Chapter 3

Gpositive cocci

2-Streptococcus

Pharmaceutical

Microbiology

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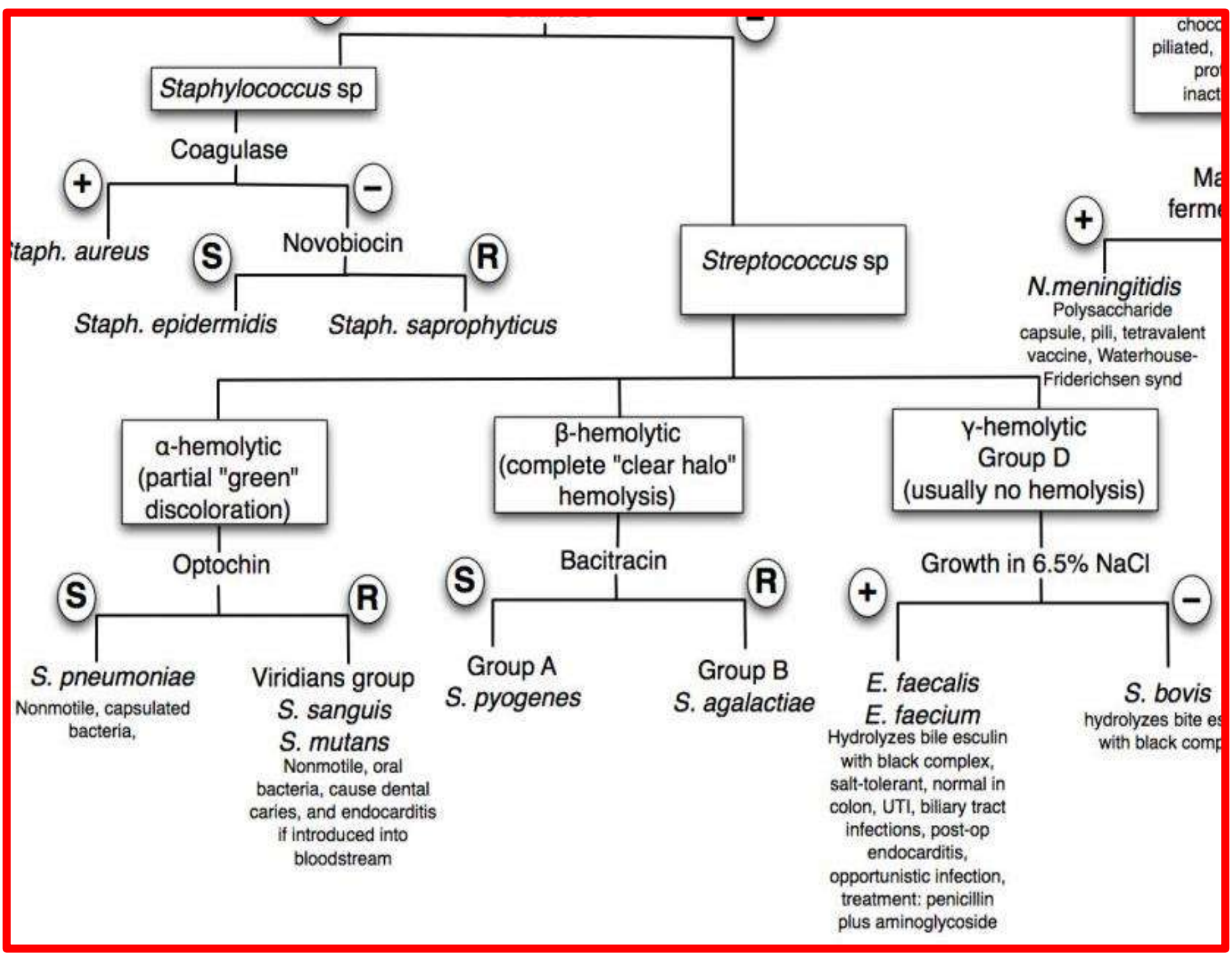

Staphylococcus sp
Coagulase
+
−
taph. aureus
S
Novobiocin
R
Staph. epidermidis
Staph. saprophyticus
Streptococcus sp
α-hemolytic (partial "green" discoloration)
β-hemolytic (complete "clear halo" hemolysis)
γ-hemolytic Group D (usually no hemolysis)
Optochin
S
R
S. pneumoniae
Nonmotile, capsulated bacteria,
Viridians group
S. sanguis
S. mutans
Nonmotile, oral bacteria, cause dental caries, and endocarditis if introduced into bloodstream
Bacitracin
S
R
Group A
S. pyogenes
Group B
S. agalactiae
Growth in 6.5% NaCl
+
−
E. faecalis
E. faecium
Hydrolyzes bile esculin with black complex, salt-tolerant, normal in colon, UTI, biliary tract infections, post-op endocarditis, opportunistic infection, treatment: penicillin plus aminoglycoside
S. bovis
+
N.meningitidis
Polysaccharide capsule, pili, tetravalent vaccine, Waterhouse-Friderichsen synd

Streptococcus

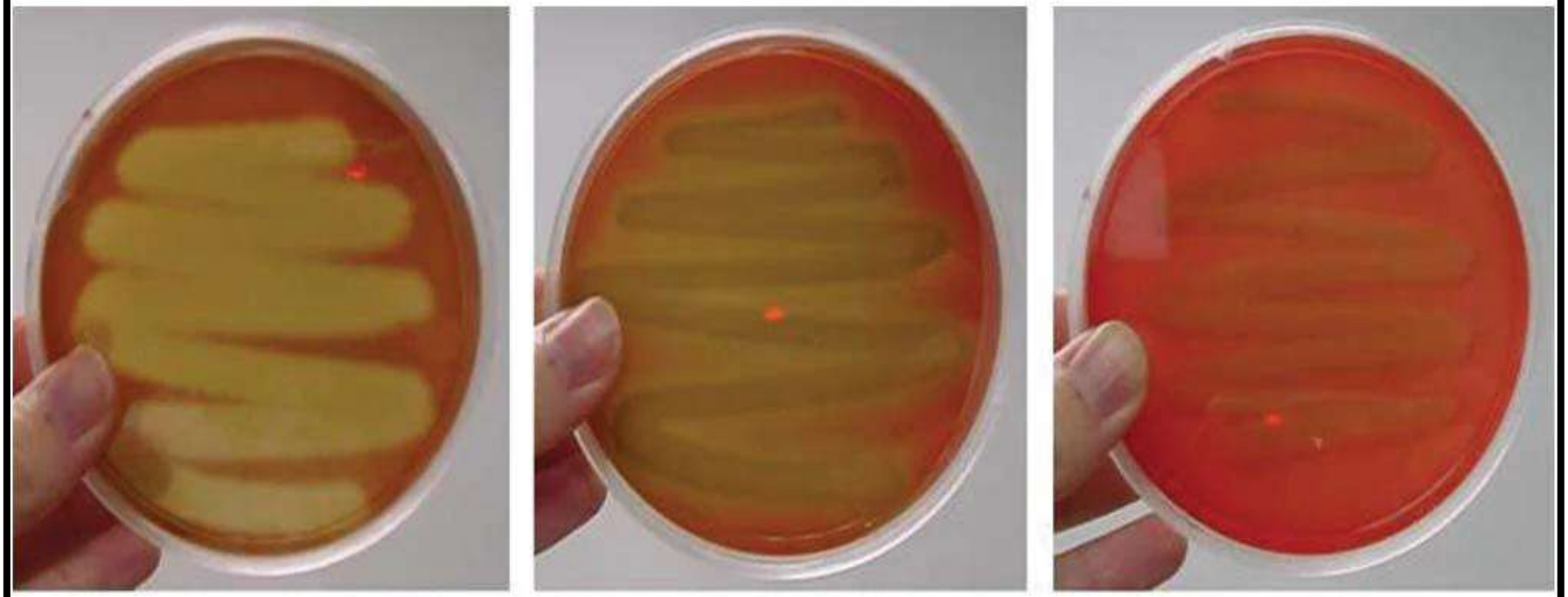
Classification oF Streptococci

- The classification of streptococci into major categories has been based on a series of observations over many years:
- (A) Colony morphology and hemolytic reactions on blood agar,
- (B) Serologic specificity of the cell wall group-specific substance (Lancefield antigens) and other cell wall
- (C) or capsular antigens,
- (D) Biochemical reactions and resistance to physical and chemical factors,

- # A. Hemolysis
- Many streptococci are able to hemolyze RBCs in vitro in varying degrees.
- Complete disruption of erythrocytes with clearing of the blood around the bacterial growth is called **β - hemolysis.**
- Incomplete lysis of erythrocytes with reduction of hemoglobin and the formation of green pigment is called **α - hemolysis.**
- Other streptococci are nonhemolytic (sometimes called **γ-hemolysis).**
- *S. pyogenes* typically produces large (1 cm in diameter) zones of β hemolysis around colonies greater than 0.5 mm in diameter.

Hemolysis test for streptococcal bacterial types

Hemolysis of Streptococci- Types and Examples



Beta Hemolysis

Alpha Hemolysis

Gamma Hemolysis

- ## B. Group-Specific Substance (Lancefield Classification)

- This carbohydrate is contained in the cell wall of many streptococci and forms the basis of serologic grouping into **Lancefield groups A – H** and **K – U.** The serologic specificity of the group specific carbohydrate is determined by **an amino sugar.**

- ## C. Capsular Polysaccharides

- The **antigenic specificity of the capsular polysaccharides** is used to classify ***Streptococcus pneumoniae*** **into more than 90 types** and to **type the group B streptococci (** ***Streptococcus agalactiae*** **).**

D. Biochemical Reactions

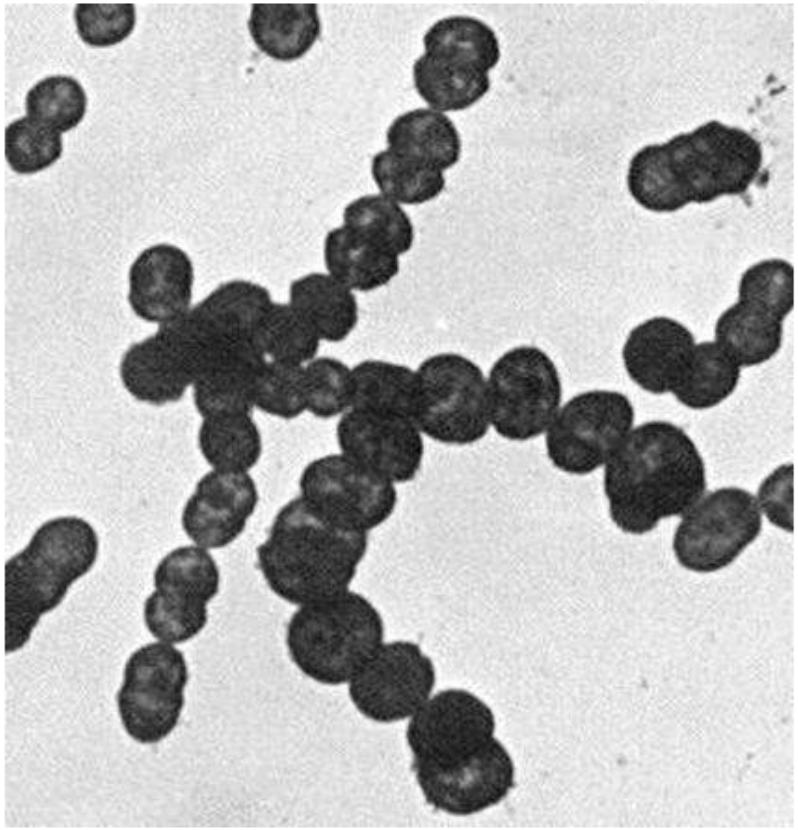
- Biochemical tests include
- sugar fermentation reactions,
- tests for the presence of enzymes, and
- tests for susceptibility or resistance to certain chemical agents.
- Biochemical tests are most often used to classify streptococci after the colony growth and hemolytic characteristics have been observed.
- Biochemical tests are used for species that typically do not react with the commonly used antibody preparations for the group-specific substances, groups A, B, C, F, and G. For example, the viridans streptococci are α-hemolytic

1- Streptococcus pyogenes

- Most streptococci that contain the group A antigen are *S pyogenes.*
- It is a prototypical human pathogen.
- *S. pyogenes* is the main human pathogen associated with local or systemic invasion and poststreptococcal immunologic disorders.
- They are usually are susceptible to bacitracin.

Streptococcus pyogenes

- Group A Streptococcus
- Gram positive
- Non-motile
- Non-spore forming
- Occurs in chains
- Has a capsule
- Adheres to surfaces such as cell walls

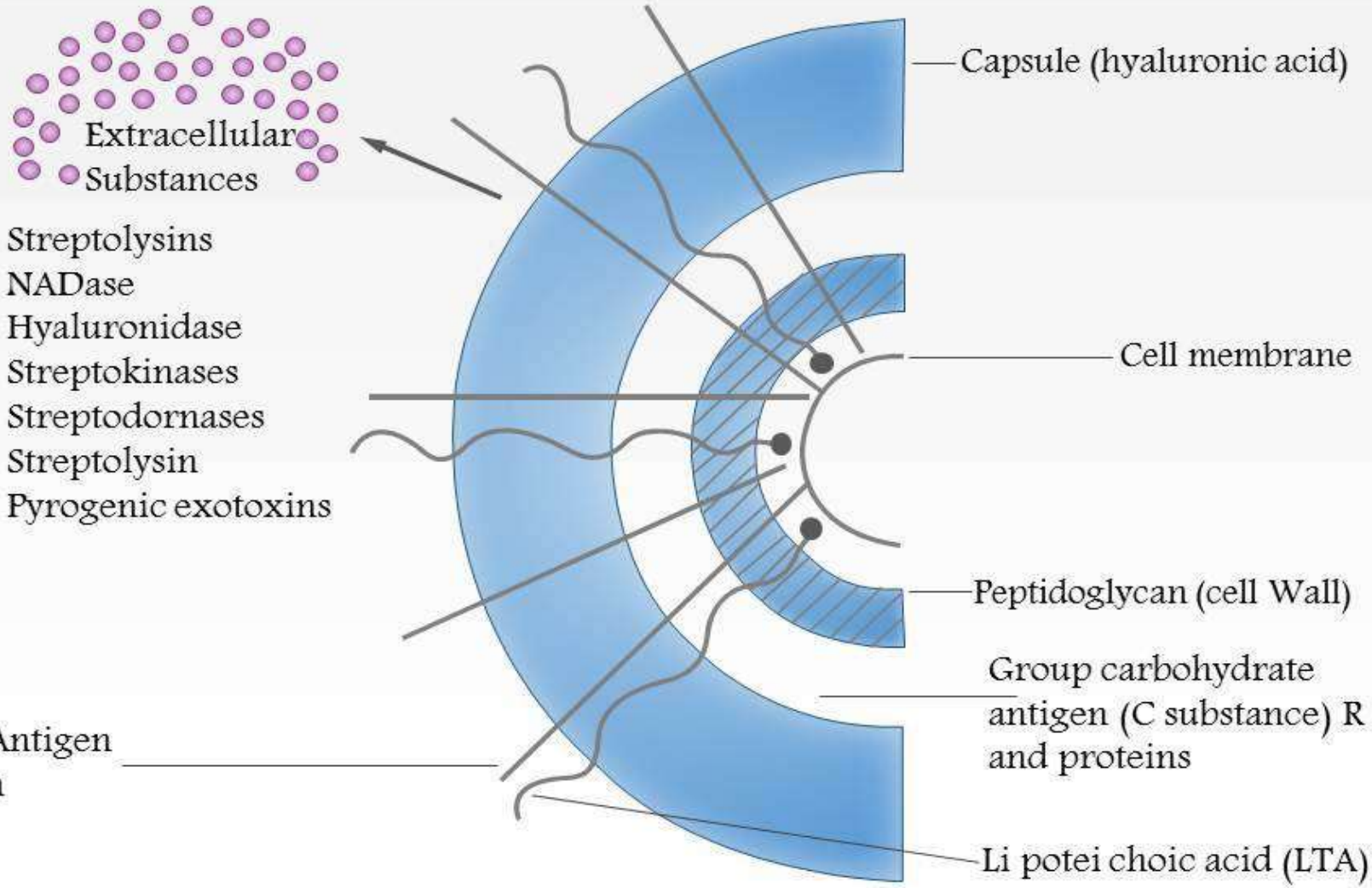


Morphology and Identification

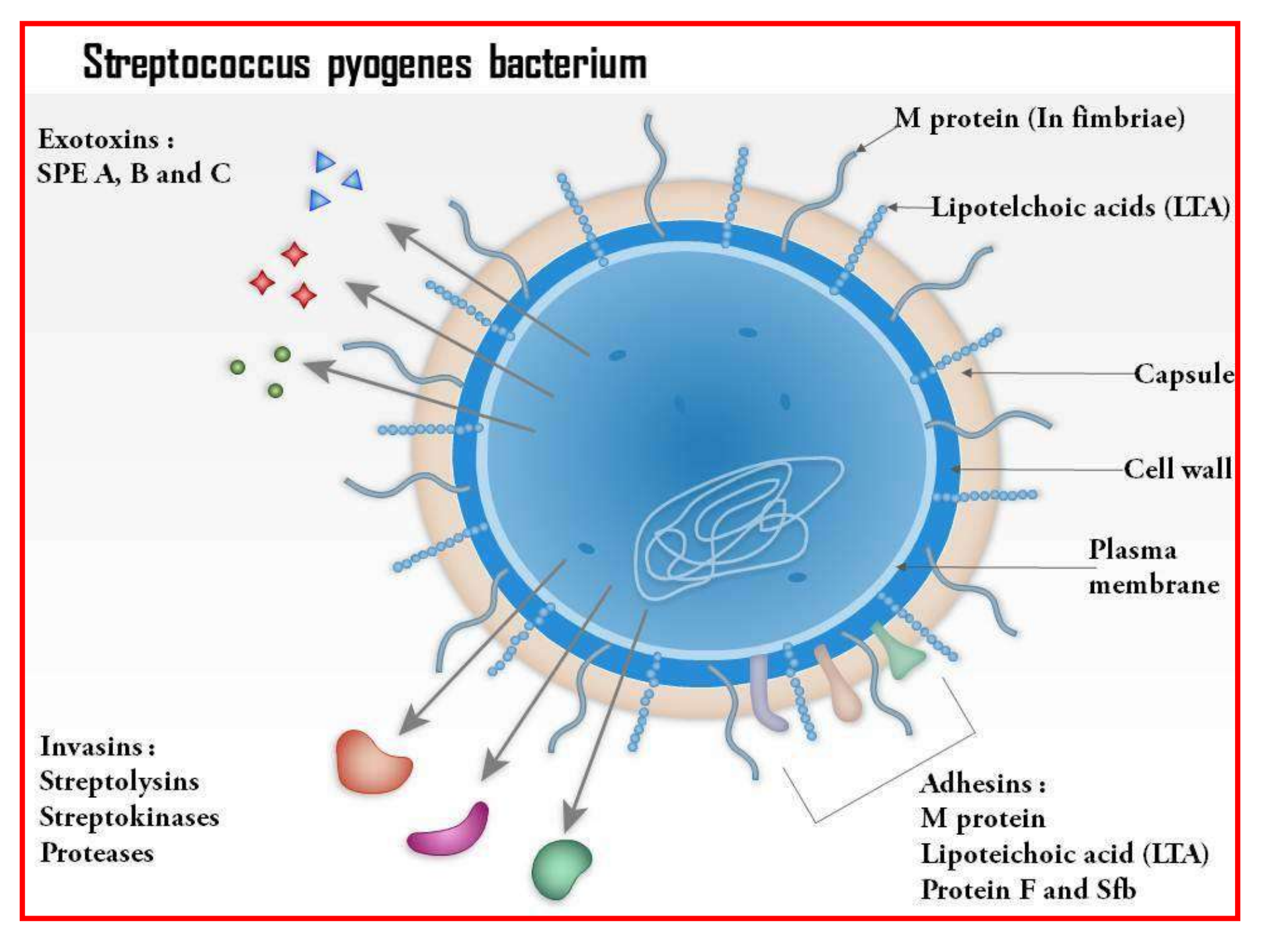
- A. Typical Organisms
- Streptococci are gram positive; Most group A strains produce capsules composed of hyaluronic acid.
- The hyaluronic acid capsule likely plays a greater role in virulence than is generally appreciated and together with M protein is believed to be an important factor in the resurgence of rheumatic fever (RF).
- The capsule binds to hyaluronic-acid-binding protein, CD44, present on human epithelial cells

- Capsules of other streptococci (eg, *S agalactiae* and *S .pneumoniae*) are different.
- The *S. pyogenes* cell wall contains proteins (M, T, R antigens), carbohydrates (group specific), and peptidoglycans.
- Hair like pili project through the capsule of group A streptococci.
- The pili consist partly of M protein and are covered with lipoteichoic acid. The latter is important in the attachment of streptococci to epithelial cells.

Streptococcus Pyogenes



Streptococcus pyogenes bacterium



- **Toxins and Enzymes**
- More than 20 extracellular products that are antigenic are elaborated by *S pyogenes*, including the following.
- A. Streptokinase (Fibrinolysin)
- B. Deoxyribonucleases
- C. Hyaluronidase
- D. Pyrogenic Exotoxins
- E. Hemolysin

Streptococcus pyogenes

Enzymes and toxins

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.

Streptodornase (DNases A to D)

Decreases viscosity of DNA suspension. A mixture of this and streptokinase is used in enzymatic debridement-liquifies exudates and facilitates removal of pus and necrotic tissue.

Hyaluronidase (spreading factor):

Destroys connective tissue and aids in spreading infecting bacteria.

A. Streptokinase (Fibrinolysin)

- Streptokinase is produced by many strains of group **A β-hemolytic streptococci.**
- **It transforms the plasminogen of human plasma into plasmin, an active proteolytic enzyme that digests fibrin and other proteins, allowing the bacteria to escape from blood clots**.

B. Deoxyribonucleases

- Streptococcal deoxyribonucleases A, B, C, and D degrade DNA (DNases) and similar to streptokinase facilitate the spread of streptococci in tissue by liquefying pus.
- Mixtures of streptokinase and DNases are used in "enzymatic debridement."
- They help to liquefy exudates and facilitate removal of pus and necrotic tissue; antimicrobial drugs thus gain better access, and infected surfaces recover more quickly.

C. Hyaluronidase

- Hyaluronidase splits hyaluronic acid, an important component of the ground substance of connective tissue.
- Thus, hyaluronidase aids in spreading infecting microorganisms (spreading factor).
- Hyaluronidases are antigenic and specific for each bacterial or tissue source.
- After infection with hyaluronidase-producing organisms, specific antibodies are found in the serum.

D. Pyrogenic Exotoxins

- **Pyrogenic exotoxins** are elaborated by ***S. pyogenes.*** There are **three antigenically distinct streptococcal pyrogenic exotoxins (Spe): A, B, and C.**
- **Spe A** has been most widely studied.
- It is produced by **group A streptococci that carry a lysogenic phage.**
- The streptococcal pyrogenic exotoxins have been associated with **streptococcal scarlet fever.**

Scarlet fever

- Strains infected with specific phage
  - Erythrogenic toxin
- Sandpaper-like rash
  - Spreads from chest across body
  - Strawberry red tongue with white coating
  - Skin peels away similar to scaled skin syndrome
- Children are at higher risk

E. Hemolysins

- The β-hemolytic group A *S pyogenes* **elaborates two hemolysins (streptolysins)** that not only lyse the membranes of erythrocytes but also damage a variety of other cell types.
- **Streptolysin O** is a protein .it combines quantitatively with **antistreptolysin O (ASO),** an antibody that appears in humans after infection with any streptococci that produce streptolysin O.

Pathogenesis and Clinical Findings

- A. Diseases Attributable to Invasion by *S. pyogenes*,

1. Erysipelas—If **the portal of entry is the skin, erysipelas results, with massive brawny edema and a rapidly advancing margin of infection.**

2.Necrotizing fasciitis (streptococcal gangrene)—

- There is **extensive and very rapidly spreading necrosis of the skin, tissues, and fascia.**

3. Cellulitis—Streptococcal cellulitis is an acute, rapidly spreading infection of the skin and subcutaneous tissues. It follows infection associated with mild trauma, burns, wounds, or surgical incisions.

- Pain, tenderness, swelling, and erythema occur. Cellulitis is differentiated from erysipelas by clinical findings: **In cellulitis, the lesion is not raised, and the line between the involved and uninvolved tissue is indistinct**.

4. Puerperal fever—

If the streptococci enter **the uterus after delivery**, puerperal fever develops, which is essentially a septicemia originating in the infected wound (endometritis).

5. Bacteremia or sepsis—

Infection of **traumatic or surgical wounds with streptococci results in bacteremia, which can rapidly be fatal**.

S. pyogenes bacteremia can also occur with skin infections, such as cellulitis .

Erispelas and cellulitis

Necrotizing fasciitis (streptococcal gangrene)

B. Diseases Attributable to Local Infection With *S. pyogenes* and by their products

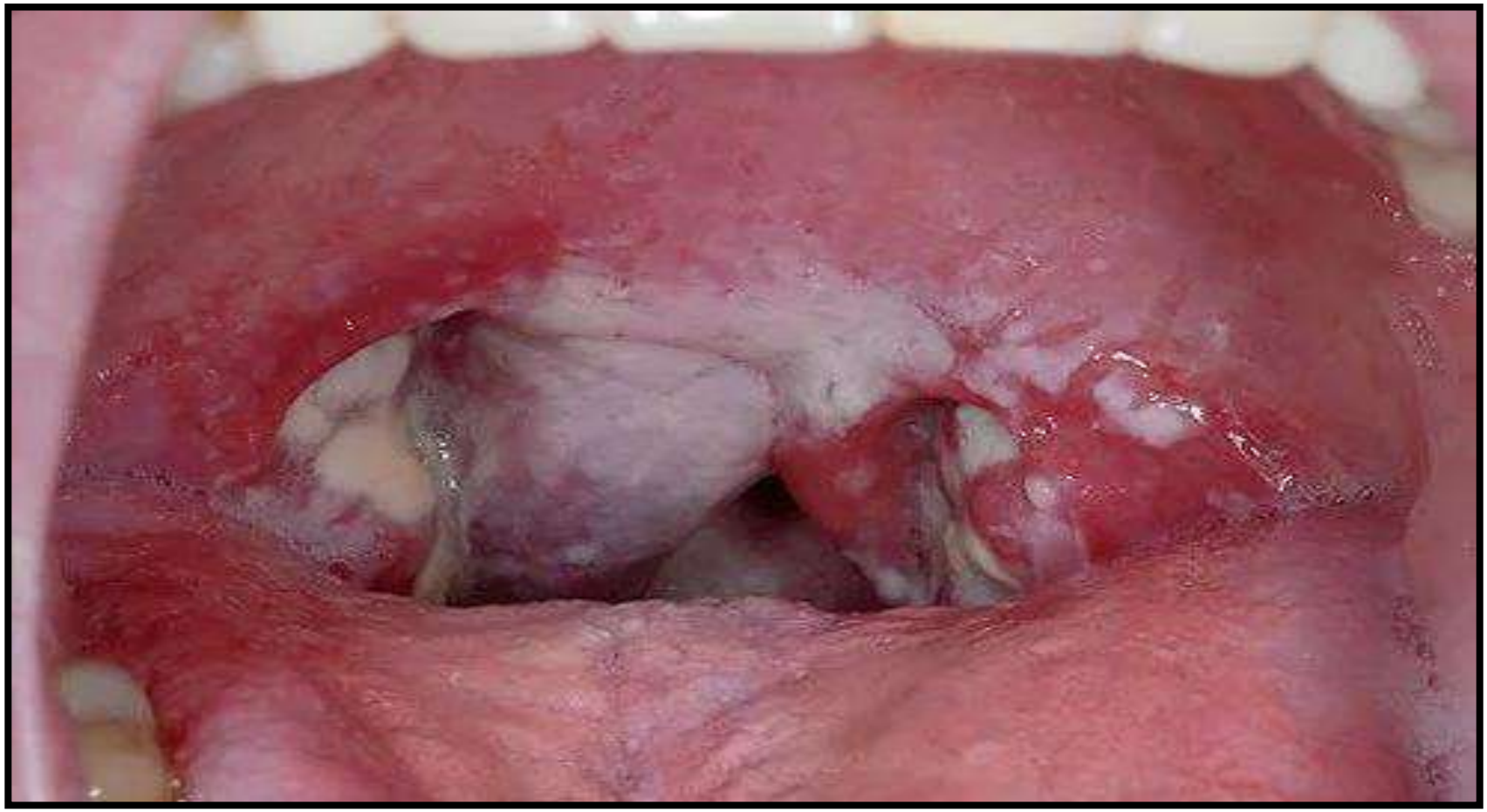
1. Streptococcal sore throat

The most common infection caused by β-hemolytic *S pyogenes* is streptococcal sore throat or pharyngitis.

S. pyogenes adhere to the pharyngeal epithelium by means of lipoteichoic acid–covered surface pili and by means of hyaluronic acid in encapsulated strains.

The glycoprotein fibronectin on **epithelial cells** probably **serves as lipoteichoic acid ligand.**

1-Streptococcal sore throat



2. Streptococcal pyoderma

- Local infection of **superficial layers of skin, especially in children, is called non bollus impetigo.**
- It consists of **superficial vesicles that break down. It spreads by continuity and is highly communicable, especially in hot, humid climates.**

3- Scarlet fever

- Pyrogenic exotoxins A–C also cause scarlet fever in association with *S pyogenes* pharyngitis or with skin or soft tissue infection.
- The pharyngitis may be severe.
- The rash appears on the trunk after 24 hours of illness and spreads to involve the extremities.

C. Poststreptococcal Diseases

(Glomerulonephritis, Rheumatic Fever)

- **1. Acute glomerulonephritis—**

- This sometimes **develops 1–4 weeks after *S pyogenes* skin infection (pyoderma, impetigo) or pharyngitis.**

- **Some strains are particularly nephritogenic.**

2. Rheumatic fever

- This is the **most serious sequela of *S. pyogenes* because it results in damage to heart muscle and valves.**
- **Certain strains of group A streptococci contain cell membrane antigens that cross-react with human heart tissue antigens**.
- The onset of rheumatic fever is often preceded by *S pyogenes* pharyngitis 1–4 weeks earlier, although the infection may be mild and may not be detected.
- In general, however, **patients with more severe streptococcal sore throats have a greater chance of developing rheumatic fever.**
-

RHEUMATIC FEVER

DUCKETT-JONES DIAGNOSTIC CRITERIA

MAJOR CRITERIA

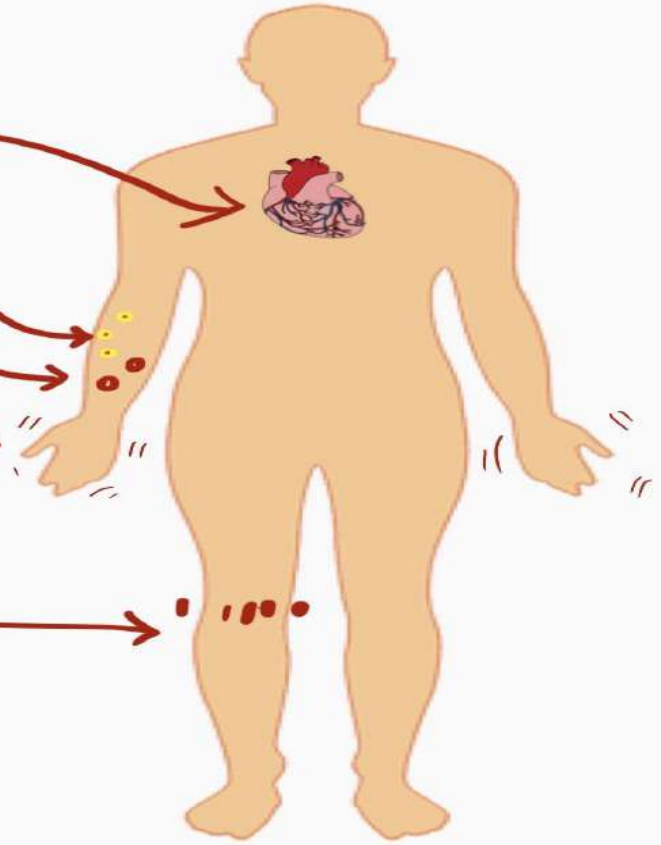
"CASES" is the Mnemonic

Carditis
Arthritis
Subcutaneous nodules
Erythema marginatum
Sydenham's chorea

MINOR CRITERIA

"FRAPP" is the Mnemonic

Fever
Raised ESR/CRP
Arthralgia
Prolonged PR Interval
Previous RF



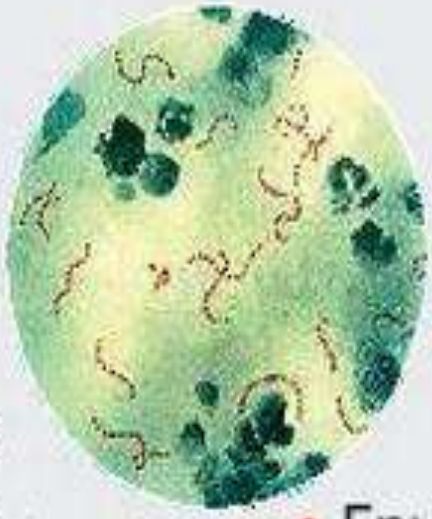
There must be evidence of streptococcal infection plus:

2 major or 1 major + 2 minor

Rheumatic fever

Signs and symptoms

- Fever
- Painful and tender joints
- Red, hot or swollen joints
- Small, painless bumps beneath the skin
- Chest pain
- Heart murmur
- Fatigue
- Outbursts of unusual behavior



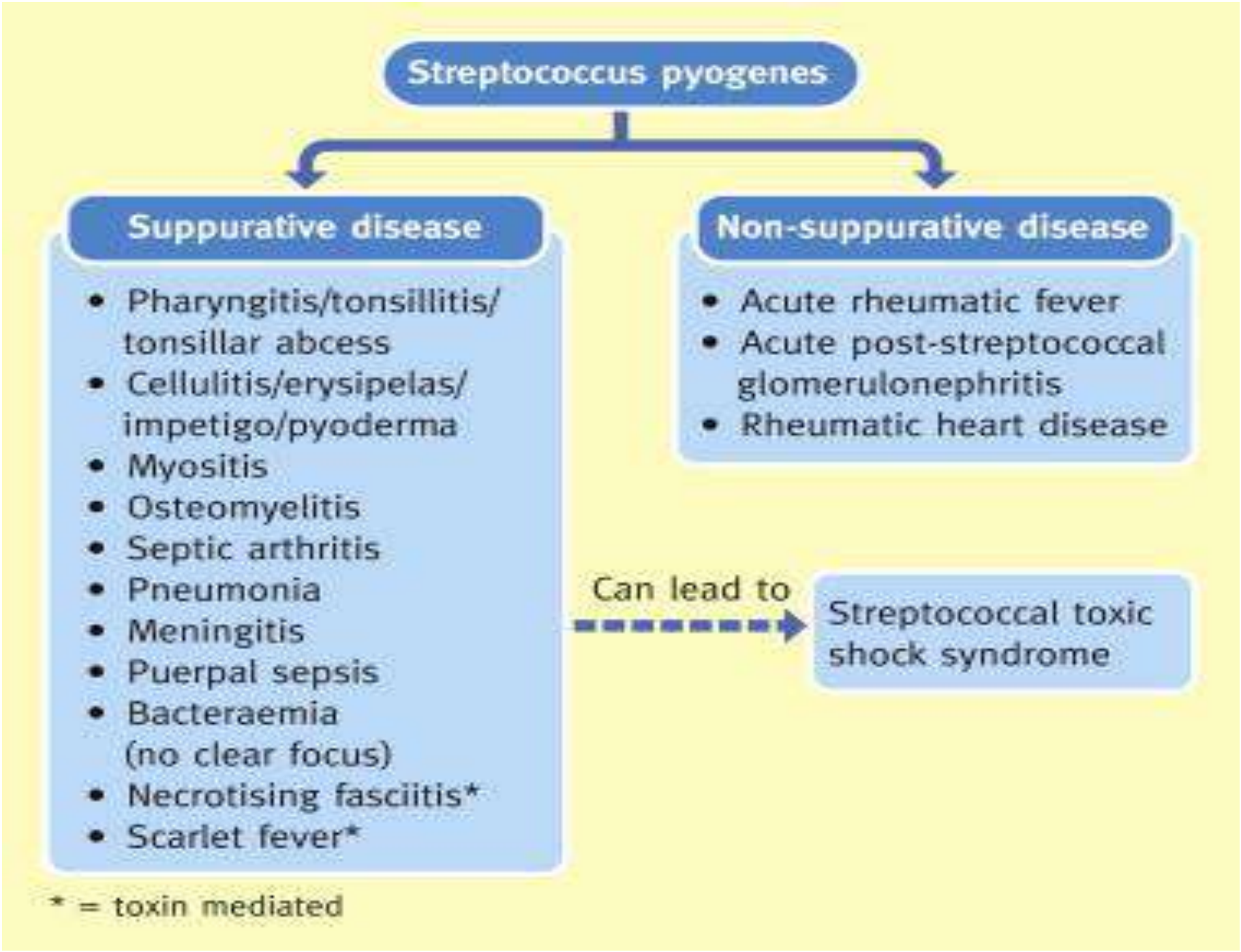
Risk factors

- Family history
- Certain strains of strep bacteria
- Environmental factors

Complications

- Valve stenosis
- Valve regurgitation
- Damage to heart muscle

- **Typical symptoms and signs of rheumatic fever** include :
- **fever, malaise, nonsuppurative polyarthritis,**
- **and evidence of inflammation of all parts of the heart (endocardium, myocardium, and pericardium).**
- It is therefore **important to protect such patients from recurrent *S pyogenes* infections by prophylactic penicillin administration.**


Streptococcus pyogenes
Suppurative disease
Pharyngitis/tonsillitis/ tonsillar abcess
Cellulitis/erysipelas/ impetigo/pyoderma
Myositis
Osteomyelitis
Septic arthritis
Pneumonia
Meningitis
Puerpal sepsis
Bacteraemia (no clear focus)
Necrotising fasciitis*
Scarlet fever*
Non-suppurative disease
Acute rheumatic fever
Acute post-streptococcal glomerulonephritis
Rheumatic heart disease
Can lead to
Streptococcal toxic shock syndrome
* = toxin mediated

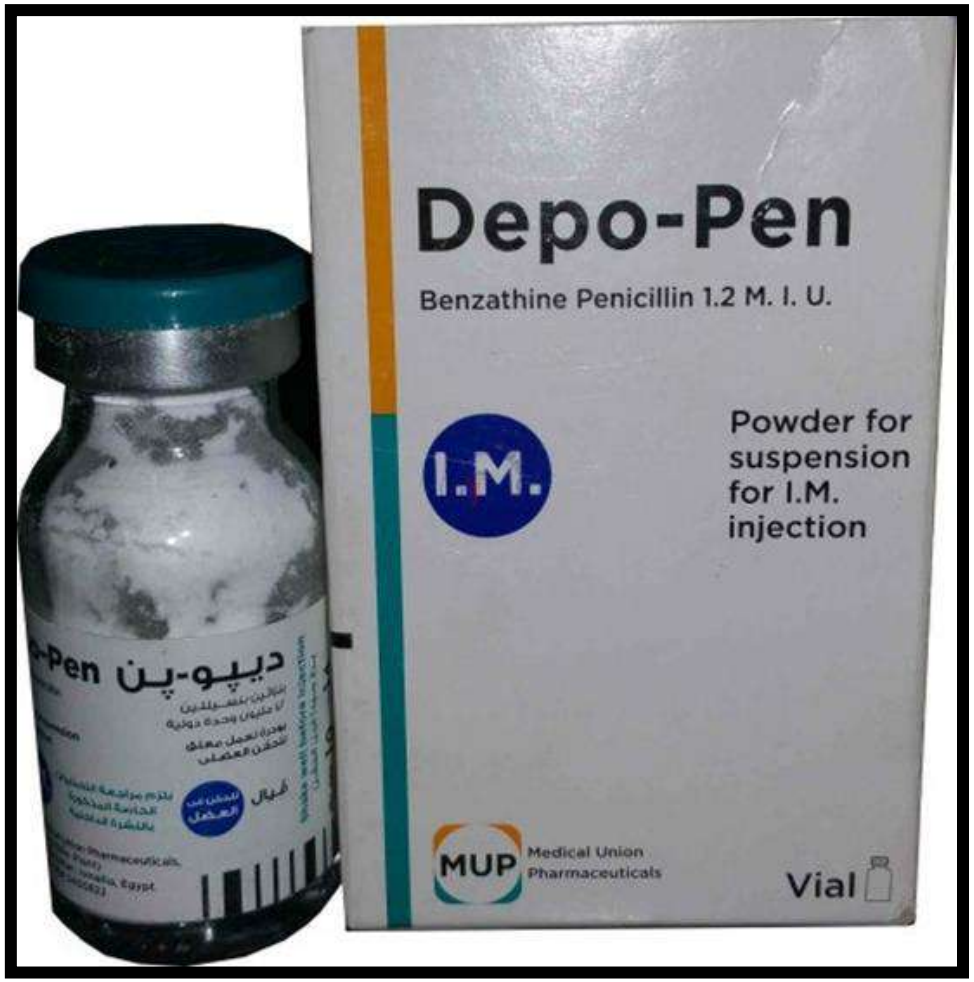
Treatment

- All *S pyogenes* are susceptible to penicillin G.
- Macrolides, such as erythromycin and clindamycin, have often been recommended for penicillin allergic patients and for patients with necrotizing fasciitis.
- Antimicrobial drugs have no effect on established glomerulonephritis and rheumatic fever.

- This requires maintenance of adequate penicillin levels in tissues for 10 days (eg, benzathine penicillin G given once intramuscularly).
- Erythromycin is an alternative drug, although many S. pyogenes are now resistant.
- Antimicrobial drugs are also very useful in preventing reinfection with β-hemolytic group A streptococci in patients with rheumatic fever.

- Antistreptococcal chemoprophylaxis in persons who have suffered an attack of rheumatic fever.
- This involves giving one injection of benzathine penicillin G... IM every 3–4 weeks or daily oral penicillin or oral sulfonamide.

Penicillin types



Streptococci

S. pyogenes (group A)	Pharyngitis, scarlet fever, pyoderma, erysipelas, cellulitis, necrotizing fasciitis, streptococcal toxic shock syndrome, bacteremia, rheumatic fever, glomerulonephritis
S. agalactiae (group B)	Neonatal infections (meningitis, pneumonia, bacteremia), urinary tract infections, amnionitis, endometritis, wound infections, pneumonia, bacteremia
Other β-hemolytic streptococci	Pharyngitis, abscess formation, bacteremia
Viridans group streptococci	Bacteremia, endocarditis, abscess formation, dental caries
S. pneumoniae	Pneumonia, meningitis, sinusitis, otitis media, bacteremia

Concept Checks

- **Streptococci** are a large group of gram-positive organisms that are catalase negative and tend to grow in pairs and long chains.

Major classifications include **the type of hemolysis (α, β, or no hemolysis [γ]), conditions for growth, and capacity to cause disease**.

- **S pyogenes** (group A β-hemolytic streptococcus) **is the most virulent pathogen in the Streptococcus family.**

It elaborates numerous proteins, **hemolysins, enzymes, and toxins responsible for the broad range of suppurative (eg, cellulitis) and immunologic diseases** (poststreptococca GN, RF) associated with this organism.

2-Streptococcus agalactiae

- **These are the group B streptococci.** They **typically are β-hemolytic.**
- Group B streptococci are **part of the normal vaginal flora and lower gastrointestinal tract in 5–30% of women**.
- **Group B streptococcal infection during the first month of life may present as fulminant sepsis, meningitis, or respiratory distress syndrome.**

3- Streptococci Viridans

- The **viridans streptococci** are the most prevalent members of the normal microbiota of the upper respiratory tract and are important for **the healthy state of the mucous membranes there.**
- They may reach the bloodstream as a result of trauma and **are a principal cause** of endocarditis on abnormal heart valves.

- (eg, *S mutans*) synthesize large polysaccharides such as dextrans or levans from sucrose and contribute importantly to the genesis of dental caries.
- **Subacute endocarditis** often **involves abnormal valves** (congenital deformities and rheumatic or atherosclerotic lesions).,

- **Subacute endocarditis** is most frequently caused by members of the **normal microbiota of the respiratory or intestinal tract** that have accidentally reached the blood.
- **After dental extraction, at least 30% of patients have viridans streptococcal bacteremia.**

4-Streptococcus pneumoniae

- The pneumococci (*S. pneumoniae*) are gram-positive diplococci, often lancet shaped or arranged in chains, possessing a capsule of polysaccharide that permits typing with specific antisera.
- Pneumococci are normal inhabitants of the upper respiratory tract of 5–40% of humans and can cause pneumonia, sinusitis, otitis, bronchitis, bacteremia, meningitis, and other infectious processes.

Treatment

- Because pneumococci are susceptible to many antimicrobial drugs, early treatment usually results in rapid recovery, and antibody response seems to play a much diminished role.
- Penicillin G has been the drug of choice.
- Some penicillin-resistant strains are resistant to cefotaxime.

- Resistance to tetracycline, erythromycin, and fluoroquinolones also occurs.
- Pneumococci remain susceptible to vancomycin.
- Because resistance profiles are not predictable, routine susceptibility testing should be performed for all pneumococcal infections

- End of chapter 3 (G positive cocci)