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Literature review: Bovine mastitis caused by Coagulase-Negative *Staphylococci*

Clara Navarro Sansano
Milk Quality Services

1. Introduction

One of the groups of bacteria that cause mastitis is called coagulase-negative *staphylococci* (CNS). These bacteria are of great interest because they are **currently the most commonly isolated microorganisms in cows** and heifers in herds, and are currently considered **emerging pathogens of bovine mastitis** (Pyörälä S. *et al.* 2009).

CNS are normally found on the healthy skin of the nipple and the hands of the milker. They are often called “opportunistic microorganisms” because they live in areas where it is easy to colonize the teat canal and penetrate the secretory tissue.

Implementing mastitis control programmes over the past 30 years has led to a reduction in the overall incidence of clinical mastitis in most herds. In some cases, the decrease has been 90%. Whereas the clinical disease caused by major pathogens such as *Staphylococcus aureus* and *Streptococcus agalactiae* decreased significantly, less important pathogens such as CNS have been increasingly taking on greater importance.

Cows and heifers can be infected with CNS before calving. In lactation, **infection due to CNS is associated with an increase in somatic cell count (SCC), which causes economic losses due to the penalty in the price of milk.**

The prevalence of mastitis by CNS is **higher in primiparous animals**. They are generally mild infections and limited to floccules in milk due to local changes in the udder. Many of these infections even heal spontaneously. But sometimes animals with intramammary infections caused by CNS are observed with symptoms at a systemic level and are animals with persistent infections that can last several months if measures are not taken. There are over 50 species of coagulase-negative *staphylococci* and perhaps it is a mistake to observe their behaviour as a group and not as individual species. Although they are not considered to be a group of bacteria as pathogenic as the main pathogens causing mastitis, their pathogenicity and resistance to antimicrobial treatments varies depending on the species of CNS.

Some investigators consider them to be secondary pathogens of the udder, but the significance of intramammary infections are still a subject of debate since, on the other hand, other works give them great importance in the aetiology of sub-clinical or clinical mastitis and increased somatic cell counts of affected cows.

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2. Aetiology and epidemiology

CNS are Gram-positive cocci that inhabit both the outside and inside of infected udders. Often they are called “opportunistic flora of the skin”, because they can be isolated from the skin of the teat, the teat canal, vagina, and the coat and nostrils.

This group of bacteria includes over 50 species and subspecies (Pyörälä S. *et al.* 2009). The most common species of CNS are isolated from cases of bovine mastitis are *Staphylococcus chromogenes*, *Staphylococcus epidermitis*, *Staphylococcus hyicus* and *Staphylococcus simulans*.

Species such as *Staphylococcus epider-mitis*, *Staphylococcus saprophyticus*, *Staphylococcus simulans* and *Staphylococcus warneri* belong to the normal bacterial flora of the teat skin, while other species such as *Staphylococcus xylosus* and *Staphylococcus sciuri* seem to come from the environment. *Staphylococcus chromogenes* may colonize the skin of the teat and other parts of an animal's body such as hair, the vagina and teat canal.

It seems that there are differences in the pathogenicity of different species of CNS that are investigated by techniques of molecular diagnosis (Zadoks and Schukken, 2006). We found species with different antimicrobial susceptibility and diverse virulence factors of CNS isolated from bovine mastitis (Taponen S. *et al.* 2009).

The incidence of new infections is highest during the cow's dry period and prior to calving; therefore, the percentage of quarters infected is high at the time of calving.

The highest prevalence of CNS is in primiparous animals rather than in mature cows.

Unfortunately, many producers mistakenly believe that their heifers are healthy, and the presence of mastitis is not observed until calving. Future breeders represent future lactation and care for the udder is basic for ensuring the profitability of dairy farms.

Many of the intramammary infections caused by CNS heal spontaneously and the prevalence decreases as lactation progresses.

Although CNS infections are usually mild or sub-clinical, it has also been shown that they **can cause more severe and persistent processes**, causing an **increase in the somatic cell counts** and a **decrease in milk quality and production**

due to damage to breast tissue (Taponen S. *et al.* 2009; Gillespie B.E. *et al.* 2009).

3. Characteristics of infections by CNS

- Are usually mild infections and cause sub-clinical cases of mastitis.
- Increase in SCC.
- Can induce persistent clinical processes that do not respond to antibiotic treatment.
- Milk appearance is normal, but it can induce intramammary infections with alterations in milk (flocules).
- High prevalence in primiparous animals (especially in the time around calving).
- Higher incidence of new infections in the cows' dry period.
- The general state of the animal is not usually affected, nor are there severe systemic signs.
- High spontaneous cure rate.

4. Diagnosis

Once the quarters with high cell counts or that display clinical mastitis are detected, samples of milk should be taken aseptically and appropriately for subsequent processing in the laboratory. Microbiological testing is the most important test for the diagnosis of mastitis control programmes.

The methodology includes the usual seeding in growth media specific for the major aetiological groups. They are incubated at 37 °C, with readings at 24 and 48 hours. Baird Parker Agar is a culture medium specific for *Staphylococci*. It makes it possible to differentiate between CNS and *Staphylococcus aureus*. The identification of the different species of CNS is important to determine their pathogenicity and to develop specific management practices to prevent mastitis. The problem is that the identification of this group of organisms is difficult and costly. That is why many laboratories do not include species identification of CNS in routine procedures.

5. Treatment

It is generally assumed that the spontaneous cure rate of CNS is high. The CNS respond much better to antimicrobial therapy than *Staphylococcus aureus* does, and **most species of CNS are**

susceptible to antibiotics commonly used to treat mastitis. The treatment by intramammary therapy in the peripartum and drying is effective for controlling infections caused by CNS. However, treatment is not always effective.

According to the National Mastitis Council (NMC), we can classify these germs as coagulase-negative *Staphylococci* sensitive to novobiocin and coagulase-negative *Staphylococci* novobiocin resistant.

Treatment of clinical mastitis due to coagulase-negative *Staphylococcus* (CNS) sensitive to novobiocin:

Penicillins and/or Penethamate or Cefalosporins (intramammary and/or parenteral route).

Treatment of mastitis due to CNS resistant to novobiocin:

The treatment is not necessary since spontaneous cures are seen.

Antibiotic treatment in drying:

Penicillins and/or Penethamate or Cefalosporins



6. Control measures

Control measures must be applied in cows in lactation, in dry cows and also breeder heifers. Rebreeding can be a source of infection on a dairy farm, particularly under the current management systems, where heifers are transported and mixed several times before coming to the dairy farm where they will give birth (Oliver and Nickerson). Generally, not much attention is given to heifers on farms, or to cows during the dry period. But if we consider that the heifers are approximately one third of the herd each year, and that together with the dry cows they are the farm's investment for the future, the health of udders and proper functioning of heifers and dry cows should be a number-one priority.

Control measures should lower the animals' contact with mastitis causing agents before calving.

Handling

- Separate the heifers in individual pens: do not allow them to suckle each other, because

this transmits bacteria and causes persistent infections that become established early in the life of the animal.

- Do not feed lactating heifers with infected milk: avoid transmission of infectious agents from the adult cows to young cows.
- Separate the heifers from the cows before calving.
- Provide clean areas for the cows to calve and for heifers.

Environment

- Control of flies: flies can be vectors of pathogenic agents and also create a lesion on the teat tip, which allows bacteria such as *Staphylococcus aureus* or CNS to become established on the skin of the teat and enter its orifice.
- Ensure a clean dry environment. Also for rebreeding.

Vaccinal schedule

We cannot ensure proper prevention and control of the health of the udder of heifers and cows on the farm without taking into account a good vaccination programme. It is important to protect

against the incidence and severity of mastitis caused by environmental microorganisms. The placement on the market of the first vaccine registered worldwide against CNS is a good tool to increase immunization of farm operations. The protocol is based on two applications before and one after calving to help decrease the incidence and severity at the time of greatest losses on the farm

Antibiotic therapy during drying and general measures

- Administer a proper antibiotic therapy during drying based on the farm operation's bacteriological profile.
- Correct the milking routine. Carry out proper disinfection of the teat tip using disinfectant dips at both pre-milking and post-milking.
- Eliminate chronically ill animals.
- Guarantee hygiene of drying period treatments.
- Verify the state of food and drinking water.
- Proper use and maintenance of the milking machine.
- Take special care of the state of beds and walkways during drying and lactation.



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Vaccinal schedule STARTVAC®

Efficacy at post-partum thanks to its vaccinal schedule

By using two applications before calving (45 and 10 days before) and one application post-partum (on day 52) **the objective of reducing mastitis is achieved** at the time of greatest risk of infections and economic losses.



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STARTVAC® Inactivated vaccine, Bovine mastitis, in injectable emulsion. COMPOSITION PER DOSE (2 ML): Inactivated *Escherichia coli* (J5) 50 REDg0*; Inactivated *Staphylococcus aureus* (CP8) SP 140 strain expressing SAAC** 50 REDg0***. Adjuvant. * REDg0: Rabbit effective dose in 60% of the animals (serology). ** SAAC: Slime Associated Antigenic Complex. *** REDg0: Rabbit effective dose in 80% of the animals (serology). **PROPERTIES:** Mastitis is one of the main problems in dairy cows, not only from an economic point of view due to losses in the quantity and quality of the milk, but also from a sanitary point of view, because the milk produced has low bacteriological quality and a high level of antibiotics, as a consequence of antimastitis treatments. The vaccine STARTVAC, which combines specific antigens and a special adjuvant, prevents and minimizes the effects of mastitis caused by *Staphylococcus aureus* (the main responsible for chronic mastitis) and *Escherichia coli* (causative agent of acute clinical mastitis). **INDICATIONS: Cows and Heifers:** To prevent Mastitis. For herd immunisation of healthy cows and heifers, in dairy cattle herds with recurring mastitis problems, to reduce the incidence of sub-clinical mastitis and the incidence and the severity of the clinical signs of clinical mastitis caused by *Staphylococcus aureus*, coliforms and coagulase-negative staphylococci. The full immunisation scheme induces immunity from approximately day 13 after the first injection until approximately day 78 after the third injection (equivalent to 130 days post-parturition). **SIDE EFFECTS:** Slight to moderate transient local reactions may occur after the administration of one dose of vaccine, which disappears within 1 or 2 weeks at most. **ADMINISTRATION ROUTE:** Intramuscular, into the neck muscles. The injections should be preferably administered on the alternate sides of the neck. It is advisable to administer the vaccine at a temperature between +15 and +25 °C. Shake before use. **DOSEAGE: Cows and Heifers:** 2 ml/animal. Generally, the following vaccination programme is recommended: **First injection:** at 45 days before the expected parturition date, **Second injection:** 35 days thereafter (corresponding to 10 days the expected parturition date), **Third injection:** 62 days after the second injection (equivalent to 52 days post-parturition). The full immunisation programme should be repeated with each gestation. The whole herd should be immunised. Immunisation has to be considered as one component in a complex mastitis control program that addresses all important udder health factors (e.g. milking technique, dry-off and breeding management, hygiene, nutrition, bedding, cow comfort, air and water quality, health monitoring) and other management practices. Can be used during pregnancy and lactation. **WITHDRAWAL PERIOD: 0 days. SPECIAL PRECAUTIONS:** Store at +2 to +8 °C, avoiding freezing. Protect from light. **PACKAGING:** Pack of 20 vials of 1 ds, 5 ds vial, 25 ds bottle. Under veterinary prescription. Marketing authorisation holder: Laboratorios Hipra, S.A. la Selva, 135, 17170-AMER (Girona) SPAIN. Legal category: UK: [POM]. ROI: [POM]. Marketing authorisation numbers: 1 dose: EU/2/08/092/003; 5 doses: EU/2/08/092/004; 25 doses: 2/08/092/006. Use medicines responsibly.



Laboratorios Hipra, S.A.
Avd. la Selva, 135
17170 Amer (Girona)
Spain

Tel.: (34) 972 43 06 60
Fax: (34) 972 43 06 61
hipra@hipra.com
www.hipra.com