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Diseases caused by *Staphylococcus aureus*

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Abstract
Staphylococcus aureus is a bacterium that can cause a variety of illnesses through suppurative or nonsuppurative (toxin-mediated) means. The sudden appearance of local erythema around the mouth (redness and inflammation), which takes over the entire body over two days, is a characteristic of Scale skin syndrome. Bullous impetigo is the topical form of scale skin syndrome. In this syndrome, specific strains of *Staphylococcus aureus* generate toxins (such as phage type 71) as well as skin surface blisters. This disease is witnessed in young children and is highly contagious. Also toxic shock syndrome is produced by *Staphylococcus aureus* species that produce TSST-1 or enterotoxin B. Previously, TSST-1 was called enterotoxin B, pyrogenic exotoxin C, and enterotoxin F. (this toxin is similar to enterotoxin F). Folliculitis is the most cutaneous infection caused by *Staphylococcus aureus*. Folliculitis is a purulent infection of hair follicles that causes redness and swelling of the hair follicle. Furuncle is a developed folliculitis, and large painful protruded nodules appear that contain dead tissue (necrotic) in its lower region. As a consequence of the furuncles joining together and their extension into the deeper subcutaneous tissues, carbuncle may develop. Staphylococcus impetigo is commonly observed in children that are mainly produced on the face and organs, especially around the nose, and most likely spreads to other parts of the face through a running nose or at the time of nose blowing. *Staphylococcus aureus* is also the common agent for bacteremia. The highest prevalence of *Staphylococcus aureus* is witnessed in patients with diabetes mellitus, cardiovascular patients, and patients with granulocytic and immune deficiency. Staphylococcus pneumonia is considered as an important disease due to its high mortality (up to 50%). It may be observed in all age groups, but it is a rare disease with the exception of its association with the flu epidemic. *Staphylococcus aureus* is the cause of most cases of primary osteomyelitis. This disease is predominantly occurring in boys under the age of 12, and is often followed by the diffusion of a primary hemorrhage (ulcer or furuncle). To design appropriate empirical therapy, physicians should be knowledgeable about the disease caused by of *Staphylococcus aureus* in their communities**.** This article reviews the some important diseases caused by *Staphylococcus aureus.*

Keywords: *Staphylococcus aureus*, staphylococcal food poisoning, toxic shock syndrome, bacteremia

Introduction
Staphylococcus aureus is a bacterium that can cause a variety of illnesses through suppurative or nonsuppurative (toxin-mediated) means. *Staphylococcus aureus* is a common cause of skin and skin structure infections as well as osteoarticular infections in the human population. *Staphylococcus aureus* is also identified in cases of septicemia, infective endocarditis, pneumonia, ocular infections, and central nervous system infections. To design appropriate empirical therapy, physicians should be knowledgeable about the disease caused by of *Staphylococcus aureus* in their communities, including toxic shock syndrome, Staphylococcal food poisoning and etc**.** This article reviews the some important diseases caused by *Staphylococcus aureus.*

Methods
Search Strategy
Searches were conducted by two independent researchers in international (PubMed, Web of science, Scopus and Google scholar) and national (SID, Magiran) databases for related studies from the inception of the databases to September 2017 (without time limitation) in English and Persian languages. To ensure literature saturation, the reference lists of included studies or relevant reviews identified through the search were scanned. The specific search strategies were created by a Health Sciences Librarian with expertise in systematic review search using the MESH terms and free terms according to the PRESS standard. After the MEDLINE strategy was finalized, it was adapted to search in other databases. Accordingly, PROSPERO was searched for ongoing or recently related completed systematic reviews. The key words used in the search strategy were "*Staphylococcus aureus*, Diseases, Infection" and Iran which were combined with Boolean operators including AND, OR, and NOT.

Study Selection
Results of the Literature review were exported to Endnote. Prior to the formal screening process, a calibration exercise was undertaken to pilot and refine the screening. Formal screening process of titles and abstracts were conducted by two researchers according to the eligibility criteria, and consensus method was used for solving controversies among the two researchers. The full text was obtained for all titles that met the inclusion criteria. Additional information was

retrieved from the study authors in order to resolve queries regarding the eligibility criteria. The reasons for the exclusion criteria were recorded. Neither of the review authors was blinded to the journal titles, the study authors or institutions.

Infections via toxins

Scale skin syndrome

In 1878, Ritter described exfoliative dermatitis in 297 infants less than one month old. The disease he described is now called Ritter. The sudden appearance of local erythema around the mouth (redness and inflammation), which takes over the entire body over two days, is a characteristic of this disease. Slight pressures result in displacement of the skin, which is referred to as the positive Nikolsky sign. Large vesicles or skin blisters appear quickly, after which epithelial desquamation is observed. The blisters contain clean and pure fluid that lack any organisms or leukocyte, which indicates that the disease is caused by bacterial toxin [1, 2].

Bullous impetigo

It is the topical form of scale skin syndrome. In this syndrome, specific strains of *Staphylococcus aureus* generate toxins (such as phage type 71) as well as skin surface blisters. Unlike patients with signs of scale skin syndrome, patients with bullous impetigo have topical blisters, culturing which is positive. In erythema impetigo, it does not extend beyond the border of the blisters and is limited to the blister line, and the nikolsky sign is not observed. This disease is witnessed in young children and is highly contagious [3].

Staphylococcal food poisoning

Staphylococcal food poisoning is one of the most common foodborne illnesses as a result of the presence of toxin in food and not due to infection. In other words, instead of being an infection, it is a kind of poisoning; therefore, instead of direct effect of the organism on the individual, the illness is due to the bacterial toxin in the food. The toxin produced is an enterotoxin, which is produced in about one-third of *Staphylococcus aureus* strains. Staphylococcus enterotoxins are a family of nine major serotypes of heat-resistant enterotoxins (A-E and G-j). Enterotoxins A and C are the major causes of food poisoning [4, 5].

Toxic shock syndrome

The first epidemic of toxic shock syndrome was reported in Australia in 1928, where the disease spread among 21 children, and 12 of whom died after being injected with *Staphylococcus aureus*-infected vaccines. Fifty years later, in 1978, the disease was named "toxic shock syndrome" and was explained among a group of seven children and youth aged 8-17 years old. In the early 1980s, a commotion was caused by several cases of toxic shock syndrome, which occurred in women who used high-absorption tampons. In addition to providing reproductive conditions for Staphylococcus, tampons provided oxygen for the expression of *tst* gene due to the presence of air bags. TSST-1 is coded by the *tst* gene and is responsible for the symptoms of toxic shock syndrome [6, 7].

In addition to what was mentioned above, the disease can also develop in people with rash or other focus areas of Staphylococcus infections, and the disease is not peculiar to women [8]. Although it was initially reported that coagulase negative Staphylococci can also be a cause of toxic shock syndrome, it is now believed that toxic shock syndrome is produced by *Staphylococcus aureus* species that produce TSST-1 or enterotoxin B. Previously, TSST-1 was called enterotoxin B, pyrogenic exotoxin C, and enterotoxin F. (this toxin is similar to enterotoxin F) [9].

Cutaneous infections

Staphylococcus and topical infections include folliculitis, furuncle, carbuncle, and impetigo [10].

Folliculitis

It is the most cutaneous infection caused by *Staphylococcus aureus*. Folliculitis is a purulent infection of hair follicles that causes redness and swelling of the hair follicle. If the pus collects under the eyelid base, it causes stye to develop. Furuncle is a developed folliculitis, and large painful protruded nodules appear that contain dead tissue (necrotic) in its lower region. The furuncle is drained spontaneously or after an incision during surgery (pus is drained off). As a consequence of the furuncles joining together and their extension into the deeper subcutaneous tissues, carbuncle may develop. Unlike patients with folliculitis and furuncle, fever is witnessed in patients with carbuncle which indicates a systemic transmission of Staphylococcus through bacteremia to other tissues [11-13].

Impetigo

It is a cutaneous infection which often affects young children. The most common symptoms of *Staphylococcus aureus* in infants are pustules or lesions similar to impetigo. Staphylococcus impetigo is also commonly observed in children that are mainly produced on the face and organs, especially around the nose, and most likely spreads to other parts of the face through a running nose or at the time of nose blowing [14].

Bacteremia and endocarditis

Staphylococcus aureus is the common agent for bacteremia. Although bacteremia produced by a large body of other organisms originates from a recognizable infection site, such as: lung, urethra, or gastrointestinal tract infections, in about one-third of patients suffering from *Staphylococcus aureus* bacteria, primary infectious areas are unknown. The infection most likely spreads from an unimportant and unobvious skin infection to the skin tissue. More than 50% of *Staphylococcus aureus* bacteremia occur after surgeries in the hospital or result from continuous use of an infected internal catheter. The highest prevalence of *Staphylococcus aureus* is witnessed in patients with diabetes mellitus, cardiovascular patients, and patients with granulocytic and immune deficiency. In addition, external objects such as intravascular prostheses and intravenous plastic catheters provide a favorable environment for vascular infection and bacteremia [15].

Pneumonia and empyema

Staphylococcus pneumonia is considered as an important disease due to its high mortality (up to 50%). It may be observed in all age groups, but it is a rare disease with the

exception of its association with the flu epidemic. Infants less than one year of age show the highest rate of infection potential and account for about 75% of cases. The primary pneumonia of *Staphylococcus aureus* is detectable in patients with abnormalities in their immune system: children with cystic fibrosis or measles, patients with flu, weak patients, and hospitalized patients treated with antimicrobial drugs, steroids or chemotherapy for cancer or immunosuppressant, necrosis, along with the formation of multiple abscesses characterizes staphylococcus pneumonia [16].

Osteomyelitis and infectious arthritis

Staphylococcus aureus is the cause of most cases of primary osteomyelitis. This disease is predominantly occurring in boys under the age of 12, and is often followed by the diffusion of a primary hemorrhage (ulcer or furuncle). The organism penetrates the diaphysis of long bones; this feature is probably due to the fact that arterial blood flow in this area is the type of capillary rings. With the progression of infection, the pus is accumulated and leaks into the bone surface; it lifts the bone crust and creates an abscess under the crust. Clinical complaints of acute osteomyelitis include fever and chills, bone pain and muscle spasm around the affected area [17].

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