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Staphylococcus aureus in broiler chickens and its virulence and resistance factors

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ABSTRACT

Staphylococcus aureus is the main cause of poultry *Staphylococcosis*, it is widely spread in the poultry farm environment, including the air, water, sewage, and dust, which usually contain it and they are significant nosocomial pathogens and members of the opportunistic bacteria. Additionally, *Staphylococcal* food poisoning is considered one of the most prevalent food-borne illnesses in the world. It is caused by enterotoxigenic strains of *S. aureus* in food. Broiler chickens may suffer from *S. aureus* infection and its enterotoxins resulting in a major public health hazard and economic losses due to decreased weight gain, mortality, and increased condemnation, so this review aims to summarize and address current knowledge about diseases caused by *S. aureus* in broiler chickens together with understanding the significant virulence and resistance factors which may help in control its occurrence in animal farms and to understand food poising in human

INTRODUCTION:

Staphylococcus aureus is a Gram-positive, non-motile, non-spore-forming, catalase-positive, coccoid bacteria that appears in grape -like clusters in stained smears. It is considered an opportunistic commensal organism of animals and the most pathogenic species of the genus *Staphylococcus* **(Quinn and Markey. 2003)**. It normally occurs on the skin and internal organs and is commonly associated with infection of skin, bones, joints, and nerves. A key factor in the development of various avian illnesses, including omphalitis, arthritis, *Staphylococcal* septicemia, synovitis, and yolk sac infections **(Smyth and McNamee. 2001).**

Transmission occurs via skin wounds, minor surgical procedures (like beak, toe, or comb trimming), vaccine injection, and compromised intestinal mucosa can introduce *Staphylococcus* to local tissue or into the bloodstream. Infection can also occur in the

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hatchery as a result of contamination of an open navel. Once in the bloodstream, *Staphylococcus* can produce systemic disease or localized lesions in tissues. *Staphylococcus aureus* can invade the metaphyseal area of joints, leading to arthritis and osteomyelitis **(Yuko Sato and Mohamed El-Gazzar. 2022).**

The isolation sites of *S. aureus* were mostly from the proximal femur, proximal tibiotarsus, tendon sheaths, hock joints, pododermatitis lesions, heart, and liver **(Andreasen. 2020).**

There is a significant death rate in broilers with swollen joints, gaseous exudates, damaged cartilage, and thickened synovial membranes with inflammatory cell infiltration **(Gu et al. 2013).**

Most *Staphylococcus* species are pathogenic and capable of producing toxins that result in health problems for both humans and animals, among them *S. aureus* produces the most toxins **(Fetsch and Johler. 2018)**.

Enterotoxin-producing *S. aureus* is the most common cause of food-borne human illness throughout the world **(Do Carmo et al. 2004).**

Prevalence of *S. aureus* in chickens:

Live birds are considered a significant reservoir for *S. aureus* strains from apparently healthy and diseased chickens **(Mamza et al. 2010)**. Also **(Suleiman et al. 2013)** found coagulase-positive *S. aureus* in 54% of apparently healthy chicken samples. **Ali et al. (2017)** found that the isolation rate of *S. aureus* from broilers was 90% of nasal and cloacal swabs. **Benrabia et al. (2020)**reported that the prevalence of *S. aureus* from nasal swab samples in broilers was 48.4%. Moreover **(Abd El-Tawab et al. 2017** and **Amen et al. 2019)** recovered *S. aureus* from 66% and 74.07% of the tested broiler chickens, respectively.

Virulence and Resistance Factors:

Staphylococcus aureus strains can grow between 15 and 45 °C in the presence of sodium chloride concentrations 10% **(Behling et al. 2010).** *Staphylococci* have a wide range of virulence factors **(Wright and Nair. 2010).**

Staphylococci produce a variety of toxins and exoenzymes that can harm host tissues and interfere with the immune system **(Gordon and Lowy. 2008)**. Several virulence factors are produced: (1) Surface proteins that aid in tissue colonization. (2) Invasion-related bacterial spread in tissues (hyaluronidase, kinases and leukocidin). (3) Surface components (capsule, Protein A) that inhibit phagocytic engulfment. (4) Catalase synthesis and carotenoids are two biochemical traits that help phagocytes survive. (5) Immunological obscures (Protein A, coagulase, coagulation factor). (6) Membrane-damaging toxins (hemolysins, leukotoxin, leukocidin) that lyse eukaryotic cell membranes. (7) Exotoxins (SEA-G, TSST, and ET) that cause host tissue destruction or other illness signs. (8) Both inherited and acquired antimicrobial agent resistance **(Toder. 2005).**

Another classification according to **Diep and Otto. (2008)** who reported that *S. aureus* virulence genes can be divided into two groups: group coding for exotoxins (secreted) and group coding for cell-surface-associated (adhesion).

A superfamily of about 23 low-molecular-weight pyrogenic exotoxins with similar structural and functional characteristics is known as *Staphylococcal* enterotoxins (SEs). According to their capacity to cause emesis, *Staphylococcal* enterotoxins can be divided into two groups: classical SEs (A to E) and newly confirmed enterotoxigenic-like proteins. By activating T cells and causing them to produce inflammatory cytokines, *Staphylococcal* enterotoxins have strong super antigenic activity and compromise adaptive immunity **(Fisher et al. 2018).** According to **Argudin et al. (2010),** SEs and SEIs can be further categorized into classic (SEA to SEE) and new (SEG to SEIU2).

Important cell-surface proteins on *S. aureus* play a role in the bacterium's pathogenicity and ability to adhere to host cells. These proteins include clumping factors A and B (clfA and clfB genes) and an elastin-binding protein (**Momtaz et al. 2013)** .Clumping factor A

(CFA) is a surface protein of *S. aureus* that binds to fibrinogen and acts as a virulence factor in certain infections by blocking phagocytosis and enhancing adherence to fibrin and fibrinogen **(Higgins et al. 2006).**

One of *Staphylococcus'* most potent pathogenic genes, is hemolysin (hlg gene). **Gundogan et al. (2013)** reported it as a crucial virulence factor that has a strong toxic effect on lymphocytes, macrophages, neutrophils, epithelial cells, fibroblasts, and other cell lineages, which is responsible for facilitating the formation of pores in red blood cells following the binding of the active proteins hlgA and hlgB.

The protein A gene, known as spa, is primarily employed to type *S.aureus*. Another illustration of a gene is the coagulase (coa) gene, which is a virulence gene of *S. aureus* considered significant because it forms an alliance with other genes that allows it to persist inside host cells and invade immune system cells in the host **(Balaban and Rasooly. 2000).** It is also a virulence marker of *Staphylococcus* which aids in the formation of fibrin around *Staphylococcal* abscesses, which promotes localized infection and guards against phagocytosis **(Sawai et al. 1997).**

In most cases, virulence genes are linked to *Staphyloccocal* infections. The initial stages of the infections are believed to include bacterial adherence. clf, fnb A, and a can according to **Arciola et al. (2005),** *Staphylococcal* adhesions A were the most significant.

Staphylococcus aureus strains that have the bla gene produce β-Lactamase enzyme which deactivates β-lactam antibiotics through cleavage with the β-lactam ring **(Kiliç and Çirak. 2006).** *Staphylococcus aureus* strains have resistance to β-Lactam antimicrobials, including cephalosporins and carbapenems (penicillin, oxacillin, cloxacillin, methicillin, flucloxacillin, and dicloxacillin) antibiotics due to a plasmid-encoded penicillinase/β-lactamase **(Watkins et al. 2019).**

Delorme et al. (2009) reported resistance of *S. aureus* isolates to other classes of antimicrobials, such as fluoroquinolones, aminoglycosides, tetracyclines, and macrolides especially those from broiler chicken origin, while 100% resistance to tetracycline, penicillin and erythromycin was reported by **Otalu et al. (2011)** of *S. aureus* isolates from live and slaughtered chickens.

Twenty different types of *Staphylococcal* enterotoxin were found including SEA through SEE, SEG through SER, and SEU. But only a small number of the *Staphylococcal* enterotoxin serotypes are regularly linked to outbreaks of food poisoning, since *S. aureus* does not produce enterotoxins in all strains, the enterotoxin genes are accessory genetic components. They are coded by plasmids, phages, and pathogenicity islands, among other mobile genetic components (**Martin et al. 2004).**

Mahmoud et al. (2018) found that *S. aureus* enterotoxins from chicken samples were (12.5%) type A, (6.25%) was type C, (6.25%) type A with B and in finally type B together with D was (6.25%) also they reported that 68.75% of the isolates without any enterotoxins secretion, while results obtained by **Harvey et al. (1982)** was different than enterotoxin type A was (2.74%), enterotoxin type D was (14.81%) and *Staphylococcal* enterotoxin C+D was (1.23%), but **Britta et al. (2016)** found that enterotoxin type A was (3.1%) and (25%) for each of the enterotoxins types G, I, M, N, O, and U.

Methicillin-resistant *S. aureus* (MRSA) is recognized as one of the most important kinds of resistant *S. aureus* since it is the cause of acquired infections linked to a high risk of bacterial death globally **(Tiemersma et al. 2004).**

***Staphylococcus aureus* Enterotoxins (SEs):**

SEs are 20–30 kDa released toxins that disrupt intestinal activity and induce *Staphylococcal* food poisoning (SFP), which is characterized by nausea, vomiting, abdominal pain, and diarrhea without indications of toxic effects, such as fever or hypotension, based on antigenic heterogeneity, more than 20 SEs (SEA—SElV) have been determined **(Hennekinne et al. 2012).** Clinical indications of SFP have been connected to inflammatory mediators in-

cluding leukotriene B4 and prostaglandin E2, both of which are produced in response to SEs, even though the receptors implicated in the emetic response to SEs have not yet been identified (**Pezato et al. 2012).**

Staphylococcal enterotoxin B (SEB) is associated with food poisoning, it has been studied for potential use as an inhaled biological weapon **(Pinchuk et al. 2010).**

***S. aureus* Toxic Shock Syndrome Toxin 1 (TSST-1):**

Unlike SEs, TSST-1 (22-kD) induces the production of a significant amount of pro-inflammatory cytokines from the host T-cells and macrophages but does not cause emesis **(Stach et al. 2014).** Toxic shock syndrome (TSS) symptoms such as high temperature, rash, desquamation, hypotension, and hypovolemic shock are brought on by this cytokine outburst, and they can lead to multiorgan failure **(McCormick et al. 2001).**

***S. aureus* in humans:**

S. aureus can produce as many as 25 different toxins causing severe food poisoning, toxins of *S. aureus* that present in human food after ingestion will be absorbed into the blood from the digestive tract, resulting in nausea, emesis, abdominal cramps, and diarrhea **(Ortega et al. 2010).** Symptoms varied according to individual susceptibility and the amount of enterotoxin ingested **(Do carmo et al. 2004).** Sometimes, severe symptoms occur which require hospitalization and can end in death in some cases **(Martin et al. 2004).** The concentration of *S. aureus* ranges from 10^6 to 10^8CFU/g in ingested food samples needed to induce food poisoning, and for sensitive persons even 10^5 CFU/g can produce enough amount SEs (around 1µ /g) to cause symptoms of food poisoning **(Alarcon et al. 2006).** According to **Nagarajappa et al. (2012),** SEs are highly thermostable; heat treatment, such as regular cooking, cannot completely inactivate them. They therefore resist thermal treatment and result in food poisoning. Outbreaks when the offending food had previously undergone heat treatment were brought on by enterotoxin in food **(Asao et al. 2003).** Some of the characteristics of SEs that lead to food poisoning include super antigenic activity, stimulation of T-cell proliferation, enhancement of endotoxic shock, suppression of immunoglobulin synthesis, and pyrogenicity **(Le loir et al. 2003).**

Recent reports of *S. aureus* food-borne illness outbreaks have been mentioned by **(Le et al. 2021)** The presence of thermostable enterotoxins of *S. aureus* in contaminated chicken meat products may cause *Staphylococcal* food poisoning in humans **(Balaban and Rasooly. 2000).** According to Larsen **et al. (2000),** infections such as gastroenteritis, heat shock-like syndrome, skin infections, lung infections, urinary tract infections, and immune-mediated disorders might occur due to enterotoxins of *S. aureus*. Also **(Fisher et al. 2018)** reported that *Staphylococcal* food poisoning (SFP) is associated with toxic shock syndrome (TSS), sepsis-related illnesses, and pneumonia.

Prevention and control:

According to **Wideman et al. (2015)** and **Andreasen. (2020),** therapeutic antimicrobial administrations can lower the prevalence of *Staphylococcal* infections, but **(McNamee and Smyth. 2000)** found that antimicrobial therapy is not appropriate to be a long-term solution to the issue due to the large number of *Staphylococci* strains that exhibit resistance to a variety of antimicrobial agents. In addition to complicating matters sick and lame birds frequently experience depression, exhibit a lack of appetite, and have trouble accessing food and water. They are less likely to receive the prescribed medication. However, bumblefoot (pododermatitis) caused by *Staphylococcus* infection when treated with antibiotics frequently leads to clinical improvement in the diseased birds, particularly when coupled with bettering the rearing environment. Birds with bumble foot have been successfully treated with levofloxacin **(Youssef et al. 2019)** and minocycline **(Satterfield and O'Rourke. 1981).**

Vaccination against *S. aureus* has been developed over many years, with some encouraging outcomes, for both humans and livestock. But to date, no such vaccination is available **(Chang et al. 2008; Proctor. 2012, Miller**

et al. 2020). Despite continued work throughout the previous years till now no licensed vaccines against *Staphylococcosis* in poultry **(Kaul et al. 2001 and El-Maghraby et al. 2020).** The effectiveness of the *S. aureus* vaccine against one disease may be lost against another since *Staphylococci* cause a variety of illness forms. Also, the development of vaccines is considered a challenge due to the genetic diversity of *S. aureus* isolates and the presence of virulence factors.

Antibiotic alternatives such as probiotics prevent *Staphylococcal* infections by reducing the amount of *Staphylococci* that enter the bloodstream through the intestinal epithelium **(Wideman et al. 2015).**

CONCLUSION:

Management of *Staphylococcal* infections is challenging. *Staphylococci* are widespread in the environment of chicken farms causing different diseases such as omphalitis, arthritis, septicemia, and synovitis. Also, *Staphylococcal* food poisoning (SFP) is a common illness that results from the presence of different types of enterotoxins (for example: type A, B, C, D, and E) which are widely affected by several factors including misdiagnosis, underreported mild outbreaks, incorrect sample collection, and improper laboratory investigations leading to social and economic importance. The presence of a wide range of virulence and resistance factors together with antibiotic resistance was reported for *S. aureus* strains. Access to genome-based technologies like using PCR to identify these factors has great importance to control the infection and minimize its economic effect.

REFERENCE

Abd El Tawab A, Fatma IH, Sahar RM, Sohila HA. 2017. Characterization of Methicillin Resistance *Staphylococcus aureus* isolated from chicken and human. Benha Univ. Med. J. 32 (1): 132- 137.

Alarcon B, Vicedo B, Aznar R. 2006. PCR-based procedures for detection and quantification of *Staphylococcus aureus* and their application in food: article. Journal of Applied Microbiology, (100):352–364.

Ali Y, Islam MA, Muzahid NH, Faruk SM, Hossain MA Marzan LW. 2017. Characterization, prevalence and antibiogram study of *Staphylococcus aureus* in poultry. Asian Pacific Journal of Tropical Biomedicine, 7 (3): 253-256.

Amen O, Hussein AG, Sayed AM, Ibrahim RS. 2019. Detection of antibiotics resistance genes in Staphylococcus aureus isolated from poultry farms. Assiut Vet. Med. J. Vol. 65 No. 163 October 2019, 1-9.

Andreasen CB. 2020. *Staphylococcosis.* In: Swayne DE, editor. *Diseases of poultry.* 14th ed. Hoboken (NJ): John Wiley & Sons, Ltd; p. 995–1003.

Arciola CR, Compoccia D, Gamberini S, Baldassarri L. 2005. Prevalenc of cna, fnb A and fnb B adhesion genes among *S. aureus* is dates fromorthopedic infections associated to different types of implant. FEMS Microbial. Lett, (246):81 – 86.

Argudín MA, Mendoza MC, Rodicio MR. 2010. Food poisoning and *Staphylococcus aureus* enterotoxins. Toxins, (2): 1751-1773.

Asao T, Kumeda Y, Kawai T, Shibata T, Oda H, Haruki K, Nakazawa H, Kozaki S. 2003. An extensive outbreak of *Staphylococcal* food poisoning due to low-fat milk in Japan: estimation of enterotoxin A in the incriminated milk and powdered skim milk. Epidemiol. Infect., 130(1): 33- 40.

Balaban N, Rasooly A. 2000. '*Staphylococcal* enterotoxins', *International Journal of Food Microbiology* 61, 1–10. 10.1016/S0168-1605(00)00377-9.

Behling RG, Eifert J, Erickson MC, Gurtler JB, Kornacki JL, Line E, Radcliff R, Ryser ET, Stawich B, Van Z. 2010. selected pathogens of concern to industrial food processors: Infectious, toxigenic, toxico-infectious, selected emerging pathogenic bacteria. In: Kornacki, J., editor. Principles of Microbiological Troubleshooting in the Industrial Food Processing Environment.

Food Microbiology and Food Safety. Springer, New York.

Benrabia I, Hamdi TM, Shehata AA, Neubauer H, Wareth G. 2020. Methicillin-resistant *Staphylococcus aureus* (MRSA) in poultry species in Algeria: long-term study on prevalence and antimicrobial resistance. Vet Sci. 7(2):54.

Britta K, Britta B, Daniel L, Bernd-Alois T, Annemarie K, Alexandra F. 2016. Antimicrobial resistances and virulence markers in Methicillinresistant *Staphylococcus aureus* from broiler and turkey: A molecular view from farm to fork: research, (200): 25 - 32.

Chang BS, Moon JS, Kang HM, Kim YI, Lee HK, Kim JD, Lee BS, Koo HC, Park YH. 2008. Protective effects of recombinant *Staphylococcal* enterotoxin type C mutant vaccine against experimental bovine infection by a strain of *Staphylococcus aureus* isolated from subclinical mastitis in dairy cattle. *Vaccine*. 26(17):2081–2091.

Delorme T, Rose S, Senita J, Callahan C, Nasr P. 2009. Epidemiology and susceptibilities of methicillin-resistant *Staphylococcus aureus* in Northeastern Ohio. Am. J. Clin. Pathol., 132(5): 668-677.

Diep BA, Otto M. 2008. 'The role of virulence determinants in community-associated MRSA pathogenesis', *Trends in Microbiology* 16(8): 361–369. 10.1016/j. tim. 2008.05.002.

Do Carmo LSC, Cummings VR, Linardi RS, Dias JM, De Suoza MJ, De Sena DA, Dos Santos JW, Shupp RK, Pereira, Jett M. 2004. A cause of massive *Staphylococcal* food poisoning incident. Foodborne Pathog. Dis. 1:241-246, PMID: 15992286 DOI: 10.1089/fpd.1.241.

El-Maghraby A, Aziz S, Mwafy A. 2020. Efficacy of *Staphylococcus aureus* vaccine in chicken. *J World's Poultry Res*. 10(2s):203–213.

Fetsch A and Johler S. (2018). *Staphylococcus aureus as a foodborne pathogen.* Current Clinical Microbiology Reports (5):88-96. https://link.springer.com/journal/40588/volumes-and-issues/5-2. Food Prot. 52**:**267–282.

Fisher EL, Otto M, Cheung GYC. 2018. Basis of virulence in enterotoxin-mediated *Staphylococcal* food poisoning. *Front. Microbiol.* 9, 436. doi: 10.3389/fmicb.2018.00436.

Gordon RJ, Lowy FD. 2008. Pathogenesis of methicillin-resistant *Staphylococcus aureus* infection. Clin Infect Dis. 46(S5):S350–S359.

Gu CQ, Hu XY, Xie Cq, Zhang WP, Wang DH, Zhou Q, Cheng GF. 2013. Observation on arthritis in broiler breeder chickens experimentally infected with *Staphylococcus aureus*. Mortality, 100: 10.

Gundogan N, Ataol O, Torlak FO. 2013. Determination of some virulence factors in *Staphylococcus aureus*, *Enterococcus faecalis* and *Enterococcus faecium* isolated from meat and milk products. J Food Safety (33):387–393.

Harvey J, Patterson JT, Gibbs PA. 1982. Enterotoxigenicity of *Staphylococcus aureus* strains isolated from poultry: raw poultry carcasses as a potential food-poisoning hazard. Journal of Applied Bacteriology, (52):251-258.

Hennekinne JA, De Buyser ML, Dragacci S. 2012. *Staphylococcus aureus* and Its Food Poisoning Toxins: Characterization and Outbreak Investigation. FEMS Microbiol. Rev. (36): 815–836.

Higgins J, Loughman A, Van Kessel PM, Foster JT. 2006. Clumping factor A of *Staphylococcus aureus* in habits phagocytosis by human polymorphnuclear leucocytes. FEMS Microbial Litt –(258): 290-296.

Kaul MK, Tanwani SK, Sharda R. 2001. Preliminary studies on bacterin against gangrenous dermatitis. *Indian Vet J*. (78):282–285.

Kiliç E, Çirak MY. 2006. Comparison of *Staphylococcal* beta-lactamase detection methods. FABAD J. Pharm. Sci., 31(2): 79 -84.

Larsen HD, Sloth KH, Elsberg C. 2000. 'The dynamics of *Staphylococcus aureus* intramammary infection in nine Danish dairy herds', *Veterinary Microbiology* 71(1–2):89–101.

Le HHT, Dalsgaard A, Andersen PS, Nguyen HM, Ta YT, Nguyen TT. 2021. Large-Scale *Staphylococcus aureus* foodborne disease poisoning outbreak among primary school children. *Microbiol. Res.* (12): 43–52. doi: 10.3390/ microbiolres12010005.

Le Loir Y, Baron F, Gautier M. 2003. *Staphylococcus aureus* and Food Poisoning: article. Genet. Mol. Res., (2): 63-76.

Mahmoud SS, Nahla AA, Sherif RA. 2018. Incidence and characterization of *S. aureus* in broiler carcasses. Benha Veterinary Medical Journal, V (34):191-200.

Mamza SA, Egwu GO, Mshelia GD. 2010. Antibiotic susceptibility patterns of beta-lactamase-producing *Escherichia coli* and *Staphylococcus aureus* isolated from chickens in Maiduguri (Arid zone), Nigeria. Vet. Arch., 80(2): 283-297.

Martin MC, Fueyo JM, Gonzalez-Hevia MA, Mendoza MC. 2004. Genetic procedures for identification of enterotoxigenic strains of *Staphylococcus aureus* from three food poisoning outbreaks. Int J Food Microbiol 94(3):279–286.

McCormick JK, Yarwood JM, Schlievert PM. 2001. Toxic Shock Syndrome and Bacterial Superantigens: An Update. Annu. Rev. Microbiol. (55):77–104.

McNamee PT, Smyth JA. 2000. Bacterial chondronecrosis with osteomyelitis ('femoral head necrosis') of broiler chickens: a review. *Avian Pathol.* 29(4):253–270.

Miller LS, Fowler VG, Shukla SK, Rose WE, Proctor RA. 2020. Development of a vaccine against *Staphylococcus aureus* invasive infections: evidence based on human immunity, genetics and bacterial evasion mechanisms. *FEMS Microbiol Rev.* 44(1):123–153.

Momtaz H, Dehkordi FS, Rahimi E, Asgarifar A, Momeni M. 2013. Virulence genes and antimicrobial resistance profiles of *Staphylococcus aureus* isolated from chicken meat in Isfahan province, Iran. J. Appl. Poult. Res., 22(4): 913-921.

Nagarajappa S, Thakur MS, Manonmani HK. 2012. Detection of enterotoxigenic *Staphylococci* by loop-mediated isothermal amplification method. J. Food. Safety, (32): 59-65.

Ortega E, Abriouel H, Lucas R, Gálvez A. 2010. Multiple roles of *Staphylococcus aureus* enterotoxins: pathogenicity, superanti-genic activity, and correlation to antibiotic resistance. Toxins (2):2117–2131.

Otalu OJ, Kabir J, Okolocha EC, Umoh VJ. 2011. Multi-drug resistant coagulase-positive *Staphylococcus aureus* from live and slaughtered chickens in Zaria, Nigeria. Int. J. Poult. Sci., 10(11): 871-875.

Pezato R, S´wierczyn´ ska-Kre¸pa M, Niz˙ankowska-Mogilnicka E, Derycke L, Bachert C, Pérez-Novo CA. 2012. Role of Imbalance of Eicosanoid Pathways and *Staphylococcal* Superantigens in Chronic Rhinosinusitis. Allergy. (67): 1347–1356.

Pinchuk IV, Beswick EJ, Reyes VE. 2010. *Staphylococcal* Enterotoxins. Toxins, (2): 2177–2197.

Proctor RA. 2012. Challenges for a universal *Staphylococcus aureus* vaccine. *Clin Infect Dis.* 54(8):1179–1186.

Quinn PJ, Markey BK. 2003. *Concise review of veterinary microbiology,* 2nd edn, Blackwell Publishing Limited, Oxford.

Satterfield WC, O'Rourke KI. 1981. *Staphylococcal* bumble foot: vaccination and immunomodulation in the early treatment and management. *J Zoo Anim Med.* 12(3):95–98.

Sawai T, Tomono K, Yanagihara K, Yamamato Y, Kaku M, Hirakata Y, Koga H, Tashiro T, Kohno S. 1997. Role of coagulase in a murine model of hematogenous pulmonary infection induced by intravenous

injection of *Staphylococcus aureus* enmeshed in agar beads. Infect. Immun., 65 (2): 466-471.

Smyth JA, McNamee PT. 2001. '*Staphylococci, Streptococci* and Enterococci', in Jordan F., Pattison M., Alexander D. & Faragher T. (eds.), *Poultry diseases*, 6th edn, 191–199, Elsevier, Amsterdam.

Stach CS, Herrera A, Schlievert PM. 2014. *Staphylococcal* Superantigens Interact with Multiple Host Receptors to Cause Serious Diseases. Immunol. Res. (59): 177–181.

Suleiman A, Zaria LT, Grema HA, Ahmadu P. (2013). Antimicrobial-resistant coagulase-positive *Staphylococcus aureus* from chickens in Maiduguri, Nigeria. Sokoto J. Vet. Sci., 11(1): 51-55.

Tiemersma EW, Bronzwaer SL, Lyytikäinen O, Degener JE, Schrijnemakers P, Bruinsma N. 2004. 'Methicillin-resistant *Staphylococcus aureus* in Europe, 1999–2002', *Emerging Infectious Diseases* (10): 1627–1634.

Toder K. 2005. *Staphylococcus* :toder's online textbook of bacteriology, Veterinary Sciences; 11(1):51-55.

Watkins RR, Holubar M, David MZ. 2019. Antimicrobial resistance in methicillin-resistant *Staphylococcus aureus* to newer antimicrobial agents. Antimicrob. Agents Chemother., 63(12): e01216-19.

Wideman RF, Al-Rubaye A, Kwon YM, Blankenship J, Lester H, Mitchell KN, Pevzner IY, Lohrmann T, Schleifer J. 2015. Prophylactic administration of a combined prebiotic and probiotic, or therapeutic administration of enrofloxacin, to reduce the incidence of bacterial chondronecrosis with osteomyelitis in broilers. *Poult Sci*. 94(1):25–36.

Wright JA, Nair SP. 2010. Interaction of *Staphylococci* with bone. Int J Med Microbiol. 300(2–3):193–204.

Youssef F, Soliman AA, Ibrahim G, Saleh H. 2019. Advanced bacteriological studies on bumblefoot infections in broiler chicken with some clinicopathological alteration. *Vet Sci Res*. 1(1).

Yuko Sato and Mohamed El-Gazzar. 2022. *Staphylococcosis* in Poultry. MSD vetrenaty manual.