Introduction to Microbiology

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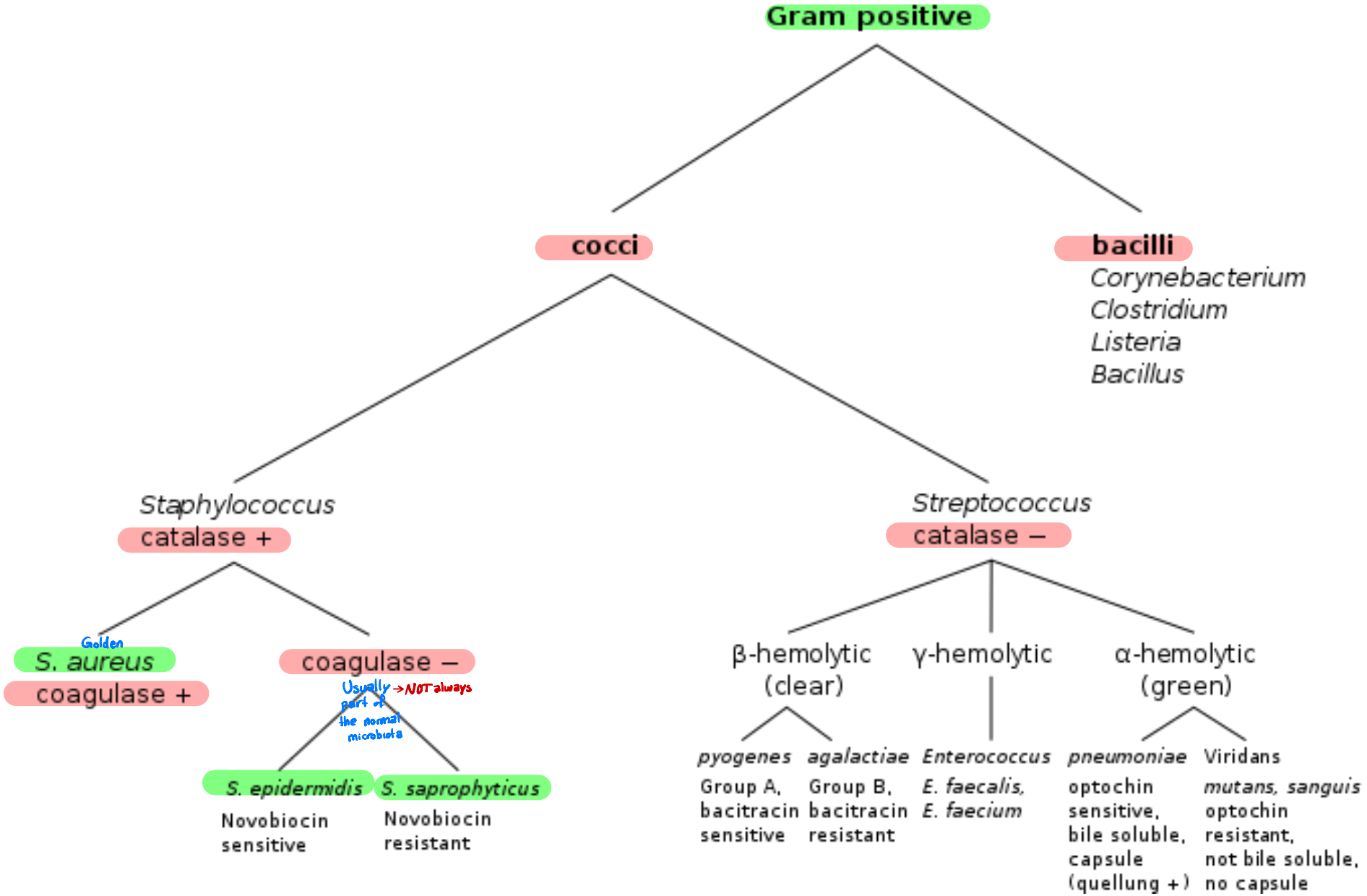
Staphylococci

Overview

Bacterial genera that will be discussed this lecture are Gram positive cocci and that cause a variety of infections in the skin and mucus membranes, and can secrete a variety of toxins:

Staphylococci


Gram positive
cocci
bacilli
Corynebacterium
Clostridium
Listeria
Bacillus
Staphylococcus
catalase +
Golden
S. aureus
coagulase +
coagulase –
Usually part of the normal microbiota → NOT always
S. epidermidis
Novobiocin sensitive
S. saprophyticus
Novobiocin resistant
Streptococcus
catalase –
β-hemolytic (clear)
γ-hemolytic
α-hemolytic (green)
pyogenes
Group A, bacitracin sensitive
agalactiae
Group B, bacitracin resistant
Enterococcus
E. faecalis, E. faecium
pneumoniae
optochin sensitive, bile soluble, capsule (quellung +)
Viridans
mutans, sanguis
optochin resistant, not bile soluble, no capsule

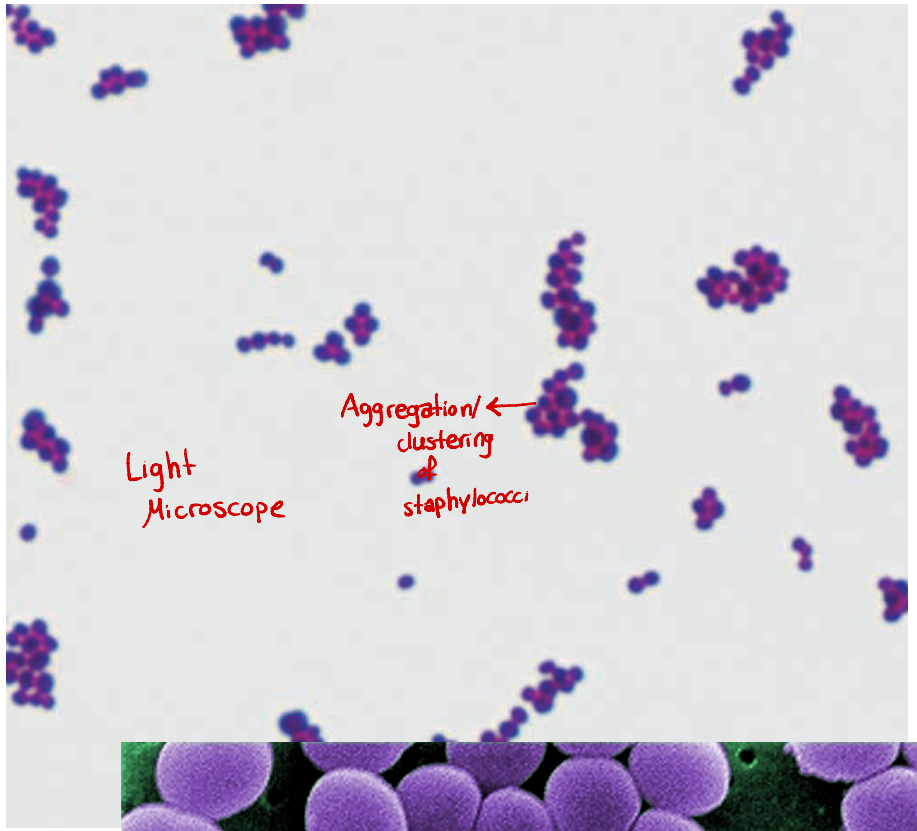
Staphylococci

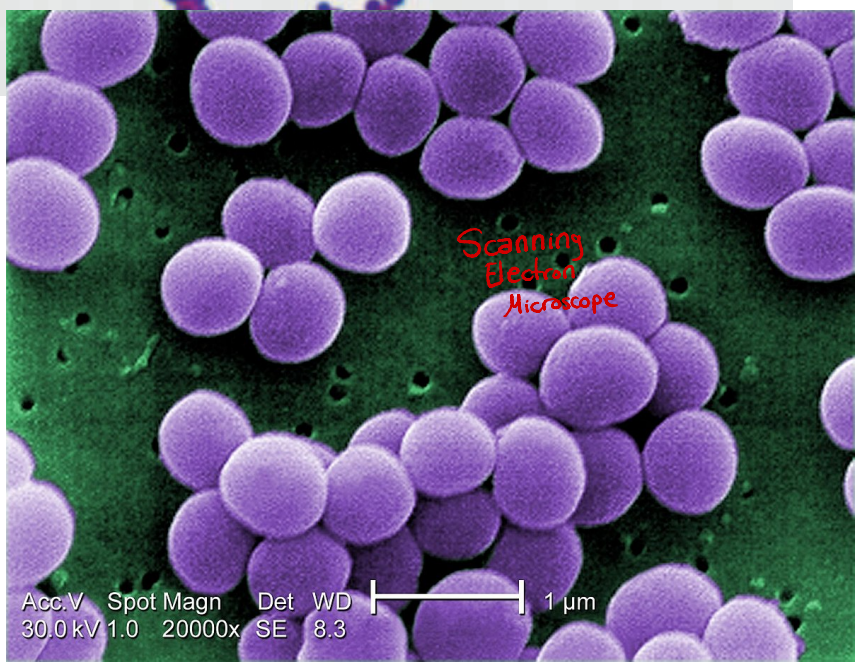
- The staphylococci are **gram-positive spherical cells**, about 1 µm in diameter usually arranged in grapelike **irregular clusters, it is non-motile.**

- The four most frequently encountered species of clinical importance are 1) ***Staphylococcus aureus,*** 2) ***Staphylococcus epidermidis,*** 3) ***Staphylococcus lugdunensis*** **, and** 4) ***Staphylococcus saprophyticus***.

Part of the human microbiota

2+3+4 are coagulase-





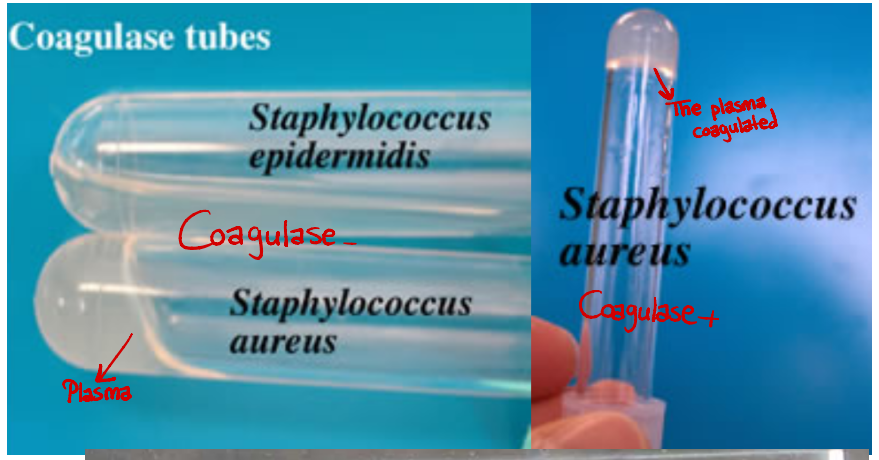
Staphylococci

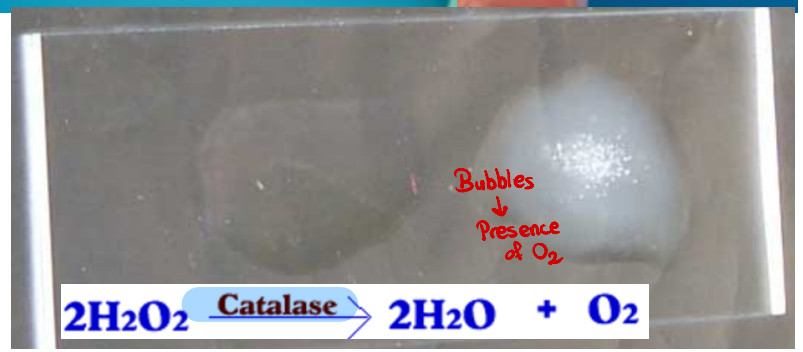
- *S aureus* is **coagulase positive,** The **coagulase-negative** staphylococci are normal human microbiota.

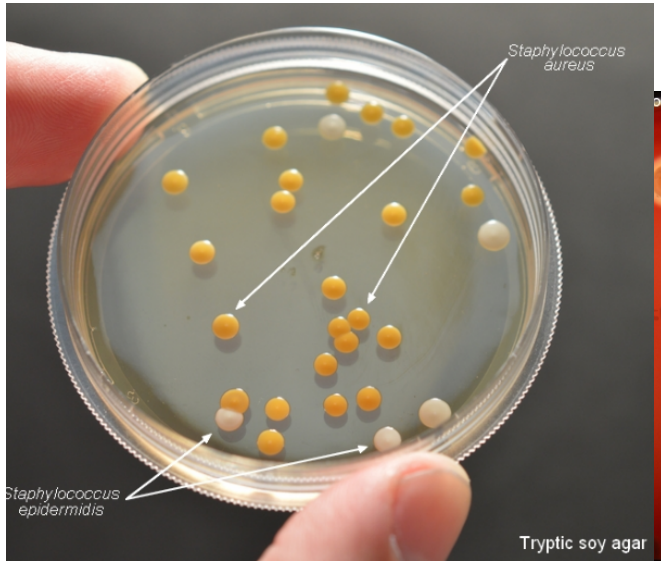
- Staphylococci produce **catalase**, which converts hydrogen peroxide into water and oxygen. The catalase test differentiates the **staphylococci**, which are **positive**, from the **streptococci**, which are **negative**.

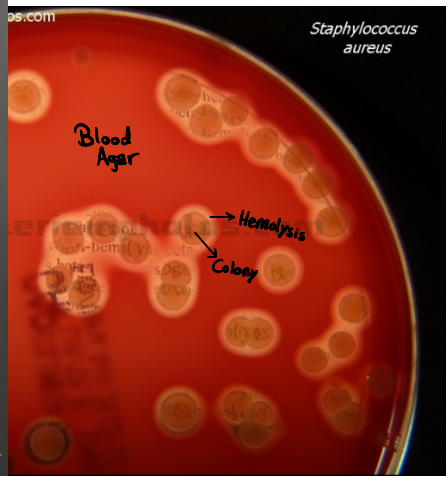
- *S aureus* usually **forms gray to deep golden yellow colonies**. *S epidermidis* colonies usually **are gray to white** on primary isolation

- Various degrees of **hemolysis** are produced by



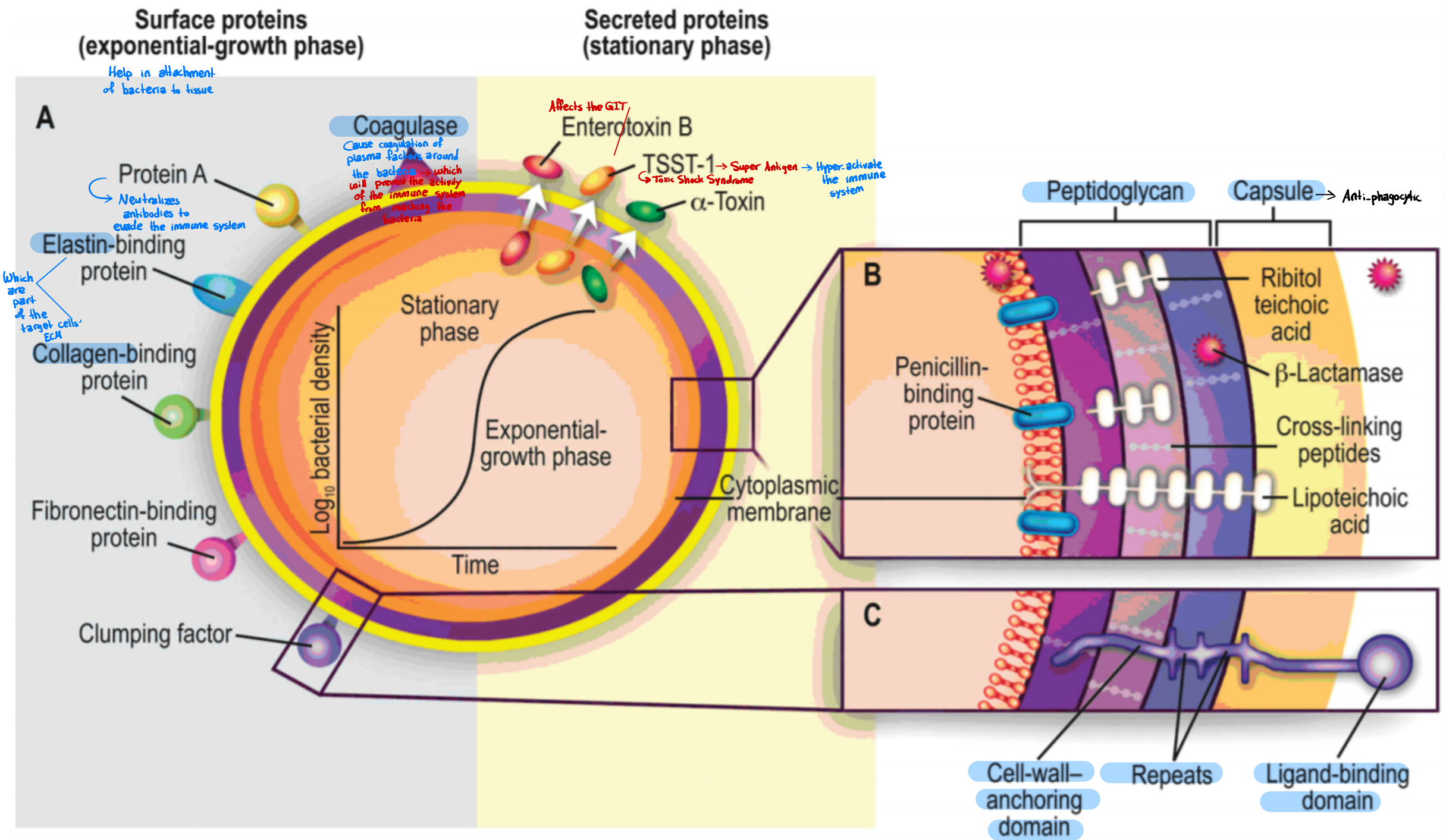






Staphylococci / Structure and physiology

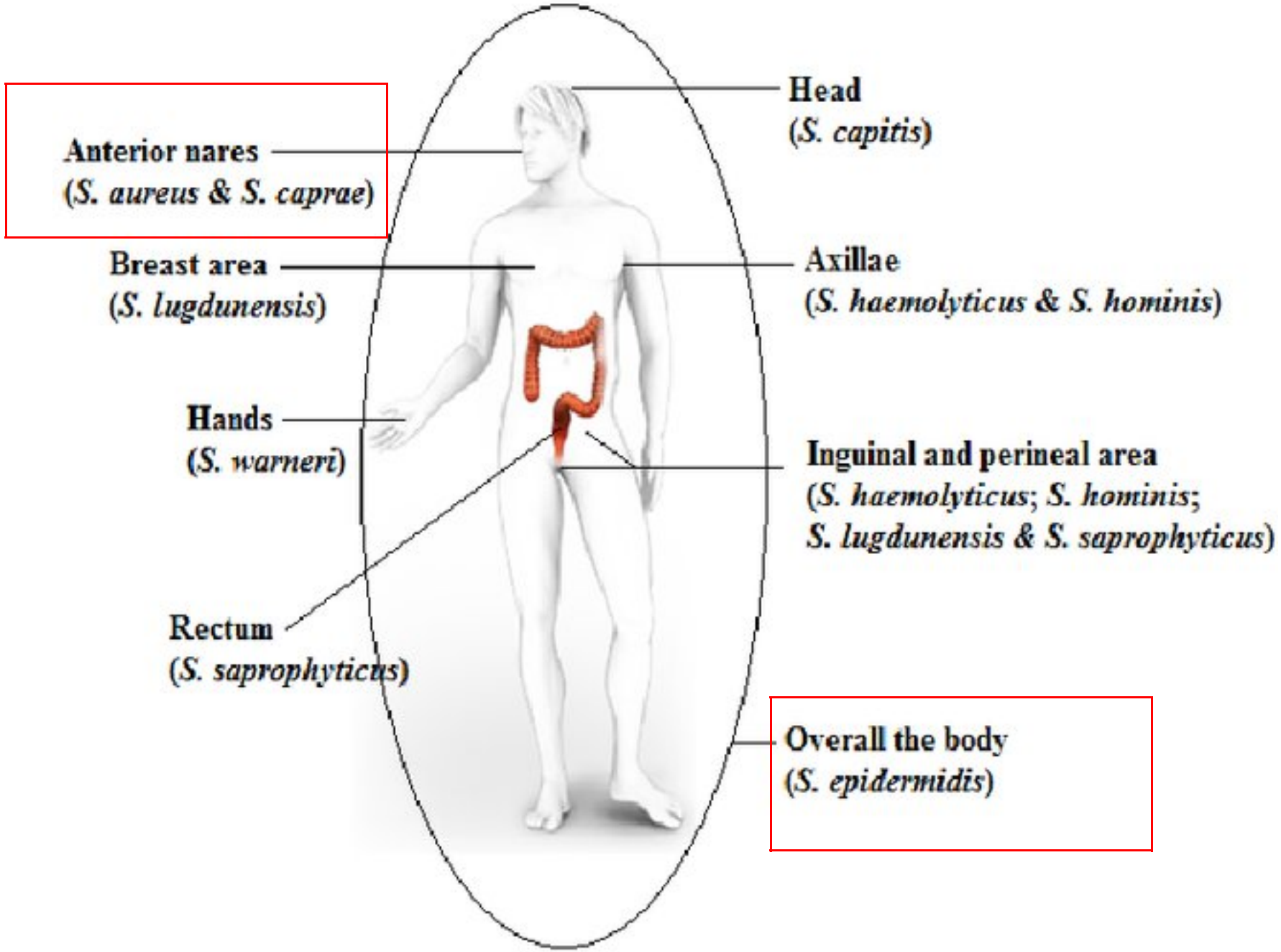
- **Peptidoglycan in the cell wall activate the immune response (**it can be a chemoattractant for polymorphonuclear leukocytes, have endotoxin-like activity, and activate complement. **)**
- Bacterial attachment to host cells is mediated by **MSCRAMM (*m*icrobial *s*urface *c*omponents *r*ecognizing *a*dhesive *m*atrix *m*olecules) proteins.** and these are important virulence factors. (e.g. Protein A, clumping factor)
- **Teichoic acids** are cross-linked to the peptidoglycan and can be antigenic.
- **Clumping factor A** is a fibrinogen-binding protein present on the surface of S. aureus that binds to fibrinogen and coats the surface of the bacterial cells with fibrinogen molecules, additionally complicating the recognition process.


Surface proteins
(exponential-growth phase)
Secreted proteins
(stationary phase)
Help in attachment of bacteria to tissue
A
Coagulase
Cause coagulation of plasma factors around the bacteria → which will prevent the activity of the immune system from reaching the bacteria
Affects the GIT
Enterotoxin B
TSST-1 → Super Antigen → Hyper-activate the immune system
↳ Toxic Shock Syndrome
α-Toxin
Protein A
Neutralizes antibodies to evade the immune system
Elastin-binding protein
Which are part of the target cells' ECM
Collagen-binding protein
Fibronectin-binding protein
Clumping factor
Stationary phase
Exponential-growth phase
Log10 bacterial density
Time
Cytoplasmic membrane
B
Peptidoglycan
Capsule → Anti-phagocytic
Ribitol teichoic acid
β-Lactamase
Penicillin-binding protein
Cross-linking peptides
Lipoteichoic acid
C
Cell-wall–anchoring domain
Repeats
Ligand-binding domain

Staphylococci / Epidemiology

- Staphylococci, particularly ***S epidermidis***, are members of the normal microbiota of the **human skin** and **respiratory and gastrointestinal tracts**.

- Nasal carriage of ***S aureus*** occurs in 20–50% of humans, with a **higher incidence** reported for **hospitalized patients**, **medical personnel**, persons with **eczematous skin diseases.** Staphylococci are also found regularly on clothing, bed linens, and other **fomites** in human environments.


Anterior nares
(S. aureus & S. caprae)
Head
(S. capitis)
Breast area
(S. lugdunensis)
Axillae
(S. haemolyticus & S. hominis)
Hands
(S. warneri)
Inguinal and perineal area
(S. haemolyticus; S. hominis;
S. lugdunensis & S. saprophyticus)
Rectum
(S. saprophyticus)
Overall the body
(S. epidermidis)

The epidemiology and molecular characterization of methicillin-resistant staphylococci sampled from a healthy Jordanian population

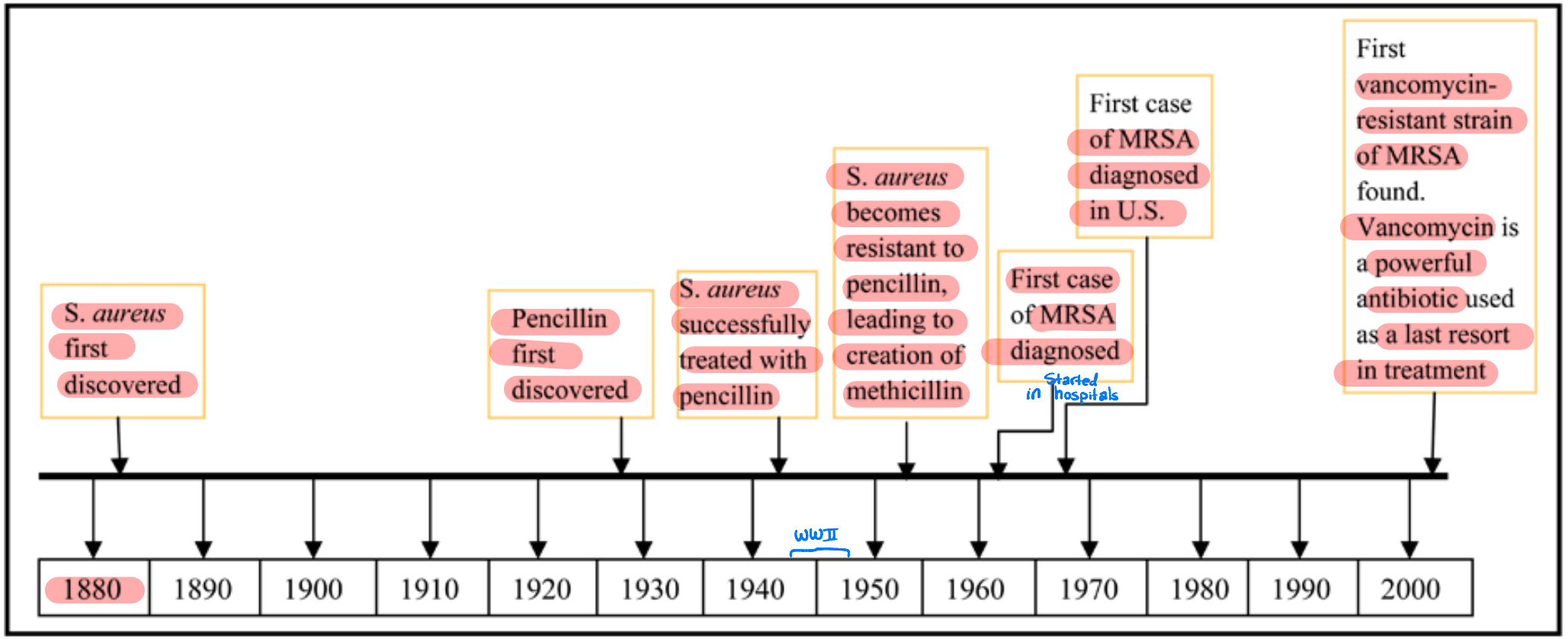
A G Al-Bakri 1, H Al-Hadithi, V Kasabri, G Othman, A Kriegeskorte, K Becker

Abstract

The prevalence of natural carriage and molecular epidemiology of methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococci (MR-CoNS) isolates in a Jordanian community were investigated. The MRSA nasal carriage rate in 227 healthy volunteers was 7·5% and the majority (81%) of MRSA harboured the resistance element **SCCmec** type IVe and were of a novel spa type t9519 (76%); other significant spa gene types were t223 (14·7%) and t044 (5·9%).

All MRSA isolates were susceptible to other classes of antibiotics, and tested positive for at least three virulence factor encoding genes, but only two harboured the pvl gene. MR-CoNS carriage was 54·2% and these isolates were characterized by single, double and untypable SCCmec elements, with Staphylococcus epidermidis SCCmec type IVa predominating. Of eight subjects with nasal co-colonization of MR-CoNS + MRSA, three shared SCCmec type IV in both groups of organisms. This is the first report of methicillin-resistant staphylococci carriage in a Jordanian community and its findings are important for epidemiological study and infection control measures of these organisms.

SCC*mec*, or **staphylococcal cassette chromosome *mec***, is a mobile genetic element of *Staphylococcus* bacterial species. This genetic sequence includes the *mecA* gene coding for resistance to the antibiotic methicillin and is the only known way for *Staphylococcus* strains to spread the gene in the wild by horizontal gene transfer.



Beginning in the 1980s, strains of Methicillin-resistant Staphylococcus aureus (**MRSA**) **spread rapidly in susceptible hospitalized patients**, dramatically changing the therapy available for preventing and treating staphylococcal infections.

MRSA began as a hospital-acquired infection, but has become **community-acquired** as well as **livestock-acquired**.

People with compromised immune systems (elderly, diabetics, HIV/AIDS), hospitalized patients and children are some of the susceptible groups to MRSA.

Staphylococci / Clinical correlations

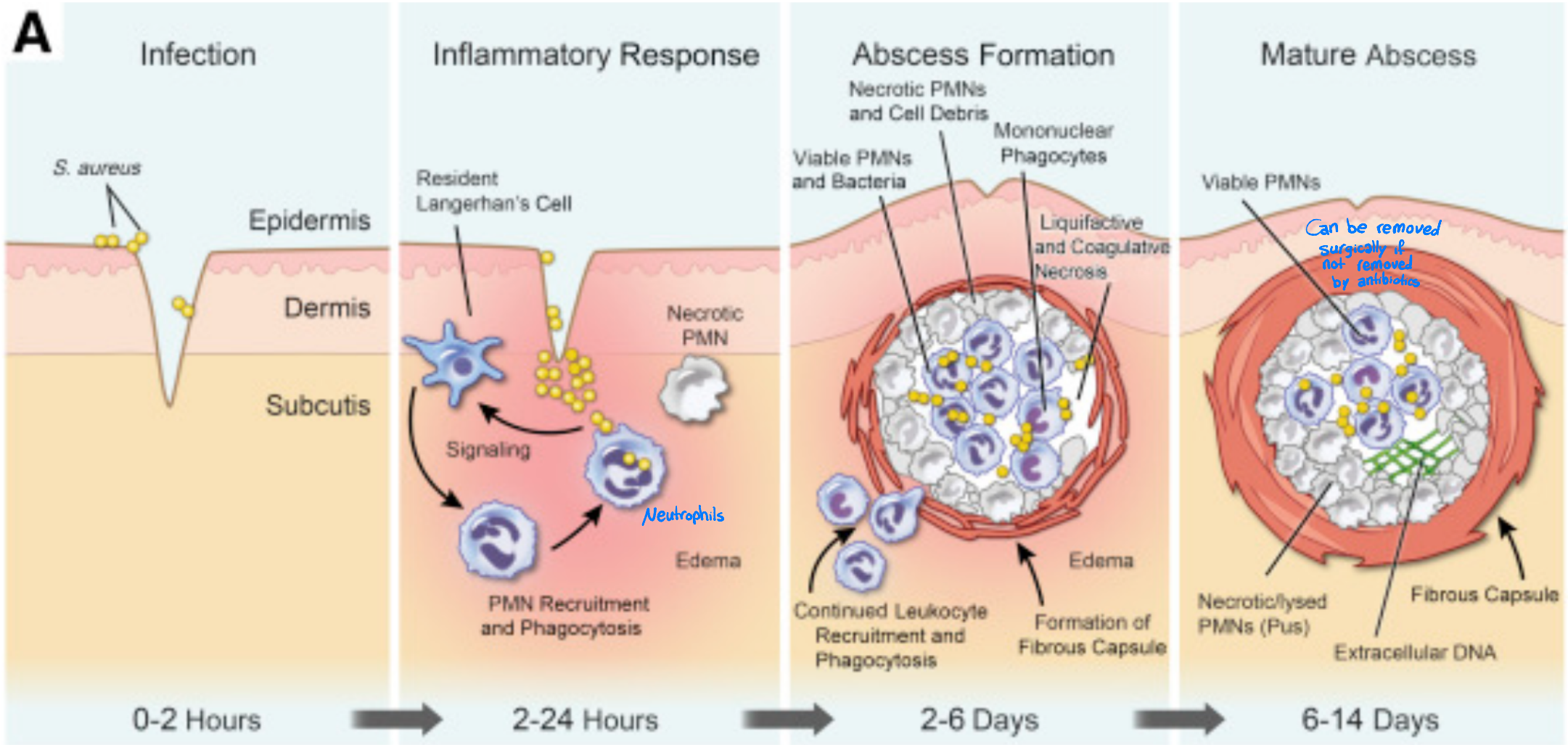
A localized staphylococcal infection appears as a **"pimple," hair follicle infection, or abscess**. There is usually an intense, localized, painful inflammatory reaction that undergoes central suppuration and heals quickly when the pus is drained.

Impetigo: localized cutaneous infection characterized by pus-filled vesicle on an erythematous base

Folliculitis: impetigo involving hair follicles

Furuncles or boils: large, painful, pus-filled cutaneous nodules

Carbuncles: Coalescence of furuncles with extension into subcutaneous tissues and evidence of systemic disease (fever, chills, bacteremia)


A
Infection
S. aureus
Epidermis
Dermis
Subcutis
Inflammatory Response
Resident
Langerhan's Cell
Necrotic
PMN
Signaling
Neutrophils
Edema
PMN Recruitment
and Phagocytosis
Abscess Formation
Necrotic PMNs
and Cell Debris
Mononuclear
Phagocytes
Viable PMNs
and Bacteria
Liquifactive
and Coagulative
Necrosis
Edema
Continued Leukocyte
Recruitment and
Phagocytosis
Formation of
Fibrous Capsule
Mature Abscess
Viable PMNs
Can be removed
surgically if
not removed
by antibiotics
Necrotic/lysed
PMNs (Pus)
Extracellular DNA
Fibrous Capsule
0-2 Hours
2-24 Hours
2-6 Days
6-14 Days

Staphylococci / Clinical correlations / S. aureus bacteremia

Simultaneously, SA (mainly MRSA) is a leading cause of **bacteremia** (way more dangerous than impetigo) and **infective endocarditis** (IE) as well as **osteoarticular**, skin and soft tissue, **pleuropulmonary**, and device-related infections.

Clinical infections with S. aureus will likely remain both common and serious. Not only have there been waves of increasing antimicrobial resistance (827), but the spectrum of clinical disease also continues to change. In the past 2 decades, we have witnessed two clear shifts in the epidemiology of S. aureus infections: first, a growing number of health care-associated infections, particularly seen in IE and prosthetic device infections, and second, an epidemic of community-associated SSTIs driven by strains with particular virulence factors. There is no doubt that there will continue to be a shifting landscape in the interactions between host and pathogen in the decades to come.

Primary foci of infection in cohorts with *S. aureus* bacteremia[a]

Region (reference)	% of MRSA cases in cohort	% of HCA cases in cohort	No. (%) of cases with focus of infection							Total no. of cases
			Infective endocarditis	Osteoarticular	SSTI	Pleuropulmonary	Line related	No focus/unknown	Other	
Central Australia (32)	21.6	25.6	9 (7.2)	20 (16)	42 (34)	11 (8.8)	9 (7.2)	30 (24)	4 (3.2)	125
Australia (59)	24.8	79.1	433 (6)	956 (13)	1,415 (20)	519 (7.2)	1,387 (19)	1,100 (15)	1,421 (20)	7,231
Sydney, Australia (65)	100	92	15 (3.8)	37 (9.3)	80 (20)	52 (13)	140 (35)	40 (10)	35 (8.8)	399
Calgary, Canada (12)[b]	11.3	75.3	79 (5.5)	227 (16)	224 (16)	220 (15)		586 (41)	104 (7.2)	1,440
Missouri, USA (64)	100	92.6	0 (0)	0 (0)	39 (24)	0 (0)	37 (23)	70 (43)	17 (10)	163
New York, USA (61)	100	97.9	91 (14)	72 (11)	112 (17)	55 (8.4)	302 (46)	0 (0)	20 (3.1)	652
Birmingham, UK (66)	100	99.5	6 (3.1)	3 (1.5)	37 (19)	0 (0)	73 (37)	68 (35)	8 (4.1)	195
Italy (57)	53.9	85.5	0 (0)	0 (0)	14 (9.3)	7 (4.6)	23 (15)	104 (69)	3 (2)	151
Israel (56)	42.8	100	55 (4.4)	71 (5.6)	294 (23)	144 (11)	172 (14)	298 (24)	227 (18)	1,261
Thailand (58)	27.6	55.1	8 (11)	9 (12)	20 (27)	16 (22)	10 (14)	0 (0)	10 (14)	73
South Korea (63)	100	95.1	9 (3.4)	16 (6)	35 (13)	24 (9)	132 (49)	36 (13)	16 (6)	268
Japan (62)	100	NA	0 (0)	0 (0)	17 (15)	10 (8.7)	27 (23)	23 (20)	38 (33)	115
Multisite (60)	11.7	NA	282 (8.3)	456 (13)	502 (15)	178 (5.2)	942 (28)	641 (19)	394 (12)	3,395
Total										15,468

aThe mean percentages of patients for each primary focus of infection from all the studies were as follows: 5% for infective endocarditis, 8% for osteoarticular, 19% for SSTI, 9% for pleuropulmonary, 26% for line related, 24% for no focus/unknown, and 11% for other foci. MRSA, methicillin-resistant *S. aureus*; HCA, health care associated; SSTI, skin and soft tissue infection.

bLine-related bacteremia was not reported in this study.

Staphylococci / Clinical correlations / Toxin mediated

Staphylococcal food poisoning, one of the most common foodborne illnesses, is an **intoxication** rather than an infection, Disease is caused by **heat stable bacterial toxin** present in food rather than from a direct effect of the organisms on the patient. With a **short incubation period (1–8 hours**); violent nausea, vomiting, and diarrhea; and **rapid convalescence**.

Staphylococcal scalded skin syndrome is a condition which predominantly affects **infants** and **children** and causes a spectrum of skin lesions.

Toxin-Mediated Diseases

Scalded skin syndrome: Disseminated desquamation of epithelium in infants; blisters with no organisms or leukocytes

Food poisoning: After consumption of food contaminated with heat-stable enterotoxin, rapid onset of severe vomiting, diarrhea, and abdominal cramping, with resolution within 24 hours

Toxic shock: multisystem intoxication characterized initially by fever, hypotension, and a diffuse, macular, erythematous rash; high mortality without prompt antibiotic therapy and elimination of the focus of infection

Staphylococci / Clinical correlations / Coagulase negative

usually harmless, but can become pathogenic due to → change in host pathogenic environment

- ***S epidermidis*** infections are difficult to cure because they occur in **prosthetic devices** where the bacteria can sequester themselves in a **biofilm**. staphylococci are a major cause of **endocarditis of artificial valves.**

- More than 50% of all infections of **catheters and shunts** are caused by **coagulase-negative staphylococci**. These infections have become a major medical problem because long-dwelling catheters and shunts are used commonly for the medical management of critically ill patients.

which can cause skin microbiota to enter the body and become pathogenic Solution: Disinfection

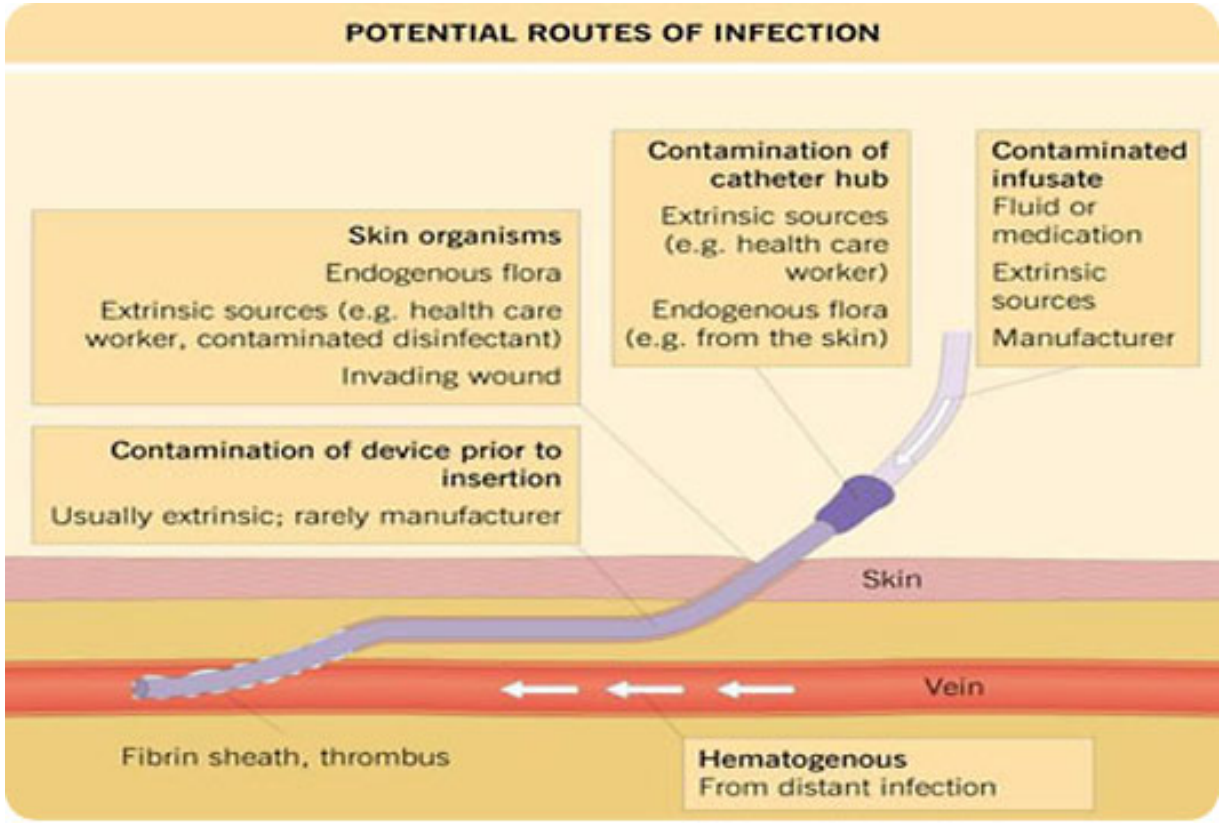
Coagulase-Negative *Staphylococcus* Species

Wound infections: Characterized by erythema and pus at the site of a traumatic or surgical wound; infections with foreign bodies can be caused by *S. aureus* and coagulase-negative staphylococci

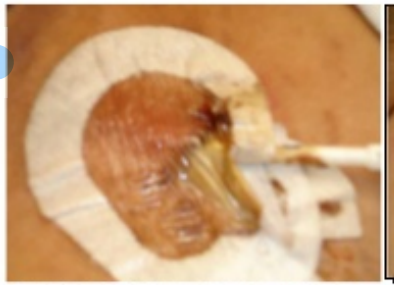
Urinary tract infections: Dysuria and pyuria in young sexually active women (*S. saprophyticus*), in patients with urinary catheters (other coagulase-negative staphylococci), or following seeding of the urinary tract by bacteremia (*S. aureus*)

Catheter and shunt infections: Chronic inflammatory response to bacteria coating a catheter or shunt (most commonly with coagulase-negative staphylococci)

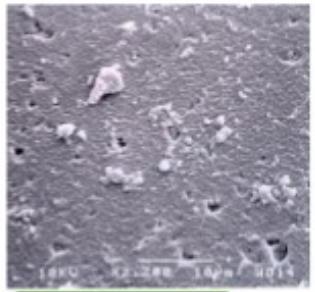
Prosthetic device infections: Chronic infection of device characterized by localized pain and mechanical failure of the device (most commonly with coagulase-negative staphylococci)



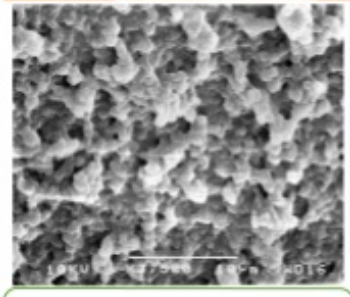
Catheter Exit Site infection



Catheter Tunnel infection



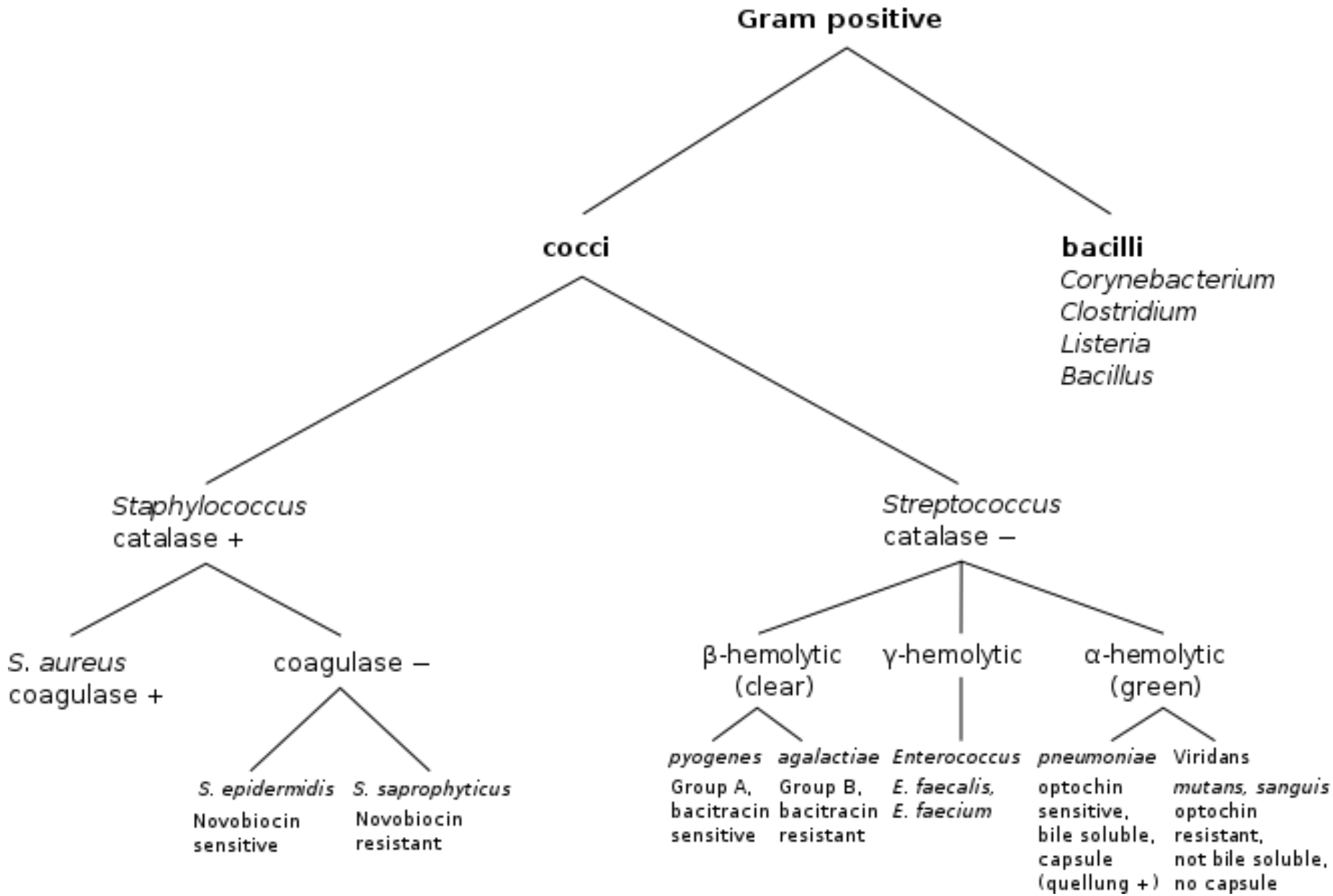
New catheter



Catheter with biofilm

Photo provided by Stephanie Booth, used with permission

Treatment: Remove the catheter where the biofilm was formed


Gram positive
cocci
bacilli
Corynebacterium
Clostridium
Listeria
Bacillus
Staphylococcus
catalase +
Streptococcus
catalase −
S. aureus
coagulase +
coagulase −
β-hemolytic
(clear)
γ-hemolytic
α-hemolytic
(green)
S. epidermidis
Novobiocin
sensitive
S. saprophyticus
Novobiocin
resistant
pyogenes
Group A,
bacitracin
sensitive
agalactiae
Group B,
bacitracin
resistant
Enterococcus
E. faecalis,
E. faecium
pneumoniae
optochin
sensitive,
bile soluble,
capsule
(quellung +)
Viridans
mutans, sanguis
optochin
resistant,
not bile soluble,
no capsule

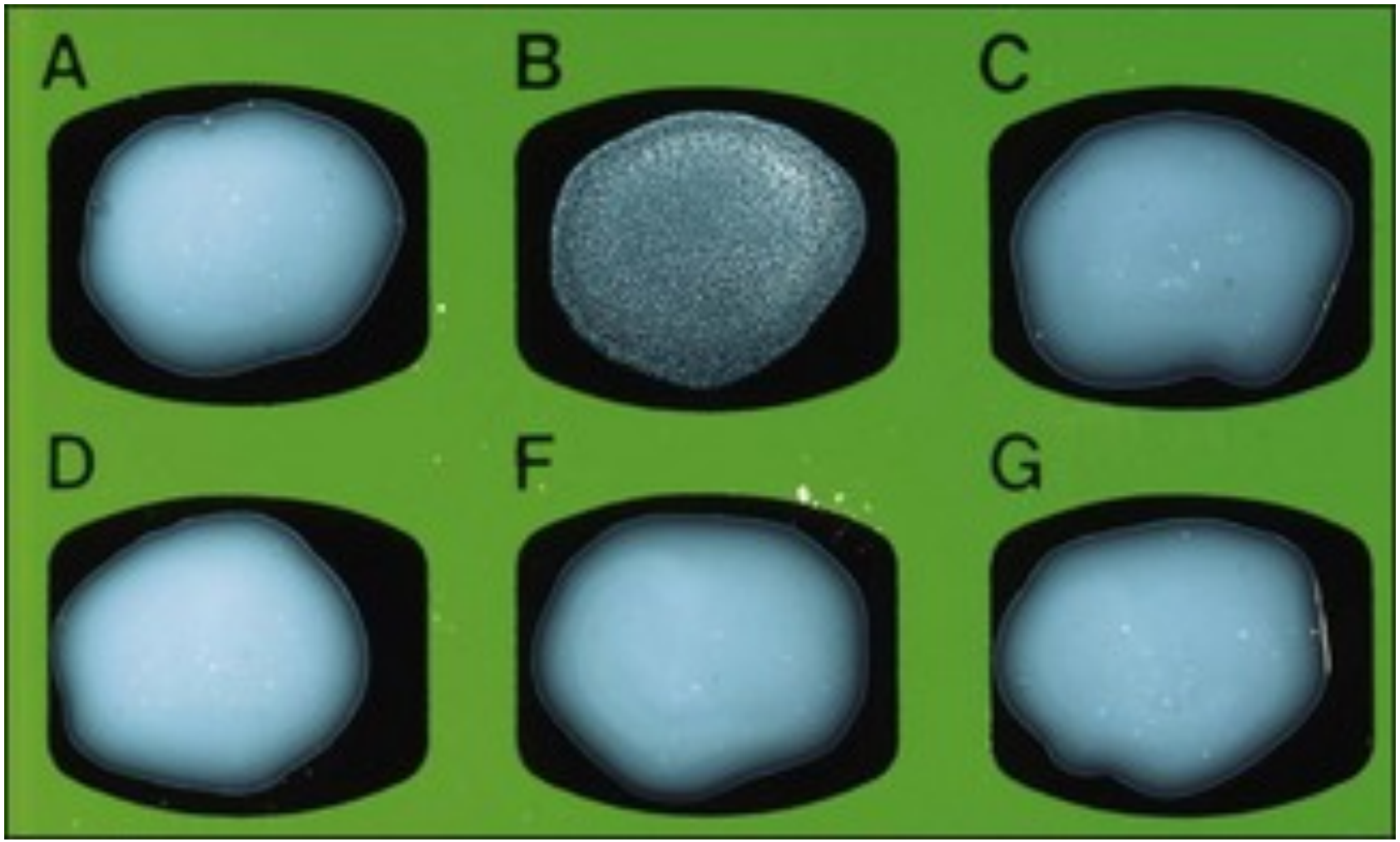
Streptococci / Classification

- The classification of more than 100 species within the genus *Streptococcus* is complicated because three different overlapping schemes are used:

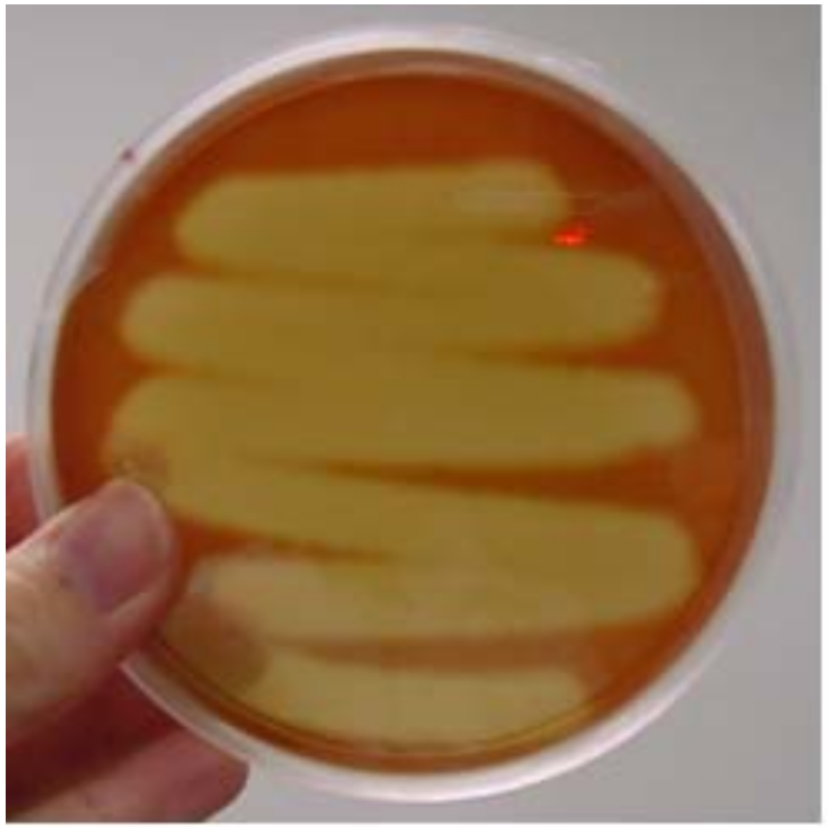
- (1) serologic properties: **Lancefield groupings** (originally A to W);
- (2) **hemolytic patterns:** complete (beta [β]) hemolysis, incomplete (alpha [α]) hemolysis, and no (gamma [γ]) hemolysis;
- (3) **biochemical (physiologic) properties.**

- The most important pathogenic streptococcal species for humans include ***Streptococcus pyogenes*** (group A streptococcus/ GAS) , **Streptococcus agalactiae** (GBS), ~~group D streptococcus (enterococci~~), ***Streptococcus pneumoniae***, and ***Streptococcus viridans*.**

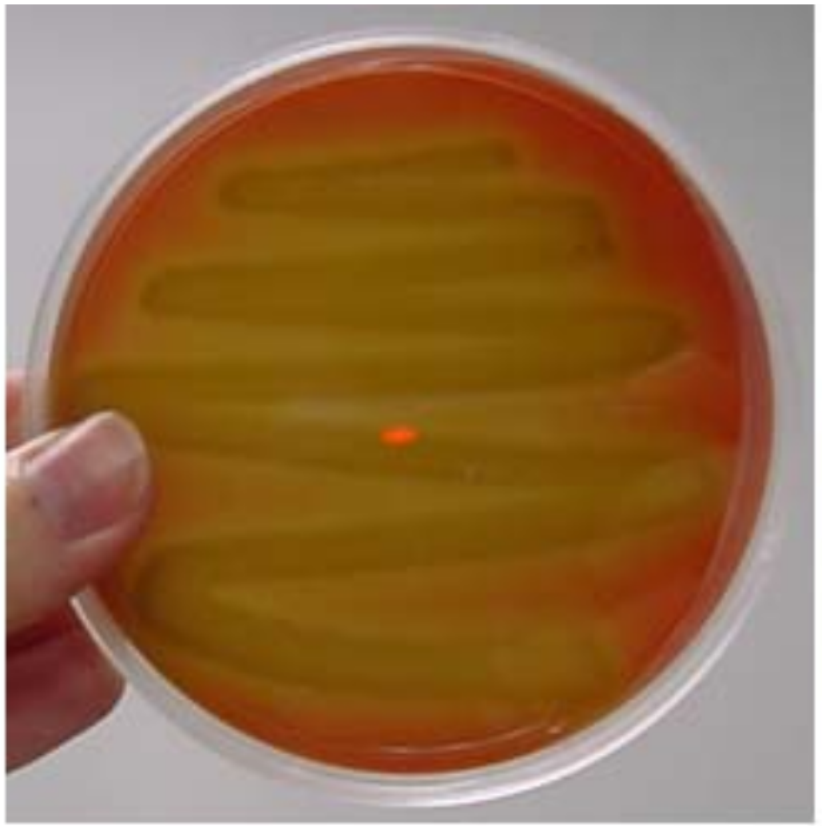
Streptococci / Classification / Lancefield groupings



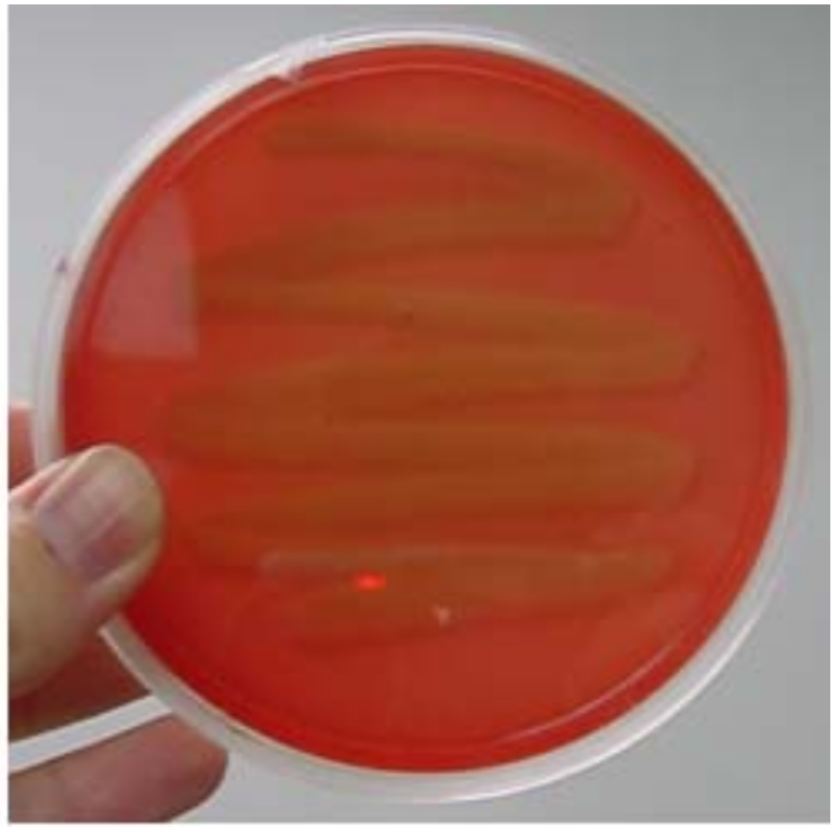
Streptococci / Classification / hemolytic patterns



Beta Hemolysis

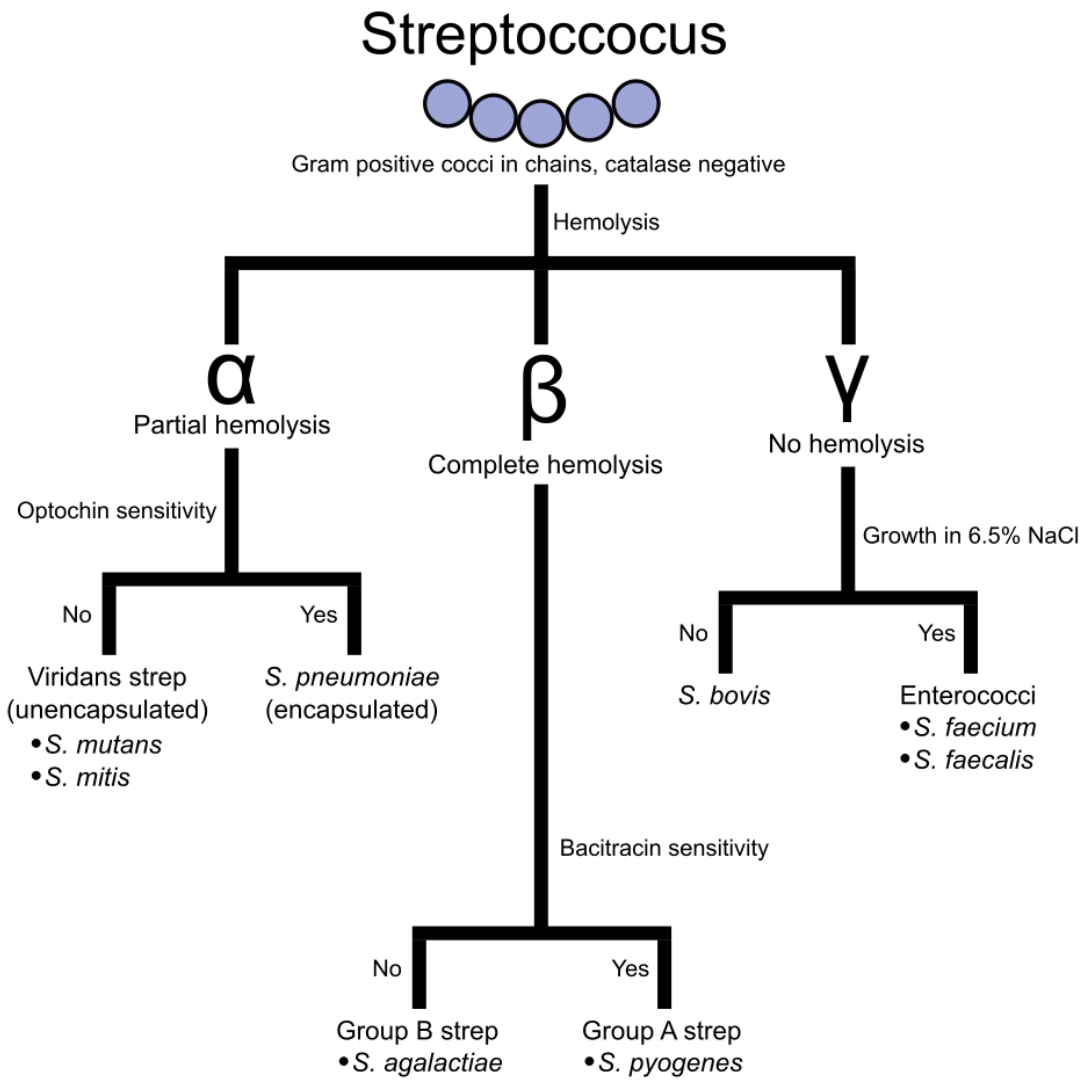


Alpha Hemolysis



Gamma Hemolysis

Streptococci / Classification / biochemical (physiologic) properties



Moises Dominguez

1. **Which of the following Staphylococcus species is most commonly associated with human infections?**

- A. *Staphylococcus epidermidis*
- B. *Staphylococcus saprophyticus*
- C. *Staphylococcus aureus*
- D. *Staphylococcus haemolyticus*

2. *Staphylococcus aureus* is known for its ability to produce several virulence factors. Which of the following toxins is primarily associated with toxic shock syndrome?

- A. Hemolysin
- B. Enterotoxin → Causes food poisoning
- C. Exfoliative toxin
- D. Toxic shock syndrome toxin-1 (TSST-1)

3. Which test is commonly used to differentiate *Staphylococcus aureus* from other staphylococcal species?

•A. Catalase test
•B. Coagulase test
•C. Oxidase test
•D. Gram stain

4. *Staphylococcus epidermidis* is part of the normal skin flora but can be pathogenic under certain conditions. Which type of infection is it commonly associated with?

•A. Urinary tract infections
•B. Skin abscesses
•C. Device-associated infections
•D. Gastrointestinal infections

5. Which of the following statements about Methicillin-resistant *Staphylococcus aureus* (MRSA) is true?

•A. MRSA is only found in healthcare settings.
•B. MRSA produces beta-lactamase, which breaks down methicillin.
•C. MRSA is resistant to all antibiotics.
•D. MRSA has an altered penicillin-binding protein (PBP2a) that reduces methicillin binding.

6. *Staphylococcus aureus* can cause food poisoning. Which of the following best describes the mechanism of food poisoning caused by *S. aureus*?

•A. Production of an endotoxin that contaminates food
•B. Production of a heat-stable enterotoxin in food
•C. Production of an exotoxin that affects the nervous system
•D. Invasion of the gastrointestinal mucosa

7. What is the primary function of Protein A in *Staphylococcus aureus*?

•A. It binds to fibrinogen to promote clotting.
•B. It enhances phagocytosis by immune cells.
•C. It binds to the Fc region of antibodies, preventing opsonization.
•D. It produces toxins that lyse red blood cells.

8. Which antibiotic class is most commonly used in treating Methicillin-sensitive *Staphylococcus aureus* (MSSA) infections?

•A. Macrolides
•B. Tetracyclines
•C. Beta-lactams
•D. Fluoroquinolones

1. **Answer:** C. *Staphylococcus aureus*
2. **Answer:** D. Toxic shock syndrome toxin-1 (TSST-1)
3. **Answer:** B. Coagulase test
4. **Answer:** C. Device-associated infections
5. **Answer:** D. MRSA has an altered penicillin-binding protein (PBP2a) that reduces methicillin binding.
6. **Answer:** B. Production of a heat-stable enterotoxin in food
7. **Answer:** C. It binds to the Fc region of antibodies, preventing opsonization.
8. Answer: C. Beta-lactams

Further reading:

Jawetz, Melnick & Adelberg's Medical Microbiology, 26th edition-
Section 3: Bacteriology-
Chapter 13: The Staphylococci

Murray - Medical Microbiology 8th Edition
Section 4: Bacteriology
Chapter 18: STAPHYLOCOCCUS AND RELATED GRAM-POSITIVE COCCI