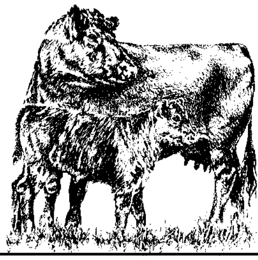

Western Beef Resource Committee Fourth Edition

Cattle Producer's Handbook

Animal Health Section 606

Antibiotic Metaphylaxis to Control Respiratory Disease

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Overview

Metaphylaxis (mass medication) to manage respiratory disease in newly received high stress or recently weaned cattle has been a common practice (USDA 1992). The beef industry's use of antibiotics is coming under more and more scrutiny. The Food and Drug Administration (FDA) and Center for Disease Control (CDC) have ongoing epidemiologic studies to assess antibiotic resistance among human bacterial pathogens and the relationship to agricultural use of antibiotics.

It is possible that many of the antibiotics cattle producers rely on today will be lost in the future. For this reason it becomes important for cattle producers to carefully consider how they select and use antibiotics [see "A Producer's Guide for Judicious Use of Anti-microbials in Cattle" (Fig. 1)].

Several questions must be addressed when considering antibiotic metaphylaxis or mass medication of newly received, high stressed or recently weaned cattle. This paper takes a look at six basic questions.

Fig. 1. A Producer's Guide for Judicious Use of Antimicrobials in Cattle. Source: NCBA Beef Quality Assurance Taskforce 2001.

Prevent Problems: Emphasize appropriate husbandry and hygiene, routine health examinations, and vaccinations.

Select and Use Antibiotics Carefully: Consult with your veterinarian on the selection and use of antibiotics. Have a valid reason to use an antibiotic. Therapeutic alternatives should be considered before using antimicrobial therapy.

Avoid Using Antibiotics Important In Human Medicine As First Line Therapy: Avoid using as the first antibiotic those medications that are important to treating strategic human or animal infections.

Use the Laboratory to Help You Select Antibiotics: Use cultures and susceptibility test results to aid in the selection of antimicrobials, whenever possible.

Avoid Using Broad Spectrum: Use narrow spectrum antimicrobials, whenever possible. Combination antibiotic therapy is discouraged.

Avoid Inappropriate Antibiotic Use: Confine therapeutic antimicrobial use to proven clinical indications, avoiding inappropriate uses, such as for viral infections, without bacterial complication.

Treatment Programs Should Reflect Best Use Principles: Regimens for therapeutic antimicrobial use should be optimized using current pharmacological information and principles.

Treat the Fewest Number of Animals Possible: Limit antibiotic use to sick or at-risk animals.

Treat for the Recommended Time Period: To minimize the potential for bacteria to become resistant to antimicrobials.

Avoid Environmental Contamination with Antibiotics: Steps should be taken to minimize antimicrobials reaching the environment through spillage, contaminated ground run off, or aerosolization.

Keep Records of Antibiotic Use: Accurate records of treatment and outcome should be used to evaluate therapeutic regimens. Always follow proper withdrawal times.

Follow Label Directions: Follow label instructions and never use antibiotics other than as labeled without a valid veterinary prescription.

Extra Label Antibiotic Use Must Follow FDA Regulations: Prescriptions, including extra label use of medications, must meet the Animal Medicinal Drug Use Clarification Act (AMDUCA) amendments to the Food, Drug, and Cosmetic Act and its regulations. This includes having a valid Veterinary-Client-Relationship.

Subtherapeutic Antibiotic Use Is Discouraged: Antibiotic use should be limited to prevent or control disease and should not be used if the principle intent is to improve performance.

Background

Respiratory disease is most often diagnosed during the first 4 weeks of the feeding period. Consistent prevention and/or control is difficult and costly. Several viruses and bacteria have been associated with acute bovine respiratory disease (BRD). Individually, these pathogens do not appear to be capable of causing disease in healthy cattle. Interactions among the respiratory pathogens and compromise of the innate respiratory defense mechanisms, especially as a result of environmental and management stresses, such as heat or cold and weaning and transportation, seems to be critical to the development of clinical BRD (Briggs and Frank 1992).

BRD in post-weaned cattle is seldom recognized as a disease entity caused by a single pathogen (Crenshaw 1968). Management strategies that focus on pre-weaning immunizations, minimizing transportation stress, and prophylactic/metaphylactic (mass medication) antibiotic treatment have yielded the most cost effective results in controlling weaning associated BRD (Cole and Hutcheson 1992; Griffin et al. 1991; Hjerpe 1990; McNeil 2000; Smith 1984).

First Question

What is the probability the group of cattle being considered for metaphylactic antibiotic use will have a high rate of bacterial respiratory disease?

The answer must include an understanding of BRD as a syndrome. Interactions among respiratory pathogens and compromise of the innate respiratory defense mechanisms, due to environmental, nutritional, and management stressors, seems to be critical to the development of clinical BRD (Briggs and Frank 1992; Cole and Hutcheson 1992; Griffin et al. 1991).

Environmental stresses include heat or cold stress, respirable dust, and fumes toxic to the respiratory epithelium (Persson et al. 1993). Management stresses that lead to dehydration and increased levels of circulating glucocortioids play an important role in disarming an animal's respiratory defense mechanisms (Persson et al. 1993; Simons et al. 1992; Vogel et al. 1998; Weiss et al. 1991).

Once the innate defense mechanisms are disarmed, potential bacterial pathogens that normally reside in the upper respiratory tract are allowed access to the lung (Collins et al. 1968; Edwards and Stokka 1986; Frank and Briggs 1992; Frank and Smith 1983; Frank et al. 1996; Frank 1986; Godson et al. 1996; Yates et al. 1983). An aerosol of pathogenic respiratory bacteria has been shown to make cattle susceptible to respiratory viral infection. Therefore, it should not be supposed that the bacterial component of BRD necessarily follows a viral infection (Griffin et al. 1991).

High stressed, newly weaned cattle have a long history for suffering from high sickness and death rates (Griffin et al. 1991; Smith et al. 1988; Smith 1984; USDA 1992; Vogel et al. 1998). Morbidity rates are commonly reported to be in excess of 50 percent of received cattle (Cole and Hutcheson 1992; Griffin et al. 1992; Smith et al. 1984).

A long list of viruses are associated with BRD: Bovine herpes virus 1 and 3 (IBR); Bovine parainfluenza 3 virus (Pl3); Bovine viral diarrhea virus (BVDV); Bovine respiratory syncytial virus (BRSV); Bovine adenovirus; Bovine rhinovirus; and Bovine coronavirus.

IBR, Pl3, BVDV, and BRSV are the common viruses associated with acute BRD (Binkhorst et al. 1990). Respiratory disease caused by these viruses can occur without significant interaction with other pathogens. These are also the only viral pathogens for which a vaccine is available. However, viral vaccination has been shown to be protective against experimentally induced bacterial pneumonia (Griffin et al. 1991; Smith et al. 1988; Smith 1984). Viral vaccination in the Texas A&M Value Added Calf (VAC) Program before weaning has been shown to be effective in controlling weaning related BRD (McNeil 2000).

Second Question

Are there any management techniques, other than metaphylactic use of antibiotics, that will reduce the pending respiratory disease in the newly received group of cattle to a manageable level?

When purchasing cattle from sources known for delivering commingled, high stress cattle, every effort should be made to ensure the cattle are handled with care and shipped to your location as quickly as possible. Once the cattle arrive there is little you can do to manage the events of the past, but handling with care after arrival should decrease the additive stresses associated with BRD development (Crenshaw 1968; Martin et al. 1988; Perino 1994).

Arrival Handling Checklist

- **Employee Training**—Don't take for granted the people you have helping you to know how you want cattle handled or how products should be used. Regular training in good management practices is available from your cattle producer's association and extension system.
- **Be Prepared**—Visit with your veterinarian and set up a processing schedule appropriate to the needs of the cattle. Have all supplies in stock. These include clean water, fresh clean feed, properly handled vaccines, sterile needles, and syringes.
- **Protect Newly Received Cattle**—Cattle are susceptible to environmental stress. Providing shade in hot weather and windbreaks in cold weather will decrease environmental stress.
- **Timing**—When the ambient temperature is predicted to be above 80°F, time processing to be completed and have the cattle in their home pen early in the day before the day's temperature reaches 80°F.

- **Keep the Cattle Calm**—Loud noises, hot shots, and rough handling increase the animal's cortisol blood level. Cortisol decreases the immune response and innate disease defense mechanisms. Rough handling will not only decrease the value of vaccines but increases the observed incidence of BRD.
- **Observe Cattle Closely**—Check cattle closely multiple times a day for early signs of disease and/or injury. Early detection of BRD is crucial to successful treatment.

Vaccination of high stressed cattle on arrival with a viral modified live vaccine that includes IBR, BVD, PI3, and/or BRSV is believed to reduce BRD incidence and severity (Griffin et al. 1991; Smith 1984). As much as a 50 percent reduction in BRD incidence has been reported (Griffin et al. 1991). Killed modern sub-unit vaccines for *Mannheimia haemolytica* (previously known as *Pasteurella haemolytica*) are thought to be effective if given well in advance of situations and stressors that lead to BRD but have little benefit if given at processing of newly received commingled high stress cattle (Griffin et al. 1991). Modern modified live vaccines that contain both *Mannheimia haemolytica* and *Pasteurella multocida* may hold more promise for use at arrival. Few studies are available to definitively support the value of vaccines in controlling respiratory disease in high stress cattle (Perino 1994).

Third Questions

Will antibiotic metaphylaxis prevent or reduce the respiratory sickness and death loss in newly purchased, commingled, highly stressed cattle?

And if so, will the reduction in health problems be sufficient to warrant the use of an antibiotic metaphylacticly?

Antibiotics have no effect on respiratory viral pathogens, and since viruses are the principle pathogenic instigators of BRD, at first glance, antibiotics given in the early stages of BRD might not be considered reasonable.

Metaphylactic use of antibiotics in high stress, commingled cattle within 72 hours of arrival have consistently proven to be effective in decreasing both morbidity and mortality associated with BRD (Thomas et al. 1978). And as one would expect when animal suffering is reduced the animal's growth improves.

These trials included the use of injectable Ceftiofur (Naxcel & Excenel), Florfenicol (Nuflor), long-acting Oxytetracycline, Tilmicosin (Micotil), and the use of feed chlortetracycline and sulfamethazine (Galyean et al. 1995; Gallo and Berg 1995; Laven and Andrews 1991; Morck et al. 1993; Musser et al. 1996; Schumann 1991; Scott 1995). Additional data, much of which dates back over 30 years, have shown metaphylactic anti-biotic use consistently lowered morbidity and mortality associated with weaning related BRD (Griffin et al. 1991). These trials reported a 20 to 44 percent reduction in sickness rate and a 0 to 24 percent reduction in death loss (Galyean et al. 1995; Gallo and Berg 1995; Laven and Andrews 1991; Morck et al. 1993; Musser et al. 1996; Schumann 1991; Scott 1995).

The Bacteria Involved and Antibiotic Selection

First consider the bacteria involved and the role they play in BRD. In general, bacteria do not serve as primary pathogens of BRD in healthy, unstressed cattle. The bacteria and bacteria-like agents that have been most commonly associated with this disease complex include *Mannheimia haemolytica* (previously known as *Pasteurella haemolytica*), *Pasteurella multocida, Hemophilus somnus, Mycoplasma* spp., and *Chlamydia* spp.

Mannheimia haemolytica type Al is commonly isolated from fatal cases of BRD (Burrows et al. 1993; Frank and Briggs 1992; Frank and Smith 1983; Frank 1986). *Pasteurella multocida* is believed to cause less fulminating respiratory disease but is reported more often than *M. haemolytica*. *P. multocida* may be more important in BRD of younger feeder cattle (Griffin and Perino 1992).

Hemophilus somnus is reported more commonly in fatal cases of BRD in the colder climates of North America. This observation has created controversy about the role of *H. somnus* in BRD in moderate climates (Griffin et al. 1991). Discrepancies in isolation rates of fatal cases of BRD may not be associated with climatic differences. Differences in livestock genetics and production practices among regions may be associated with the reported isolations of the organism (Griffin et al. 1991).

Mycoplasma bovis is commonly isolated by some diagnostic laboratories. While this organism is not considered a primary pathogen in weaned or yearling cattle, a *Mycoplasma*-like lesion is frequently observed in finished cattle at the packing plant (Griffin et al. 1991). These organisms are often isolated in association with other bacterial respiratory pathogens, and their role in BRD may be interactive with other pathogens (Smith 1984). Vaccines have either been ineffective or have made *Mycoplasma* related BRD worse (Griffin et al. 1991; Smith 1984). Prophylactic antibiotic use has not consistently been reported to change the incidence of *Mycoplasma* isolation or severity of *Mycoplasma* lesions (Griffin et al. 1991; Musser et al. 1996).

Cattle as prey animals are extremely good at hiding their symptoms. Clinical signs develop within 14 days, but because of the multitude of etiologic factors involved, the clinical signs may vary (Griffin 1996; Griffin et al. 1991). Generally, clinical signs include loss of appetite, rapid respiration, generalized depression and weakness, coughing, increased nasal and ocular discharge, stiff movement and shortened stride, and high body temperatures (Smith 1984). The onset can be very dramatic, with the occasional animal found dead and a large percentage of cattle in a group showing severe depression (Daoust 1989; Griffin et al. 1991).

The value of metaphylactic antibiotics in part is related to the ability of cattle to hide symptoms and the explosive nature of the bacterial phase of BRD once viral damage has crippled the bacterial defense mechanisms in the upper respiratory tract. The decrease in the potential pathogenic bacterial populations in the upper respiratory region by metaphylactic antibiotic use may be related to the improved health parameters observed (Briggs and Frank 1992; Cole and Hutcheson 1992; Edwards and Stokken 1986; Frank and Smith 1983). Additionally, metaphylactic antibiotics may decrease the role of bacteria, such as *M. bovis,* that are marginally pathogenic but that may have a significant additive effect in BRD development.

Metaphylactic antibiotic selection should be discussed with your veterinarian. Your veterinarians will consider age and source of the cattle, the type of stress the cattle will endure, and previous laboratory antibiotic sensitivities for isolated bacterial pathogens (Burrows et al. 1993; Salmon et al. 1996).

Some antibiotics should never be considered for metaphylactic use. These include injected gentamicin, injected neomycin, and enrofloxacin (Baytril). Also, cattle producers must understand it is a violation of federal law to use antibiotics other than as directed on the label unless prescribed by a veterinarian. Before writing a prescription, federal law requires a veterinarian have personal knowledge of the cattle and their management, determine that use other than as labeled is required, that the veterinarian is available for follow up, and the withdrawal time is significantly extended so that no violative residues will be found.

Fourth Question

Will the reduction in suffering caused by respiratory disease be great enough to offset the cost of antibiotic metaphylaxis?

Detailed breakeven analysis of the cost of BRD shows reduction from 30 percent sickness to 20 percent sickness will be worth approximately 4 percent higher cattle purchase price in health cost savings. Cattle producers commonly fall for this trap. When breakeven analysis considers performance losses over the backgrounding period the value appears to be worth an additional 4 percent, or about $4.00 per hundredweight (cwt). Less data are available for analysis of performance loss for the entire feeding period but suggests losses will cost in excess of 30 pounds gain and a 2 percent decrease in carcass value (Griffin 1996; Salman et al. 1991; Salman et al. 1990; Thomas et al. 1978).

Fifth Question

Will the use of antibiotic metaphylaxis decrease the response seen to antibiotics in future cases of respiratory disease in cattle in the group treated with antibiotics metaphylacticly?

Few studies are available to answer this important question. But the available data suggest metaphylactic antibiotic use does not alter the effectiveness of the medication if used on clinical BRD cases from the same group (Morck et al. 1993; Vogel el al. 1998).

Sixth Question

Will the long-term effects on bacterial antibiotic resistance make it difficult to treat future cases of bacterial disease in your cattle or humans working around the cattle?

Data available for BRD bacterial pathogens do not support observations of significant changes in the antibiotic resistance pattern. Perhaps this is because BRD bacterial pathogens tend to be kept isolated within groups of cattle and terminate at the packers.

The FDA and CDC are concerned about antibiotic resistance in animal pathogens such as *Salmonella* that could be transferred to humans. For the past few years a national antibiotic resistance monitoring program has been in place, but little is presently available to support a relationship.

The FDA has initiated a new "Framework" for evaluating antibiotics that are cleared for use in agriculture. The new approach to antibiotic approval considers the significance of an antibiotic for treatment of human disease and the duration the antibiotic is typically used. Pharmaceutical companies are now required to continually monitor antibiotic resistance changes. It has become important for cattle producers to work with their veterinarian when selecting and using anti-biotics and to adopt judicious antibiotic use guidelines (Fig. 1).

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