RESOURCES MILK MONEY

Evaluating the Effectiveness of Mastitis Vaccines

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Introduction

Mastitis control is based upon adoption of preventive control strategies including good milking hygiene, the use of properly functioning milking equipment, provision of clean and dry housing areas, sound nutritional programs and proper identification and treatment of cows that are infected with subclinical and clinical mastitis. Worldwide, many dairy farmers have adopted these procedures and produce high quality milk. However, mastitis remains the most common and costly disease of dairy cattle and many producers continue to struggle to achieve their quality goals.

Mastitis results when pathogenic bacteria are able to gain entrance to the udder, overcome the cows' immune defenses, establish an infection and produce inflammation of udder secretory tissue.

The use of vaccination to control infectious diseases in dairy cattle is common and vaccination against mastitis pathogens is a control strategy used by some dairy farmers. Research on mastitis vaccines has been conducted for at least 30 years and several mastitis vaccines are commercially available.

The objective of this paper is to review current concepts about vaccines used to control mastitis in dairy cattle.

Mastitis Vaccines

Commercial mastitis vaccines are currently available in the United States for immunization against mastitis caused by *Staphylococcus aureus* and *E. coli*. There are two *Staph aureus* bacterins marketed to U.S. dairy producers but they are simply separate licensures of the same product.

The vaccines are marketed as Somato-Staph® and Lysigin® and are labeled as somatic antigen containing phage types I, II, III, IV and miscellaneous groups of *Staph aureus*. There are three coliform mastitis vaccines marketed but two of the products are identical. The two identical coliform bacterins are marketed as J-5 Bacterin and Mastiguard.™ A separate bacterin-toxoid (J Vac®) is also available. A 4th gram negative mastitis vaccine (Endovac-Bovi®) contains re-17 mutant Salmonella typhimurium bacterin toxoid. All coliform mastitis vaccine formulations use gram-negative core antigens to produce non-specific immunity directed against endotoxic disease.

Effective immunization against mastitis has been a goal of mastitis researchers for many years. Several authors have reviewed the problems associated with vaccination against mastitis.[2,11,18] The nature of the disease creates a number of unique challenges for the production of successful immunity against mastitis.[18] Mastitis is defined as inflammation of the mammary gland, yet the purpose of vac-

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cination is to enhance the immune response. In the case of mastitis, an enhanced immune response is not always considered beneficial.

One component of the immune response is the migration of large numbers of white blood cells (in the udder called somatic cells) to the infected gland. The presence of somatic cells in the milk is not considered a positive outcome as somatic cells are evidence of mastitis and reduce milk quality. Effective immunization is difficult because of the very nature of milk.[18]

The volume of milk present in the gland dilutes the number of immune cells available to fight infection and milk components such as fat and casein reduce the bactericidal abilities of the infection- fighting immune cells. Additionally, the cow is exposed to numerous organisms that have the potential to cause mastitis and milk is an excellent substrate for bacterial growth.

The definition of a successful mastitis vaccine may vary depending upon the herd situation. Farmers may expect mastitis vaccines to reduce the severity and frequency of mastitis, prevent new infections and eliminate existing infections.[18] While these expectations seem reasonable, it is unlikely that any one vaccine will be able to achieve all of these outcomes. Furthermore, the evaluation of mastitis vaccines is complicated by the underlying biology of the various mastitis pathogens.

One of the most frustrating mastitis pathogens is *Staph aureus*. This organism is a highly successful mastitis pathogen in that it has evolved to produce infections of long duration with limited clinical signs. Most infections with this pathogen are subclinical in nature and are detected by the production of poor quality milk. While clinical mastitis may occur sporadically, affected animals rarely become seriously ill and the major economic effect of this disease is reduced milk yield and quality premiums received by the producer.

Animals are at risk for this organism throughout lactation and often becoming infected after prolonged periods of exposure. Unless a vaccine can prevent new infections throughout lactation and dramatically reduce the SCC of affected animals, it may be difficult for a producer to recognize the benefit of using a *Staph aureus* vaccine.

In contrast, mastitis caused by coliforms (*E. coli, Klebsiella spp*. and others) is usually of short duration and <15% of affected animals usually develop chronic infections. Coliform mastitis is generally clinical in nature and many affected animals exhibit systemic signs of disease.

The clinical symptoms associated with coliform infections are the result of endotoxin released from the cell wall of dying gram-negative bacteria. There is rarely a long-term impact of coliform infections on SCC. Losses attributable to coliform mastitis are associated with the clinical episode and are the result of reduced milk yield, discarded milk, treatment costs, death and culling.

The highest risk period for coliform mastitis is during the immediate periparturient period. Therefore, a vaccine may be judged effective if it successfully reduces symptoms of coliform mastitis during this limited “at-risk” period.

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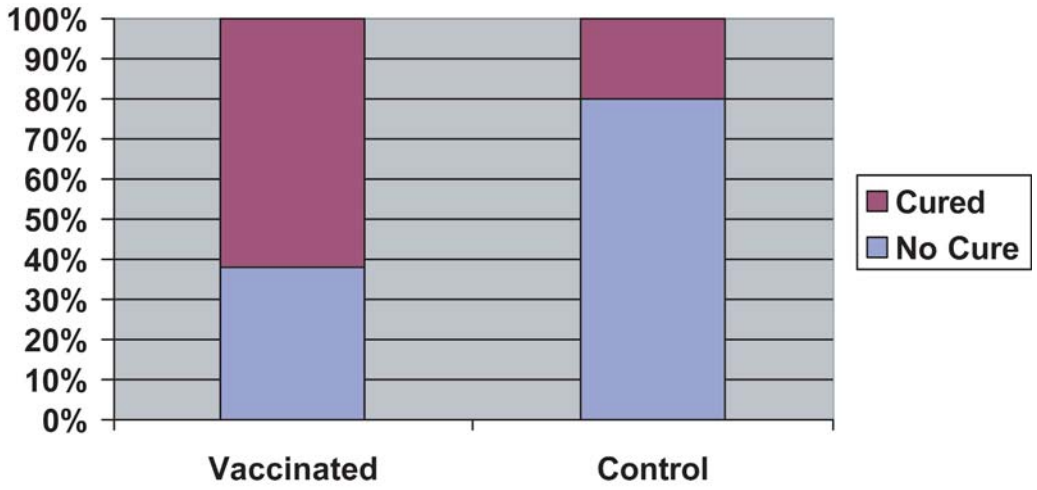
Assessing Vaccine Efficacy

Staph aureus Vaccines

It is generally accepted that commercially available *Staph aureus* vaccines have limited ability to prevent new infections.[11,18] A 3-lactation trial failed to demonstrate a reduction in the number of new *Staph aureus* infections in cows vaccinated with a commercial vaccine.[14] This study did document an increase in the spontaneous cure rate of cows that received the vaccine. Similar results were found in a separate study conducted in 3 commercial dairy herds in New Zealand (Figure 1).[13]

Figure 1. Spontaneous Cure Rate



There are several other studies that support the ability of commercially available *Staph aureus* vaccines to enhance spontaneous cure rates. Literature published by representatives of the manufacturer suggests that the best use of this vaccine is the reduction of chronic infections rather than prevention of new infections.[17] The ability of commercial *Staph aureus* vaccines to reduce the development of chronic infections may be useful in some herds that are involved in *Staph aureus* control programs, but for most herds the successful control of *Staph aureus* mastitis will result from the prevention of new infections. The failure to prevent new infections is probably the reason that this vaccine is used on a limited basis in mastitis control programs.

There have been several approaches to the development of experimental vaccines directed toward the control of *Staph aureus* mastitis. Researchers have attempted to develop vaccines directed toward specific virulence factors responsible for the development of mastitis. Vaccines have been formulated based on bacterial cell wall components (protein A), adhesion factors (bacterial factors that allow Staph aureus to attach to mammary epithelial cells) and *Staph aureus* pseudocapsules (a slime layer that surrounds the bacteria and reduces the ability of WBC to destroy the bacteria). The outcomes of these studies have been inconsistent and confusing to interpret.

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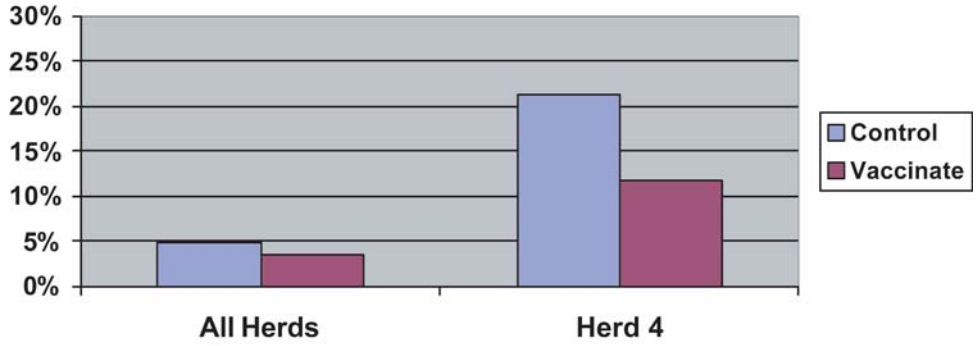
Australian researchers have published several papers describing results of vaccine trials using an inactivated vaccine produced from *Staph aureus* strains that produce pseudocapsules.[15,16] An experimental challenge study documented that this vaccine can successfully stimulate the development of anti-pseudocapsule antibody and reduce the development of clinical symptoms.[15] The vaccine did not significantly reduce SCC or increase milk yields of infected cows. This particular vaccine was further evaluated in a 7-herd field study.[16] The results of this study were interesting because there was no significant effect of vaccination on SCC or clinical mastitis when data from all 7-herds were included in the analysis. However, this study did demonstrate that differences were seen between herds (Figure 2).

Figure 2. Clinical Mastitis Caused by Staph aureus



When analysis was restricted to a single herd that had a high prevalence of *Staph aureus* mastitis, the vaccinated animals had a reduction in signs of clinical mastitis and reduced development of new subclinical mastitis infections.

A Norwegian researcher enrolled 108 heifers from 16 farms in a study of a vaccine that included pseudocapsule and toxoids.[12] Almost 20% of the cows in the enrolled herds were infected with *Staph aureus* mastitis. Vaccination did not significantly affect the rate of clinical mastitis or the SCC of enrolled cows. Vaccination did seem to lessen the development of clinical mastitis from subclinically infected cows.

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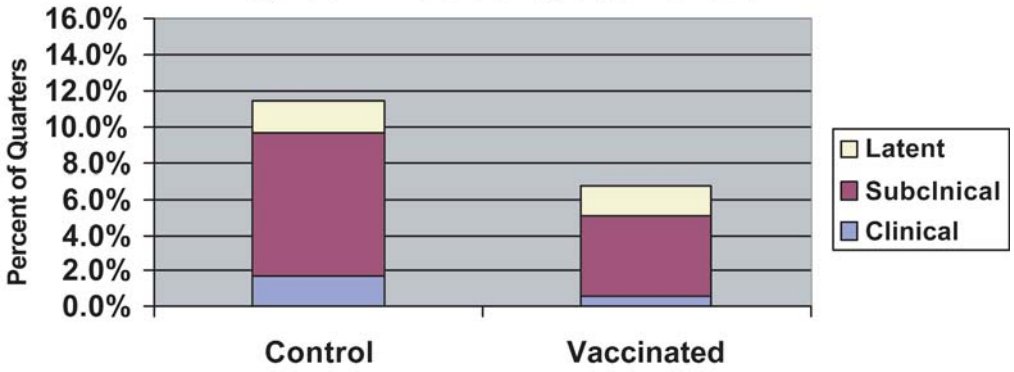
A vaccine consisting of inactivated, highly encapsulated *Staph aureus*, unencapsulated *Staph aureus* and exopolysaccharides has been developed and tested in Argentina.[3,6] The field trial portion of the studies was conducted in dairy herds with poor milk quality and a moderate prevalence of existing *Staph aureus* infections.[3] The experimental unit was quarters and the researchers excluded quarters that were infected prior to beginning the study. Under these conditions, the vaccine successfully reduced new intramammary infections with *Staph aureus* (Figure 3) but did not significantly affect the SCC.

Figure 3. IMI Caused by Staph aureus



In general, there seems to be progress in the development of an effective *Staph aureus* vaccine but the efficacy of these vaccines seems to vary by herd. The greatest effect of *Staph aureus* vaccines appears to be a decrease in the development of clinical symptoms and preventive management programs are needed to effectively reduce the new infection rate.

Coliform Vaccines

The use of vaccines against gram-negative bacterial mastitis ("J5 vaccines") has become standard practice on many dairy farms in the United States. The efficacy of these vaccines has been demonstrated in both experimental challenge trials and in field trials in commercial dairy herds.[7,8,9] The biologic principle of these bacterins is based upon their ability to stimulate production of antibodies directed against common core antigens that gram-negative bacteria share. These vaccines are considered efficacious even though the rate of intramammary infection is not significantly reduced in vaccinated animals because they significantly reduce the clinical effects of the infection. Experimental challenge studies have demonstrated that J5 vaccines are able to reduce bacterial counts in milk and result in fewer clinical symptoms.[8] The prevailing theory is that J5 vaccines enhance the ability of WBC to destroy the bacteria.

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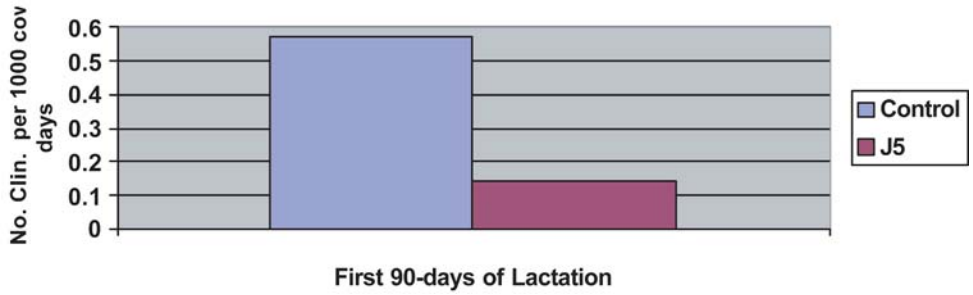
Vaccinated cows therefore may become infected with gram-negative mastitis pathogens at the same rate as control animals but have a lower rate of development of clinical mastitis (Figure 4).[7]

Figure 4. Rate of gram-negative Clinical Mastitis



Researchers have also demonstrated that vaccination with J5 bacterins reduced the duration of IMI from 130 hours in control animals to 80 hours in animals that received the vaccine.[9] The use of J5 vaccines has been justified in several economic models because of reduced production, culling and death losses.[1,4] The significant economic benefit from the use of these vaccines has resulted in mastitis consultants recommending their use in most dairy herds.

Other vaccines

The increased frequency of mastitis caused by environmental streptococci has resulted in a number of attempts to produce vaccines against these pathogens. There has been a sustained, focused research effort for vaccines directed against *Streptococcus uberis*.[10] Repeated immunization with a killed *S. uberis* vaccine was effective in reducing the number of bacteria in milk from animals that were experimentally challenged with the same strain of *S. uberis*.[5] Immunization did not reduce the SCC level in this study. One strain each of *Streptococcus uberis* and *Streptococcus agalactia* were included in an experimental multivalent killed mastitis bacterin that was tested in a field trial.[3,6] This vaccine had no significant effect on the occurrence of mastitis caused by Streptococcus organisms but the study may not have been designed with enough power to be able to detect a difference if one did exist. Researchers have also investigated live vaccines against *Strep uberis* but have concluded that the strain-specific nature of protection obtained will limit the applicability of live antigen vaccines.[10] At this time, there are no commercial vaccines available that protect against Streptococcus mastitis.

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Current Recommendations

In most herds the most effective control strategy is prevention of new infections by the use of good management practices. The use of *Staph aureus* vaccines is not universally recommended but may be useful in some herds as an adjunct to prevention oriented control programs. J5 vaccines are economically viable for many dairy herds.

The manufacturer of J-Vac© has created a partial budget program that can be used to perform a cost to benefit analysis for herds at various levels of milk price, mastitis incidence and milk yield. A key assumption of this model is that E. coli causes 10% reduction in milk yield and that the vaccine efficacy is 80%.

It is also important to emphasize that vaccines must be handled properly, used before the expiration date and given to healthy immune competent cattle in the manner recommended by the manufacturer.

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