Different European Perspectives on the Treatment of Subclinical Mastitis in Dairy Cows

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Abstract

As part of the European Network for Optimization of Veterinary Antimicrobial Treatment (ENOVAT), a webinar on the topic "Different European Perspectives on the Treatment of Subclinical Mastitis in Lactation" was held on September 21, 2022, during which eight mastitis experts from different European countries (France, Hungary, Italy, the Netherlands, Portugal, Slovenia, Sweden, and the United Kingdom) presented their treatment approaches for subclinical mastitis during lactation. The information provided by the experts is based on experience, guidelines, surveys, and opinions of the university to which they belong. The aim of this study was to compare the therapeutic approaches to identify commonalities and differences. It was not the aim of the webinar to identify the best approach for the treatment of subclinical mastitis, but to better understand the different approaches in the different countries in order to find starting points for long-term harmonization. The definition of subclinical mastitis varies from country to country. However, in all countries the definition is based on the presence of increased somatic cell count (SCC) in the quarter milk but without clinical signs or visual changes in the milk and is usually caused by an intramammary infection (IMI). Particularly regarding the cell count limit, the definitions differ between countries. In all participating countries, treatment of subclinical mastitis is not standard practice. This varies from a general rejection of treatment during lactation to treatment in special situations, involving the risk of penalties if a certain threshold of cells in the bulk tank milk is exceeded. Diagnostically, in its simplest form, subclinical mastitis in cows is determined by an individual cow SCC being greater than a threshold. The SCC numbers are most commonly received via regular monthly dairy herd milk recording (DHI). It was reported that the importance of bacteriological analyses has increased significantly, leading to more targeted interventions. Whether a cow is treated or classified as unworthy of treatment depends on various factors such as age, fertility, pathogens present, and duration of intramammary infection (chronicity) based on DHI data and other criteria.

It was reported that in some countries a trend over the past ten years is evident showing a decrease in treatment frequency and a concomitant decrease in antibiotic use, while the use of alternative agents, often non-evidence-based, is increasing. At the same time, no increase in the bulk milk somatic cell count (BMSCC) is evident but rather BMSCC continues to decrease despite the reduced use of antibiotics and increased use of alternative agents implying better cow management.

The aim of the Enovat project on mastitis therapy is to produce evidence-based guidelines. The collection of expert opinions is an essential step towards a better understanding of mastitis therapy in different European countries, especially in the absence of common guidelines. Unfortunately, the quality of databases in European countries on the use of antibiotics in mastitis therapy is still rather imprecise. Therefore, to understand the practices and make them more evidence-based in the long run, it is even more important to hear the opinions of key opinion leaders. In principle, there is common ground and consensus on certain points of treatment. For example, treatment is generally considered appropriate only after bacteriological diagnosis. However, the results of the webinar show that there are still differences in the definition and treatment of subclinical mastitis. Only through exchange and communication, a reasonable guideline for the treatment of subclinical mastitis can be found. The exchange could generate important research questions. Answering these questions could contribute to the development of common evidence-based guidelines.

Keywords: mastitis; subclinical bovine mastitis; lactational treatment; treatment approaches; Europe; ENOVAT

Introduction

Subclinical mastitis is an inflammatory response of the mammary gland that may be the result of an intramammary infection (IMI). The threshold for defining subclinical mastitis varies. In Germany, a threshold of more than 100,000 cells/ml milk at the quarter or individual animal level is commonly described and generally accepted [1]. Subclinical mastitis leads to decreased milk yield, an increase in somatic cell count (SCC), increased risk of clinical mastitis, increased culling rate, and a possible spread of pathogens [2-5]. This results in major economic losses in the dairy industry. It is important to develop effective concepts to reduce the prevalence of subclinical mastitis. The IMI present in subclinical mastitis can be stopped by self-cure or by therapy. Antibiotic therapy can take place directly after identifying subclinical mastitis, with or without bacteriologic diagnostics, or at the end of lactation – at drying-off. IMIs can cause inflammation that persists beyond the initial infection and may progress to clinical mastitis. The frequency of this disease on the dairy farm, the microorganisms involved, the bacteriological and cytological cure rates that can be achieved, and societal opinions on the use of antibiotics in dairy farming are criteria that should be considered when making decisions [5]. There are many possible approaches in the management of subclinical mastitis. Although the efficacy and economic effects of subclinical mastitis treatments during lactation are in general questionable [6-7], such treatments may be of value in recently acquired subclinical mastitis cases [8-9].

The European Network for Optimization of Veterinary Antimicrobial Treatment (ENOVAT) aims to optimize the treatment of subclinical mastitis in order to develop guidelines for antimicrobial treatment and improving microbiological diagnostic procedures. To further advance the development of treatment strategies and the prudent use of antibiotics in the therapy of subclinical mastitis, it is important to compare and interpret current strategies and approaches in different European countries. Therefore, a webinar entitled "Different European Perspectives on the Treatment of Subclinical Mastitis in Lactation" was held as part of working Group 4 of the ENOVAT project, in which 8 mastitis experts from different European countries described how subclinical mastitis is usually treated in their countries. The aim of the study was to record and compare different therapeutic strategies and approaches and to highlight similarities and differences. The exchange should lead to a convergence of treatment strategies in European countries in order to create a common standard for the treatment of subclinical mastitis. The scientific exchanges between key opinion leaders (practicing veterinarians and researchers) can help identify the scientific questions that need to be addressed in future research. This can improve the identification of treatable subclinical mastitis and optimize therapy.

Materials and Methods

To reach the goal of optimizing the therapy of subclinical mastitis in veterinary medicine, members of the ENOVAT project aim to generate an overview of the current state of veterinary treatment and microbiological diagnostic procedures in Europe. To gain an understanding of the current treatment methods for subclinical mastitis in lactation in Europe, an international webinar was scheduled. Various mastitis experts from several European countries were contacted via email and asked to participate in the webinar. The article provides expert opinions on udder health of dairy cows from different European countries. The selection of European countries is based on the different production conditions and aims to provide an overview of the variation of perspectives and approaches in European countries. The speakers from the respective countries were selected because they are proven experts with practical relevance and represent their countries in corresponding bodies - such as the European Mastitis Panel (EMP) or the Nordic Mastitis Network (NKJ). The selection was made by the last author (VK), who is well connected within European mastitis researchers and key opinion leaders. Mastitis experts from France (F), Hungary (H), Italy (I), the Netherlands (NL), Portugal (P), Slovenia (SLO), Sweden (S) and the United Kingdom (UK) took part.

The mastitis experts were asked to prepare a 10-minute presentation on treatment approaches for subclinical mastitis in their country. They were instructed to base their presentation on what is recommended by doctrine or current research in their country and, if applicable, to classify the extent to which this is common practice. To provide some orientation, a list of possible aspects to focus on in their presentations was prepared in advance. The list included the following:

- 1. How is subclinical mastitis defined?
- 2. What is the cell count threshold? How is subclinical mastitis diagnosed (SCC, other diagnostic systems)? Who diagnoses subclinical mastitis on the farms (farmer, manager, veterinarian)?
- 3. At what point are subclinical mastitis cases treated? Who makes the treatment decision? Are they not treated after a certain lactation day?
- 4. Are animals excluded from subclinical antibiotic mastitis therapy due to unworthiness for therapy? Which criteria for unworthiness for therapy are used?
- 5. Are the results of cyto-microbiological examinations used for animal and/or therapy selection?
- 6. Is the choice of therapy made on the basis of key pathogens (frequent findings on the farm) or is a standard therapy used?
- 7. Are the cows treated at all? Is the treatment an emergency measure (so that the herd milk cell count drops, or to prevent the spread of pathogens on the farm), or is it routine treatment?
- 8. What is the average duration of treatment? How are antibiotic treatments usually administered? Are alternatives to antibiotics used? Are there differences in the treatment of recently acquired subclinical mastitis and chronic subclinical mastitis?
- 9. Are there differences in the treatment of subclinical mastitis between the different farming practices (organic/conventional)?
- 10. Have there been significant changes in the treatment of subclinical mastitis in the last 10 years? Are there emerging trends that will change the way subclinical mastitis is managed?
- 11. Do you have any other comments?

The presenting veterinarians are active in a wide variety of fields related to cattle health and mastitis control (Table 1). The speakers were free to choose whether to address all of the topics on the orientation list in their presentation or to choose a few points that they felt were particularly relevant. Around 100 listeners followed the webinar and actively participated via chat. The webinar took place within the framework of a virtual mobility grant from the ENOVAT project to strengthen existing networks, share knowledge, and learn new techniques. It was held online via a platform of Copenhagen University, Denmark and was recorded for subsequent editing. In order to give their answers to the questions posed, different methods were chosen (national guidelines, own experiences/expert knowledge, or interviews with experts/clinicians in their own country) to answer the different aspects of the therapy of subclinical mastitis. The different approaches are briefly described below. They are listed in the order in which they were presented during the webinar.

Sweden: Dr. Persson Waller based her answers mainly on the Nordic guidelines and the National (Swedish) guidelines for mastitis therapy. A study from 2021 by Rajala-Schultz et al. described the implementation of the Nordic Guidelines and explained that the guidelines are a supplement to the legal regulations on the dispensing of antibiotics and provide guidance on the use of antibiotics [10]. Her information can be seen as an approach to subclinical mastitis in the Scandinavian countries.

Mastitis expert	Country Sweden	Field of expertise	
Karin Persson Waller		State veterinarian at the National Veterinary Institute (SVA), DVM^1 , PhD^2	
Christian Scherpenzeel	The Netherlands	Dairy veterinary specialist, DVM, PhD at Royal GD Animal Health	
Jože Starič	Slovenia	Professor, DVM, MSc ³ , PhD, spec. Buiatrics at Veterinary Faculty, University of Lj bljana	
Luís Pinho	Portugal	Lecturer at the University of Porto teaching milk hygiene/mastitis, Dairy consultan on udder health, DVM, PhD	
Peter Kovacs	Hungary	Lecturer at the University of Veterinary Medicine in Budapest at the Department o Animal Hygiene, Herd-Health and Mobile Clinic and an udder health consultant, Ph	
Olivier Salat	France	Practitioner with a special focus on mastitis control in Saint-Flour in the Cantal regio of France, DVM	
Andrew Biggs	The United Kingdom	Practitioner with a special focus on mastitis control in Devon, UK, and head of h own mastitis lab, DVM	
Paolo Moroni	Italy	Professor at University of Milan at the Department of Veterinary Medicine and A imal Sciences; Associate Professor in Practice at Cornell University, USA, DVM, Pf	

The Netherlands: Dr. Scherpenzeel based his comments on the different topics with his own opinion respectively on the opinion of Royal GD Animal Health and the guidelines and dairy formulary of the Royal Dutch Veterinary Association (KNMvD). The approaches of the Netherlands may be representative for the basic ideas of the "Benelux countries" for the therapy of subclinical mastitis.

Slovenia: Dr. Starič stated his personal opinion as well as speaking on behalf of the University of Ljubljana, for which he speaks. Since the situation in Slovenia is similar to other countries in Southeastern Europe in terms of cattle population, herd size, etc., his comments can be considered as representative for this region.

Portugal: Dr. Pinho had sent a survey with the questions of the orientation list to five specialized veterinarians in bovine mastitis in Portugal, eleven clinicians, eight managers, and twenty-one farmers representing all four dairy basins from Portugal mainland and the Azores Islands and incorporated their responses into his presentation.

Hungary: Dr. Kovacs presented the findings of an (online) survey he had conducted where practicing colleagues were asked to assess the given questions.

France: Dr. Salat referred to the French Guidelines in his comments and included his own experience. In France, new guidelines for mastitis therapy are in progress by commission Qualité du lait SNGTV 2023 (forthcoming).

The United Kingdom: Dr. Biggs based his remarks primarily on his own opinion and experience of over 40 years gained as a practicing veterinarian, providing continuing education for veterinarians, and as director of his own mastitis laboratory, as well as speaking to other UK mastitis key opinion leaders.

Italy: Dr. Moroni used a survey to obtain the opinions of ten practicing veterinarians, three veterinarians working for pharmaceutical companies, two veterinarians working in laboratories and one university, and presented these findings in his lecture.

Results and Discussion

Looking at the therapeutic approaches for subclinical mastitis during lactation in the European countries considered, both differences and similarities become apparent. Table 2 provides an overview of the comparative management of subclinical mastitis. A more detailed description of the content of each country and the sources used by the speakers can be found in Appendix A. The results are based on national guidelines (e.g. F, S), surveys of practicing colleagues and experts (e.g. H, I, P) or the own experience and knowledge (e.g. UK, SLO) of the experts who are key opinion leaders in their field. This must be considered in the context of the discussion in order to classify the influence of the speakers on the results.

1a. Definition of subclinical mastitis	IMI ¹ ; no clinical signs, no visible changes in milk	SCC ² >100,000-150,000 cells/ mL	SCC >200,000 cells/mL	Not specified
	All countries	Ş3	H ⁴ , I ⁵ , P6, SLO ⁷ , NL ⁸ (>250,000), UK ⁹ (most >400,000), F ¹⁰ (2x month in a row >200,000)	/
1b. Definition differs between multiparous and primiparous	Yes	No	Not Specified	
	F, NL, S, SLO	I, P	H, UK	
2. Diagnostics	SCC (monthly DHI ¹¹)	CMT ¹²	AMS ¹³ (color, temperature, conductivity, etc.)	
	All countries	F (rarely), H, I, P, S, SLO	F, H, NL, PT, S, SLO, UK	
3. Person – treatment decision	Mostly vet	Mostly farm personnel	Both equal	Not specified
	Н, Р, UK	/	F, I, NL, S, SLO	/
4. Bacteriological analysis	Routinely	Often	Rarely	Not specified
	F, NL, S, UK	H, I, P, SLO	/	/
5. Cow – treatment decision	Just "cows most damaging" to BMSCC ¹⁴	Just herds with overall BMSCC issues $ ightarrow$ penalties	Usually not treated at all (excl. dry off)	Monthly routine
	SLO	F, H, P (mostly), SLO, UK (in~5 to 10 % of herds with BMSCC price penalty issues)	I, S, UK (mostly)	P (smaller farms)
6. Time of treatment	At dry off	At any time	In early lactation	Not specified
	All	H, SLO	UK	I, NL
7. Definition for treatment unworthy cows	Multiple high SCC in a row (3x >700,000)	3 months above 800,000 cells/ ml	Decision depends on age, pathogen, fertility, chronicity and other criteria	Not specified
	F, UK	Р	F, H, P, S, SLO	I, NL
8. Way of treatment	Just intramammary AB ¹⁵	Intramammary + parenteral AB	Alternatives (Excl. NSAIDs ¹⁶)	Not specified
	H, I, S, SLO, UK (long-acting at dry off)	F, H (rarely), P, SLO	Н	NL
9. Changes in last 10 years	Critically important antimicro- bials restricted/ enforcement of legislation on the reduction of antimicrobials use in farm animals	Less treatment because of crisis of milk pricing	Alternatives (NSAIDs etc.) increasing	BMSCC decreasing
	F, I, NL, P	Р	I, P, SLO	F, P, SLO, UK

¹intramammary infection, ² somatic cell count, ³ Sweden, ⁴Hungary, ⁵Italy, ⁶Portugal, ⁷Slovenia, ⁸the Netherlands, ⁹United Kingdom, ¹⁰France, ¹¹dairy herd improvement, ¹²California mastitis test, ¹³automatic

milking system, ¹⁴bulk milk somatic cell count, ¹⁵antibiotics, ¹⁶non-steroidal anti-inflammatory drugs

* Explanations of the results can be found in Appendix A.

Definition of subclinical mastitis

The definition of subclinical mastitis is mostly uniform in all countries represented. It is based on the presence of increased SCC in the quarter and single animal milk but without clinical signs or visual changes in the milk and is caused by IMI. Only the thresholds and the opinion, whether there are differences in the threshold for primiparous or multiparous animals, differ slightly (for thresholds see Table 2). The speakers also discussed the cell count limit at which a cow is considered worthy of treatment, if treatment is to be carried out. The circumstances under which treatment is carried out during lactation are described in more detail in the section "Treatment of subclinical mastitis". The SCC for a cow to be considered worthy of treatment is usually diagnosed at a cell count threshold of >200,000 cells/mL, in some cases even higher (see Table 2). In addition, according to Mr. Salat, the practice in France is that a SCC of >200,000 cells/mL must be present for at least two consecutive months. In Sweden, subclinical mastitis is diagnosed at a SCC of >100,000 cells/mL, but as the Swedish guidelines, as explained later, generally do not recommend treatment during lactation, there is no specific threshold for defining subclinical mastitis worthy of treatment.

Diagnostic of subclinical mastitis

Diagnostics also show a predominantly uniform picture. SCC from the monthly DHI is used in all countries considered to identify cows with subclinical mastitis. In addition, there are California Mastitis Test (CMT) results, usually performed by farmers to identify the infected quarter, as well as milking machine milk conductivity meter, milk flow, and quantity meter during self-monitoring. For automatic milking systems, various factors such as color, milk temperature, conductivity, etc. are also included in the diagnosis.

In all countries, the use of bacteriological analyses to identify pathogens present and to select further interventions is an essential element. This procedure is routine in F, NL, S and UK. In H, I, P and SLO, bacteriological analyses are also used frequently or with increasing frequency, but still veterinarians or farmers work without a bacteriological result.

Treatment of subclinical mastitis

Treatment of subclinical mastitis in lactation in most countries is used only under special conditions or is basically excluded. It frequently takes place at drying off or is postponed from a particular lactation day until drying off. In P, treatment is postponed from the 150th day of gestation until dry-off. Exceptions are possible especially in smaller farms. In H and SLO, treatment may occur at any time during lactation. In the UK, it is becoming increasingly common to treat new IMIs in early lactation on farms with good practices and udder health to prevent the spread of pathogens as early as possible, according to Andrew Biggs.

When treatment does occur, opinions differ as to which cows should be treated. Different reasons are given for treatment. In SLO, there are farms which only treat cows that have the most negative impact on BMSCC, which are often those animals with the most chronic IMIs and likely to be treatment unworthy, according to Dr. Starič. If treatment is carried out in some countries (F, H, P, SLO), it is because the cell count in the tank milk is so high that penalties are to be expected. Treatment during lactation is generally excluded in I, S and most of the UK. In P it is common, especially on smaller farms, that treatment of subclinical mastitis is part of the monthly routine. In S, where treatment during lactation is normally excluded, an exception from the recommendation is made in herds with *Streptococcus (Sc.) agalactiae*-infections (Åsa Lundberg, Växa, Stockholm, Sweden, personal communication 2019). The literature also describes the treatment of subclinical mastitis as an option, mainly during the dry period, but sometimes also during lactation. The aim is to reduce the duration of the infection and its transmission to other cows [11-12]. However, studies on whether antibiotic treatment helps in the long term are rare and, when available, are limited to specific cases such as subclinical mastitis caused by *Staphylococcus (S.) aureus*. One study showed that treatment of subclinical mastitis during lactation reduced SCC but had no positive effect on milk yield or the development of clinical mastitis. It is concluded that treatment should only be carried out in exceptional cases [5]. This conclusion is consistent with the consensus of the speakers.

There are different approaches to decide whether a cow is unworthy of treatment, with most countries indicating that the decision is made on an animal-by-animal basis using various parameters such as age, pathogen present, chronicity, fertility, and other factors. In all countries, animals with certain pathogens that have been associated with little to no chance of a bacteriological cure are no longer treated with antibiotics [13]. The speakers mentioned *S. aureus*, yeasts, and *Prototheca* spp. as examples. In F, P and UK, multiple exceedance (mostly three times) of a certain threshold (F; UK: 700,000 cells/mL, P: 800,000 cells/mL) is described as a decision criterion against antibiotic treatment. This ensures that cows with chronic or recurrent mastitis are not repeatedly treated with antimicrobials [14]. When treatment is administered, it is predominantly intramammary. In some cases, in F, H, P and SLO, combined intramammary and parenteral treatment is also used sometimes. Studies have shown that this can have a positive effect on reducing SCC and reducing the spread of pathogens in the herd [15-16]. In H, alternative, non-antibiotic preparations are used regularly in daily practice.

Changes in recent years

The representatives of many countries describe changes in the treatment of subclinical mastitis in the last ten years. In the context of the restriction of certain antibiotic preparations, there has been a decrease in treatment (I, NL, P, UK). As this is mainly a matter of restricting antibiotics, the use of alternative agents is increasing, although their effect cannot be considered evidence based.

Despite reduced or no treatment of subclinical mastitis during lactation, there has been a decrease in BMSCC in some countries over the past ten years or the trend seems to be towards a further decrease.

Recommendations for future research

The differences observed between the participating countries as well as the developments in recent years, mainly related to restrictions on the use of antibiotic products in the treatment of subclinical mastitis in lactation, raise some research questions that need to be addressed by the scientific community in the near future:

- Is treatment of subclinical mastitis with antimicrobials during lactation necessary and useful?
- Is treatment of subclinical mastitis at all economically and healthily sustainable?
- Does treatment of subclinical mastitis have a detectable effect on the level of BMSCC?
- On which farms does treatment have a lasting effect or is it acceptable as an emergency measure?
- Does increased use of bacteriological analysis lead to a more targeted treatment and thus better cure rates?
- Does the increased use of bacteriological analysis lead to decreased treatment incidence?
- Can treatment of subclinical mastitis be limited to certain pathogens, certain time points during lactation, certain antimicrobials?
- Does the cure rate decrease if subclinical mastitis with proven infections is not treated within two months?
- Does a shift in pathogen distribution occur in the absence of treatment with antimicrobials?

Conclusions

The effectiveness of treatment of subclinical mastitis during lactation has been questioned for a long time. The basic consensus in European countries is that subclinical mastitis should not be treated during lactation. However, in exceptional cases or under certain conditions, it can have a visible positive effect. These conditions include, for example, the presence of bacteriological tests and a good udder health on the farm. It is therefore necessary to test and define the exact conditions under which treatment is appropriate. It can be concluded that in the future, treatment will be based on bacteriological analysis and precise cow selection. This will increase the cure rate and reduce the use of antibiotics.

In many of the participating European countries, there are recognizable trends that point to a reduction in the use of antibiotics. The use of antibiotic drugs is already decreasing in many countries due to pressure from the government, and the routine use of bacteriological analyses and preventive measures are on the rise. The successes achieved in the dairy industry in the Nordic countries with minimizing treatments can be seen as a positive example for other countries. The findings addressed in this manuscript are limited in that they are based on national guidelines, the opinion/experience or surveys of experts and not based on new studies. However, the data can be used to identify relevant questions that should be answered

scientifically, because the speakers are key opinion leaders from their respective countries. The randomized clinical trials based on these research questions, as well as the recognizable common ground that has become clear in the webinar, can then contribute to the development of future guidelines.

Disclosure of conflicts of interest

The authors declare no potential conflicts of interest.

Compliance with Ethical Standards

This study has been conducted in compliance with ethical standards.

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Appendix

Treatment methods for subclinical mastitis in lactation

Sweden: A network of mastitis researchers in the Nordic countries of Denmark, Finland, Norway, and Sweden have developed cooperative Nordic guidelines for mastitis therapy [17]. Practices, legislation, and availability of drugs, mastitis-associated pathogens, and antimicrobial resistance differ to some extent among these countries, but the general approach is similar. There are explicit Swedish guidelines (National guidelines) on mastitis therapy and use of antibiotics available, but these are based on the Nordic guidelines [18]. The definition of subclinical mastitis involves intramammary infection (IMI), without clinical signs of mastitis. At the cellular level, an SCC of >100,000-150,000 cells/mL is considered as mastitis. At cow inspection (DHI, animals are classified into udder health classes based on SCC from 2-3 monthly milk recordings. From an udder health class of 3 and higher (corresponding to >130,000 cells/mL), inflammation is assumed. Diagnosis is usually based on cow control data (monthly SCC), CMT, or in automatic milking systems on conductivity or other parameters. To differentiate between subclinical mastitis and infectious subclinical mastitis, bacteriological examination is essential. This procedure is regulated in the aforementioned guidelines. The Nordic and National guidelines describe that subclinical mastitis generally has a too high self-cure or a too low cure rate in relation to the cost of treatment within lactation. Only herds where it is intended to eradicate Sc. agalactiae are generally exempt from this principle. This means that no treatment of subclinical mastitis with antibiotics during lactation is generally administered. Treatment is performed by other measures, such as group sorting at milking, drying off affected udder quarters, and culling of chronic cases. Treatment with antibiotics is used only at dry-off in selected cases. Since only a few antibiotic products are available (mainly benzyl penicillin), antibiotic treatment is basically based on milk sample bacteriology. In Sweden, there have been no major changes in the recommendations on treatment of subclinical mastitis during lactation over the past 10 years. There are recently introduced (developed in 2021) guidelines for dry cow therapy [19].

The Netherlands: In the Netherlands, there were about 1,500,000 cows in 2021. The average SCC is about 180,000 cells/mL. Regarding the definition of subclinical mastitis, a distinction is made in the Netherlands between heifers and multiparous cows. For heifers, a threshold of 150,000 cells/mL and for multipara 250,000 cells/mL is set. Diagnostically, this is mainly determined via test-day results (DHI). About 85 % of farmers routinely use the DHI records. For this purpose, mainly cow-level thresholds, but recently also quarter-level SCC thresholds, are used. In the automatic milking systems, conductivity and other factors are also considered. In the Netherlands, there is a farm-specific dairy formulary that contains an official list giving details of prescribable medicines for specific indications. The treatment of subclinical mastitis is based on the resulting herd-specific guidelines. The aim of treatment should be to prevent the transmission and development of persistent infections [20]. For achieving successful cures, the right selection of cows for treatment must be made. Criteria are cows with less than three lactations, less than two infected quarters, an SCC less than <1,000,000 cells/mL, a short duration of infection, low growth in culture, and sensitivity for the antimicrobial of first preference. Other cows are more likely to be considered unworthy of therapy. In the last 10 years, political pressure to reduce antimicrobial use has increased in the Netherlands. Both farmers and veterinarians are obliged to contribute to a substantial reduction in antibiotic usage. The use of antibiotic drugs has decreased significantly. At the same time, the average BMSCC has also decreased, although a slight increase was observed in the last four years.

Portugal: According to Luis Pinho (personal communication, 2023), in Portugal, the number of dairy cows was about 230,000 with an average herd size of 58 to 236 dairy cows depending on the region (highest in Alentejo, lowest in the Azores). In 2022, milk production was about 2 million tons, with a slightly increasing level and an average productivity of 305 DIM of about 9,500 with a significant increase in recent years. The average cell count shows a decreasing level with an average value of 242,000 cells/mL in 2019. In Portugal, according to the survey, the definition of subclinical mastitis generally does not distinguish between primiparous and multiparous cows. The cell count limit is 200,000 cells/mL in combination with no macroscopic alterations in milk or clinical signs in the udder or cow. DHI-testing was performed in 52 % of the national farms [21]. Mainly subclinical mastitis is diagnosed by SCC. Additionally, farmers use CMT for fresh cows and at drying off. In accordance with the survey, treatment of subclinical mastitis is carried out when the number of problem cows (noted in the DHI report) increases or the BMSCC increases to such an extent that penalties are to be expected. Treatments are based on protocols/decisions by the assistant veterinarian or as indicated by the veterinary microbiologic laboratory. For this purpose, microbiological tests are often requested by the farmer or carried out directly by on farm-culture systems. Therapy is largely based on the type of mastitis and cow characteristics. Therapy can be performed at any time but is usually postponed after the 150th day of gestation until the dry period. In order to define cows unworthy of therapy, individual analyses are carried out. Fertility, age, number of clinical

mastitis and treatments in the same lactation, pathogens (especially *S. aureus* and pathogens that are not treatable with AB) as well as chronic cases (3 or more months over 800,000 cells/mL) are considered. Usually, intramammary treatment is used, but parenteral treatment may be applied in grazing systems or in chronic cases. Alternative agents, other than NSAIDs, are not used. In Portugal, from 2017 to 2021, the use of cefquinome and quinolones was increased due to the emergence of various products in the market, but since the beginning of 2022, the use of critically important antimicrobials (CIAs) is restricted to identification of causative bacteria and antibiograms. There was a change to other beta-lactam antibiotics. During the milk price crisis, subclinical infected cows were not treated or received delayed treatment. A lower incidence of contagious pathogens is visible in the last 10 years, which has also led to less treatment of subclinical mastitis (observational information from participants and personal communication SVA laboratory, SEGALAB laboratory, CAVC laboratory).

Hungary: In Hungary, there are mainly larger farms, so the average number of cows per farm was 455 (381 milked cows/farm). The total number of cows in Hungary was 420,000. Holstein Friesian is the predominant breed, but some farms also have Hungarian Simmental or Jersey. The main definition criteria for subclinical mastitis are an elevated SCC, no visible changes in the milk, no visible changes in the udder, and generally no clinical signs on the cows. In some cases, reduced milk production is also used as a criterion. The threshold value is mainly set at 400,000 cells/mL. However, lower (100,000-300,000 cells/mL) or even higher (500,000 cells/mL) thresholds are sometimes applied. Commonly, CMT and DHI test results (monthly SCC) are used for diagnosis. More rarely, electrical conductivity is also included as a factor. In Hungary, it is quite common for many farms to treat subclinical mastitis whenever necessary. Nonethless, there are also farms where treatment is only applied more than one month before the dry period, only at drying off, or only in the first month of lactation. In more than half of the cases, treatment is only performed during lactation in rare cases. However, only a few farms generally reject the treatment of subclinical mastitis during lactation. The main reasons for treatment are emergency measures to reduce the cell count and to prevent the spread of pathogens. For some farms, treatment is also a routine procedure. In most cases, intramammary treatment alone is used, but sometimes intramammary and parenteral treatment are used in combination. Besides antibiotics, some alternatives such as antibiotic-free infusions, boluses, NSAIDs, and creams/ointments are also used in Hungary. Microbiologic examinations are usually used for animal and therapy selection. Routine therapy is carried out less frequently. The microbiologic profile of subclinical mastitis is dominated by Streptococcus uberis and NAS (Non-aureus staphylococci). S. aureus, Prototheca (P.) bovis, yeasts, and Escherichia (E.) coli as well as a few other pathogens are also observed. Several reasons are given for the unworthiness of a cow for therapy. Among other things, lameness, infertility, certain pathogens (e.g., S. aureus, P. bovis), disorders of the udder structure, low milk production, and several unsuccessful treatments are given as factors. Recently, due to new regulations on the use of antimicrobial substances, there has been an increase in the use of microbiological examinations and requests for antibiograms.

France: From the French point of view, subclinical mastitis is defined as an increased somatic cell count without clinical signs at two consecutive monthly controls. There are differences in the SCC thresholds between the views of veterinarians (>200,000 cells/mL) and dairy control technicians (>300,000 cells/mL) as well as between primiparous (>150,000 cells/mL) and multiparous animals. A higher SCC is usually indicated for multiparous animals, but there is no general value. The monthly SCC check-up is also the main diagnostic method. Only in automatic milking systems are other factors also taken into account and on an individual scale, CMT is also applied. Treatment is mainly performed when farms are at risk of having milk collection stopped. This is the case at a threshold of 400,000 cells/mL in the bulk tank milk. Farmers also decide individually to treat animals if the cell count in the bulk tank milk is significantly elevated or if they feel that the situation is currently worsening significantly. As the results of treatment are often unsatisfactory, a bacteriological examination and an assessment of the animal's condition should always be carried out beforehand, according to Olivier Salat. Blind treatment should be rejected. After preliminary assessment of the cows, there are three options. Treatment during lactation, waiting for dry off therapy, or culling [22]. Olivier Salat stated that several criteria should be considered before treatment. In the literature the age of the cow, the chronicity of the mastitis, the parity, the number of infected guarters, other udder abnormalities, and the presence of micro-abscesses are cited as factors [23]. If these criteria indicate that treatment will be unsuccessful, consideration must be given to whether therapy is appropriate. Other factors that classify a cow as unworthy of treatment are the isolation of certain pathogens (β-lactamase-producing S. aureus, gram-negative bacteria, Enterococcui), or if the cow has been in milk for too long (last two months of lactation). In France, the use of bacteriologic analyses, including Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF), has increased significantly. As a result, blind therapy should be almost non-existent.

The United Kingdom: In the UK, the number of dairy cows is approximately 1,800,000. The milk production varies between 3,000 (extensive pasture based) to 12,000 kg (intensively housed all year round) per cow/year depending on the management and housing conditions. In the UK, as in most European countries, subclinical mastitis is defined as an intramammary infection without visible changes in the milk or udder. The most common limit is 200,000 cells/mL, although some farms also use lower (e.g., 150,000 cell/mL) limits. Diagnostics routinely include monthly DHI recordings (in 70% of herds), ad hoc individual cow somatic cell counts testing, CMT, and on farms with automatic milking systems, a variety of color, temperature, and conductivity measurements. A cultural examination is usually performed. Considering therapy, more than 10 years ago it was not uncommon to treat cows that had the greatest impact on BMSCC. Now the approach has changed, and treatment is mainly given in herds with BMSCC problems (~5-10 % of herds at any one time) that could lead to financial penalties. According to Andrew Biggs, cows with high SCC should not be treated indiscriminately or routinely. Animals are categorized and only relatively new IMIs are considered for treatment. In selected well managed herds with low BMSCC (<150,000 cells/mL), early treatment of recently identified subclinical IMIs can reduce the spread of pathogens [10-11], such as S. aureus reducing the need for lactation or dry cow antibiotic in cows where the spread may otherwise have occurred. Cows with new, first, or newly qualified chronic mastitis (only two consecutive high SCCs) may be considered most worthy of treatment. Cows later in lactation (e.g., three months before dry-off) are postponed for treatment until dry off. Two main criteria are used to sort out cows unworthy of treatment. Firstly, cows with multiple high SCC in the current lactation (e.g., 3x >700,000 cells/mL) and secondly, cows with multiple clinical cases (e.g., three clinical cases in current lactation). Only intra-mammary treatment of subclinical mastitis is recommended. Systemic (injectable) antibiotics should not be used. In recent years, the average BMSCC has dropped significantly and was in 2022 at 160,000cells/mL [24].

Italy: In Italy, based on the survey, the predominant opinion on the definition of subclinical mastitis is an increase in SCC >200,000 cells/mL without

clinical signs of mastitis. Only occasionally a distinction is made between multiparous and primiparous cows. The diagnosis is performed mainly by SCC or CMT. In some cases, electrical conductivity is included, especially in automatic milking systems. In the majority of cases, the treatment of subclinical mastitis is carried out in consideration of bacteriologic examination. Generally, cows are not treated during lactation in the presence of subclinical mastitis. There are exceptions, such as the presence of certain contagious pathogens or based on SCC and culture results. Some farms use a specific therapy depending on the bacteriological analyses and, standard therapies are still frequently used. Nonetheless, a trend from standard therapy to target therapy based on herd epidemiology can be seen. In Italy, treatment of subclinical mastitis with antimicrobials has decreased sharply over the past four years due to enforcement of legislation to reduce the use of antimicrobials in livestock. The trend will be to further reduce antibiotic treatment for subclinical mastitis, with increased use of alternative products and treatment of affected cows in the form of milk discharge from affected quarters and culling policies.

Slovenia: In Slovenia, the cattle population was 482,619 (126,617 cows/97,686 dairy cows) in 28,178 holdings (5,182 performed commercial dairy production) at the end of 2021 [25]. The majority (>98 %) of cattle farms are family farms. An average Slovenian dairy farm reared 18,9 dairy cows. There were only 41 farms with more than 100 cows. Unlike in many other European countries, the percentage of Holstein accounted for only 17,2 % of the total cattle population. Limousin, Charolais, crossbreeds, and Simmental made up the largest percentage thereof with 27,2 %. The average milk production was 7,292kg per standard lactation depending on the breed (Simmental 6,073kg/Holstein 8,545kg). In 2021, 60,4 % of test day milk samples obtained for DHI had an SCC of less than 150,000 cells/mL and 39,6 % of samples were above this level. The greater the number of cows per farm, the lower the average SCC was [26]. In Slovenia, the definition of subclinical mastitis is the same as in the other presented countries. However, a difference is made between primiparous and multiparous cows by veterinarians. The limit for primipara is set at >100,000 cells/mL and for multipara at >200,000 cells/mL. Suspicion of subclinical mastitis is mostly made by farmers based on milk records (80 % of dairy cows participated in DHI in Slovenia) and by milkers detecting decreased milk production, higher milk conductivity, or CMT. Veterinarians are always involved in mastitis diagnosis and treatment as they are legally exclusively responsible for antimicrobial drug prescribing and dispensing to farm animals. Especially in problematic herds (BMSCC >400,000 cells/mL), they are often involved in mastitis control program development. The number of farms performing tests (culture) before drying off is increasing. Besides classical bacteriology, MALDI-TOF and polymerase chain reaction (PCR) are also available in Slovenia. Treatment is mainly administered on farms with overall BMSCC issues and especially with cows that negatively affect the BMSCC. These cows usually have chronic IMI and are partly unworthy of treatment. There are farms that perform microbiologic testing before treatment, but blanket treatment is also common. Generally, the decision whether to treat cows during lactation is based on the pathogen present, the farm, and the veterinarian's experience. Intramammary treatment is performed either solely or in combination with parenteral administration. Blanket antimicrobial treatment at drying off is common. The decision whether a cow is considered unworthy of treatment depends on age, the pathogen present, fertility, and other factors. In Slovenia, it is observed that the use of alternatives has increased in the last ten years.

References

- 1. DVG (Deutsche Veterinärmedizinische Gesellschaft [German Veterinary Association]). Leitlinien zur Bekämpfung der Mastitis des Rindes als Bestandsproblem [Guidelines for combating bovine mastitis as a herd problem], 2012, 5th edition. Gießen, Germany: Deutsche Veterinärmedizinische Gesellschaft (DVG).
- 2. Zadoks RN, Allore HG, Barkema HW, Sampimon OC, Gröhn YT, Schukken YH. Analysis of an Outbreak of Streptococcus uberis Mastitis. Journal of Dairy Science. 2001 Mar;84(3):590–9. doi:10.3168/jds.S0022-0302(01)74512-2.
- 3. Miller RH, Norman HD, Wiggans GR, Wright JR. Relationship of Test-Day Somatic Cell Score with Test-Day and Lactation Milk Yields. Journal of Dairy Science. 2004 Jul;87(7):2299–306. doi:10.3168/jds.S0022-0302(04)70051-X.
- van den Borne BHP, Vernooij JCM, Lupindu AM, van Schaik G, Frankena K, Lam TJ, Nielen M. Relationship between somatic cell count status and subsequent clinical mastitis in Dutch dairy cows. Preventive Veterinary Medicine. 2011 Dec;102(4):265–73. doi: 10.1016/j.prevetmed.2011.07.013.
- 5. van den Borne BHP, van Schaik G, Lam TJGM, Nielen M, Frankena K. Intramammary antimicrobial treatment of subclinical mastitis and cow performance later in lactation. Journal of Dairy Science. 2019 May;102(5):4441–51. doi:10.3168/jds.2019-16254.
- Barlow JW, Zadoks RN, Schukken YH. Effect of lactation therapy on *Staphylococcus aureus* transmission dynamics in two commercial dairy herds. BMC Veterinary Research. 2013 Jan 1;9(1):28–8. doi:10.1186/1746-6148-9-28.
- Steeneveld W, Swinkels JM, Hogeveen H. Stochastic modelling to assess economic effects of treatment of chronic subclinical mastitis caused by Streptococcus uberis. Journal of Dairy Research. 2007 Oct 9;74(4):459–67. doi:10.1017/S0022029907002828.
- van den Borne BHP, van Schaik G, Lam TJGM, Nielen M. Therapeutic effects of antimicrobial treatment during lactation of recently acquired bovine subclinical mastitis: Two linked randomized field trials. Journal of Dairy Science. 2010 Jan;93(1):218–33. doi: 10.3168/jds.2009-2567. PMID: 20059920.
- van den Borne BHP, Halasa T, van Schaik G, Hogeveen H, Nielen M. Bioeconomic modeling of lactational antimicrobial treatment of new bovine subclinical intramammary infections caused by contagious pathogens. Journal of Dairy Science. 2010 Sep;93(9):4034–44. doi:10.3168/jds.2009-3030.
- 10. Rajala-Schultz P, Nødtvedt A, Halasa T, Persson Waller K. Prudent Use of Antibiotics in Dairy Cows: The Nordic Approach to Udder Health. Frontiers in Veterinary Science. 2021 Mar 5;8. doi:10.3389/fvets.2021.623998.
- 11. Barkema HW, Schukken YH, Zadoks RN. Invited Review: The Role of Cow, Pathogen, and Treatment Regimen in the Therapeutic Success of Bovine *Staphylococcus aureus* Mastitis. Journal of Dairy Science. 2006 Jun;89(6):1877–95. doi:10.3168/jds.S0022-0302(06)72256-1.
- 12. Barlow J. Mastitis Therapy and Antimicrobial Susceptibility: a Multispecies Review with a Focus on Antibiotic Treatment of Mastitis in Dairy Cattle. Journal of Mammary Gland Biology and Neoplasia. 2011 Oct 9;16(4):383–407. doi:10.1007/s10911-011-9235-z.
- 13. Ahlman T, Berglund B, Rydhmer L, Strandberg E. Culling reasons in organic and conventional dairy herds and genotype by environment interac-

tion for longevity. Journal of Dairy Science. 2011 Mar;94(3):1568-75. doi:10.3168/jds.2010-3483.

- 14. Ruegg PL. Antibiotic treatments for bovine mastitis. American Association of Bovine Practitioners Conference Proceedings. 2013 Sep 19;72–8.
- St Rose SG, Swinkels JM, Kremer WD, Kruitwagen CL, Zadoks RN. Effect of penethamate hydriodide treatment on bacteriological cure, somatic cell count and milk production of cows and quarters with chronic subclinical Streptococcus uberis or Streptococcus dysgalactiae infection. J Dairy Res. 2003;70(4):387-394. doi:10.1017/s0022029903006460.
- 16. Owens WE, Watts JL, Boddie RL, Nickerson SC. Antibiotic Treatment of Mastitis: Comparison of Intramammary and Intramammary Plus Intramuscular Therapies. Journal of Dairy Science. 1988 Nov;71(11):3143–7. doi:10.3168/jds.S0022-0302(88)79915-4.
- 17. Anonymous. 2009. Nordic guidelines for mastitis therapy. The NMSM Annual Conference June 12, Lund, Sweden https://www.sva.se/media/ qsJjw2yb/nordic-guidelines-for-mastitis-therapy.pdf.
- 18. Anonymous. 2017. Guidelines for the use of antibiotics in production animals. Cattle, pigs, sheep and goats. The Swedish Veterinary Association, Stockholm, Sweden. SVS guidelines 2017.indd (svf.se).
- 19. National Veterinary Institute (SVA). Recommandations for dry cow therapy with antibiotics. 2021. http://juverportalen.se/media/1249/recommendations-for-dry-cow-therapy-with-antibiotics-210615.pdf.
- 20. Barlow JW, White LJ, Zadoks RN, Schukken YH. A mathematical model demonstrating indirect and overall effects of lactation therapy targeting subclinical mastitis in dairy herds. Preventive Veterinary Medicine. 2009 Jul;90(1-2):31–42. doi:10.1016/j.prevetmed.2009.03.016.
- 21. PublicaçãodeResultados2021[Internet].[cited2024Feb14].Available from:https://www.ruralbit.com/client_manager/files/1661941681-1903. pdf.
- 22. David V, Beaugrand F, Gay E, Bastien J, Ducrot C. Evolution of antimicrobial usages in dairy and beef cattle industries: state of progress and prospects. INRAE Productions Animales. 2019 Apr 16;291–304. doi:10.20870/productions-animales.2019.32.2.2469.
- 23. Samson O, Gaudout N, Schmitt E, Schukken YH, Zadoks R. Use of on-farm data to guide treatment and control mastitis caused by Streptococcus uberis. Journal of Dairy Science. 2016 Sep;99(9):7690–9. doi:10.3168/jds.2016-10964.
- 24. GB milk hygiene | AHDB [Internet]. ahdb.org.uk. Available from: https://ahdb.org.uk/dairy/gb-milk-hygiene.
- 25. Slika na naslovnici: Kmetija Stopar, krave cike Foto: Franci Stopar, osebni arhiv [Internet]. [cited 2024 Feb 14]. Available from: https://www. govedo.si/wp-content/uploads/2022/08/POROCILO_2021.pdf.
- 26. Sadar M, Jeretina J, Logar B, Opara A, Pečnik Ž, Perpar T, Podgoršek P. Rezultati kontrole prireje mleka in mesa Slovenija 2021/Results of Dairy and Beef Recording Slovenia 2021., Ljubljana: Kmetijski inštitut Slovenije (2022). www.govedo.si.

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