Staphylococcus and Staphylococcal Disease

Lec.3

This microorganism is widely distributed in our environment some of them are members of the normal flora of humans.

Staphylococci are spherical in shape usually arranged in grape like clusters, grow rapidly on many types of ordinary bacterial media ferment CHO and produced pigments varying from white to deep yellow.

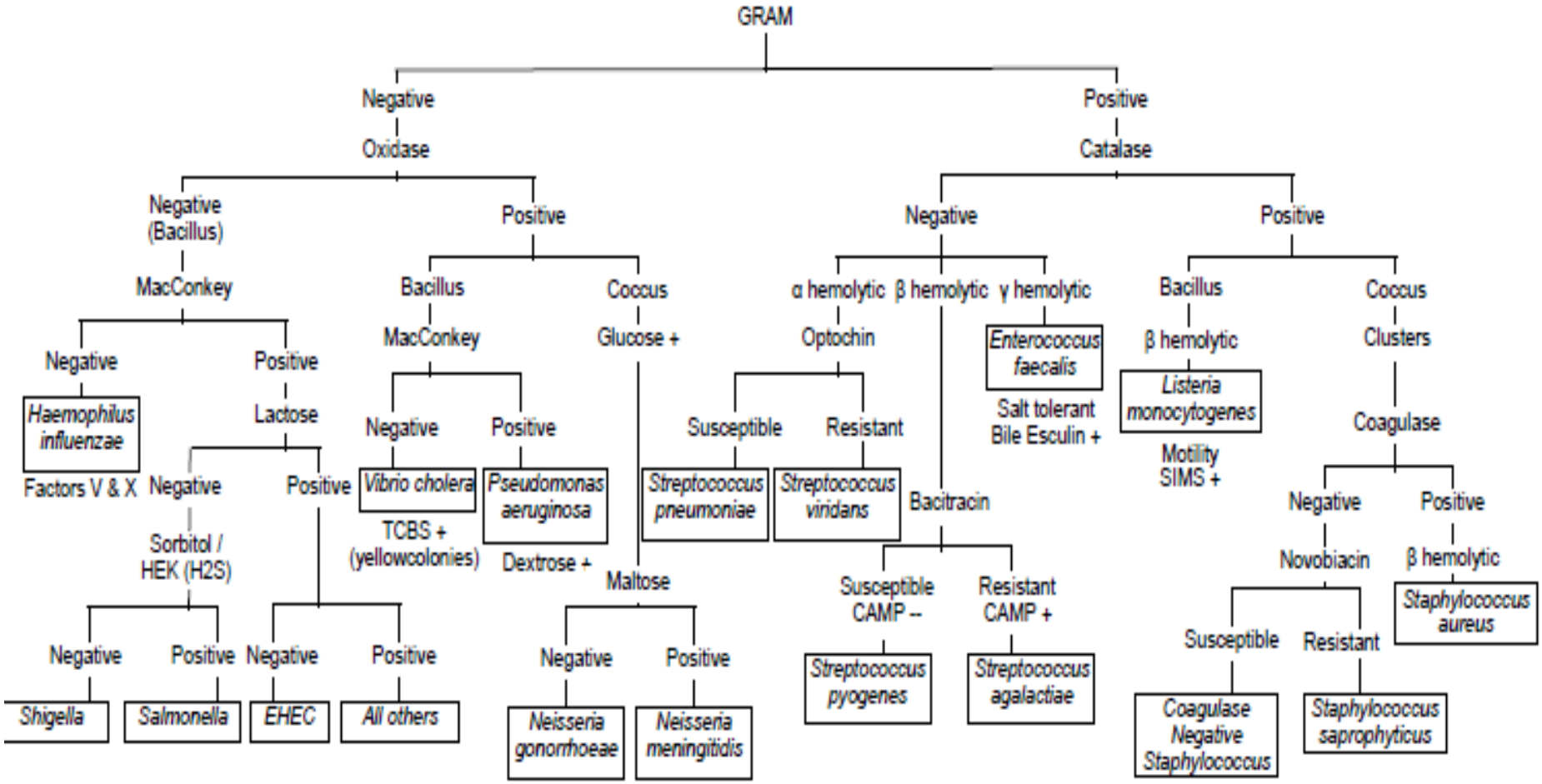
important human pathogens
Staphylococcus aureus
Staphylococcus epidermidis
Staphylococcus saprophyticus.

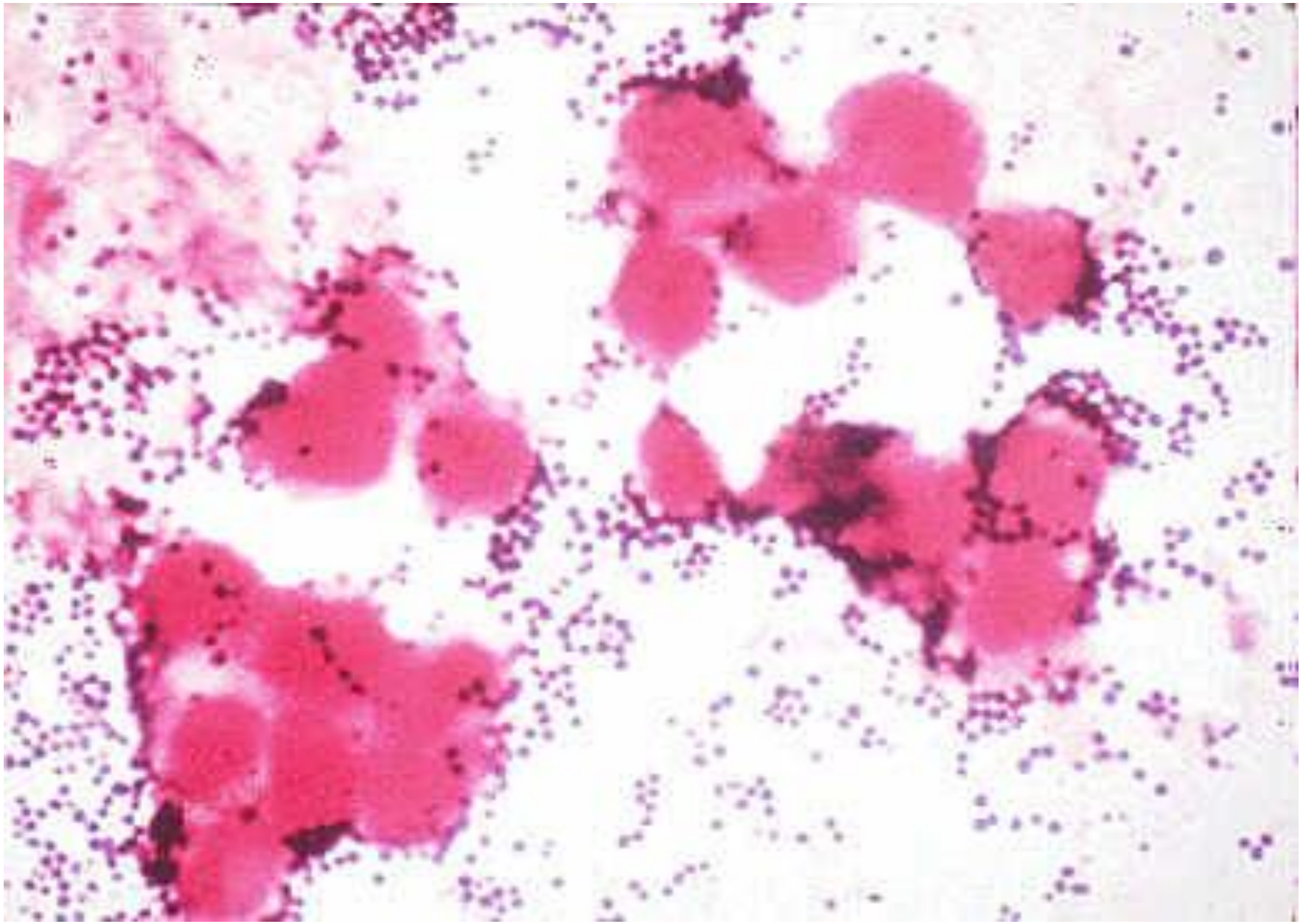
Important phenotypic characteristics of *Staphylococcus aureus*

Gram-positive, cluster-forming coccus
nonmotile, nonsporeforming facultative anaerobe
fermentation of glucose produces mainly lactic acid
ferments mannitol (distinguishes from *S. epidermidis)*
catalase positive
coagulase positive
golden yellow colony on agar
normal flora of humans found on nasal passages, skin and mucous membranes
pathogen of humans, causes a wide range of suppurative infections, as well as food poisoning and toxic shock syndrome

Resistance to environmental condition:

Staphylococcus aureus considered one of the hardest of all non spore forming bacteria most strain are relatively heat stable, with stand a temperature as high as 60 c for 30 min. also resist a high concentration of salt (7.5% - 9% Nacl).


GRAM
Negative
Positive
Oxidase
Catalase
Negative (Bacillus)
Positive
Negative
Positive
MacConkey
Bacillus
Coccus
α hemolytic
β hemolytic
γ hemolytic
Bacillus
Coccus
Negative
Positive
MacConkey
Glucose +
Optochin
Enterococcus faecalis
β hemolytic
Clusters
Haemophilus influenzae
Lactose
Negative
Positive
Susceptible
Resistant
Salt tolerant
Bile Esculin +
Listeria monocytogenes
Coagulase
Factors V & X
Negative
Positive
Vibrio cholera
Pseudomonas aeruginosa
Streptococcus pneumoniae
Streptococcus viridans
Bacitracin
Motility
SIMS +
Negative
Positive
Sorbitol / HEK (H2S)
TCBS + (yellowcolonies)
Dextrose +
Maltose
Susceptible CAMP --
Resistant CAMP +
Novobiacin
β hemolytic
Negative
Positive
Negative
Positive
Negative
Positive
Susceptible
Resistant
Staphylococcus aureus
Shigella
Salmonella
EHEC
All others
Neisseria gonorrhoeae
Neisseria meningitidis
Streptococcus pyogenes
Streptococcus agalactiae
Coagulase Negative Staphylococcus
Staphylococcus saprophyticus



Gram stain of *Staphylococcus aureus* in pustular exudate

Pathogenesis of *S. aureus* infections

Staphylococcus aureus causes a variety of suppurative (pus-forming) infections and toxinoses in humans.
Superficial skin lesions such as **boils**, **styes** and **furuncules**
More serious infections such as **pneumonia**, **mastitis**, **phlebitis**, **meningitis**, and **UTI**
Deep-seated infections, such as **osteomyelitis** and **endocarditis**.

S. aureus is a major cause of **hospital acquired (nosocomial) infection** of surgical wounds and infections associated with indwelling medical devices.

S. aureus causes **food poisoning** by releasing enterotoxins into food, and **toxic shock syndrome** by release of superantigens into the blood stream.

Although **methicillin-resistant Staph aureus** (**MRSA**) have been entrenched in hospital settings for several decades, MRSA strains have recently emerged outside the hospital becoming known as **community associated- MRSA(** (**CA-MRSA**).

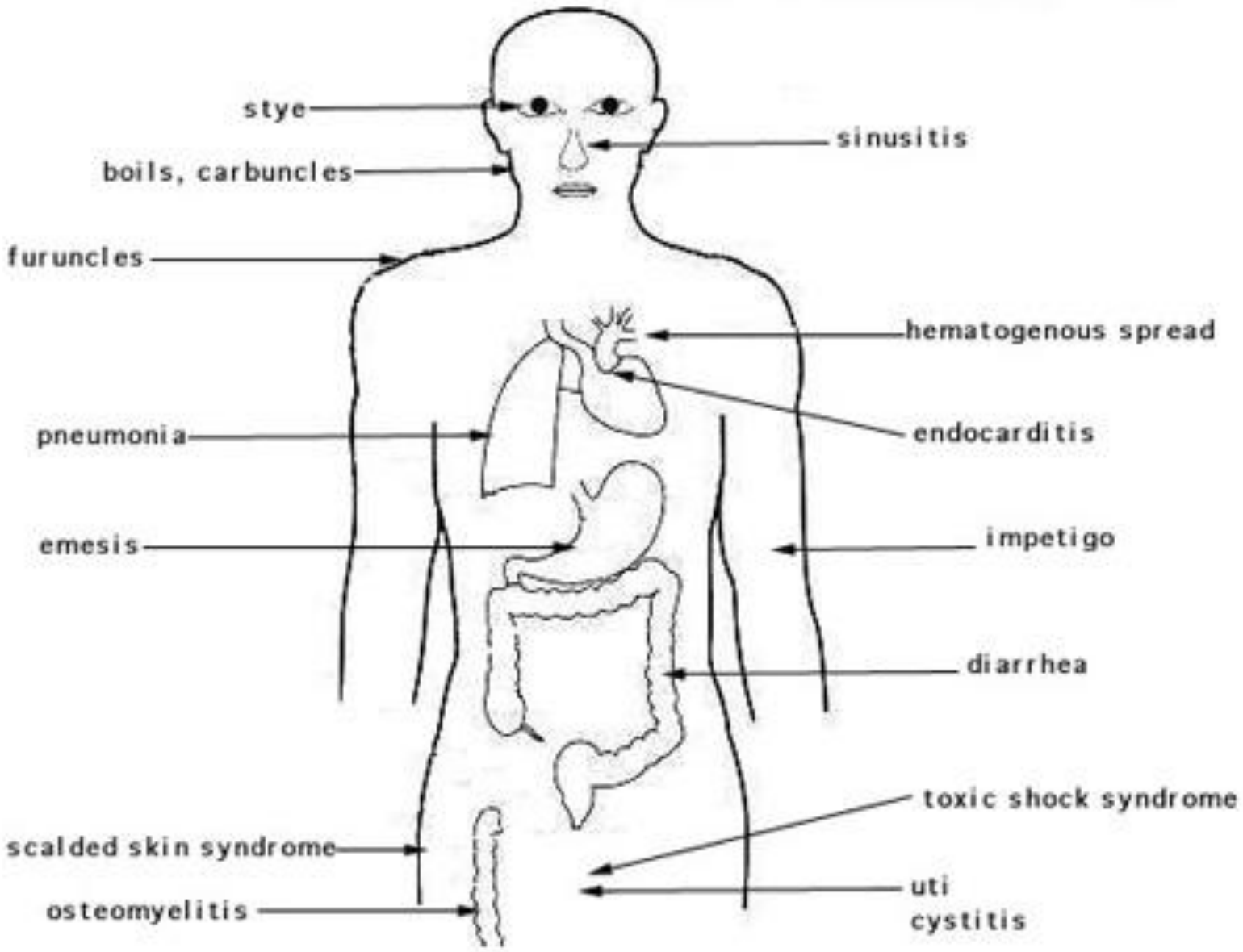
Human staphylococcal infections are frequent, but usually **remain localized at the portal of entry by the normal host defenses**.

The portal may be a hair follicle, but usually it is a break in the skin which may be a minute needle-stick or a surgical wound. Foreign bodies, including sutures, are readily colonized by staphylococci, which may make infections difficult to control. Another portal of entry is the respiratory tract. Staphylococcal pneumonia is a frequent complication of influenza.

The localized host response to staphylococcal infection is inflammation, characterized by an elevated temperature at the site, swelling, the accumulation of pus, and necrosis of tissue. Around the inflamed area, a fibrin clot may form, walling off the bacteria and leukocytes as a characteristic pus-filled boil or abscess. More serious infections of the skin may occur, such as furuncles or impetigo.

Localized infection of the bone is called osteomyelitis.

Serious consequences of staphylococcal infections occur when the bacteria invade the blood stream. A resulting septicemia may be rapidly fatal; a bacteremia may result in seeding other internal abscesses, other skin lesions, or infections in the lung, kidney, heart, skeletal muscle or meninges.


stye
boils, carbuncles
furuncles
pneumonia
emesis
scalded skin syndrome
osteomyelitis
sinusitis
hematogenous spread
endocarditis
impetigo
diarrhea
toxic shock syndrome
uti
cystitis

Antigenic structure of Staphylococcus aureus:

1. **Peptidoglycan: a polysaccharide polymer provides rigid** exoskeleton of the cell wall characterized by:

* Can be destroyed by exposure to strong acids and lysozymes.
* Stimulate the production of IL-1.
* Stimulate the production of opsonic antibodies.
•The peptidoglycan has endotoxin activity.

2. **Teichoic acids:**

They are polymers of glycerol or ribitol phosphate. These polymers are linked to the peptidoglycan and can be antigenic. Antiteichoic acid antibodies may be found in patients with active endocarditis caused by Staphylococcus aureus.

3. **Protein A :**

Is a cell wall component of Staphylococcus aureus strains that binds to the FC portion of IgG molecule.

4. **Extracellular substances: (enzymes and toxin)**

Most extracellular substances produced by Staphylococcus aureus are antigenic (stimulate the production of antibodies). (catalase, coagulase, proteinase, lipase, hyaluonidase, beta lactamase)

virulence factors:

(1) *S. aureus* cells express **surface proteins** that promote attachment to host proteins such as laminin and fibronectin that form the extracellular matrix of epithelial and endothelial surfaces. In addition, most strains express a fibrin/fibrinogen binding protein (**clumping factor**) which promotes attachment to blood clots and traumatized tissue.

(2) invasins that promote bacterial spread in tissues (**leukocidin**, **kinases**, **hyaluronidase**)

(3) surface factors that inhibit phagocytic engulfment (**capsule**, **Protein A**)

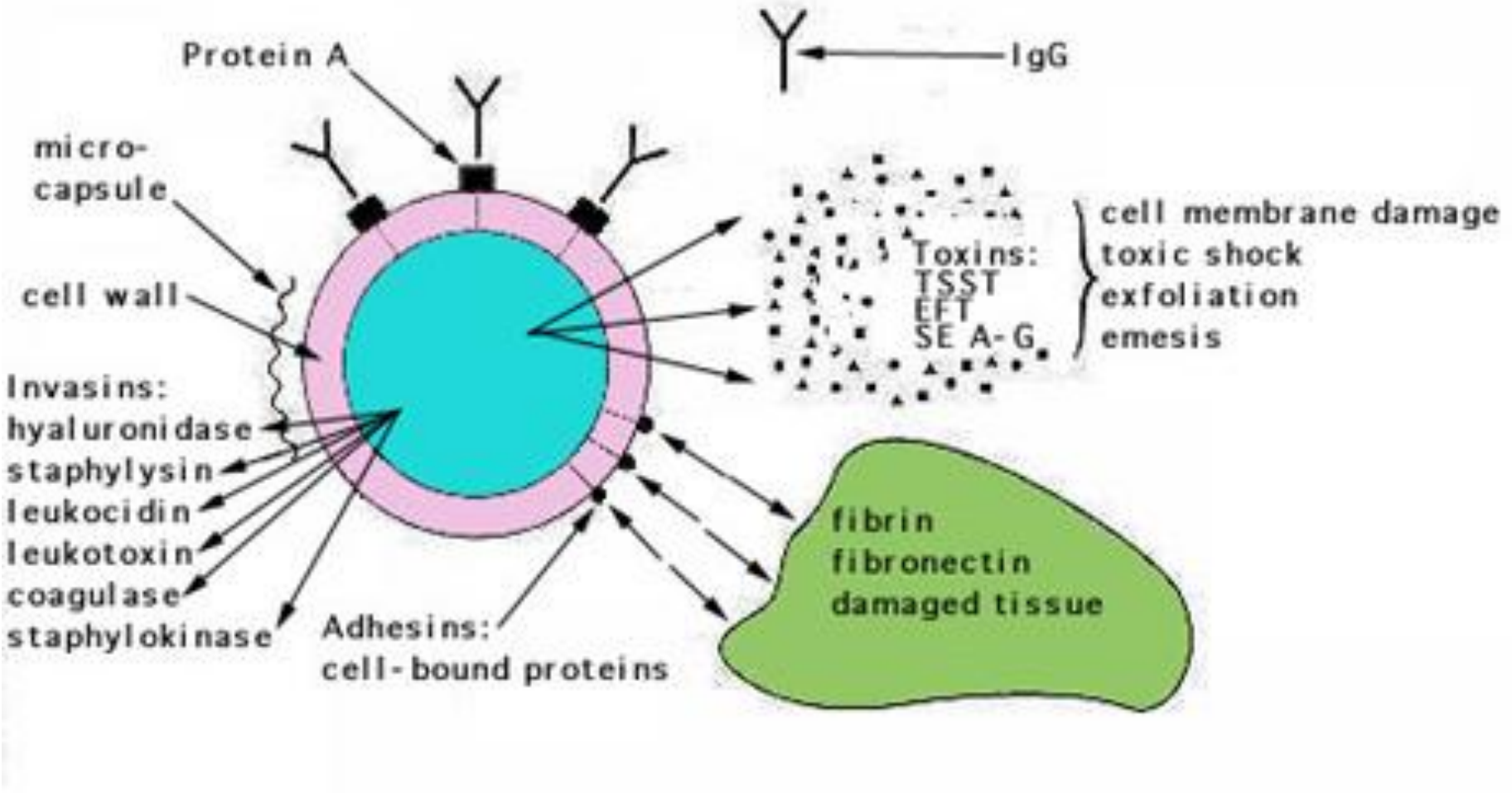
(4) biochemical properties that enhance their survival in phagocytes (**carotenoids**, **catalase** production)

(5) immunological disguises (**Protein A**, **coagulase**)

(6) membrane-damaging toxins that lyse eucaryotic cell membranes (**hemolysins**, **leukocidin)**

(7) exotoxins that damage host tissues or otherwise provoke symptoms of disease (Enterotoxin, **TSST**, Exfoliatin toxin **ET**)

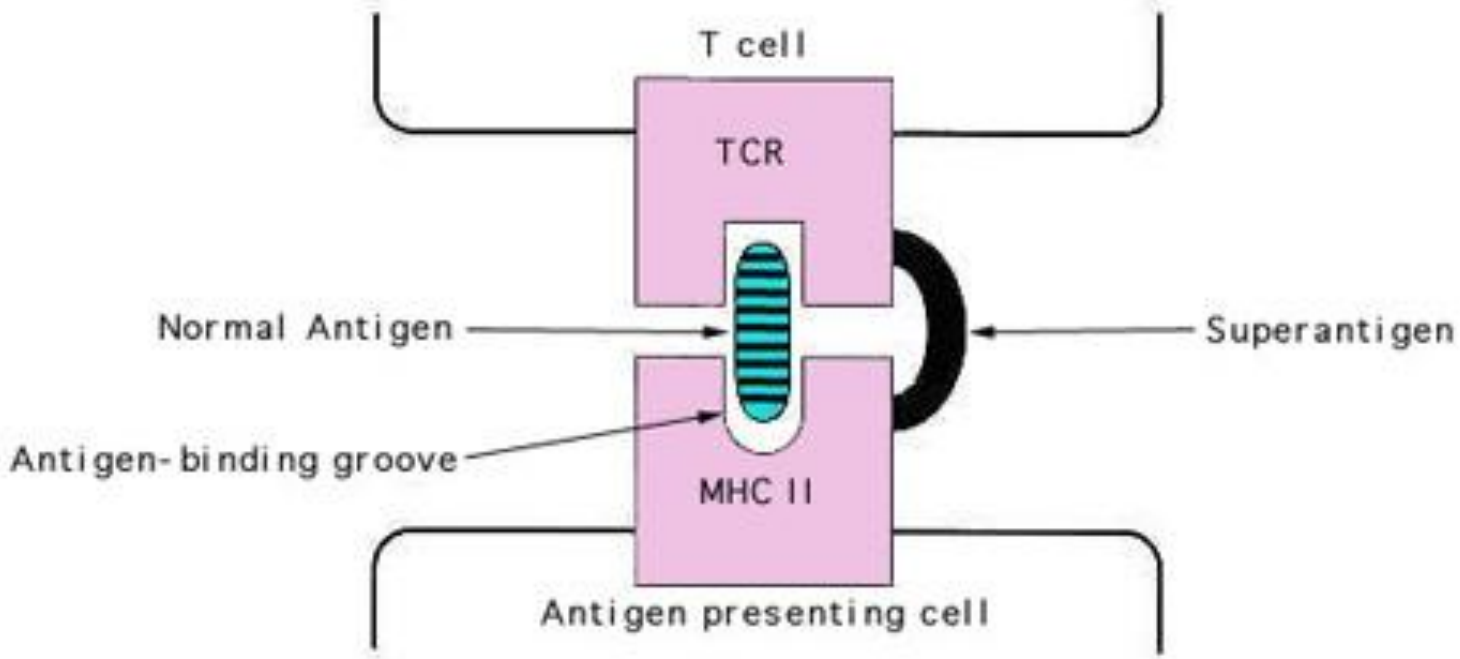
(8) inherent and acquired **resistance to antimicrobial agents**.


Protein A
IgG
micro-
capsule
cell wall
Invasins:
hyaluronidase
staphylysin
leukocidin
leukotoxin
coagulase
staphylokinase
Toxins:
TSST
EFT
SE A-G
cell membrane damage
toxic shock
exfoliation
emesis
fibrin
fibronectin
damaged tissue
Adhesins:
cell-bound proteins

Superantigens: enterotoxins and toxic shock syndrome toxin

S. aureus secretes two types of toxins with superantigen activity, **enterotoxins**, of which there are six antigenic types (named **SE-A, B, C, D, E and G**), and **toxic shock syndrome toxin** (**TSST-1**). Enterotoxins cause diarrhea and vomiting when ingested and are responsible for staphylococcal food poisoning. TSST-1 is expressed systemically and is the cause of toxic shock syndrome (TSS).
Superantigens stimulate T cells non-specifically without normal antigenic recognition (Figure).
Up to one in five T cells may be activated, whereas only 1 in 10,000 are stimulated during a usual antigen presentation.
Cytokines are released in large amounts, causing the symptoms of TSS.

Superantigens bind directly to class II major histocompatibility complexes of antigen-presenting cells outside the conventional antigen-binding grove. This complex recognizes only the Vb element of the T cell receptor. Thus any T cell with the appropriate Vb element can be stimulated, whereas normally, antigen specificity is also required in binding.


T cell
TCR
Normal Antigen
Superantigen
Antigen-binding groove
MHC II
Antigen presenting cell

Staphylococcus epidermidis

All humans carry this bacteria in the deep layer of skin its usually associated with nosocomial infections and with foreign objects (i.e. catheters, shunts, pacemaker wires, heart valves replacement).

Virulence factors is production of an exopolysaccharide “slime”

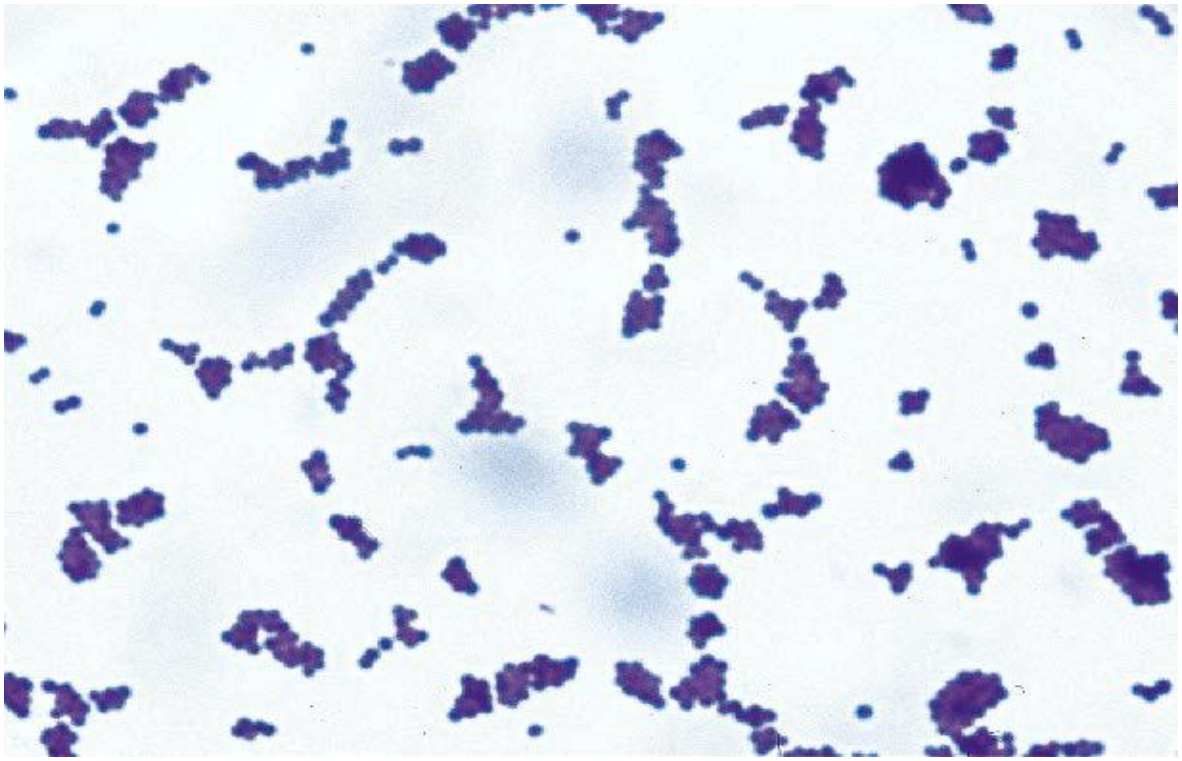
The slime layer around the bacterial cell wall :

- promotes adherence to plastic surfaces
- increase resistance to phagocytosis
- inhibits enterance of antibiotics to the cell.

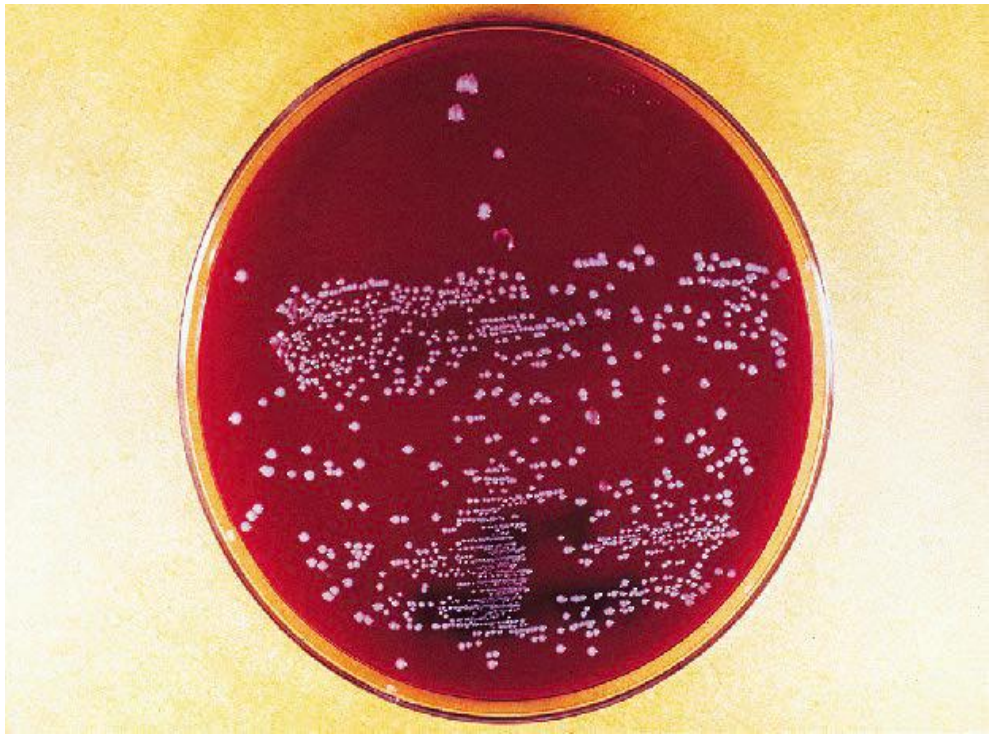
Staphylococcus saprophytics:

Normal flora when become pathogenic, it causes upper and lower urinary tract infection in young women.

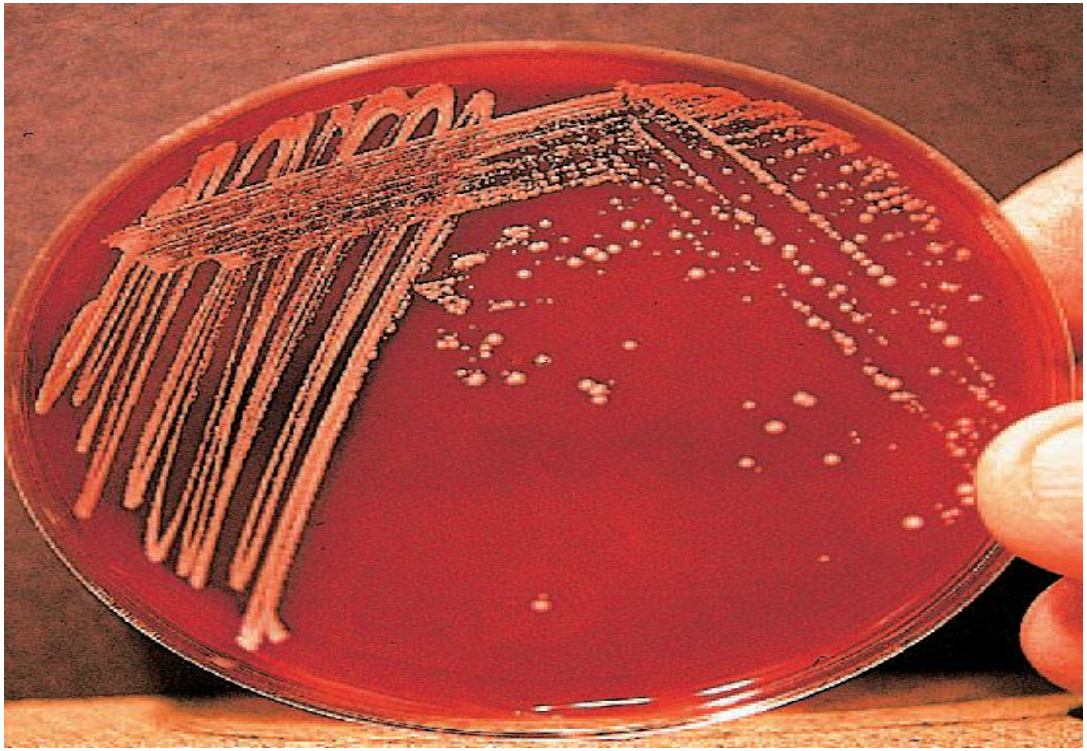
Lab Dx



Morphology of Staphylococci. grapelike clusters of gram-positive cocci



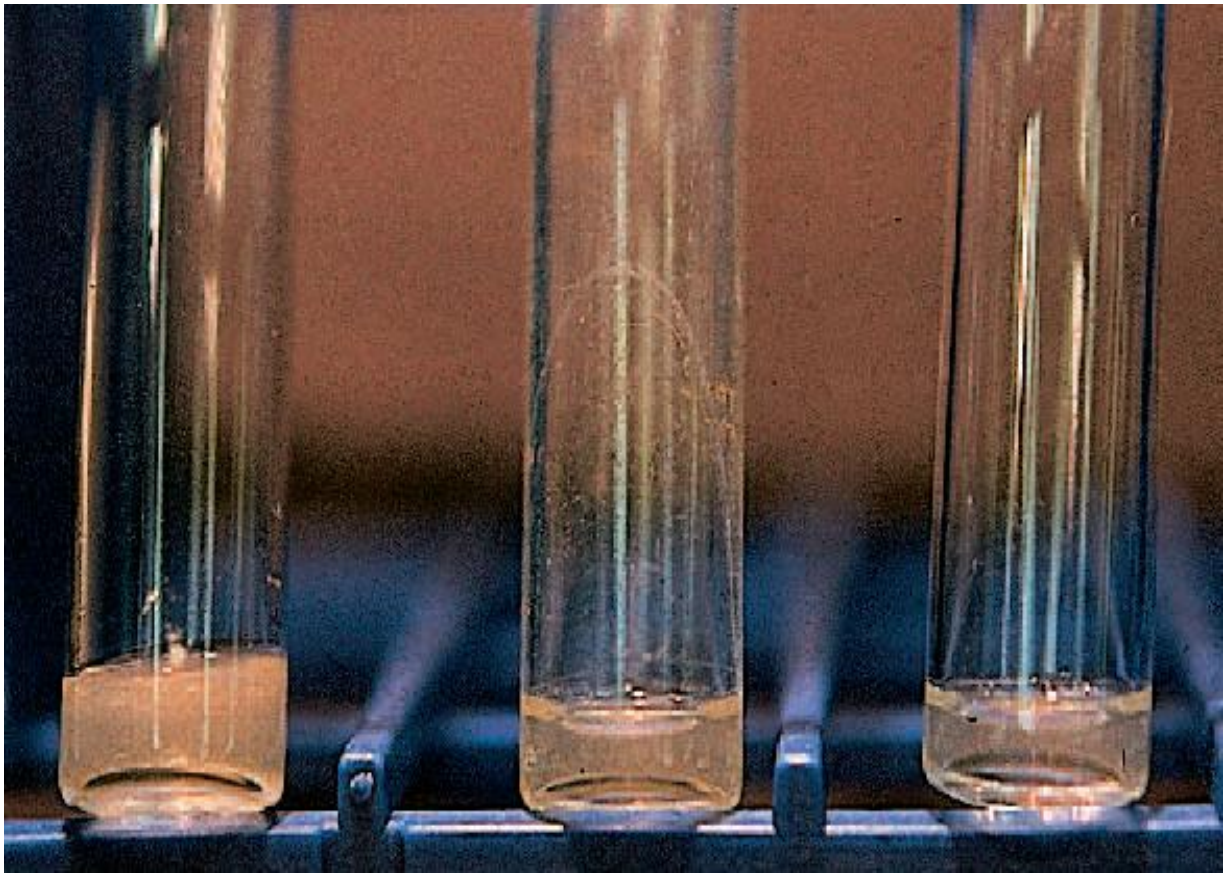
Culture of *Staphylococcus epidermidis* on Blood Agar. Notice the white, opaque, nonhemolytic, smooth colonies characteristic of *S. epidermidis.*



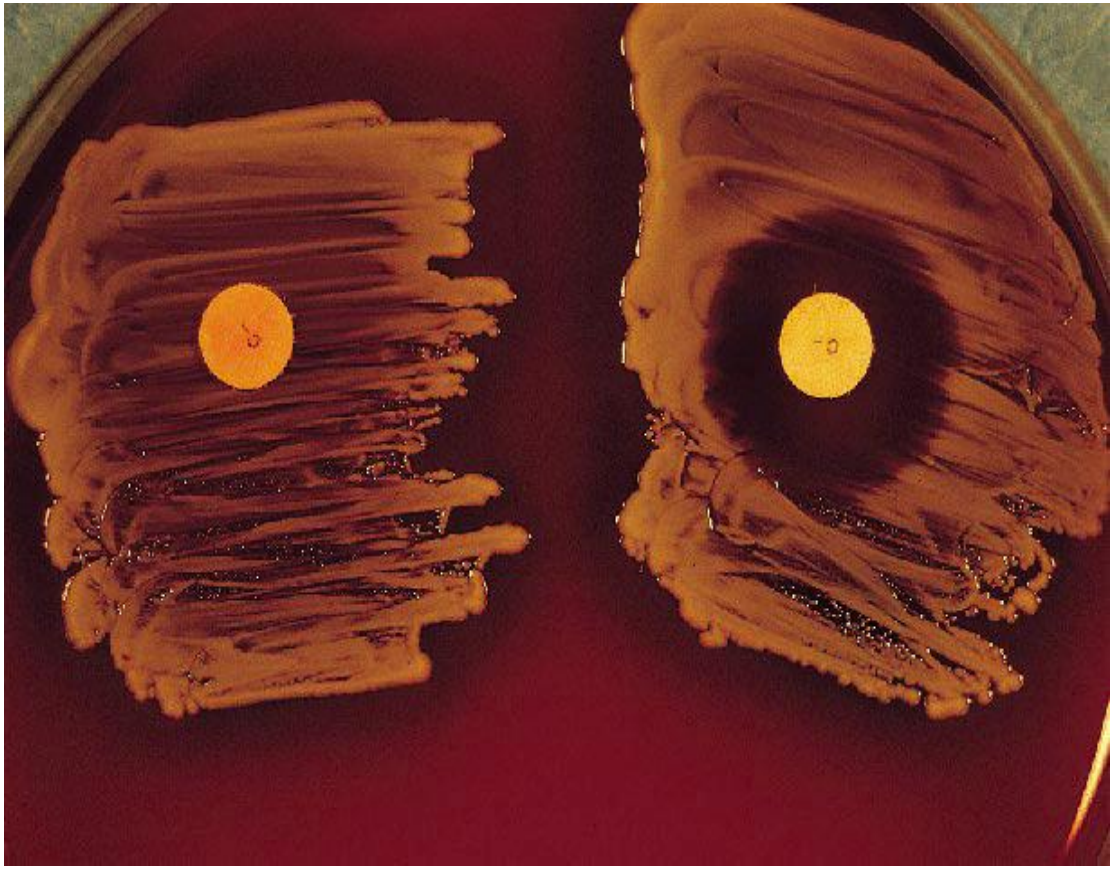
Culture of Staphylococci on Blood Agar. Blood agar plate on which large, smooth, β-hemolytic colonies of *S. aureus* are growing. The lysis of the RBCs is due to alpha toxin production.

Culture of *Staphylococcus aureus* on Mannitol Salt Agar. Notice that the medium has turned yellow around the growing bacteria since the bacteria are able to ferment the mannitol and produce an acid pH.

Culture of *Staphylococcus epidermidis* on Mannitol Salt Agar. Notice the small white colonies that do not use the mannitol; that is, no color change is observed since no acid has been produced.



Coagulase Test. Coagulase producing strains of *S. aureus* form a clot (solid fibrin gel) when grown in plasma (tube on the left), whereas coagulase negative staphylococci (*S. saprophyticus* [middle tube] and *S.epidermidis* [tube on the right]) do not form a clot



Novobiocin Susceptibility Test. (Left on plate) Novobiocin resistance evidenced by lack of zone of inhibition (or a zone less than 17 mm) surrounding a novobiocin disk. Resistance is typical of *Staphylococcus saprophyticus.* (Right on plate) Novobiocin susceptibility evidenced by a zone of inhibition greater than 16 mm surrounding the novobiocin disk. Sensitivity is typical of *Staphylococcus epidermidis* and other coagulase-negative staphylococci, other than *S. saphrophyticus.*