

*Industry Presentation*  
**The Role of Nutrition In Udder Health**

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**Introduction to Udder Health**

Mastitis is an inflammation of the mammary gland or udder tissue. Inflammation is the response of the body to injury. In cows, this response, i.e. mastitis, is usually provoked by infection with bacteria. Mastitis can also be the result of non-infectious causes, such as mechanical damage. A poorly adjusted milking machine, or narrow stalls and poorly trimmed claws, may cause mechanical injuries to the teats and the udder. Even when bacteria are not present, the body will respond to such injuries with inflammation, much like the redness, swelling, and pain that is associated with a twisted ankle. Mechanical damage and bacterial infections can both result in mastitis. Furthermore, mechanical damage may open the way for bacterial infections.

The response of the body, the inflammation, may be visible or invisible. If a response is visible, the mastitis is considered to be clinical. Clinical signs can be mild, moderate or severe. In mild cases, visible abnormalities are limited to the milk only, e.g. clots, flakes or watery milk. Of course, one has to look to see such changes. If cows are not fore-stripped before the milking unit is attached, mild clinical mastitis will go unnoticed. In the case of moderate clinical mastitis, both milk and udder show abnormalities. The udder may show redness, swelling, or pain, and can be warm to the touch. Usually, the function (milk production) is affected too. Redness,

swelling, pain, increased temperature and abnormal function are the typical characteristics of inflammation. In severe cases milk, udder, and cow are affected. The animal may have a fever, be off-feed, depressed, and down. Very severe cases are also described as *toxic cases* (Figure 1). Some herds only consider the severe cases to be *clinical cases*, thus underestimating the real number of clinical cases. When discussing or comparing the number of clinical cases, make sure that everybody has the same understanding of what they mean by clinical mastitis. Severe clinical mastitis is often called *acute* mastitis. Strictly speaking, acute refers to the duration of the mastitis, rather than to the severity. Clinical mastitis can be acute (just started) or chronic (e.g. chronic *E. coli* mastitis).

When no signs of clinical mastitis are visible, the mastitis is subclinical. Because subclinical mastitis often goes unnoticed and unaddressed, the duration of subclinical mastitis is usually longer than the duration of clinical mastitis. For many people *chronic mastitis* and *subclinical mastitis* are more or less synonymous, although the first term refers to duration and the latter term to severity. Even though subclinical mastitis can't be seen with the naked eye, it is very important. It is associated with high somatic cell count (SCC) and production losses, and subclinical mastitis cases can be a source of infection for other animals in the herd.

**Figure 1.** Examples of moderate and severe clinical mastitis in left rear quarters. In the moderate case (left) the udder is visibly abnormal (swollen), but the cow is healthy. In the severe case (right) the udder is grossly abnormal (blue, "toxic") and the cow is sick and down.



Many subclinical mastitis cases show up as clinical mastitis cases when a cow is in heat, when there is a change in the weather, or at some other point in time. High SCC are associated with lower milk and cheese yields, shorter shelf life of processed milk, and lower milk prices. Usually, 200,000 cells/ml is used as a threshold between normal and abnormal milk, but any cow level SCC over 50,000 cells/ml is associated with a decrease in production relative to the cow's genetic potential. In practical terms, milking cows with high SCC means you are milking more cows than necessary to produce the same amount of milk. Each extra cow needs to be housed, managed, fed, inseminated, vaccinated, and milked. From an economic point of view, subclinical mastitis is probably more important than clinical mastitis, even though we cannot see it in the milking parlor. To *see* subclinical mastitis, additional tests such as SCC measurement, CMT (California Mastitis Test or *paddle test*), culture of bacteria, or conductivity measurements must be used (Figure 2).

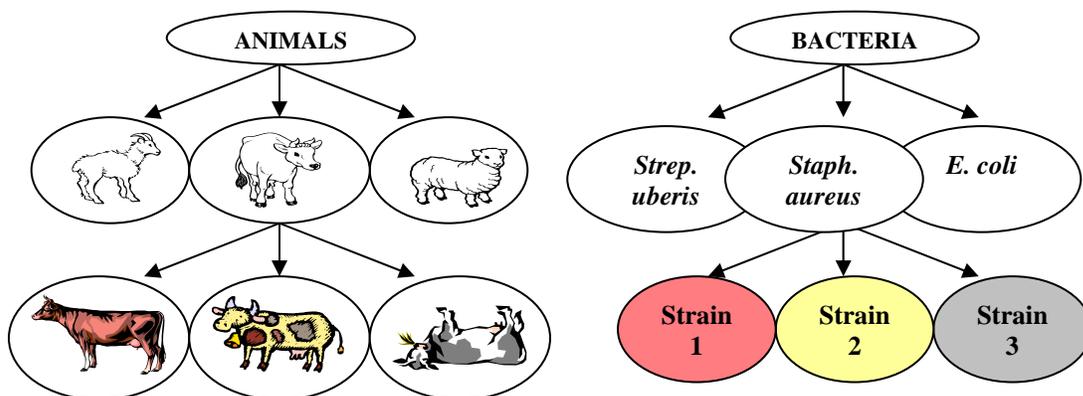
For mastitis management, the way mastitis spreads is more important than the

way it shows up. Once we understand how and where cows become infected with bacteria, we can take management action to prevent infections and new mastitis cases from occurring. Bacterial mastitis is characterized in two groups, based on the way the bacteria are spread. On the one hand, there is contagious mastitis. For contagious mastitis, the cow's udder is the main source of bacteria. Spread of bacteria mostly happens during milking, via udder cloths, liners, or milkers' hands. To solve a contagious mastitis problem, the source of bacteria needs to be identified and removed. In other words: infected cows are detected based on high SCC and culture results, and these animals are subsequently treated, culled, or segregated from the rest of the herd. On the other hand, there is environmental mastitis. As the name implies, the environment is the main source of bacteria in this scenario. The environment includes the cow itself: manure, skin, mucous membranes, and anything outside of the udder, as well as water, bedding, pets, pests, etc. Because the bacteria can be anywhere, exposure can happen anywhere and at anytime, even in non-milking animals such as dry cows and heifers.

**Figure 2.** Cows with subclinical mastitis look normal (left). To detect subclinical mastitis, the CMT test (center) and culture of bacteria from the milk sample (right) can be used.



**Figure 3.** Animals can be divided in species, and animal species can be subdivided into breeds. Similarly, bacteria can be divided in species, and bacterial species can be subdivided into strains.



### Contagious and Environmental Mastitis

How can we tell whether we are dealing with a contagious or an environmental problem? There are three factors that play a major role in the occurrence of mastitis: the cow, the environment, and the bacteria. Therefore, there are three things we need to look at: the cows, their environment, and the bacteria.

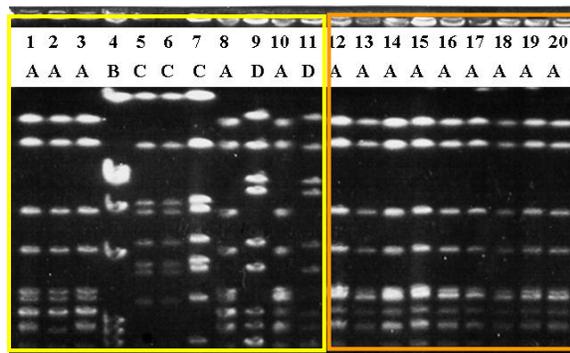
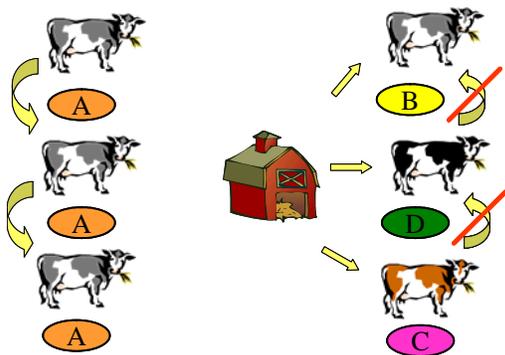
Start with the cows. Where does the problem occur? Do you mainly see a problem in the dry cows or the heifers? Those animals are not exposed to milking, so transmission during milking and contagious mastitis is out of the question. Do you mainly see a problem in the milking herd? In that case, there may be contagious transmission in the milking herd, or there may be something wrong with the cows' resistance, or with the bacterial load in their environment.

Next, look at the environment. Don't forget that the environment includes the milking machine, the people handling, feeding and milking the cows, and nutrition. Are the cows out on pasture or in a barn? If inside, what is the air quality? Is it fresh inside the barn, or dusty and muggy? When dust and moisture have a chance to

accumulate, bacteria do too. Is the paddock dry and evenly used, or do cows gather under shades, creating a high density of animals, bacteria, and manure and urine for the bacteria to grow in? What is the bedding material that is used? Straw and manure pellets may harbor lots of Streptococci. Manure also contains *E. coli* and *Klebsiella*. In the north, *Klebsiella* is also found in sawdust and shavings. Make sure to check the environment of the lactating cows, dry cows and heifers and, most importantly, the close-up and transition groups.

Finally, look at the bacteria. Submit milk samples to identify the main bacteria causing mastitis, and environmental samples (bedding, water, teat dip) to identify environmental sources of bacteria. In special cases, strain typing may be considered to determine whether bacteria are of environmental or contagious origin. When a predominant strain is found, the problem is probably contagious. If a large variety of strains are found, the source of the bacteria is in the cows' environment. Strains are subgroups within bacterial species, just like breeds are subgroups within animal species (Figure 3).

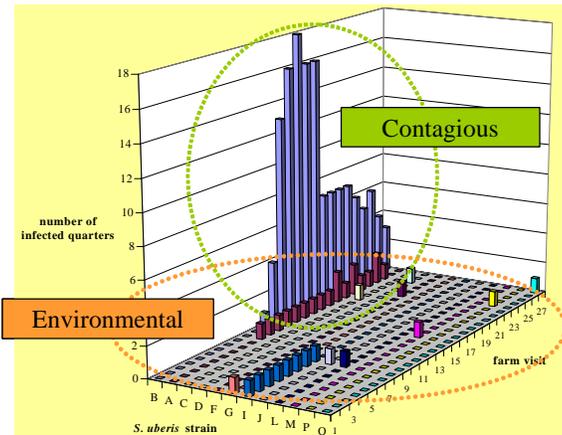
**Figure 4.** Left hand panel: schematic representation of contagious or cow-to-cow transmission (each cow infected with the same strain, called A) and environmental origin of mastitis (each cow infected with a different strain, called B, C and D). Right hand panel: DNA fingerprinting results for *Staphylococcus aureus* isolates from two herds: in columns 12-20, a herd with contagious or cow-to-cow transmission (each cow infected with the same strain, called A), and in columns 1-11 a herd with environmental origin of mastitis (cows infected with four different strains of *S. aureus*, called A, B, C and D, showing that at least four sources of infection must have existed. Both herds had been closed herds for years.



Strain typing, also known as *DNA fingerprinting* can help to determine whether a mastitis problem is contagious or environmental. If a cow is infected with a certain strain of, say, *S. aureus*, and she transmits that to the next cow, and on to the next cow, etc., most cows in the herd would be infected with the same strain of *S. aureus*. In the environment, many different sources of *S. aureus* are present, e.g. on the cow's skin, bedding, flies, dogs, people, etc. Different sources contain different strains. Thus, if cows don't get the infection from each other but from the environment, each cow would probably get a different strain of *S. aureus*. In fact, this is what happens in most herds: the majority of *S. aureus* infections are the result of cow-to-cow transmission, but a proportion of *S. aureus* cases comes from the environment (Zadoks et al., 2000; Figure 4).

Traditionally, bacterial species have been categorized as either contagious or environmental. Some bacteria are highly contagious, for example *Streptococcus agalactiae* and *Mycoplasma bovis*. Other bacteria are usually contagious, but they can also come from the environment, as shown above for *Staphylococcus aureus*. Bacteria that usually come from the environment include: *E. coli*, *Klebsiella*, *Pseudomonas*, *Prototheca*, and a number of others. In some parts of the world, all Streptococci other than *Streptococcus agalactiae* are considered to be environmental, and they are called environmental streptococci or *E-streps*. In reality, these so-called E-streps, also known as *non-agalactiae streptococci* or *strep species* can be environmental or contagious. In fact, contagious and environmental mastitis caused by E-streps can co-exist in a herd (Zadoks et al., 2003; Figure 5).

**Figure 5.** Example from a 95-cow herd. The graph shows 27 herd visits at monthly interval (1-27). For each visit, the number of quarters with *Streptococcus uberis* mastitis is shown (0-18). The letters (B, A-Q) and colors indicate the different strains of the bacteria. Most strains (C-Q) cause only one infection of short duration (environmental mastitis). Strain B caused an outbreak of contagious mastitis..



### Managing Mastitis

The key to managing mastitis is understanding mastitis. Determine whether you are dealing with contagious or environmental mastitis in your herd. If you have *Streptococcus agalactiae* mastitis, you can be 99.9 % certain that you are dealing with contagious mastitis. If you have *Staphylococcus aureus* mastitis or mastitis caused by non-agalactiae streptococci, you may be dealing with contagious or environmental mastitis. You will need to look at the cows, the environment, and the herd management to determine which one it is. Some bacterial species and strains are more likely to spread from cow-to-cow than others, but the ability of bacteria to spread in a contagious manner strongly depends on herd management. The outbreak of mastitis in Figure 5 caused by *S. uberis* (one of the so-called non-agalactiae streptococci or E-streps) occurred at a time that the herdsman stopped using post-milking teat-disinfection. The number of new infections stopped increasing as soon as post-milking teat-disinfection was re-instated. Contagious transmission of E-streps has been described in New York, Tennessee, California, and

other places. Just because something is called an *environmental strep* doesn't mean it has to be environmental. As long as you keep that in mind, and look at what is going on in your herd, contagious transmission is easy to control:

1. Always use post-milking teat-disinfection with a proven disinfectant that is also a skin conditioner.
2. Maintain and use the milking machine properly, without overmilking, vacuum fluctuations, air inlet, cracked liners, etc. Train milkers on how to prep and milk the cows, in English or Spanish, as needed.
3. Use blanket dry cow treatment to treat existing infections and to prevent new cases of mastitis.
4. Treat cows with clinical mastitis. If possible, the choice of treatment should be based on knowledge of the bacteria that are causing mastitis. On-farm culture can be used to identify bacteria.
5. Cull chronically infected cows that don't respond to treatment.

Managing environmental mastitis is a different story. Managing environmental mastitis is about managing the balance between exposure to bacteria in the environment, and the cow's ability to overcome this bacterial challenge. Sometimes, specific environmental sources of bacteria can be identified and removed, e.g. a load of contaminated bedding material, contaminated cow-care products, or contaminated water. In many situations, there is no specific source, for example because the bacteria are shed by the animals in their feces. Keeping the environment as clean and dry as possible is the best way to manage bacterial loads. Many factors influence a cow's resistance to mastitis. This provides us with many tools to work with to control environmental mastitis. Some tools, like breeding, may provide solutions in the long term; whereas other tools provide short or medium term solutions. Key factors in host resistance include: (1) **Teat end integrity**. This is affected by teat shape (breeding), teat dip (skin conditioning), machine-on time (avoid over-milking both before and after peak flow), and vacuum level and pulsations; (2) **Vaccination**. Vaccines are available for coliform mastitis. "Nutrition is the best vaccine"; and (3) **Nutrition**. Specifically negative energy balance and vitamins and minerals influence resistance.

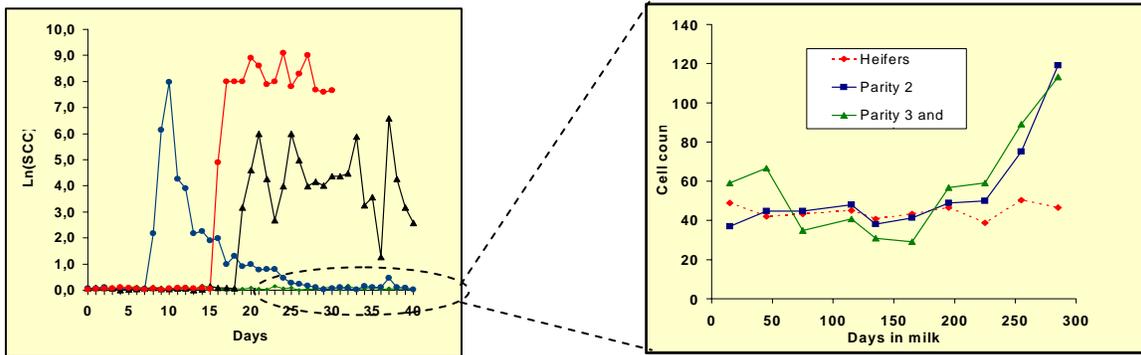
### **Infection and Immune Response**

The host immune response consists of innate and acquired immunity. Innate

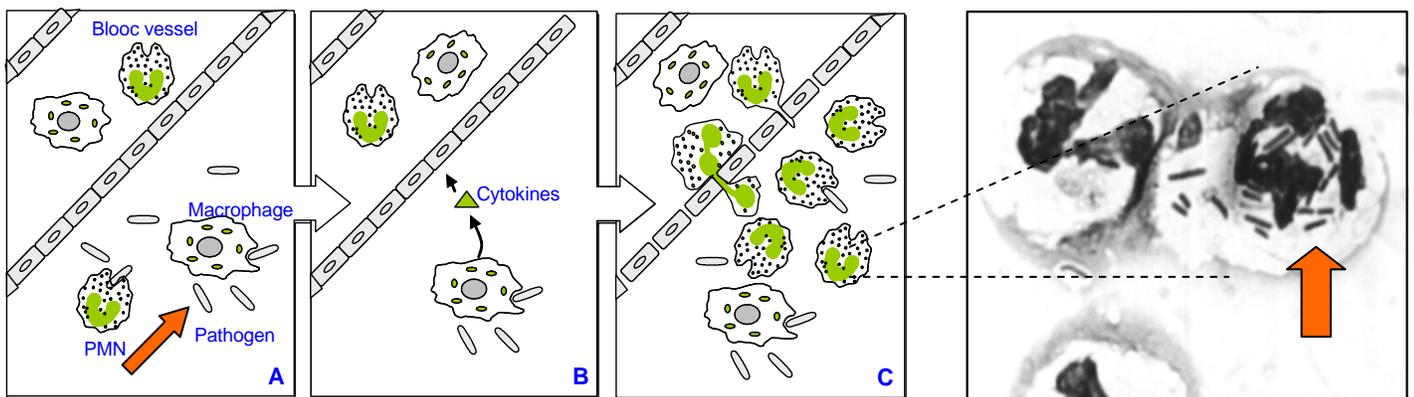
immune defenses are not specific for any organism, but work against many organisms. That is an advantage. Another advantage is that the innate immune system is always present. There is no delay between bacterial invasion and host response. Elements of the innate immune system include lactoferrin and enzymes such as glutathione peroxidase (**GSH-PX**). The innate immune response is not very strong. The acquired immune response is much stronger. The down side of the acquired response is that it takes time to develop. We can stimulate this response with vaccines, such as coliform vaccines. Unfortunately, the acquired response is specific for certain organisms, so the coliform vaccine does not protect against other types of mastitis.

In healthy cows, SCC is low, lower than 200,000 cells/ml, irrespective of lactation stage or parity (Figure 6, right side). In the healthy udder, different types of white blood cells occur in similar numbers: macrophages, lymphocytes, and leucocytes. When these cells notice invading bacteria, they release signal molecules (cytokines) that attract a large influx of leucocytes. These leucocytes or PMNs (polymorphonuclear leucocytes), are the *killer cells*. They engulf and kill invading bacteria. The numbers of cells increase dramatically, from hundreds to millions per ml (Figure 6, left side). If the cells win, the bacteria are captured, killed and removed, and SCC decreases. If the bacteria win, they cause chronic infection and SCC stays high. The infection process is shown in Figure 7.

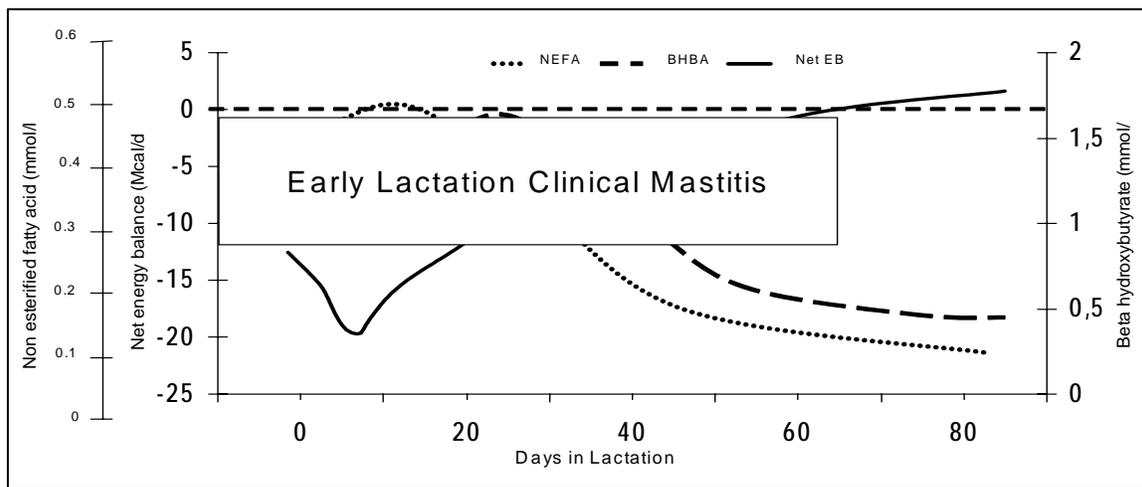
**Figure 6.** SCC in healthy cows (right) and cows with mastitis (left). In healthy cows, SCC is below 150,000 cells/ml irrespective of parity or lactation stage (SCC scale runs from 0 to 140,000 cells/ml). In cows with mastitis, SCC can be in the millions (SCC scale runs from 0 to 2.2 million cells/ml). SCC can be high for a few days (left, blue curve, short infection), for weeks (left, red curve, chronic infection) or SCC can vary (left, black curve, chronic infection, SCC fluctuates from normal to high).



**Figure 7.** A: Macrophages and PMN in the udder recognize bacteria (grey arrow). B: Macrophages release signal molecules, cytokines. C: In response to the cytokines, white blood cells (PMNs) from the blood stream migrate to the infected udder (SCC increase). D: Picture of white blood cells from milk with *E. coli* bacteria inside of them (grey arrow). (Suriyasathaporn et al., 1999; van Werven et al., 1997).



**Figure 8.** Negative energy balance (full black line) in early lactation. NEFA levels (dotted line) mirror energy balance, and BHBA levels (dashed black line) follow with some delay. BHBA levels >0.8 mmole/l are associated with slow response of white blood cells to infection, resulting in a high risk of clinical mastitis in early lactation (Suriyasathaporn et al., 2000).



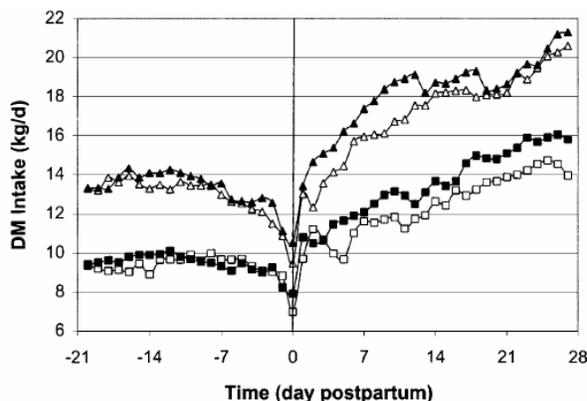
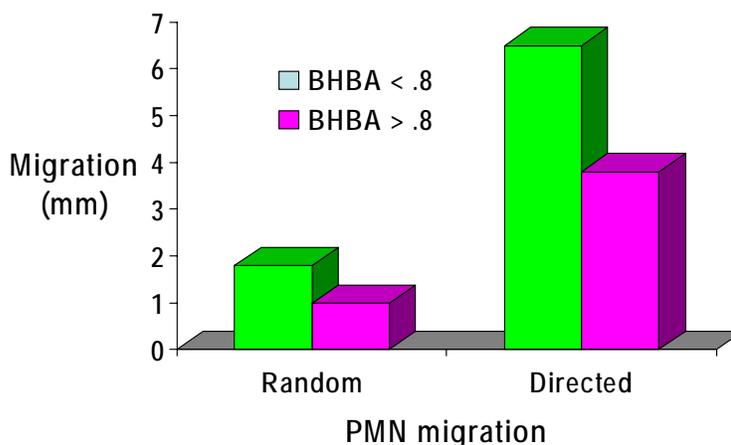
### Negative Energy Balance and Mastitis

Negative energy balance has a major impact on the immune response that is described in the preceding section. Around calving, the appetite of every cow is depressed, and in early lactation every cow is in a negative energy balance. The energy demand for milk production is larger than the energy intake with feed. As a result, cows mobilize their internal energy reserves, which is reflected in higher levels of non-esterified fatty acids (**NEFAs**) and beta-hydroxybutyric acid (**BHBA**) in blood, loss of body condition score, high fat:protein ratios in milk (>1.5), and in severe cases, in clinical ketosis (Figure 8). Cows in negative energy balance are at a higher risk of ketosis. In a Canadian study, 21 % of cows with pre-partum ketosis developed clinical mastitis, versus only 9 % of cows without pre-partum ketosis. More severe ketosis results in more severe clinical mastitis (Kremer et al., 1993). BHBA limits the ability of PMN to move. In practical terms: a cow with high BHBA levels (negative energy balance) can't recruit PMNs to the udder fast enough to outcompete the growth

of bacteria (Suriyasathapornetal., 1999; Figure 9).

To screen a herd for negative energy balance, have at least 12 animals tested. NEFA testing is done 2-14 days before calving and BHBA testing at 2-21 days after calving. If more than 10-15 % of animals have NEFA levels above 0.40 mEq/L (milliequivalent per liter) or BHBA levels above 14 mg/dl (milligrams per deciliter), the herd is considered to be suffering from excessive negative energy balance (Nydam and Stokol, 2005). Prevention of negative energy balance in early lactation starts in the previous lactation. Strive for moderate body condition score in late lactation, and maintain this score during the dry period. It is easy to overfeed dry cows, especially if the dry period is longer than expected. Transition cow ration and management are very important. Minimize stress, and provide the most attractive high quality food to transitioning animals. The more they eat, the better. Make it attractive to them. Dietary supplements, specifically live yeast, can improve dry matter intake (Figure 10) and significantly limit loss of BCS

**Figure 9.** The ability of white blood cells (PMN) to migrate depends on the level of beta-hydroxy butyric acid (BHBA) in the cow's blood. PMNs move randomly, and towards specific stimuli from cytokines, e.g. in the infected udder (directed migration). Both types of migration are faster for cells from cows with low BHBA levels (light grey bars) than for cells from cows with high BHBA levels (dark grey bars) in their blood. If cells move slowly, they are outcompeted by bacteria, resulting in clinical mastitis. (Suriyasathaporn et al., 1999).



**Figure 10.** Impact of live yeast on dry matter intake (DMI) of cows (triangles) and heifers (squares) around calving. Open symbols represent animals on control diet. Closed symbols represent animals that received live yeast culture diets. (Robinson and Garrett, 1999).

(Robinson and Garrett, 1999). Feeding of yeast culture also contributes to higher milk production.

### Vitamins, Minerals and Mastitis

In terms of udder health, vitamin E and selenium (Se) are by far the most important vitamin and mineral, as shown in experimental studies and field studies in many parts of the world. To a lesser extent, vitamin A and beta-carotene, copper (Cu)

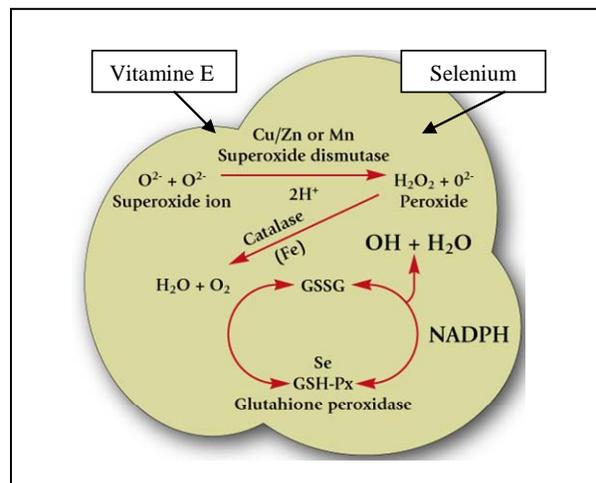
and zinc (Zn) may play a role in reducing occurrence or severity of mastitis (Scaletti et al., 2003; Weiss, 2002). All of these vitamins and minerals exert their effect by influencing the cow's immune function. Adequate vitamin and mineral levels make for adequate immune function, enabling the cow to deal efficiently with invading bacteria. Depending on soil type and ration, supplementation of vitamins and minerals may or may not be needed. The concentration of supplemental Se in dairy

cattle diets is regulated by the FDA at 0.3 ppm. The same level is recommended for dry cows by the NRC. Vitamin E requirements depend on age and lactation stage (Weiss, 2002).

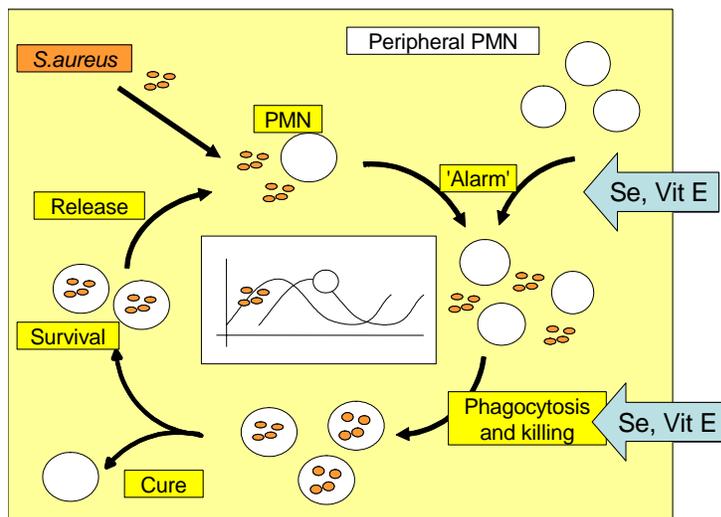
When bacteria invade the udder, they are recognized, and, if all goes well, killed by white blood cells as shown in Figure 8. To kill the invading bacteria, PMNs release toxins: reactive oxygen species (ROS) such as superoxide and peroxide (Figure 11). While the goal of ROS is to damage bacterial cells, they may also damage the cow's white blood cells. Vitamine E and Se both act to remove ROS from the host cell. This prevents damage to the host cell and prolongs host cell survival. Vitamine E acts on the cell wall, while Se acts inside the cell, as co-factor of GSH-PX (Smith et al., 1997).

Vitamine E and Se also play a role in the metabolism of polyunsaturated fatty acids in cell membranes, including arachidonic acid (Smith et al., 1997).

Arachidonic acid is a precursor for leukotriene B<sub>4</sub>, one of the messenger molecules that is produced by macrophages and PMN in the early stages of bacterial invasion (see Figure 8, panel B). Inflammatory mediators such as leukotriene B<sub>4</sub> and cytokines are important for initiation and amplification of the host response. Vitamin E and Se increase the random migration and the directed migration of PMN (Ndiweni and Finch, 1996). This effect is similar to the effect of BHBA shown in Figure 10. Thus, vitamin E and Se are important to generate a quick response, and also to generate an efficient response. If an efficient response is not generated, host cells may capture invading bacteria, but fail to kill them. Once the host cell dies, the bacteria are released and a new infection cycle starts. This is common in *S. aureus* (Figure 12).



**Figure 11.** Vitamine E, Se and other minerals limit the effect of reactive oxygen species in the cell wall and the cell cytosol, respectively.



**Figure12.** Bacteria (*S. aureus*) invade and are recognized by PMN (white). Resident PMN in the udder raise alarm. Peripheral PMN from the bloodstream respond, and SCC rises. PMN take up bacteria and kill them. If the PMN fail to kill the bacteria, surviving bacteria are set free once the cell dies, and a new cycle begins. The center graph shows the cyclic increase and decrease in bacteria counts and SCC over time. (Adapted from Daley et al., 1991). Vitamin E and Se play a role in quick recruitment of cells, and in efficient killing of bacteria.

In experimental studies, *E. coli* mastitis has been induced in Se-deficient and Se-supplemented cows. In Se-deficient cows, bacteria counts are higher, clinical signs are more severe, SCC is higher, and duration of infection is longer (Erskine et al., 1989). PMN of vitamin E or Se-deficient cows are less efficient at killing *S. aureus* than PMN of supplemented animals (Grasso et al., 1990; Hogan et al., 1990). What happens on a farm does not always mirror what happens in experiments. In the case of vitamin E and Se, it does. Dietary supplementation is associated with a reduction in the proportion of cows in a herd with high SCC, in the duration of udder infection, in the number of clinical mastitis cases, and in the number of animals that freshen with mastitis (Smith et al., 1997). At herd level, the mean Se concentration in plasma or whole blood from cows is correlated with bulk milk SCC: higher Se or GSH-PX activity levels are associated with lower SCC, lower incidence of clinical mastitis, and lower prevalence of subclinical mastitis. (Erskine et al., 1987; Hemingway, 1999; and Weiss et al., 1990). Different sources of Se exist, most importantly inorganic sources such as sodium selenite and organic sources such as Se-yeast. The

bioavailability of Se-yeast is superior to that of sodium selenite. Se-yeast is associated with higher GSH-PX levels in blood, higher Se levels in blood and milk, and lower levels of mastitis and SCC (Malbe et al., 1995). Similarly, bioavailability of organic copper lysine is better than the availability of inorganic copper sulfite (Rabiansky et al., 1999).

## Conclusion

Mastitis is a multi-factorial disease. The cow, the bacteria, the management and the environment all play a role in the risk of mastitis, and hence in the prevention and control of mastitis. Some bacteria have adapted to long-term survival in the host without severe disease symptoms. These bacteria usually spread in a contagious manner from cow-to-cow, and identification and removal of infected cows is the key to control of this type of mastitis. Other bacteria have adapted to environmental survival, and cause opportunistic infections, sometimes with severe clinical symptoms, when they are present in large numbers, or when the host is immunocompromised.

Control of environmental bacterial populations and improvement of host resistance are the keys to control of environmental mastitis. Host resistance is affected by genetics, teat end integrity, vaccination, and nutrition. The most important aspects of nutrition are prevention of negative energy balance in early lactation and maintenance of adequate levels of vitamins and minerals. Negative energy balance, high blood levels of NEFA's or BHBA and ketosis reduce the response capacity of white blood cells so that invading bacteria can out compete the immune system. To prevent this, keep cows in adequate condition during the dry period, maximize feed intake around calving, and optimize energy content of early lactation rations. Addition of live yeast to the ration promotes feed intake and reduces body condition score losses and negative energy balance.

Vitamin E and Se enhance the ability of white blood cells to move to the infected udder, and in their ability to kill bacteria. To a lesser extent, Zn and Cu play a role in the ability of white blood cells to move to the site of infection or kill bacteria. Availability of minerals from organic sources is better than availability of minerals from inorganic sources.

Understanding which type of mastitis you are dealing with, prevention of cow-to-cow transmission, environmental hygiene, and adequate nutrition are the foundation of a successful mastitis control program.

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