Staphylococcus

Classification

- **Family** **Micrococcaceae**
- **Genus** ***Micrococcus and Staphylococcus***
- **Species** ***S. aureus***
  S. saprophyticus
  S. epidermidis
  M. luteus

more than 20 species

Gram-Positive Cocci

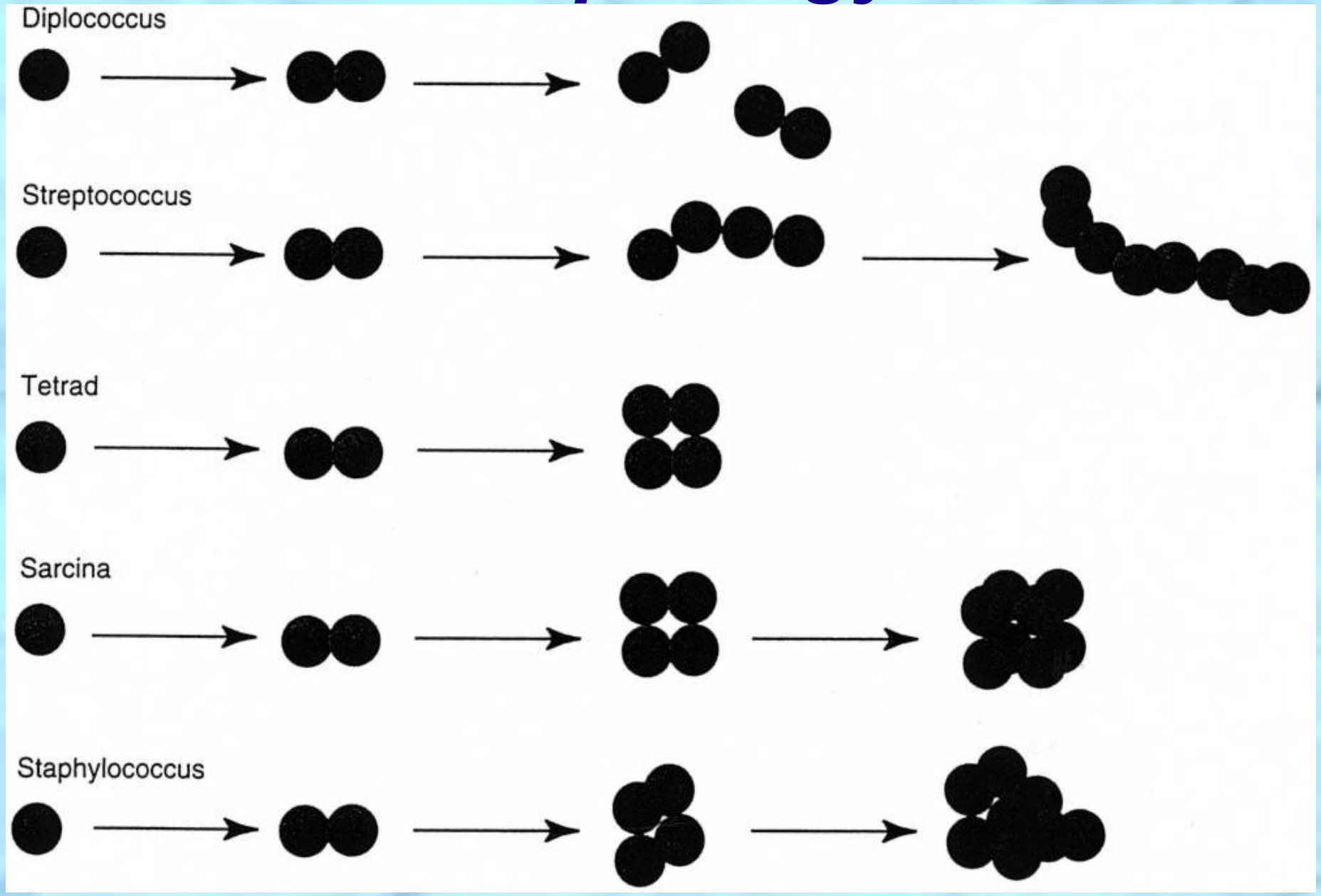
FAMILY Streptococcaceae (catalase negative)

- **Group A: β-hemolytic *Streptococcus pyogenes***
- **Group B: β-hemolytic (occasionally α or γ) *S. agalactiae***
- **Group C: β-hemolytic (α or γ) *S. anginosus, S. equismilis***
- **Group D: α or γ hemolytic (β) *S. bovis***
- **Group F: β-hemolytic *S. anginosus***
- **Group G: β -hemolytic *S. anginosus***
- **Viridans streptococci: (no group specific CHO)**
  - **α or γ hemolytic *S. mutans* and**
  - ***S. salivarius*, *S. sanguis*, *S. mitis and S. milleri* groups**
- ***Streptococcus pneumoniae* (no group CHO)(α-hemolytic)**
- ***Enterococcus* (Group D CHO) γ hemolytic (α or β)**
  - ***Enterococcus faecalis, E. faecium***

FAMILY Micrococcaceae (catalase positive)

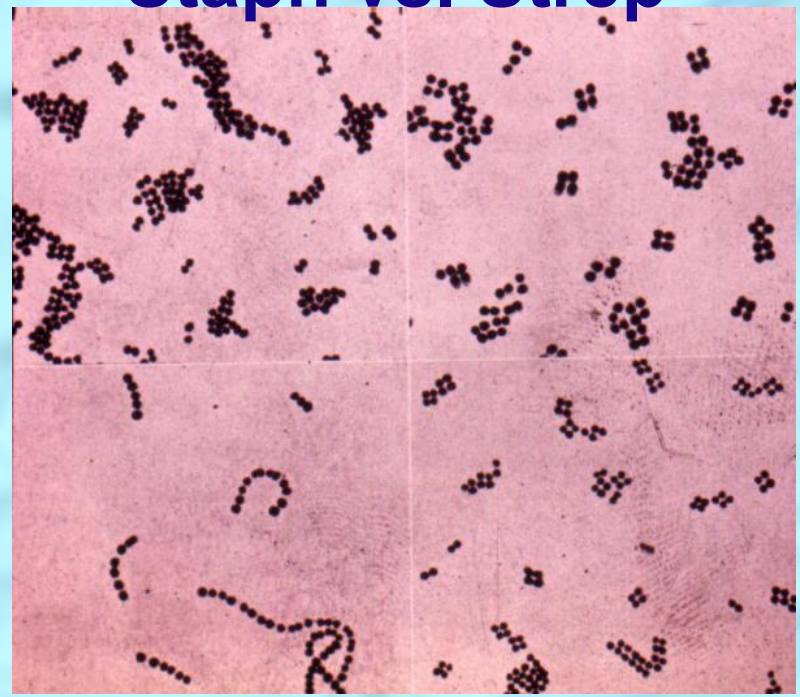
- **Coagulase-positive *Staphylococcus aureus***
- **Coag.-neg. *Staphylococcus epidermidis, S. saprophyticus***

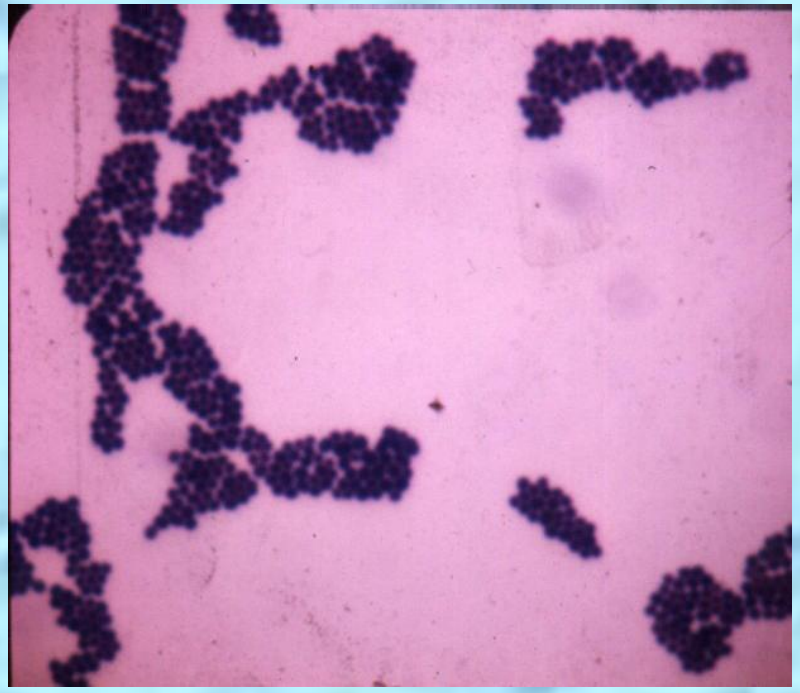
Morphology


Diplococcus
Streptococcus
Tetrad
Sarcina
Staphylococcus

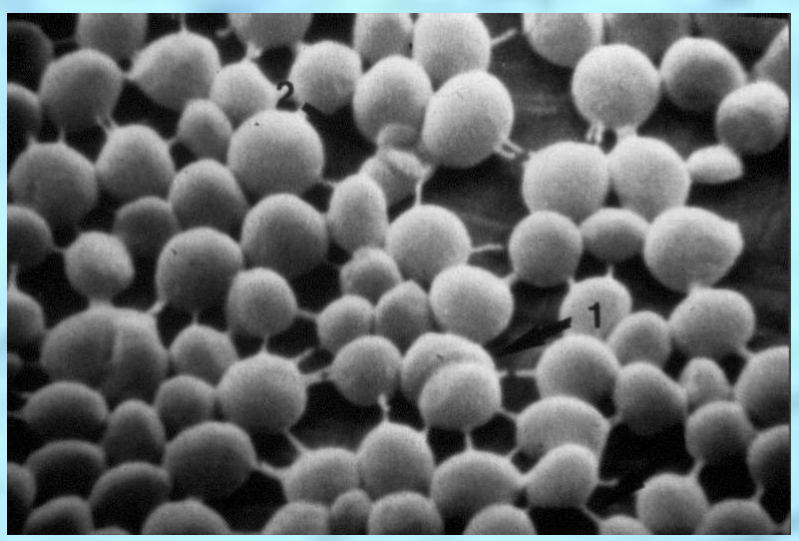
Morphology

Staph vs. Strep

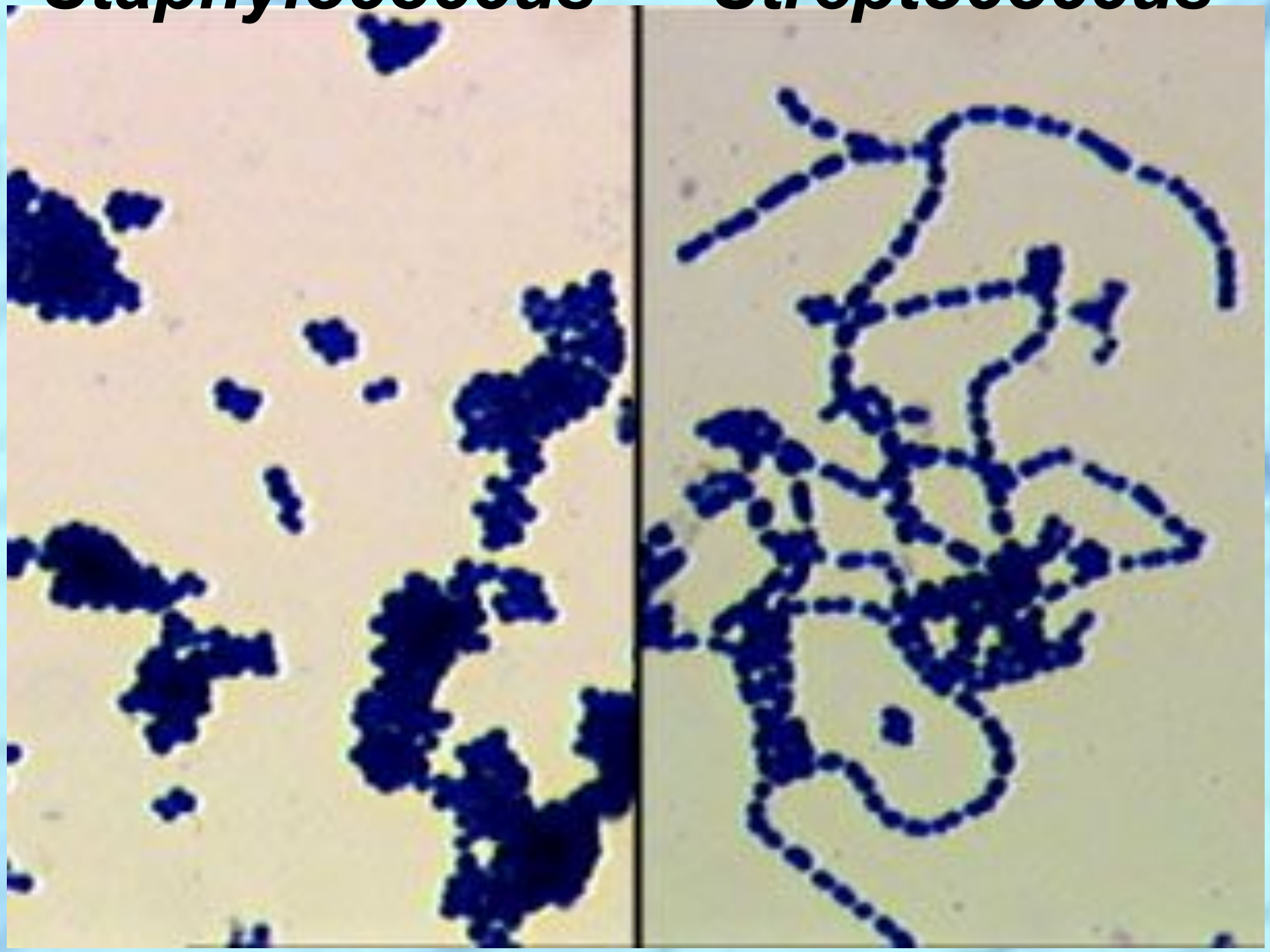




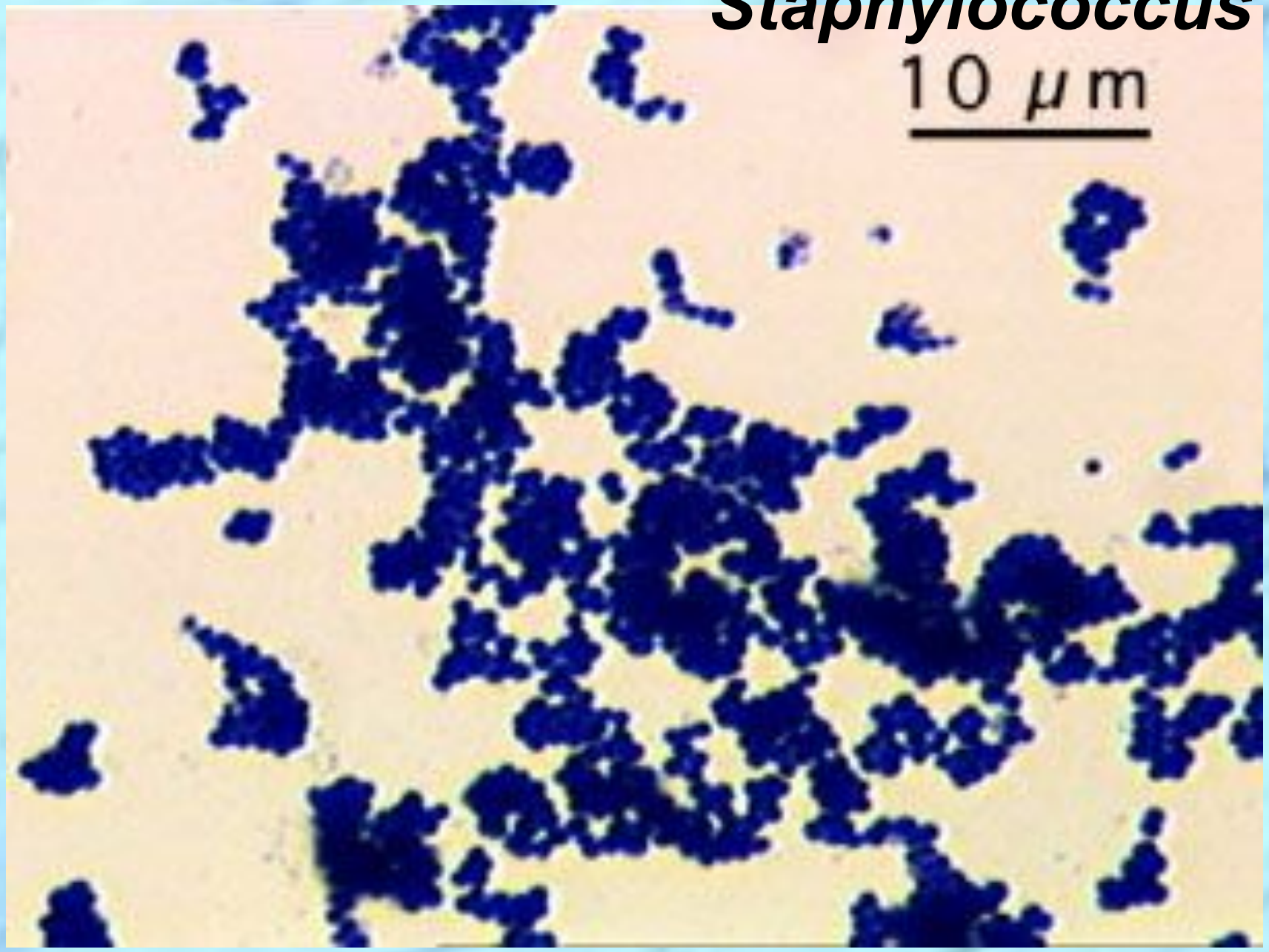
Gram-positive cocci in clusters



Staphylococcus ***Streptococcus***



Staphylococcus



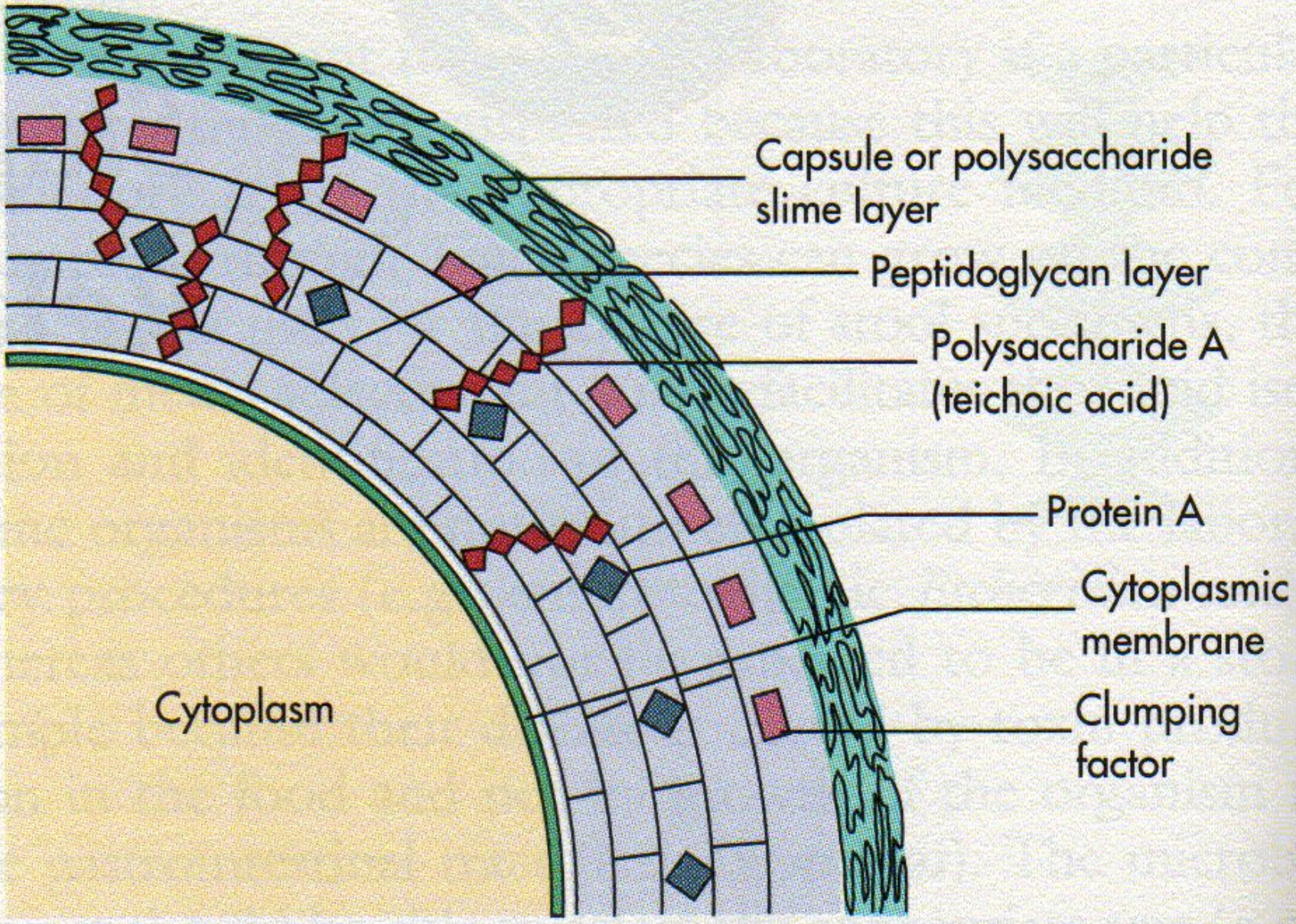
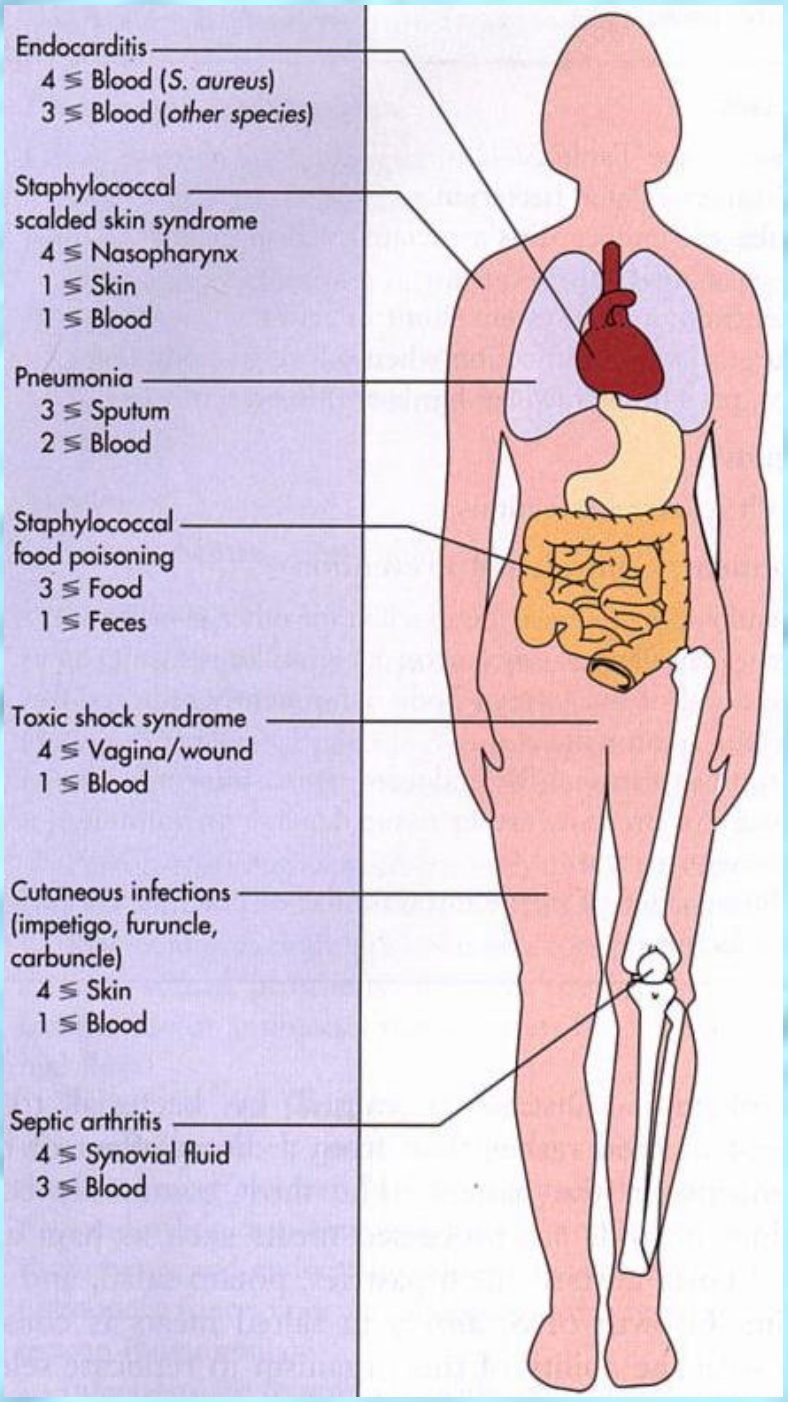

Capsule or polysaccharide slime layer
Peptidoglycan layer
Polysaccharide A (teichoic acid)
Protein A
Cytoplasmic membrane
Clumping factor
Cytoplasm

TABLE 22–2. ***Staphylococcus*, *Micrococcus*, *Stomatococcus*, and *Alloiococcus* and Their Diseases**

Organism	Diseases
Staphylococcus aureus	Toxin-mediated (food poisoning, toxic shock syndrome); cutaneous (impetigo, folliculitis, furuncles, carbuncles, wound infections); other (bacteremia, endocarditis, pneumonia, empyema, osteomyelitis, septic arthritis)
Staphylococcus epidermidis	Bacteremia; endocarditis; surgical wounds; urinary tract infections; opportunistic infections of catheters, shunts, prosthetic devices, and peritoneal dialysates
Staphylococcus saprophyticus	Urinary tract infections, opportunistic infections
Staphylococcus capitis	Bacteremia, endocarditis, urinary tract infections, wound infections, pneumonia, bone and joint infections, opportunistic infections
Staphylococcus haemolyticus	Bacteremia, endocarditis, urinary tract infections, wound infections, and opportunistic infections
Micrococcus spp.	Opportunistic infections
Stomatococcus mucilaginosus	Bacteremia, endocarditis, opportunistic infections
Alloiococcus otitidis	Chronic middle ear infections


Endocarditis
4 ≤ Blood (S. aureus)
3 ≤ Blood (other species)
Staphylococcal scalded skin syndrome
4 ≤ Nasopharynx
1 ≤ Skin
1 ≤ Blood
Pneumonia
3 ≤ Sputum
2 ≤ Blood
Staphylococcal food poisoning
3 ≤ Food
1 ≤ Feces
Toxic shock syndrome
4 ≤ Vagina/wound
1 ≤ Blood
Cutaneous infections (impetigo, furuncle, carbuncle)
4 ≤ Skin
1 ≤ Blood
Septic arthritis
4 ≤ Synovial fluid
3 ≤ Blood

See Overheads

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TSS

Foodborne Intoxication

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TABLE 22–3. *Staphylococcus aureus* **Virulence Factors**

Virulence Factors	Biologic Effects
Structural Components	
Capsule	Inhibits chemotaxis and phagocytosis; inhibits proliferation of mononuclear cells; facilitates adherence to foreign bodies
Peptidoglycan	Provides osmotic stability; stimulates production of endogenous pyrogen (endotoxin-like activity); leukocyte chemoattractant (abscess formation); inhibits phagocytosis
Teichoic acid	Regulates cationic concentration at cell membrane; binds to fibronectin
Protein A	Inhibits antibody-mediated clearance by binding IgG_1, IgG_2, and IgG_4 Fc receptors; leukocyte chemoattractant; anticomplementary
Cytoplasmic membrane	Osmotic barrier; regulates transport into and out of cell; site of biosynthetic and respiratory enzymes
Toxins	
Cytotoxins (α, β, δ, γ, P-V leukocidin)	Toxic for many cells, including leukocytes, erythrocytes, macrophages, platelets, and fibroblasts
Exfoliative toxins (ETA, ETB)	Serine proteases that split the intercellular bridges in the stratum granulosum epidermis
Enterotoxins (A–E, G–I)	Superantigens (stimulates proliferation of T cells and release of cytokines); stimulates release of inflammatory mediators in mast cells, increasing intestinal peristalsis and fluid loss, as well as nausea and vomiting
Toxic Shock Syndrome Toxin-1	Superantigen (stimulates proliferation of T cells and release of cytokines); produces leakage or cellular destruction of endothelial cells
Enzymes	
Coagulase	Converts fibrinogen to fibrin
Catalase	Catalyzes removal of hydrogen peroxide
Hyaluronidase	Hydrolyzes hyaluronic acids in connective tissue, promoting the spread of staphylococci in tissue
Fibrinolysin	Dissolves fibrin clots
Lipases	Hydrolyzes lipids
Nucleases	Hydrolyzes DNA
Penicillinase	Hydrolyzes penicillins

MICROBIAL PATHOGEN	ADHESIN	RECEPTOR
Staphylococcus aureus	**Lipoteichoic acid**	Unknown
Staphylococcus spp.	**Slime layer**	Unknown
Group A *Streptococcus*	**LTA-M protein complex**	**Fibronectin**
Streptococcus pneumoniae	Protein	N-acetylhexosamine-gal
Escherichia coli	Type 1 fimbriae	D-Mannose
	CFA 1 fimbriae	GM ganglioside
	P fimbriae	P blood grp glycolipid
Other Enterobacteriaceae	Type 1 fimbriae	D-Mannose
Neisseria gonorrhoeae	Fimbriae	GD_1 ganglioside
Treponema pallidum	P_1, P_2, P_3	Fibronectin
Chlamydia spp.	Cell surface lectin	N-acetylglucosamine
Mycoplasma pneumoniae	Protein P1	Sialic acid
Vibrio cholerae	Type 4 pili	Fucose and mannose

Cell-Associated Virulence Factors

- **Capsule** or **slime layer (glycocalyx)**
- Peptidoglycan (PG)
- **Teichoic acid** is covalently linked to PG and is species specific:
  - ✔ S. aureus **ribitol teichoic acid** (polysaccharide A)
  - ✔ S. epidermidis **glycerol teichoic acid** (polysaccharide B)
- **Protein A** is covalently linked to PG
- **Clumping factor** (bound **coagulase**)

Virulence Factors Extracellular Enzymes

- **Coagulases** (bound or free)
  - ✔ Antigenic
- **Hyaluronidase**
  - ✔ “spreading factor” of *S. aureus*
- **Nuclease**
  - ✔ Cleaves DNA and RNA in *S. aureus*
- **Protease**
  - ✔ Staphylokinase (fibrinolysin)
- **Lipases**
- **Esterases**

Virulence Factors: Exotoxins

- **Cytolytic** (cytotoxins; cytolysins)
  - ✔ **Alpha** toxin - hemolysin
    - Reacts with RBCs
  - ✔ **Beta** toxin
    - Sphingomyelinase
  - ✔ **Gamma** toxin
    - Hemolytic activity
  - ✔ **Delta** toxin
    - Cytopathic for:
      - RBCs
      - Macrophages
      - Lymphocytes
      - Neutrophils
      - Platelets
    - Enterotoxic activity
  - ✔ **Leukocidin**

Virulence Factors: Exotoxins

- **Enterotoxin**
- **Exfoliative toxin** (epidermolytic toxin)
- **Pyrogenic exotoxins**

Pathogenesis

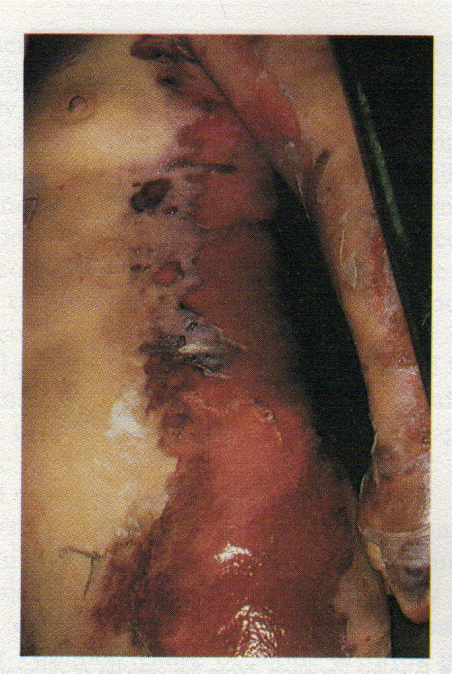
- Pass skin – first line of defense
  - ✔ Benign infection
    - Phagocytosis
    - Antibody
    - Inflammatory response
  - ✔ Chronic infections
    - Delayed hypersensitivity

Clinical Manifestations/Disease

- **SKIN**
  - ✔ **folliculitis**
  - ✔ **boils (furuncles)**
  - ✔ **carbuncles**
- ✔ **impetigo** (bullous & pustular)
- ✔ **scalded skin syndrome**
  - •Neonates and children under 4 years

Clinical Manifestations/Disease

- **Other infections**
  - ✔ Primary staphylococcal pneumonia
  - ✔ **Food poisoning vs. foodborne disease**
  - ✔ **Toxic shock syndrome**



Metastatic Infections

- **Bacteremia**
- **Osteomyelitis**
  - ✔ disease of growing bone
- Pulmonary and cardiovascular infection

Coagulase-Negative Staphylococci

- ***Staphylococcus epidermidis***
- ***S. saprophyticus***

BOX 22–2. Summary of Coagulase-Negative Staphylococcal Infections

Physiology and Structure

Gram-positive cocci arranged in clusters.

Facultative anaerobe (capable of aerobic and anaerobic growth).

Catalase-positive but coagulase-negative.

Species-specific teichoic acid.

Capsule ("slime" layer) present.

Virulence

Refer to Table 22–3.

Epidemiology

Normal human flora on skin and mucosal surfaces.

Organisms can survive on dry surfaces for long periods.

Person-to-person spread through direct contact or exposure to contaminated fomites (although most infections are with the patient's own organisms).

Patients at risk are those with foreign bodies (e.g., suture, prosthesis, shunt, catheter).

The organisms are ubiquitous, so there are no geographic or seasonal limitations.

Diseases

Diseases—see Table 22–2.

Catheter-related bacteremia.

Subacute endocarditis associated with previously damaged or artificial heart valve.

Central nervous system shunt infection.

Surgical wound infection when a foreign body (e.g., suture, prosthesis, medical hardware) is present.

Diagnosis

As with *S. aureus* infections.

Treatment, Control, and Prevention

The antibiotics of choice are oxacillin (or other penicillinase-resistant penicillin) or vancomycin for oxacillin-resistant strains.

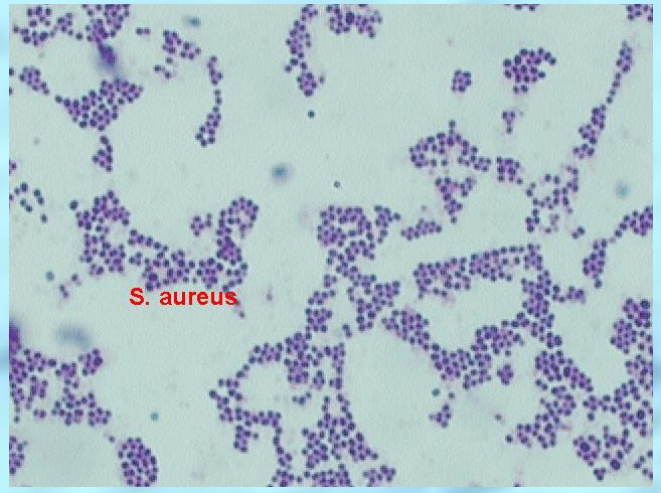
Removal of the foreign body is frequently required for successful treatment.

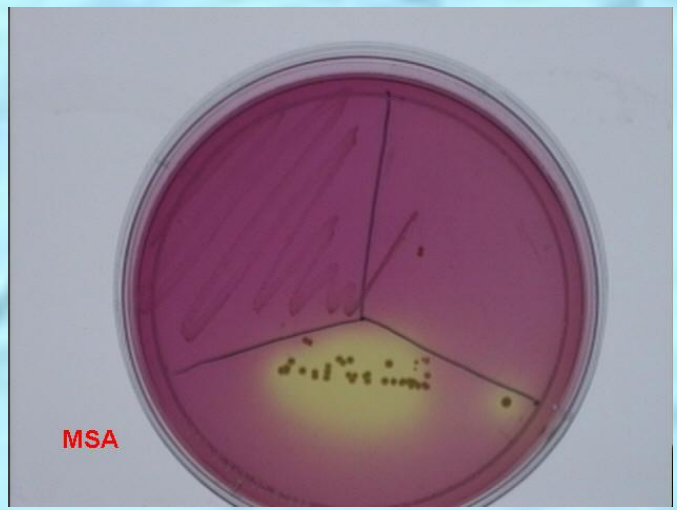
Prompt treatment for endocarditis or shunt infections is necessary to prevent further tissue damage or immune complex formation.

Maintenance of sterile intravascular catheters helps prevent infections.

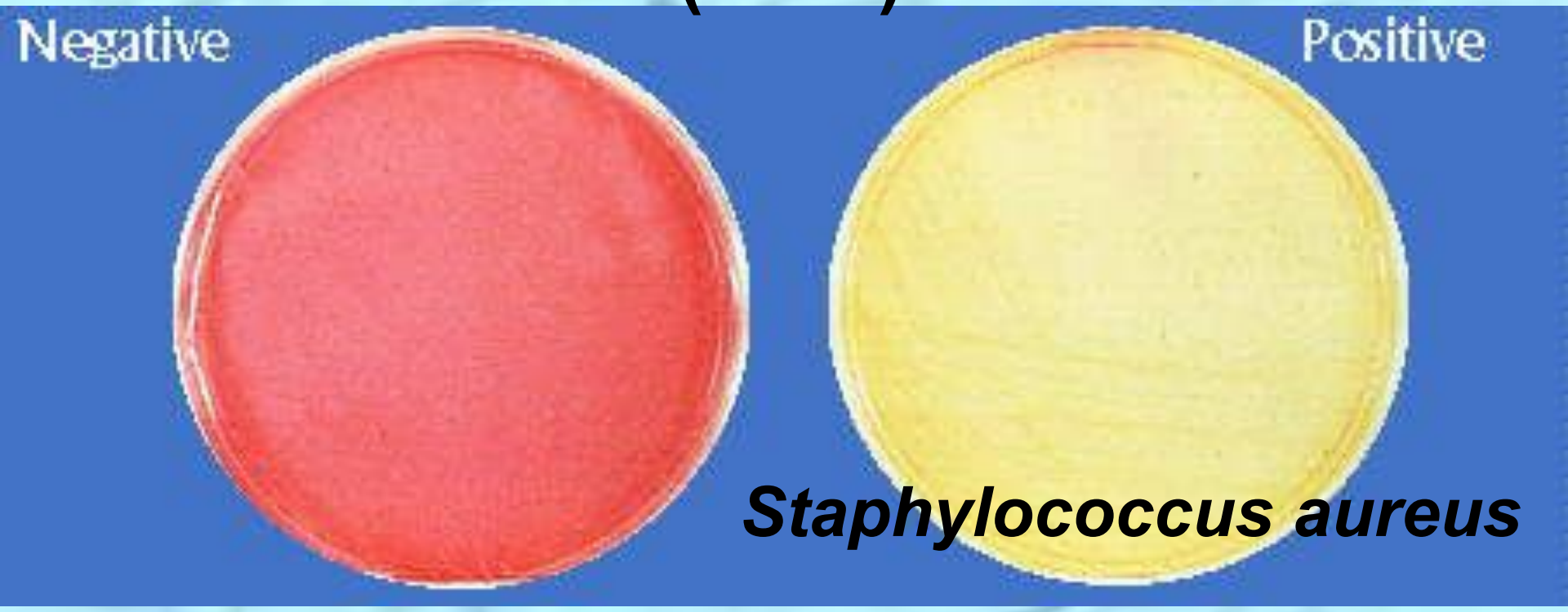
Staphylococcal Lab ID & Diagnostic Tests

- Microscopic
- Lab isolation
- **Coagulase positive**
  - ✔ ***S. aureus***





Mannitol Salts Agar (MSA)

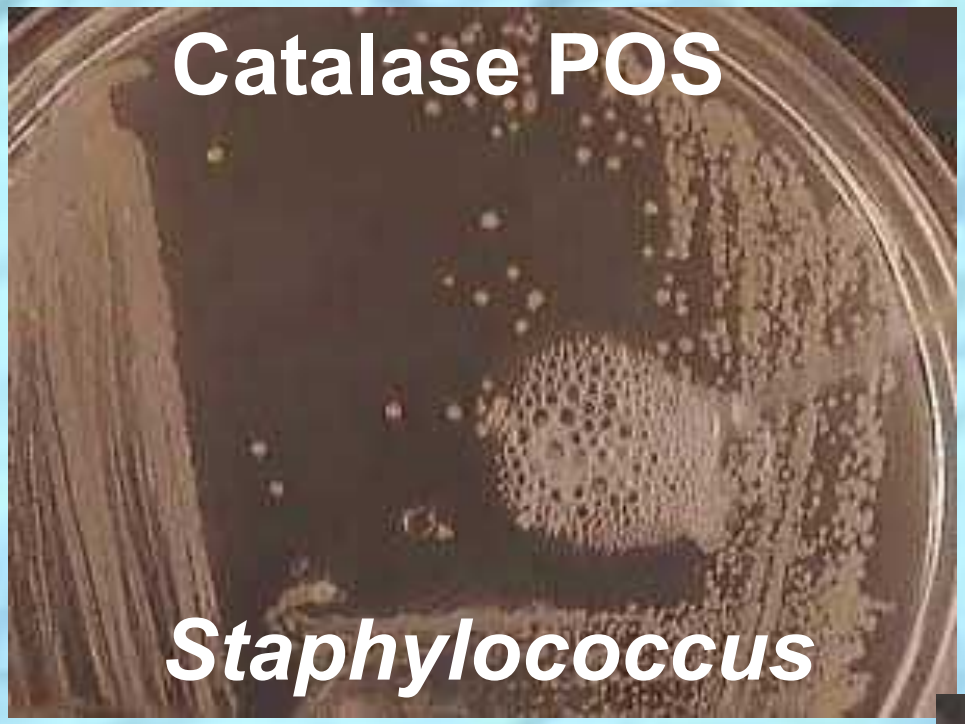


Differential Characteristics

Catalase

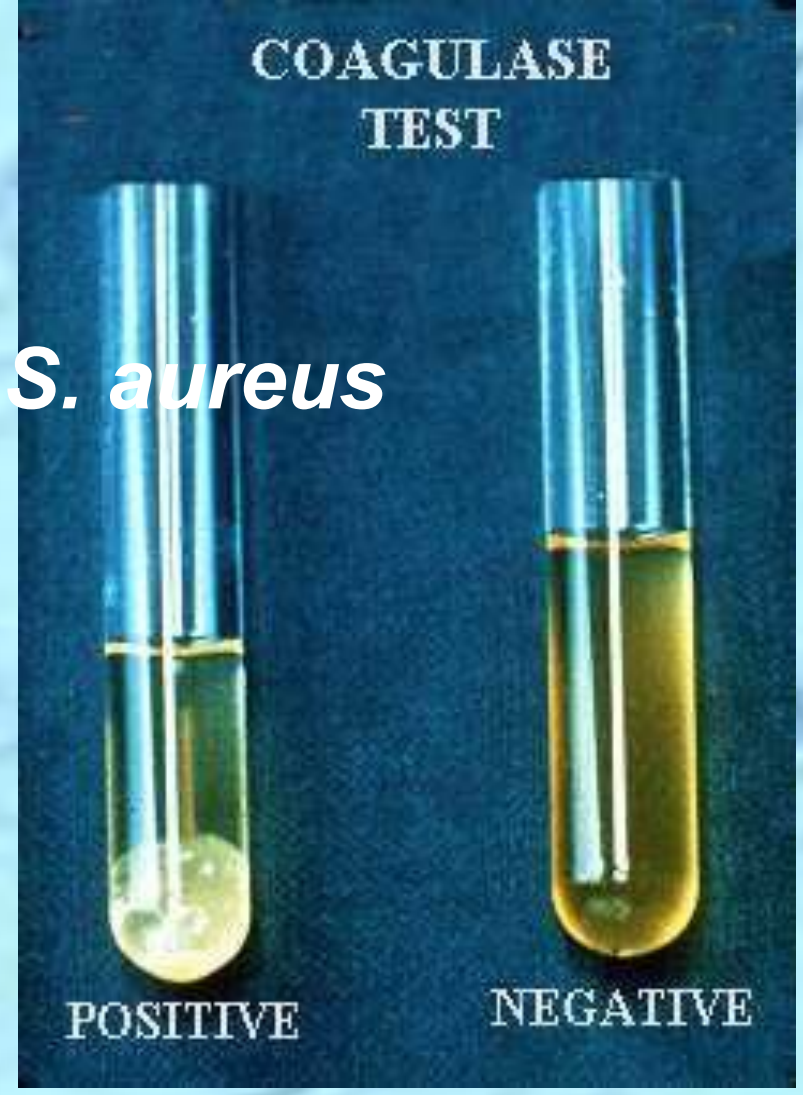
$$2H_2O_2 \square O_2 + 2H_2O$$

Streptococci vs. Staphylococci


Catalase POS
Staphylococcus

Catalase NEG

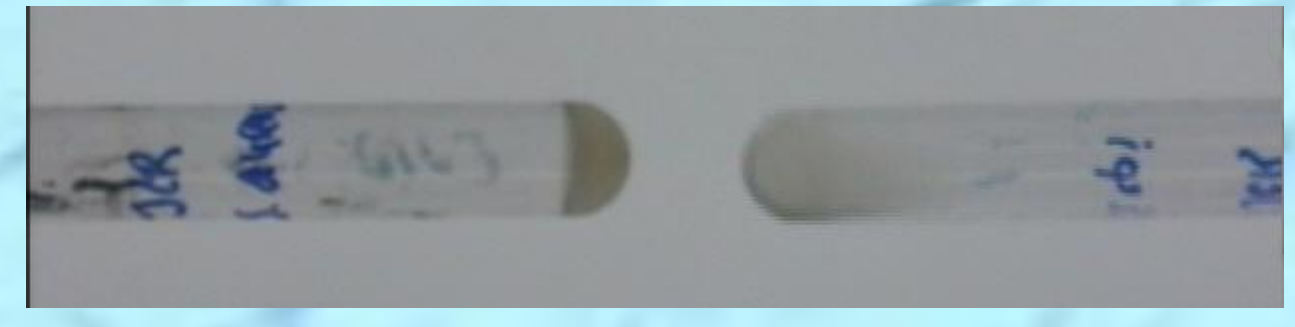
Differential Characteristics

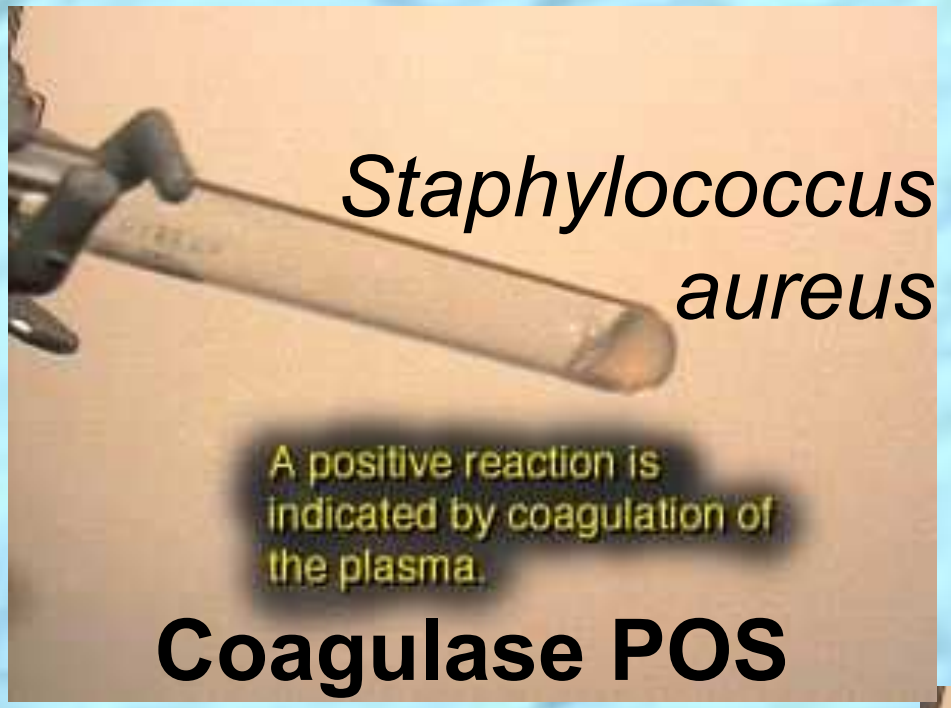


S. aureus

Coagulase

Fibrinogen Fibrin




Staphylococcus aureus
A positive reaction is indicated by coagulation of the plasma.
Coagulase POS

If the cells did not produce coagulase, the plasma remains fluid.
Coagulase NEG

Treatment

- **Drain infected area**
- **Deep/metastatic infections**
  - ✔ **semi-synthetic penicllins**
  - ✔ **cephalosporins**
  - ✔ **erythromycin**
  - ✔ **clindamycin**
- **Endocarditis**
  - ✔ **semi-synthetic penicillin + an aminoglycoside**

Prevention

- **Carrier** status prevents complete control
- Proper hygiene, segregation of carrier from highly susceptible individuals
- Good **aseptic techniques** when handling surgical instruments
- **Control of nosocomial** infections

REVIEW

Gram-Positive Cocci

FAMILY Streptococcaceae (catalase negative)

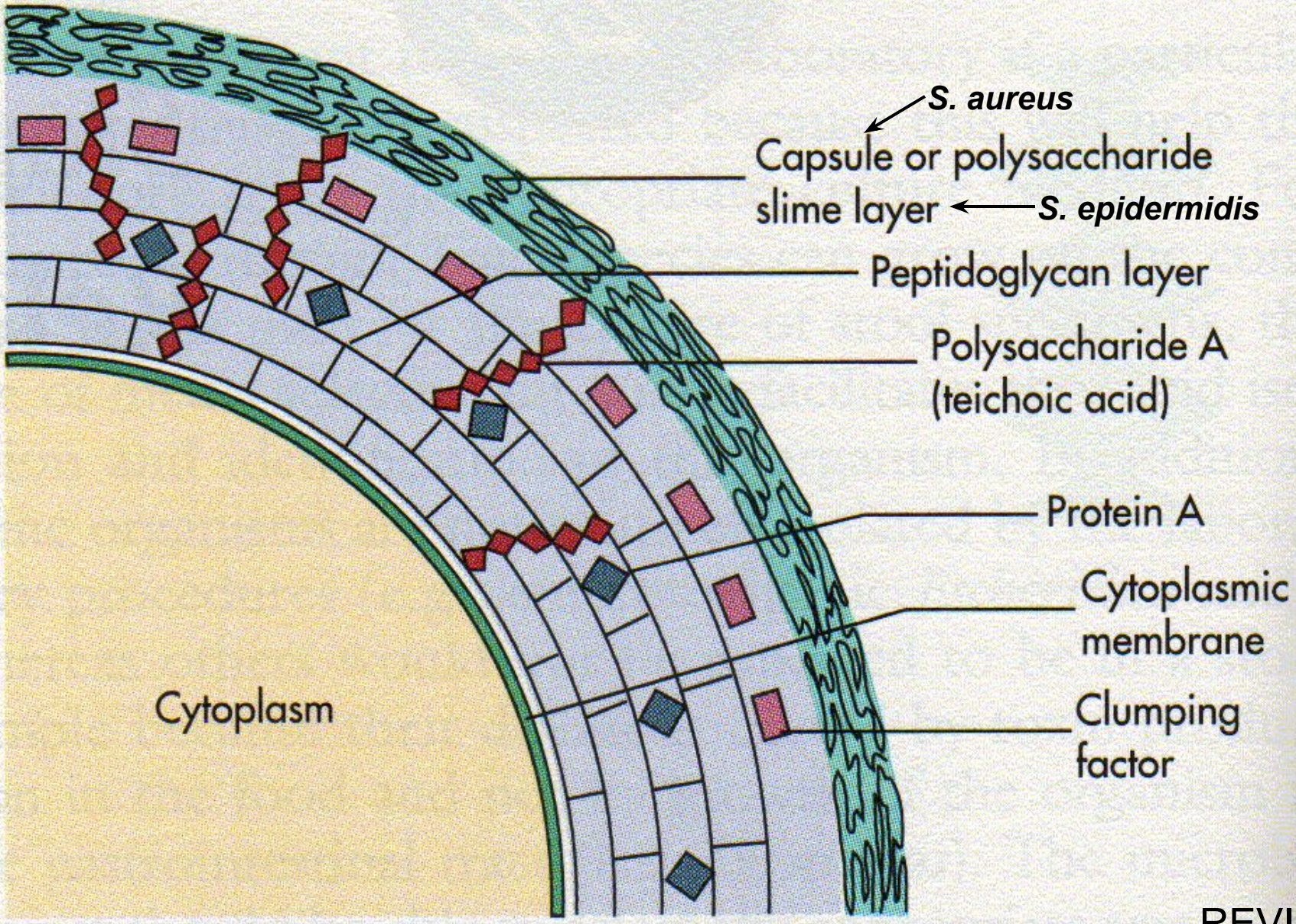
- **Group A: β-hemolytic *Streptococcus pyogenes***
- **Group B: β-hemolytic (occasionally α or γ) *S. agalactiae***
- **Group C: β-hemolytic (α or γ) *S. anginosus, S. equismilis***
- **Group D: α or γ hemolytic (β) *S. bovis***
- **Group F: β-hemolytic *S. anginosus***
- **Group G: β -hemolytic *S. anginosus***
- **Viridans streptococci: (no group specific CHO)**
  - **α or γ hemolytic *S. mutans* and**
  - ***S. salivarius*, *S. sanguis*, *S. mitis and S. milleri* groups**
- ***Streptococcus pneumoniae* (no group CHO)(α-hemolytic)**
- ***Enterococcus* (Group D CHO) γ hemolytic (α or β)**
  - ***Enterococcus faecalis, E. faecium***

FAMILY Micrococcaceae (catalase positive)

- **Coagulase-positive *Staphylococcus aureus***
- **Coag.-neg. *Staphylococcus epidermidis, S. saprophyticus***

REVIEW

Which features are only found in *S. aureus*?



REVIEW

TABLE 22–2. ***Staphylococcus*, *Micrococcus*, *Stomatococcus*, and *Alloiococcus* and Their Diseases**

Organism	Diseases
Staphylococcus aureus	Toxin-mediated (food poisoning, toxic shock syndrome); cutaneous (impetigo, folliculitis, furuncles, carbuncles, wound infections); other (bacteremia, endocarditis, pneumonia, empyema, osteomyelitis, septic arthritis)
Staphylococcus epidermidis	Bacteremia; endocarditis; surgical wounds; urinary tract infections; opportunistic infections of catheters, shunts, prosthetic devices, and peritoneal dialysates
Staphylococcus saprophyticus	Urinary tract infections, opportunistic infections
Staphylococcus capitis	Bacteremia, endocarditis, urinary tract infections, wound infections, pneumonia, bone and joint infections, opportunistic infections
Staphylococcus haemolyticus	Bacteremia, endocarditis, urinary tract infections, wound infections, and opportunistic infections
Micrococcus spp.	Opportunistic infections
Stomatococcus mucilaginosus	Bacteremia, endocarditis, opportunistic infections
Alloiococcus otitidis	Chronic middle ear infections

REVIEW

BOX 22–1. Summary of *Staphylococcus aureus* Infections

Physiology and Structure

Gram-positive cocci aranged in clusters.

Facultative anaerobe (capable of aerobic and anaerobic growth).

Coagulase ("clumping factor") positive (key identification test).

Species-specific teichoic acid.

Protein A (useful for identification).

Capsule.

Virulence

Virulence factors—see Table 22–3.

Epidemiology

Normal flora on human skin and mucosal surfaces.

Organisms can survive on dry surfaces for long periods (owing to thickened peptidoglycan layer and absence of outer membrane—characteristics of all gram-positive bacteria).

Person-to-person spread through direct contact or exposure to contaminated fomites (e.g., bed linens, clothing).

Risk factors include presence of a foreign body (e.g., splinter, suture, prosthesis, catheter), previous surgical procedure, use of antibiotics that suppress the normal microbial flora).

Patients at risk for specific diseases include menstruating women (toxic shock syndrome), infants (scalded skin syndrome), young children with poor personal hygiene (impetigo and other cutaneous infections), intravascular catheters (bacteremia and endocarditis); patients with compromised pulmonary function or an antecedent viral respiratory infection (pneumonia).

Infections are found worldwide and generally with no seasonal prevalence (except that food poisoning is more common in summer and during late-year holidays).

Diseases

Refer to Table 22–2.

Toxin-mediated diseases include food poisoning, toxic shock syndrome, and scalded skin syndrome.

Pyogenic diseases include impetigo, folliculitis, furuncles, carbuncles, and wound infections.

Other systemic diseases (frequently associated with bacteremia) include pneumonia (typically after viral respiratory infection), empyema (complication of pneumonia or surgical intervention), septic arthritis, osteomyelitis, acute endocarditis, and catheter-related bacteremia.

Diagnosis

Microscopy is useful for pyogenic infections but not blood stream infections or toxin-mediated infections.

Staphylococci grow rapidly when cultured on nonselective media.

Detection of staphylococcal antigens by serology are generally of low value.

Treatment, Control, and Prevention

The antibiotics of choice are oxacillin (or other penicillinase-resistant penicillin) or vancomycin for oxacillin-resistant strains.

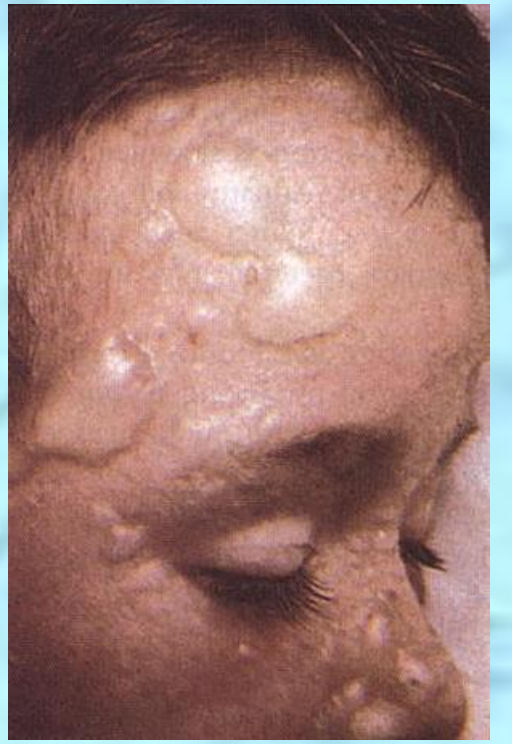
The focus of infection (e.g., abscess) must be identified and drained.

Treatment is symptomatic for patients with food poisoning (although the source of infection should be identified so that appropriate preventive procedures can be enacted).

Proper cleansing of wounds and use of disinfectant help prevent infections.

Thorough hand washing and covering of exposed skin helps medical personnel prevent infection or spread to other patients.

REVIEW



REVIEW

TABLE 22–3. *Staphylococcus aureus* **Virulence Factors**

Virulence Factors	Biologic Effects
Structural Components	
Capsule	Inhibits chemotaxis and phagocytosis; inhibits proliferation of mononuclear cells; facilitates adherence to foreign bodies
Peptidoglycan	Provides osmotic stability; stimulates production of endogenous pyrogen (endotoxin-like activity); leukocyte chemoattractant (abscess formation); inhibits phagocytosis
Teichoic acid	Regulates cationic concentration at cell membrane; binds to fibronectin
Protein A	Inhibits antibody-mediated clearance by binding IgG_1, IgG_2, and IgG_4 Fc receptors; leukocyte chemoattractant; anticomplementary
Cytoplasmic membrane	Osmotic barrier; regulates transport into and out of cell; site of biosynthetic and respiratory enzymes
Toxins	
Cytotoxins (α, β, δ, γ, P-V leukocidin)	Toxic for many cells, including leukocytes, erythrocytes, macrophages, platelets, and fibroblasts
Exfoliative toxins (ETA, ETB)	Serine proteases that split the intercellular bridges in the stratum granulosum epidermis
Enterotoxins (A–E, G–I)	Superantigens (stimulates proliferation of T cells and release of cytokines); stimulates release of inflammatory mediators in mast cells, increasing intestinal peristalsis and fluid loss, as well as nausea and vomiting
Toxic Shock Syndrome Toxin-1	Superantigen (stimulates proliferation of T cells and release of cytokines); produces leakage or cellular destruction of endothelial cells
Enzymes	
Coagulase	Converts fibrinogen to fibrin
Catalase	Catalyzes removal of hydrogen peroxide
Hyaluronidase	Hydrolyzes hyaluronic acids in connective tissue, promoting the spread of staphylococci in tissue
Fibrinolysin	Dissolves fibrin clots
Lipases	Hydrolyzes lipids
Nucleases	Hydrolyzes DNA
Penicillinase	Hydrolyzes penicillins

REVIEW

BOX 22–2. Summary of Coagulase-Negative Staphylococcal Infections

Physiology and Structure

Gram-positive cocci arranged in clusters.

Facultative anaerobe (capable of aerobic and anaerobic growth).

Catalase-positive but coagulase-negative.

Species-specific teichoic acid.

Capsule ("slime" layer) present.

Virulence

Refer to Table 22–3.

Epidemiology

Normal human flora on skin and mucosal surfaces.

Organisms can survive on dry surfaces for long periods.

Person-to-person spread through direct contact or exposure to contaminated fomites (although most infections are with the patient's own organisms).

Patients at risk are those with foreign bodies (e.g., suture, prosthesis, shunt, catheter).

The organisms are ubiquitous, so there are no geographic or seasonal limitations.

Diseases

Diseases—see Table 22–2.

Catheter-related bacteremia.

Subacute endocarditis associated with previously damaged or artificial heart valve.

Central nervous system shunt infection.

Surgical wound infection when a foreign body (e.g., suture, prosthesis, medical hardware) is present.

Diagnosis

As with *S. aureus* infections.

Treatment, Control, and Prevention

The antibiotics of choice are oxacillin (or other penicillinase-resistant penicillin) or vancomycin for oxacillin-resistant strains.

Removal of the foreign body is frequently required for successful treatment.

Prompt treatment for endocarditis or shunt infections is necessary to prevent further tissue damage or immune complex formation.

Maintenance of sterile intravascular catheters helps prevent infections.

REVIEW