

Practical pharmacology for the new graduate

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Abstract

New veterinary graduates can be helped by guidance for therapeutic decision-making when using antimicrobial drugs in bovine practice. Aspects to be considered include empirical therapy in the absence of a definitive diagnosis, governmental regulations, client compliance, therapeutic indications, cost, food safety, and extra-label drug administration.

Key words: antimicrobial, drug, therapy

For the new graduate, therapeutic decision-making in practice can feel like a challenge even when there has been good preparation in veterinary school and through practice externships (though what one learns in veterinary school and what one observes in externship or in practice may differ substantially). Making therapeutic decisions about the use of antimicrobial drugs is a privilege to be taken seriously. The process can be simplified as a series of steps, as follows.

Step 1: A VCPR and a patient that is ill or at risk

The first step is always to establish a Veterinarian-Client-Patient Relationship (VCPR), if the client is one you wish to work with. Fortunately, the VCPR is established in the process of making the most accurate diagnosis possible. Resistance to making the most accurate possible diagnosis is often encountered in the form of client reluctance, limited resources, limited time, or all of the above. In the context of livestock practice, it is important to look at the management of the affected animal or animals within the production system, whether it is a backyard hobby farm or a feedlot. What factors may have led to this problem? How can those factors be adapted to enhance the likelihood of recovery and decrease the likelihood of more animals being affected?

Of course, obtaining microbial culture and sensitivity is ideal and even when empirical therapy (in the absence of that information) is undertaken, a sample may be obtained and submitted to the diagnostic laboratory, or held to be submitted in the event of treatment failure (for example, freezing a milk sample from a cow with mastitis).

Step 2: Should you treat it?

Once a diagnosis is obtained within the context of a valid VCPR, the next question is whether or not to treat the condition with antimicrobial drugs. Some conditions, for example mastitis of mild or moderate severity (especially when caused by a Gram-negative pathogen), are likely to resolve on their own without antimicrobial drug treatment. Some conditions, such as chronic mastitis that has recurred across lactations, are unlikely to resolve no matter the treatment. And of course, many conditions are not caused by bacterial infection, so treatment with antimicrobial drugs is not indicated.

Step 3: What is the most likely causative pathogen?

There are over 40 different antimicrobial drugs approved for use in livestock species. That can seem a bit overwhelming, but for the treatment of the individual patient, there are fewer drugs to choose from, making the process simpler.

The most common infectious diseases encountered in cattle are bovine respiratory disease (BRD) and mastitis. For BRD, which may have both viral and bacterial components, the most common bacterial pathogens are *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*. In mastitis, the most common pathogens include streptococci, staphylococci and *Escherichia coli*. When choosing an antimicrobial drug for a first-time treatment of infectious disease in the absence of microbial culture results or if treatment is necessary pending their receipt, it is prudent to target the pathogens that occur most commonly in the condition. If the condition is something other than BRD or mastitis, the internet is your friend; for example, a quick search of “bovine wound infections” on a large search engine (not a specifically scholarly one), quickly turned up information from 2021 that bovine wound infections are most often caused by *Actinomyces bovis*, *Bacteroides melaninogenicus*, *Staphylococcus aureus*, *S. hyicus*, *Streptococcus dysgalactiae*, *Fusobacterium necrophorum*, *Moraxella bovis* and *Trueperella pyogenes*.¹

Step 4: How should this infection be treated?

Assuming you have made it to this step, having established a VCPR and that the animal has a bacterial infectious disease that may benefit from antimicrobial drug treatment, the next step is to select an appropriate drug.

The first question must be, “what are the options”? What drugs do you have available to you for treatment of this animal? For individual animal treatment of cattle, drug classes (with example drugs) with FDA-approved products available include:

- Penicillins: penicillin G, ampicillin, amoxicillin, cloxacillin (IMM) and ampicillin
 - Cephalosporins*: cephapirin (1st gen, IMM only) and ceftiofur (3rd gen)
 - Fluoroquinolones*: danofloxacin and enrofloxacin
 - Macrolides: gamithromycin, tildipirosin, tilmicosin, tulathromycin, and tylosin
 - Sulfonamides*: sulfadimethoxine
 - Tetracyclines: oxytetracycline
- * Extra label drug use in this drug class is restricted or prohibited

For the treatment of BRD, there are a relatively high number of drugs approved by the FDA, with their label-indicated spectra of antimicrobial activity including some or all of the most common bacterial BRD pathogens. For mastitis, there are

intramammary tubes available containing drugs with both Gram-positive and Gram-negative bacteria in their spectrum of activity (and none that are active against *Mycoplasma*). Of course, the activity listed on the label indicates what the drug may do, not what it will do in any particular circumstance, given the many variables including the state of the patient's immune system and bacterial resistance patterns.

Another consideration in drug selection is client compliance. Some drugs are labeled for single-dose use, while others require repeated dosing to complete a full treatment regimen. Generally, the cost per dose is higher in the single-dose products. Compliance may be a problem with multiple doses for some clients, and multiple doses will require multiple episodes of stress associated with restraint for the patient.

Many articles that discuss antimicrobial drug treatment approaches include extensive discussions of pharmacokinetic and pharmacodynamic considerations in the design of dosing regimens. At this point, as a new graduate practitioner, that kind of analysis is usually unnecessary; it is acceptable to trust that the pharmaceutical company and the FDA have successfully collaborated to approve a label dosing regimen that maximizes the likelihood of therapeutic success for labeled indications. Another advantage of sticking to the dosing regimen on the drug label is the protection from veterinary liability should a violative drug residue occur, provided that the veterinarian followed the label dosing regimen and provided notice of the label withholding time in writing to the client. Withdrawal times relative to plans for the animal during the proposed withholding period must be discussed with the client prior to treatment.

In addition to selecting antimicrobial drug treatment (if necessary), consider what other treatments might be beneficial. Should the animal be isolated during treatment, or will the social stress of isolation outweigh the convenience or benefit isolation? Measures should be taken to enhance nutritional support and mitigate environmental or other stressors. Conditions associated with the infection, such as pain and dehydration, must also be addressed in the treatment plan in order to maximize the likelihood of treatment success.

Finally, determine what treatment success or failure will look like and when the evaluation(s) of treatment effect will be conducted, and by whom. Make a plan for follow up with the client to monitor and record the outcome of treatment (and if necessary, confirm that treatments to be done by the client were done as directed). Veterinary technicians can be a great help in ensuring treatment protocol compliance and evaluating and recording treatment outcomes.

Step 5: What to do afterward...and before the next time

For the most common causes of infectious diseases, it is helpful for the practitioner to have handy a definition of a case and of successful and unsuccessful treatment outcomes; this becomes essential if the practitioner is designing protocols to be used in production systems.

Keeping records of treatment outcomes for infectious diseases on a farm or ranch or at a veterinary clinic is tremendously helpful. Sometimes drugs do not work as expected for a variety of reasons, including the development of resistance, and becoming aware of patterns of treatment failure is an irreplaceable tool for guiding future decisions. Of course, this is most helpful when information about the causative microbial pathogens is also obtained and recorded. Veterinary diagnostic labs often compile records such as pathogen identification and drug susceptibility among BRD cases submitted to the laboratory over the course of a year, and they may share them if asked or post them on the laboratory website. Although cases submitted to a diagnostic laboratory may not perfectly represent all cases encountered, the data may give some clues as to general resistance patterns in the region. In addition, I have found that most diagnosticians at veterinary diagnostic laboratories are happy to help practitioners interpret diagnostic findings from their lab, including antimicrobial drug susceptibility testing, and apply the information to therapeutic decision-making. A veterinary practice can also make a record of their own using cases and outcomes from their own clientele; this document would have the advantage of specifically reflecting the outcomes of the types of cases most often encountered and treatments most often used at the practice.

Summary

In summary, when a new graduate is gaining their footing as practitioner, a systematic approach to antimicrobial drug selection will make decision-making easier and less stressful. Weighing factors such as probable pathogen, cost, likelihood of compliance and withholding time, along with excellent record keeping, case definition, and monitoring of outcomes, will decrease stress while enhancing the likelihood of therapeutic success and a satisfied client.

References

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