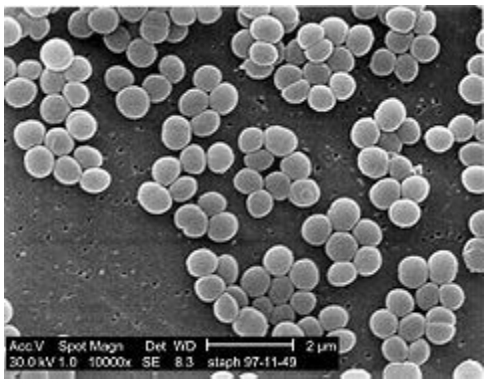
Staphylococcus

Staphyle means in Greek "bunch of grapes" and ***kókkos***, "granule"). *Staphylococcus* is a genus of Gram positive bacteria. Under the microscope they appear round (cocci), and form in grape-like clusters.

The *Staphylococcus* genus include just thirty-three species. Most are harmless and reside normally on the skin and mucous membranes of humans and other organisms. Found worldwide, they are a small component of soil microbial flora.

Staphylococcus



Electron microscopy of *S. aureus* colonies; grape-like clustering common to *Staphylococcus* species.

Scientific classification

Kingdom : Bacteria

Phylum : Firmicutes

Class : Bacilli

Order : Bacialles

Family : Staphylococcaeae

Genus : ***Staphylococcus***

Species

S. epidermidies

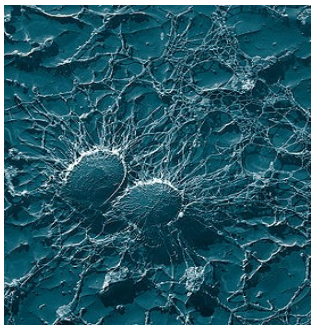
S. aureus
S. caprae
S. haemolyticus
S. hominis
S. intermidius
S. saprophyticus
S. schleiferi
S. simulans

Staphylococcus species can be differentiated from other aerobic and facultative anaerobic gram positive cocci by several simple tests. *Staphylococcus spp.* are facultative anaerobes. Facultative anaerobes are capable of growth both aerobically and anaerobically. All species grow in the presence of bile salts and are catalase positive. Growth also occurs in a 6.5% NaCl solution. On Baird Parker Medium *Staphylococcus spp.* show as fermentative, except for *S. saprophyticus* which is oxidative. *Staphylococcus spp.* are resistant to Bacitracin and susceptible to Furazolidone .

Staphylococcus aureus

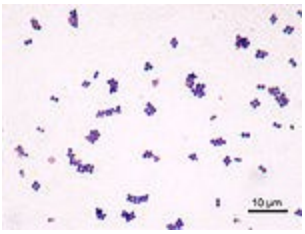
(literally the "golden cluster seed" or "the seed gold" and also known as *golden staph*) is the most common cause of staphylococcus infection. It is a spherical bacterium, frequently found in the nose and skin of a person. About 20% of the population are long-term carriers of *S. aureus*.*S. aureus* can cause a range of illnesses from minor skin infections, such as pimples, boils, cellulities, folliculitis, furuncles, carbuncles and abcesses to life-threatening diseases such as pneumonia, meningities, osteomyelitis, endocardities, Toxic shock syndrome (TSS), and septicemia. Its incidence is from skin, soft tissue, respiratory, bone, joint, endovascular to wound infections. It is still one of the four most common causes of nosocomial infections, often causing postsurgical wound infections.

S. aureus was discovered in Aberdeen, Scotland in 1880 by the surgeon Sir Alexander Ogston in pus from surgical abscesses.Each year some 500,000 patients in American hospitals contract a staphylococcal infection.



Staphylococcus aureus

Microbiology



Gram stain of *S. aureus*.

S. aureus is a facultative anaerobic, Gram positive coccus, which appears as grape-like clusters when viewed through a microscope and has large, round, golden-yellow colonies, often with haemolysis, when grown on blood agar plate.

S. aureus is catalase positive (meaning that it can produce the enzyme "catalase") and able to convert hydrogen peroxide (H_2O_2) to water and oxygen, which makes the catalase test useful to distinguish staphylococci from enterococci and streptococci. A small percentage of *S. aureus* can be differentiated from most other staphylococci by thec oagulase positive: *S. aureus* is primarily coagulase-positive (meaning that it can produce "coagulase", a protein product, which is an enzyme) that causes clot formation while most other *Staphylococcus* species are coagulase-negative.However, while the majority of *S. aureus* are coagulase-positive, some may be atypical in that they do not produce coagulase. Incorrect identification of an isolate can impact implementation of effective treatment and/or control measures.

Role in disease

S. aureus may occur as a commensal on human skin; it also occurs in the nose frequently (in about a third of the population)and throat less commonly. The occurrence of *S. aureus* under these circumstances does not always indicate infection and therefore does not always require treatment (indeed, treatment may be ineffective and re-colonisation may occur). It can survive on domesticated animals such as dogs, cats and horses, and can cause bumble foot in chickens. It can survive for some hours on dry environmental surfaces, but the importance of the environment in spread of *S. aureus* is currently debated. *S. aureus* can infect other tissues when normal barriers have been breached (e.g., skin or mucosal lining).

Toxic shock syndrome and *S. aureus* food poisoning

Some strains of *S. aureus*, which produce the exotoxin TSST-1, are the causative agents of toxic shock syndrome. Some strains of *S. aureus* also produce an enterotoxin that is

the causative agent of *S. aureus* gastroenteritis. The gastroenteritis is self-limiting with the person getting better in 8-24 hours. Symptoms include nausea, vomiting, diarrhea, and abdominal pain.

Mastitis in cows

S. aureus is one of the causal agents of mastitis in dairy cows. Its large capsule protects the organism from attack by the cow's immunological defenses.

Protein A

Protein A is a protein that is anchored to staphylococcal peptidoglycan pentaglycine bridges by the transpeptidase Sortase A. Protein A is an IgG-binding protein which binds to the Fc region of an antibody.

Virulence factors

Toxins

Depending on the strain, *S. aureus* is capable of secreting several toxins, which can be categorized into three groups. Many of these toxins are associated with specific diseases.

Pyrogenic toxin superantigens(PTSAgs) -have superantigen activities that induce toxic shock syndrome (TSS). The staphylococcal enterotoxins, which cause a form of food poisoning, are included in this group.

Exfoliative toxins(EF)- toxins are implicated in the disease staphylococcal scalded-skin syndrome (SSSS), which occurs most commonly in infants and young children. It also may occur as epidemics in hospital nurseries. The protease activity of the exfoliative toxins causes peeling of the skin observed with SSSS.

Other toxins

> Staphylococcal toxins that act on cell membranes include alpha-toxin, beta-toxin, delta-toxin, and several bi-component toxins.

Role of pigment in virulence

Some strains of *S. aureus* are capable of producing *staphyloxanthin* - a carotinoid pigment that acts as a virulence factor. Its has an antioxidant action that helps the microbe to evade killing with reactive oxygen used by the host immune system. It is thought that staphyloxantin is responsible for S. aureus' characteristic golden colour.

Diagnosis

Depending upon the type of infection present, an appropriate specimen is obtained accordingly and sent to the laboratory for definitive identification by using biochemical or enzyme-based tests. A agram stain is first performed to guide the way, which should show typical gram-positive bacteria, cocci, in clusters. Secondly, culture the organism in mannitol salt agar, , which is a selective medium with 7–9% NaCl that allows *S. aureus* to grow producing yellow-colored colonies as a result of salt utilization and subsequent drop in the medium 'pH. Furthermore, for differentiation on the species level, catalase (positive for all species), coagulase (fibrin clot formation), DNAse (zone of clearance on nutrient agar), lipase (a yellow color and rancid odor smell), and phosphatase (a pink color) tests are all done. For staphylococcal food poisoning, phage typing can be performed to determine if the staphylococci recovered from the food to determine the source of infection.

Pathogenesis of *S. aureus* infections

***S. aureus* expresses many potential virulence factors: (1) surface proteins that promote colonization of host tissues; (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, clotting factor); (6) membrane-damaging toxins that lyse eucaryotic cell membranes (hemolysins, leukotoxin, leukocidin; (7) exotoxins that damage host tissues or otherwise provoke symptoms of disease (SEA-G, TSST, ET); and (8) inherent and acquired resistance to antimicrobial agents.**

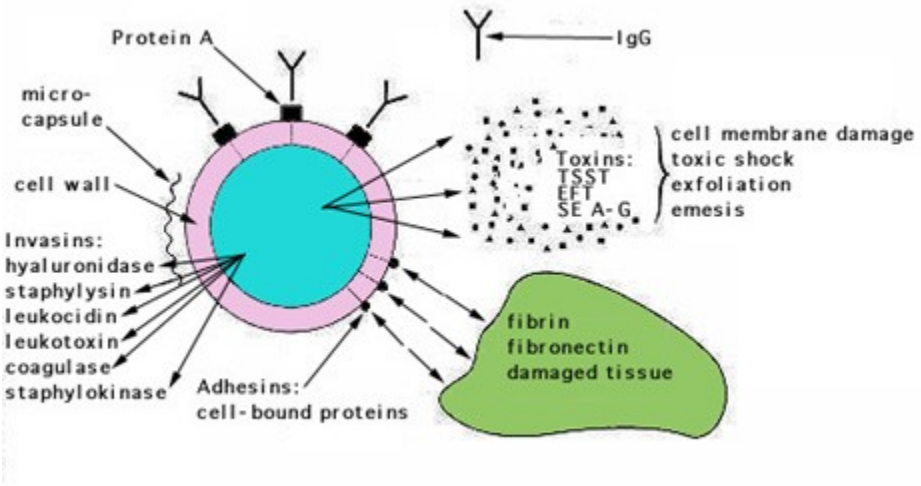


FIGURE 2. Virulence determinants of *Staphylococcus aureus*

Adherence to Host Cell Proteins

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. Most strains of *S. aureus* express both fibronectin and fibrinogen-binding proteins. In addition, an adhesin that promotes attachment to collagen has been found in strains that cause osteomyelitis and septic arthritis.

Invasion

The invasion of host tissues by staphylococci apparently involves the production of a huge array of extracellular proteins, some of which may occur also as cell-associated proteins. These proteins are described below with some possible explanations for their role in invasive process.

Membrane-damaging toxins

alpha toxin (alpha-hemolysin) The best characterized and most potent membrane-damaging toxin of *S. aureus* is alpha toxin. In humans, platelets and monocytes are particularly sensitive to alpha toxin. The mode of action of alpha hemolysin is likely by osmotic lysis.

ß-toxin is a sphingomyelinase which damages membranes rich in this lipid. The classical test for ß-toxin is lysis of sheep erythrocytes. The majority of human isolates of *S. aureus* do not express ß-toxin.

delta toxin is a very small peptide toxin produced by most strains of *S. aureus*. It is also produced by *S. epidermidis*. The role of delta toxin in disease is unknown.

Leukocidin is a multicomponent protein toxin produced as separate components which act together to damage membranes. Leukocidin is hemolytic, but less so than alpha hemolysin. It is an important factor in necrotizing skin infections.

Coagulase and clumping factor

Coagulase is an extracellular protein which binds to prothrombin in the host to form a complex called staphylothrombin. The protease activity characteristic of thrombin is activated in the complex, resulting in the conversion of fibrinogen to fibrin. Coagulase is a traditional marker for identifying *S aureus* in the clinical microbiology laboratory. However, there is no overwhelming evidence that it is a virulence factor, although it is reasonable to speculate that the bacteria could protect themselves from phagocytic and immune defenses by causing localized clotting.

There is some confusion in the literature concerning coagulase and clumping factor, the fibrinogen-binding determinant on the *S. aureus* cell surface. Partly the confusion results from the fact that a small amount of coagulase is tightly bound on the bacterial cell surface where it can react with prothrombin leading to fibrin clotting. However, genetic studies have shown unequivocally that coagulase and clumping factor are distinct entities. Specific mutants lacking coagulase retain clumping factor activity, while clumping factor mutants express coagulase normally.

Staphylokinase

Many strains of *S aureus* express a plasminogen activator called staphylokinase. This factor lyses fibrin. The genetic determinant is associated with lysogenic bacteriophages. A complex formed between staphylokinase and plasminogen activates plasmin-like proteolytic activity which causes dissolution of fibrin clots.

Other extracellular enzymes

S. aureus can express proteases, a lipase, a deoxyribonuclease (DNase) and a fatty acid modifying enzyme (FAME). The first three probably provide nutrients for the bacteria, and it is unlikely that they have anything but a minor role in pathogenesis. However, the FAME enzyme may be important in abscesses, where it could modify anti-bacterial lipids and prolong bacterial survival.

Vaccines

No vaccine is generally available that stimulates active immunity against staphylococcal infections in humans. A vaccine based on fibronectin binding protein induces protective immunity against mastitis in cattle and might also be used as a vaccine in humans. The pharmaceutical company Nabi has developed a trivalent staphylococcal polysaccharide conjugate vaccine called TriStaph™. It contains the two main capsular types, 5 and 8, found in the outer coating of more than 80% of *S. aureus* strains, conjugated to nontoxic recombinant *Pseudomonas* exotoxin A.

References

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