

Mastitis

Antibiotic treatment cannot compensate for poor practice in respect of environmental hygiene, teat dipping, milking machine cleaning and maintenance and culling. To neglect the last in cases of recurrent or chronic mastitis cases is to expect too much of antibiotic treatment.

RUMA guidelines suggest culling be considered in cows with more than three episodes in a lactation, in poorly-responding animals and in those with an average somatic cell count in excess of 500 000. Culling is strongly advised for chronic recurring mastitis cases or high somatic cell cases that had dry cow treatment the previous year. Pyorala S. (2009) points out that in one large study antibiotic treatment only raised the bacteriologically-cured proportion of subclinical mastitis during lactation from 68% to 75% of cases and that for staphylococcal mastitis there was in fact no apparent effect of antibiotic use upon bacteriological cure during lactation. However, the use of antibiotics for cases for *Staphylococcus aureus* and *Streptococcus agalactiae* is likely to reduce the risk of contagion.

For lactating therapy, RUMA guidelines advise:

- Early identification of cases
- Strip as often and as completely as possible
- Treat using a complete course, particularly in heifers. Courses of treatment should be completed, even if the milk returns to being visibly normal before completion.
- Culture some typical pre-treatment cases to identify the organisms and their sensitivity to antimicrobials. (Samples can be frozen for up to 6 weeks and glycerol can be included to enhance keeping quality)
- If clinical cases stop responding or respond more slowly check more pre-treatment samples. In order to select the most appropriate treatment regime a sufficient range of clinical and/or subclinical cases should be cultured and the sensitivity of the organisms determined.
- Farmers and vets should agree a defined treatment protocol within the health plan along with guidelines on identification of cows that are systemically ill, that should be examined by a veterinary surgeon.
- Segregation or use of separate units for cows known to be positive for *Staph Aureus*, can be an effective control on the spread of mastitis.
- Effective treatment of clinical cases, with appropriate 'quarantine' of their milk will remain one of the most effective means of controlling the spread of mastitis. Pyorala S (2009) reviewed lactating cow antibiotic therapy. Bactericidal drugs are preferred, as bacteria are not readily destroyed by immune mechanisms in the diseased udder. Intra-mammary therapy achieves high concentrations but an uneven distribution, and is particularly effective against streptococci and coagulase-negative staphylococci, plus *Corynebacterium*. For these pathogens, penicillin G (procaine +/- benzathine penicillin) or related drugs (penethamate) are optimal. Culture diagnosis allows efficient targeting of these cases. Monitoring of therapy can be done with cell counts or (more practically) the California Milk Test and it is recommended to treat every case for at least three days (i.e. longer than some standard course durations). Systemic therapy can struggle to achieve effective tissue and milk

concentrations, and Tetracycline, Trimethoprim-Sulpha and (perhaps surprisingly) the 3rd-generation Ceftiofur have poor distribution and efficacy. Macrolides have poor activity in milk, although Tylosin is effective against streptococcal mastitis.

For acute Gram-negative (generally *E. coli*) mastitis cases, some systemic antibiotics have shown clinical benefit in experimental trials (Fluoroquinolones and Cefquinome) and a field study (Ceftiofur). However, fluid support and anti-endo-toxic therapy remains the core approach with such cases. Specific guidelines arising from these considerations are as follows:

- Establish prevailing pathogens and resistance patterns by means of recent culture surveys. It is recommended to collect, freeze and culture a selection of fresh cases every 6 months at least. Culturing occasional samples or only small numbers can be unrewarding, as some bacteria may be shed intermittently. Samples can be frozen for up to six weeks and glycerol can be included in the sample pot to enhance keeping quality of the frozen sample
- Where such results indicate susceptibility, treat clinical cases of likely streptococcal or staphylococcal origin with benzyl penicillin-based intramammary tubes. Ideally narrow spectrum preparations ...but these are not available in lactating cow form.
- Only resort to broader-spectrum tubes (Amoxicillin+Glavulanic, Cephalosporins) as second-line treatment, or where resistance of the likely pathogen to penicillin has been established
- With known or likely *Staph. aureus*, systemic treatment is recommended in addition to Intra-mammary, this could be Penicillin/Penethemate or Tylosin, depending on susceptibility patterns on-farm and the tube being used.
- Treatment should be prolonged in cases of *Staph. aureus* and *Strep. uberis*.
- Antibiotic treatment of *E. coli* mastitis should be reserved for severe cases, with Marbofloxacin or Ceftiofur, probably the drugs of choice. These would normally be 'reserve' antibiotics, so using them for milder cases raises the risk of having resistance to these antibiotics on the farm, yet providing little or no benefit to the treated cow.
- Dry cow treatment (DCT) also should be selected on the basis of resistance patterns in the lactating cow pathogens, but 'repeat offenders' need to be considered for culling rather than hoping DCT will fix them.

Procaine Penicillin: (targeting streptococci and susceptible staphylococci), streptomycin plus neomycin (theoretically synergistic with penicillin for staphylococci and streptococci), novobiocin (targeting staphylococci). Provided there is no evidence of resistance to penicillin (*Strep*) or novobiocin (*Staph*), this is a suitable first-line tube, with injectable penethamate as a systemic complement. It covers most bases, although resistance by staphylococci to penicillin, streptomycin and neomycin is common, and investigations have shown no benefit of including aminoglycoside (Strepto/Neomycin) in the mix for penicillin-susceptible mastitis (Taponen 2003).

Whereas it would be preferable to use a narrow-spectrum tube for Streptococcal or

Staphylococcal cases (based upon resistance data), there just aren't any on the lactating cow tube market at present. The Gram-negative spectrum of streptomycin/neomycin components are not very relevant, as Gram-negative (toxic) mastitis is not effectively treated by tube therapy.

Potentiated Amoxicillin: targeting streptococci and staphylococci, also with a Gram-negative spectrum, (but note previous comments about limited benefit of tubes in Gram negative infections). LESS active against susceptible Streptococci than penicillin, but a useful second line if penicillin-resistant Streps and/or Novobiocin-resistant Staphs are present, and compatible systemic treatment available.

Cephalexin plus Kanamycin: covering a broad spectrum including penicillin as producing organisms. Advise reserve its use for cases where penicillin resistance is known or strongly suspected. Cannot be regarded as a 'stronger' preparation, and farms should generally stick to one or the other, only changing if resistance data are indicative. Injection is a compatible systemic treatment.

Cefquinome: Broad-spectrum 4th-generation cephalosporin. Again, may be LESS active against Streps and Staphs than other drugs, provided resistance to penicillin and Novobiocin, respectively, is not present. Should be reserved (3rd line) for cases where resistance to other drugs is an established issue. Possible use with injectable Cefquinome in acute severe *E. coli*-type mastitis, but value is dubious, especially as therapy involves frequent stripping out.

Penethemate + procaine penicillin: (targeting streptococci and susceptible staphylococci) plus framycetin (synergistic with penicillin components, plus Gram-negative spectrum including *E. coli*). Recent European data (published by Boehringer; Pillar et al 2014) indicates >89% susceptibility of all major groups of mastitis pathogens to this combination. Suitable as a first-line, unless penicillinase Staphylococcus is the main problem.

Cloxacillin: Spectrum is restricted to Streptococci and Staphylococci but will include penicillinase-producing Staphs, so useful for attempting a cure if these have been during lactation or are prevalent in the herd. No Gram-negative spectrum, so may be wise to avoid if postpartum toxic mastitis is a problem.

Cephalonium: a veterinary-only-licensed 1st generation cephalosporin. Spectrum includes Streptococci, Staphylococci (including penicillinase-producers) and most environmental Gram-negative organisms. Sensible to reserve for use where penicillin as producing pathogens are prevalent AND post-calving toxic mastitis is an issue. Long-lasting in the udder (minimum 54-day interval to calving), but the value of this for clinical cure of Gram-positive cases during dry period is unclear, and Gram-negative cover by Framycetin is claimed to be similarly prolonged.

(RUMA), Responsible Use of Medicines in Agriculture Alliance