Lesson 9.

The main principles, aim and tasks of microbiological diagnostics. Microbiology diagnosis of diseases, caused by Gram positive cocci (staphylococci, streptococci and enterococci)

Discussed questions:

1. The main tasks of special medical microbiology.
2. Importance of selection of pathological material for clinical diagnosis. Collection of pathological material, storage, sending to the laboratory. Disinfection of pathological material left after the examination.
3. Gram-positive cocci, the causative agents of purulent-inflammatory processes
4. Staphylococci, classification, morpho-biological characteristics, pathogenicity factors and antibiotic-resistant forms (methicillin-resistant Staphylococcus aureus (MRSA), methicillin-resistant coagulase-negative staphylococcus (MRCNS)).
5. Microbiological diagnosis of diseases caused by staphylococci
6. Specific treatment and prevention of staphylococcal infections.
7. Streptococci, their classification, morpho-biological properties, antigenic structure, pathogenicity factors and diseases caused by them. The role of streptococci in the development of rheumatism and glomerulonephritis.
8. Microbiological diagnosis of diseases caused by streptococci.
9. Specific treatment and prevention of streptococcal infections
10. Pneumococci (Streptococcus pneumoniae), morpho-biological properties, antigenic structure, diseases caused by them and signs that distinguish pneumococci from other streptococci.
11. Microbiological diagnosis of pneumococcal infections.
12. Specific treatment and prevention of pneumococcal infections.
13. Enterococci, their morpho-biological properties, pathogenic factors, diseases they cause, antibiotic-resistant forms (vancomycin-resistant enterococcus (VRE)), microbiological diagnosis, specific treatment and prevention
14. Other medically important streptococci (S.agalactiae, S.mutans, S.mitis, etc.)

Purpose of the lesson:

- Introduction to special microbiology for students, clinically important bacteria: pathogenic and opportunistic Gram-positive cocci, especially antibiotic-resistant forms (Staphylococcus (methicillin-resistant Staphylococcus aureus (MRSA), methicillin-resistant coagulase-negative staphylococcus (MRCNS)), Streptococcus, vancomycin- resistant enterococcus (VRE)), to provide information about their morpho-biological characteristics, pathogenicity, diseases, microbiological diagnostisis, specific treatment and prevention.

➢*Special medical microbiology*

Medical microbiology - studies the characteristics of microorganisms that cause disease in humans and the pathological processes that occur in the organism during these diseases.

Development of laboratory diagnosis, specific prevention and treatment methods of diseases caused by microorganisms are the main tasks of medical microbiology.

- Special microbiology - studies the characteristics of various microorganisms and is divided into the following departments depending on this:

- bacteriology (science of bacteria)

- virology (science of viruses)

- - mycology (science of fungi)

- - protozoology (the science that studies protozoas)

Gram-positive cocci:

- **Aerobic genus**: Micrococcus, Planococcus və Deinococcus
- **Facultative anaerobic genus:** Staphylococcus, Stomatococcus, Streptococcus, Leuconostoc, Pediococcus, Aerococcus and Gemella
- **Anaerobic genus:**

  Peptococcus, *Peptostreptococcus*, *Ruminococcus*, *Coprococcus*, *Sarcina*

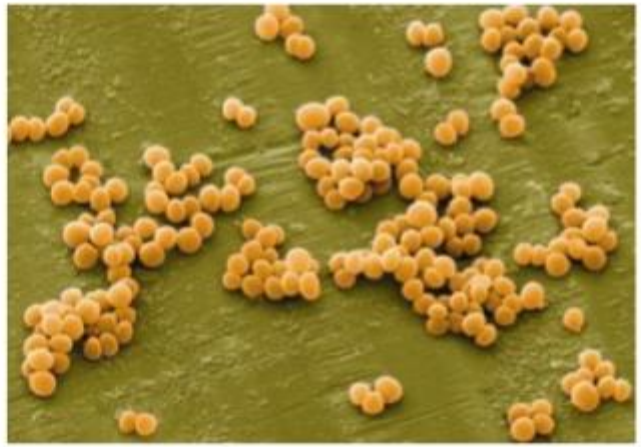
Staphylococcaceae family (new taxonomy)

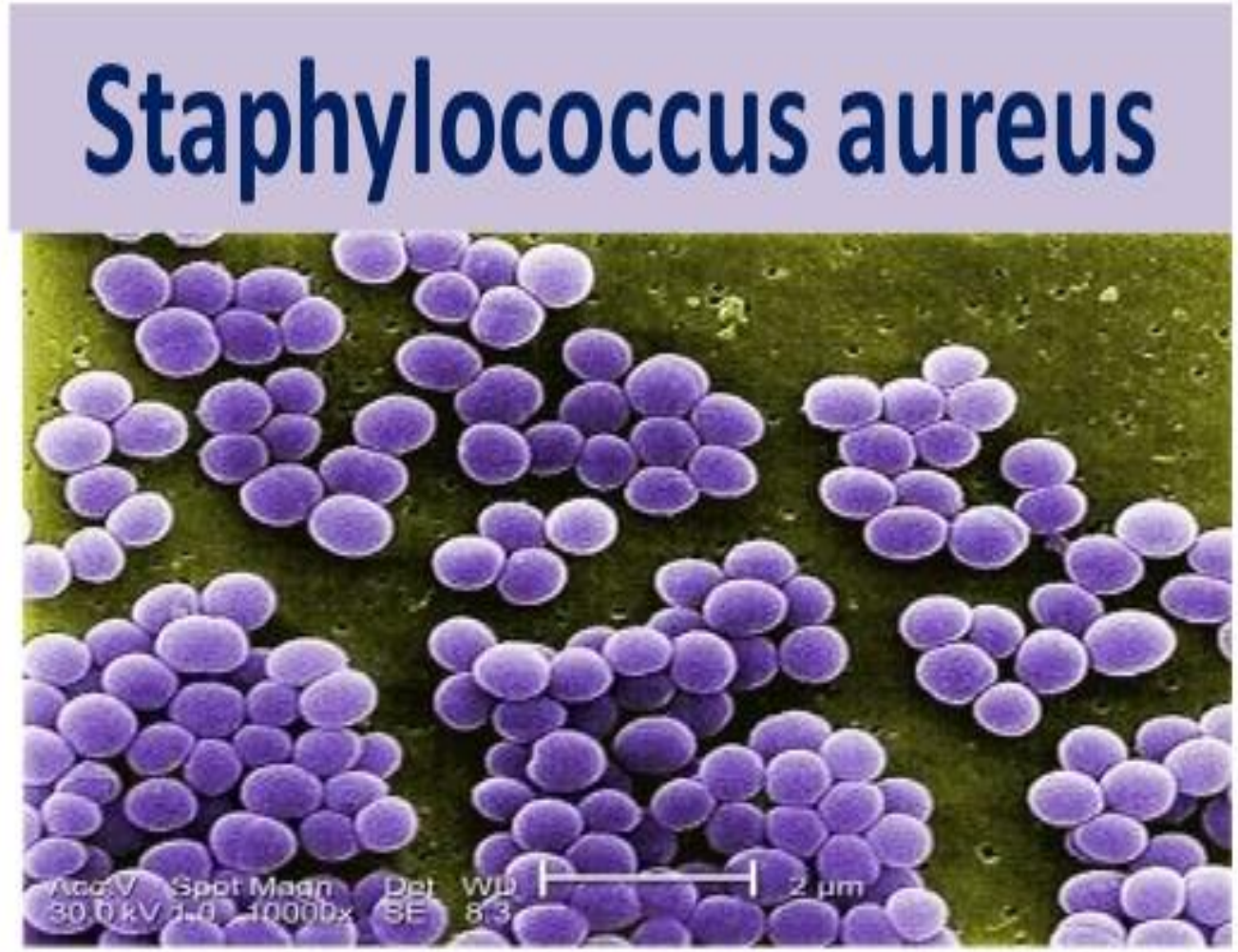
- **Domain: Bacteria**
- **Kingdom: Bacillota**
- **Class: Bacilli**
- **Order: Bacillates**
- **Family: Staphylococcaceae**
- **Genus: Staphylococcus**

- **Genus:**
  - Abyssicoccus
  - Aliicoccus
  - Auricoccus
  - Corticicoccus
  - Gemella
  - Jeotgalicoccus
  - Macrococcus
  - Nosocomiicoccus
  - Salinicoccus
  - **Staphylococcus**
    - **Species**: It consists of about 40 species (S.hominis, S.albus, S.haemolyticus, S.simulans, S.sciuri, etc.). But medically important species are ***S.aureus, S.epidermidis, S.saprophyticus.***

Schleifer and Bell 2010

STAPHYLOCOCCI





INTRODUCTION

- Family: Micrococceae (consists of Gram positive cocci, arranged in tetrads, clusters)
- Genus : Staphylococcus
- Term “staphylococcus” derived from Greek :Staphyle = bunch of grapes and Kokkos = berry, meaning bacteria occurring in grapelike clusters or berry.

S.aureus

- Natural habitat:-Nostril and skin

Morphology:-

- Gram-positive, cocci, 0.5-1.5µm in diameter; occur characteristically in group, also singly and in pairs
- Form irregular grapelike clusters (since divide in 3 planes)
- Non-motile, non- sporing and few strains are capsulated

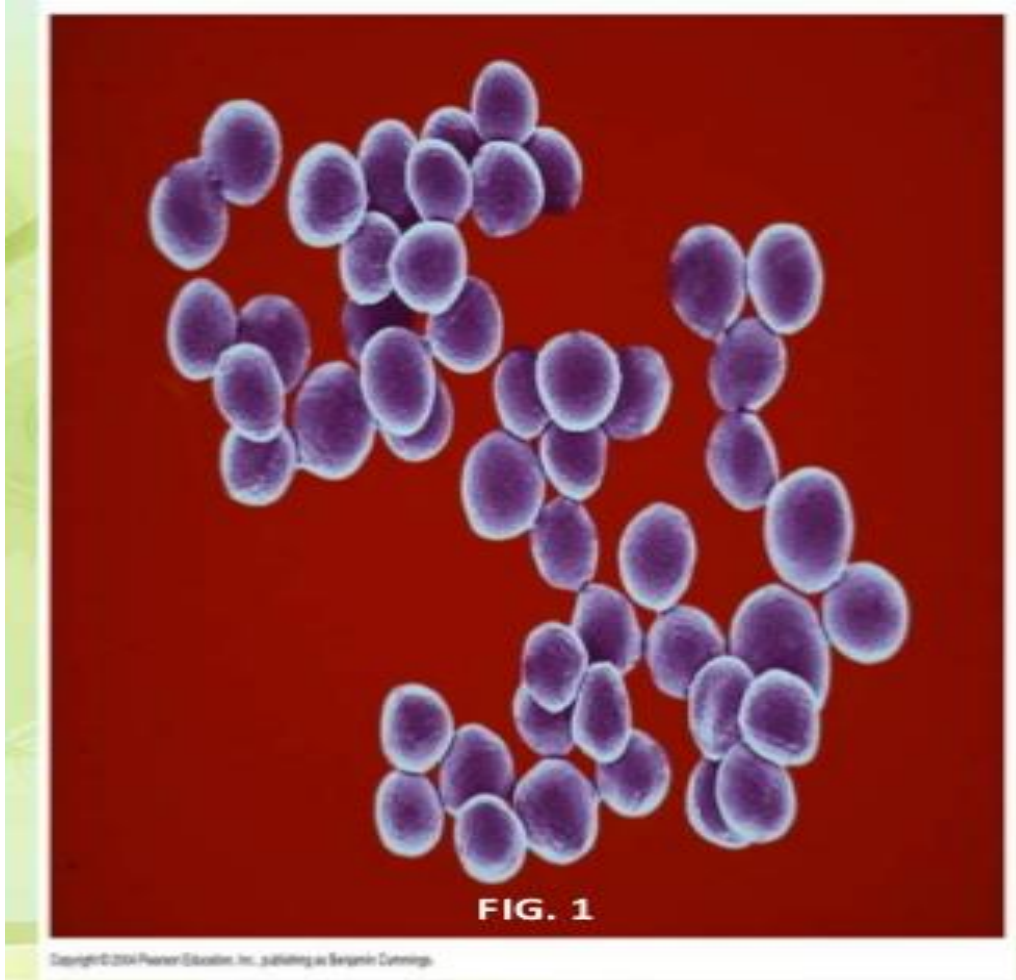
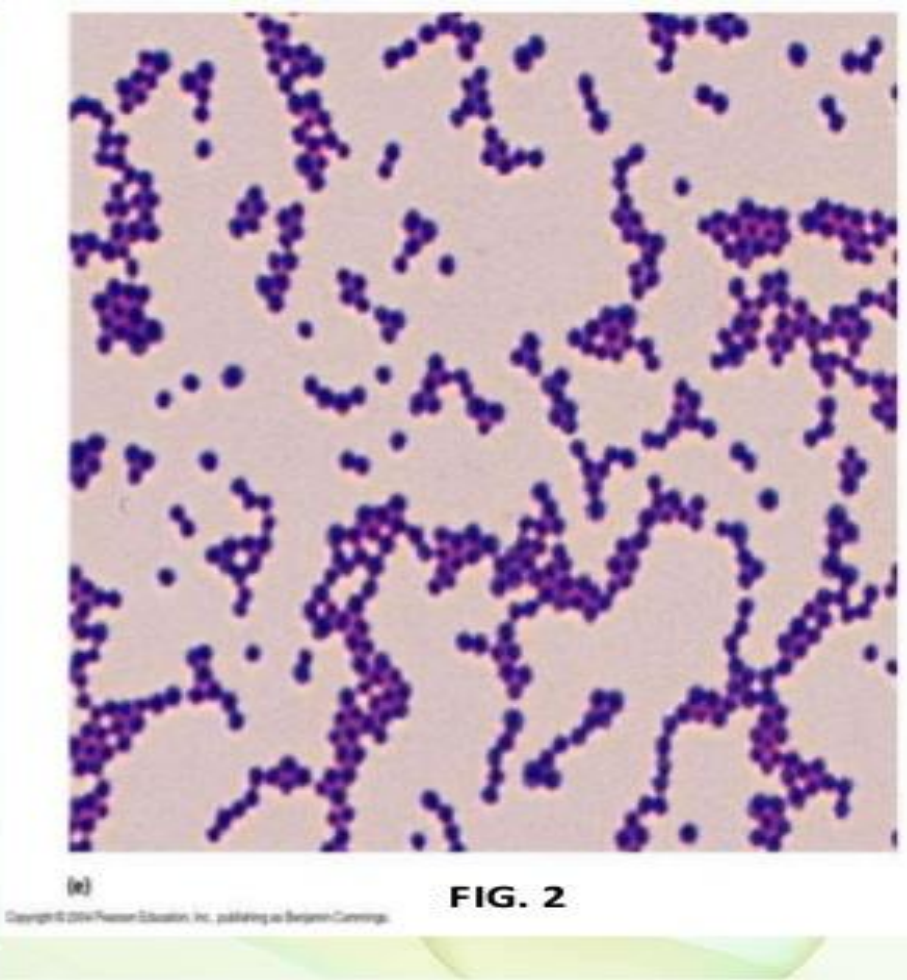


FIG. 1



(a)

FIG. 2

GRAM STAIN

Classification

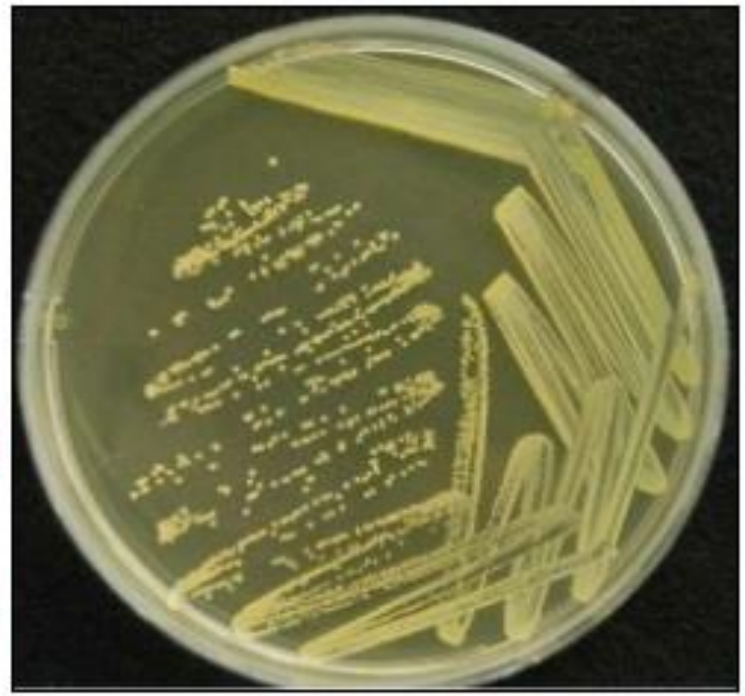
- Based on pigment production:
  - *S.aureus* :-golden-yellow pigmented colonies
  - *S.albus* :- white colonies
  - *S.citrus* :-lemon yellow colonies

S. albus , S. aureus , S. citrus on Nutrient Agar

- Based on pathogenecity:
  - Pathogenic:- includes only one i.e., *S.aureus*
  - Non-pathogenic:- includes *S.epidermidis, S.saprophyticus, S.albus, S. citrus, S.hominis,etc.*
- Based on coagulase production:
  - Coagulase positive: *S. aureus*
  - Coagulase negative: *S. epidermidis, S. saprophyticus*

Culture

- Aerobes and facultative anaerobes
- Opt. Temp. For growth= 37°C
- Opt. pH for growth= 7.5
- On Nutrient agar,
  - golden yellow and opaque colonies with smooth glistening surface, 1-2 mm in diameter (max. pigment production@22 °C)



culture characteristic

colony morphology on many types of agars:

-**On nutrient agar**

Staphylococcus aureus

colonies are:

large, circular, smooth ,

shiny surface and are

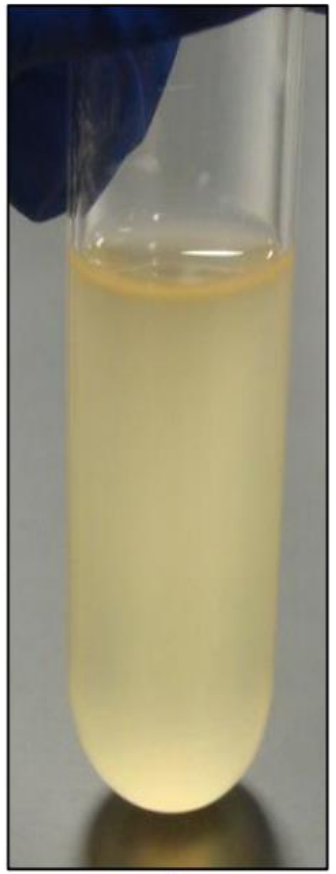
pigmented (golden-yellow).

Staphylococcus aureus
Cultural characteristics:

In a liquid nutrient media, it forms a sedimentary diffuse turbidity.

They develop better in sugary media.

Egg yolk-salt or milk-salt agars are selective nutrient media for them.



Staphylococcus aureus
liquid nutrient media

Staphylococcus aureus

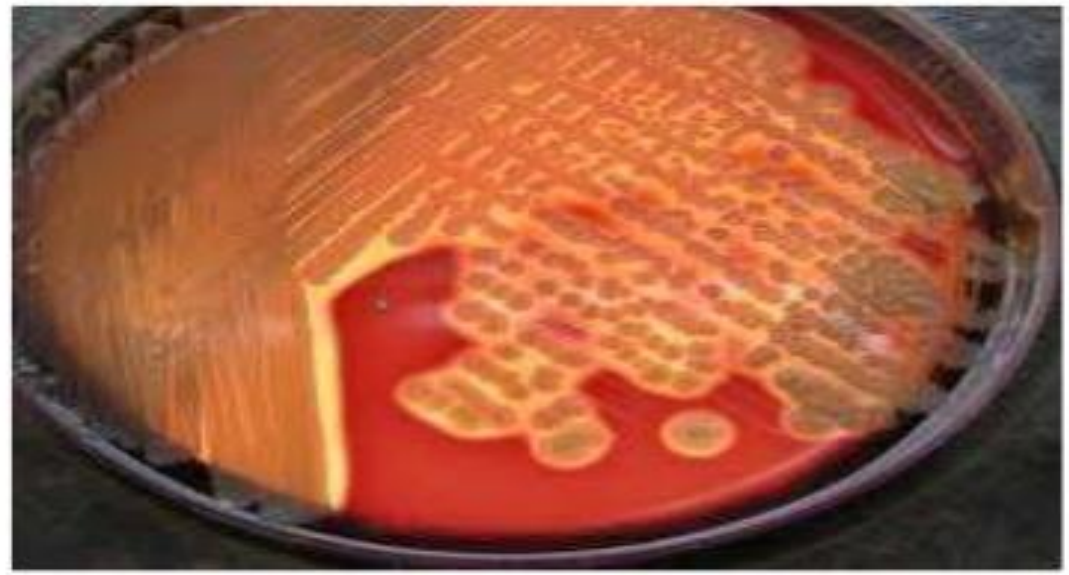
(lecithinase test in egg yolk-salt agar)

***Lecithinase test* -** due to the action of lecithinase enzyme, a crown-shaped blurred border is formed around S.aureus colonies.

-**On blood agar**

- ***S. aureus***

β-hemolysis /clear zone around the colonies.



- ***S.epidermidis***

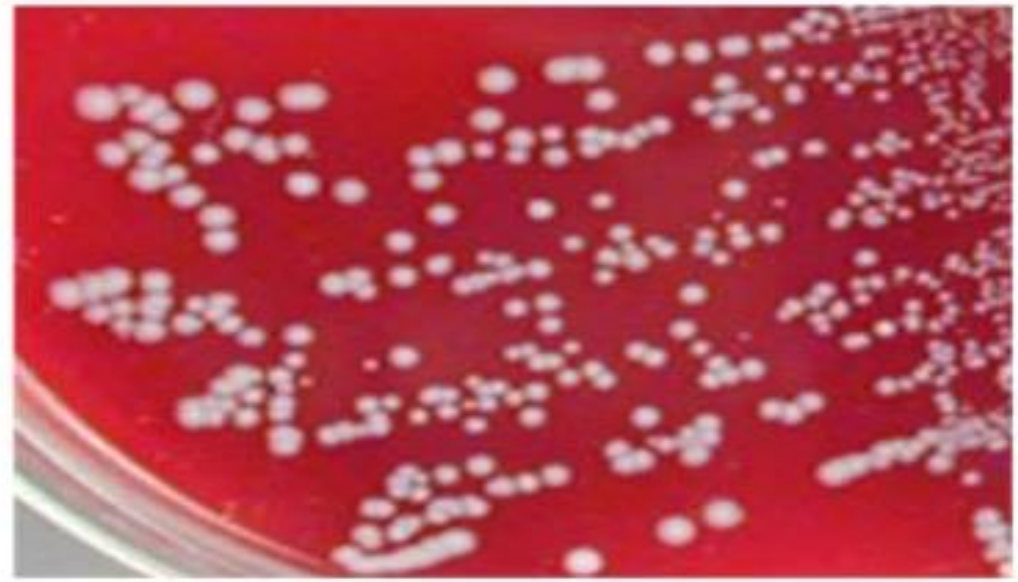
-White-creamy colonies

-no hemolysis of red blood cells.

- ***S. Saprophyticus***

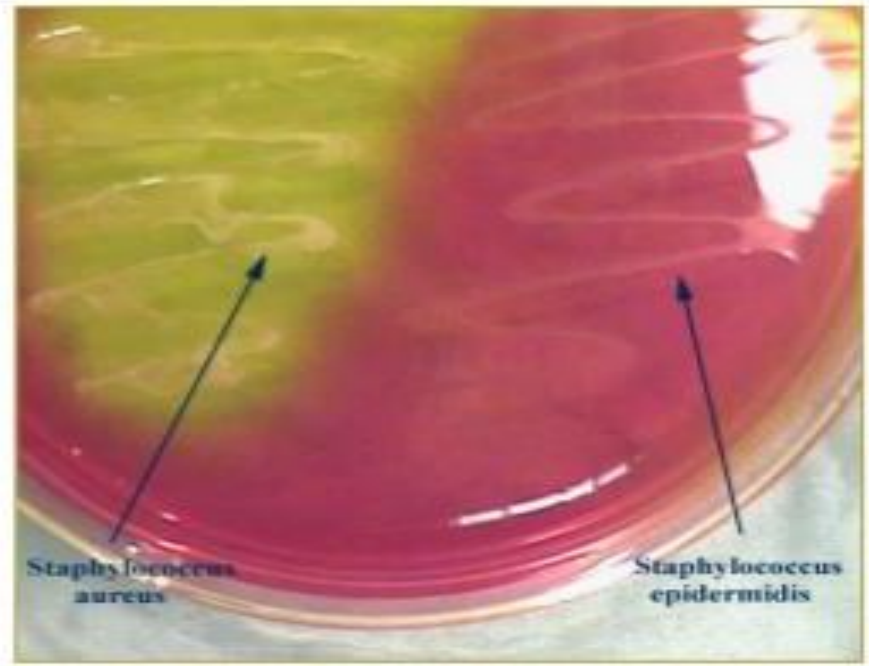
  - white-yellow colony

  -no haemolysis of red blood cells



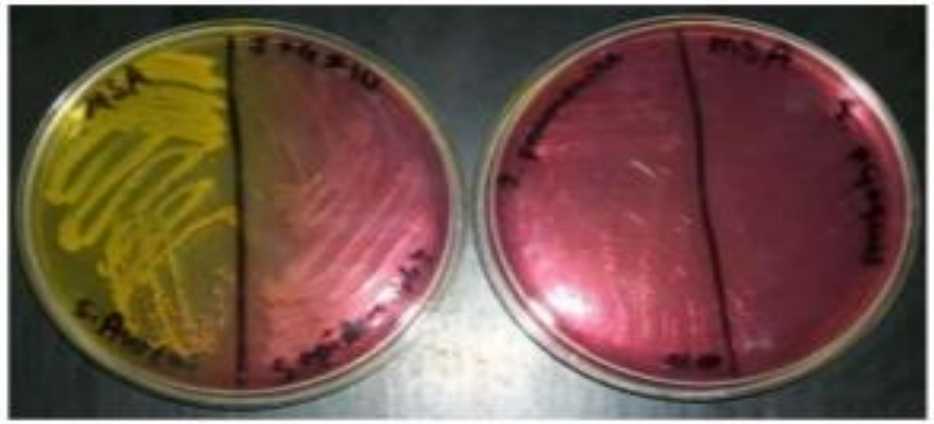
Culture (….contd)

- On Mannitol salt agar,
  - *S.aureus* ferments mannitol and appear as yellow colonies
  - MSA is a useful selective medium for recovering *S.aureus* from faecal specimens, when investigating food poisoning



Biochemical Properties

- Catalase positive; oxidase negative
- Ferment glucose, lactose, maltose, sucrose and mannitol, with production of acid but no gas
- Mannitol fermentation carries diagnosis significance



Biochemical Properties(....contd)

- Indole test= negative
- MR test= positive
- VP test= positive
- Urease test= positive
- Hydrolyse gelatin
- Reduces nitrate to nitrite
- Phospahatase= positive
- DNA-ase test= positive
- Coagulase test= positive

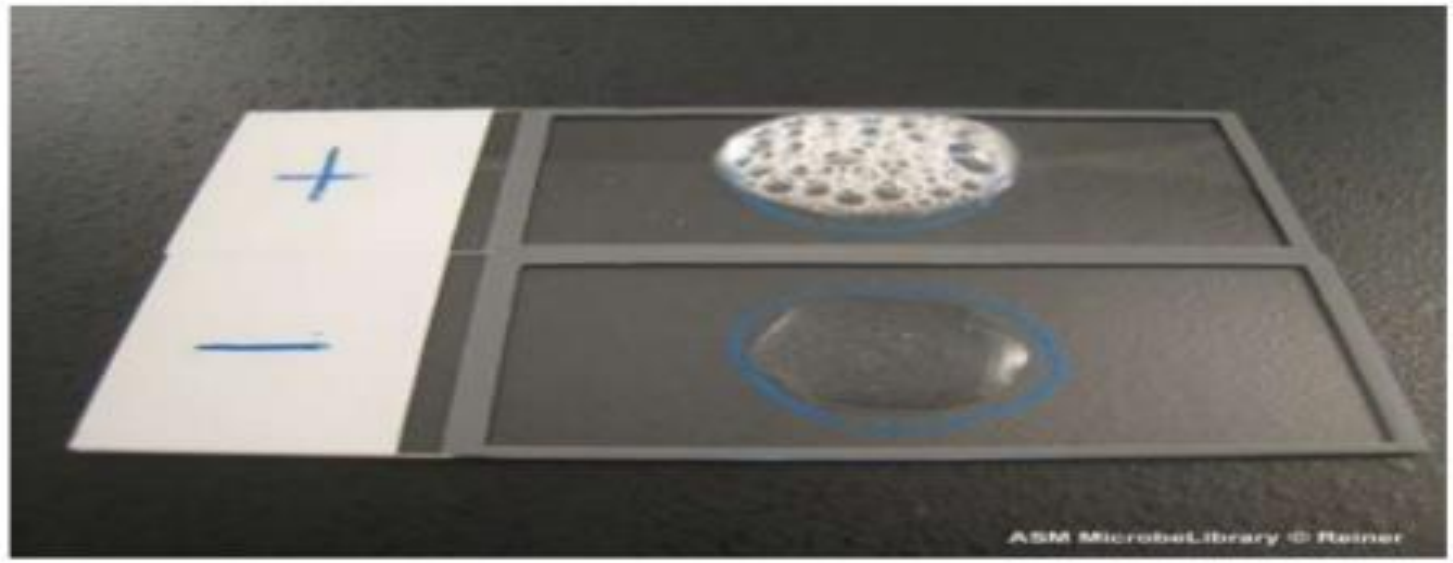
Slide test (clumping factor)

Tube test (free coagulase)

Biochemical tests

- **Catalase test:**

- Is used to differentiate between staphylococci (catalase +ve) and streptococci(catalase –ve).



- **Coagulase test**

is used to differentiate *Staphylococcus aureus* from coagulase-negative staphylococci.

fibrinogen —(coagulase)→ fibrin

(clot formation)

Staphylococcus aureus

Coagulase negative staphylococci, e.g. *S. epidermidis*

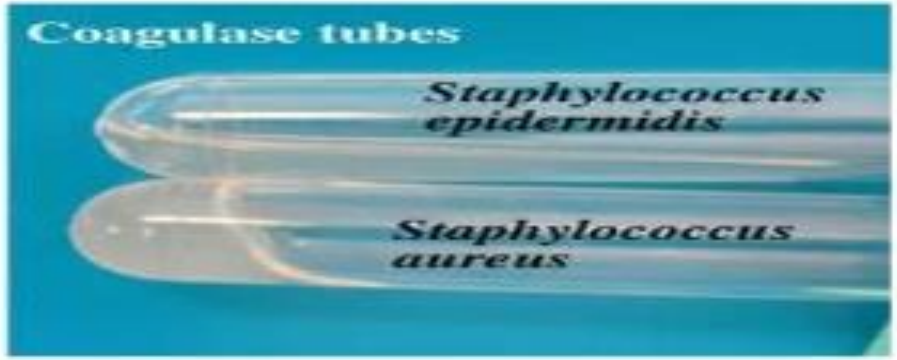
slide coagulase test

- Procedure
  - Place a drop of sterile water on a slide and emulsify a colony
  - Add a drop of rabbit plasma to the suspension
  - Observe
    - Agglutination = Positive (*S. aureus*)
    - No agglutination= Negative (other *staphylococcci)*

tube Coagulase Test

- Causes a clot to form when bacterial cells are incubated with plasma.

- **Procedure**
  - Inoculate rabbit plasma with organism and incubate at 35-37 ^{0} C
  - Observe at 30 minutes for the presence of a clot
  - Continue for up to 24 hours, if needed.



Staphylococcus aureus

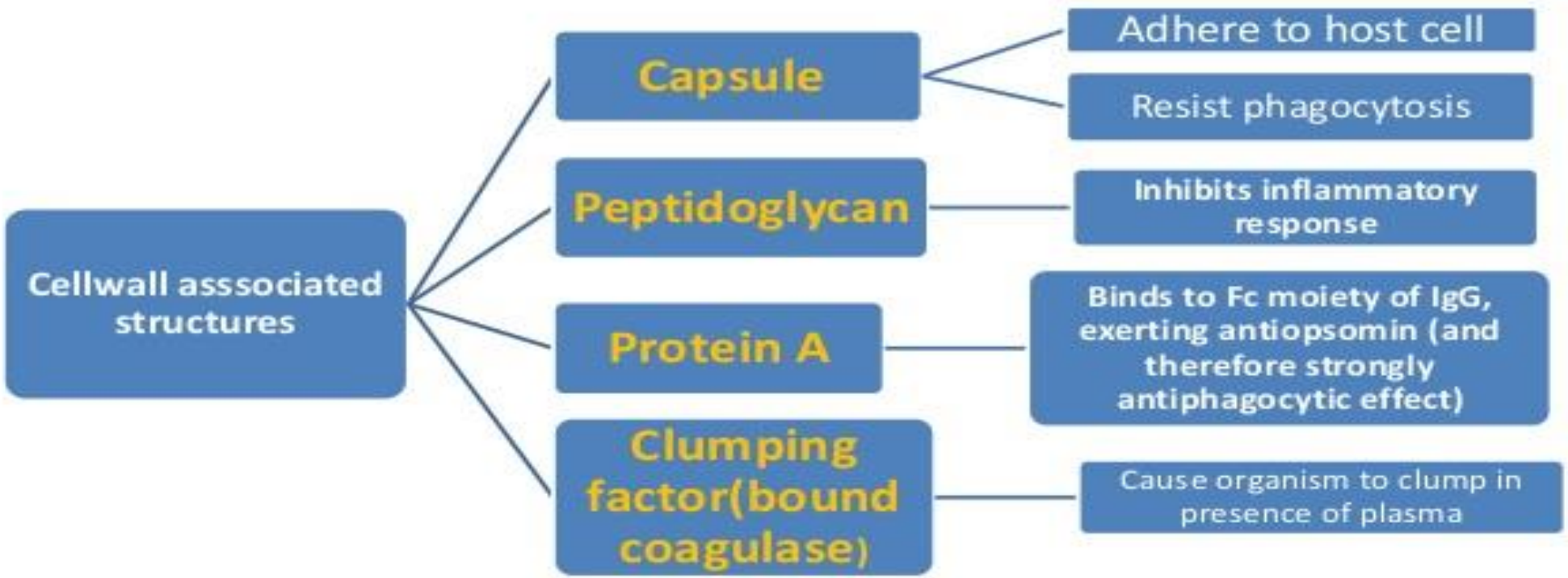
Antigenic structure

- Capsule
  - Prevents phagocytosis
  - Promotes adherence to cells of prosthetic devices
- Peptidoglycan
  - Acts as endotoxin
  - Chemotactant for neutrophils
  - Stimulates complement and coagulation
- Teichoic acid
  - Adherence to mucosal surface
- Protein A
  - Binds to Fc portion of IgG
  - Phagocytosis is reduced

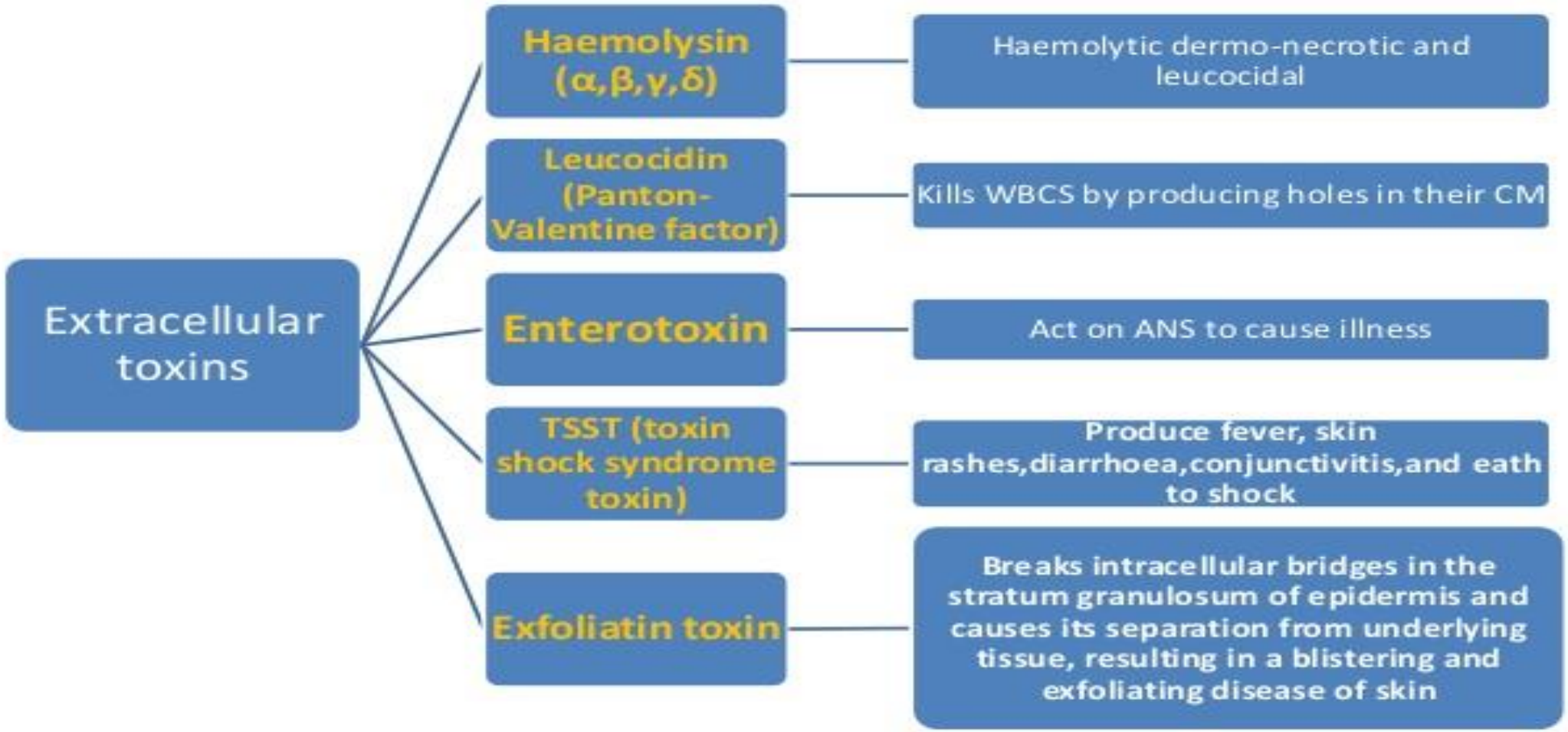
Virulence Factors

Cellwall associated structures	Extracellular toxins	Coagulase
• Peptidoglycan • Capsule • proteinA • Clumping factor (bound coagulase)	• Haemolysin • Leukocidin • Enterotoxin • TSST • Exfoliatin toxin	• staphylokinase • DNAase • Phosphatase • lipase • Phospholipase • hyaluronidase • serokinase • protease

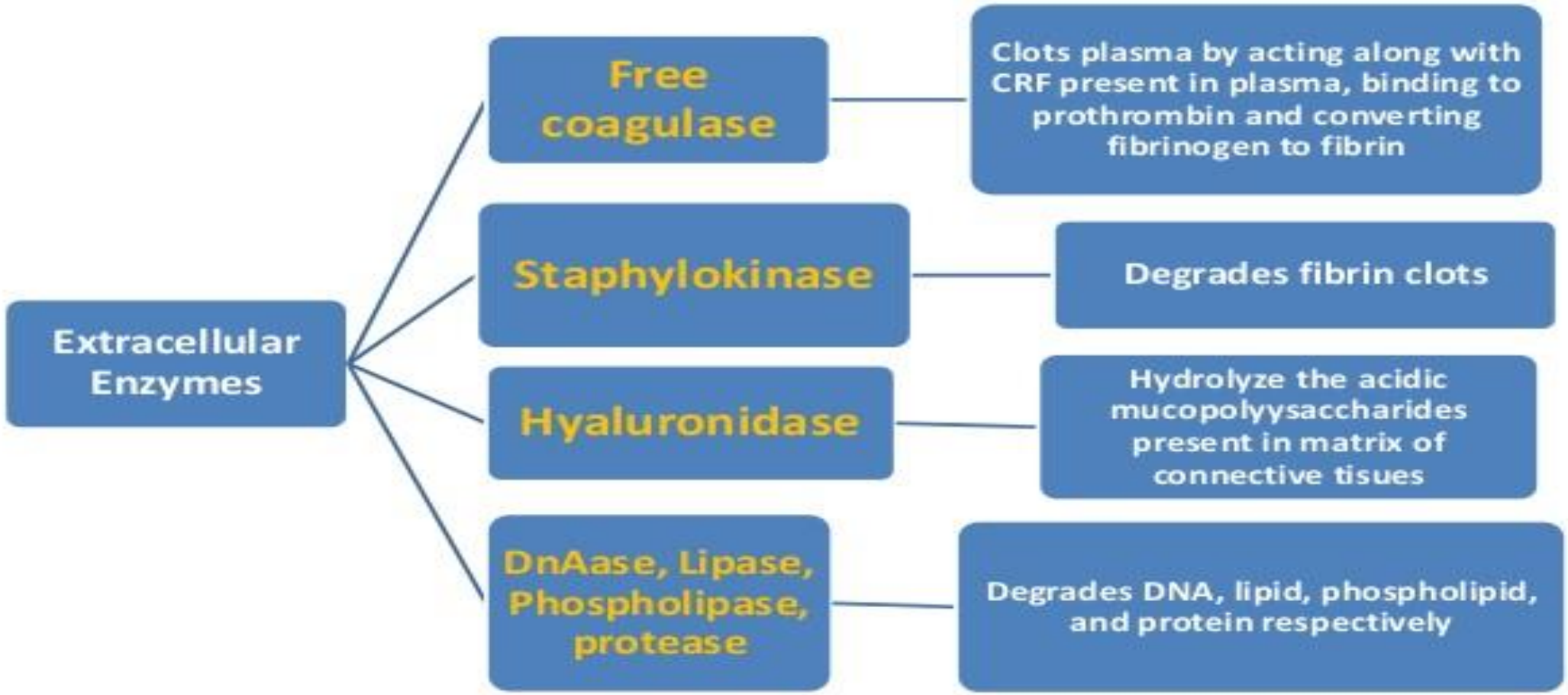
Virulence Factors(contd....)



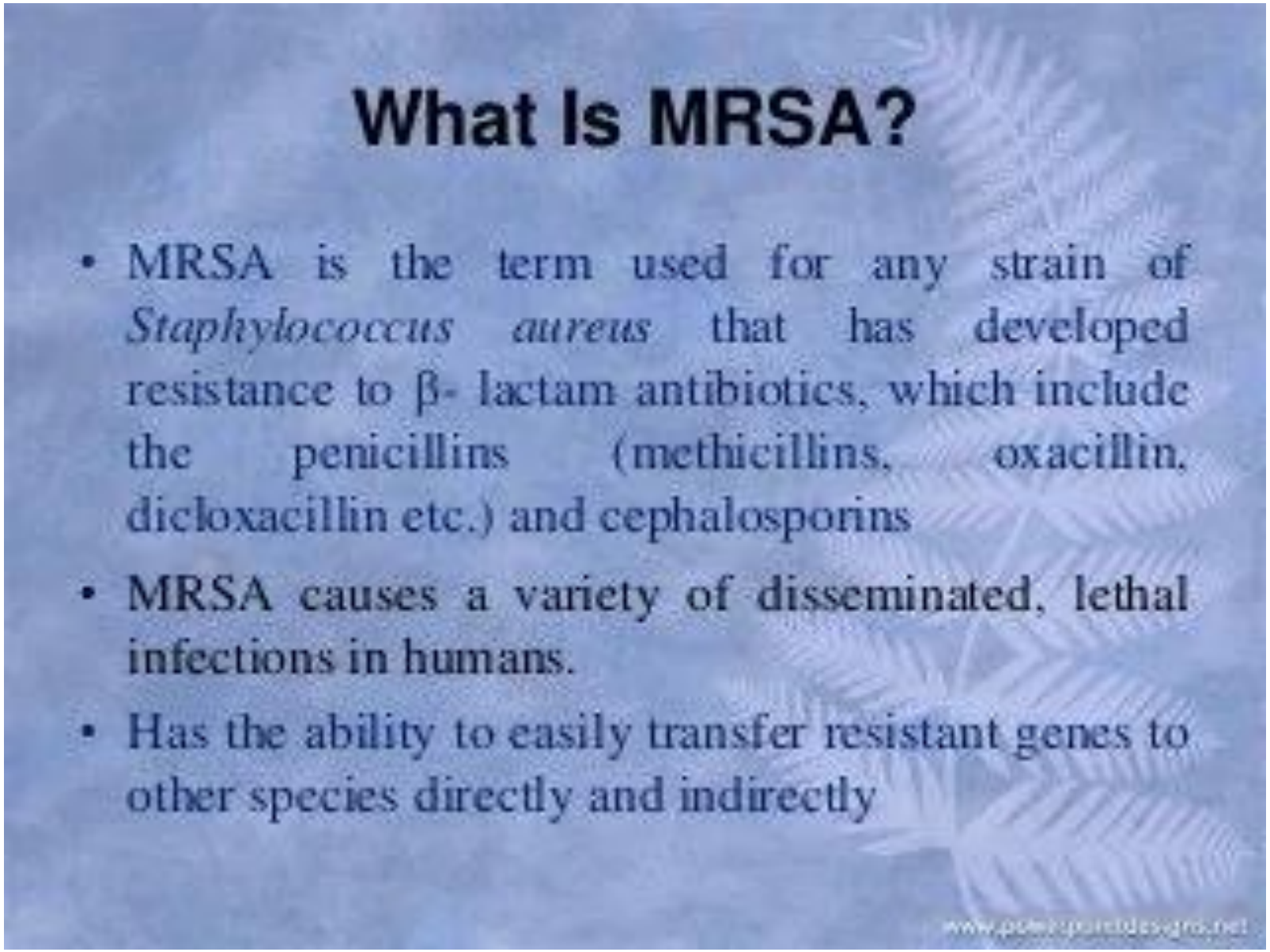
Virulence Factors(contd....)



Virulence Factors(....contd)



Methicillin-resistant Staphylococcus aureus (MRSA),



Pathogenesis

- Adhere to damaged skin, mucosa or tissue surfaces
  - At these sites, they evade defence mechanisms of the host, colonize and cause tissue damage
- *S.aureus* produces disease by
  - Multiplying in tissues
  - Liberating toxins,
  - Stimulating inflammation

PATHOGENICITY

Source of infection:

A) Exogenous: patients or carriers

B) Endogenous: From colonized site

Mode of transmission:

A) Contact: direct or indirect(through fomites)

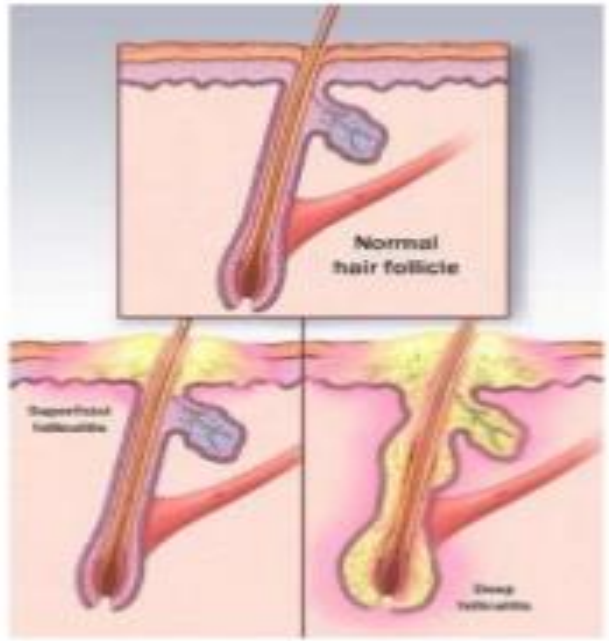
B) Inhalation of infected air borne droplets

Clinical Syndromes

1. **Cutaneous infections**
   - Folliculitis
   - Boils/furuncles
   - Carbuncle
   - Impetigo
   - Wound infections
2. **Deep infections**
   - Osteomyelitis
   - Periostitis
   - endocarditis
3. **Exfoliative diseases**
4. **Toxin shock syndrome**
5. **Staphylococcal food intoxication**

1) Cutaneous Infections

- **Folliculitis**: It is inflammation of the hair follicles.
- A small red bump or pimple develops at infection sites of hair follicle.



•**Sty**: A sty is folliculitis affecting one or more hair follicles on the edge of the upper or lower eyelid.

Cutaneous Infections(contd....)

- **Furuncle/boils**: Furuncle is deep seated infection, originating from folliculitis,(if infection extends from follicle to neighbour tissue)
- Causes redness, swelling, severe pain
- Commonly found on the neck, armpit and groin regions

- **Carbuncle**: Carbuncle is an aggregation of infected furuncles. Carbuncles may form large abscesses.
- It is a large area of redness, swelling and pain, punctuated by several sites of drainage pus.

Cutaneous Infections(contd....)

- Impetigo: a very superficial skin infection common in children, usually produces blisters or sores on the face, neck, hands, and diaper area.
- It is characterized by watery bristles, which become pustules and then honey coloured crust

impetigo with vesicles, pustules, and sharply demarcated regions of honey-colored crusts.

2) Deep Infections

- **Osteomyelitis**: inflammation of bone
- Bacteria can get to the bone
  - Via bloodstream
  - Following an injury

  Clinical features: pain, swelling, deformity, defective healing, in some case pus flow,

  Diagnosis: X-ray, MRI, bone aspirates

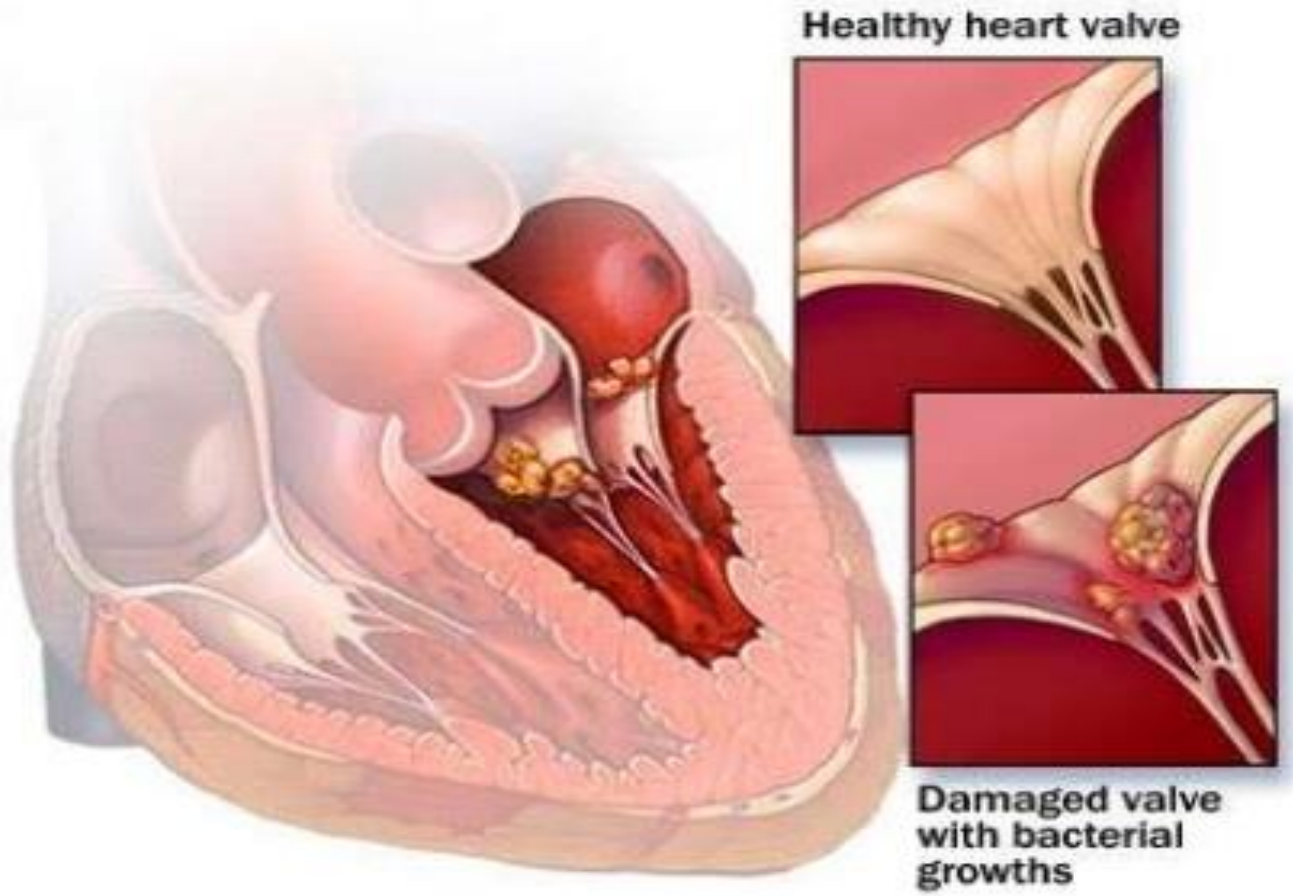
Deep Infections(contd....)

- **Periostitis**: inflammation of periosteum
- Clinical features: fever, localised pain, leucocytosis
- Diagnosis: needle aspiration of subperiosteal fluid

Deep Infections(....contd)

- **Endocarditis**: It is an inflammation of the inner layer of the heart, the endocardium

- Endocarditis occurs when bacteria enter bloodstream, travel to heart, and lodge on abnormal heart valves or damaged heart tissue.



3)Exfoliative Disease

- (Exfoliate= scaling off tissues in layers)
- Also known as **'Staphylococcal skin scalded syndrome'**

- previously called dermatitis exfoliativa, pemphigus neonatorum, Lyell's disease and Ritter's disease

- Epidermal toxin produced by *S.aureus* at skin and is carried by bloodstream to epidermis , where it causes a split in a cellular layer i.e., this toxin separates outer layer of epidermis from underlying tissue

4) Toxic Shock Syndrome

- Caused when Toxin shock syndrome toxin (TSST) liberated by S.aureus enters bloodstream
- It is a multisystem illness, characterized by:

High Fever

Headache

Vomiting

Diarrhoea

Conjunctival reddening

Hypotension

Skin rashes

Kidney failure

5) Staphylococcal Food Poisoning

- Caused when consuming food in which S.aureus has multiplied and formed endotoxin
- Symptoms:
  - Nausea
  - Vomiting
  - Severe abdominal cramp
  - Diarrhoea
  - Sweating
  - Headache,etc.

- **Respiratory**
  - Tonsilitis
  - Pharyngitis
  - Sinusitis
  - Otitis
  - Bronchopneumonia
  - Lung abscess
  - empyema

- **Endovascular**
  - Bacteremia
  - Septicemia
  - Pyemia
  - Endocarditis

- **Urinary**
  - Urinary tract infection

- **Central nervous system**
  - Abscess
  - Meningitis
  - Intracranial thrombophlebitis

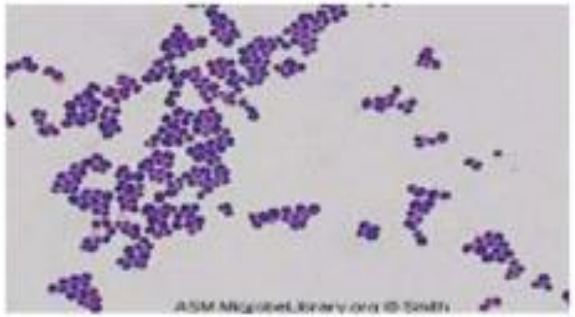
Laboratory diagnosis

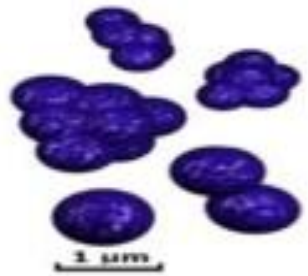
microscopic examination

1-Gram stain → gram positive.

2-Morphology → cocci (spherical).

3-Arrengment → single cell or pairs or in short chain but appear predominantly in grape-like clusters.





Laboratory Diagnosis (contd....)

B. Bacteriological Investigation:

- Specimens:
  - Pus: from wound or abscess or burns]
  - Nasal Swab: from suspected carrier
  - Food: to diagnose staphylococcal intoxication
  - Blood: to diagnose endocarditis and bacteremia
  - Sputum: to diagnose lower respiratory tract infection

LABORATORY DIAGNOSIS:

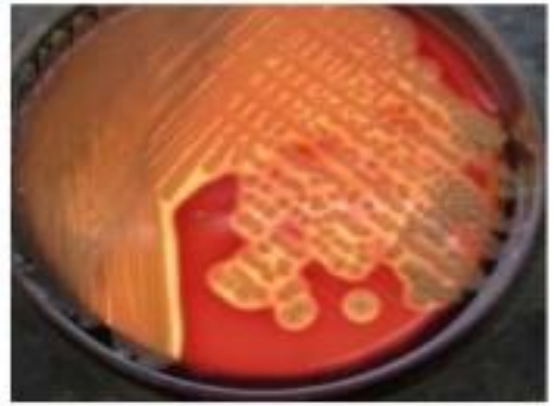
Specimen collection

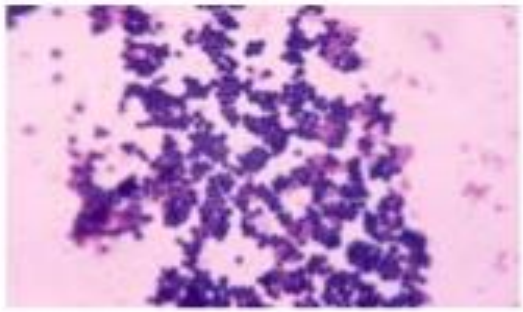
- **Pus** from pyogenic lesions.
- **blood** from septicaemia.
- **Cerebrospinal fluid** from meningitis.
- **sputum** from respiratory infection
- suspected **food, vomit or faeces** from food poisoning.
- Mid-stream **urine** in urinary tract infection.
- Anterior **nasal swab** from suspected carriers.

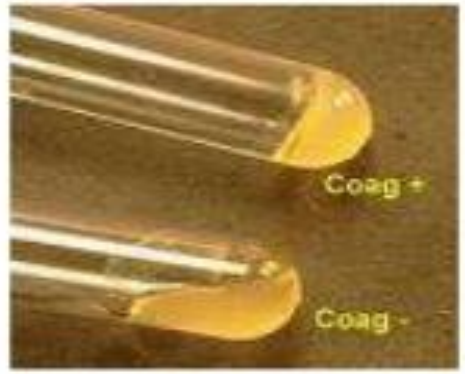
Laboratory Diagnosis (contd....)

- **Culture and isolation:**
  - Specimens are cultured on BA plate and are incubated @ 37 °C for 24 hours
  - After incubation, BA plate is observed for significant bacterial growth (> 2mm in diameter)
  - Then, Gram-staining is performed of the isolated organisms
  - Then, subcultured on NA plate for further biochemical tests

- **Tube coagulase test:**
  - i. Mix 0.5ml of human plasma with 0.1ml of an overnight broth culture of S.aures
  - ii. Incubate the mix in a water bath @ 37°C for 3-6 hours
  - Result: plasma clots and doesn't flow if the tube is inverted







Prevention

Wash your hands

Keep wounds covered

Reduce tampon risks

Avoid sharing personal care items

Cooking and storing food properly

Treatment and Drugs

Antibiotic therapy

Wound drainage

Device removal

Removal of dead tissue

STREPTOCOCCUS

Classification of Streptococci

- Brown`s classification
- Lancefield grouping
- Griffith typing

Streptococcus

α-hemolytic
green,
partial hemolysis

- **pneumoniae**
  optochin sensitive,
  bile solube,
  capsule –>
  quellung +
- **Viridans**
  mutans, sanguis
  optochin resistent,
  not bile soluble,
  no capsule

β-hemolytic
clear,
complete hemolysis

- **pyogenes**
  Group A,
  badtradn sensitive
- **agalactiae**
  Group B,
  badtradn resistant

γ-hemolytic
no hemolysis

- **Enterococcus**
  E. faecalis,
  E. faecium

Group A betahemolytic Streptococci

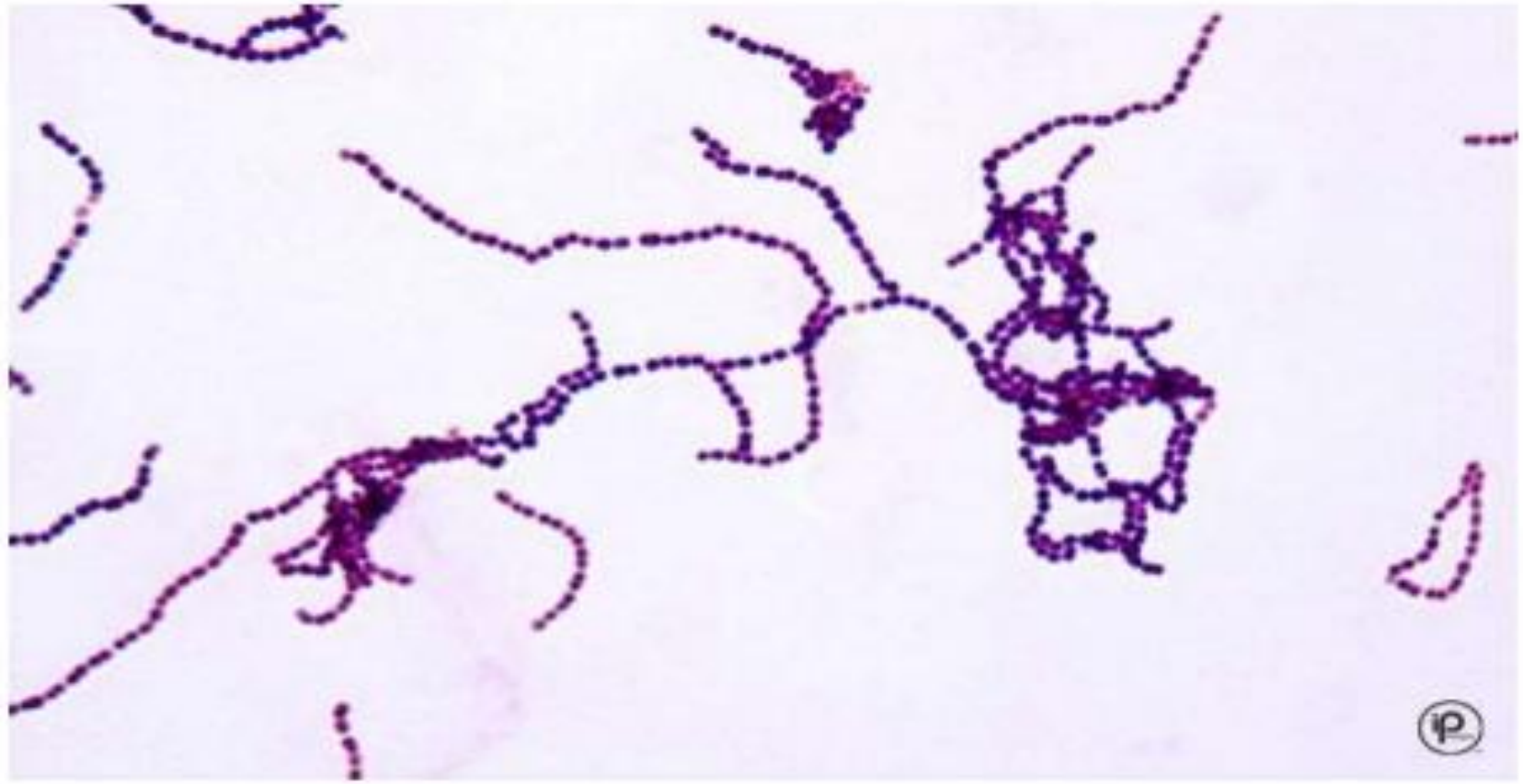
Streptococcus pyogenes

Streptococcus pyogenes

Morphology

- Ovoid to spherical in shape
- Gram-positive cocci arranged in chains or pairs
- Chain formation is due to the cocci dividing in one plane only and the daughter cells failing to separate completely
- Chains are longer in liquid than in solid media
- Non motile and non-sporing
- Capsulated (hyaluronic acid; non-immunogenic)
- Group A b-hemolytic streptococci

Gram positive cocci in chains



Cultural characteristics

- Aerobes and facultative anaerobes
- Optimum temperature: 37C
- Growth occurs only in media containing fermentable carbohydrates or enriched with blood or serum

i. Blood agar:

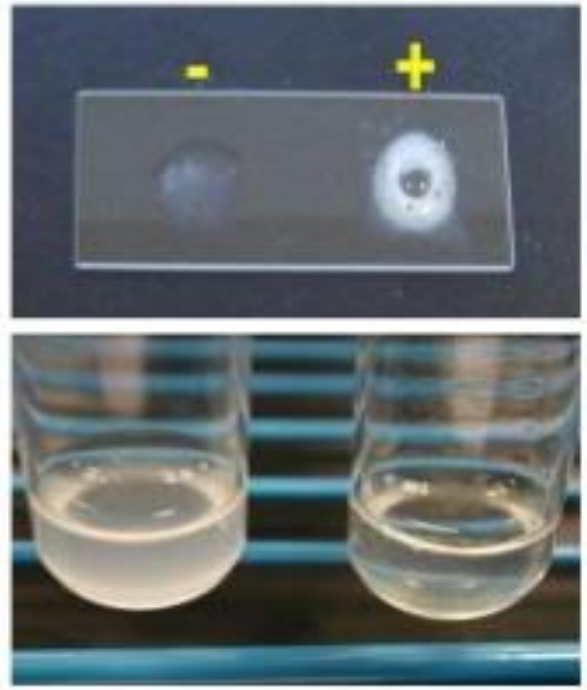
- Small (0.5-1mm), circular, semi-transparent colonies
- Produce wide zone of β- hemolysis
- Growth and hemolysis are promoted by 5-10% CO2
- Virulent strains, on fresh isolation form lesions, produce a 'matt' (finely granular) colony while avirulent strains form 'glossy' colonies
- Mucoid colonies are formed by strains that produce large capsules

ii. Liquid media:

- Glucose or serum broth
- Growth occurs as a granular turbidity with a powdery deposit
- No pellicle is formed

Biochemical reactions

- Catalase negative
- Bile insoluble
- Ferments sugars producing acid but no gas
- PYR test positive



Bile insoluble

- Hydrolyse pyrrolidonyl-beta-napthylamide (PYR) due to presence of peptidase, the resulting napthylamide produces a red colour upon the addition of 0.01% cinnamaldehyde reagent
- Faliure to ferment ribose

Antigenic structure

- Structural antigens – Cell wall antigens
- Toxins
- Enzymes

Capsular hyaluronic acid:

- Non antigenic as **hyaluronic acid** is identical to that found in human connective tissue and hence bacteria can disguise themselves with an immunological self substance
- Has weak anti-phagocytic activity but protects streptococci against immunological attacks

Antigenic structure

A. **Cell wall:**

1. Outer layer: Protein and lipoteichoic acid
2. Middle layer: Group specific carbohydrate
3. Inner layer: Peptidoglycan (mucoprotein)

- Responsible for cell wall rigidity
- Enhances non specific resistance (pyrogenic and thrombolytic activity)

Toxins and enzymes

1. **Hemolysins (Streptolysins)**
2. **Erythrogenic toxin**
3. **Streptokinase (Fibrinolysin)**
4. **Deoxyribonucleases (Streptodornase, DNAase)**
5. **Hyaluronidase**

Hemolysins (Streptolysins)

- Produce complete disruption of RBC
- Contribute to tissue invasion and destruction
- There are two types of Streptolysins
  - **Streptolysin O**
  - **Streptolysin S**

Pathogenicity

- Produces pyrogenic infection with a tendency to spread locally, along lymphatics and through blood stream
- Disease caused can be:
  - **Suppurative** or
  - **Non suppurative**

- Suppurative diseases:
1. Respiratory infections
2. Skin and soft tissue infections
3. Genital infections

- Non suppurative sequelae:
1. Acute rheumatic fever
2. Acute glomerulonephritis

Enterococcus

- E.faecalis
- E.faecium
- E.durans

Laboratory Diagnosis

a. Throat swab culture: Detection of group A antigen
b. Specific nucleic acid based test
c. Elevation of anti hyaluronidase antibodies(strong evidence)

1. **Specimen:**

- Throat swab, pus swab or exudates are collected.

2. **Microscopy:**

- Gram-staining of pus can be examined
- Presence of Gram-positive cocci in chains can be indication.

3. Culture:

- Swab from the affected area is collected and are either plated immediately or sent to laboratory in Pike's medium.

- The specimen should be plated on blood agar and incubated at 37°C anaerobically or under 5-10% CO_2 ,as hemolysis develops better.

4. Identification:

- Rapid diagnostic test kits are available for the detection of streptococcal group A antigen from throat swab

- **Bacitracin sensitivity:**
- Based on Maxted's observation that they are more sensitive to bacitracin than other streptococci
- A filter paper disc of 0.04U is applied on the surface of an inoculated blood agar
- After incubation, a wide zone of inhibition is seen with *S.pyrogenes* but not with other streptococci

5. Serology:

a) **Antistreptolysin O titration**

Standard test ASO titres higher than 200 are indicative of prior streptococcal infection. High levels are usually found in acute rheumatic fever but in glomerulonephritis, times are often low

b) **Antideoxyribonuclease B (anti-DNAase B):**

Commonly used

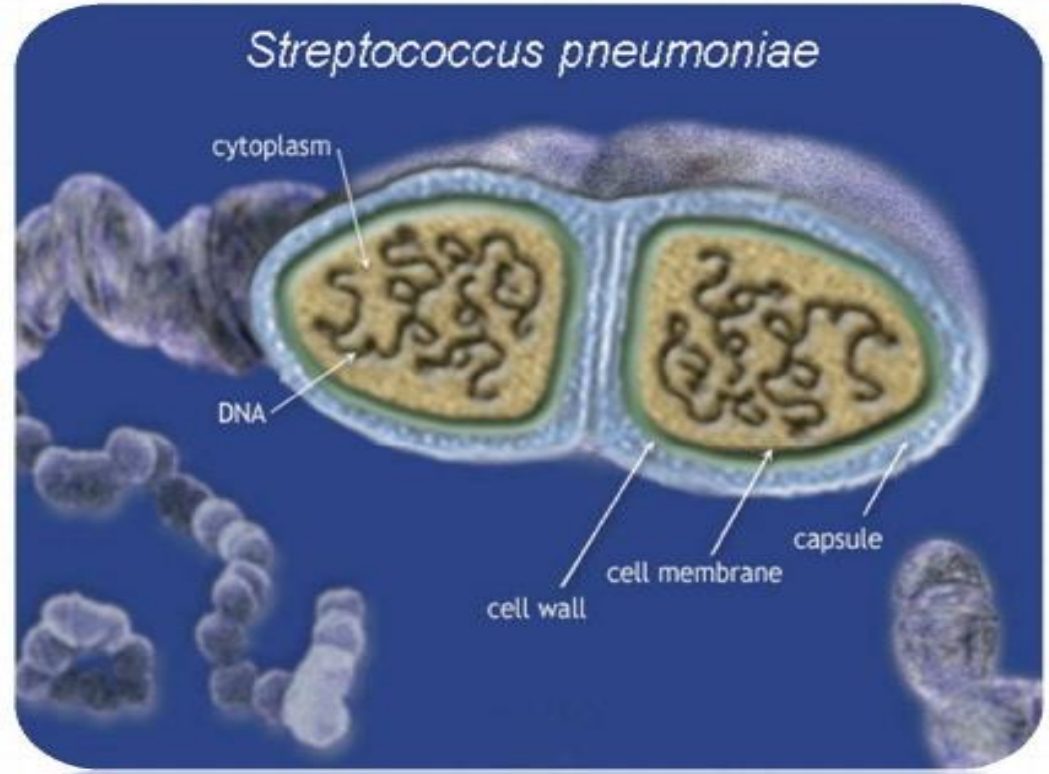
Titres higher than 300 are taken

c) **Streptozyme test:**

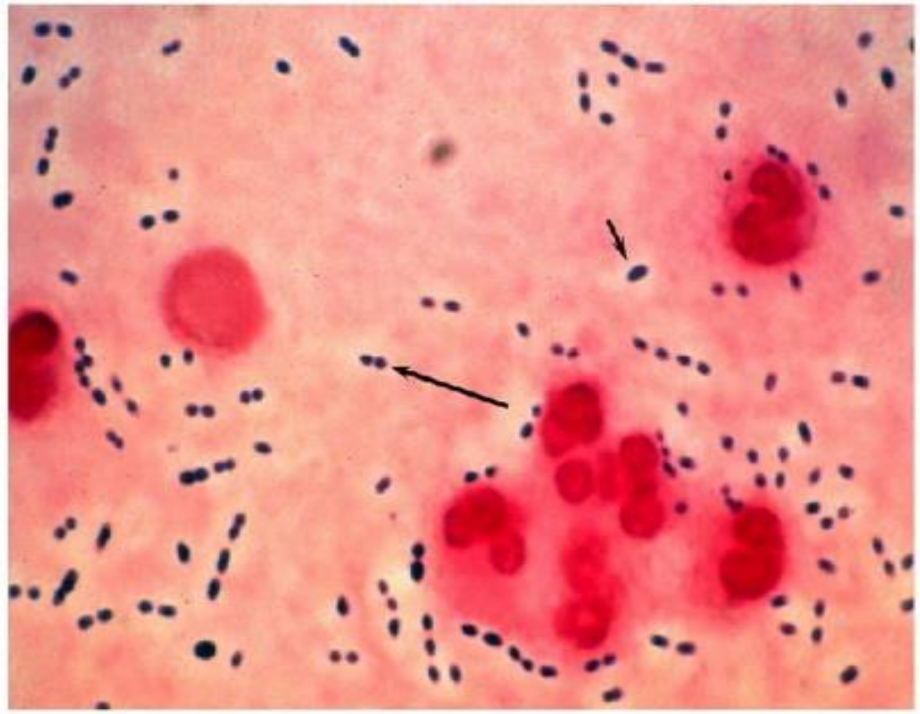
- A passive slide hemagglutination test using erthyrocytes sensitised with a crude preparation of streptococci
- It is a convenient, sensitive and specific screening test.

Streptococcus pneumoniae

- **Streptococcus pneumoniae cells are Gram-positive, lancet-shaped cocci (elongated cocci with a slightly pointed outer curvature). Usually, they are seen as pairs of cocci (diplococci), but they may also occur singly and in short chains. When cultured on blood agar, they are alpha hemolytic**



Streptococcus pneumoniae



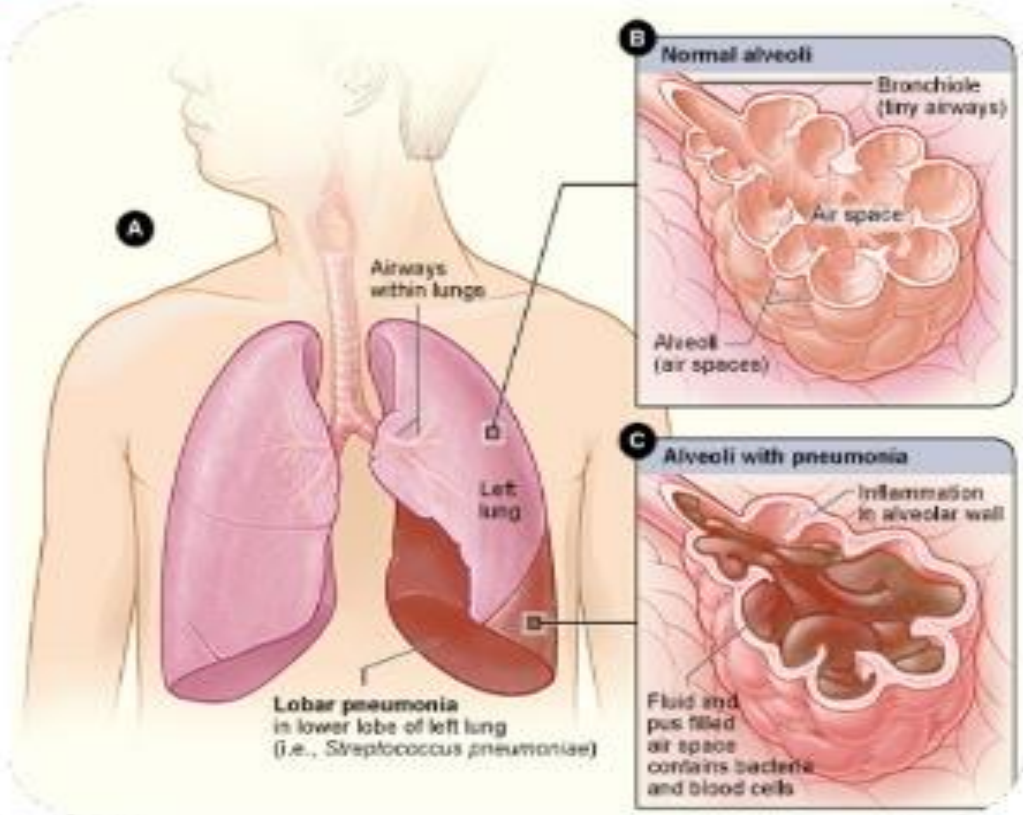
- Individual cells are between 0.5 and 1.25 micrometers in diameter. They do not form spores, and they are nonmotile. Like other streptococci, they lack catalase and ferment glucose to lactic acid

Pneumococcal Disease Clinical Syndromes

A. Pneumonia

B. Bacteremia

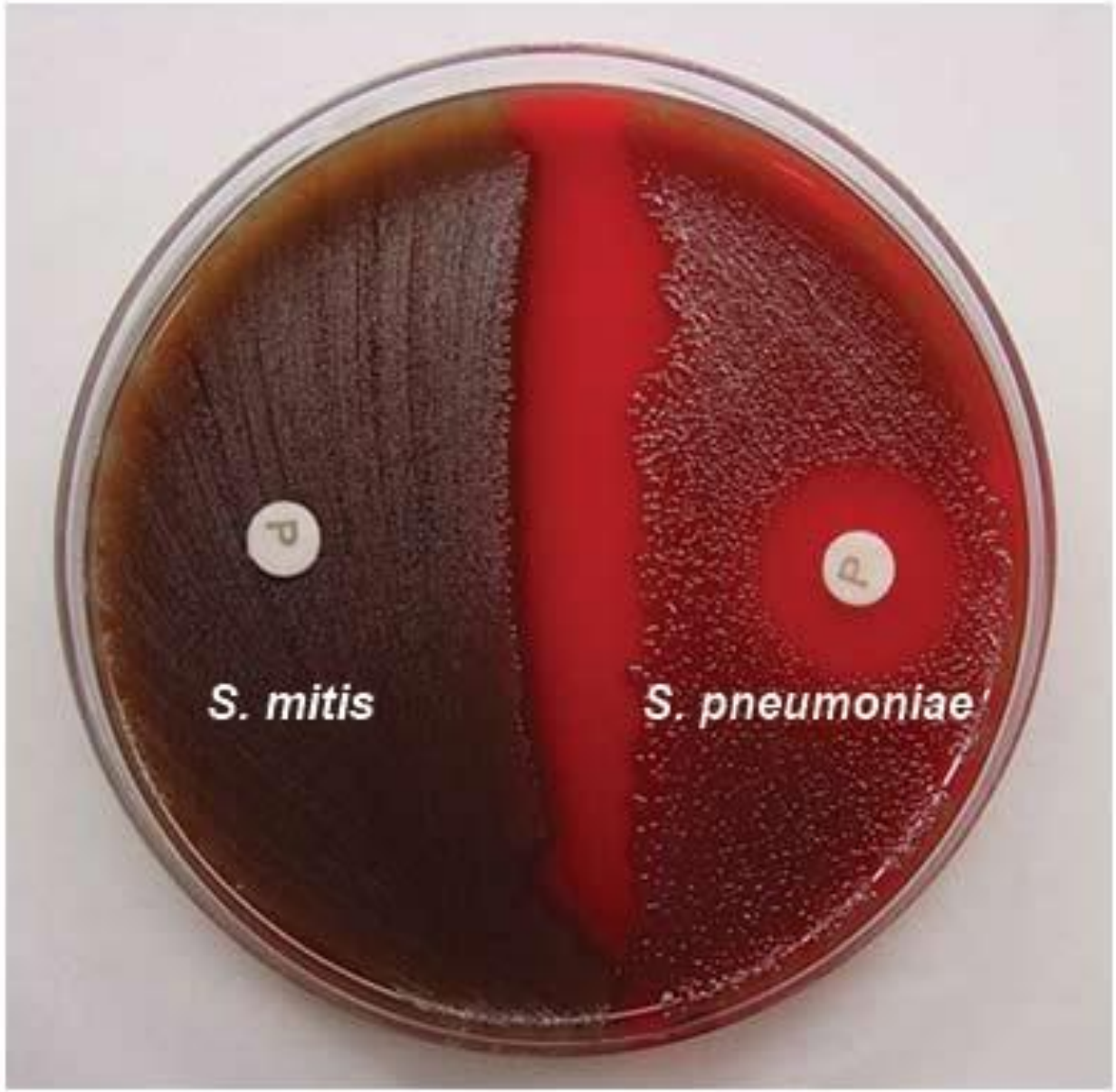
C. Meningitis



Streptococcus pneumoniae

E. Laboratory Diagnosis

1. Direct examination of Sputum
   - Gram-stain (PRESUMPTIVE DIAGNOSIS)
1. Culture
   - Appearance of α-hemolytic colonies that are bile soluble & optochin sensitive & positive Quellung reaction: (if typing sera is available - simplest, most rapid & accurate)



Left Side

S. mitis

Resistant to optochin

Right Side

S. pneumoniae

Susceptible to optochin

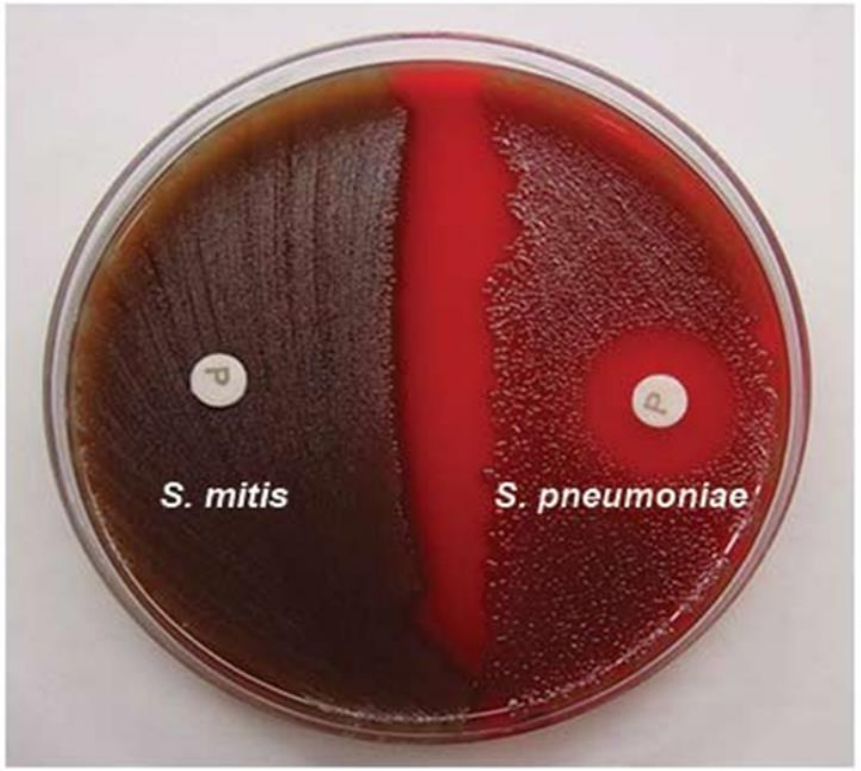
Streptococcus pneumoniae

E. Laboratory Diagnosis

3. Serologic Diagnosis
   i. Detection of pneumococcal antibodies
      - radioimmunoassay
   i. Detection of capsular polysaccharide
      - counterimmunoelectrophoresis

Signs that distinguish pneumococci from other streptococci:

- pneumococcal colonies are not confluent
- produces alpha hemolysis
- breaks down inulin to form acid
- is lysed by bile and bile acids
- has a high sensitivity to optoxin



OPTOXİN testi

S.mitis - davamlı

S.pneumoniae - həssas

Treatment, prevention and control

DRUGS USED:

- For streptococcal pharyngitis: Oral penicillin V or amoxicillin
- Oral cephalosporin or macrolides can be used for penicillin sensitive patients
- For severe, systemic infection: Combined use of intravenous penicillin with protein synthesis inhibiting antibiotics(clindamycin) is recommended
- *Streptococcal pyogenes* have developed resistance over tetracyclines and sulfonamides, newer macrolides
- Antimicrobial drugs has no effect on glomerulonephritis and rheumatic fever

Viridans group

- Streptococci normally resident in the mouth and upper respiratory tract
- Alpha lysis on blood agar
- Cannot be categorised under lancefield antigenic groups
- Types:

1. S.mitis
2. S.mutans
3. S.salivarius
4. S.sanguis

- Causes dental caries
- Tooth extraction – seeding into blood stream - endocarditis – hence give prophylactic antibiotics

DENTAL CARIES

--Progressive bacterial damage to teeth exposed to saliva.

--one of the most major causes of all diseases and major cause of tooth loss.

--ultimate effect-to breakdown enamel and dentin and open a path for bacteria to reach pulp.

Consequences-inflammation of pulp and periapical tissues.

AETIOLOGY

- Four major factors involved in etiology:-
- Cariogenic bacteria
- Bacterial plaque
- Susceptible tooth surface
- Fermentable bacterial substrate (sugar)

Bacteriology of Dental Caries

- Major organisms responsible for caries are:-
- Strep mutans
- Lactobacilli
- Other strains of streptocooci

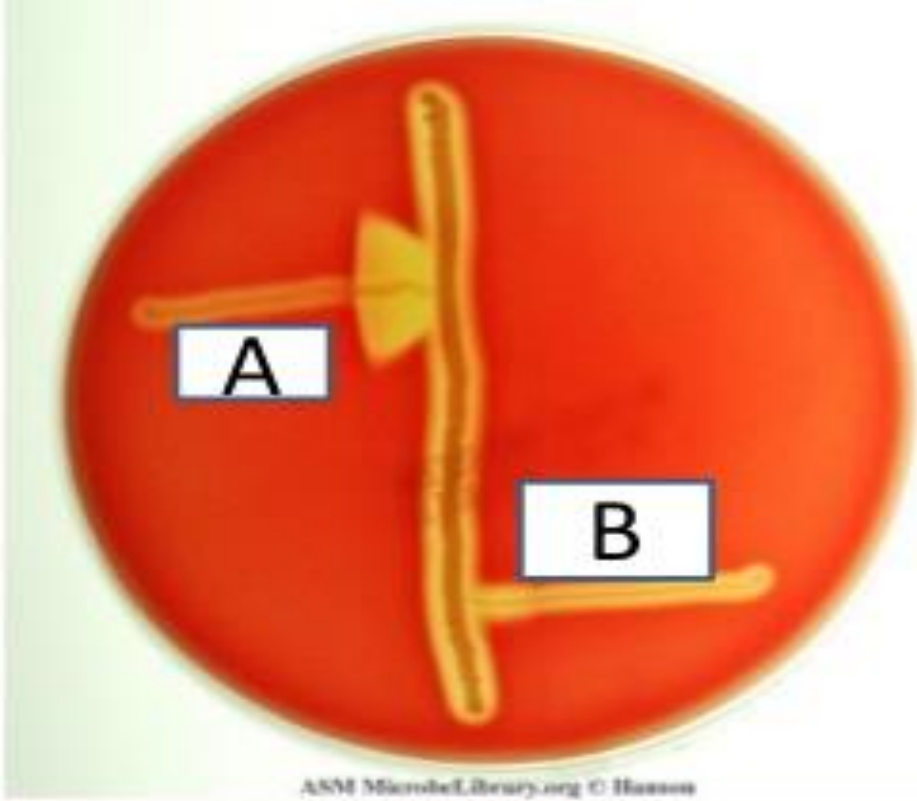
Group B beta hemolytic Streptococci

Streptococcus agalactiae

- Neonatal infection
- Most common cause of neonatal meningitis
- Source – from the maternal vagina during birth
- GBS – puerperal sepsis, pneumonia
- Diagnostic markers – Hippurate hydrolysis, CAMP test

CAMP test

- Christie, Atkins and Munch-Peterson
- When S.agalactiae is inoculated perpendicular to a streak of S.aureus grown on blood agar → an accentuated zone of hemolysis occurs



Name of the test: CAMP test
Example A: Positive - Strept agalactiae (Arrow shaped)
Example B: Negative - Strept pyogens
Principle : Strept agalactiae produce CAMP factor (a diffusible extracelluar protein) that synergistically acts with the beta-lysin of *Staphylococcus aureus* and enhances the lysis of red blood cells.

Enterococcus

- Gram positive cocci, non motile, non sporing
- Catalase Negative
- Previously classified as group D streptococci
- Natural inhabitants of GIT
- Distinct features
  - Ability to grow at 10°C and 45°C
  - Ability to grow in 6.5%NaCl
  - Ability to grow at 9.6pH
  - Ability to hydrolyze esculin in 40% bile
  - Ability to process pyrrolidonyl arylamidase (PYR)

Introduction

- Evolved from intestinal commensal to 2nd most common nosocomial pathogen.
- Common species
  - Entrococcus fecalis
  - Enterococcus fecium
  - E *gallinarum*
  - E *casseliflavus*
  - E *durans*
  - E *avium*
  - E *hirae*

Enterococcal Infections

- Group D cell wall antigen
- *Enterococcus faecalis; Enterococcus faecium*
- GI tract of humans and animals
- UTI most common; wound infections; bacteremia; endocarditis
- Most infections from endogenous source
- Prolonged hospitalization and broad-spectrum antibiotics increase risk
- Antibiotic resistance (VRE)

Vancomycin-Resistant Enterococci

- (VRE), are bacterial strains of the genus *Enterococcus* that are resistant to the antibiotic vancomycin. Enterococci are gram-positive coccoid-shaped bacteria found in the digestive tract of some humans. To become VRE, vancomycin-sensitive enterococci typically obtain new DNA in the form of plasmids or transposons which encode genes that confer vancomycin resistance.