🦠 "Gram-Positive Cocci"

📌 Introduction

- Two medically important genera:
  - Staphylococcus
  - Streptococcus
- Both are non-motile and non-spore-forming.

🔑 Key Differences ⭐

Feature	Staphylococcus	Streptococcus
Microscopic arrangement	Grape-like clusters 🍇	Chains ⛓️
Catalase test	Positive ✅	Negative ❌
Principle	Breaks $H_2O_2 \rightarrow H_2O + O_2$	No catalase enzyme

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🧬 Staphylococcus

🚨 Diseases Caused

Staphylococcus aureus (most pathogenic)

Localized infections

- Abscesses (classic lesion ⭐)
- Folliculitis, cellulitis, impetigo
- Bacterial conjunctivitis 👁️

Systemic / serious infections

- Endocarditis
- Septic arthritis
- Osteomyelitis
- Hospital-acquired pneumonia
- Septicemia
- Surgical wound infections

Toxin-mediated diseases

- Food poisoning 🍲
- Scalded skin syndrome
- Toxic shock syndrome (TSS)

Other Clinically Important Staphylococci

MRSA (Methicillin-Resistant S. aureus)

- Common cause of skin abscesses (especially in USA)
- Causes pneumonia, necrotizing fasciitis, sepsis

Staphylococcus epidermidis

- Prosthetic valve endocarditis
- Prosthetic joint infections
- CNS shunt infections
- Neonatal sepsis 👶

Staphylococcus saprophyticus

- Urinary tract infection (cystitis)
- Common in young sexually active women

Kawasaki Syndrome

- Possible association with toxigenic *S. aureus* strains

🔬 Important Properties of Staphylococci

Morphology

- Gram-positive cocci
- Spherical
- Irregular clusters

Catalase Test

- All staphylococci are catalase-positive ✅
- Catalase:
  - Converts $H_2O_2 \rightarrow H_2O + O_2$
  - Helps bacteria survive oxidative killing by neutrophils

Clinically Important Species

- S. aureus → coagulase positive
- S. epidermidis → coagulase negative
- S. saprophyticus → coagulase negative

Coagulase Test (Very High-Yield ⭐)

- S. aureus produces coagulase:
  - Activates prothrombin → thrombin

- Converts fibrinogen → fibrin clot 🩸
- Walls off bacteria from immune cells

- Coagulase-negative staphylococci (CONS):
  - S. epidermidis
  - S. saprophyticus

📊 Staphylococci of Medical Importance

Species	Coagulase	Hemolysis	Key Feature	Typical Disease
S. aureus	+	β	Protein A, golden pigment	Abscesses, food poisoning, TSS
S. epidermidis	–	None	Novobiocin sensitive, skin flora	Prosthetic valve/joint infections, CNS shunts
S. saprophyticus	–	None	Novobiocin resistant	UTI (cystitis)

📈 Flowchart: Differentiation of Staphylococci

Gram-positive cocci in clusters → Catalase positive → Staphylococcus

- Coagulase positive → S. aureus
- Coagulase negative
  - Novobiocin sensitive → S. epidermidis
  - Novobiocin resistant → S. saprophyticus

✨ Exam Points

- Catalase test distinguishes Staphylococcus vs Streptococcus.
- Coagulase test distinguishes S. aureus from CONS.
- Abscess formation strongly suggests S. aureus.

🧬 Staphylococcus aureus – Virulence & Resistance

🎨 Pigment Production

- Produces staphyloxanthin (carotenoid pigment)
- Colonies appear golden ✨
- Function:
    - Neutralizes reactive oxygen species (ROS)
    - Enhances survival inside neutrophils

➡️ S. epidermidis lacks pigment → white colonies ⚪ → less virulent

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🍬 Fermentation & Hemolysis

S. aureus

- Ferments mannitol (basis of Mannitol Salt Agar)
- Produces hemolysins:
    - Lyse RBCs
    - Release iron → used in cytochrome enzymes

S. epidermidis & S. saprophyticus

- Do not ferment mannitol
- Non-hemolytic

💊 Antibiotic Resistance

β-lactamase Production

- ~90% of *S. aureus* strains
- Plasmid-encoded β-lactamase
- Inactivates many penicillins

MRSA (Methicillin-Resistant S. aureus)

- Due to mecA gene
- Encodes altered PBP (PBP-2a)
- Resistant to:
  - Methicillin
  - Nafcillin
  - Other β-lactams

Types:

- HCA-MRSA 🏥
- CA-MRSA 🏡 (often P-V leukocidin positive)

➡️ Common US strain: USA300

Vancomycin Resistance

- VISA – intermediate resistance
- VRSA – full resistance
- Resistance genes acquired from enterococci
- Mechanism:
  - D-alanine → D-lactate substitution in peptidoglycan

🧩 Cell Wall Components & Antigens

1️⃣ Protein A 🛡️

- Major surface protein of *S. aureus*
- Binds Fc portion of IgG
- Blocks complement activation
- ↓ Opsonization & phagocytosis
- Used in diagnostic coagglutination tests
- Absent in CONS

2️⃣ Teichoic Acids

- Ribitol phosphate polymers
- Functions:
  - Adherence to mucosal cells
  - Lipoteichoic acids → IL-1, TNF release → septic shock
- Act as bacteriophage receptors (phage typing)

3️⃣ Polysaccharide Capsule 🎭

- Anti-phagocytic
- 11 serotypes
- Types 5 & 8 → ~85% infections
- Poorly immunogenic → vaccine challenge

4️⃣ Peptidoglycan

- Structural rigidity
- Endotoxin-like effects:
  - Macrophage activation
  - Cytokine release
  - Complement & coagulation activation

➡️ Explains septic shock without LPS.

📈 Flowchart: Antibiotic Resistance in S. aureus

Penicillin-sensitive strain → Acquisition of β-lactamase plasmid → Penicillin-resistant strain → mecA gene → altered PBPs → MRSA / NRSA → Vancomycin pressure → VISA / VRSA (D-Ala → D-Lac)

🔄 Transmission of Staphylococci

🧍 Reservoir

- Humans are primary reservoir

📍 Sites of Colonization

S. aureus

- Nose 👃 (≈30% carriers)
- Skin
- Vagina (~5%) → risk of TSS

S. epidermidis

- Normal skin flora

S. saprophyticus

- Genital tract mucosa

📤 Modes of Transmission

- Direct contact (hands ✋ - most important)
- Shedding from lesions
- Fomites (towels, clothes)

➡️ Handwashing 🚿 = best preventive measure

⚠️ Predisposing Factors for S. aureus

- Contaminated environment
- Immune defects:
  - ↓ Antibodies
  - ↓ Complement

    - ↓ Neutrophils
- Diabetes mellitus 🍬
- IV drug use 💉
- Chronic Granulomatous Disease (CGD)

🌡️ Transmission Pathways

-> S. aureus

Nasal colonization → Autoinoculation → Skin infections

Vaginal colonization → Toxic shock syndrome

Lesion shedding / fomites → Community spread

Hand contact→ Hospital transmission

-> S. epidermidis

Skin flora → IV catheter entry → Sepsis / prosthetic infections

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-> S. saprophyticus

Genital colonization → Ascending infection → Cystitis (UTI)

🧪 Pathogenesis of Staphylococci

🔴 Staphylococcus aureus

Mechanisms

1. Toxin-mediated disease
2. Pyogenic inflammation → abscess formation ⭐

Foreign bodies (catheters, sutures) greatly increase risk.

⚡ Important Exotoxins

☐ Enterotoxins (A–F) 🍔

- Food poisoning
- Vomiting + watery diarrhea
- Superantigen activity

- Heat & acid stable
- Preformed toxin → rapid onset (2–6 h)

2️⃣ TSST-1 🚺

- Tampons, wounds, nasal packing
- Superantigen → IL-1, IL-2, TNF
- Shock without bacteremia
- Occurs if no neutralizing antibody

3️⃣ Exfoliatin 👶

- Protease
- Cleaves desmoglein
- Scalded Skin Syndrome
- Epidermal separation at granular layer

4️⃣ Leukocidins ⚔️

- Kill WBCs
- Alpha toxin → membrane pores
- Panton-Valentine leukocidin:
  - CA-MRSA
  - Necrotizing pneumonia

- Severe skin infections

🔬 Enzymes

- Coagulase
- Fibrinolysin
- Hyaluronidase
- Proteases, nucleases, lipases

⚪ Coagulase-Negative Staphylococci

S. epidermidis

- No exotoxins
- Prosthetic device infections

S. saprophyticus

- No exotoxins
- UTIs in young women

🧩 Flowchart: Pathogenesis of S. aureus

S. aureus infection

-> Toxigenic pathway

Enterotoxin → Food poisoning

TSST → Toxic shock syndrome

Exfoliatin → Scalded skin syndrome

P-V leukocidin → Necrosis, pneumonia

-> Pyogenic pathway

Local → Abscess, impetigo, wound infection

Disseminated → Sepsis, endocarditis, osteomyelitis, arthritis

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✨ Exam Pearls

- Abscess = hallmark of *S. aureus*
- Food poisoning = preformed toxin
- TSS = toxemia without bacteremia
- P-V leukocidin = CA-MRSA marker

🦠 Clinical Findings of Staphylococcus aureus

The clinical spectrum of *S. aureus* infections is classically divided into two major categories:

1. Pyogenic (pus-producing) infections
2. Toxin-mediated diseases

👉 *S. aureus* is a leading cause of infections of skin, soft tissues, bone, joints, lungs, heart, kidneys, and eyes, making it one of the most versatile human pathogens.

🔹 1. Pyogenic Diseases (Suppurative Infections)

(a) Skin & Soft Tissue Infections

Most common and characteristic manifestations 🔥

- Abscesses (hallmark lesion)
  → Central necrosis + pus formation

- Impetigo
- Furuncles (boils)
- Carbuncles 🔥 → Deep abscesses with multiple draining sinuses

- Paronychia (nail fold infection)
- Cellulitis
- Folliculitis
- Necrotizing fasciitis (severe, rapidly progressive)
- Hidradenitis suppurativa

- Ocular & adnexal infections:
  → Conjunctivitis 👁️
  → Blepharitis
  → Hordeolum (stye)

- Mastitis (especially postpartum women)

➡️ Lymphangitis may complicate hand infections.

➡️ Severe necrotizing infections are strongly associated with CA-MRSA strains producing Panton-Valentine (P-V) leukocidin.

High-risk groups ⚠️

- IV drug users 💉
- Homeless populations
- Athletes in close-contact sports (wrestling, football)

📌 Exam Pearl:

- CA-MRSA is the most common cause of skin & soft tissue infections in the USA.
- HCA-MRSA accounts for ~50% of nosocomial S. aureus infections.

(b) Septicemia (Sepsis)

- Usually originates from:
  → Wound infections
  → IV drug abuse 💉
- Clinical picture resembles gram-negative sepsis (e.g., *Neisseria meningitidis*):
  → Fever

→ Hypotension

→ Multiorgan involvement

(c) Endocarditis ❤️

• Can involve normal or prosthetic valves.

• Right-sided (tricuspid) endocarditis: → Common in IV drug users

• Prosthetic valve endocarditis: → Commonly caused by *S. epidermidis*

(d) Osteomyelitis & Septic Arthritis

• Routes of infection:

→ Hematogenous spread 🩸

→ Direct inoculation (trauma, surgery)

• Children are especially susceptible.

(e) Post-Surgical Wound Infections 🏥

- *S. aureus* is the leading cause.
- Associated with high morbidity & mortality.
- Common around:
  → Pacemaker sites
  → Surgical sutures

(f) Pneumonia 🫁

- Occurs:
  → Postoperatively
  → After viral infections (especially influenza)
- Complications:
  → Empyema
  → Lung abscess
- Nosocomial pneumonia:
  → *S. aureus* = most common cause overall
  → Major cause of ventilator-associated pneumonia (VAP)

- CA-MRSA:
  → Causes severe necrotizing pneumonia

(g) Conjunctivitis 👁️

- Features:
  → Unilateral burning pain
  → Red conjunctiva
  → Purulent discharge
- Transmission:
  → Fingers → eye (autoinoculation)
- Adults:
  → *S. aureus* most common cause
- Children:
  → *S. pneumoniae, H. influenzae* more common
- Neonatal conjunctivitis:
  → Gonococcal or Chlamydial (during birth)

(h) Metastatic Abscesses

- Result from hematogenous spread (bacteremia).
- Can involve any organ:
  → Liver
  → Kidney
  → Brain

📊 Flowchart: Clinical Spectrum of *S. aureus*

S. aureus infection

⬇️

-> Pyogenic (Suppurative) 🟠

- Skin & soft tissue infections
- Sepsis
- Endocarditis
- Osteomyelitis & septic arthritis
- Post-surgical wound infection
- Pneumonia

- Conjunctivitis
- Metastatic abscesses

-> Toxin-mediated 🔴

- Food poisoning (enterotoxin)
- Toxic shock syndrome (TSST-1)
- Scalded skin syndrome (exfoliatin)

🦠 Toxin-Mediated Diseases of *S. aureus*

1️⃣ Food Poisoning 🍗

- Cause:
  → Ingestion of preformed enterotoxin
- Incubation period:
  → 1–8 hours (very short)
- Clinical features:
  → Vomiting 🤢 (dominant)
  → Watery, non-bloody diarrhea

- Special point ⭐:
  → No fever (toxin-mediated, non-invasive)

2️⃣ Toxic Shock Syndrome (TSS) 🚺

- Etiology:
  → TSST-1 (superantigen)
- Risk factors:
  → Tampon use 🩸
  → Nasal packing
  → Infected wounds
- Clinical features:
  → Fever 🌡️
  → Hypotension (shock)
  → Diffuse macular sunburn-like rash
  → Later desquamation
  → Involvement of ≥3 organ systems:
    - Liver
    - Kidney

- GI tract
- CNS
- Muscle
- Blood

📌 Exam Pearl:

- Blood cultures are often negative because disease is toxin-mediated.

3️⃣ Scalded Skin Syndrome (SSS) 👶

- Cause:
  → Exfoliatin toxin (protease)
- Population:
  → Mainly infants & young children
- Features:
  → Fever
  → Erythematous macular rash
  → Large bullae

→ Epidermal sloughing (granular layer)

→ Fluid & electrolyte loss

- Prognosis:

  → Recovery in 7–10 days with proper care

📊 Flowchart: Toxin-Mediated Diseases

S. aureus toxins

⬇️

Enterotoxin → Food poisoning (rapid vomiting & diarrhea)

TSST-1 → Toxic shock syndrome (fever, shock, rash, multiorgan failure)

Exfoliatin → Scalded skin syndrome (bullae & skin sloughing in children)

❤️ Kawasaki Disease (KD)

📌 Not directly caused by *S. aureus*, but resembles superantigen-mediated diseases like TSS.

- Type:
  → Vasculitis of small & medium arteries (especially coronary arteries)

- Epidemiology:
  → Most common cause of acquired heart disease in children (USA)
  → Age <5 years
  → More common in children of Asian ancestry

🔎 Clinical Features

- High fever ≥5 days 🌡️
- Bilateral non-purulent conjunctivitis 👁️
- Oral changes:
  → Strawberry tongue 🍓
  → Lip edema
- Cervical lymphadenopathy
- Diffuse erythematous maculopapular rash

- Hands & feet:
  → Erythema & edema → later desquamation
- Cardiac involvement (most important) ❤️
  → Myocarditis
  → Arrhythmias
  → Valvular regurgitation
  → Coronary artery aneurysms (major cause of mortality)

🛠️ Treatment

→ High-dose IVIG + Aspirin
→ Prevents coronary artery aneurysms

🧫 Coagulase-Negative Staphylococci (CONS)

🟦 *Staphylococcus epidermidis*

- Normal habitat:
  → Skin & mucous membranes

- Infections:
  - → IV catheter-related sepsis
  - → Prosthetic valve & joint infections
  - → CSF shunt infections
  - → Neonatal sepsis 👶
  - → Peritonitis (peritoneal dialysis)
- Virulence factor:
  - → Glycocalyx → adherence to prosthetic devices
- Epidemiology:
  - → Mostly hospital-acquired 🏥

2️⃣ *Staphylococcus saprophyticus*

- Habitat:
  - → Genital tract mucosa of young women
- Disease:
  - → Community-acquired UTI (cystitis) 💧

- Epidemiology:
  → 2nd most common cause after *E. coli*
- Trigger:
  → Often follows sexual intercourse

3️⃣ *Staphylococcus lugdunensis*

- Less common but more virulent than other CONS
- Causes:
  → Prosthetic valve endocarditis
  → Skin & soft tissue infections

🔬 Laboratory Diagnosis of Staphylococci

- Smear:
  → Gram-positive cocci in grape-like clusters 🍇

- Culture:
  - → *S. aureus*: Golden-yellow, β-hemolytic colonies ✨
  - → CONS: White, non-hemolytic colonies ⚪
- Biochemical tests:
  - → *S. aureus*: Coagulase-positive
  - → CONS: Coagulase-negative
- Mannitol salt agar:
  - → *S. aureus*: Ferments mannitol → yellow agar 💛
  - → *S. epidermidis*: No fermentation → pink agar 💗
- Novobiocin test:
  - → *S. epidermidis*: Sensitive
  - → *S. saprophyticus*: Resistant 🚫

📌 Special points:

- No serologic tests used routinely
- TSS diagnosis is clinical
- Phage typing used for epidemiologic tracing

💊 Treatment of Staphylococcal Infections

- >90% strains resistant to Penicillin G (β-lactamase production)

MRSA

- Mechanism:
  → Altered PBPs (PBP2a)
- Resistant to:
  → All β-lactams
- Drug of choice:
  → Vancomycin
- Alternatives:
  → Daptomycin
  → Linezolid
  → Clindamycin
  → TMP-SMX
  → Ceftaroline (only effective β-lactam)

VISA / VRSA

- Drugs:
  - → Daptomycin
  - → Quinupristin-Dalfopristin

Special Clinical Situations

- Toxic shock syndrome:
  - → Supportive care
  - → Nafcillin
  - → Source removal
  - → IVIG may help
- Skin abscess:
  - → Incision & drainage = cornerstone 🚑
- Topical therapy:
  - → Mupirocin (skin + nasal decolonization)
  - → Chlorhexidine washes

🛡️ Prevention

- No vaccine available 🚫
- Hand hygiene 🧼 = most effective measure
- Aseptic hospital practices
- Decolonization of carriers when indicated
- Perioperative prophylaxis: → Cefazolin commonly used

-> The End <-