Antimicrobial Resistance

LESSON 1 CASE STUDY: Canine Pruritus

Instructor's Information

LEARNING OUTCOMES

- In the absence of culture results, make an empirical selection of antibiotic regimen, utilizing animal welfare, ethical, and scientific frameworks.
- Select an antimicrobial drug and regimen based on susceptibility data, and justify the decision.

PREPARATION

Required Preparation:

- Student understanding of breakpoints, pharmacodynamic and pharmacokinetic factors of antimicrobials (time-dependent vs. concentration-dependent).
- Students can review online component or else this should be taught by instructors at their discretion.

Recommended Preparation:

- Remainder of online module

CLASS SETUP

- If this activity is utilized in a large-group setting, the class should be pre-divided into groups of no more than 4 – 6. The ideal setup will depend on your classroom environment.
- If this activity is utilized during clinical rounds, students can complete the activity individually, in pairs, or in small groups.

ACTIVITY AGENDA OPTION A

Option A requires pre-work to be completed prior to class. This option provides more time for the instructor to devote to discussion, particularly in regards to antimicrobial selection. The instructor is likely to complete 1 – 2 cases over a 2-hour period.

Canine Pruritus Part 1: Empirical Treatment

- Step I, Before Class:
  - Distribute the case scenario to each group.
  - Groups will converse on their own time to answer the guiding questions in preparation for class.
- Step II, In Class:
  - Provide a set time period for students to convene in their groups and for each group to come to a consensus on the guiding questions.
  - Hold a facilitated discussion on their group answers. Instructors should use the teaching tools with which they are most comfortable.

Canine Pruritus Part 2: AST Testing

- Step III, In Class:
  - Provide each group a set of AST results and a set time period to interpret the data.
  - Hold a facilitated discussion on their group answers. Instructors should use the teaching tools with which they are most comfortable.

ACTIVITY AGENDA OPTION B

Option B takes place completely in the classroom environment. The instructor is likely to complete no more than 1 case over a 2-hour period. The general process is the same as option A, except Step I takes place during the class session.

Canine Pruritus Case Scenario

CASE SCENARIO

Presenting Complaint:

Fiona, a 3-year-old, female spayed, Shih Tzu presents to you for a 5-week history of pruritus.

History:

Five weeks ago, Fiona started itching along her abdomen and rump, but this has progressed to include the neck, armpits, and paws. Her pruritus only partially responded to prednisone. Other than skin disease, Fiona seems normal. Standard inoculations are up-to-date (DA2PLP to distemper, adenovirus type 2, parvovirus, leptospirosis, parainfluenza virus, and rabies) and were last given 7 months ago. Fiona had successful corrective surgery for an intussusception as a puppy. Rarely, her left knee cap luxates (medial grade 1) causing her to skip a few strides on this limb.

Physical Exam:

T = 101.1 °F (38.4 °C)

P = 98/min

R = 20/min

BW = 7.2 kgs (15.8 lbs)

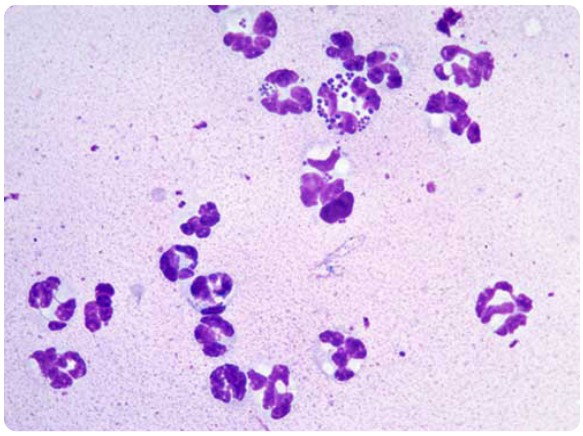
BCS = 5/9

Fiona is bright, alert, and responsive, but is actively biting, rubbing, and/or scratching her axillae, groin, paws, rump, and perineum in the exam room. Negative pinnal-pedal response/reflex AU. Excoriated patches of alopecia are present at the base of the tail. The ventral neck and trunk is mildly to moderately erythematous and partially lichenified with a slight surface oily hue. Linear excoriations are seen in the axillae. Perineal skin is erythematous, lichenified, and excoriated. Dorsal pedal surfaces are partially alopecic. Interdigital spaces are erythematous. The pinnae and ear canals are normal. The nasal planum, oral cavity, claws, and paw pads do not have lesions suggestive of dermatological disease. Both anal sacs are empty, normally sized, and nonpainful. With manipulation, the left patella can be luxated medially, but it spontaneously returns to its normal position. The rest of the exam is normal.

Diagnostics:

Cytology: Cocci 2+

Skin Scrape (deep + superficial): Negative



ACTVITY GUIDE: STEP I

Distribute the Canine Pruritus: Case Scenario to each group. This can be done prior to class to be completed on their own time, or at the beginning of the class session. Students without extensive pharmacological knowledge might benefit from pre-designed drug regimens. Consider providing students with the following options instead of allowing them free choice of drugs.

- Amoxicillin/Clavulanic Acid 25mg/kg PO q12h
- Cefovecin 8mg/kg SC
- Cephalexin 30mg/kg PO q12h
- Doxycycline 5mg/kg PO q12h
- Enrofloxacin 20mg/kg PO q24h
- Trimethoprim/Sulpha 30mg/kg PO q12h

The provided regimens have been extracted from:

Hillier, A., Lloyd, D. H., Weese, J. S., Blondeau, J. M., Boothe, D., Breitschwerdt, E., ... & Sykes, J. E. (2014). Guidelines for the diagnosis and antimicrobial therapy of canine superficial bacterial folliculitis (Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases). *Veterinary dermatology*, 25(3), 163-e43.

In their groups, students should work to answer the following guiding questions.

CASE SCENARIO GUIDING QUESTIONS

1. What bacteria do you expect to find at this body site?
2. Would you empirically treat this patient with antibiotics? If so, answer the following questions.
    a. Name three drugs that you would consider using for that site, and how you would administer them (dose, route, duration).
    b. Justify your decisions. Comment on the legal/ethical, welfare, and scientific considerations regarding your decisions

ACTVITY GUIDE: STEP II

Provide time for students to convene in their groups and for each group to come to a consensus. If Step I was completed prior to class, students should be able to complete this task in no more than 10 minutes. Hold a facilitated discussion to solicit group answers. Use the teaching tools with which you are most comfortable. Examples include:

- Online polling software – each group submits their answers and the instructor can read the responses to the class. For example, **"I see from your responses that a number of groups chose not to empirically treat this patient with antibiotics. Would a group like to volunteer their thought process?"**
- Pull a group number out of a hat – each group elects a spokesperson to provide the group answer if called upon. For example, **"group #12, what are the top 3 bacteria you expect to find at this site?"**
- Colored index cards – each group holds up an index card with a color that corresponds to a given answer. For example, **"If your group elected to empirically treat with drug A, hold up the green card. If your group treated with drug B, hold up the pink card."**

The following sections are divided into various discussion points that might arise during the class session. It is recommended to keep the focus of drug selection on why an empirical selection was made, rather than whether the "correct" drug was selected. In this respect, you might find it beneficial to dedicate time to the discussion points about the legal/ethical, welfare, and scientific reasoning behind group decisions.

INSTRUCTOR DISCUSSION POINTS (DRUGS AND REGIMENS)

The provided regimens have been extracted from:

Hillier, A., Lloyd, D. H., Weese, J. S., Blondeau, J. M., Boothe, D., Breitschwerdt, E., ... & Sykes, J. E. (2014). Guidelines for the diagnosis and antimicrobial therapy of canine superficial bacterial folliculitis (Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases). *Veterinary dermatology*, 25(3), 163-e43.

Discussion points for the provided regimens are included. Please feel free to modify your discussion as appropriate for your class session.

Amoxicillin/Clavulanic Acid 25mg/kg PO q12h

- Pros: Labeled for dogs; Labeled for skin/soft tissue (SST); Supported by published evidence; Resistance in most settings is unlikely; Tablet or liquid formulation (depending on patient size)
- Cons: Potential for selection for resistance
- Note: The majority of staphylococci carry the beta-lactamase enzyme and will be resistant to amoxicillin without the clavulanate

Cefovecin 8mg/kg SC

- Pros: Labeled for dogs; Labeled for skin/soft tissue (SST); Supported by published evidence; Resistance in most settings is unlikely; Can charge for services (practice management); Improved client adherence
- Cons: Potential for selection for resistance; "Medically-important antimicrobial" (3rd generation cephalosporin, may not be appropriate for first-line therapy); Unable to change regimen once instituted

Cephalexin 30mg/kg PO q12h

- Pros: Labeled for dogs; Labeled for skin/soft tissue (SST); Supported by published evidence; Resistance in most settings is unlikely; Cost
- Cons:

Doxycycline 5mg/kg PO q12h

- Pros: Supported by published evidence; Resistance in most settings is unlikely
- Cons: Not labeled for dogs

Enrofloxacin 20mg/kg PO q24h

- Pros: Labeled for dogs; Labeled for skin/soft tissue (SST); Supported by published evidence; Susceptibility is likely
- Cons: Potential for selection for resistance; "Medically-important antimicrobial" (May not be appropriate for first-line therapy); Potential for adverse effects; Cost
- Notes: All fluoroquinolones are not interchangeable (e.g., ciprofloxacin cannot be substituted for enrofloxacin due to reduced bioavailability compared to humans)

Trimethoprim/Sulpha 30mg/kg PO q12h

- Pros: Supported by published evidence; Susceptibility is likely; Cost
- Cons: Potential for adverse effects

INSTRUCTOR DISCUSSION POINTS (FRAMEWORKS)

Legal/Ethical

- Not selecting for resistance (MRSA/MRSP)
- Select a narrow scope of drug

Welfare

- Human-animal bond
- What protocol can the clients reasonably adhere to?
- Financial considerations

Scientific

- What evidence supports their decision? For example, have there been randomized controlled trials performed in dogs, or is their decision supported by lower-quality evidence such as expert opinion or cohort studies?

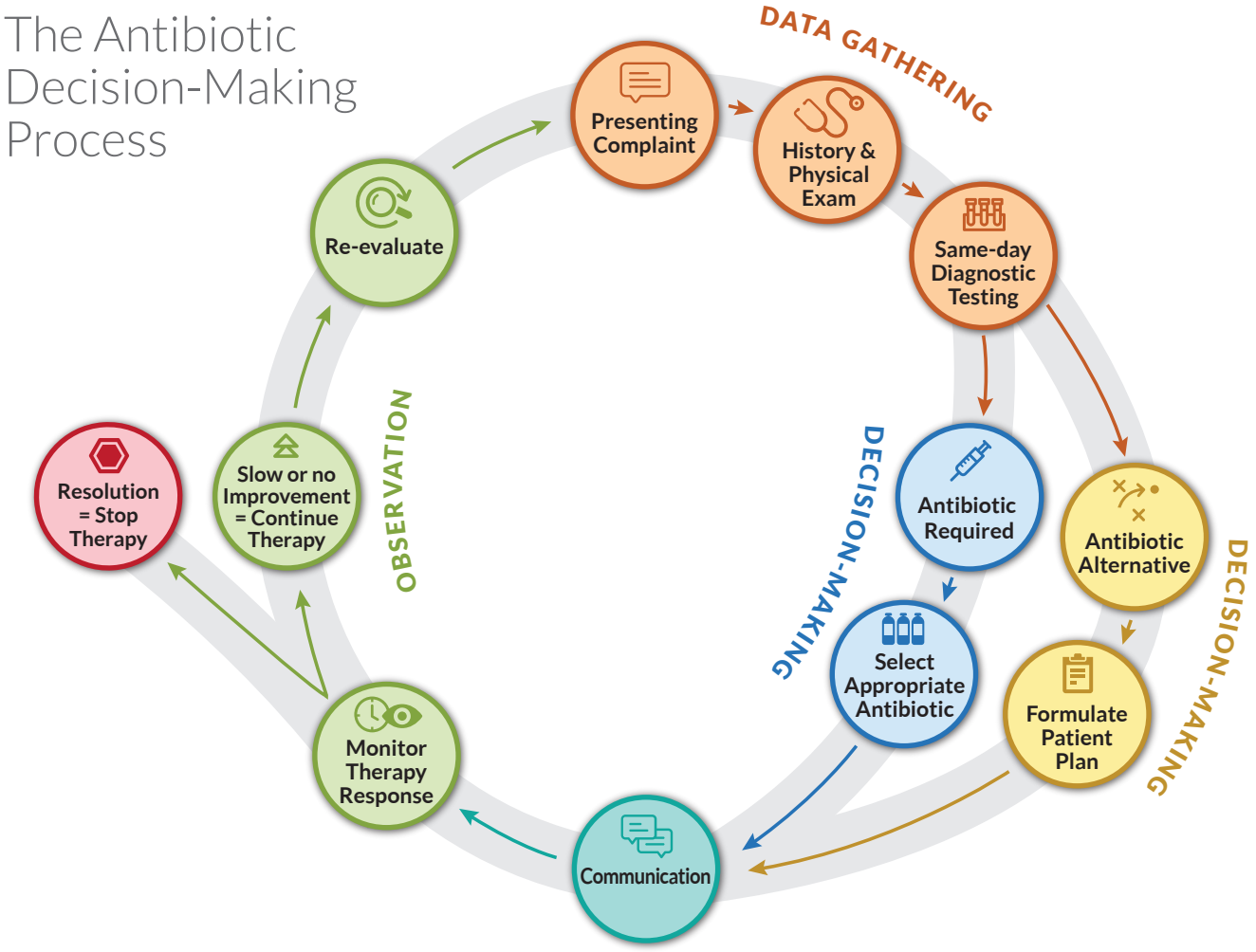
INSTRUCTOR DISCUSSION POINTS (MISCELLANEOUS)

The following are discussion points that you might use with the class. This is not an exhaustive list, and each instructor should use their discretion to determine which information is pertinent for their own curriculum.

- Many laboratories arbitrarily exclude contaminants and/or normal flora from susceptibility data. In this example, it would be common to find normal flora (Staphylococcus aureus, Staphylococcus epidermidis) at this site.
- Because many labs exclude contaminants and/or normal flora, it is critical that diagnostic submission forms are completely and correctly filled out.
- Sometimes empirical treatment needs to occur based on the patient's clinical presentation. Is the patient stable? Can treatment wait until diagnostic test results have returned?
- Other times, empirical treatment is not recommended. If this is the patient's third visit for a particular condition, for example, the veterinarian and client should discuss further diagnostic testing rather than empirical treatment.
- Consider your clients. Clients have differing expectations and limitations. How might you discuss this?
- Consider your practice. How might other DVMs address this same case? Could your preferred method of empirical treatment differ from another individual in your practice? If so, how do you have a conversation with your clients about this? How do you speak to the other DVM?

The "Antibiotic Decision-Making Process" chart may be used to provide students a visual illustration of a clinician's thought process. Each point on the chart will have associated questions for the practitioner to consider. For example, one cannot simply "select an appropriate antibiotic" without asking questions such as:

- What drug can be legally used?
- What drug is likely to be effective?
- What are the possible adverse effects of the drug?
- Will that drug reach the site of infection?
- Will the client be able to administer this drug?
- Will the patient allow the client to administer this drug?



ACTVITY GUIDE: STEP III

Select from one of three provided "difficulty levels" for antimicrobial susceptibility testing (AST) data to provide to students.

a. Patient with methicillin-susceptible *Staphylococcus pseudintermedius*
b. Patient with methicillin-resistent *Staphylococcus pseudintermedius* (MRSP) but susceptible to other drug classes
c. Patient with MRSP that is resistant to several other drug classes, but susceptible to fluoroquinolones

Distribute the Canine Pruritus, part 2: AST Testing information to each group with the preferred AST data. Students without extensive pharmacological knowledge might benefit from receiving the pre-designed drug regimens provided in Step I. In their groups, students should work to answer the following guiding questions. After a set time period, hold a discussion about their findings using the teaching tools with which you are comfortable.

Canine Pruritus, Part 2: AST Testing

ANTIMICROBIAL SUSCEPTIBILITY TESTING GUIDING QUESTIONS

1. Based on the susceptibility data, evaluate your empiric therapy. How successful do you think it would have been?
2. What would you do next for this patient? Why?

INSTRUCTOR DISCUSSION POINTS (GENERAL)

The following are discussion points that you use with the class. This is not an exhaustive list, and each instructor should use their discretion to determine which information is pertinent for their own curriculum.

- How do you make decisions in a practice? Veterinarians need to consider the cost of treatment, owner and patient compliance, which drugs are in their inventory, etc.
- Some labs will suppress results for certain drugs, particularly drugs of last resort for use in humans such as imipenem or vancomycin.
- For drugs with no established breakpoints for that species, refer to the CLSI VET09 document to make defensible extrapolations of breakpoints from other species.

INSTRUCTOR DISCUSSION POINTS (CASE-SPECIFIC)

The Clinical and Laboratory Standards Institute (CLSI) provides the current VET01S, the Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals, online at no cost. It can be found using the search terms “CLSI” and “Free” =/- “VET01S”. The standard provides additional information in the comments section of the breakpoints tables that are useful for evaluating a therapeutic regimen.

Patient with methicillin-susceptible *Staphylococcus pseudintermedius*

- Many drugs have breakpoints for *Staphylococcus pseudintermedius* for dogs.
- For this *Staphylococcus* species, any drug with an established breakpoint and recorded as “susceptible” should result in likely clinical efficacy when the dosing regimen used to establish the breakpoint is used..
- Those drugs that do not have established breakpoints (recorded as “no interpretation”) are also drugs that would not generally be the first to use. Many of these drugs have adverse effects (e.g., aplastic anemia with chloramphenicol) or are not first-line drugs. The laboratory may interpret the results for some drugs (like chloramphenicol) using human breakpoints when an appropriate canine breakpoint for *Staphylococcus pseudintermedius* is unavailable. This is important because not all drugs without a canine breakpoint will be listed as “no interpretation”.
- The results for ampicillin and penicillin have been suppressed in this report because this bacterium has a resistance mechanism (beta-lactamase positive).
- Starting topical therapy in this patient could be beneficial as a multi-modal approach to therapy, potentially reducing the possibility of creating resistant bacteria.

Patient with MRSP but susceptible to other drug classes

- Methicillin-resistant *Staphylococcus pseudintermedius* is resistant to all beta-lactams and carbapenems.
- Results have been suppressed for any drugs to which the bacterium is resistant.
- There are still multiple treatment options available in various drug classes with appropriate breakpoints and are recorded as “susceptible”.

Patient with MRSP that is resistant to several other drug classes, but susceptible to fluoroquinolones

- This strain of methicillin-resistant *Staphylococcus pseudintermedius* has also acquired other resistance mechanisms.
- Some patients with these findings may have had recurring infections and could have been treated with multiple drugs over time.
- For this patient, the veterinarian will need to be creative to find appropriate treatment options. Topical therapy will be necessary.
- Although it might be possible to use vancomycin in this patient, it is not recommended. This is a medically important drug for humans and requires IV therapy, hospitalization, etc.