

## A REVIEW

# Treating mastitis in the cow – a tradition or an archaism

J.E. Hillerton and E.A. Berry

*Institute for Animal Health, Compton, Newbury, UK*

2004/1024: received 2 September 2004, revised 7 March 2005 and accepted 7 March 2005

1. Summary, 1250
2. Mastitis in the dairy cow, 1250
3. Causes of mastitis, 1250
4. Incidence of mastitis, 1251
5. Costs of mastitis, 1251
6. Progress in control of mastitis, 1252

7. Refinement of controls and use of antibiotics, 1252
  - 7.1 Treating mastitis in lactating cows, 1252
  - 7.2 Treating mastitis in nonlactating cows, 1253
8. Problems in control of mastitis, 1253
9. Conclusions, 1254
10. References, 1254

### 1. SUMMARY

Intramammary infection of the dairy cow is much less common than 40 years ago due to the impact of a control programme. This has changed the aetiology of the infection. The problem remains one of the costliest affecting farm animal health, estimated at £300 million annually in the UK. The successful control relies much on antibiotic treatments. The use of antibiotics in food animals is under challenge, particularly use of broad spectrum, multicomponent products and use of prophylactic treatment. Recent research has confirmed that antibiotic treatment is practical and cost-effective. Moreover, it remains essential for animal welfare.

### 2. MASTITIS IN THE DAIRY COW

Mastitis, an inflammatory response of the mammary gland caused usually by bacteria, is probably the most costly of the infectious, endemic diseases to affect dairy cows and other dairy species. Its impact is on animal production, animal welfare and the quality of the milk produced.

Mastitis is usually recognized by clinical signs, most obviously by abnormalities in the milk and the udder. The disease is usually local but may become systemic, although rarely, in immunocompromised animals. The incidence of the disease varies with the age of the animal and the stage of lactation, some 50% of cases occurring in the first 60 days or so after calving (Dodd and Jackson 1971). Clinical mastitis is less likely in younger animals. Reduction in clinical mastitis

has been a major success over the past 35 years, in countries with a developed dairy industry. The average rate has been reduced from some 150 cases per 100 cows per year to approximately 40 cases per 100 cows per year (IDF 2001).

Most mastitis occurs as a low grade infection, a subclinical state, which affects 10–15% cows, increasing milk leucocyte content, reducing milk production and increasing milk bacterial content. These all contribute to reduced milk value as a food and in monetary terms (Barbano 2004). The prevalence of such infections is a significant risk to uninfected animals in the herd as many mechanisms exist to expose the animals to new infection. Most commonly these include the common lying areas in housing or at pasture, the milking machine and successive contact of different cows or teats by the milker preparing the teats for milking.

### 3. CAUSES OF MASTITIS

Bacterial infection is the usual cause of mastitis with *Staphylococcus aureus*, *Streptococcus agalactiae*, *Strep. dysgalactiae*, *Strep. uberis* and various Gram-negative bacteria comprising the five common pathogen types, although more than 130 micro-organisms have been reported to cause disease in the mammary gland of cows (Watts 1988). *Staphylococcus aureus* causes relatively low grade mastitis but co-infections may lead to systemic disease and even death. Some 40 years ago this pathogen infected up to 50% of dairy cows and was the predominant cause of clinical disease, but now it is only a problem on particular farms and under particular circumstances. It is highly infectious and its control requires diligence.

The contagious, group B *Streptococcus*, *Strep. agalactiae*, has been virtually eradicated from the dairy cow by

Correspondence to: Dr J. Eric Hillerton, Institute for Animal Health, Compton, Newbury, Berks RG20 7NN, UK (e-mail: eric.hillerton@bbsrc.ac.uk).

appropriate use of penicillin-based antibiotics. This was one of the first successful and durable demonstrations of use of antibiotics to improve significantly animal health and food quality (Stableforth *et al.* 1949). The presence of *Strep. agalactiae* in any UK milk is an indicator of poor management and missing biosecurity. This problem may however, assume new international importance because it is much less well controlled elsewhere. This follows the recent demonstration (Bisharat *et al.* 2004) that Sequence Type 17 of *Strep. agalactiae*, of high importance in neonatal infections, has a possible bovine origin.

The type of *Streptococcus*-causing mastitis varies locally, with geography and animal husbandry. Overall, *Strep. uberis* is of most importance causing on average one-third of all clinical mastitis cases and often being the dominating pathogen on many farms.

Various Gram-negative bacteria, from environmental exposure and poor hygiene, may cause 50% of all cases of clinical mastitis. *Escherichia coli*, *Pseudomonas* and *Klebsiella* spp. are commonest, each related to particular management and hygiene problems, especially related to bedding materials and poor cleanliness (Rendos *et al.* 1975).

The changing aetiology is well described from the principal causes of mastitis in the Institute for Animal Health herd over 36 years (Table 1). In 1964, 43% cases were caused by *Staph. aureus* declining to 16% in 2000 whilst *Strep. uberis* had increased from 20 to 33% cases and Gram-negative bacteria from 2.4 to 43% of cases. The incidence of mastitis had declined by half so that the actual number of cases showed less dramatic changes. The dynamics of mastitis are largely because of the impact of control measures introduced from 1970 onwards.

#### 4. INCIDENCE OF MASTITIS

The likely impact on the UK dairy herd is that some 880 000 clinical cases occur in the 2.2 million cows annually but that up to 50% of all lactating cows are infected at some time each year in one or more of the four secretory quarters of the mammary gland. On average 25% of cows in the herd suffer clinical mastitis, with an average incidence of 40 cases

per 100 cows per year. Treatment may be unsuccessful resulting in a recurrence rate of up to 60%. Recurrence results from a failure to eliminate infection either naturally from not applying treatment, or a failure of the treatment. In the past, when milk was bought largely for volume, the main aim of treatment was to restore milk production and the failure to eliminate infection was not of major priority. Now milk price depends much more on quality and so treatment is more orientated to bacterial elimination rather than clinical resolution.

The reported incidence of clinical mastitis may be an underestimate as the person milking may only detect 80% of all cases showing clinical signs (Dodd *et al.* 1969). However, if cases are not detected then their severity, duration and impact may not be especially relevant. The prevalence or number of infected cows (quarters) is an unknown to most farms. These cases show no obvious signs and can only be determined from microbiological examination of milk or measurement of nonvisible milk abnormality. The most common method is to count the somatic cells (mostly leucocytes) in milk. Cells in milk occur naturally with a discrete threshold for the uninfected gland that varies with the species of mammal. The count in a healthy udder quarter of the cow should be fewer than 100 000 cells ml<sup>-1</sup> (Hamann 2002). A level >200 000 cells ml<sup>-1</sup> indicates infection (Smith *et al.* 2001). In a typical farm 3–4% quarters is the usual prevalence of subclinical mastitis. The farm should target fewer than 10% of cows with an elevated leucocyte content in milk.

#### 5. COSTS OF MASTITIS

Each clinical case of mastitis incurs costs that vary with the severity of the case and the response of the farmer. The major components are treatment costs, time and drugs, and the necessary discard of abnormal milk and milk-containing drug residues (Table 2). Averaging for a typical case suggests a net cost per case of £131 (Berry *et al.* 2004). This takes account of less food consumed to produce less milk, a factor not usually considered, and so is probably a

**Table 1** Causes of clinical mastitis in the Institute for Animal Health dairy herd (% positive identifications)

|                                   | 1964 | 1985–90 | 2000 |
|-----------------------------------|------|---------|------|
| <i>Streptococcus agalactiae</i>   | 1.9  | 0       | 0    |
| <i>Streptococcus dysgalactiae</i> | 22   | 8.3     | 0    |
| <i>Streptococcus uberis</i>       | 20   | 43      | 33   |
| <i>Staphylococcus aureus</i>      | 43   | 20.3    | 16   |
| Coliforms                         | 2.4  | 22.8    | 43   |
| <i>Arcanobacterium pyogenes</i>   | 4.5  | 5.4     | 1.2  |

**Table 2** Cost of an average case of clinical mastitis in a dairy cow producing 7000 kg milk per lactation (from Berry *et al.* 2004)

| Factor                   | Cost (£) |
|--------------------------|----------|
| Labour, 2 h at £6        | 12       |
| Treatment, drugs and vet | 11.3     |
| Discarded milk           | 26       |
| Production loss (10%)    | 135      |
| Reduced food intake      | –56.25   |
| Fatality (1%)            | 3        |
| Total                    | 131      |

realistic estimate. The national cost, given average incidence rates, would be approximately £105 million. Whilst sub-clinical mastitis has no direct costs, the infected udder produces up to 5% less milk for every additional 100 000 cells  $\text{ml}^{-1}$  in the milk (Hamann 2002). This adds up to a cost two to three times that of the overt disease making the UK 'losses' from mastitis in dairy cows £300 million  $\text{year}^{-1}$ .

## 6. PROGRESS IN CONTROL OF MASTITIS

A series of experimental and field studies from 1962 onwards at the National Institute for Research in Dairying in the UK led to a 5-point Mastitis Control Plan (Dodd and Jackson 1971). Its impacts have been to reduce the incidence of mastitis in the UK and elsewhere, by more than 70%, from more than 140 cases per 100 cows per year to approximately 40 cases (Booth 1988) and to reduce the prevalence of infection, measured by somatic cells in milk. The cell count of milk sold from farms declined from 550 000 cells  $\text{ml}^{-1}$  in 1972 to a national average of fewer than 170 000 cells  $\text{ml}^{-1}$  in 2000 (Fig. 1). Since then the national level has gradually increased to nearly 200 000 cells  $\text{ml}^{-1}$  in 2004. This has also been reported from several other major dairying nations including Germany and New Zealand. It is unclear why milk quality has deteriorated, it may be related to low milk prices paid to farmers. It is indicative of an increased prevalence of mastitis.

The aims of the mastitis control plan are to reduce the duration of existing infections and to reduce the likelihood of new infection by managing exposure and means of transmission (Dodd and Neave 1970). The components are:

- i Treat all case of clinical mastitis promptly with an effective remedy, to limit exposure and reduce duration.
- ii Use a longer acting antibiotic on all quarters of all cows at the end of the lactation to eliminate persisting infections

and prevent new infections in the dry period, to reduce duration and minimize exposure.

- iii Cull all cows suffering recurrent infection, usually more than three cases in the same quarter in one lactation, to reduce exposure and duration.
- iv Dip all teats of all cows in an effective disinfectant after every milking to reduce exposure.
- v Ensure, by at least annual testing that the milking machine is operating properly to minimize the impact of this route of transmission.

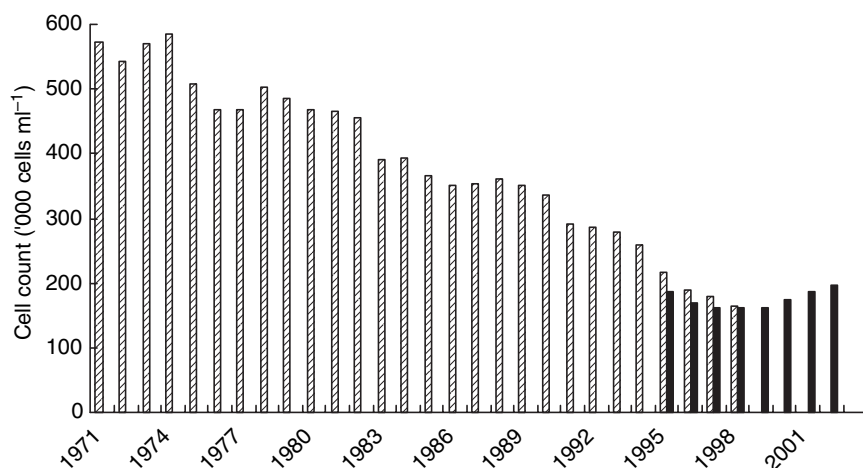
## 7. REFINEMENT OF CONTROLS AND USE OF ANTIBIOTICS

### 7.1 Treating mastitis in lactating cows

Most mastitis occurs in lactating cows, often soon after calving, with the abnormal milk having to be discarded. Conventional treatment is to use antibiotic therapy, although alternatives including herbal and homoeopathic approaches assume some importance.

The use of antibiotics to treat mastitis is contentious in itself with the methods varying internationally. Australasia, the USA and the UK amongst others, treat mastitis by intramammary inoculation of an antibiotic-containing paste, using one syringe every one or two milkings for up to 3 days. Others, principally in Nordic countries, use intramuscular injection as the preferred route of treatment.

The intramammary preparations are usually multicomponent including more than one antibiotic and often a corticosteroid to treat inflammation. The intramuscular products are usually single active products, often simply penicillin G. Arguments exist on the formulation and the pharmacodynamics to reach the site of infection, a problem with an organ that is relatively dense and weighs several kilograms.



**Fig. 1** National average milk cell counts for England and Wales. Open bars from Milk Marketing Board/Milk Marque data, filled bars from successor groups

**Table 3** Efficacy of antibiotic treatment with commercial products in treating experimental clinical mastitis caused by *Streptococcus uberis* (from Hillerton and Kliem 2002)

| Treatment              | Clinical cure (%) |        | Bacteriological cure (%) |
|------------------------|-------------------|--------|--------------------------|
|                        | 3 days            | 6 days | 6 days                   |
| None                   | 0                 | —      | —                        |
| 3 syringes (label)     | 27                | 91     | 70                       |
| 6 syringes             | 70                | 100    | 80                       |
| Injection              | 18                | 91     | 80                       |
| 6 syringes + injection | 55                | 100    | 75                       |

Ziv (1980) showed that approximately 97% of intramammary product stays in the udder and is void in milk whilst systemic treatment results in only 3% product becoming intramammary with the rest void mostly in urine, after systemic dispersal. The basic argument weighs use of nonspecific and broad spectrum intramammary treatment against simple products, nontargeted and used in significantly greater amounts. It would also appear that there might be good reasons to use more treatment than recommended on the label of the products.

A recent study, comparing efficacy in treating experimental mastitis caused by *Strep. uberis* (Hillerton and Kliem 2002), showed similar efficacy between the label recommended use of intramammary (one syringe at three successive milkings) and intramuscular (daily for 3 days) treatment antibiotics (Table 3). More aggressive treatment (extending the intramammary treatment to six successive milkings) resulted in more cure whilst combining intramammary syringes and injections was marginally better in some aspects only. However, the intramuscular injection contained significantly more antibiotic such that successful treatment required 15 times more penicillin equivalent and was much less targeted.

Despite considerable advances in the antimicrobial products available for treatment little improvement in efficacy has been reported. Interestingly, farmers appear to use almost twice the amount of treatment recommended. This is equivalent to the amount shown to give maximum effect (Hillerton and Kliem 2002).

One other advance has been the demonstration experimentally that the earlier treatment is given then the better the prospect of bacterial elimination (Milner *et al.* 1997). If the development of clinical mastitis can be predicted, then treatment prior to the appearance of visible signs results in fewer cases of clinical mastitis developing, reduces the severity measured by cell count at detection, and halves the length of the convalescent period, the return of cell count to a normal level. However, advances in detection systems have not produced effective cow-side methods to achieve this better cure.

**Table 4** Efficacy of dry cow intramammary antibiotic treatment in preventing new infections as determined at calving (from Berry and Hillerton 2002a)

| Treatment group | Number of quarters | New infections     |
|-----------------|--------------------|--------------------|
| Dry cow product | 443                | 19                 |
| No treatment    | 499                | 58 ( $P < 0.001$ ) |

## 7.2 Treating mastitis in nonlactating cows

It is desirable to have all dairy cows spend a period, 6–10 weeks prior to calving (usually annually), in a dry or resting period, a nonlactating phase. At this time the cow remains susceptible to new intramammary infections especially soon after the 'drying off' or cessation of milking, and around calving.

The original trials developing dry cow treatment (DCT) with antibiotics showed a prophylactic benefit of 82% reduction in the rate of new intramammary infections in the dry period as well as a much higher rate of eliminating infections than achieved by treating in lactation (Smith *et al.* 1967). In practical use the benefit has been shown to average 67%. However, as shown above, the aetiology of mastitis and incidence of mastitis has been changed significantly. This has led to criticism of unnecessary prophylactic use of antibiotic in cows with no infection when treated with a low probability of future infection.

The prophylactic benefit of DCT has been re-examined and remains substantial (Table 4), significantly controlling infection by *Strep. uberis* (Berry and Hillerton 2002a) and coliforms (Bradley and Green 2001). DCT is also cost-effective (Berry *et al.* 2004).

## 8. PROBLEMS IN CONTROL OF MASTITIS

The need for prophylactic treatment to control mastitis is contentious but it remains part of the recommended control programme and its efficacy and cost-benefit have been recently reconfirmed. Recently an alternative, an internal teat seal, has been introduced that is equal to DCT in preventing new infections but has no curative benefits (Berry and Hillerton 2002b; Huxley *et al.* 2002). This means it makes no contribution to reducing the duration of infection, a key aim of the mastitis control plans, and so it is only suitable for animals proven to be uninfected at dry off.

Antibiotic treatment remains necessary to achieve bacteriological cure of infection and usually clinical cure. A no-treatment group was completely unsuccessful in resolving experimental *Strep. uberis* infection and intervention for animal welfare was required (Hillerton and Kliem 2002). No treatment of clinical mastitis appears to increase the

prevalence of infection as determined at dry off, especially by *Staph. aureus* (Berry and Hillerton 2002a).

A criticism of use of antibiotics to treat mastitis is that it leads to development of resistant strains of bacteria that can be transferred to man. The UK data show that *Staph. aureus* (47%) have resistance to penicillins but that relatively little resistance exists to any antibiotic commonly used to treat the other mastitis-causing pathogens contrary to the levels found in enteric coli (Teale and David 1999). This suggests that if antibiotics used are targeted to the mammary gland and systemic treatment limited then any development of resistance can be minimal. The work of Devriese *et al.* (1997) in Belgium suggests that the proportion of mastitis-causing *Staph. aureus* resistant to penicillin G has declined from 80% to under 50%. A recent review (NMC 2004) found no evidence that antibiotic therapy has led to a problem of resistance in mastitis-causing bacteria.

Finally, mastitis is a painful disease. A prompt and effective treatment is a requirement to fulfil the 'Five Freedoms of Animal Welfare' in the UK especially 'Freedom from pain, injury and disease' and a growing international requirement of proper animal care in the new Code of Good Dairy Practice (IDF/FAO 2004).

## 9. CONCLUSIONS

A mastitis control plan devised more than 30 years ago has achieved huge success in reducing the incidence of disease and the prevalence of infection in the mammary gland of dairy cow principally in developed dairy countries. The aetiology of the disease has changed such that contagious pathogens such as *Staph. aureus* and *Strep. agalactiae* have been significantly reduced in importance. The progress made to a great extent has been achieved by the diligent use of therapeutic and prophylactic antibiotics treatments. It appears that on-farm use rates of antibiotic introduced directly into the mammary gland can give the optimal cure. Similarly a strong case exists on the basis of efficacy and cost-effectiveness for the prophylactic application of intra-mammary antibiotic at the end of each lactation. Convincing evidence is quite lacking that such use of antibiotic to treat or prevent mastitis has resulted in any development of resistance to antimicrobial products. Further control of mastitis in the cow is a necessity being a major welfare requirement on the dairy farmer.

## 10. REFERENCES

- Barbano, D. (2004) *The Role of Milk Quality in Addressing Dairy Food Marketing Opportunities in a Global Economy*. Proceedings of the 43rd Annual Meeting of NMC, Charlotte, NC, USA, pp. 284–285.
- Berry, E.A. and Hillerton, J.E. (2002a) The effect of selective dry cow treatment on new intra mammary infections. *J Dairy Sci* **85**, 112–121.
- Berry, E.A. and Hillerton, J.E. (2002b) The effect of an intra mammary teat seal on new intra mammary infections. *J Dairy Sci* **85**, 2512–2520.
- Berry, E.A., Hogeveen, H. and Hillerton, J.E. (2004) Decision tree analysis to evaluate dry cow strategies. *J Dairy Res* **71**, 409–418.
- Bisharat, N., Crook, D.W., Leigh, J., Harding, R.M., Ward, P.N., Coffey, T.J., Maiden, M.C., Peto, T. *et al.* (2004) Hyperinvasive neonatal group B *Streptococcus* has arisen from a bovine origin. *J Clin Microbiol* **42**, 2161–2167.
- Booth, J.M. (1988) Progress in controlling mastitis in England and Wales. *Vet Rec* **122**, 299–302.
- Bradley, A.J. and Green, M.J. (2001) An investigation of the impact of intramammary antibiotic dry cow therapy on clinical coliform mastitis. *J Dairy Sci* **84**, 1632–1639.
- Devriese, L.A., Haesebrouck, F., Hommez, J. and Vandermeersch, R. (1997) A 25-year survey of antibiotic susceptibility testing in *Staphylococcus aureus* from bovine mastitis in Belgium, with special reference to penicillinase. *Vlaams Diergeneeskundig Tijdschr* **66**, 170–173.
- Dodd, F.H. and Jackson, E.R. (eds) (1971) *Control of Bovine Mastitis*. UK: British Cattle Veterinary Association.
- Dodd, F.H. and Neave, F.K. (1970) *Progress in Mastitis Control*. Shinfield, Reading: Biennial Reviews of the National Institute for Research in Dairying, 21 pp.
- Dodd, F.H., Westgarth, D.R., Neave, F.K. and Kingwill, R.G. (1969) Mastitis – the strategy of control. *J Dairy Sci* **52**, 689–695.
- Hamann, J. (2002) Relationships between somatic cell counts and milk composition. Bulletin of the International Dairy Federation No. 372, Brussels, Belgium, pp. 56–59.
- Hillerton, J.E. and Kliem, K.E. (2002) Effective treatment of clinical mastitis to minimize the use of antibiotics. *J Dairy Sci* **85**, 1009–1014.
- Huxley, J.N., Green, M.J., Green, L.E. and Bradley, A.J. (2002) Evaluation of the efficacy of an internal teat sealer during the dry period. *J Dairy Sci* **85**, 551–561.
- IDF (2001) *Mastitis Newsletter No. 24*. Bulletin of the International Dairy Federation No. 367, Brussels, Belgium, 53 pp.
- IDF/FAO (2004) *Guide to Good Dairy Farming Practice*. Rome: United Nations Food and Agriculture Organization, 28 pp.
- Milner, P., Page, K.L. and Hillerton, J.E. (1997) The effects of early antibiotic treatment following diagnosis of mastitis detected by a change in electrical conductivity of milk. *J Dairy Sci* **80**, 859–863.
- NMC (2004) *Bovine Mastitis Pathogens and Trends in Resistance to Antimicrobial Drugs*. National Mastitis Council Research Committee Report. Proceeding of the 43rd Annual Meeting of NMC, Charlotte, NC, USA, pp. 400–414.
- Rendos, J.J., Eberhardt, R.J. and Kesler, E.M. (1975) Microbial populations of the teat ends of dairy cows and bedding materials. *J Dairy Sci* **58**, 1492–1500.
- Smith, A., Westgarth, D.R., Jones, M.R., Neave, F.K., Dodd, F.H. and Brander, G.C. (1967) Methods of reducing the incidence of udder infections in dry cows. *Vet Rec* **81**, 504.
- Smith, K.L., Hillerton, J.E. and Harmon, R.J. (2001) *National Mastitis Council Guidelines on Normal and Abnormal Milk based on Somatic Cell Counts and Signs of Clinical Mastitis*. Madison, WI, USA: National Mastitis Council, 3 pp.

- Stableforth, A.W., Hulse, E.C., Wilson, C.D., Chodhowski, A. and Stuart, P. (1949) Herd eradication of *S. agalactiae* by simultaneous treatment of all cows with five doses of 100 000 units of penicillin at daily intervals and disinfection. *Vet Rec* **61**, 357–362.
- Teale, C.J. and David, G. (1999) *Antibiotic Resistance in Mastitis Bacteria*. Proceedings of the British Mastitis Conference, Institute for Animal Health, pp. 24–29.
- Watts, J.L. (1988) Etiological agents of bovine mastitis. *Vet Microbiol* **16**, 41–66.
- Ziv, G. (1980) Drug selection and use in mastitis: systemic versus local therapy. *J Am Vet Med Assoc* **176**, 1109–1128.