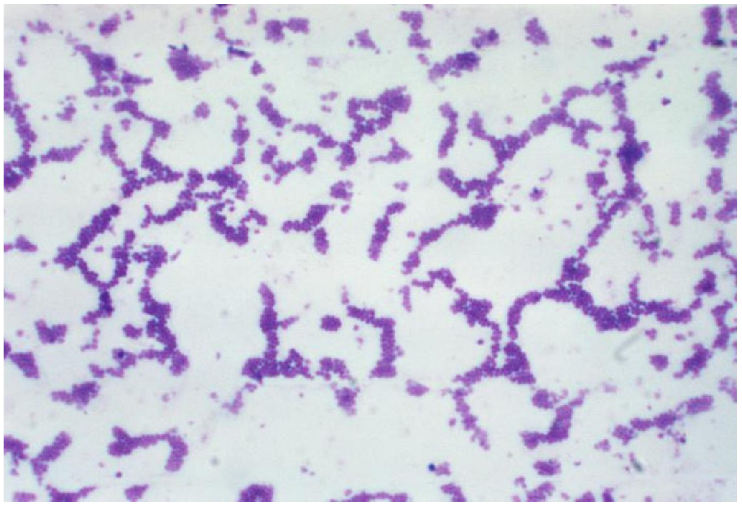
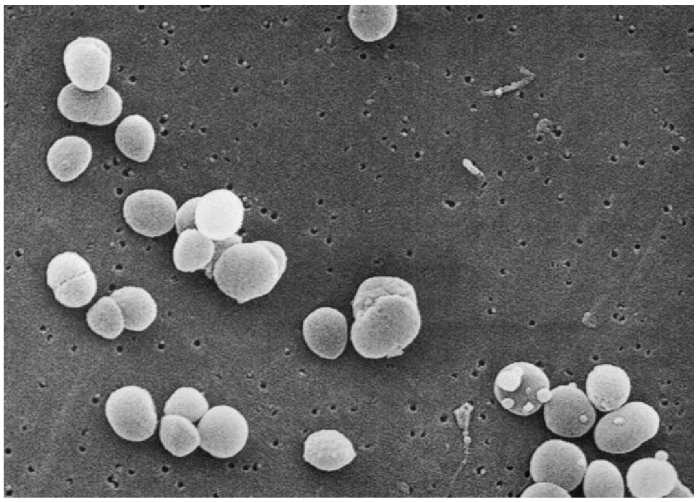
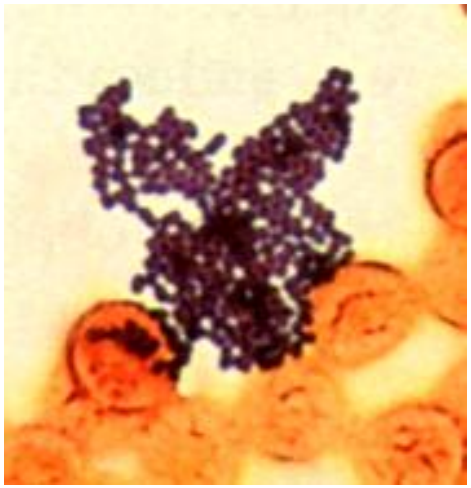


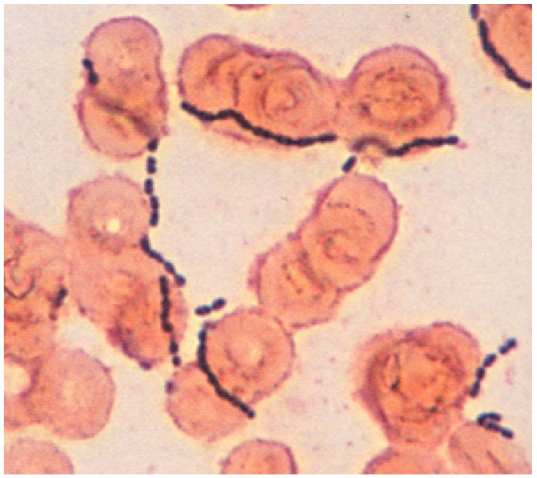


Staphylococcal Food Poisoning

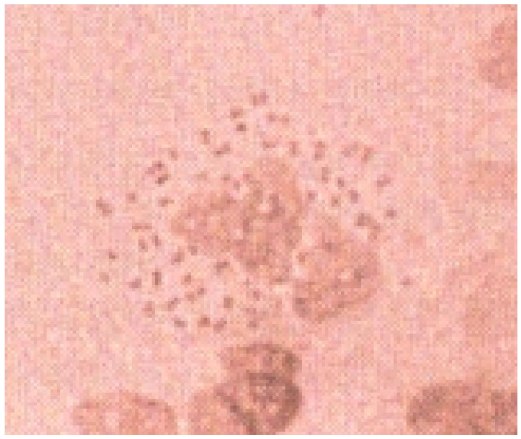
Pyogenic Cocci



Staphylococcus
gram-positive



Streptococcus
gram-positive



Neisseria
gram-negative

Stapylococcus and related organisms

***S. aureus*:** major pathogen for humans, may cause suppuration, abscess formation, scalded skin syndrome, toxic shock syndrome and food poisoning.

***S. epidermidis*:** may cause infection from prosthetic devices.

***S. saprophyticus*:** may cause urinary tract infections (UTI) in young women.

***S. haemolyticus*:** endocarditis, UTI, and opportunistic infections.

***Micrococcus* spp.:** opportunistic infections.

***Stomatococcus* spp.:** endocarditis, opportunistic infections.

***Alloiococcus otitidis*:** chronic middle ear infection.

Morphology and Identification

Staphylococci

Gram-positive cocci
(a bunch of grapes)

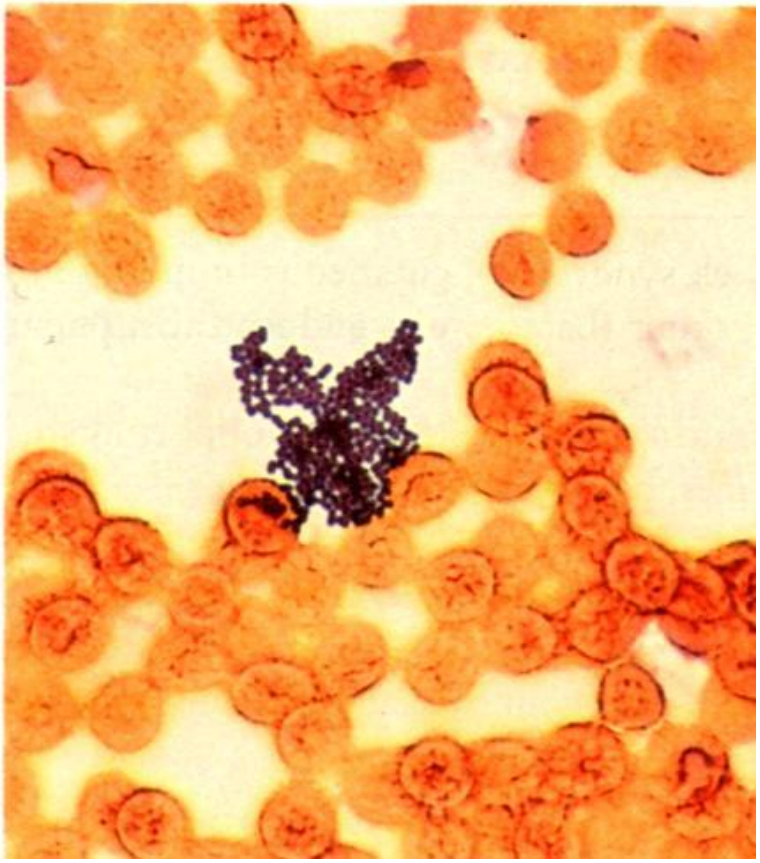
Nonmotile.

Grow readily on most bacteriological media; facultative anaerobic.

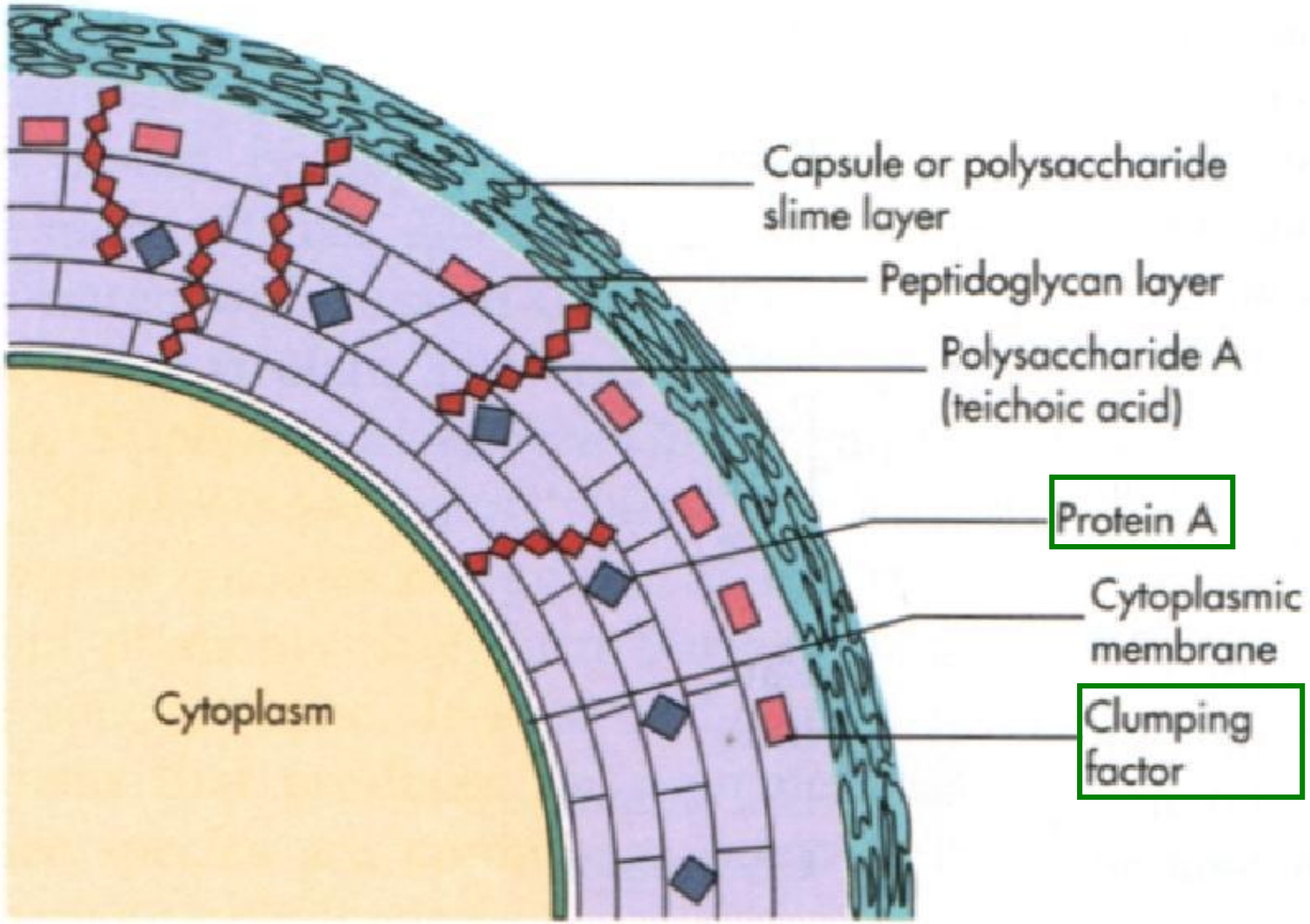
Grow most rapidly at 37 °C, but form carotenoid pigment best at room temperature under aerobic condition on solid medium.

Produce catalase.

Relatively resistant to drying, heat (40°C) and 10% NaCl.



Structure of staphylococcal cell wall



Capsule

Not readily seen *in vitro*

At least 11 types in *S. aureus*

Inhibiting phagocytosis by polymorphonucleocytes

Slime layer

Loose-bound, water-soluble film

Facilitates bacterial adherence to tissues or foreign bodies and, consequently, biofilm formation (important for the pathogenesis of coagulase-negative staphylococci)

Peptidoglycan

Has endotoxin-like activity

- induces production of cytokines
- activates complement
- induces aggregation of polymorphonucleocytes

Teichoic acids and lipoteichoic acids

Bind covalently to peptidoglycan; species-specific; bind to fibronectin of host cells (adherence); antibodies may be found in systemic staphylococcal disease, particularly endocarditis.

Protein A: present on the surface of *S. aureus* strains, but not other species. Binds to the Fc portion of IgG except IgG3, preventing clearance of bacteria.

Coagulase (clumping factor)

Produced by most *S. aureus* on the cell wall surface; binds to fibrinogen and converts it to fibrin, resulting in aggregates of bacteria.

Coagulase-positive vs. coagulase-negative staphylococci

Other adhesins bind with collagen, elastin and fibronectin

Pathogenesis and Immunity

***S. aureus* can produce diseases both through invasiveness and production of toxins.**

Toxins

Cytotoxins

α-toxin: pore-forming , cytotoxic to many types of cells including muscle cells.

β-toxin: degrades sphingomyelin and is toxic for many kinds of cells, including human RBCs.

γ-toxin: bicomponent toxins, pore-forming.

δ-toxin: has detergent-like activity.

P-V leukocidin: similar to γ-toxin in structure, kills WBCs of many animals and release the lysosomal enzymes. Associated with severe pulmonary and cutaneous infections.

Toxins (continued)

Exfoliative (epidermolytic) toxins: proteases that split desmoglein 1 of the intercellular bridges in epidermis; produced by about 5-10% of *S. aureus*; causes the generalized desquamation of the staphylococcal scalded skin syndrome (SSSS).

Toxic shock syndrome toxin-1 (TSST-1): superantigen, associates with fever, shock, desquamative skin rash of toxic shock syndrome in humans.

Enterotoxins: superantigens, at least 10 (A, B, C1, C2, C3, D, E, G, H, and I) soluble toxins produced by about 50% of *S. aureus*.

Heat-stable (100^{o}C, 30 min.) and resistant to the gastric acid and gut enzymes.

Enterotoxins are produced in carbohydrate and protein foods.

Causing emesis, a characteristic of staphylococcal food poisoning.

Enzymes

Coagulase: bound and free forms. May deposit fibrin on the surface of staphylococci and alter their ingestion by and destruction within the phagocytic cells (associated with invasiveness).

Fibrinolysin (staphylokinase): to dissolve fibrin clot.

Catalase: to remove H_2O_2.

Hyaluronidase: to facilitate spread of *S. aureus* in tissue.

Lipase: associated with superficial skin infection.

Nuclease: produced only by *S. aureus*.

Penicillinase

Epidemiology

Staphylococci can permanently (coagulase-negative strains) or transiently (*S. aureus*) colonize various areas of the human body, with the anterior nasopharynx as the most common colonization site for *S. aureus* in older children and adults (30% of healthy adults.)

Nasopharyngeal or skin carriers of *S. aureus* are responsible for many hospital infections.

S. aureus can be transmitted through direct personal contact or contact with contaminated fomites.

Areas at highest risk for severe infections: new born nursery, ICU, operating rooms and cancer chemotherapy wards.

What is *Staphylococcus*?

Staphylococcus aureus **is a common bacterium found on the skin and in the noses of up to 25% of healthy people and animals.**

Staphylococcus aureus **is important because it has the ability to make seven different toxins that are frequently responsible for food poisoning.**

What is staphylococcal food poisoning?

Staphylococcal food poisoning is a gastrointestinal illness. It is caused by eating foods contaminated with toxins produced by *Staphylococcus aureus*. The most common way for food to be contaminated with *Staphylococcus* is through contact with food workers who carry the bacteria or through contaminated milk and cheeses. *Staphylococcus* is salt tolerant and can grow in salty foods like ham. As the germ multiplies in food, it produces toxins that can cause illness. Staphylococcal toxins are resistant to heat and cannot be destroyed by cooking. Foods at highest risk of contamination with *Staphylococcus aureus* and subsequent toxin production are those that are made by hand and require no cooking. Some examples of foods that have caused staphylococcal food poisoning are sliced meat, puddings, some pastries and sandwiches.

What are the symptoms of staphylococcal food poisoning?

Staphylococcal toxins are fast acting, sometimes causing illness in as little as 30 minutes. Symptoms usually develop within one to six hours after eating contaminated food. Patients typically experience several of the following: nausea, vomiting, stomach cramps, and diarrhea.

The illness is usually mild and most patients recover after one to three days. In a small minority of patients the illness may be more severe.

How do I know if I have staphylococcal food poisoning?

Toxin-producing *Staphylococcus aureus* can be identified in stool or vomit, and toxin can be detected in food items. Diagnosis of staphylococcal food poisoning in an individual is generally based only on the signs and symptoms of the patient. Testing for the toxin-producing bacteria or the toxin is not usually done in individual patients. Testing is usually reserved for outbreaks involving several persons. If you think you may have food poisoning, contact your physician.

How can staphylococcal food poisoning be prevented?

It is important to prevent the contamination of food with *Staphylococcus* before the toxin can be produced.

- •Wash hands and under fingernails vigorously with soap and water before handling and preparing food.
- •Do not prepare food if you have a nose or eye infection.
- •Do not prepare or serve food for others if you have wounds or skin infections on your hands or wrists.
- •Keep kitchens and food-serving areas clean and sanitized.
- •If food is to be stored longer than two hours, keep hot foods hot (over 140°F) and cold foods cold (40°F or under).
- •Store cooked food in a wide, shallow container and refrigerate as soon as possible.

Fatal Staphylococcal Food Poisoning

Southern Medical Journal. 66(6):703-705, June 1973.

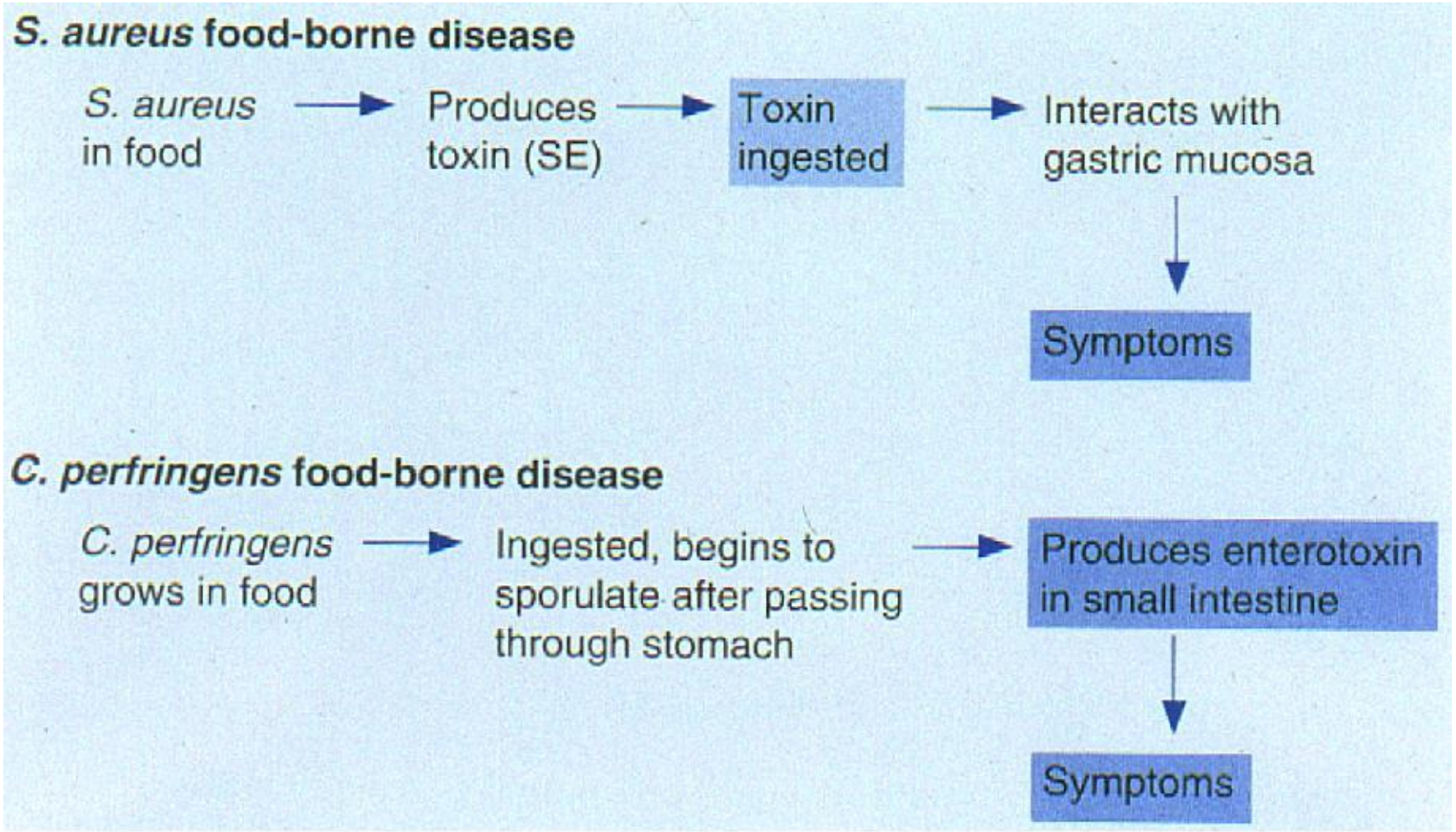
Four persons experienced the sudden onset of vomiting, diarrhea and shock approximately three and one half hours after eating a "cold plate" lunch served at a restaurant; the illness was fatal in one individual. Food specific attack rates implicated ham from which staphylococci were isolated. This report demonstrates the potential seriousness of staphylococcal food poisoning and emphasizes the role of the practicing physician in reporting such outbreaks to the appropriate health authorities.

Clinical Diseases

Food poisoning: caused by ingestion of preformed enterotoxin in food (meat and carbohydrates). Short incubation (1-8 hr). Violent nausea, vomiting and watery diarrhea; no fever; rapid convalescence.

Staphylococcal enterocolitis occurs in patients who have received broad spectrum antibiotics (antibiotic-associated diarrhea).

Toxic shock syndrome: abrupt onset of high fever, vomiting, diarrhea, myalgia, scarlatini form rash, desquamation of palms and soles, and hypotension with cardiac and renal failure. This disease has occurred in children injected with contaminated vaccine (1928), and young women who used tampons (1980). This may also occur in children or in men with staphylococcal wound infections (half cases are caused by enterotoxin B and, rarely, enterotoxin C.)


S. aureus food-borne disease
S. aureus in food
Produces toxin (SE)
Toxin ingested
Interacts with gastric mucosa
Symptoms
C. perfringens food-borne disease
C. perfringens grows in food
Ingested, begins to sporulate after passing through stomach
Produces enterotoxin in small intestine
Symptoms

Laboratory Diagnosis

Specimen: pus, sputum, blood, anterior nasal and perineal swabs, left-over food etc.

Smear: except for abscess material, gram stain of the smear is usually not informative.

Serology: antibodies against teichoic acid can be detected in patients with staphylococcal endocarditis, but not those with osteomyelitis or wound infection. Elevated antibody titers is an indication for prolonged antibiotic treatment.

Laboratory Diagnosis

Culture: blood agar plates. Use 7.5% NaCl to inhibit contaminants. Mannitol-salt agar can be used as a selective medium for *S. aureus*. Hemolysis and pigment production may not occur until several days later and are optimal at room temperature.

Identification: catalase test; coagulase test. Fluorescent in situ hybridization (FISH) with a *S. aureus*-specific DNA probe can be used for identification of this organism in clinical specimens.

Various subtyping methods (such as pulsed-field gel electrophoresis) are used for epidemiological purpose.

Treatment

Drug resistance of *S. aureus*

Tetracycline are used for long term treatment of acne or furunculosis. Abscess and other closed suppuration lesions are treated by drainage and antibiotics.

Bacteremia, endocarditis, pneumonia and other severe staphylococcal infections: prolonged i.v. therapy with β-lactamase-resistant penicillins (e.g. methicillin, oxacillin, etc.)

Vancomycin is the most effective drug against staphylococci, but its use is restricted in most hospitals.

Drug resistance of *S. aureus*

1) Resistance to penicillin G, ampicillin, and similar drugs is common.

2) Resistance to nafcillin, methicillin and oxacillin

MRSA (ORSA): methicillin (oxacillin)-multiresistant *S. aureus*, resulting from acquisition of *mecA*, which encodes a novel PBP (PBP2') that is not bound by β-lactams.

3) MRSA strains are usually also resistant to tetracyclines, erythromycins and aminoglycosides.

4) Remain susceptible to vancomycin. However, many strains have become moderately resistant to vancomycin (called vancomycin-intermediate SA, VISA) and, notably, two vancomycin-resistant strains (VRSA), have been isolated in USA since 2002.

New chemotherapy target: staphyloxanthin

Staphyloxanthin, the carotenoid pigment, acts as an anti-oxidant and helps the bacteria resist killing by the reactive oxygen species (ROS), such as O_2^-, H_2O_2 and HOCl, in neutrophils. Bacteria that lack this pigment grow normally, but are deficient in skin abscess formation.

Liu GY *et al*., *J. Exp. Med.* 202, 209 (2005)

Early enzymatic steps in staphyloxanthin production resemble those for cholesterol biosynthesis. A cholesterol biosynthesis inhibitor blocks staphyloxanthin biosynthesis, resulting in colorless bacteria with diminished virulence that were cleared by the innate immune system

Liu CI *et al*., *Science* 319, 1391 (2008)

Prevention and control

Chief sources of infection: shedding human lesions, contaminated fomites, human respiratory tract and skin.
Prevention of infection: cleansing of the wound and the application of an effective disinfectant.

Prevention of wide dissemination from staphylococci carriers is very important (aerosols and UV of air have little effect).
Rifampin plus a second antibiotics, or some topical agents, may suppress or cure of nasal carriage.

Areas at highest risk for severe infections: new born nursery, ICU, operating rooms and cancer chemotherapy wards.

While cases of infection by MRSA are mainly hospital-acquired, there are increasing numbers of community-acquired infections by newly emerging MRSA recently.