Antibiotic resistance continues to be a growing concern in veterinary and human medicine.

The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) in humans and methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) and methicillin-resistant *Staphylococcus schleiferi* (MRSS) in companion animals is compelling veterinary practitioners to reevaluate how they are treating patients.

By gaining a clear understanding of the published guidelines for treating skin disease and following modern treatment concepts, veterinarians can act as good antimicrobial stewards, helping to reduce the development and spread of antimicrobial resistance.

**THE EXPERTS**

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Mark G. Papich, DVM, MS, DACVCP
Vanessa M. Schmidt, BVSc (Hons), PhD, CertVD, DECVD, MRCVS
Jeffrey L. Watts, PhD, RM(NRCM), M(ASCP)
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A panel of experts in veterinary and human medicine was convened to provide practitioners with insight into their principles of treatment for skin infection, including recommendations for selection and judicious use of antimicrobials in general practice and how these factors relate to antibiotic resistance.
ANTIBIOTIC RESISTANCE AND PRINCIPLES OF TREATMENT IN VETERINARY DERMATOLOGY

THE ISCAID GUIDELINES PLACE SYSTEMIC DRUGS INTO TIERS:

FIRST TIER—Drugs in this category are appropriate choices as a first empirical selection for superficial folliculitis caused by *S. pseudintermedius*. These include first-generation cephalosporins, clindamycin or lincomycin, and trimethoprim- and ormetoprim-potentiated sulfonamides.

FIRST OR SECOND TIER—This middle ground between tiers was chosen for third-generation cephalosporins.

SECOND TIER—These include drugs such as aminoglycosides, fluoroquinolones, and rifampin, which are to be used when empirical selection of first-tier systemic antimicrobials AND topical therapy are not appropriate and cultures indicate susceptibility.

THIRD TIER—Drugs in this category include linezolid, teicoplanin, and vancomycin and are indicated when first- and second-tier choices are not appropriate and cultures indicate susceptibility. Use of these drugs is strongly discouraged.

GUIDELINES ON TREATING BACTERIAL SKIN INFECTIONS

A number of guidelines on the treatment of bacterial dermatologic infections exist. These guidelines focus on recommendations regarding diagnostics, appropriate antibiotic selection, and case management. With the guidelines often providing conflicting information, how can a general practitioner decide which recommendations to follow?

The expert panel focused on the guidelines for treating superficial bacterial folliculitis published by the International Society for Companion Animal Infectious Diseases (ISCAID). The panel included dermatologists, internal medicine clinical pharmacologists, and microbiologists; Dr. Papich served on the consensus committee that developed the ISCAID guidelines. Guidance is provided for both topical and systemic modalities and includes recommendations to address MRSP.

*Staphylococcus pseudintermedius* is commonly found on the skin, nose, and mouth and in the gut microbiome in dogs and cats (and some humans). As with other commensal bacteria, it can become pathogenic and cause disease. MRSP is a form of the bacterium that is resistant to all beta-lactam antibiotics and frequently resistant to other commonly used antibiotics of other classes. Typically used antimicrobials may not be effective against MRSP infections.

“When the third-generation cephalosporins were placed as either first or second tier, the concern was about the gram-negative organisms, particularly about the selection of the highly resistant, extended-spectrum beta-lactamase (ESBL)-producing organisms,” Dr. Papich explains. “This is a concern all over the world in food animals, companion animals, and human medicine. These are bacteria, primarily *Escherichia coli*, that produce an ESBL that renders the organisms resistant to the extended-spectrum drugs, particularly the third-generation cephalosporins.”

“The placement of the third-generation cephalosporins in the ISCAID guidelines was based on the risk of selecting for resistance among the Enterobacteriaceae and the potential risk that they may pose for human health.”

—Dr. Papich

Selecting an Appropriate Antibiotic

“We have a number of guidelines to help us in the selection of antibiotics for the treatment of pyoderma. Each has slight differences, which I think has to do with geographic variation and perhaps the regulatory environment in which we live,” explains Dr. Fadok. “My advice to veterinarians is to try to interpret the guidelines in light of what you know about your own geographic area. One of the problems that I see is that there are big differences in patterns of susceptibility or response in different parts of the country. I think it’s important for veterinarians to try to get some local information, so that when you’re picking an antibiotic empirically, you have some idea of whether that empiric choice makes sense for your locale or not. This information is often available through your local specialist. It might be a little skewed toward the more severe cases, but it’s a place to start.”

“We have come a long way since penicillin. Not only do we have new drugs that go beyond penicillin, but we understand how they work better and how to use them better based on
pharmacokinetic and pharmacodynamic principles,” Dr. Papich says. “We have enough background that we can get some ideas of what would be an ideal antibiotic: one that’s safe and that we can give to all of the patients we see—some old, some young, and those with other comorbidities or on other drugs. Drug selection is favored toward agents that have minimal adverse effects. That’s why beta-lactams like amoxicillin–clavulanate and the cephalosporin class of antibiotics have been so popular.

“From a resistance standpoint, the ideal antibiotic would be one that is targeted at the bacteria that we want to treat. If we’re talking about pyoderma, it’s bacteria in the skin. We prefer an antibiotic that has less of an effect on the bacteria in other parts of the body—those that we refer to as the ‘innocent bystanders,’ particularly those in the intestine. That means that the drug is either not active against those bacteria, perhaps because of differences in minimum inhibitory concentration (MIC), or perhaps the drug doesn’t distribute to the intestinal tract or gets inactivated in the intestinal tract.”

“The reason these ‘innocent bystanders’ are a concern when selecting an antibiotic is that those bacteria can get into the environment and our homes, and people could be exposed to them. They can also be a source for future infections, particularly lower urinary tract infections or skin/soft tissue infections that could result from contamination of intestinal bacteria, in both people and pets.”

—Dr. Papich

Minimum Inhibitory Concentration

The MIC is the lowest concentration of the drug tested that inhibits the growth of the bacteria. “If the drug concentration is below the MIC, theoretically, it shouldn’t do anything because the organism is not inhibited,” Dr. Papich explains. “It should not select for resistance. Those bacteria should be able to survive because there is not sufficient selection pressure of antibiotics at concentrations below the MIC. Once we’re at this subtherapeutic level, the drug is also not going to be effective. There’s no reason to suggest that the drug is going to select for a resistant strain of bacteria.”

Study Shows That Antimicrobial-Resistant Fecal E. coli in Dogs Recovers to Pretreatment Levels Regardless of the Antibiotic or Antibiotic Class Used

A recent prospective study by Dr. Vanessa Schmidt and colleagues was conducted to determine what effect systemic antimicrobials (both oral and injectable) have on the resistance profile of fecal E. coli populations in dogs requiring routine antibiotic therapy.

Dr. Schmidt explains that the study focused on E. coli because it is often used as a marker of the presence of antimicrobial resistance. An important member of the gut microbiome, E. coli is carried within all people and animals and can be shared between people, between pets, and between people and pets within a household.

Included in the study were 131 dogs that were prescribed amoxicillin–clavulanate, cephalexin (a first-generation cephalosporin), cefovecin (a third-generation cephalosporin), clindamycin (a lincosamide), or enrofloxacin (a fluoroquinolone). “We wanted to compare the impact of different antimicrobials, including cephalosporins that are commonly used by general practitioners to treat infections in dogs,” Dr. Schmidt says. “We also wanted to compare both oral and injectable forms and to compare beta-lactams within the class.”

Risk factors, such as repeated veterinary visits, procedures within the hospital, and contact with healthcare workers, were taken into account in the modeling of the study analysis to screen out potential biases.

The results suggest a trend toward increased antimicrobial resistance in fecal commensal E. coli immediately after antimicrobial treatment was stopped with all antimicrobials, except for the more narrow-spectrum drug clindamycin.

This study, however, did show subsequent recovery to pretreatment (baseline) levels within 1 to 3 months after treatment in this population of dogs, regardless of the antibiotic or antibiotic class used. Dr. Schmidt points out that frequent repeated exposure to antimicrobials, although not investigated in this study, may be expected to prolong these effects.³
Preventing Antibiotic Resistance

“I believe we can use antibiotics safely and effectively when they’re needed,” says Dr. Fadok. “What we know about antibiotics is that they tend to select for resistant strains, particularly when long or multiple courses of antibiotics are used. That’s why it’s important to understand our organism when we’re starting with the first pyoderma.

“What we know about the *Staphylococcus* organism is that, in general, it is resistant to penicillins and tetracycline derivatives. It’s often exquisitely sensitive to beta-lactams, such as the cephalosporins. We have a long history of using beta-lactams in veterinary medicine because they’re safe and effective. They seem to resolve infections rapidly, and this allows us to meet the needs of our clients and patients without the fear of causing resistance. So rather than long, drawn-out courses of antibiotics, we want to select an antibiotic that we know resolves an infection quickly and to use that antibiotic only as long as it needs to be used.”

**Antibiotic resistance** refers to the ability of bacteria to resist the effects of an antibiotic. When bacteria are resistant to the drug or drugs being used, the bacteria will survive and continue to multiply. Antibiotics themselves don’t cause resistance; they select for resistant strains that are already present. All antibiotics select for resistance.

“In human medicine in the 1980s, 1990s, and 2000s, our thoughts were that the main driver of *Staphylococcus* spp. resistance was beta-lactam use—penicillins and cephalosporins—but also total antimicrobial use,” Dr. Zhanel says.

“Antibiotic resistance and principles of treatment in veterinary dermatology

**THE meca GENE ENCODES BACTERIA TO BE METHICILLIN RESISTANT.**

“Because we know that when you are using any antimicrobial class such as a fluoroquinolone, a macrolide, or a tetracycline, you have the capability to drive resistance to *S. aureus* and presumably *S. pseudintermedius*, so I would take the cause of resistance to be all antimicrobial use, not just beta-lactam use.”

“Even in veterinary medicine, some studies have shown that restriction of certain classes of antibiotics has had little effect on reducing resistance,” Dr. Papich says. “If there are restrictions on certain antibiotics or overall antibiotic use, it may reduce antimicrobial prescriptions and can reduce antibiotic resistance. However, it’s difficult to identify one particular drug or class of drug that is responsible for the increase in antibiotic resistance. If there are restrictions on one particular drug or class of drug, the use of other classes of drugs may increase. Therefore, other drugs could also drive resistance. So it sounds like an easy solution to just say we’re not going to use a certain drug, but it might also be naive to think that bacteria would not develop resistance to the alternative selection.”

“The available evidence shows that it has not been one particular drug or class of drug that has caused the emergence of methicillin-resistant strains of staphylococcal pyoderma. The conclusion is that any antibiotic has been a risk factor in driving resistance for that organism. Not just second-tier drugs, not just first-tier drugs—any antibiotic.”

― Dr. Papich

“There is no evidence that one class of cephalosporins is any more likely to select for methicillin-resistant *Staphylococcus* spp. than another group of cephalosporins,” Dr. Papich says. “Therefore, all the cephalosporins, with respect to *Staphylococcus* spp., may carry a similar risk for selecting for resistance.”

“I think any time you are using antimicrobial therapy, you know that you will be selecting for resistance,” Dr. Zhanel says. “So you ask yourself, ‘Does the benefit of using the antimicrobial to treat and cure the infection outweigh the potential selection of resistance?’”

“I completely agree. It’s the same situation in veterinary medicine,” Dr. Fadok says. “We’ve learned this from the studies where they have tried to identify one particular class of drug, or one particular drug, as being the driver of resistance. What we’ve learned, based on our literature and some of our own experiences, is that any antibiotic exposure can lead to resistance. So it’s always a concern. In order to mitigate that, we pick a good drug: one that is going to work.”
Staphylococcal Resistance Levels Return to Near Pretreatment Levels 3 Months After Therapy

In addition to Dr. Schmidt’s work on E. coli (see the sidebar on page 3), she and colleagues also conducted a prospective study to examine mucosal staphylococcal populations in dogs before and after therapy with systemic antimicrobials. A group of dogs (N=126) requiring routine systemic antimicrobial therapy with either cephalexin (n=31), amoxicillin–clavulanate (n=29), cefovecin (n=25), clindamycin (n=28), or a fluoroquinolone (n=13) without prior antimicrobial treatment or veterinary admission were enrolled in the study. Outcome measures included the presence of oxacillin resistance, mecA gene carriage, and multidrug resistance.

The study showed an overall trend for the percentage of resistant canine commensal staphylococci to increase at the end of therapy and return to near pretreatment levels 3 months post-therapy, without further antimicrobial prescription.

Culture and Susceptibility

If the chosen empirical antibiotic fails, Dr. Papich and Dr. Fadok recommend doing a culture and susceptibility to determine which drugs the bacteria are resistant to. “I really think you need to be guided by a susceptibility test because if the drug has failed, it could be poor compliance, and you need to evaluate that,” Dr. Papich explains. “In some types of pyoderma (for example, deep pyoderma), it could be a different organism. But the biggest reason for failure these days is the fact that it’s a methicillin-resistant strain.”

Besides being resistant to all of the penicillins and cephalosporins, most MRSP are also multi-drug resistant. Thus, most of these strains are resistant to other drugs that might ordinarily be considered in these cases, such as erythromycin, clindamycin, trimethoprim sulfonamides, tetracyclines, or a fluoroquinolone. “So it’s difficult to predict what drug is going to reliably work,” Dr. Papich says, “which is why you need to be guided by a diagnostic test.”

THE ROLE OF ANTIMICROBIAL SURVEILLANCE IN COMPANION ANIMAL PRACTICE

In both human and veterinary medicine, surveillance has been recognized as a fundamental component in the control of organisms with resistance to antimicrobial agents. Surveillance information can:

- Enable assessment of the disease burden regionally and locally
- Allow for determination of risk factors associated with resistant pathogens
- Allow the identification of resistance trends over time

Zoetis Surveillance Programs

To give clinicians better guidance regarding antibiotic resistance patterns, Zoetis began investing in surveillance programs in 1998, focusing on target pathogens in livestock. The companion animal surveillance program began in 2011. Important pathogens of the skin, soft tissue, and urinary tract of dogs and cats are collected from state/provincial diagnostic and commercial laboratories in North America. Currently, the program has 19 participating laboratories and has collected samples of around 2,000 isolates.

CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI)

CLSI standards state that if a Staphylococcus strain carries the mecA gene or is oxacillin or methicillin resistant, laboratories must report that isolate as resistant to all beta-lactam antibiotics. The only exception is in human medicine, with the new fifth-generation cephalosporins (ceftaroline and ceftobiprole) that have specific activity against MRSA infections.

“We encourage labs to always use the CLSI standards. Most reputable labs in the United States are using them. These will state how to interpret the test, oxacillin resistance, and so forth.”

–Dr. Papich
Sampling Bias in Surveillance Programs

“What we’ve learned over the years of building our program is that all surveillance programs contain sampling bias, or ‘skew,’” Dr. Watts says. “You have to understand what causes that bias.”

He further points out that the program should clearly identify the bias in the data, including sampling methods, types of isolates (pretreatment vs posttreatment), and frequency of sampling intervals. It should also avoid sampling multiple strains from the same outbreak to prevent overrepresentation of a single strain from biasing the data.

For the Zoetis Companion Animal Surveillance Program, samples are received from general practices where a culture was deemed necessary based on clinical response, history of antibiotic use, or other suspicion of resistance.

Other surveillance programs use isolates from diagnostic labs, which may be from tertiary care hospitals, or they may be isolates from animals that have previously failed therapy. This means their data will be skewed to show more resistance. Surveillance programs should be designed to reduce bias as much as possible within the objectives of the program.

Focus on MRSP in Surveillance

With the concern surrounding MRSP, all staphylococci in the Zoetis Companion Animal Surveillance Program are tested to see if they are methicillin resistant. Methicillin resistance is mediated by production of a modified penicillin-binding protein 2a (PBP2a) that is encoded by the mecA gene. The modified PBP resists the effects of beta-lactam antibiotics.

Rates of MRSP for skin/soft tissue infections (SSTIs) in companion animals have consistently remained around 25% to 30% of isolates tested since 2011, when the surveillance program began (Figure 1).

The emergence of MRSP since 2000 has been remarkable, with a rapid rise in prevalence from 2004 through 2009 and rates plateauing from 2010 to present.6 In the Zoetis surveillance program, MRSP levels have ranged from 24.9% to 32.2% from 2011 to 2015. This has represented a significant therapeutic challenge to veterinarians because it significantly limits treatment options.

“The parallel with the MRSP data and community-acquired MRSA in the human setting is startling. We had an analogous, skyrocketing increase in the late 1990s/early 2000s, and thereafter it plateaued exactly the same way as the data for MRSP show. MRSA is very regionally based, with rates of 5% to 50%, but on average, rates fall somewhere around 30%.”

–Dr. Zhanel

TREATING INFECTIOUS DISEASES IN HUMANS

Unfortunately, not a lot of information is available about antibiotic compliance in veterinary medicine. Dr. Zhanel provided insight into human compliance that may offer correlations to ideal antibiotic regimens for companion animals.

Compliance and Clinical Cure Rates

Compliance (referred to as adherence in human medicine) with an antibiotic treatment regimen is associated with higher clinical cure rates. Antibiotics kill pathogens, but patients need to take the antibiotics for them to cause clinical resolution of the infection (Figure 2).
Combining less frequent dosing with a short course of therapy correlates with the highest compliance. The ultimate is that you have one-dose therapy," Dr. Zhanel says. "There are advantages and disadvantages of one-dose therapy, but to me, the advantages far outweigh the disadvantages. The thought is that you give one dose, compliance is theoretically going to be 100%, and the infection has been treated. It may take some time (days) to achieve clinical improvement, but the course of therapy is finished, and now you’re not worried about, ‘Will the patient take his or her antimicrobials and finish the course?’ Good compliance equals good clinical cure.”

Compliance and Longer Half-Life
A current trend in human medicine is to select a systemic antibiotic with a longer half-life to ensure compliance. However, there has been some discussion about whether the length of the drug’s half-life may play a role in driving resistance.

"The worry has been, if you treat with a 3- or 5-day azithromycin treatment regimen, the drug due to its long half-life (68-72 hours) may hover around (above and below) the MIC for several weeks," says Dr. Zhanel. "Could azithromycin with its long half-life be selecting out organisms that are less susceptible or resistant to macrolides (pathogens or normal flora) at a higher rate than macrolides with short half-lives, such as clarithromycin? When azithromycin, which has a long half-life, came out, we were asked, ‘Is azithromycin more likely to select out resistance than clarithromycin or erythromycin?’ So we looked into this.”

Dr. Zhanel and colleagues examined 15 years’ worth of data in Canada and the United States. They looked at regions that were using more clarithromycin and those that were using more azithromycin and asked, "Was there a relationship between using shorter half-life macrolides versus longer half-life macrolides in their selection of macrolide-resistant Streptococcus pneumoniae?" In that study, they showed that the driving force for selecting macrolide-resistant S. pneumoniae was using all or total macrolides. There was no preferential effect of long half-life in terms of driving out resistant S. pneumoniae. They concluded that whether you’re using erythromycin, which has a half-life of 1 hour, clarithromycin, which has a half-life of 5 to 8 hours; or azithromycin, which has a half-life of 68 to 72 hours, they did not find that half-life was a driving factor in the development of resistance.8

"I think poor compliance is more likely to drive resistance than long half-life," says Dr. Zhanel. "We know that patients with tuberculosis who don’t take their antitubercular antimicrobials (e.g., rifampin, isoniazid) are associated with development of resistance. That data is indisputable.9 I personally am not worried that the long half-life is driving resistance.”

“When we look at the available data, we just don’t have the evidence that long half-life antibiotics select for more resistance than shorter half-life agents. I do worry about the selection and development of resistance with long half-life agents, but I don’t worry any more than I would with a medium or a shorter half-life antimicrobial.”

–Dr. Zhanel
Selecting for resistance is a risk when using traditional daily oral medications as well. "A lot of the discussion around resistance is related to intestinal bacteria," says Dr. Papich. "With an oral antibiotic, concentrations are high in the intestine. Regardless of the class of drug, there is potential to alter the intestinal population and select for resistant bacteria, even with an oral antibiotic that is administered intermittently (once or twice a day). Most oral antimicrobial agents have a risk of resistance because of the method of administration."

"I worry about antibiotic resistance, whether you’re using an agent orally, subcutaneously, or intravenously," Dr. Zhanel says. "Antimicrobials help to select resistant pathogens in different parts of the body. Treating companion animals or humans with any antibiotic has its risks and benefits. No data exist that show an antimicrobial with a long half-life selects for resistance. Knowing that the antimicrobial you use will achieve the bacterial killing and clinical cure far outweighs any potential worry that we would have about a long half-life."

"There are no data to show whether long half-life drugs select for resistance more than intermittent doses of drugs with a short half-life," Dr. Papich says. "As we’ve discussed, the concern has been that selection of resistance in the intestine is caused by long-acting third-generation cephalosporins. But if the long half-life drug concentrations eventually fall below the minimum inhibitory concentration, the bacteria shouldn’t be affected one way or another."

**Compliance and Duration of Therapy**

Studies conducted in human medicine show that shorter courses of therapy are associated with the same or greater clinical outcome versus long-term therapy.\(^{10,11}\)

We’ve learned that in food animals as well, because there’s so much concern about the use of antibiotics in food animals and the exposure to humans. "Almost by necessity, food animal veterinary practitioners have learned in some cases to use a single-shot therapy and have found that it’s effective for diseases as severe as pneumonia," Dr. Papich explains. He also points out that on the companion animal side, some evidence shows that shorter courses of treatment for a urinary tract infection, for instance, are just as effective as a longer course of treatment.\(^{12}\)

"There’s limited evidence, but there is some that encourages us to challenge the need for some long courses of treatment. Some of these treatment regimens are handed down from one book chapter or one textbook to another without much challenge. We encourage more clinical studies to evaluate duration of antibiotic administration for various infections."

–Dr. Papich

Dr. Fadok would like to see duration of therapy based on response of the patient rather than set periods of time that there is no evidence to support. "I’m finished treating a pyoderma when there are no active lesions," she says. "Once I don’t see active lesions, I’m not convinced I need to go a week or two beyond or have a set date. This makes it much more individualized, and because of that, it might be more challenging to a practitioner to monitor patients this way. But I think it’s the best way to go. It will come back to instilling confidence that we’re doctors. We know what we’re doing. We have your interests and your pets’ interests at heart, and we’re going to treat this until it’s gone. We’re not going to treat it any longer than that."

**TREATING CANINE PYODERMA**

Decades ago when treating infections, such as canine pyoderma, veterinarians were taught to pick the most narrow-spectrum antibiotic first. If that didn’t work, the next step would be to pick a more active drug, sometimes in the same class. Unfortunately, this 1980s microbiology thinking won’t work when treating 21st-century infections.

**Understanding Selection Pressure**

Using antibiotics in companion animals or humans is a risk-versus-benefit issue, Dr. Zhanel explains, because antibiotic use selects antibiotic-resistant (or less susceptible) organisms on (e.g., fur, skin) or in (e.g., gastrointestinal tract) subjects. "Antibiotics don’t know where in the body the infection is," he says. "Their job is to kill organisms all over the body, which leads to collateral damage, meaning the selection of resistant organisms in our normal bacterial microbiota."
“What we’ve learned from dealing with MRSP is that once you’ve tried a beta-lactam and it doesn’t work, you can’t try another in that class for the same infection,” Dr. Fadok explains. “If the Staphylococcus strain is resistant to one beta-lactam, it is essentially resistant to all beta-lactams. That’s why I believe the best approach is to start with the best-in-class antibiotic—the one that is expected to achieve the fastest outcome.”

“Empirical choice of antibiotics in the treatment of pyoderma requires that we know a little bit about our organism, and when the organism is what we would call a ‘methicillin-sensitive Staph,’ we know that it is very responsive to beta-lactam antibiotics,” Dr. Fadok says. “There are other antibiotics we could choose, but I think a lot of dermatologists and practitioners like cephalosporins because they are very safe and work quickly. I would anticipate recommending a cephalosporin if it’s a first-time pyoderma. I think the likelihood of that bug being resistant is low.”

Standard practice used to suggest treating a superficial pyoderma for at least 3 or 4 weeks with antibiotics or 1 to 2 weeks after clinical remission. “I now recommend shorter courses of oral antibiotics coupled with topical therapy for the treatment of superficial pyoderma. Whether longer courses are needed is based on response to therapy,” Dr. Fadok says. “In addition, pulse antibiotic therapy is no longer considered effective.”

“There may be benefits to a shorter course of treatment. The pet owner is happier because she doesn’t have to keep struggling with giving the pet an antibiotic, and that improves the human–animal bond. We’re also reducing overall antibiotic exposure, to both the pet and environment.”

—Dr. Papich

Although there is no optimal duration of antibiotic therapy for pyoderma, Dr. Fadok recommends treating until the infection is gone (no pustules, papules, crusts, or epidermal collarettes). Shortening the course of treatment can also be a good way to improve compliance. Although there are no reliable data on compliance specifically in veterinary medicine, as in human medicine, compliance likely remains higher with a once-a-day or twice-a-day dose. Additionally, the shorter the course, the more likely owners may be to remember to give the drug.

Incorporating Multimodal Therapy

Topical therapy can be extremely effective in helping to reduce the duration of systemic antibiotics and prevent relapse. Evidence has shown that using a multimodal approach, including both systemic and topical therapy, can provide better outcomes for dogs with pyoderma. In fact, the ISCAID guidelines give recommendations on the use of topical therapy for treating superficial pyoderma. The guidelines promote the use of chlorhexidine-based shampoos, based on evidence of their superiority when compared with benzoyl peroxide, ethyl lactate, chloroxylenol, or lactic acid/boric acid. One study in particular found that the use of a combined protocol of 4% chlorhexidine digluconate shampoo and solution reduces the time to resolution and prevents relapse.

“Perhaps some relapses have to do with not incorporating topical therapy. Topical therapy gives us a great chance to physically remove a lot of the bacteria that are present on the surface of the skin. To me, combining the two modalities—systemic antibiotic and topical therapy—is even more powerful.”

—Dr. Fadok

Dr. Fadok strongly recommends bathing or some form of topical antisepsis as a part of therapy for every canine patient with pyoderma. Clients, especially those with difficult-to-bathe dogs, may push back. Explaining the rationale behind bathing should result in greater buy-in. In addition, veterinarians can offer other topical therapy options, such as sprays, mousses, or spot-ons, or offer the client the bath as a service performed at the hospital.
**BEYOND RESPONSIBLE USE**

Dr. Watts stresses that antimicrobial stewardship encompasses more than just responsible use. Although a veterinarian’s first responsibility is to individual patients, instituting certain practices will allow you to make good stewardship choices on a practice-wide basis. He suggests:

1. Know your pathogens and understand local resistance patterns by getting access to surveillance programs and requesting antibiogram patterns of your cases from your laboratory. That way, you can switch empiric therapy if a resistant organism emerges.

2. Implement biosecurity and hygiene practices, such as handwashing and sterilizing stethoscopes between patient exams, which can also have an impact. “As an example, the most recent European data I’ve seen in humans showed that the UK was the only country that had a decrease in MRSA in their hospitals,” Dr. Watts says. “They attribute that to one thing: strict handwashing protocols.”

**Managing MRSP Infections**

MRSP may be more common than veterinarians think: In one surveillance program, approximately 30% of dogs with skin infections that a veterinarian cultured had MRSP. The ISCAID guidelines for the treatment of pyoderma suggest that if empirical therapy doesn’t provide a 50% or better improvement in skin lesions in 2 weeks, a methicillin-resistant staphylococcal infection may be present.

In general, *S. pseudintermedius* is almost always resistant to penicillin, amoxicillin, ampicillin, and tetracycline, which is why these drugs are not good empirical choices. Scheduling recheck exams around the 2-week mark will help practitioners determine whether the chosen therapy worked. These rechecks will also help ensure that the veterinarian, rather than the pet owner, is determining whether the therapy is working.

“Unfortunately, it’s typically not possible to determine whether the staphylococcal strain is resistant simply by the way a lesion looks. MRSP is also not more virulent than a susceptible strain and doesn’t require a longer course of treatment. It isn’t possible to predict what methicillin-resistant infections will respond to, so if the infection is suspected to be MRSP, the only way to know which antibiotic will be effective is to do a culture and susceptibility.”

**THE IMPORTANCE OF ANTIBIOTIC STEWARDSHIP**

Antimicrobial stewardship is critical to preserving antibiotic effectiveness for decades to come. The concept can be implemented in any practice, regardless of size. Our experts reviewed how to use antibiotics judiciously, how surveillance programs can help reduce resistance, and why avoiding resistance in individual animals is just one aspect of antibiotic stewardship.

“To me, the most important aspect of antimicrobial stewardship is asking yourself the question: ‘Do you need to treat?’” Dr. Zhanel says. “If you do not need to treat the infection or you’re not sure it’s an infection, we ask that you do not use an antibiotic. On the other hand, if you really think it’s an infection, be aggressive. Microbiologists like to say, ‘Dead bugs don’t mutate.’ Use a good-quality antimicrobial, and you’ll kill the pathogen, get clinical cure, and will not be selecting for resistant organisms.”

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“We don’t do enough recheck exams when dogs have skin infections. We dispense a course of antibiotics, and we assume that the infection goes away if the owners don’t call us back. But a lot of times, they just don’t call back because we’ve beaten the infection back to a point where they don’t find it to be a problem anymore.”

— Dr. Fadok
“Stewardship also means not using antibiotics that aren’t going to work. If we can reduce overall exposure for drugs that are going to fail, we’ve also accomplished something. We need to pause and ask, ‘Does this animal require an antibiotic?’ Then we need to reevaluate, probably earlier than what we have been doing, within 2 weeks.”

–Dr. Papich

Dr. Fadok agrees: “It’s actually more cost-effective and better antibiotic stewardship to get a culture and susceptibility and then select the antibiotic that will actually work, so that we don’t use antibiotics that have no chance of working in some of these patients.”

“Some pet owners are reluctant to pick up the phone or let us know that the therapy hasn’t worked, while during that entire time, the pet’s been miserable,” Dr. Papich says. “They’ve been exposing the pet and the environment to unnecessary antibiotics, when we could have stopped this earlier. That applies not just to skin infections, but to urinary tract and other infections as well.”

“Going forward, we need to encourage more studies to be done on decreasing duration of antibiotic use and other interventions, such as topical therapy. We’re not going to get a lot of new antibiotic classes and new agents available to us. There’s just not a lot in the pipeline, unfortunately. That’s why stewardship is so important—to use the drugs that we have appropriately, so that we can preserve them for the future.”

– Dr. Zhanel

“As we try to institute antimicrobial stewardship practices, one goal of the surveillance program is to continue to monitor the impact of those practices on the level of resistant organisms, both at the regional and national level. Hopefully, we will see the resistance go down.”

–Dr. Watts

“To me, using antibiotics effectively and safely means: Know the nature of your infections. The good thing about pyoderma is we know how this pathogen tends to behave when it is a sensitive bug, and we know how to dose and treat with antibiotic therapy,” says Dr. Fadok. “We suspect that when we have to use multiple courses of antibiotics, though, that we increase the risk of selecting for a resistant mutant.”

“Good stewardship is using antibiotic therapy that is administered once or twice daily, or as a single-dose therapy,” Dr. Zhanel reiterates. “Your goal is to try to kill the pathogen, and you do that by optimizing compliance. Bad compliance is bad antimicrobial stewardship, so I don’t like prescribing antibiotics 3 or 4 times a day or more, because I know that patients only take a dose twice daily, and that’s not killing the organism and is helping to select resistance. That applies in the human or animal care setting.”

“We can’t assume that what we do in veterinary medicine does not affect human medicine, and the same is true for human medicine. We’re all in this together,” Dr. Papich says. “There’s been some good evidence modeling to show that if we’re going to try to solve the problem of antibiotic resistance, the same kinds of stewardship programs and stewardship principles have to be applied to human and veterinary medicine alike.”

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