A review of animal diseases caused by staphylococci

Una revisión de las enfermedades animales causadas por estafilococos

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Abstract

Staphylococci are opportunistic microorganisms that may cause severe infections in both humans and animals under certain conditions. Staphylococcus spp is the most important microorganism that may cause major economic losses in animal farms. This manuscript aims to provide an overview of some animal diseases caused by Staphylococcus spp.

Keywords: Staphylococcus spp., virulence factors, animal diseases, mastitis, poultry diseases.

Resumen

Los estafilococos son microorganismos oportunistas que pueden causar infecciones graves tanto en humanos como en animales bajo ciertas condiciones. Staphylococcus spp. son los microorganismos más importantes que pueden causar importantes pérdidas económicas en las granjas de animales. Este manuscrito tiene como objetivo proporcionar una descripción general de algunas enfermedades animales causadas por Staphylococcus spp.

Palabras clave: Staphylococcus spp., Factores de virulencia, enfermedades animales, mastitis, enfermedades avícolas.

History and Etymology

Staphylococci are a group of Gram-positive bacteria that belong to the Staphylococcus genus of the Micrococcaceae family. These microorganisms can be grown and multiply everywhere, water, soil, air, plants, and are also considered as normal flora on the skins and nasal cavities of animals and humans[1-3]. Staphylococci were first discovered in the 19th century by Scottish surgeon and bacteriologist Alexander Ogston in 1880. Who observed grape-like clusters of bacteria in surgical abscess of a knee joint and called them Staphylococcus (Greek Staphylo "a bunch of grape"; Kokkos "berry")[4,5]. In 1884, the German physician Friedrich Julius Rosenbach noticed that these microorganisms have two different colors (white and yellow) on pure bacterial media, so he classified them into two groups; Staphylococcus albus (albus means white) and Staphylococcus aureus (aurum means gold). In 1928, Alexander Fleming accidentally discovered the effect of Penicillium on the growth of S. aureus. In 1940, penicillin-resistant S. aureus was reported for the first time by the English biochemist Sir Edward Penley Abraham[6,7]. In 1959, a British pharmaceutical company developed semisynthetic penicillin (methicillin) to treat infections caused by penicillin-resistant S. aureus[8-10]. In the early 1960s, some researchers discovered the presence of methicillin-resistant S. aureus (MRSA)[11-13]. In 1996, vancomycin-intermediate S. aureus (VISA), was isolated from a Japanese patient[14,15]. In 2002, vancomycin-resistant S. aureus (VRSA) was first isolated from a clinical sample in the United States[16,17].

Etiology

1. Capsule

Capsules enhance microbial virulence by increasing bacterial resistance to phagocytosis. A few strains of S. aureus produce a capsule, and there are eight different serotypes. Serotype 5 and 8 were the most detected serotypes in animal specimens (cows, rabbits, poultry, pigs, and horses). The capsulated strains are characterized by producing mucoid colonies[18,19].

2. Protein A

Protein A is an IgG-binding protein found on the cell wall of S. aureus, which is also known as Staphylococcal Protein A (SPA). SPA can assist S. aureus to avoid phagocytosis by polymorphonuclear leukocytes (PMNs) via capturing IgG in an inverted orientation. In addition, the binding of the SPA with IgG reduces the opsonization by antibodies. Moreover, SPA is one of the virulence factors in S. aureus due to its ability to inhibit phagocytosis[20,21].

SPA can adhere to the soluble and immobilized von Willebrand factor (vWF), which is a glycoprotein present in the blood and plays a vital role in endovascular infections and adheres to the platelets to the damaged endothelial sites[9].

3. Enzymes

3.1. Coagulase

Staphylococci are divided into two groups based on their ability to produce coagulase; Coagulase Positive Staphylococci (CPS) and Coagulase Negative Staphylococci (CNS). S. aureus is distinguished clinically from other less pathogenic species by its ability to produce coagulase. S. aureus secretes two proteins that promote coagulation, coagulase and von Willebrand factor binding protein (vWbp). Both of these proteins activate prothrombin non-proteolytically. These two proteins interact with prothrombin in the blood to form a " Staphylothrombin " complex. Staphylothrombin activates protease to convert fibrinogen to fibrin and to form a clot in the bloodstream. Since coagulase is tightly bound to the surface of S. aureus, it can form a layer of fibrin on the surface of S. aureus. This fibrin layer may protect S. aureus from phagocytosis and isolate it from other host defenses[21-23].

3.2. DNase

DNase is one type of nuclease that can hydrolyze phosphodiester bonds between nucleotides. DNase can destroy neutrophil extracellular traps (NETs) by degrading their chromatin. Almost all CPS produce DNase, also known as staphylococcal nuclease (SNase). It is active toward both DNA and RNA. The optimum pH range is between 8.6 and 10.3, and the enzyme activity varies inversely with Ca2+ concentration. SNase also been hypothesized to play a role in disseminating and spreading S. aureus by liquifying pus[24,25].

3.3. Hyaluronidase

Hyaluronic acid is a major component of the mammalian extracellular matrix, which acts as a physical barrier, controlling the migration of both host and invasive cells. Staphylococci produce hyaluronidase to destroy the hyaluronic acid and spread easily through the host's tissues[12,16].

3.4. Staphylokinase

Plasminogen is an inactive form of plasmin, which is secreted from the liver to digest fibrin clots in the bloodstream in a process called "Fibrinolysis". Staphylococci produce staphylokinase during the late exponential phase of the growth cycle, which converts plasminogen into plasmin for fibrinolysis[7].

3.5. Protease

Protease hydrolyses the peptide bonds in proteins and therefore breaks the proteins down into their constituent amino acids. Staphylococcal proteases include; 2 cysteine proteases (staphopain A and staphopain B), one serine protease (V8), and one metalloproteinase (aureolysin). Staphopain A degrades elastin, fibrinogen, and collagen, causing destruction and ulceration of tissue, while staphopain B prevents the interaction of neutrophils and monocytes with macrophages. V8 degrades human immunoglobulins. Aureolysin inactivates the complementary system by cleaving the C3 into imperfect C3b, which is then rapidly degraded by factor H and factor I present in serum. Thus, avoiding phagocytosis and killing by neutrophils[23,26,27].

4. Exotoxins

4.1. Hemolysins

Hemolysins are exotoxins consisting of (lipid and protein), that can destroy red blood cells of different mammals by a process called "Hemolysis". Hemolysins can also destroy other blood cells such as leukocytes, monocytes, lymphocytes, and macrophages, leading to autolysis and death. Staphylococci produce four different types of hemolysins (α, β, γ, and δ).

4.1.1. Alpha Hemolysin

Staphylococcal α-hemolysin lyses RBCs by forming pores on the RBC membrane. These pores are responsible for increasing osmotic phenomena, cell depolarization, and loss of vital molecules. This hemolysis is also called incomplete or partial hemolysis because RBCs are not lysed completely; thus α-hemolysin shows yellowish-green hemolysis on blood agar[28,29].

4.1.2. Beta Hemolysin

The β-hemolysin has a phosphorylase C activity to destroy the RBCs completely, so it causes complete hemolysis. β-hemolysin is an Mg2+ dependent protein and specified for the sphingomyelin and lysophosphatidylcholine[13,30].

4.1.3. Gamma Hemolysin

Almost all S. aureus strains produce γ-hemolysin. This toxin can lyse neutrophils, macrophages, and many types of mammalian RBCs. The effects of γ-hemolysin cannot be observed on blood agar because the agar has an inhibition role on the activity of toxin[9,31].

4.1.4. Delta Hemolysin

Almost 97 % of the S. aureus strains produce δ-hemolysin. δ-hemolysin has a broad cytotoxic activity, like its ability to lyse RBCs and other animal cells; on the other hand, it can

also destroy subcellular structures such as spheroplasts and protoplasts[15,32].

4.2. Panton-Valentine Leukocidin

Leukocidin is one of the staphylococcal toxins, forming pores in host cell membranes and destroying cells. Panton-Valentine Leukocidin (PVL) is the main reason for the necrotic lesions in the skin of humans and many animals[27].

4.3. Exfoliative Toxins

Exfoliative toxins (ETs) are also known as epidermolytic toxins. The staphylococcal exfoliative toxin is the main reason for a highly contagious skin disease known as "Staphylococcal Scalded-Skin Syndrome (SSSS)".

5. Superantigens

5.1. Toxic Shock Syndrome Toxin-1 (TSST-1)

Approximately 25% of S. aureus strains produce Toxic Shock Syndrome Toxin-1 (TEST-1), which causes Toxic Shock Syndrome (TSS). TSST-1 is one of the staphylococcal superantigens, which can stimulate the proliferation of T cells nonspecifically by binding to the MHC-II complex and inducing IL-1 and TNF-α[12,33].

5.2. Staphylococcal Enterotoxins

aureus produces two groups: staphylococcal enterotoxins (SEs) and staphylococcal enterotoxins-like proteins (SE). Both of these enterotoxins are potent gastrointestinal exotoxins, which can cause staphylococcal food poisoning (SFP). The only difference between these two groups is that SEs have an emetic activity while SE s have not. This family of enterotoxins is resistant to conditions such as heat treatment and low pH[34,35].

6. Antimicrobial Resistance

S. aureus is one of the important pathogens that can cause many zoonotic diseases. This etiological pathogen can withstand a wide range of inappropriate conditions. S. aureus has been reported to have the ability to resist most of the available antibiotics[19-21]. It has also been reported that S. aureus strains have genetic diversity in their ability to resist antimicrobial agents, and one of the most widely known strains is methicillin-resistant S. aureus (MRSA). MRSA can tolerate the presence of most β-lactam antimicrobial agents. However, the ability to form biofilms influences the multidrug resistance (MDR) of S. aureus. This diversity in the antimicrobial resistance of S. aureus strains decreases the recovery rate of diseases. In addition, MDR has been reported to be one of the major challenges in bovine mastitis treatment measurements[36,37].

Livestock animals are considered the main potential source of MRSA for humans, as several cases of human MRSA infections have been reported in humans who have been dealing with animals. Moreover, MRSA strains are highly anxious zoonotic pathogens that can threaten human and animal health in recent years[5,18].

The β-lactam agents (Penicillin) are the most commonly used antibiotic group, which kills microorganisms by inhibiting the synthesis of their cell walls. S. aureus produces β-lactamase (Penicillinase), which degrades the β-lactam ring of penicillin[3,32].

Epidemiology

Staphylococci are Gram-positive cocci belonging to the Micrococcaceae family that commonly colonize the skin, respiratory tracts, alimentary tracts, and urogenital tracts of many animals and birds. These microorganisms are opportunistic pathogens that may cause many different contagious diseases in animals and humans. The interest in studying the epidemiology of these microorganisms has been increased in the last years because of the emergence of some strains that have shown resistance to all available antibiotics[28]. Abuse of antibiotics promotes the development of antibiotic resistance of these microorganisms[24].

S. aureus is the main causative agent of mastitis in cattle, sheep, goats, and horses, as well as may cause dermatitis in sheep and goats, botryomycosis in pigs and horses, and suppurative infections in cats and dogs. S. aureus subsp. anaerobius can cause lymphadenitis in sheep[14].

S. intermedius causes various pyogenic diseases in dogs and cats and may also cause some other suppurative infections (endometritis, cystitis, and otitis externa) in this animal species. S. hyicus causes exudative epidermitis and arthritis in pigs, S. schleiferi causes otitis externa in dogs, and S. delphini causes suppurative skin lesions in dolphins[11,19].

Among the coagulase-negative staphylococci, S. chromogenes, S. simulans, S. epidermidis, S. xylosus, and S. caprae are the most important species that have been implicated in bovine mastitis in Turkey[13-16].

Diseases

Mastitis

Mastitis is an inflammation of the mammary glands, threatening the dairy industries and leading to real economic losses. Non-steroidal anti-inflammatory drugs can suppress the inflammatory process.[31] According to the report of the United States Department of Agriculture (USDA) in 2016, clinical mastitis cases had been increased from 13% to 25% between 1996 and 2016.[22] Although mastitis can be caused by a variety of environmental pathogens such as (Enterobacteriaceae, Streptococcus spp., Lactococcus spp., Prototheca spp., and almost all Staphylococcus species), S. aureus remains a challenge for some herds[8,16]. S. aureus can cause clinical, subclinical, acute, or chronic mastitis[1].

Pathogenicity

Staphylococci enter into the mammary gland through the teat channel, followed by bacterial multiplication in the mammary gland and the destruction of the delicate mammary tissues, which stimulates an inflammatory reaction.[21] The destruction of alveolar and ductal cells leads to the accumulation of leukocytes and blockage of the milk ducts, which reduces milk production. The spread of staphylococci within the mammary gland leads to form clumps of abscesses in the udder. These abscesses prevent antibiotics from reaching the bacteria, making the treatment process more difficult[26, 6].

Symptoms

Mastitis is characterized by visible changes, as the infected animals produce clotted, watery, or bloody milk, in addition to decreased milk production. Physical changes may also be seen in the udder of the animal-like (high temperature, rough skin, pain, external swelling, and redness)[20].

S. aureus is involved in acute, chronic, and mild mastitis. In acute mastitis, it appears that the infected animal suffers from high fever, depression, anorexia, losing weight, and sometimes lameness. In some cases, gangrene may occur[5].

Treatment and control

To control staphylococcal mastitis infections, some hygienic procedures must be taken: Using different gloves for each individual cow, using dry disposable towels, examination of teat ends to check for cracks or lesions, infected cows should be milked at last or separately, and milking equipment should be sterilized continuously[30,36].

In addition, vaccination may reduce the incidence of mastitis, as vaccinated animals show a less severe inflammatory reaction compared to unvaccinated animals[29,34].

However, antibiotics are the most common effective agents that can be used to treat mastitis infections. Although antibiotics such as penicillin, streptomycin, tetracycline, erythromycin, novobiocin, and methicillin can be used to treat staphylococcal mastitis infections, some strains are multi-drug-resistant. Dry cow therapy (DCT) is more effective in eliminating infections. In DCT, cows must be milked out completely, and an effective antibiotic injected into the udder using an antibiotic tube (1/8 inch)[11].

Botryomycosis

Botryomycosis is a rare bacterial infection that occurs in equids, cattle, and canines[25]. Botryomycosis is a sporadic disease that may occur in cutaneous and visceral forms. It is characterized by forming fistulous irritations or fibrous tumors, especially in mammary tissues and castration wounds[29]. The first case of botryomycosis was reported in a horse's lung in 1870, and it was believed to be an animal infection. In 1913 Eugene L. Opie reported the first case of human botryomycosis[4].

Pathogenicity

S. aureus is a normal-flora of many animals' skin and nasal cavity. The presence of wounds, dents, or scratches on the skin facilitates the entry of S. aureus into the body and creates an infection, especially in mammary tissues and castration wounds.

Symptoms

Botryomycosis may be dermal or subcutaneous, and the early stages are characterized by forming painless, non-itchy papules. Primary lesions may show draining tracts with granules (1-2 mm diameter). Moreover, chronic cases may involve muscles or bones[29,31].

Treatment and control

Treatment of botryomycosis often involves a combination of both long-term medical (antimicrobial) treatment and surgical resection of the affected tissue. Sulphonamides, cephalosporins, and erythromycin have been reported to be a successful treatment of staphylococcal botryomycosis in horses and following surgical resection of affected tissue[17].

Tick Pyaemia

Pyaemia is a blood poisoning (septicemia) that the spread of bacterial toxins may cause into the bloodstream. Tick pyaemia is septicemia associated with the presence of ticks as a vector. This disease is a pyogenic staphylococcal infection that occurs in lambs less than ten-week-old and is limited to hill-grazing of Britain and Ireland due to the widespread of Ixodes ricinus ticks[14].

Pathogenicity

M'Fadyean first described this disease in 1894; he assumed that the Ixodes ricinus tick may act as a true vector. When the tick feeds on a sheep suffering from pyaemia, it may carry S. aureus in its body and transfer it to another sheep. Tick pyaemia can be acute (septicemic) or chronic (metastatic)[14,17].

Symptoms

In acute cases, sudden death may occur without any symptoms. In chronic cases, infected animals are lame and have warm and painful swelling in their leg joints; death may occur within 4-10 days. Recovered animals may remain lame[5].

Treatment and control

Prophylactic treatment of lambs with antibiotics, such as long-acting tetracycline, can be initiated at one week of age. Tick-control measures such as dipping should be introduced[15].

Poultry diseases

Some Staphylococcus spp. are considered opportunistic bacteria, which can cause several poultry diseases like

synovitis, bumblefoot, and omphalitis under appropriate conditions[3].

a) Synovitis is also known as arthritis, an acute to chronic, systemic disease of chickens. It occurs in the joints, tendons, or bones. S. aureus is believed to be a secondary pathogen of synovitis, and the reovirus is the main causative agent, as S. aureus causes synovitis after septicemia[18].

   Pathogenicity: This disease begins as systemic infection or a local injury followed by cellular infiltration of lymphocytes, plasma cells, and macrophages. The accumulation of these cells leads to the formation of extensive fibrosis in the synovial membranes[28].

   Symptoms: Symptoms include swollen, hot joints with limping and reluctance to walk. Joints contain increased amounts of fluid, tendons and tendon sheaths are inflamed, and bone sections can contain focal areas of necrosis known as osteomyelitis[14].

b) Bumblefoot: It is a debilitating chronic disease mainly caused by S. aureus. Bumblefoot is also known as pododermatitis, which is a common poultry disease in males. It is often caused by injuries that allow contamination of the subcutaneous tissue in the footpad[15].

   Pathogenicity: It begins after the entry of S. aureus into the toes, hocks, and pads of the chicken feet through cuts, scratches, or injuries and creates an abscess full of pus.

   Symptoms: During the early stages of bumblefoot, it may initially appear as a small, superficial lesion, rough abrasion, or mild discoloring of the foot. Infected chickens may often begin to show slight behavioral changes and varying degrees of lameness[33].

   This disease is characterized by a pus-filled abscess covered by a black scab and is paired with lameness, swelling, and the infected bird's reluctance to walk[3].

c) Omphalitis is also called infection of the yolk sac, a common disease caused by S. aureus in young chicks and poultry.

   Pathogenicity: The yolk sac is an enriched source of nutrients and antibodies for chicks. In general, chicks absorb the entire yolk sac just before hatching. However, chicks that cannot absorb the entire yolk sac are less likely to survive. Because the yolk sac is necessary for unhealed navel and open lesions that make chicks more susceptible to bacterial infections[30]. There are two ways for bacterial entry into eggs vertical and horizontal transmission. In vertical transmission, bacteria are introduced from infected reproductive tissues to eggs before shell formation. In horizontal transmission, fecal contamination on the egg usually occurs as bacteria may enter through pores or cracks on the shell of eggs[11].

   Symptoms: Most chicks with a yolk sac infection die within 24 hours of hatching, peaking at 5 to 7 days. Recovered chicks will have a poor immune system, making them more susceptible to infection with other opportunistic pathogens and developing chronic respiratory diseases. The most common signs are the soft and swollen abdomen, wet or open navel, unabsorbed yolk sac, discoloration of the navel, foul odor, weakness, and droopy head[30].

Treatment and control

Staphylococcal infections can be successfully treated with antibiotics. Antibiotics such as penicillin, erythromycin, lincomycin, spectinomycin, cloxacillin, and amikacin can be used to treat staphylococcal infections. Proper management to prevent injury may help to prevent infections. Because wounds are the primary route by which staphylococci can enter the body, it is important to reduce all potential sources of injury to the bird. Good litter management is important in controlling footpad injuries to prevent bumblefoot. Hatchery sanitation and good egg management practices are also important to reduce navel infections and omphalitis[35].

Conclusions

Staphylococcus is a bacterial genus that includes members that can cause many infections in animals as well as humans because members of this genus have various virulence factors that increase their tolerance to different environmental conditions. Thus, the more virulence factors these microorganisms produce, the more pathogenic they are. So CPS is more pathogenic than CNS because of their ability to produce 'coagulase', which increases their pathogenicity by forming a layer of fibrin that protects them from phagocytosis. Moreover, capsulated strains are the most resistant strains. In addition to virulence factors, the antimicrobial resistance ability of some strains reduces the possibility of antibiotic therapy. Therefore, the increase in the number of multidrug-resistant strains of Staphylococcus strongly suggests discontinuation of antibiotic misuses and depending on antimicrobial sensitivity tests to detect the appropriate antibiotic to be used.

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