Toxic Shock Syndrome (TSS)
Staphylococcal

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Disease Etiology, Pathology, and Epidemiology:

Toxic Shock Syndrome, otherwise known as TSS, is a systemic infection that is associated with the bacteria *Staphylococcus aureus* [1]. *S. aureus* exists as part of the human body's normal bacteria, and does not cause infection since most people develop antibodies against the bacteria. Infection can be result in people that have not developed these antibodies, or may develop in people that have another infection if the bacteria is introduced [2]. If fact, *S. aureus* is the cause of many nosocomial infections [3].

*S. aureus* produces Toxic Shock Syndrome Toxin (TSST)[4]. These toxins possess superantigen activity, and are released into the human blood stream [3]. The role of superantigens is to bind to and activate T helper cells. These superantigens can activate up to 20% of the T helper cells. “When activated they produce Interleukin 2 and other cytokines that cause the symptoms of TSS. The bacteria do not usually invade the tissues or the bloodstream. This is usually the result of an intoxication with TSST-1” [1].

Transmission:

TSS can occur in both women, as well as men. However it is most commonly seen in women with the start of menstruation [1]. Menstrual linked TSS is far more common in women that use high absorbent tampons, use tampons excessively, use a single tampon for a long period of time, or use tampons past the end of their cycle [5]. Although most cases of TSS are consequences of menstruation, there has been an increasing amount of non-menstrual TSS reported [6]. Clinical or hospital acquired infections can result from biofilms on intravenous catheters, implants, and even prosthetic joints [3]. Fortunately TSS is not usually considered to be contagious since the presence of infection or disease depends on if a person has antibodies against the bacteria [2].

Reservoirs:

Humans serve as the main reservoir. *S. aureus* is typically found in the groin, nose, axillae, perineal area of males, mucus membranes, mouth, mammary glands, hair, intestines, genitourinary tract, and upper respiratory tracts. Additionally, TSS can exist as a zoonotic disease, as many animals serve as reservoirs, especially cows that contain infected udders [7]. Biofilms on intravenous catheters, implants, prosthetic joints can also serve as a reservoir [3].
**Microorganism characteristics:**

*Staphylococcus aureus* is a bacterium that exists as part of the normal bacteria in the human body, and is considered to be an opportunistic pathogen. *S. aureus* are gram-positive cocci (0.5-1.0 um in diameter) that grow in clusters, pairs, and sometimes in short chains. This is different from *Streptococci*, which grow in longer chains. Observations and identification of *S. aureus* must be made from cultures grown in broth, not in solid agar as they may appear as clumps [3]. *S. aureus* is catalase positive, non-motile, non-spore-forming, and are mostly all facultative anaerobes. Several strains produce enterotoxins, the superantigen exotoxin TSST, as well as exfoliative toxins [7]. Many strains of *S. aureus* are becoming antibiotic resistant. For example, methicillin-resistant *S. aureus* (MRSA) is a known nosocomial infection [3].

**Key tests for identification:**

Epidemiological testing of *S. aureus* involves phage typing, molecular typing, biotype analysis, agglutination tests, ELISA, PCR, coagulase (coagulase negative), and hemolysins [3]. Identification of *Staphylococci* involves the catalase test (catalase positive), as well as observing the structure of the bacteria grown in broth cultures ( cocci that are 0.5-1.0 um in diameter, and grow in clusters, pairs, or even in short chains) [3]. A gram stain can also be performed (gram positive) [3].

Diagnosis is based on blood cultures, blood blotting, bleeding times, cell counts, electrolytes, liver function, urine tests, as well as lumbar puncture to test for the presence of the bacteria [2].

**Signs and symptoms of disease:**

TSS begins with general signs and symptoms that resemble the flu, such as high fever, chills, muscle aches, headaches, vomiting, dizziness, lightheadedness, and low blood pressure [8].

Later signs and symptoms of TSS develop into a rash that resembles a sunburn, which then further develops to a rash on the palms of the hands and soles of the feet about 1-2 weeks after the onset of acute infection [5, 8]. TSS is also characterized by multi-organ failure, which involves three or more organs of organ systems, as well as non-focal neurological abnormalities [5]. Additionally signs of vaginal hyperemia, and uremia are manifestations [1]. Early symptoms can be alike to symptoms of many other infections, but can progress rapidly and become fatal [2].

Diagnosis of TSS should be considered when presented with cases that include "unexplainable fever associated with an erythematous rash and diffuse organ involvement, especially in menstruating women" [1].
**Historical information:**

TSS was initially acknowledged in 1978 and was associated with tampon use in menstruating women [5]. In May 1980, 55 cases of TSS were reported, of those 55 cases, 52 cases were in women. CDC (Centers for Disease Control and Prevention) issued national surveillance to assess the degree of infection and to follow trends of incidence cases. In June 1990, a follow-up report established an association between TSS and menstruating women. Further studies were done and identified that women who used RelyPr brand of tampons were had a higher risk of developing TSS. In September 1980 following these studies, RelyPr brand tampons were taken off the market [9].

**Virulence factors:**

*S. aureus* contains several virulence factors. From surface proteins that induce colonization of host tissues, to factors such as a capsule and immunoglobulin binding protein A, that inhibit phagocytosis.

In order to express the signs and symptoms of disease and infections *S. aureus* must first get into the host and attach to host cells or tissues. The bacteria cells express surface proteins such as laminin and fibronectin that form part of their extracellular matrix and promote adhesion. Many strains of *S. aureus* contain fibrinogen/fibrin binding protein, which is a clumping factor that promotes adhesion to blood clots and damaged tissue [3].

The release of toxins that damage host tissue and cause disease is yet another factor [3]. Some exotoxins are hemolysins and can lyse erythrocytes. Additionally *S. aureus* can also produce a toxin that contains leukocidin activity and specifically acts on polymorphonuclear leukocytes [4]. Many clinical isolates of *S. aureus* have a surface polysaccharide (serotype 5/8) that is known as a microcapsule due to the fact that it can only be visualized by an electron microscope [4]. This is different from the typical bacterial capsule, which can be viewed by a light microscope.

Coagulase is a known marker for the presence of *S. aureus*, however there is no evidence that it is a virulence factor [3]. In fact, the “division of staphylococci into coagulase positive and negative is artificial and indeed, misleading in some cases” [3].

**Treatment and control:**

Upon diagnosis of TSS recommended treatment includes fluid replacement, and beta lactamase resistant antibiotics such as oxacillin or nafcillin [1]. “Phagocytosis is the major mechanism for combatting staphylococcal infection. Antibodies are produced which neutralize toxins and promote opsonization” [3]. Hospital acquired TSS infection is typically the result of antibiotic resistant strains. These infections can only be treated with vancomycin [3]. For persons who develop renal failure, dialysis may be required. Furthermore, deep surgical cleaning of the infected area may be necessary [2].
*S. aureus* is susceptible to 70% ethanol, chlorhexidine, 2% glutaraldehyde, formaldehyde, 1% sodium hypochlorite, and 0.25% benzalkonium chloride; also to dry heat treatment of 160-170 degrees Celsius for at least an hour [7].

**Prevention and vaccination:**

Fortunately TSS can be prevented. Menstruating females should avoid the use of tampons, or foreign vaginal items, especially if they have a history of TSS. Timely. Thorough wound care is required for avoidance of TSS [2]. Although there is no current available vaccine for the public, antibiotics can help neutralized toxins and enzymes [3].

Recently however, researchers from the Department of Clinical Pharmacology, Medical University Vienna, have developed a newly tested successful vaccine for TSS. The injected vaccine is “a recombinant detoxified toxic shock syndrome toxin-1 variant (rTSST-1v) from a Staphylococcus toxin, and has been found to be immunogenic and well-tolerated in a clinical Phase I trial after being given to 46 young men and women” [8]. This study plays a crucial role in the prevention of TSS.

**Local and global cases/outbreaks:**

Infections caused by *S. aureus* are worldwide. The last population-based evaluation of TSS was back in 1986. A recent study published in 2011 examined the “incidence of both menstrual and non-menstrual TSS in the years 2000–2003 compared to the late 1980s, with the highest incidence among women aged 13–24 years.” “There was also no significant increase in annual TSS incidence over the years 2000–2006.”

After the initial epidemic, the number of reported cases decreased considerably. In 1986, active surveillance was conducted in several regions in the United States (with a total population of 34 million) to assess the trend. “The cumulative incidence (0.5 per 100,000 population) confirmed the substantial decrease in the incidence of menstrual TSS observed in the passive surveillance system. Incidence rates decreased from 6 to 12 per 100,000 among women 12 to 49 years of age (10,11) in 1980 to 1 per 100,000 among women 15 to 44 years of age in 1986” [10].

Since December 2015, five new cases of TSS were reported in Michigan [11]. Unfortunately there is extremely limited data on global outbreaks and cases.

**REFERENCES:**


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