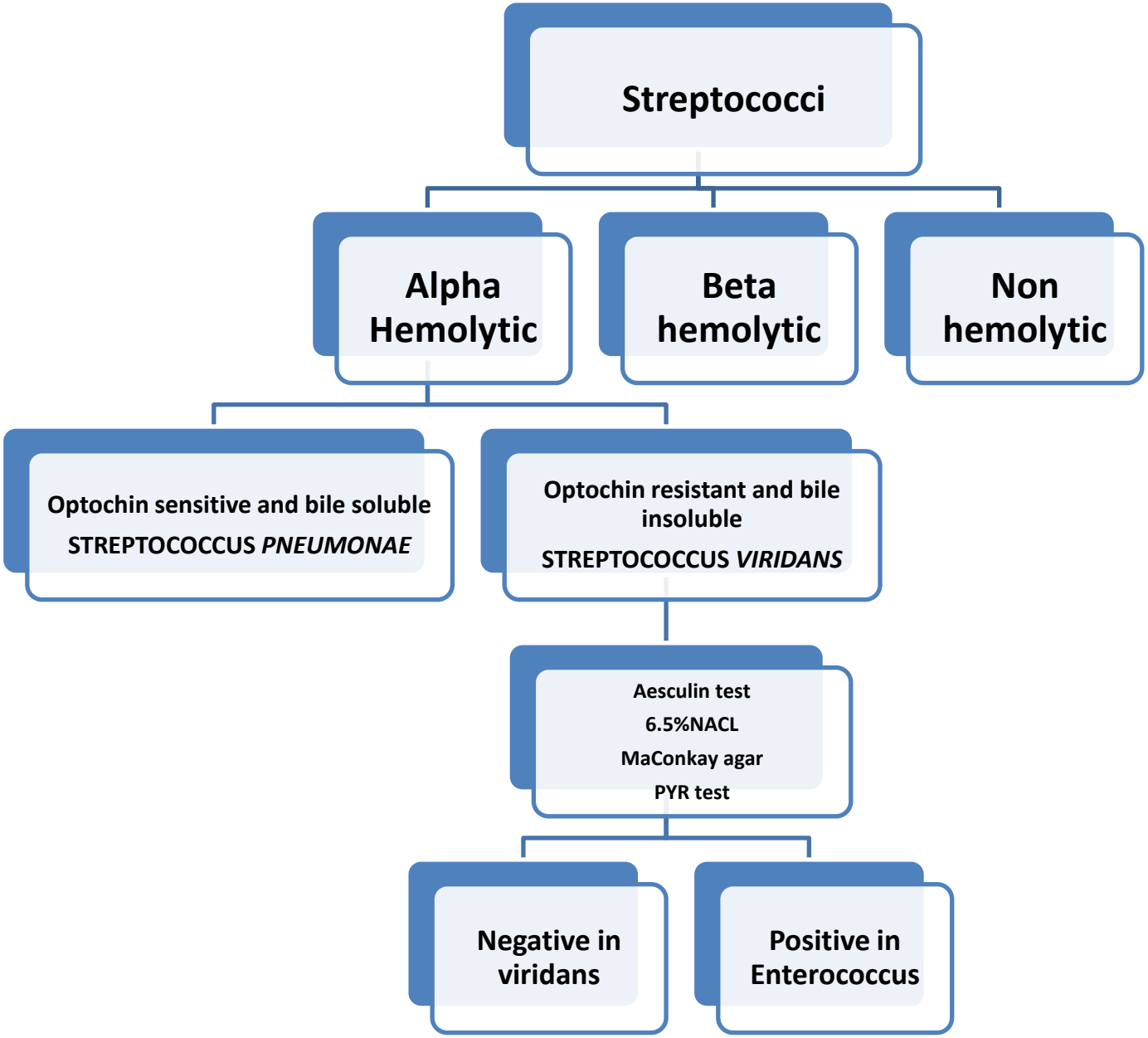
- **Optochin test : resistant to optochin**
- **Bile solubility test: Not soluble in bile**
- **Inulin fermentation: not fermenting inulin**
- **Acid production: some strains produce acids from mannitol, sorbitol , sucrose**
- **Aesculin test: negative**
- **PYRase test : negative**
- **Salt tolerance test : negative**

TREATMENT:

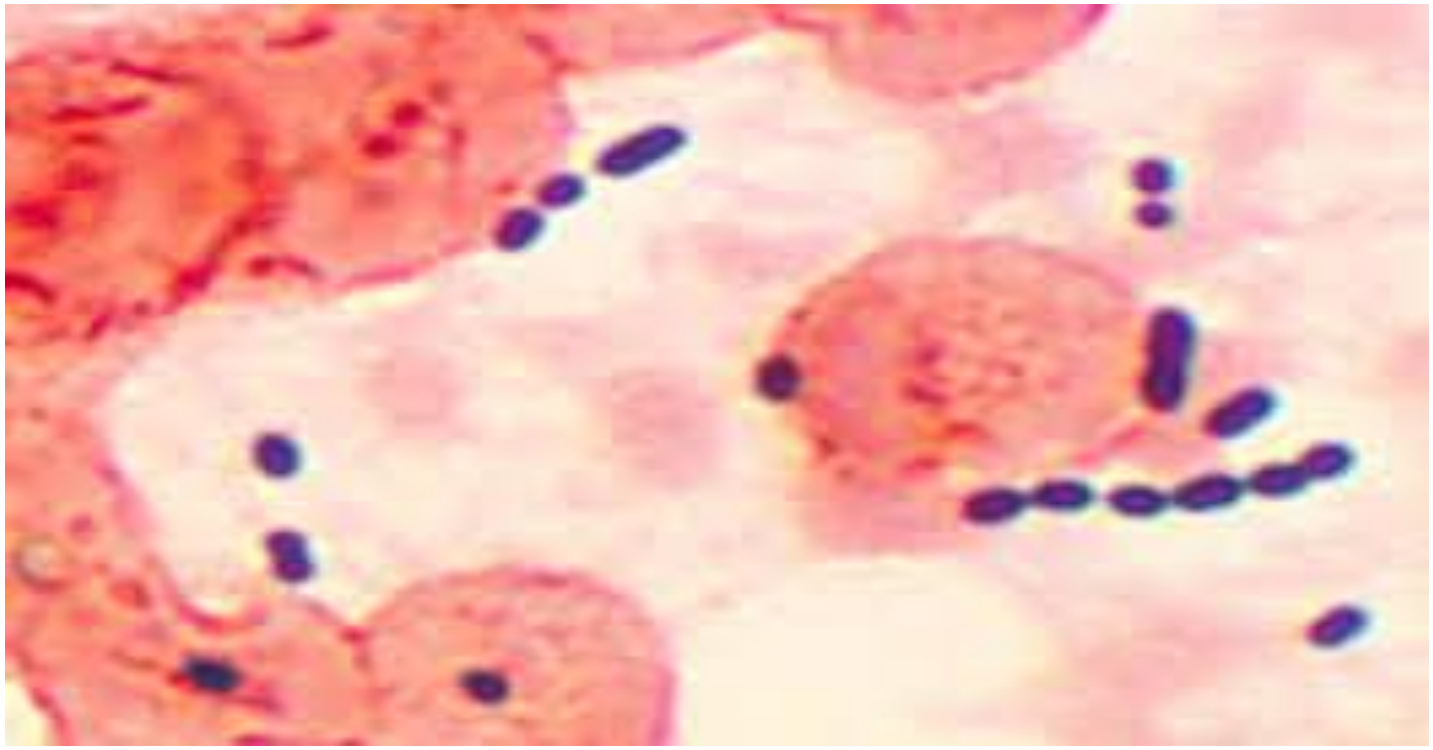
- Treated with penicillin
- Bactericidal activity is enhanced by aminoglycosides.

DIFFERENCE BETWEEN PNEUMOCOCCAI & VIRIDANS STREPTOCOCCAI

CHARACTER	PNEUMOCOCCUS	VIRIDANS. STREPT
MORPHOLOGY	Ovoid or lenceolate diplococci, short chains	Short or long chains of round cocci
CAPSULE	Present	Usually absent
COLONIES	Low convex , flattened to draughtsman	Convex
BLOOD AGAR	Narrow zone of alpha hemolysis	Wide or narrow
OPTOCHIN SENSITIVITY	Sensitive	Resistant
BILE SOLUBILITY	Soluble	Not soluble
INULIN FERMENTATION	Present	Absent
VIRULENCE IN MICE	Present	Absent


Streptococci
Alpha Hemolytic
Beta hemolytic
Non hemolytic
Optochin sensitive and bile soluble
STREPTOCOCCUS PNEUMONAE
Optochin resistant and bile insoluble
STREPTOCOCCUS VIRIDANS
Aesculin test
6.5%NACL
MaConkay agar
PYR test
Negative in viridans
Positive in Enterococcus

GROUP D Streptococci



Group D Streptococcus

- **Enterococcal**
- *Enterococcus faecalis*
- *Enterococcus faecium*

- **Non enterococcal**
- Enterococci are members of the normal flora of the colon and cause urinary, biliary, and cardiovascular infections

General characteristics

- They are very hardy organisms.
- They can grow in hypertonic (6.5%) saline or in bile and are not killed by penicillin G.
- A synergistic combination of penicillin and an aminoglycoside (e.g., gentamicin) is required to kill enterococci.
- Vancomycin -resistant enterococci (VRE) have emerged and become an important and much feared cause of life-threatening nosocomial infections.
- *Ent. faecium* are more vancomycin-resistant than are strains of *Ent. faecalis.*

General characteristics

- Non enterococcal group D streptococci, such as *Strep. bovis,* can cause similar infections but are much less hardy organisms (e.g., they are inhibited by 6.5% NaCl and killed by penicillin G).
- Hemolytic reaction of group D streptococci is variable:
- Most are α-hemolytic, but some are β-hemolytic, and others are non hemolytic.

Important features of pathogenesis by Enterococci

Organism	Type of Pathogenesis	Typical Disease	Main Site of Disease (D), Colonization (C), or Normal Flora (NF)
Ent. faecalis (group D)	Pyogenic	Urinary tract infection, endocarditis	Colon (NF)
S. bovis (group D)	Pyogenic	Endocarditis	Colon (NF)

Clinical Findings

- Enterococci cause **urinary tract infections,** especially in hospitalized patients.
- Indwelling urinary catheters and urinary tract instrumentation are important predisposing factors.
- Enterococci also cause endocarditis, particularly in patients who have undergone gastrointestinal or urinary tract surgery or instrumentation.
- They also cause intra-abdominal and pelvic infections, typically in combination with anaerobes.

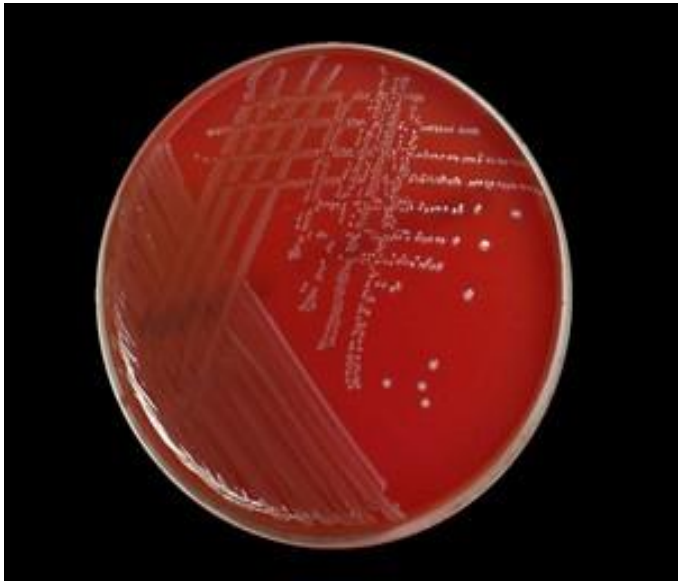
Clinical Findings

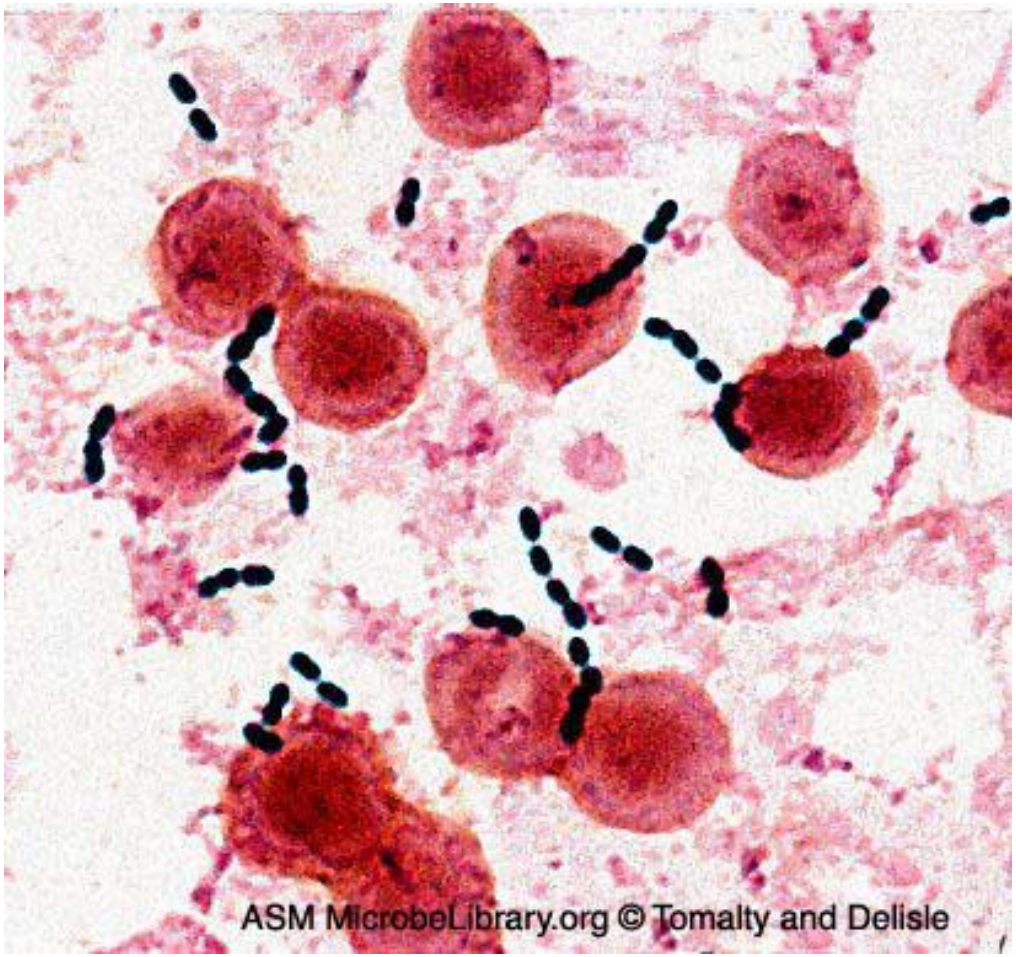
- *Strep. bovis,* a non enterococcal group D streptococcus, causes **endocarditis,** especially in patients with carcinoma of the colon.

- This association is so strong that patients with *Strep. bovis,* bacteremia or Endocarditis should be investigated for the presence of colonic carcinoma.

Lab diagnosis - Enterococcus

- Specimens: urine, pus, blood.
- Microscopy: Gram stain - GPC in pairs or short chains .
- Culture: BA - alpha / beta / no hemolysis

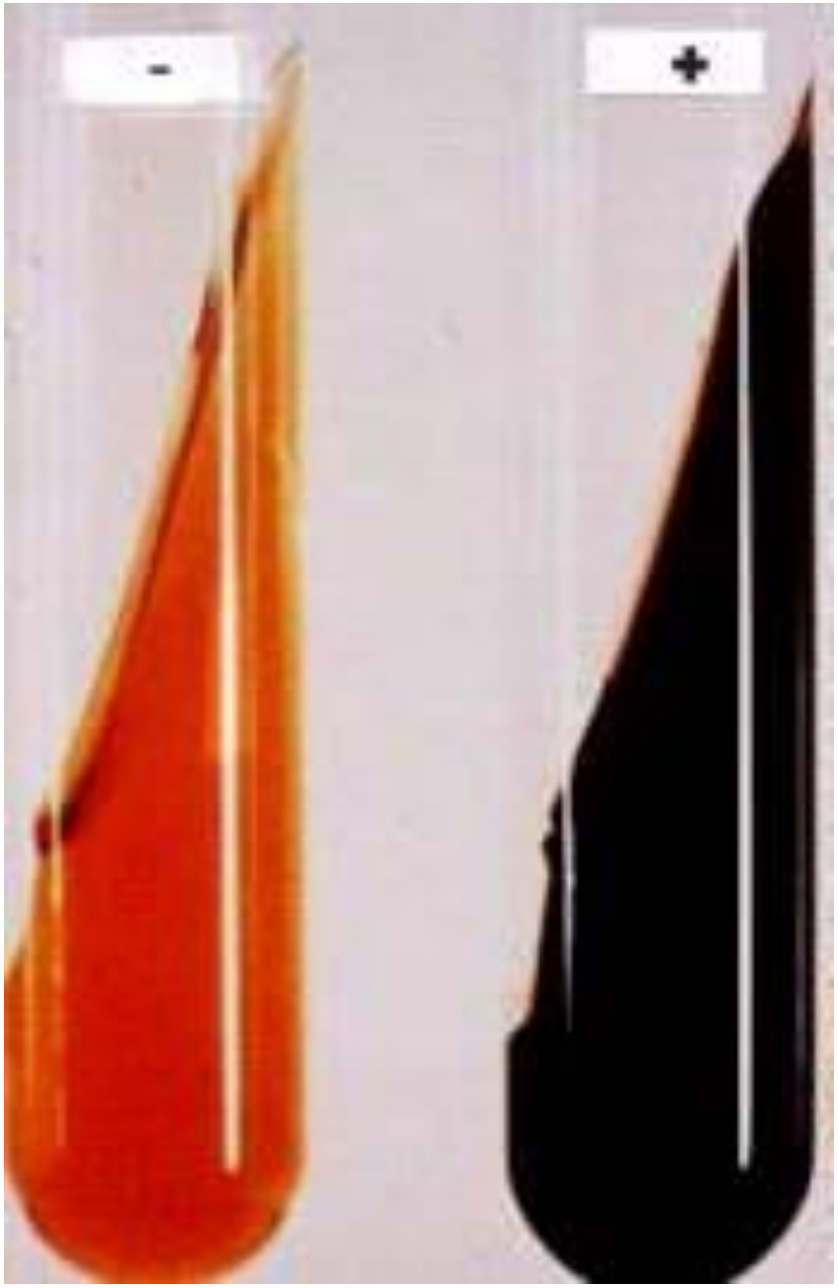



ASM MicrobeLibrary.org © Tomalty and Delisle

Laboratory diagnosis

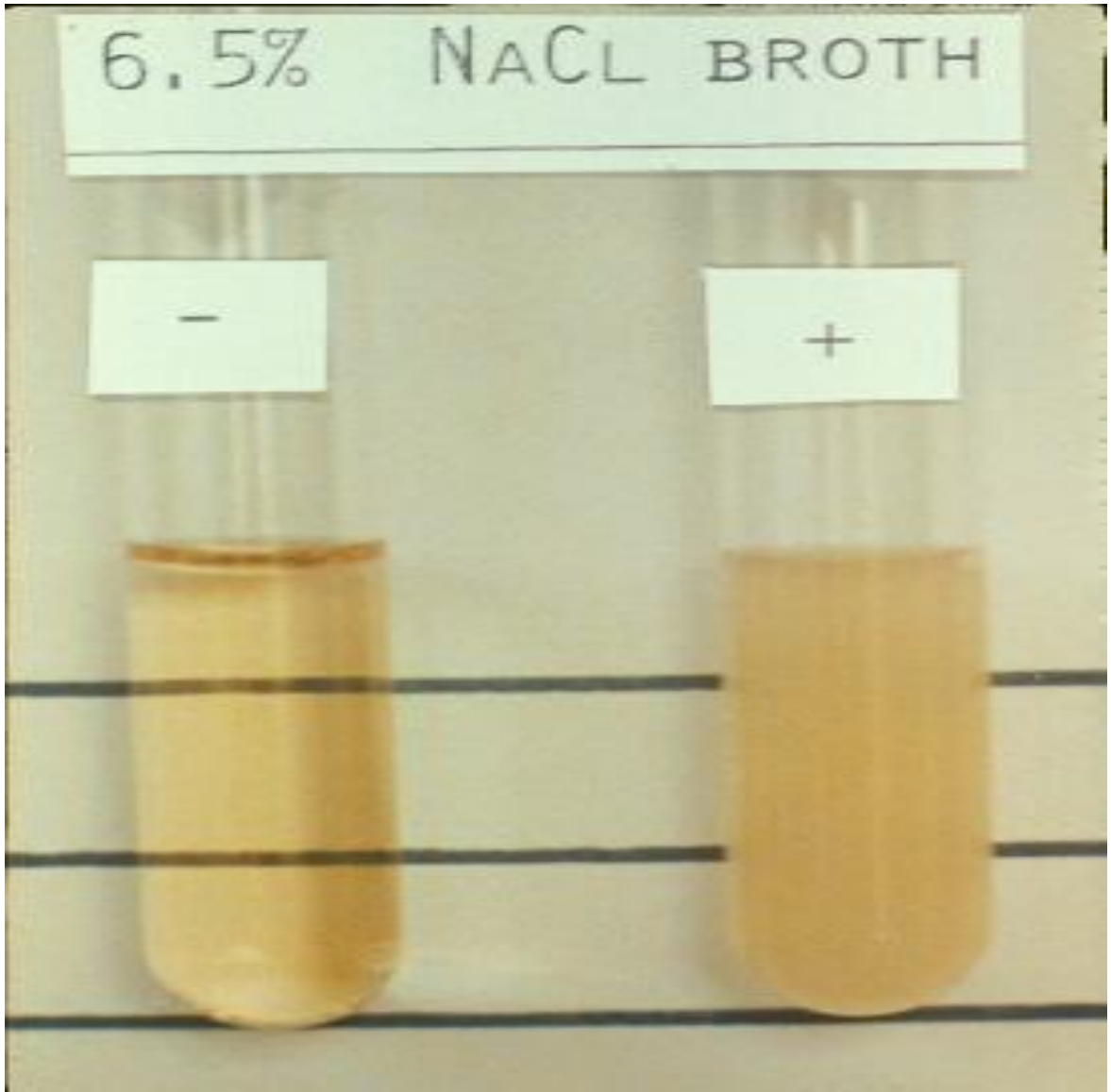
- They are catalase negative.
- Gives magenta coloured colonies on MacConkey Agar.
- Group D streptococci hydrolyze esculin in the presence of bile(i.e., they produce a black pigment on bile-esculin agar).

- The group D organisms are further subdivided: the enterococci grow in hypertonic (6.5%) NaCl, whereas the non enterococci do not.

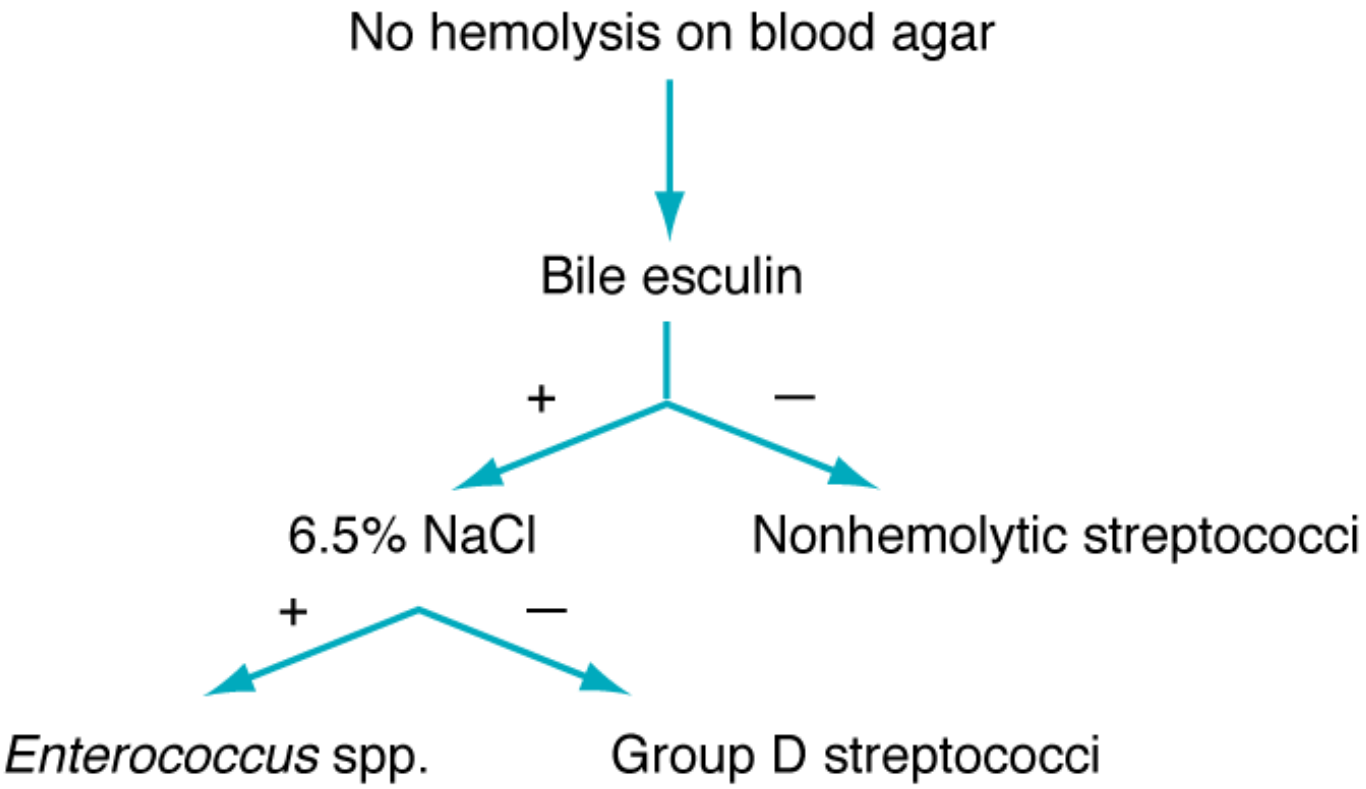


Esculin Bile Assay

6.5 % NaCl Broth



Identification Schema



Schema to differentiate *Enterococcus* and Group D streptococci from other nonhemolytic streptococci

Resistance mechanism

- 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.*
- VREs are now an important cause of nosocomial infections.
- Non enterococcal group D streptococci (e.g., *Strep. bovis*) are not highly resistant and can be treated with penicillin G.

Treatment for Vancomycin resistant Enterococci

- There is no reliable antibiotic therapy for these organisms.
- At present, two drugs are being used to treat infections caused by VRE: linezolid (Zyvox) and daptomycin (Cubicin).