Antibiotic use
Andy Wales, Oct 2014

General principles for selecting and using antibiotics

Is an antibiotic needed?
Many diseases are not a result of bacterial infection and, especially when not severe, do not need antibiotics to manage them. Relevant examples include mild calf scours and outbreaks of coughing without other signs among growing cattle. Even in more severe cases of scour and pneumonia, the effect of antibiotics may be to protect the animal from secondary infection rather than to cure the underlying (often viral) cause.

Antibiotics should be seen as a useful addition to control of many diseases, but the fundamentals of hygiene, ventilation, stocking density, attention to early signs of disease and to colostrum intake, etc. will do far more to reduce disease and suffering plus the associated costs. Antibiotics given as a blanket or preventive treatment will not prevent infections if the bacterial challenge is high enough or the animal’s immunity is poor, as is often the case when there are problems with stock management.

What is/are the likely infectious agent(s) and where are they?
To be effective, an antibiotic’s ‘spectrum’ needs to cover the bacteria present, and it needs to be present at effective concentrations in the important tissues. A straightforward view of an antibiotic’s spectrum is to consider it in terms of two bacterial classifications: cell wall type (Gram-positive vs. Gram–negative) and oxygen tolerance (aerobes vs. anaerobes). ‘Broad-spectrum’ antibiotics cover a wide range of Gram-positive and –negative bacteria, whilst ‘narrow-spectrum’ antibiotics affect a smaller subset.

It might be imagined that Broad-spectrum antibiotics are generally preferred, but in fact for many purposes the opposite is true. Narrow spectrum antibiotics may penetrate or concentrate especially well, and/or be the most lethal agent against certain bacteria, provided they are selected with due regard for the particular problem. In addition, they pose less risk of generating antibiotic resistance among other bacteria present on the farm. With all the considerations of spectrum, distribution and resistance, it should be evident that the idea of there being ‘stronger’ and ‘weaker’ antibiotics is at best misleading.

Ideally, all infections should be sampled and cultured to establish the presence of susceptible organisms before antibiotic treatment is started. For many reasons (cost, severity of illness requiring immediate treatment, limitations of diagnostics and sampling access, etc.) this happens far less frequently in farm practice than in the human field. However, in situations where an animal or (particularly) a group of animals is not responding well to treatment, or where a problem keeps coming back despite sensible measures, then sampling for culture to establish the most suitable antibiotic is strongly recommended. This has been usual practice with bovine mastitis for years, but it should be a primary consideration whenever a first-line antibiotic approach has not been successful. Even if results do not arrive in time to affect treatment of one animal, they can be very useful to inform treatment of future cases.
diagnostic tests, based on molecular genetic approaches, for identifying bacteria and their resistance profiles are likely to become available in the near- to mid-term.

‘New’ antibiotics and problems of resistance
There are a limited number of classes of antibiotics, and bacteria that acquire or develop resistance to one member of a class often gain partial or similar resistance to other members of that antibiotic class, owing to similar mechanisms of chemical attack between members of a class. ‘New’ veterinary antibiotic preparations are generally reformulations or novel combinations of well-established antibiotics. There are well-founded anxieties over antibiotic resistance in the human field, where whole areas of practice such as cancer treatment, transplants and other advanced surgery are heavily reliant on antibiotics. It therefore seems highly unlikely that any important ‘new’ classes of antibiotic will be licensed for veterinary use in the foreseeable future. In consequence, in order to keep the antibiotics we already have, and to keep them effective, vets and clients need to use them carefully and effectively.

It used to be thought that resistance to an antibiotic would fade away once the ‘selective pressure’ of the antibiotic use was stopped. It is now evident that the situation is far more complex than that, with resistance persisting and sometimes spreading between premises even when antibiotic use has stopped. The view of authorities remains quite balanced for the moment, but there are many who would like to see the range and availability of veterinary antibiotics drastically curtailed, and the patterns of veterinary use are scrutinised for evidence of inappropriate use. In particular, the usefulness of fluoroquinolone and 3rd and 4th generation cephalosporin antibiotics for human Salmonella infections have prompted the British Veterinary Association (among others) to advise that their use be reserved for the treatment of clinical conditions that have responded poorly, or are expected to respond poorly, to other classes of antimicrobials. Furthermore their use for groups or flocks of animals should be strongly discouraged, except in very specific situations, and off label use should be strongly discouraged.

Timing, dosing, frequency and duration of treatment
Once a bacterial infection (e.g. mastitis, foot infection) is noticed or strongly suspected, the faster that antibiotic is given (along with other suitable treatment), the less tissue damage and bacterial multiplication will occur and the better the outcome is likely to be.

Benefit is likely to be maximised and the risk of generating resistance minimised if dosing errs on the generous side and for longer, i.e. a single jab (of anything but a long-acting preparation) at a low dose may well be worse than useless. Treatment until clinical cure is highly desirable, both in terms of preventing recurrence or a chronic ‘grumbling’ condition, and for preventing survival of bacteria with some level of resistance. For most antibiotics, daily or even twice-daily administration achieves much better tissue concentrations than does a single dose of long-acting preparation. For some antibiotics (e.g. procaine penicillin) the spectrum is significantly affected by the dose, with more of the Gram-negative bacterial spectrum being included at above-normal dosing.
Licensing requirements

Although in most cases regulations require that a product licensed for a particular condition be used to treat that condition, the Veterinary Medicines Directorate has recently issued a statement including the following: “The VMD therefore considers that it is justified, on a case-by-case basis, to prescribe an antibiotic on the cascade in the interests of minimising the development of resistance ... that is, the prescription of a narrow spectrum antibiotic on the cascade over a broad spectrum antibiotic that has a specific authorised indication for that condition” (Eckford, 2014). This appears to provide significant freedom to select more focussed antibiotics, provided they are likely to work.
Recommendations

These are based upon consideration of likely bacteria present in certain conditions, and are consistent with guidelines produced by the Responsible Use of Medicines in Agriculture Alliance (RUMA), and other more specific reference sources for certain conditions. Drug product datasheets are available online (http://www.noahcompendium.co.uk/, http://www.norbrook.com/), as is further information in the form of Summary of Product Characteristics (SPC) sheets on all veterinary licensed medicines at: http://www.vmd.defra.gov.uk/ProductInformationDatabase/

It is prudent to limit first-line antibiotics to one or two classes on any given farm, and to change these only if repeated resistance problems are encountered.

Table: Usage not covered by recommendations on specific conditions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Commercial preparation(s)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tylosin (narrow-spectrum macrolide)</td>
<td>Tylan (Cattle, Sheep, Pigs)</td>
<td>For Gram-positive and certain Gram-negative (Pasteurella, Mycoplasma) infections. NOT active against Enterobacteraceae e.g. E. coli. It's well-distributed including into pus and wounds although beware lack of anaerobe activity. Activity for approx. 12h after injection.</td>
</tr>
<tr>
<td>Procaine penicillin (narrow-spectrum)</td>
<td>Norocillin (Cattle, Sheep, Pigs)</td>
<td>Bactericidal, active against anaerobes, spectrum broadens from Gram-positives into some Gram-negatives with increased dosing (4-6x standard dose of 10mg/kg)</td>
</tr>
<tr>
<td>Penicillin +/- Streptomycin (broad-spectrum combination of penicillin plus aminoglycoside)</td>
<td>Penstrep (Cattle, Sheep, Pigs)</td>
<td>Bactericidal combination., Both components short-acting in sheep; would suggest 12-hourly re-dosing in this species. Superficial advantages as a cheap 'broad-spectrum' preparation are not borne out by the evidence: see comment in footnote about spectrum and efficacy.*</td>
</tr>
<tr>
<td>Amoxycillin (broad-spectrum penicillin)</td>
<td>Betamox 150mg/ml (Cattle, Sheep, Pigs)</td>
<td>Bactericidal, similar spectrum to Penstrep although probably more consistent duration of activity.</td>
</tr>
<tr>
<td>Trimethoprim-potentiated sulphonamide (broad-spectrum)</td>
<td>Norodine 24 (Cattle, Pigs)</td>
<td>Bactericidal, limitations include quite short half-lives of active ingredients, in cattle especially, and low activity in presence of pus. However, can be given intravenously to achieve rapid distribution. Could increase frequency of administration if desired (off-label use, requiring standard 28-day meat withdrawal).</td>
</tr>
<tr>
<td>Oxytetracycline (broad-spectrum)</td>
<td>Alamycin, Engemycin (Cattle, Sheep, Pigs)</td>
<td>Bacteriostatic, resistance among both Gram-positive and Gram-negative organisms appears widespread. Probably not a first choice for routine antibiotic, but good activity against respiratory bacteria (including mycoplasmas) and prolonged activity after a double dose.</td>
</tr>
<tr>
<td>Drug</td>
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<tr>
<td>Lincomycin (Narrow-spectrum)</td>
<td>Lincocin (Pigs)</td>
<td>Lincosamide; similar spectrum and distribution to Tylosin but good anaerobic cover</td>
</tr>
<tr>
<td>Potentiated amoxycillin (Broad-spectrum)</td>
<td>Combioclav</td>
<td>Same spectrum and distribution to amoxycillin, but active against penicillinase-producing bacteria that are resistant to amoxycillin. Frequency of resistance currently low, but does develop by changes to cell membranes</td>
</tr>
<tr>
<td>Cephalaxin (Broad-spectrum 1st-generation cephalosporin)</td>
<td>Ceporex, (Cattle)</td>
<td>Bactericidal, active against most penicillinase-producing bacteria. Probably better reserved as a systemic complement to Ubrolexin in mastitis cases, rather than a ‘routine’ second line antibiotic.</td>
</tr>
<tr>
<td>Amoxycillin (Broad-spectrum)</td>
<td>Betamox 150mg/ml (Cattle, Sheep, Pigs)</td>
<td>Potentially useful second-line for Sheep and Pigs, comments on activity as above</td>
</tr>
<tr>
<td>Ceftiofur (Broad-spectrum 3rd generation cephalosporin)</td>
<td>Excenel (Cattle), Naxcel (Cattle, Pigs)</td>
<td>Extended Gram-negative spectrum. Data sheet states ‘should be reserved for … clinical conditions which have responded, or are expected to respond, poorly to … first line treatment…Whenever possible use should only be based upon susceptibility testing’ Selects for Gram-negative extended-spectrum beta-lactamase-producers that may constitute a risk to human health.</td>
</tr>
<tr>
<td>Cefquinome (broad-spectrum)</td>
<td>Cobactan (Cattle, Pigs)</td>
<td>4th generation cephalosporin. Comments as for ceftiofur.</td>
</tr>
<tr>
<td>Marbofloxacin (Broad-spectrum fluoroquinolone)</td>
<td>Marbocyl (Cattle, Pigs)</td>
<td>Licensed for respiratory disease and acute E. coli mastitis. Data sheet states ‘ should be reserved for … clinical conditions which have responded, or are expected to respond, poorly to other classes of antimicrobials…Whenever possible use should only be based upon susceptibility testing’.</td>
</tr>
<tr>
<td>Enrofloxacin (Broad-spectrum fluoroquinolone)</td>
<td>Baytril (Cattle, Pigs)</td>
<td>Comments as for Marbofloxacin, licensed additionally for alimentary conditions</td>
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</table>

*Note re Pen & Strep. Whittem and Hanlon (1997) point out that streptomycin is documented as the drug of choice for only leptospirosis and wooden tongue in cattle. Also that major textbooks recommend the combination of Pen and Strep only for wooden tongue and dermatophilosis; for the former streptomycin alone is effective and for the latter, tetracycline appears to have better efficacy. Where the pathogens involved are uncertain, it is suggested that procaine penicillin alone would have similar efficacy. Furthermore, increasing the dose of penicillin broadens its spectrum among Gram-negative bacteria whilst avoiding potential renal toxicity and residues associated with high-dose aminoglycosides. The famed ’synergy' between penicillin and aminoglycosides cannot be regarded as a general property, but differs between target organisms. Drug companies in the USA were put on notice in 1971 of the need to provide evidence of the efficacy of penicillin plus (dihydro)streptomycin combinations, and these combinations were eventually withdrawn from the US market in 1993 as no such evidence was forthcoming, despite the market value of these products to the companies concerned. It therefore seems preferable to prefer the use of straight procaine penicillin, over Pen & Strep, as a first-line drug where susceptible organisms are likely to be present. This is likely to achieve similar or better efficacy, while minimising potential residues and constituting a more prudent use of antibiotics. Where a broader spectrum is desired, then Pen & Strep is unlikely to match the effect of a genuinely broad-spectrum penicillin (amoxycillin +/- clavulanate).
Usage in 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. Pyörälä (2009) points out that in one large study antibiotic treatment only raised the bacteriologically-cured proportion of subclinical mastitis during a 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 a 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.

Pyörälä (2009) reviewed lactating cow antibiotic therapy. Bactericidal drugs are preferred, as bacteria are not readily destroyed by immune mechanisms in the diseased udder. Intramammary 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
(Excenel/Naxcel) 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 [Cobaclan]) and a field study (ceftiofur [Excenel/Naxcel]). However, fluid support and anti-endotoxic 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 staphyloccocal 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 (combi-clav, 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 intramammary; this could be Penicillin/penethemate (Mamyzin) Combi-clav, Ceporex 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 (Marbocyl/Forcyl) or ceftiofur (Excenel/Naxcel) 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.

Details of lactating tubes in use

**Tetra-delta:** 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 (Mamyzin) 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 mastitides (Tapponen 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.

**Combiclav:** Potentiated amoxycillin, 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 (combiclav injection) available.

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

**Cobactan MC:** 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 (Cobactan) in acute severe *E. coli*-type mastitis, but value is dubious, especially as therapy involves frequent stripping out.

**Details of dry cow tubes in use**

**Ubro (Leo) Red:** 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.

**Orbenin DC:** Cloxacillin. Spectrum is restricted to Streptococci and Staphylococci but will include penicillinase-producing Staphs, so useful for attempting a cure if these have been identified 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.

**Cepravin Dry Cow:** 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 penicillinase-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 in Ubro Red is claimed to be similarly prolonged.
Usage in neonate diarrhoea and gastroenteritis

RUMA guidelines are as follows. “Treatment for scours is very similar regardless of the cause. It should be directed toward correcting the dehydration, acidosis, and electrolyte loss. Antimicrobial treatment can be given simultaneously with the treatment for dehydration but is not always necessary. Dehydration can be overcome with simple fluids given by mouth early in the course of the disease. If dehydration is allowed to continue, intravenous fluid treatment becomes necessary.”

The emphasis should be on fluid therapy, with antibiotics reserved for calves that are dull or have haemorrhagic diarrhoea. For older calves of around a month plus, due consideration should also be given to coccidiosis as a cause of diarrhoea. 'Scour boluses' may have a non-specific diarrhoea-suppressing effect, but will tend to generate resistance that will cause problems when calves are more severely sick, and will not adequately compensate for dehydration, poor colostral immunity and high environmental challenge.

Bolus preparations available for oral treatment of calves with scour are trimethoprim-potentiated sulphonamide (Norodine) and clavulanate-potentiated amoxycillin (Synulox). As potentiated amoxycillin is useful in a wide number of on-farm situations, it should be reserved as a second-line oral antibiotic in cases of calf scours.

Spectinomycin (Spectam) is licensed for prevention of enterotoxaemia (watery mouth) in lambs. Its spectrum and resistance pattern is very similar to streptomycin, and resistance is consequently likely to be common although high local concentrations in the gut may partially overcome this. There are no other licensed preparations, and its use may be unnecessary if there is a suitable concentration on hygiene and the provision of colostrum, adequate milk supply and shelter.

Usage for lameness and conditions of the foot

RUMA guidelines include the following

- Treat all cows as soon as lameness is noted
- Interdigital necrobacillosis (foul in the foot) is one of the few conditions likely to be responsive to systemic antimicrobials.
- Digital dermatitis, which is characterised by acute lameness with varying degrees of circumscrip dermatitis classically at the bulbs of the heel, responds to topical antimicrobial rather than systemic.
- All lame feet should be checked before using antimicrobials.
- Hoof trimming is an important part of routine foot care as well as often being necessary to make a diagnosis and as part of treatment of lame animals.
- Consider using a footbath to increase hoof strength.

Foul in the foot/Bovine footrot, should respond well to antibiotic, provided it is identified early and the foot is examined for any other problems. There are specific claims for treatment with tylosin (Tylan) or tilmicosin (Micotil), both macrolides, and these are the preferred antibiotics in view of their relatively narrow spectrum. The zero milk withhold of ceftiofur (Excenel/Naxcel) is financially attractive for lactating dairy cow treatment, although far from ideal from an antibiotic resistance control perspective.

For digital dermatitis, topical treatment is more effective than systemic, with individual application of oxytetracycline spray, and/or herd treatments with copper sulphate footbaths being
recommended (Laven and Logue, 2006; Logue et al., 2012). Suggested protocols range from 5% solution twice daily for 3 days a week or a fortnight, to 2% solution for less severe cases. It is not uncommon for lincomycin or lincomycin/spectinomycin to be used in footbaths to control digital dermatitis. It should be noted that this is unlicensed, invoking a standard 7-day milk withdrawal period, is based on anecdotal recommendations only, and to be discouraged. Use of hypochlorite-containing parlour washings for footbathing appears to be ineffective against digital dermatitis.

Contagious Ovine Digital Dermatitis (CODD) involves severe tissue damage, and is not as susceptible to trimming and topical treatment as conventional footrot, nor is there evidence of a benefit to using footrot vaccine, except perhaps in situations where both conditions are present. However, both tilmicosin (Micotil) and long-acting amoxicillin (Betmox LA) have been reported as effective (Davies, 2011; Duncan et al., 2012), and should be regarded as reasonable elements of a control programme.

**Usage in respiratory Disease**

RUMA guidelines emphasise good husbandry, but make no other specific recommendations. Viral causes dominate considerations for prevention and control.

Antibiotic spectra for calf pneumonia should aim to cover the common bacterial genera (*Mannheimia*, *Pasteurella*, *Histophilus/Haemophilus* and *Mycoplasma*). Synthetic macrolides are probably the narrowest-spectrum option here: Tilmicosin (Micotil), Gamithromycin (Zactran) and Tulathromycin (Draxxin). Oxytetracycline, Florfenicol (Nuflor) and fluoroquinolones (Baytril and Marbocyl) also cover these pathogens but with a broader spectrum of action.

The prevailing bacterial pathogens and resistance patterns for bovine respiratory disease will not be readily determined in the same way as for mastitis, and the primary causes will likely be viral in most cases. It is recommended to use non-steroidal anti-inflammatory drugs in all cases, this sometimes being the only treatment in milder cases.

- It is difficult to provide confident further guidelines, however fluoroquinolones should be reserved for unresponsive or severe cases.
- Oxytetracycline or the narrower-spectrum macrolides (Micotil, Zactran, Draxxin) may be preferred as first-line choices.
- Penicillins (Betamox, Combiyclav) do not cover mycoplasmas; whether this is significant in most cases is difficult to know. However, this spectrum gap and the need for daily injections (as opposed to the longer-acting macrolides) make them less attractive as first-line treatments.
- Florfenicol is broad-spectrum and shows cross-resistance with chloramphenicol, therefore logically it should be retained for less frequent use. Its combination with flunixin (Resflor) makes its use convenient. However, the flunixin is relatively short-acting, given the single-dose licensing, and farmers should consider the benefits of giving separate antibiotic and anti-inflammatory injections at appropriate intervals.
Topical applications

There is little choice to be had in the licensed topical preparations. The first-generation cephalosporin cefapirin is licensed for intra-uterine use (Metricure). Prudent use would advise against the indiscriminate applications of 'washout' treatments, with study evidence suggesting that Metricure treatment of endometritis before four weeks post-calving does not shorten time to conception (LeBlanc et al., 2002). The data sheet indication is for use after two weeks post-calving.

Topical licensed eye treatment is restricted to cloxacillin in a long-acting base, and as a narrow-spectrum product that is active against the likely pathogen (*Moraxella bovis*) in the concentration achieved by topical application, it is the antibiotic of choice in this circumstance. Severe cases may benefit from bulbar subconjunctival injection of penicillin, oxytetracycline or a cephalosporin (technically difficult), or systemic treatment with an antibiotic covering the Gram-negative spectrum.
References


Eckford, S., 2014. Responsible use of antimicrobials under the prescribing cascade. Veterinary Record 175, 207–207. doi:10.1136/vr.g5326


