

***Staphylococcus aureus* mastitis**

Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTTOOLS group of experts on *Staphylococcus aureus* (*S. aureus*) infections of the mammary gland. They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details are available on the web site at <http://www.discontools.eu/> and can be downloaded by selecting Disease Database, then the specific disease and highlighting the variables of interest. This is completed by selecting “create a report” which can then be downloaded as either a PDF or Excel spread sheet.

Disease profile

2. *S. aureus* causes a variety of diseases in man and animals. Mastitis is the main disease caused in ruminants, including cows, sheep, goats, camels and water buffalo. Many other animal species can be affected including horses, pigs, dogs, cats, rabbits and poultry. Asymptomatic carriage is also observed in most species. In dairy cows, ewes and goats the most economically important condition caused by *S. aureus* is a contagious mastitis. The pathogen is primarily transmitted during the milking process as the bacteria are spread to uninfected quarters by teat cup liners, milkers' hands, wash cloths, and flies (fomites). Most infections in dairy cattle are subclinical and chronic, persisting frequently over the ongoing lactation and possibly the following lactations, with more or less clinical flare-up. Severe forms are more frequent in goats and ewes than in cows.

3. The main reservoir in herds is constituted by infected mammary glands and skin/mucosae, but *S. aureus* can survive for some time in the environment (milking equipment and facilities). Strains of human origin are known to survive for weeks on fabrics and plastics. Different *S. aureus* strains infect humans, cows, sheep, poultry, and pigs. There is considerable genetic and gene content diversity within the species. Cow and sheep specific clones of *S. aureus* exist which indicates host-specialization. In a given herd, mastitis isolates often belong to a dominant type or clone.

Risk

4. Direct mortality in bovine dairy herds is low but the indirect loss resulting in premature culling due to *S. aureus* incurable mastitis can be high in problem herds. Direct mortality can be high in heifers, ewes and goats due to peracute (gangrenous) mastitis. *S. aureus* is a major pathogen for human beings where it can cause a variety of pathologies.

5. Human infection caused by bovine-specialized clones is rare as most strains of ruminant origin are not well-equipped to induce disease in humans. There is a need for continued epidemiological surveillance for emergence of strains common to both ruminants and humans. The flow of strains from humans to cows and the potential for cows/milk as a source of zoonotic infection need additional investigation. Yet, a few isolates from bovine mastitis are related to methicillin-resistant *S. aureus* (MRSA) human strains, and exchange of genetic mobile elements between human and bovine strains is likely. The fact that coagulase negative staphylococci (the most common bacteria isolated from milk) frequently carry antimicrobial resistance genes, such as *mecA*, that can potentially transmit to *S. aureus* is also of concern and surveillance of mastitis pathogens for antimicrobial resistance genes seems prudent.

Diagnostics

6. Currently diagnosis of inflammation is routinely performed by determining the concentration of cells in milk samples but this is not specific for *S. aureus* mastitis. Etiological diagnosis is currently by bacteriological analysis of aseptically taken milk samples from individual mammary glands. The risk of contamination during sampling, phases of low shedding and time to get result are impediments to bacteriological diagnosis. A rapid, cow side or in-line pathogen specific

diagnostic kit would allow timely implementation of pathogen-oriented treatment. Diagnostics would need to be both sensitive and specific to avoid false-negative and, more importantly, false positive diagnoses.

7. Specific polymerase chain reaction (PCR) can be used to identify bacterial DNA in aseptically taken milk samples. Tests based on bacterial nucleic acids detection and quantification show promise and deserve research and development. Quantitative PCR-based commercial reagent kits for detection of mastitis-causing pathogen are available but a rapid, specific cow-side screening test is not currently available. The application of newer diagnostic methods such as PCR may allow the development of improved diagnostics but the biggest hurdle to development of a new diagnostics is cost, and the need for definite interpretation rules.

Vaccines

8. Vaccines based on killed bacterins are currently approved in both the EU and US. Their efficacy is either limited or variable or in need of large scale field evaluation. Numerous attempts to induce protection with subunit vaccines have been carried out or are on-going, so far without convincing results. Current vaccines primarily stimulate humoral immunity but the level of opsonising antibody in milk is poor. These vaccines show some efficacy in decreasing the clinical severity of mastitis, but reduce the rate of new infection by 15-25%.only. Since the mammary gland is the predominant reservoir for contagious transmission, there is a need for a vaccine that prevents intramammary infection or accelerates cure after infection, or which contributes to increasing treatment efficiency. None of the vaccines studied to date have achieved these goals. Most vaccines rely on humoral immunity and humoral immunity may not be sufficient since many hosts already possess a repertoire of anti-staphylococcal antibodies at the onset of infection. Identification of protective immune mechanisms and correlate of protection is necessary. There is a need for effective vaccines but also for a good definition of effectiveness for mastitis vaccines.

Pharmaceuticals

9. Numerous products are marketed and both lactating and dry cow therapies are widely available. Antibiotic therapy during lactation may improve the clinical condition but usually does not eliminate infection. Dry-cow therapy is considered the most effective, but may also be unsuccessful, especially for long lasting infections. In vitro antimicrobial resistance of mastitis-causing strains is not the main reason of failure, and does not appear to be on the rise. Access of antimicrobials to infection foci including intracellular bacteria, and growth phase of staphylococci may contribute to this in vivo resistance. Chronic infections become more and more difficult to cure as time passes. Late diagnosis of infection, late onset of treatment, and short duration of therapy contribute to poor treatment outcomes. Standard commercial treatment is limited to 2-3 days whereas several scientific studies have shown that cure rates are higher with 5-8 day treatment.

10. Improved therapies that utilize flexible treatments that are pathogen dependent will be needed in the future. The use of improved diagnostics and vaccines will help to maximize treatment efficacy. The use of peptide antimicrobials may offer the option of no withdrawal times, blanket fresh cow therapy and heifer treatments. Novel antimicrobial compounds that act intracellularly are under development. Narrow spectrum antibacterials that are not considered critical for human use are needed.

Knowledge

11. There are many significant areas of uncertainty in the knowledge about *S. aureus* infections especially in relation to genetics, pathogenesis, immunology, vaccinology, epidemiology and control. Research is needed to fill these knowledge gaps as many of these are closely linked to the research requirements to develop more effective tools for the control of the disease. Full details of the gaps are shown in the Disease and Product Analysis for *S.aureus* on the DISCONTTOOLS web site.

Conclusions

12. *S. aureus* is a multifaceted pathogen which has the potential to express a myriad of virulence factors and is fully capable of evading immune surveillance and treatment compounds. These complexities are illustrated by the lack of efficacy of currently available vaccines and antimicrobial treatments. To effectively combat this disease a multifaceted approach must be taken. Control measures aimed at preventing *S. aureus* from entering the teat canal, namely milking time hygiene, has reduced the prevalence of this disease on many modern farms, yet the disease is still prevalent worldwide.