



AVMA/Committee on Antimicrobials
**ANTIMICROBIAL RESISTANT
PATHOGENS AFFECTING
ANIMAL HEALTH IN THE
UNITED STATES**

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EXECUTIVE SUMMARY

The Priority list of antimicrobial-resistant bacteria affecting animal health in the United States, 2020 is a cross-section of the impact of antimicrobial-resistant bacteria on select species of animals in the United States. Some of the bacteria in this report also impact the health of humans. Infections caused by these bacteria have been identified by the American Veterinary Medical Association Committee on Antimicrobials to be increasingly associated with resistance to first-line antimicrobials, thus affecting the health of animals and presenting a growing challenge for veterinarians. The purpose of this report is to raise awareness of the threat that antimicrobial resistance poses and to encourage action to address the threat.

This report covers bacteria causing animal infections and the antimicrobials used to treat those infections. Existing and emerging resistance of viruses and fungi is not included, nor is drug resistance among parasites; these are beyond the scope of this report. The report consists of summaries of cross-cutting and bacteria-specific antimicrobial resistance topics.

The first section of the report provides context and an overview of the impact of antimicrobial resistance on animal health in the United States. We describe what can be done to combat this growing threat, including information on current AVMA antimicrobial stewardship resources.

In the second section of the report, AVMA provides host-species specific summaries of pathogens of concern. These one-pagers are designed for printing and posting in high-flow areas to raise the awareness of resistance among veterinarians and other personnel.

In the third section of the report, AVMA provides “report cards” for each pathogen of concern. These are organized by host species and, in some sections, the host species are divided up by production type to better describe the health threats of different pathogens within the species. These summaries can aid in discussions about bacteria, how to manage infections, and implications for animal health and veterinary management.

The final section of the report is the technical appendix. This provides more detailed and specific research data to support the report cards, as well as key references identified by our technical committees.

In summary, the report includes actionable information about what groups such as veterinarians, producers, breeders, and those seeking medical care for their animals can do to combat antimicrobial resistance. Slowing and limiting the emergence and spread of antimicrobial resistance can only be achieved with widespread engagement, especially among leaders in veterinary medicine, animal agriculture, and public health. Only through concerted commitment and action will those caring for the health and welfare of animals be able to succeed in reducing this threat.

Any comments and suggestions that would improve the usefulness of future publications are appreciated and should be sent to Dr. Michael Costin at mcostin@avma.org.

Antimicrobial resistance is a global One Health issue. One Health is an approach that recognizes the interconnectedness of the health of people, animals, and the environment. Antimicrobial use in animals, people, and the environment all contribute to the emergence of resistance, and resistance spreads across species and settings. This report is a snapshot of the current situation in animal health in the United States; however antimicrobial resistance impacts animal health throughout the world and requires a global response.

INTRODUCTION

Antimicrobial resistance occurs when bacteria are able to survive in the presence of antimicrobials that are used to treat them. Although the development of resistance is not a new phenomenon, the health challenges associated with it have increased considerably in the last several decades because of a lack of investment in and development of new-generation antimicrobials that can be used when other antimicrobials lose effectiveness. In fact, antimicrobial resistance has become one of the greatest sustained public health challenges of our time. As a One Health issue, antimicrobial resistance impacts animal, human and environmental health. All uses of antimicrobials exert selective pressure that promotes the emergence of resistant bacteria; thus it is critical that health professionals tasked with prescribing antimicrobials be aware of the issue, knowledgeable about ways that they can mitigate resistance, and on the alert for cases where a risk of treatment failure exists due to resistant bacteria.

In 2019, the United States Centers for Disease Control and Prevention (CDC) released its updated report “Antibiotic Resistance Threats in the United States, 2019”. This report highlighted the importance of antimicrobial resistance in human medicine and discussed the underlying importance of One Health in combating the issue. In an effort to highlight the growing importance of antimicrobial resistance in bacteria that cause diseases in animals, the American Veterinary Medical Association commissioned this report to serve as a current summary of the issue in veterinary medicine, and to highlight specific bacteria responsible for animal diseases that show evidence of increasing resistance. This report is intended to serve as a baseline for continued efforts to identify and monitor these bacterial pathogens and their impact on animal health.

WHAT IS ANTIMICROBIAL RESISTANCE?

Antimicrobial resistance can result when bacteria are able to survive in the presence of antimicrobials that are used during the treatment of disease. In some situations, certain classes of antimicrobials were never effective against specific species of bacteria due to inherent structural or functional characteristics of those bacteria. This is termed intrinsic resistance and is not further addressed in this report. In this report we are focused on acquired antimicrobial resistance that results in an antimicrobial that previously worked to kill a given bacteria losing its effectiveness. As with many complex issues, differences in nomenclature can result in confusion related to antimicrobial resistance. Much of the complexity in this situation relates to how the resistance is identified or how antimicrobial prescribers are alerted to the potential for resistance.

While fully addressing these complexities is beyond the scope of this report, it is important for readers to recognize that these differences are important and will likely impact decision-making regarding antimicrobial prescribing. In many diagnostic laboratories resistance is identified through antimicrobial susceptibility testing (AST). These approaches generally rely on identifying the concentration of an antimicrobial drug necessary to inhibit growth of the bacteria and are expressed as the minimal inhibitory concentration (MIC). Since these concentrations are inherently difficult to interpret on their own, approaches to provide some context around these concentrations have been developed in order to try and simplify prescriber decision-making. Examples of such approaches include the development of breakpoints by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Clinical and Laboratory Standards Institute (CLSI) that can be applied to specific animal species-bacteria-drug combinations to classify the isolate as susceptible, intermediate or resistant. Unfortunately, these breakpoints are not consistently applied, which can make comparing “resistance” rates or monitoring trends difficult since the actual concentration at which the bacteria is deemed resistant is not always the same. Additional approaches to predicting antimicrobial resistance rely on the identification of the presence of specific genes that have the potential to encode proteins that confer resistance in the bacteria. Like breakpoints, this approach has important limitations, such as the gene not being expressed or containing mutations that render the protein less effective at conferring resistance.

For the purpose of this report we have asked our panels to use their expertise and the scientific literature to identify bacterial pathogens of significance in animals where data exist to raise concern that acquired antimicrobial resistance is increasing. As with all medical decisions, antimicrobial prescribing is a complex decision process, and we encourage the veterinary users of this report to consider the data presented here in context with the AVMA’s antimicrobial stewardship core principles when making clinical prescribing decisions. We endeavor to make clear what evidence is being used to identify the concern for rising resistance. In some cases that is based on phenotypic resistance (AST breakpoints), while in other cases it is based on identification of organisms carrying potential resistance genes, i.e., part of the organism’s genotype. While both situations should raise the clinician’s awareness of potential resistance, decisions should be made based on the full understanding of the data in any given clinical case and situation.

WHAT SHOULD BE DONE TO CONTROL THE RISK OF ANTIMICROBIAL RESISTANCE?

Antimicrobial resistance is a complex issue and requires human, animal and environmental health experts to work together to mitigate the continued development and spread of resistance. It is important to recognize that we cannot eliminate the emergence of resistance. Due to the rapid replication of bacteria, their ability to share resistance genes with other bacteria or to acquire them from their environment, and their propensity for rapid evolution, any use of antimicrobials will continue to select for resistance. Therefore, our efforts must be focused on assuring that we are using antimicrobials as judiciously as possible and only in situations where the health or welfare of the patient would be compromised by a failure to treat.

WHAT IS ANTIMICROBIAL STEWARDSHIP AND ITS CORE PRINCIPLES?

Antimicrobial stewardship refers to the actions veterinarians take individually and as a profession to preserve the effectiveness and availability of antimicrobial drugs through conscientious oversight and responsible medical decision-making while safeguarding animal, public, and environmental health. The AVMA has identified and provided helpful guidance on how veterinarians can assure good antimicrobial stewardship. Full information is available at avma.org/Antimicrobials, along with a helpful Stewardship Checklist. Briefly, antimicrobial stewardship involves maintaining animal health and welfare by implementing a variety of preventive and management strategies to prevent common diseases; using an evidence-based approach in making decisions to use antimicrobial drugs; and then using antimicrobials judiciously, sparingly, and with continual evaluation of the outcomes of therapy. The five core principles are further summarized in the infographic on the next page.

HOW TO USE THIS REPORT

This report has been designed with ease of use in mind. We include several tables and infographics that can be used to help discuss antimicrobial resistance and antimicrobial stewardship with your colleagues and stakeholders. They focus on the key concepts and overarching issues and assist in framing the issue.

The second section of the report is designed to provide a host species-level summary of the potential pathogens of concern for that host species. We have included summary reports for dogs and cats, cattle, chickens and turkeys, equine, fish and shrimp, sheep and goats, and swine. These are designed to concisely summarize the issues and to provide reminders of the core principles of stewardship and practice that may assist in mitigating emergence and spread of resistant infections in your patients. We encourage users to download information pertinent to their practice and print for posting in the pharmacy or work-room areas.

The third section of the report provides a detailed “report card” for each of the specific bacterial pathogens identified as a concern for elevated resistance to antimicrobials in a host species. These are organized by host species and provide the key details that will assist veterinary prescribers in evaluating the risk of resistance in their clinical cases. Although some of the pathogens listed can cause disease in multiple host species they are only included in the sections for the host where resistance has been identified as a concern. We have limited the complexity of these summaries for clarity and have provided additional scientific and research details that underpin the recommendations in the technical summary for each organism.

The fourth and final section of the full report is the technical summaries for each bacterial pathogen. As with section three they are organized by host species group and provide important references and details that may be useful in interpreting the report.

Antimicrobial stewardship

DEFINITION

Antimicrobial stewardship refers to the actions veterinarians take to preserve the success and availability of antimicrobial drugs through careful oversight and responsible medical decision-making while protecting animal, public, and environmental health.

CORE PRINCIPLES

Antimicrobial stewardship maintains animal health and welfare by using several strategies to prevent common diseases; using an evidence-based approach in judging the use of antimicrobial drugs; and then using antimicrobials wisely, cautiously, and with frequent evaluation of therapy results, respecting the client's available resources.

The following principles can be used to create antimicrobial stewardship plans in any veterinary practice setting. Use these principles to improve disease prevention strategies and antimicrobial drug prescribing, evaluate outcomes, and adjust plans accordingly.



Commit to stewardship

Involve practice members and stakeholders in the stewardship effort. Create stewardship plans for disease prevention and to improve the usage and supervision of antimicrobial drugs. Focus on high-priority conditions commonly treated with antimicrobial drugs. Commit to thoroughly evaluating the results of antimicrobial drug therapy. Identify individuals to lead the stewardship plan and deliver accountability.



Advocate for care systems to prevent common diseases

Recognize barriers to successful disease prevention. Work with clients to find strategies that minimize the need for antimicrobial drugs. Such strategies include animal husbandry and hygiene, biosecurity and infection control, nutrition, and vaccination programs. Consider options other than antimicrobial drugs.



Select and use antimicrobial drugs sensibly

Recognize barriers to proper antimicrobial prescribing and usage. Use an evidence-based approach for making a diagnosis and deciding if an antimicrobial drug is specified. Make an informed selection of a suitable antimicrobial drug and regimen. Refer to applicable veterinary medical guidelines for sensible therapeutic use. Evaluate results of antimicrobial use.



Evaluate antimicrobial drug practices

Urge the creation of a program for the assessment of antimicrobial drug use at the veterinary practice or aggregated levels. Confirm that feedback is given. Support examining and sharing of antimicrobial drug use data while keeping veterinarian-client privacy. Involve clients in finding barriers to application of stewardship programs and to assess antimicrobial storage, usage, and other practices.



Educate and build expertise

Offer resources to support the development of expertise in antimicrobial stewardship. Stay up-to-date on disease prevention strategies, antimicrobial alternatives, and choice of antimicrobial drugs. Critically evaluate and execute relevant clinical guidelines for antimicrobial use. Deliver client education on antimicrobial stewardship. Research antimicrobial drug use and resistance.

Animal pathogens of heightened concern

	Aminoglycosides	Amphenicols	Carbapenems	Cephalosporins	Fluoroquinolones	Lincosamides	Macrolides	Penicillins	Pleuromutilins	Sulfonamides	Tetracyclines	Trimethoprim
<i>Aeromonas</i> spp		●									●	●
<i>Campylobacter jejuni</i>	●				●	●	●				●	
<i>Edwardsiella</i> spp		●									●	●
<i>Enterobacteriales</i>	● ● ●	●		● ● ●	● ●			● *		● ●	● ● ●	●
<i>Enterococcus</i> spp					*		●	●				
<i>Flavobacterium psychrophilum</i>		●									●	●
<i>Moraxella</i> spp							●				●	
<i>Ornithobacterium rhinotracheale</i>								●		●	●	
<i>Pasteurellaceae</i>					● ●		●	● ●	●	●	● ● ●	
<i>Pseudomonas aeruginosa</i>	●		●		●							
<i>Salmonella</i> spp	●	●		●	●		●	●	●	●	●	
<i>Staphylococcus</i> spp	●			●	●	●	● ●	● *			● *	
<i>Streptococcus</i> spp				●	●			●				
<i>Vibrio</i> spp	●	●		●	●		●	●		●	●	●

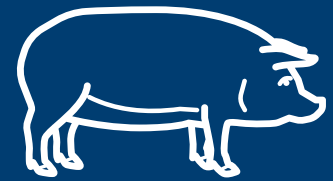
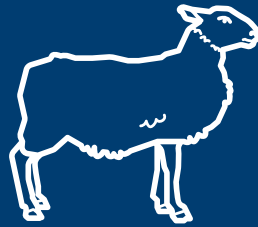
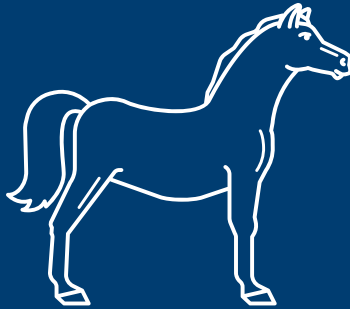
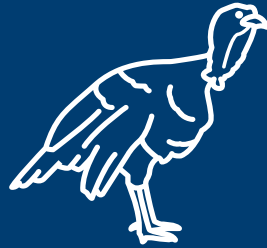
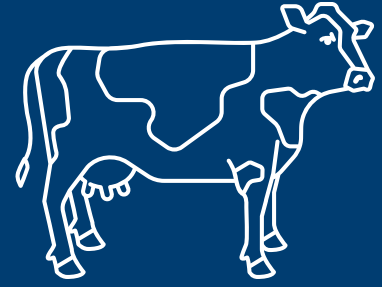
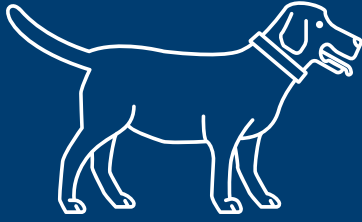
● Dogs & Cats ● Cattle ● Chickens & Turkeys ● Equine ● Fish & Shrimp ● Sheep & Goats ● Swine

*Note: Some of the resistance noted for these organisms has been long-established

Intrinsic resistance

- Enterobacteriales*: Clindamycin, Fusidic acid, Glycopeptides (e.g vancomycin), Macrolides (azithromycin+, clarithromycin and erythromycin), Rifampin
- Pseudomonas aeruginosa*: Ampicillin-sublactam, Cefotaxime, Chloramphenicol, Tetracyclines, Trimethoprim-sulfamethoxazole
- Enterococcus* spp.: Aminoglycosides, Cephalosporins, Clindamycin, Fusidic acid, Trimethoprim, Trimethoprim-sulfamethoxazole
- Campylobacter jejuni*: Cephalothin, Fusidic acid, Streptogramins, Trimethoprim

*Derived from Vet09 Table 8 and Vet08 Appendix B, both of which are available from the Clinical Laboratory Standards Institute at CLSI.org



HOST SPECIES



DOGS & CATS

One of the risk factors leading to the emergence of antimicrobial-resistant bacteria is prior exposure to antimicrobial therapy. Therefore, any measures that reduce overall antimicrobial drug use in dogs and cats may help reduce antimicrobial resistance. This could include establishing infection prevention programs and developing antimicrobial stewardship plans in veterinary settings.

PATHOGEN OF CONCERN:

- *Staphylococcus* spp.
 - *S. aureus*
 - *S. pseudintermedius*
 - *S. schleiferi*
- *Enterobacteriaceae*
 - *Escherichia coli*
 - *Proteus* spp.
 - *Klebsiella* spp.
- *Acinetobacter* spp.
- *Pseudomonas aeruginosa*
- *Enterococcus* spp.
 - *Enterococcus faecalis*
 - *Enterococcus faecium*
- *Campylobacter jejuni*

Antimicrobial-resistant infections affect dogs and cats. Preventing infections is crucial to preventing resistant infections.

What you need to know

- Prevalence of resistant pathogens in dogs and cats is largely unknown. Additional information is needed to learn more about how often resistant infections occur.
- Resistant infections can be difficult to treat.
- Antimicrobial stewardship helps to prevent development of antimicrobial-resistant bacteria.
- The International Society for Companion Animal Infectious Diseases (ISCAID) has developed clinical guidelines to highlight diagnostic and treatment choices for bacterial infections of the skin, respiratory tract and urinary tract.
- The American Animal Hospital Association (AAHA) and the Ontario Animal Health Network (OAHN) have developed guidelines to control the spread of disease within hospital environments.

WHAT VETERINARIANS CAN DO:

- Use antimicrobials only when indicated.
- Use diagnostic testing to inform treatment decisions.
- Implement infection prevention and antimicrobial stewardship programs in veterinary settings (AAHA, ISCAID, and OAHN referenced above).



CATTLE

Antimicrobial resistance has been documented in the bacterial pathogens that affect cattle health and can have significant economic consequences. Therefore, preventing infections and preserving the efficacy of antimicrobials to treat, prevent and control infections is crucial.

PATHOGEN OF CONCERN:

- *Moraxella* spp.
 - *M. bovis*
 - *M. bovoculi*
- *Bovine respiratory disease*
 - *Mannheimia haemolytica*
 - *Pasteurella multocida*
 - *Histophilus somni*

What you need to know

- Efforts to promote herd health, including good management practices and routine use of vaccines, can help prevent disease.
- Early identification of infectious bovine keratoconjunctivitis and bovine respiratory disease can help prevent outbreaks and reduce morbidity and mortality.
- Resistant infections can be difficult to treat.
- More research is needed regarding strategic approaches for disease prevention, diagnostic testing, and use of antimicrobials to treat both individual disease cases and outbreaks of infections in herds.

Antimicrobial-resistant infections affecting cattle can have significant impacts on health, animal welfare, herd health, and economic consequences for cattle producers.

WHAT VETERINARIANS CAN DO:

- Assist producers in development of comprehensive herd health programs to prevent infections which may minimize the need for antimicrobial use.
 - Vaccines can be a tool used to prevent infections as part of a comprehensive herd health program.
 - Modify the practices that introduce stressors which can adversely impact animal health and the immune system (e.g., weaning, transport, commingling, crowding, dust, inadequate ventilation, parasites, and poor nutrition).
 - Utilize biosecurity and biocontainment practices to prevent introduction of pathogens or prevent effective contacts.
- Use diagnostic testing to inform treatment decisions – for example, to justify the need for antimicrobial therapy.
- Monitor antimicrobial treatment outcomes to evaluate past therapeutic performance and guide future therapeutic protocols.



CHICKENS & TURKEYS

Antimicrobial resistance has been documented in the bacterial pathogens that affect chicken and turkey health and can have significant economic consequences. Therefore, preventing infections and preserving the efficacy of antimicrobials to treat, prevent and control infections is crucial.

PATHOGEN OF CONCERN:

- *Escherichia coli*
- *Ornithobacterium rhinotracheale* (turkeys)
- *Pasteurella multocida*

Infections in broiler and layer chickens, and turkeys, can impact animal health. More research is needed regarding methods to prevent and control infections.

What you need to know

- Opportunistic pathogens can significantly impact chicken and turkey health.
- More research is needed regarding disease transmission, recognition of disease and prevention strategies

WHAT VETERINARIANS CAN DO:

- Biosecurity is critical to preventing infections.
- Assist producers in development of comprehensive biosecurity programs to prevent infections.
 - Vaccines can be a tool used to prevent infections; however, in many cases vaccines may not be available.
 - Modification of environmental factors such as water sanitation, rodent control and ventilation may help prevent disease.



EQUINE

Antimicrobial resistance has been documented in the bacterial pathogens that affect equine health and can have significant economic consequences. Therefore, preventing infections and preserving the efficacy of antimicrobials to treat, prevent and control infections is crucial.

PATHOGEN OF CONCERN:

- *Staphylococcus* spp.
 - *S. aureus*
- *Enterobacteriaceae*
 - *Escherichia coli*
 - *Proteus* spp
 - *Enterobacter* spp
 - *Klebsiella* spp
- *Pseudomonas aeruginosa*

Preserving the efficacy of antimicrobials to treat infections is critical. Antimicrobials currently FDA-approved for horses are often not active against the resistant pathogens discussed in this document; legal extralabel use of human and animal drugs may be necessary for treatment.

What you need to know

- Resistant infections can affect horses and may be spread to horses from other animals, from people, or from the environment.
- Some of the pathogens affecting equine health may be resistant to multiple antimicrobials and therefore be difficult to treat.

WHAT VETERINARIANS CAN DO:

- Infection control is critical to preventing resistant infections among equine patients.
- Infection control and prompt resolution of the infection is important when resistant infections are identified.
- Use diagnostic testing to inform treatment decisions.



FISH & SHRIMP

Antimicrobial resistance has been documented in bacterial pathogens that affect aquatic animal health and can have significant economic consequences. Therefore, preventing infections and preserving the efficacy of antimicrobials to treat, prevent and control infections is crucial.

PATHOGEN OF CONCERN:

- *Edwardsiella* spp.
 - *E. ictaluri*
 - *E. piscicida*
- *Aeromonas* spp.
 - *A. salmonicida*
 - *A. hydrophila*
 - *A. liquefaciens*
- *Flavobacterium psychrophilum*
- *Vibrio parahaemolyticus*
- *Vibrio vulnificus*

Antimicrobial-resistant infections affecting fish and shrimp can have significant economic and health impacts on animals and the environment.

What you need to know

- Some antimicrobial drugs used in aquatic animal medicine are available through over-the-counter and online sales, many of which are prohibited. Their extralabel use may be illegal, potentially compromising our ability to treat both aquatic animal and human infections. Taking these prohibited antimicrobials off the market may help reduce the development and spread of antimicrobial resistance.
- Antimicrobial-resistant aquatic animal and human pathogens have been found in fish and shellfish.

WHAT VETERINARIANS CAN DO:

- Maintain strict biosecurity practices to prevent or minimize the spread of disease within an aquaculture facility.
- Enact proactive management techniques in fish culture settings, such as:
 - Remove dead or moribund fish as soon as possible.
 - Reduce fish stressors as much as possible.
 - Monitor fish for signs of early infection.
- Provide judicious and evidence-based stewardship approaches to antimicrobial use.



SHEEP & GOATS

Resistant pathogens that impact small ruminant health can result in mastitis, including sub-clinical and severe presentations. Resistant pathogens may also be associated with abortion events. Both mastitis and abortion affect sheep and goat health and production and can result in significant economic loss. Because there are no approved susceptibility breakpoints for sheep and goats for any bacterial pathogens or antimicrobials, resistance may not be immediately recognized. Resistant infections can be more difficult to treat and may only be recognized as non-responsive infections. This may then lead to additional rounds of treatment or retreatment with an alternative antimicrobial drug, which can result in significant production loss in affected herds.

PATHOGEN OF CONCERN:

- *Staphylococcus* spp.
 - *S. aureus*
 - Coagulase-negative
- *Campylobacter jejuni*

Antimicrobial-resistant infections affect sheep and goats. Preventing infections through good milking practices, vaccine use—when available—and using diagnostic testing to rapidly identify pathogens affecting herd health are crucial to preventing all infections, including resistant infections.

What you need to know

- The prevalence of resistant mastitis pathogens in sheep and goats is largely unknown. Additional information and studies are needed to learn more about how often resistant mastitis infections occur and impact animal health. The prevalence of tetracycline resistance in *C. jejuni*-associated abortions is extremely high, and the organism should be considered resistant until proven otherwise.
- Resistant infections can be difficult to treat with antimicrobials.
- Antimicrobial stewardship helps to prevent development of antimicrobial resistant bacteria.

WHAT VETERINARIANS CAN DO:

- Use antimicrobials only when needed.
- For *Staphylococcus*
 - Use diagnostic testing to inform treatment decisions related to mastitis.
 - Work with producers to implement best practices for milking of small ruminants including principles associated with mastitis prevention.
- For *Campylobacter*
 - Make sure that sheep and goat clients follow up with veterinarians to submit fetuses and placentas to a diagnostic laboratory when abortions occur.
 - Veterinarians can make sure that *Campylobacter* isolates are typed, and if *C. jejuni* is isolated, assure that antimicrobial susceptibility patterns are determined before using antimicrobials in the flock. Discourage the use of antimicrobials in the feed when infection has not been diagnosed, particularly tetracyclines, as this may encourage selection of antimicrobial resistant organisms.



SWINE

Antimicrobial resistance has been documented in the bacterial pathogens that affect swine health and can have significant economic consequences. Therefore, preventing infections and preserving the efficacy of antimicrobials to treat, prevent and control infections is crucial.

PATHOGEN OF CONCERN:

- *Escherichia coli*
- *Streptococcus suis*
- *Pasteurella multocida*
- *Salmonella* spp
 - *S. Choleraesuis*
 - *S. enterica* serotype Choleraesuis
 - *S. enterica* serotype I, 4,[5],12:i:-

Infections in swine can significantly impact animal health; following the core principles of swine health management is important to preventing infection.

What you need to know

- Young pigs may be more susceptible to infection with certain pathogens.
- Infection with viruses might result in subsequent bacterial infections that require treatment.
- Development and use of vaccines may help prevent diseases such as salmonellosis.

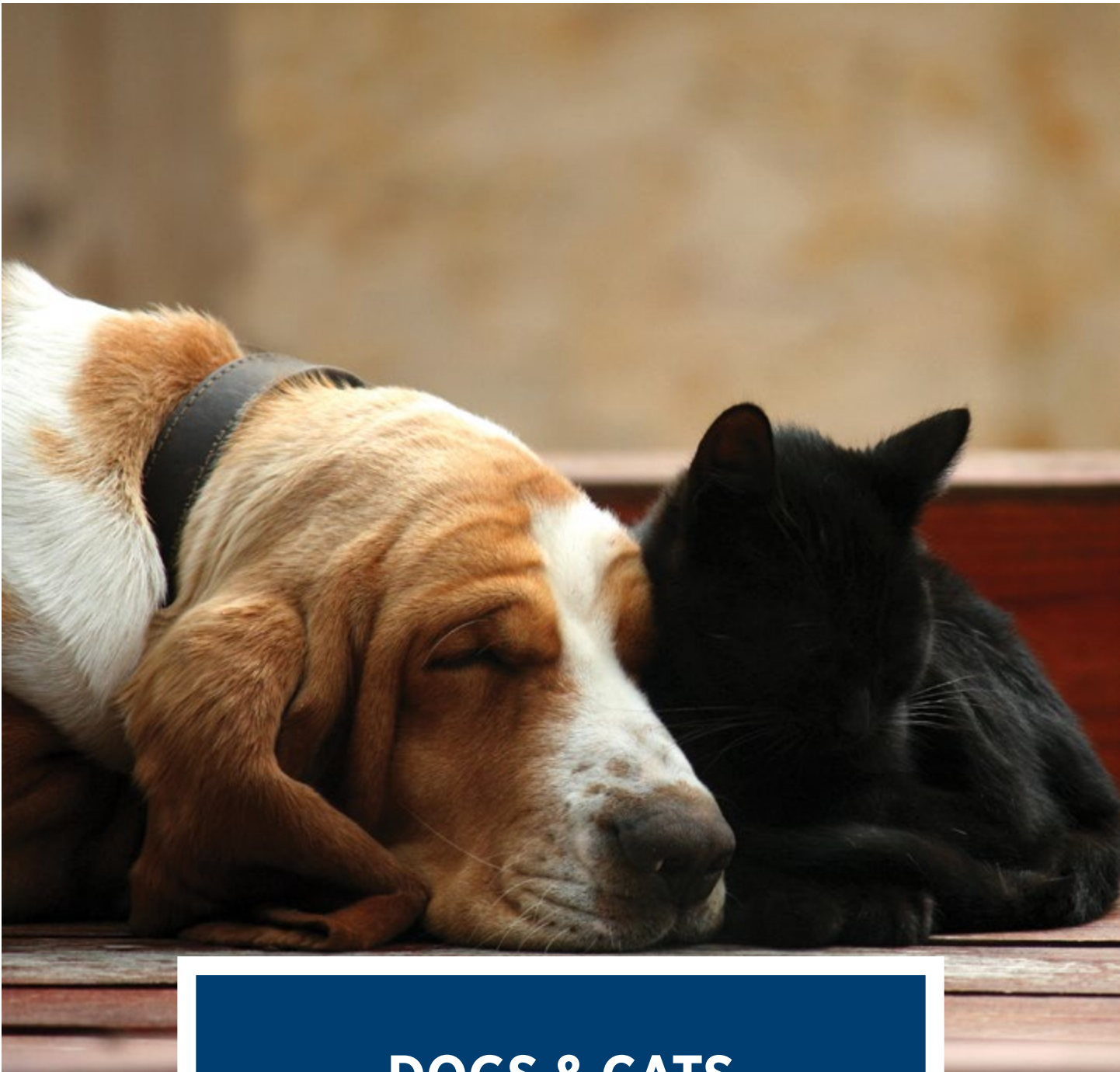
WHAT VETERINARIANS CAN DO:

Working with producers to follow the core principles of swine health management is critical to preventing infections, including those that are resistant to antimicrobials. This includes:

- Avoid mixing pigs from different sources.
- Adopting all-in/all-out management whenever practical.
- Maintaining good hygiene.
- Minimizing environmental stresses due to temperature fluctuations and poor ventilation.



PATHOGENS



DOGS & CATS

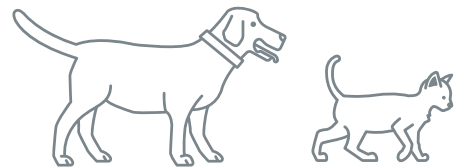
CAMPYLOBACTER JEJUNI

Campylobacter jejuni is a gram-negative, “gull-winged,” microaerophilic, opportunistic bacterial pathogen that inhabits the intestinal and genital tracts of animals.

What you need to know

- Most dogs do not need antimicrobial treatment for campylobacteriosis. At this time, it is unknown whether resistant strains cause more serious problems than susceptible strains.
- Multidrug resistant *C. jejuni* can spread from pets (particularly puppies and kittens) to people and can cause human disease with symptoms that may include diarrhea (which can be bloody), fever, and abdominal cramps.
- In people, particularly those with weakened immune systems, *C. jejuni* can also spread in the blood and cause arthritis, irritable bowel syndrome, or Guillain-Barré syndrome.

SPECIES:

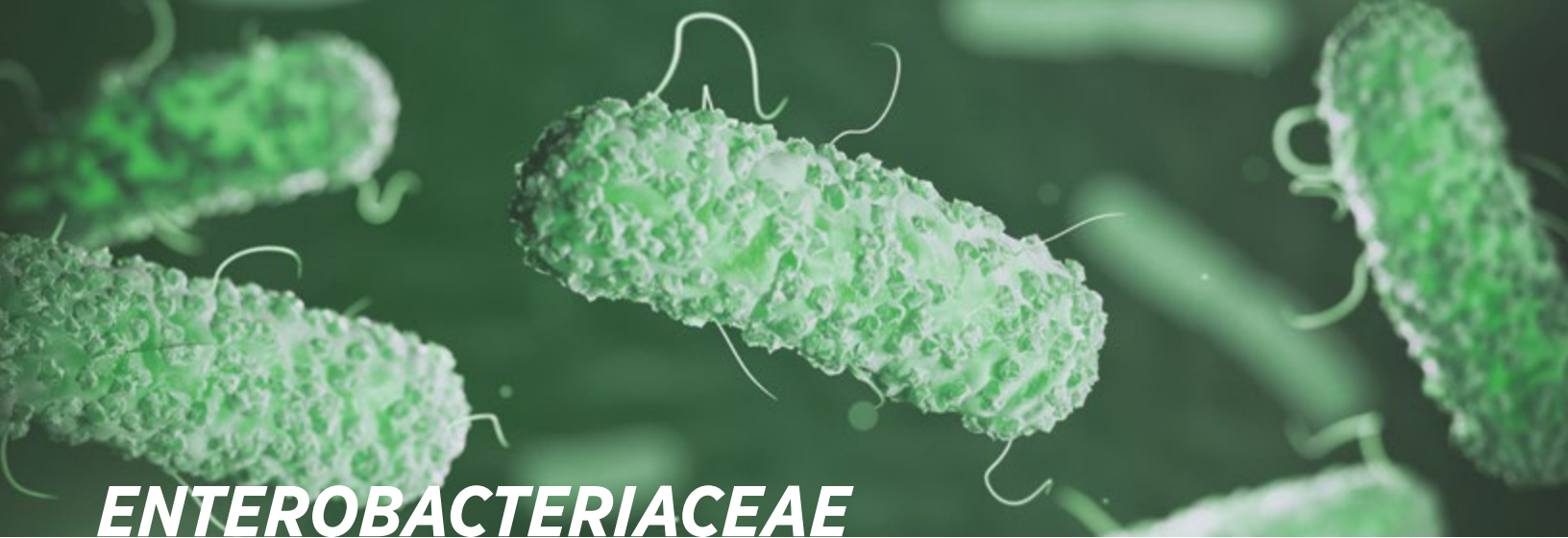


PREVENTION ACTIONS:

- Always wash hands thoroughly with soap and water after touching patients, after handling their food, and after cleaning up after them.
- Avoid feeding raw food including treats to pets.
- Use disposable gloves or a plastic bag to pick up stool right away. Dispose of the stool in the trash, and wash hands with soap and warm water afterwards.
- Thoroughly clean and disinfect surfaces and equipment that have been in contact with stool.
- Use antimicrobials only when indicated.

RESISTANCE PROFILE:

- Aminoglycosides
- Fluoroquinolones
- Lincosamides
- Macrolides
- Tetracycline
- Multidrug resistant *C. jejuni* is an emerging concern in puppies and dogs obtained through pet stores.
- *C. jejuni* has intrinsic resistance to several antimicrobial drugs including bacitracin, novobiocin, rifampin, streptogramin B, trimethoprim, and vancomycin.



ENTEROBACTERIACEAE

Enterobacteriaceae (*Escherichia coli*, *Proteus* spp., *Klebsiella* spp.) and *Acinetobacter* spp.

Enterobacteriaceae and *Acinetobacter* spp. are a group of gram-negative, facultatively anaerobic, non-spore-forming rods that can be found in the environment as well as in humans and animals.

What you need to know

- Extended-spectrum beta lactamase (ESBL)-producing *Escherichia coli*, *Proteus* spp., *Klebsiella* spp. and *Acinetobacter* spp. occur in humans, animals, and the environment. Feeding raw diets to dogs and cats has been implicated as a route of transmission to small animals; however, other modes of transmission are possible.
- There are no antimicrobial drugs approved by FDA for dogs and cats to treat ESBL-producing strains in animals. Some antimicrobials approved for animals may be active against ESBL-producing strains; however, this must be confirmed through susceptibility testing.

SPECIES:



PREVENTION ACTIONS:

- Always wash hands thoroughly with soap and water after touching animals, after handling their food, and after cleaning up after them.
- Avoid feeding raw food, including treats, to cats and dogs.
- Use disposable gloves or a plastic bag to pick up stool right away. Dispose of the stool in the trash, and wash hands with soap and warm water afterwards.
- Thoroughly clean and disinfect surfaces and equipment that have been in contact with stool or urine.
- Develop an infection prevention program in the veterinary clinic.

RESISTANCE PROFILE:

- Penicillins*
- Cephalosporins
- Fluoroquinolones

*Note: Some of the resistance noted for these organisms has been long-established and there available therapeutic options which may be successfully used for treatment.

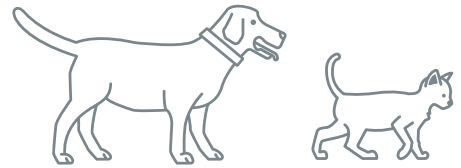
ENTEROCOCCUS SPP.

Enterococcus spp. are gram-positive cocci that most commonly behave as non-pathogenic commensal (or naturally occurring) organisms but can be opportunistic pathogens causing healthcare-associated infections. The most common disease-causing species are *Enterococcus faecalis* and *Enterococcus faecium*, with the latter typically demonstrating more extensive resistance patterns.

What you need to know

- In some cases, the presence of *Enterococcus* spp. in patient samples can be interpreted as a contaminant, or non-pathogenic isolate, and no treatment is required. Clinicians should consider the patient's clinical signs and refer to existing guidelines when interpreting culture and susceptibility test results.
- Use the results of culture and susceptibility testing to determine the most appropriate antimicrobial agent to treat infections due to the broad intrinsic and acquired resistance patterns.
- When patients are co-infected with *Enterococcus* spp. and other bacteria, (e.g., in wounds, the bladder, or body cavities), treatment should be directed to the likely cause of infection.

SPECIES:



PREVENTION ACTIONS:

- Always wash hands thoroughly with soap and water after touching patients, after handling their food, and after cleaning up after them.
- Thoroughly clean and disinfect surfaces and equipment that have been in contact with stool or urine.
- Develop an infection prevention program in the veterinary clinic.

RESISTANCE PROFILE:

- Penicillins
- Fluoroquinolones*
- Macrolides

Note: Some of the resistance noted for these organisms has been long-established and there available therapeutic options which may be successfully used for treatment. *Enterococcus* spp. are intrinsically resistant to cephalosporins, fluoroquinolones, trimethoprim-sulfonamides, clindamycin, and macrolides (erythromycin or tylosin).

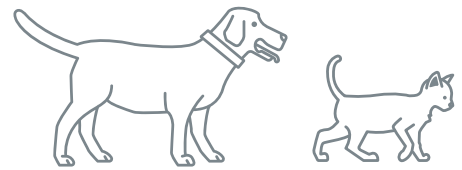
PSEUDOMONAS AERUGINOSA

Pseudomonas aeruginosa is a gram-negative rod that prefers moist environments and can be found widely in the environment.

What you need to know

- *Pseudomonas aeruginosa* is intrinsically resistant to many common antimicrobials including most penicillins, most cephalosporins, glycopeptides, macrolides, tetracyclines, trimethoprim-sulfonamides, rifampin, and chloramphenicol. Antimicrobial susceptibility testing is the only way to determine if *Pseudomonas* is resistant and to tailor antimicrobial therapy, when indicated.
- *Pseudomonas aeruginosa* transmission animal-to-animal or animal-to-human is not known to occur. This is an environmental contaminant, and infection of the ears and nasal passages and wound management are the most important treatment issues.

SPECIES:



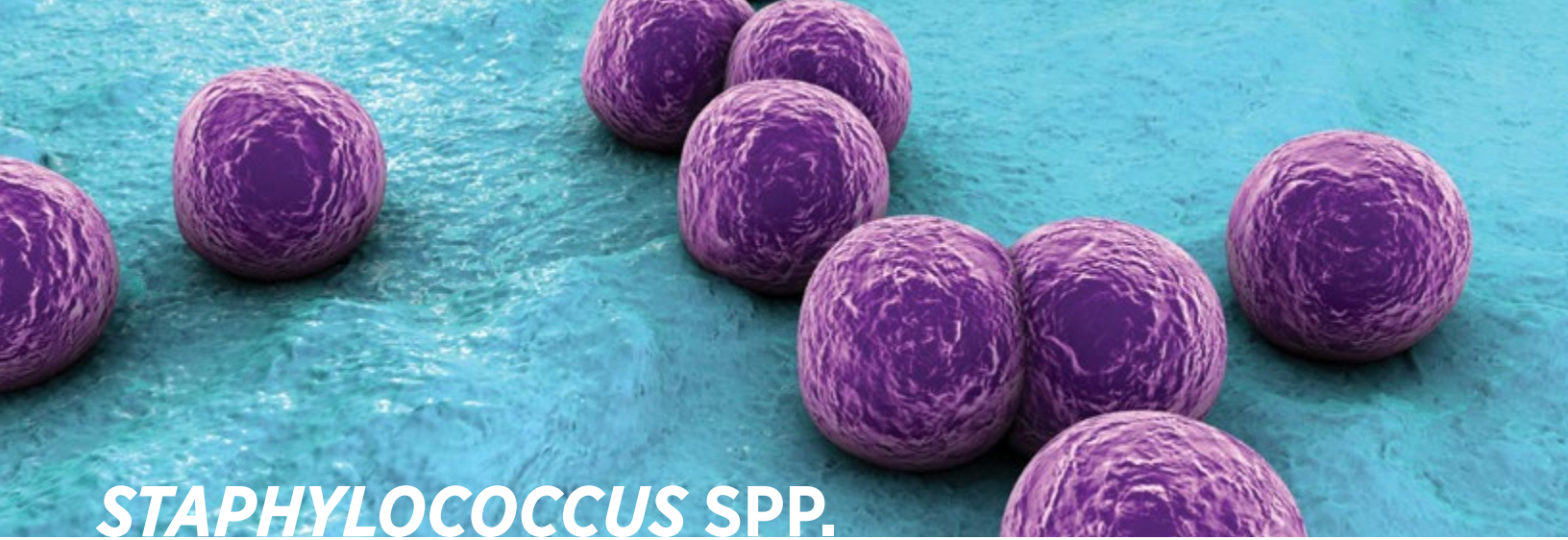
PREVENTION ACTIONS:

- Manage any underlying problems (e.g., allergy and ear infections).
- Good biosecurity and infection control are critical. This organism is ubiquitous in the environment.

RESISTANCE PROFILE:

- Fluoroquinolones
- Carbapenems (rare)

Note: Some of the resistance noted for these organisms has been long-established and there available therapeutic options which may be successfully used for treatment. *Pseudomonas aeruginosa* is intrinsically resistant to many common antimicrobials including most penicillins, most cephalosporins, tetracyclines, trimethoprim-sulfonamides and chloramphenicol. FDA-approved antimicrobials for companion animals, including fluoroquinolones, are not active against resistant strains of *Pseudomonas*.



STAPHYLOCOCCUS SPP.

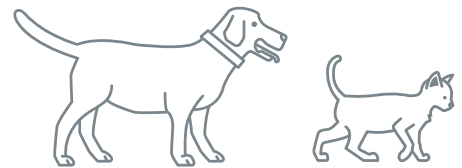
(*S. aureus*, *S. pseudintermedius*, *S. schleiferi*)

Staphylococcus spp. are gram-positive cocci that commonly inhabit the skin and mucous membranes (nose, mouth, perineum). Resistance to antimicrobials in these organisms is increasing.

What you need to know

- The most common risk factors for methicillin-resistant *S. pseudintermedius* (MRSP) in animals are a) prior antimicrobial exposure, and b) visits to veterinary hospitals. However, MRSP colonization and infection can occur in dogs that do not have any known risk factors.
- There are few antimicrobials approved by FDA for dogs and cats that are active against MRSP strains of *Staphylococcus* spp.; therefore, legal extralabel use of human and animal drugs may be necessary when antimicrobial treatment is indicated.
- Methicillin-resistant *S. pseudintermedius* is a canine pathogen but is rarely the cause of illness in people.

SPECIES:



PREVENTION ACTIONS:

- Reduce the risk of *Staphylococcus* infection by treating underlying conditions (skin parasites or atopic/allergic dermatitis). Topical treatment should be considered, if possible, to minimize the use of systemic antimicrobials.
- Promote infection control and biosecurity in veterinary settings.
- Practice good hand hygiene when examining patients.
- Only use antimicrobials when indicated.
- Develop an infection prevention program in the veterinary clinic.

RESISTANCE PROFILE:

Resistance has been reported to these antimicrobials:

- Cephalosporins
- Fluoroquinolones
- Lincosamides
- Macrolides
- Penicillins*
- Tetracyclines*

*Note: Some of the resistance noted for these organisms has been long-established and there available therapeutic options which may be successfully used for treatment.



CATTLE

MANNHEIMIA HAEMOLYTICA, PASTEURELLA MULTOCIDA, HISTOPHILUS SOMNI

Image Credit: Dr Karen Olsen University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

Mannheimia haemolytica and *Histophilus somni* are pathogens of concern primarily in cattle. *Pasteurella multocida* causes bacterial infections in a wide range of mammalian species, including cattle. *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* are three important bacteria causing bovine respiratory disease (BRD) and are isolated routinely from animals at necropsy (Bell et al., 2012).

What you need to know

These pathogens cause clinical disease in all sectors and stages of cattle production (cow-calf, stocker, feedlot, and dairy, especially pre- and post-weaned) and are responsible for a significant portion of the antimicrobial use in the United States cattle industry. One of the key challenges of BRD therapy is the lack of a reliable and affordable “cow-side” test for diagnosis. Currently, BRD is diagnosed based on the presence of clinical signs, physical examination, and presence of fever. Even trained observers cannot reliably classify animals as true BRD cases.

SPECIES:



PREVENTION ACTIONS:

- Modification of environmental factors that can serve as stressors which adversely impact animal health and the immune system (e.g., weaning, transport, commingling, crowding, dust, and inadequate ventilation). In addition, certain factors such as crowding and inadequate ventilation, can enhance the transmission.
- Proper nutrition and vaccination in advance of challenge by risk factors can reduce morbidity and mortality.

RESISTANCE PROFILE:

Multidrug / Extensively-drug resistant, including the following classes:

- Aminocyclitols
- Fluoroquinolones
- Phenicol
- Penicillins
- Tetracyclines
- Macrolides

MORAXELLA SPP.

Image Credit: Dr. Kristin Clothier UC Davis College of Veterinary Medicine

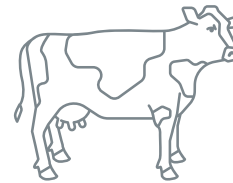
Moraxella bovoculi and *Moraxella bovis*

Moraxella bovis has been identified as a cause of infectious bovine keratoconjunctivitis (IBK, also known as “pinkeye”). *Moraxella bovoculi* has been associated with IBK outbreaks. IBK causes ocular ulcers and in some cases blindness; therefore, it is both an animal welfare concern and an economically important disease for beef and dairy cattle farms.

What you need to know

- IBK has been a challenge for cattle producers for more than a century. However, the emergence of strains that contain as many as 10 co-located antimicrobial resistance genes and confer resistance in vitro to all antimicrobials approved for this disease is concerning. A collection of resistance genes has also been found in *M. bovoculi* (Dickey et al., 2016) and were found in 12% of isolates subjected to whole genome sequencing in a recent study (Dickey et al., 2018). *Moraxella* isolates with multiple resistance genes were from a genotype that has been found associated with IBK outbreaks. IBK has significant welfare and production concerns, and new disease prevention strategies and tools are critical to reduce incidence and reduce the need for antimicrobial therapy.

SPECIES:



PREVENTION ACTIONS:

- Vector control
- Vaccination
- Commercial and autogenous bacterins.
- Efforts to prevent infection and outbreaks can help prevent the need for antimicrobial administration which can lead to resistant bacteria.

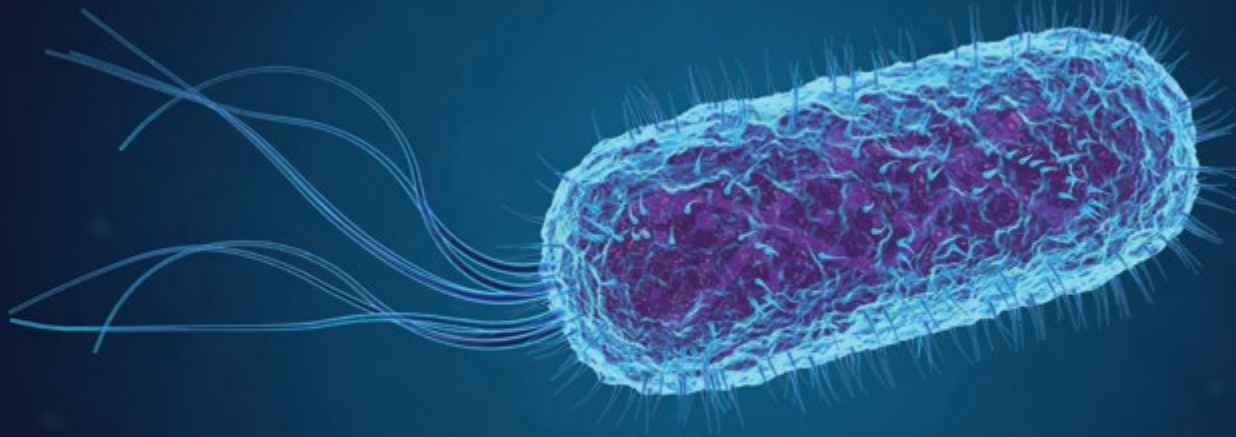
RESISTANCE PROFILE:

Resistance to these antimicrobials has been reported:

- Tetracyclines
- Macrolides



CHICKENS & TURKEYS



ESCHERICHIA COLI

Escherichia coli is a gram-negative rod in the family *Enterobacteriaceae* and is considered a facultative anaerobe that is ubiquitous in all environments. In chickens and turkeys, the *E. coli* associated with disease are generally referred to as avian pathogenic *E. coli* (APEC) and are the primary cause of colibacillosis. The disease syndromes making up the colibacillosis definition include septicemia (colisepticemia), airsacculitis/polyserositis, swollen-head syndrome, coliform cellulitis (aka inflammatory or infectious process), osteomyelitis/synovitis, salpingitis, panophthalmitis, and omphalitis/yolk sac infection. Colibacillosis in either broilers or turkeys is typically a localized or systemic disease occurring secondarily to viral infections and environmental stressors. In an annual survey, colibacillosis was ranked as the #2 health issue that turkey veterinarians faced in 2016, 2017 and 2018.

What you need to know

- *E. coli* is an important opportunistic pathogen of broiler and layer chickens and turkeys.
- Few antimicrobials are approved for use in broiler, layer and turkey production in the United States for treatment and control of *E. coli* diseases, and the antimicrobials that are available have limited efficacy against APEC.
- Whereas the majority of APEC were previously assigned to three main serogroups - O1, O2, and O78 - more recent research has shown that there is great diversity in the serogroups of APEC causing colibacillosis. A high percentage of APEC isolates cannot be grouped using current methods.
- Robust preventive medicine programs that include a vaccination program developed in consultation with a veterinarian and appropriate housing conditions will help minimize the occurrence of colibacillosis.

SPECIES:



PREVENTION ACTIONS:

- Eliminate predisposing factors by vaccinating birds against mycoplasmas, IBV, NDV, and HEV.
- Thorough cleaning of poultry houses may reduce exposure to pathogenic strains of *E. coli*.
- Ensuring proper ventilation and chlorination of drinking water also reduces the levels of environmental contamination.
- Treatment of colibacillosis relies on antimicrobial therapy; however, *E. coli* are becoming increasingly resistant to frequently used antimicrobials so this treatment may fail.

RESISTANCE PROFILE:

- Tetracyclines
- Sulfonamides
- Streptomycin

ORNITHOBACTERIUM RHINOTRACHEALE

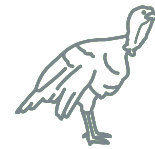
Image credit: Dr Karen Olsen University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

Ornithobacterium rhinotracheale (ORT) is a highly contagious respiratory disease caused by a gram-negative pleomorphic rod-shaped bacterium. ORT was originally recognized in Europe and South Africa and was confirmed for the first time in the United States in turkeys in 1993. In an annual survey, ORT ranked #4 out of 36 priority health issues that turkey veterinarians faced in 2018 and has ranked in the top 5 health issues affecting turkey production since 2015. Research on ORT in turkeys has been identified as critical research needed by the turkey industry as the options for prevention are very limited.

What you need to know

- The key to ORT prevention is strict biosecurity to prevent the introduction of the pathogen in a turkey farm. Once introduction has occurred, the disease becomes endemic and is nearly impossible to eradicate in multiple-age farms or in geographical areas densely populated with turkeys.
- No commercial vaccine is approved for this widespread disease in the turkey industry. Understanding of the antigenic epitopes and cross protection between serotypes of ORT is limited and needs to be better understood in order to identify the characteristics and requirements of good vaccine candidates.
- The only extensive antimicrobial susceptibility testing conducted in the United States is outdated (1998). Sixty-eight isolates of *O. rhinotracheale* were tested for susceptibility to a panel of antimicrobials, and all were found to be susceptible to ampicillin, erythromycin, penicillin, spectinomycin, and tylosin. In addition, 54 out of the 68 isolates tested were found to be susceptible to neomycin, sarafloxacin, and tetracycline. This is not reflective of the resistance profile of more contemporary *O. rhinotracheale* isolates.

SPECIES:



PREVENTION ACTIONS:

- Biosecurity is critical for preventing ORT infections.
- Proper water sanitation can minimize the severity and spread of *O. rhinotracheale*.
- Limited application of controlled exposure efforts on individual flocks have shown value.

RESISTANCE PROFILE:

- Tetracyclines
- Sulfonamides
- Penicillin

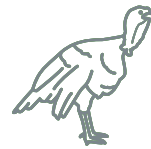
PASTEURELLA MULTOCIDA

Pasteurella multocida is a gram-negative, nonmotile, coccobacillus belonging to the *Pasteurellaceae* family and is the cause of fowl cholera. This disease often presents as a non-specific severe respiratory disease of older (>8 weeks old) turkeys although young turkeys can also be affected. Antimicrobial sensitivity is highly variable. When flocks are infected with a strain that does not have any treatment options, mortality rates can exceed 3-5% losses per day.

What you need to know

- Biosecurity is critical to preventing infections with *P. multocida*, especially rodent control and limiting barn access to cats.
- Commercially available live vaccines need to be used carefully as they can induce clinical disease and mortality.
- Antimicrobial therapy may help reduce the severity of the disease but will not typically eliminate *P. multocida* from the infected flock.

SPECIES:

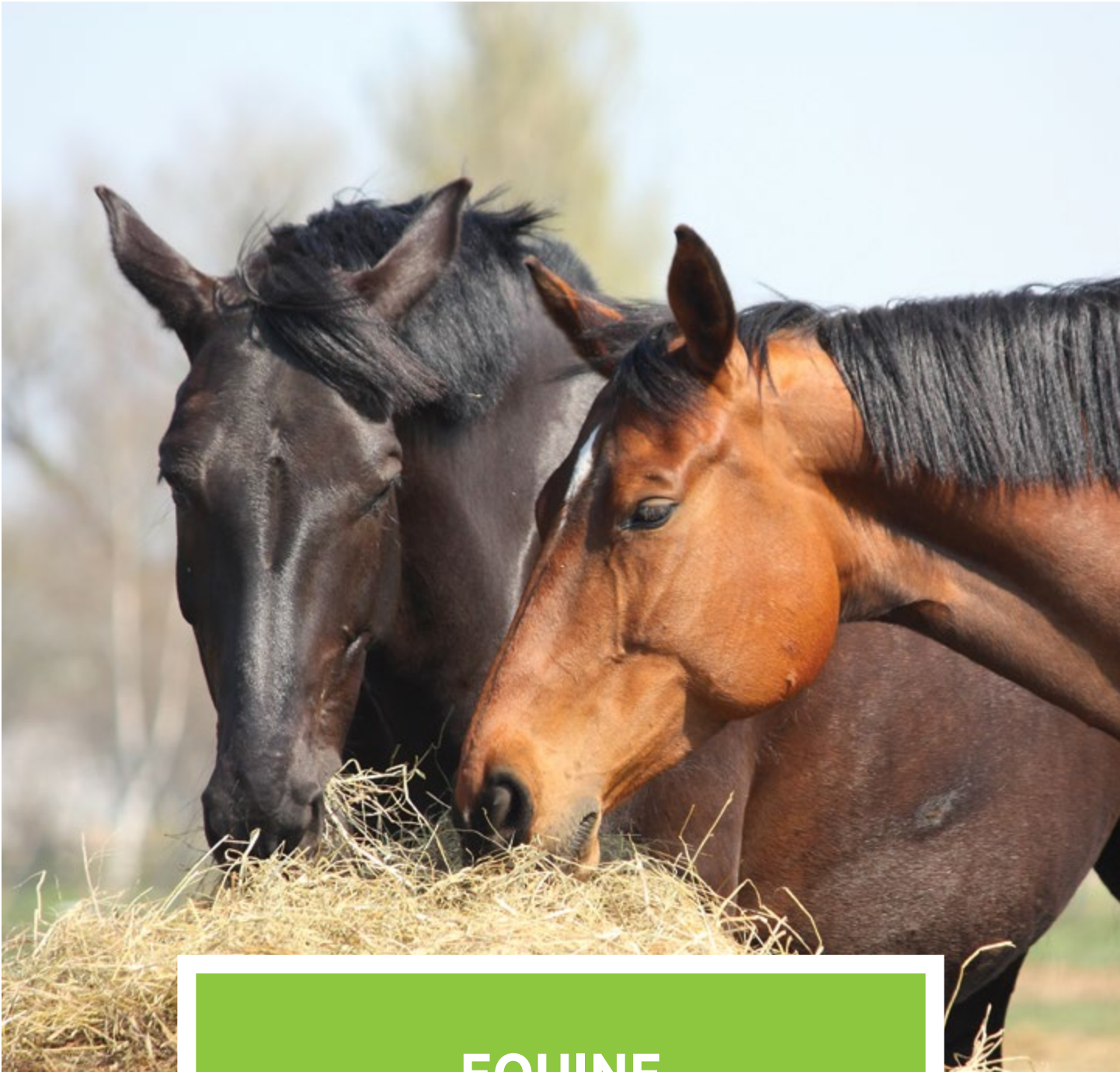


PREVENTION ACTIONS:

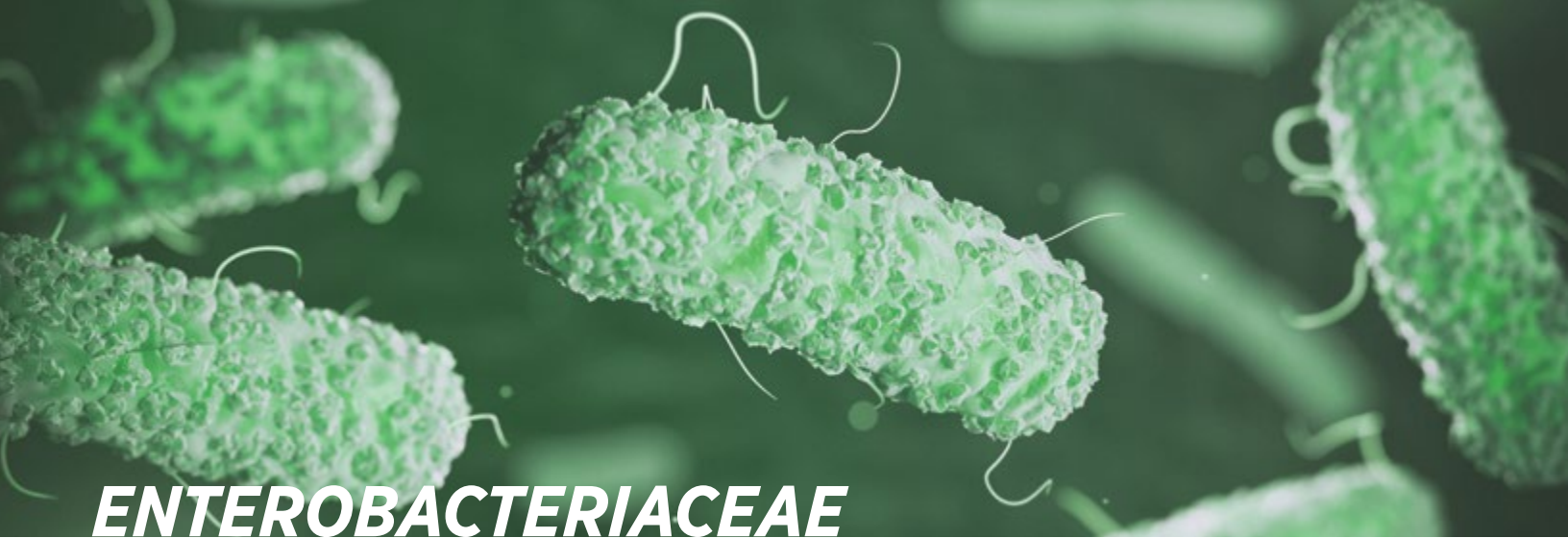
- Biosecurity is critical for preventing infections.
- Adequate rodenticide rotations are important to reduce rodent pressure around turkey barns as well as biosecurity programs that prohibit domestic species, especially cats, from being on the farm.
- Commercially available live fowl cholera vaccines can cause moderate to severe disease in turkeys.

RESISTANCE PROFILE:

- Tetracyclines
- Sulfonamides
- Penicillin



EQUINE



ENTEROBACTERIACEAE

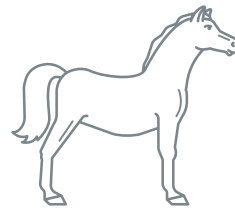
Escherichia coli, *Proteus* spp., *Enterobacter* spp., *Klebsiella* spp.

Enterobacteriaceae are commonly identified as commensal gastrointestinal flora in horses. These are uncommonly implicated as the cause of equine clinical disease, but due to their location in the body, they are commonly exposed to antimicrobial agents when horses are treated for infections. This is a strong selective pressure for the development of resistance, and this family of bacteria can therefore play a major role in dissemination of resistance to other bacterial species and act as a reservoir for resistance genes.

What you need to know

- Multidrug resistant *Enterobacteriaceae* – specifically ESBL producing strains – are an important human health risk.
- The most important risk factors for emergence of ESBL-producing strains of *Enterobacteriaceae* have not been identified for horses. Use of antimicrobials on the farm could be a factor. Transmission from other sources (e.g., people) could also be a factor.
- The FDA-approved antimicrobial drugs for horses are usually not active against resistant strains of *Enterobacteriaceae*. Therefore, legal extralabel use of human or animal drugs often is needed for treatment.

SPECIES:



PREVENTION ACTIONS:

As with the other animal species and bacteria, infection control and prompt resolution of the infection is important when resistant infections are identified.

RESISTANCE PROFILE:

- This family of bacteria are intrinsically resistant to penicillins and commonly demonstrate resistance to trimethoprim-sulfonamides, cephalosporins, and tetracyclines.
- Extended-spectrum beta-lactamase (ESBL) *Enterobacteriaceae* are of even more concern as most demonstrate resistance to other classes of antimicrobials including third-generation cephalosporins, gentamicin, tetracyclines, fluoroquinolones, and chloramphenicol.

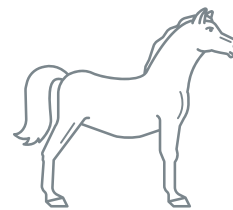
PSEUDOMONAS AERUGINOSA

Pseudomonas aeruginosa is often resistant to many of the antimicrobials commonly used in veterinary medicine. It is ubiquitous in the environment, and infections are usually opportunistic following primary infection with another pathogen or due to patient immunocompromise. Infection in horses is generally uncommon, but severe lesions and advanced disease can predispose to secondary infection with *P. aeruginosa*. Resistance in these instances poses an additional complication for the animal and can make treatment of the disease process all the more difficult.

What you need to know

- Most strains are multidrug resistant. Transfer of this pathogen from animals to people is not known.
- The most important risk factors for emergence of resistant strains are not known because incidence is low. These are most often opportunistic infections.
- There are no antimicrobials in the United States approved by FDA for horses that are active against drug-resistant strains of *P. aeruginosa*. Therefore, drugs used extralabel such as amikacin, tobramycin, and carbapenems may be needed for treatment. If treatment can be accomplished with topical treatment or local infusion, this may avoid systemic drug administration.

SPECIES:



PREVENTION ACTIONS:

- Infection control and prompt resolution of the infection is important when resistant infections are identified.
- Keeping the environment clean and dry should be a priority for hospitals, but it is likely to be overtly challenging if not impossible to completely eliminate this pathogen from any animal housing facility.
- Surgical sites and open wounds should also remain covered to prevent contamination with environmental debris.

RESISTANCE PROFILE:

- *Pseudomonas aeruginosa* is inherently resistant to macrolides, penicillin (including ampicillin), tetracyclines, trimethoprim-sulfonamides, chloramphenicol, rifampin, and cephalosporins (except ceftazidime).
- Resistant strains may be resistant to fluoroquinolones, gentamicin, and carbapenems, but resistance can be highly variable among isolates.
- *P. aeruginosa* is almost always susceptible to amikacin.



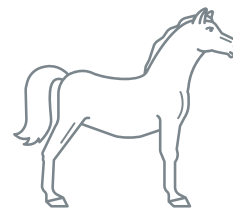
STAPHYLOCOCCUS SPP.

Staphylococcaceae are among the most commonly isolated gram-positive bacteria found to be colonizing the skin of equine patients, particularly those that present to referral settings for treatment of bacterial infections. The trend, over time, of the prevalence of methicillin-resistant *S. aureus* (MRSA) has not been reported in horses. It has increased in people and other animals over the past 20 years, and this may have also occurred in horses. Most MRSA are also multi-drug resistant (MDR). MRSA infections in horses are associated with a variety of types of infections including wounds, surgical- and catheter-site infections, dermatitis, septic arthritis, pneumonia, and others. These infections are often associated with another primary problem such as surgery, skin disease, a joint infection in an immunocompromised foal, or patient with joint disease. Zoonotic transmission is possible but rare.

What you need to know

- MRSA has been identified from isolates taken from horses, but it is possible that transmission came from humans.
- The most common risk factors for MRSA in horses are prior antimicrobial exposure and transmission from people.
- There are few (if any) antimicrobials approved by the FDA for horses that are active against MRSA infections. Therefore, legal extralabel use of human and animal drugs is often needed for treatment. Trimethoprim-sulfadiazine is approved for use in horses and may be active against some MRSA strains, but this is based on using human susceptibility testing standards for trimethoprim-sulfamethoxazole, which may not apply to isolates from horses.

SPECIES:

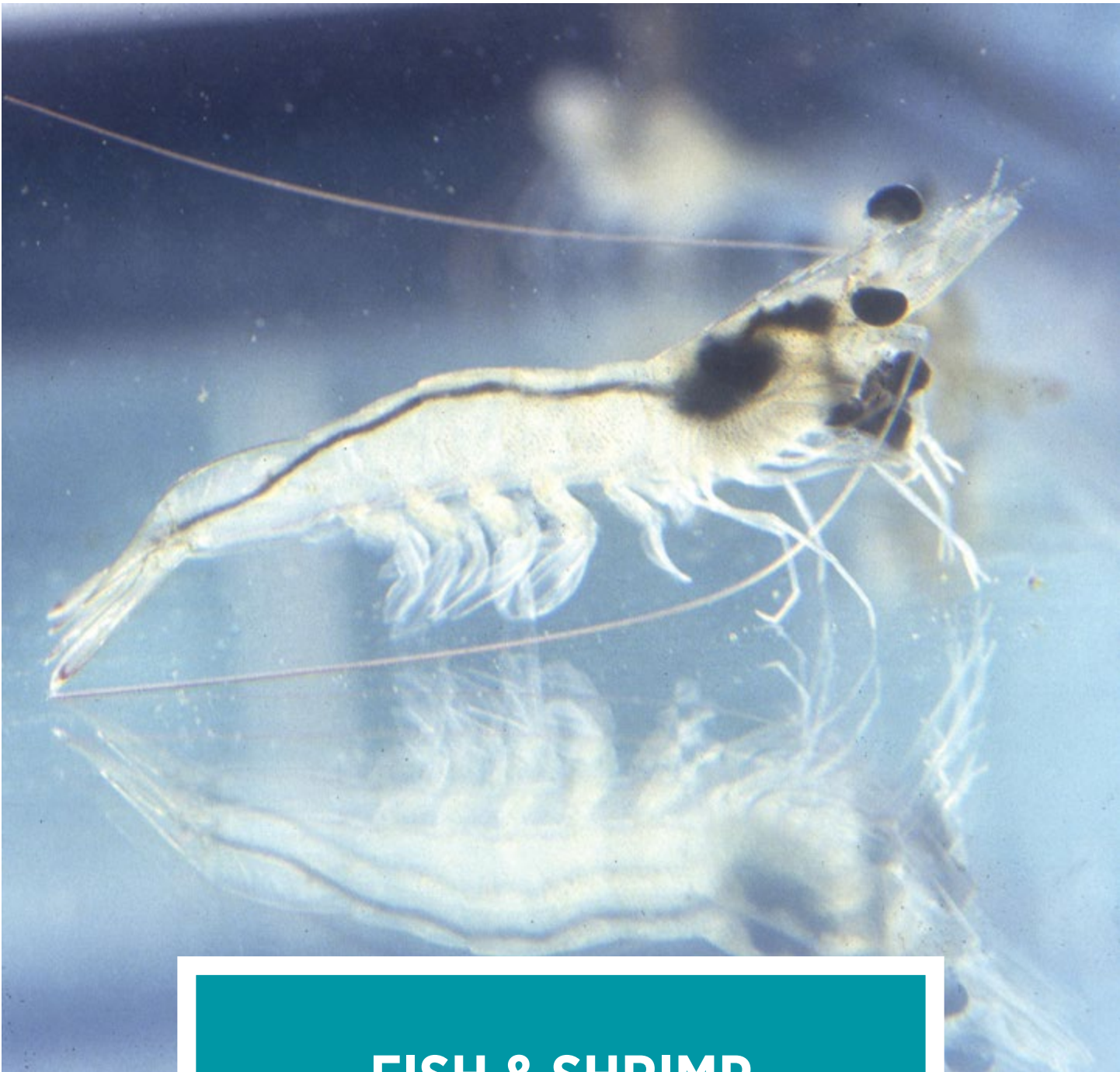


PREVENTION ACTIONS:

Infection control policies in hospitals can be effective to prevent spread of infection, and hospital-associated sources of methicillin-resistant *Staphylococcus* contribute to a number of equine staphylococcal infections. Infection control measures can include identification and isolation of patients with drug-resistant infections, simple hygiene measures (washing hands, use of hand disinfectant stations, and use of disposable gloves when working with horses that have wounds), and limiting the exposure to other animals in the hospital.

RESISTANCE PROFILE:

Methicillin resistant *S. aureus* (MRSA) are resistant to all beta-lactam antimicrobials. Most strains are multi-drug resistant (MDR) and resistant to lincosamides (although not used in horses), macrolides, tetracyclines, and fluoroquinolones.



FISH & SHRIMP

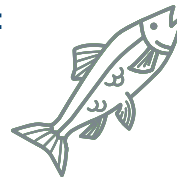
AEROMONAS SPP.

Aeromonas salmonicida, *A. hydrophila*

Aeromonas spp. are oxidase-positive, facultative anaerobic gram-negative bacteria. Outbreaks often present with general clinical and behavioral signs, which can be difficult to distinguish from other diseases. Behavioral changes such as lethargy, stoppage of eating, and riding high in the water column may prelude clinical signs. Non-specific clinical signs such as ulcerative lesions of the skin, hemorrhage around the base of the fins and anus, raised scales, abdominal distension, and exophthalmia are associated with external, internal, and/or systemic infections. These bacteria can be divided into mesophilic motile and psychrophilic nonmotile groups.

- Mesophilic motile strain: *A. hydrophila* is found ubiquitously in warm-water environments but is an opportunistic pathogen that can cause disease in coolwater and coldwater species. It is also part of the normal bacterial microbiota in the gastrointestinal tract of fish. For clinical outbreaks, *A. hydrophila* can result in motile *Aeromonas* septicemia (MAS). MAS outbreaks are often secondary to stress due to suboptimal water parameters, poor husbandry, parasitism, etc.
- Psychrophilic nonmotile strain: *A. salmonicida* has been identified in both fresh and marine fish species but has been typically associated with salmonid aquaculture. It is an obligate pathogen that can cause septicemia and is often referred to as Furunculosis. The disease can occur in several different forms: peracute; acute; subacute; chronic; and latent. An atypical *A. salmonicida* strain has been identified that infects both salmonid and non-salmonid species. The atypical *A. salmonicida* has been responsible for ulcerative diseases in goldfish and flounders. In carp, the atypical *A. salmonicida* can also cause erythrodermatitis.

SPECIES:



- *A. hydrophila* mainly impacts the following warmwater aquaculture species: minnows, bait fishes, carp (*Cyprinus carpio*), channel catfish (*Ictalurus punctatus*), striped bass (*Morone saxatilis*), largemouth bass (*Micropterus salmoides*) and tilapia (*Oreochromis aureus*). Foreign countries have documented *A. hydrophila* multi-drug resistance in cultured shrimp and fish.
- *A. salmonicida* mainly impacts salmonid aquaculture but outbreaks in goldfish, carp, and flounder aquaculture have been documented.



AEROMONAS SPP. CONT'D.

What you need to know

- Antimicrobial resistance can be transferred within and between species of bacteria through gene transfer.
- *Aeromonas* spp. in countries other than the United States may have increased multidrug resistance due to less-regulated use of antimicrobial drugs in those countries compared to the United States.
- *A. hydrophila* has been isolated from seafood, meat and meat products, milk and dairy products, and vegetables.
- *A. hydrophila* can cause illness in humans.

RESISTANCE PROFILE:

Increased resistance to FDA-approved aquatic antimicrobials:

- Oxytetracycline
 - Florfenicol
 - Ormetoprim/sulfadimethoxine

PREVENTION ACTIONS:

- The first line of defense in disease prevention is sanitation in fish culture. These methods include disinfecting hands, boots, and culture equipment before entering fish-rearing facilities to prevent diseases from being introduced to young fish and between different lots of fish. Maintaining strict biosecurity practices can also prevent or minimize the spread of disease within an aquaculture facility.
- All-in/all-out rearing practices, where fish of a specific lot are kept as an individual group within a facility, should be implemented. This is where groups are kept separate from other species and year classes.
- Vaccines for *A. salmonicida* can help prevent or minimize outbreaks.
- Recent studies suggest feeding probiotics can also help to minimize outbreaks with *A. hydrophila*.
- Antimicrobial use should only be under the direction of a veterinarian and prescribed judiciously in accordance to regulations.

EDWARDSIELLA SPP.

Image credit: Dr. Esteban Soto U C Davis College of Veterinary Medicine

Edwardsiella ictaluri and *E. piscicida*

Edwardsiella ictaluri is a gram-negative rod. It is considered an economically important cause of disease of United States catfish and tilapia, and is a threat in zebrafish research colonies because of its associated high morbidity and mortality.

Edwardsiella piscicida is a distinct species of *Edwardsiella* that was previously identified as *E. tarda* (based on indole + assay). Current molecular techniques have clarified that this bacteria of catfish and largemouth bass in the United States is primarily *E. piscicida*.

What you need to know

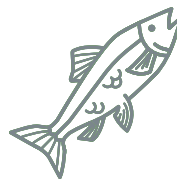
- *Edwardsiella ictaluri* was found to develop and transfer plasmid mediated antimicrobial resistance to all three FDA-approved antimicrobials for fish.
- There are genetic differences between the *E. ictaluri* strains from catfish, zebrafish, and tilapia, but it is unknown what role those genetic differences play in their susceptibility to antimicrobials.
- Resistance is seen with increased antimicrobial use. There are only two medicated feeds approved for use to control mortality associated with *E. ictaluri* in catfish. In the Mississippi Delta, florfenicol is widely used. Diagnostic laboratory records from the Aquatic Diagnostic Laboratory at Stoneville, Mississippi, show a trend in decreased susceptibility based on annual reports (2006-present).

RESISTANCE PROFILE:

Increased resistance to FDA-approved antimicrobials approved for aquatic animals:

- Oxytetracycline
- Florfenicol
- Ormetoprim/sulfadimethoxine

SPECIES:



Isolates of *E. ictaluri* and *E. piscicida* are considered problematic in the catfish industry, particularly channel catfish (*Ictalurus punctatus*) and hybrid catfish (*Ictalurus punctatus* x *Ictalurus furcatus*). Also affected in the United States: zebrafish (*Danio rerio*), Blue Catfish (*I. furcatus*), Tadpole Madtom (*Noturus gyrinus*), Green Knifefish (*Eigemannia virescens*), Devario Devario (*Danio devario*), the Rosy Barb (*Puntius conchonius*) and Nile Tilapia (*Oreochromis niloticus*), and Large Mouth Bass (*Micropterus salmoides*).

PREVENTION ACTIONS:

- Veterinarians can follow the AVMA's Judicious therapeutic use of antimicrobials in aquatic animal medicine policy to reduce resistance from developing in the three approved antimicrobials in aquaculture (Vaccine use, quality brood stock, stocking density, all-in/all-out rearing practice).
- Fish discards should be disposed of properly and should not be dumped into bodies of water that could lead to contamination of other fish.
- For zebrafish colonies, the managers of laboratories should follow strict biosecurity including quarantine in their facilities. Make sure that the source of animals coming into the facility is sound. This is especially important given the lack of FDA approved treatments for bacterial infections in cultured shrimp in the United States.
- Prohibited antimicrobial drugs in aquaculture should be taken off the market. Their use is illegal and may compromise future treatment of infections in both animals and humans.

FLAVOBACTERIUM PSYCHROPHILUM

Image credit: Dr. Esteban Soto U C Davis College of Veterinary Medicine

Flavobacterium psychrophilum, formerly known as *Cytophaga psychrophila* and *Flexibacter psychrophilus*, is a psychrophilic, slow-growing, gram-negative rod. *F. psychrophilum* is associated with bacterial cold-water disease of salmonids and has been responsible for massive die-offs of cultured salmonids since it was first isolated in 1948. This bacterium does not, as of yet, have a zoonotic risk.

What you need to know

- *F. psychrophilum* is an important pathogen in cold water fish culture and wild fish conservation.
- *F. psychrophilum* is ubiquitous in cold, freshwater environments.
- Antimicrobial treatment remains the sole method for reducing losses associated with *F. psychrophilum* infection in cultured finfish, as viable vaccinations have not been developed and eradication of the pathogen is not feasible.
- *F. psychrophilum* is a pathogen of special concern in wild fish stocks as climate change alters water flow and water temperature in migratory waterways.

SPECIES:



Cultured and wild cold water finfish, particularly salmonids

PREVENTION ACTIONS:

- Enact proactive management techniques in fish culture settings, such as removing dead or moribund fish as soon as possible, reducing fish stressors as much as possible, and carefully monitoring fish for signs of early infection (i.e.: fin abrasion, skin surface changes, behavioral changes).
- Provide judicious and evidence-based stewardship for antimicrobial use in cases of suspected *Flavobacterium psychrophilum* infection.

RESISTANCE PROFILE:

- Multidrug resistance has been reported.
- In North America resistance genes for oxytetracycline, florfenicol, and ormetoprim/sulfadimethoxine have been identified.

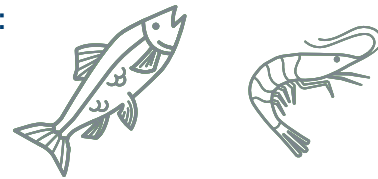
VIBRIO PARAHAEMOLYTICUS

Vibrio parahaemolyticus is a gram-negative, curved bacillus. A halophilic organism, it inhabits temperate and tropical estuarine, marine, and coastal environments around the world. *Vibrio parahaemolyticus* is zoonotic; not only can it cause mass mortality in shellfish (especially shrimp), it is a leading cause of foodborne illness in humans, predominantly via consumption of undercooked seafood.

What you need to know

- *Vibrio parahaemolyticus* is responsible for the majority of bacterial foodborne infections in humans that result from consumption of raw or undercooked shellfish (in particular, oysters). Symptoms in humans include watery diarrhea, nausea, abdominal cramping, vomiting, headache, and fever. Severe disease is generally rare in humans and occurs more commonly in individuals with weakened immune systems. In addition, wound infections can develop when an open wound is exposed to seawater.
- Although acute hepatopancreatic necrosis disease (AHPND) outbreaks in shrimp have not been observed at the same frequency in the United States as in other parts of the world, the ubiquitous nature of the etiological agent, the potential for growth of the shrimp industry in the United States, and *V. parahaemolyticus*' role in food-borne illnesses in humans make it an organism worth paying attention to in the United States
- The majority of antimicrobial resistance studies used isolates from outside of the United States (i.e., Europe and Asia); however, because *V. parahaemolyticus* is zoonotic and because the United States imports the majority of its consumable seafood from international markets, the observed antimicrobial resistance patterns should be considered relevant to shellfish and human health in the United States as well. The source countries often lack antimicrobial use regulations that have been implemented in the United States or simply don't enforce the regulations they do have. These include widespread use of medically important antimicrobials as well as use of antimicrobials banned for use in food animals in the United States (e.g., nitrofurans and chloramphenicol).

SPECIES:



PREVENTION ACTIONS:

- Strict biosecurity practices are imperative to prevent the spread of disease both within and among facilities.
- Use of prohibited drugs in aquaculture is not only illegal; it can be unsafe and may compromise our ability to treat infections in both animals and humans.
- As *V. parahaemolyticus* is responsible for food-borne infections in humans, proper preparation of shellfish (i.e., sufficient cooking) is important to prevent foodborne illness.

RESISTANCE PROFILE:

Resistance to these antimicrobials has been reported:

- Beta-lactams (amoxicillin, ampicillin, penicillin, imipenem)
- Tetracycline
- Cephalosporins (cefoxitin, cefazolin, cephalothin, cefepime, cefotaxime)
- Chloramphenicol, florfenicol
- Aminoglycosides (amikacin, gentamicin, streptomycin, apramycin, kanamycin)
- Fluoroquinolones (enrofloxacin, nalidixic acid)
- Sulfonamides (sulfathiazole, sulfamethoxazole, trimethoprim-sulfa)
- Macrolides (erythromycin)
- Rifampin
- Trimethoprim
- Fosfomycin
- Bicozamycin

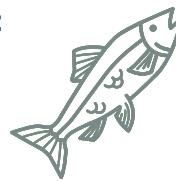
VIBRIO VULNIFICUS

Vibrio vulnificus is a halophilic, gram-negative bacillus that has been associated with opportunistic infections in humans resulting in deadly septicemia and is an emergent pathogen of fish particularly in brackish and marine environments. It is also frequently recovered from molluscan shellfish, primarily oysters. Although some isolates have been found to be particularly virulent to fish, most are part of the normal flora of marine animals.

What you need to know

- *V. vulnificus* is an important zoonotic pathogen capable of causing severe infections and mortality in fish, animals, and humans.
- *V. vulnificus* is ubiquitous in marine environments and marine animals.
- Treatment of *V. vulnificus*-infected fish is dependent on the type of fish (pet fish vs. food destined for human consumption) and the availability of antimicrobial susceptibility data as resistance, suggested by high minimal inhibitory concentration of several drugs, is not uncommon.

SPECIES:



Cultured and wild fish and shellfish

PREVENTION ACTIONS:

- Always wash hands thoroughly with soap and water after touching fish, shellfish and life support systems (fish tank, nets, filters).
- If you work at a pet store, aquarium, or aquaculture facility, report sick animals to the appropriate manager and have them examined by a veterinarian.
- Avoid feeding raw shellfish to cultured or wild fish.
- Use disposable gloves when cleaning tanks and other inanimate objects in aquatic systems or when touching live and dead fish and shellfish.
- Thoroughly clean and disinfect surfaces and equipment that have been in contact with dead fish or shellfish.
- Develop appropriate biosecurity and aquatic animal health management plans with veterinarian.

RESISTANCE PROFILE:

Resistance to the following antimicrobials has been reported:

- Apramycin
- Nalidixic acid
- Azithromycin
- Chloramphenicol
- Ampicillin
- Doxycycline
- Tetracycline



SHEEP & GOATS

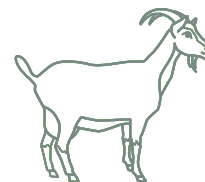
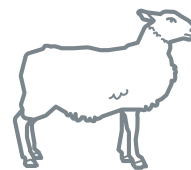
CAMPYLOBACTER JEJUNI

Campylobacter jejuni is a motile gram-negative rod and is found in the intestinal and genital tracts. *C. jejuni* more commonly affects sheep than goats, causes abortion in late pregnancy and can also result in weak or stillborn lambs. A single genetic clone of this organism (ST-8, termed clone SA for sheep abortion) has emerged as the most common cause of *C. jejuni* abortion in sheep and was identified in 87.6% of United States sheep abortion isolates. This clone appears to be hypervirulent with respect to abortion; the gene responsible for this virulence appears to be *porA* encoding the major outer membrane protein. Previously, DeLong and colleagues (1996) found that *C. jejuni* isolates from the western United States associated with abortion in sheep were heterogeneous with respect to biotype, but evidence strongly suggests this is no longer true.

What you need to know

Abortion due to *C. jejuni* in sheep appears to be an emerging disease in the United States. Almost all abortions are due to clone SA, a highly tetracycline resistant and abortifacient type. This clone has been identified in a number of cases of human illness associated with consumption of raw milk.

SPECIES:



PREVENTION ACTIONS:

- Traditionally *C. jejuni* abortion was controlled through the use of a chlortetracycline feed additive in the United States. This made treatment of a flock in the midst of an abortion outbreak fairly easy, particularly in animals out on pasture. Injection of multiple animals in a pasture setting can be challenging. However, the clone SA currently isolated from the majority of sheep abortion cases has been found to be highly resistant to tetracyclines as it almost always carries the *tet(O)* gene.
- Vaccination may be effective.

RESISTANCE PROFILE:

Tetracyclines as a result of the clone SA, a highly tetracycline-resistant and abortifacient type.

STAPHYLOCOCCUS SPP

Staphylococcus aureus and coagulase-negative *Staphylococcus*

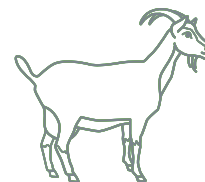
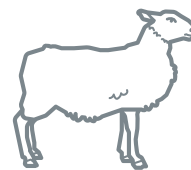
Staphylococcus aureus is an important clinical pathogen, but coagulase negative staphylococci (CNS) are the most prevalent *Staphylococcus* spp. isolated in subclinical mastitis. When these pathogens affect dairy goats, farms can experience significant economic losses due to reduction in milk production and poor milk quality.

About the Pathogen: *S. aureus* is a gram-positive coccus that is coagulase-positive. While it may be responsible for other infections, mastitis is the most important of these in small ruminants. It infects the mammary gland leading to mastitis and often results in microabscesses in the udder. It can also be isolated from teat, nasal, and vaginal swabs of goats and sheep. Infections can be acute or chronic and may be subclinical, meaning that the only indication of infection is an elevated somatic cell count in the milk or when it is isolated from routine milk cultures. *S. aureus* is also the most common cause of peracute necrotic mastitis, a less common but more devastating disease. It can lead to complete sloughing of one or both glands and has a reported case fatality rate of up to 40%. The organism is considered a contagious pathogen and typically passes between animals during milking. Coagulase-negative staphylococci are a type of bacteria that normally lives on the skin or mucous membranes of people and animals and often does not cause infection. However, it is one of the most common bacteria implicated in preclinical mastitis of small ruminants.

What you need to know

- *Staphylococcus aureus* is considered a contagious mastitis pathogen and can be transmitted via milking equipment, milkers' hands, and other fomites.
- Poor milking routines or improperly functioning milking machines are often involved in maintaining the high prevalence of CNS.
- Resistance to beta-lactam antimicrobials has been reported.
- Prevention of infection through efforts to prevent mastitis are also effective in preventing resistant infections.

SPECIES:

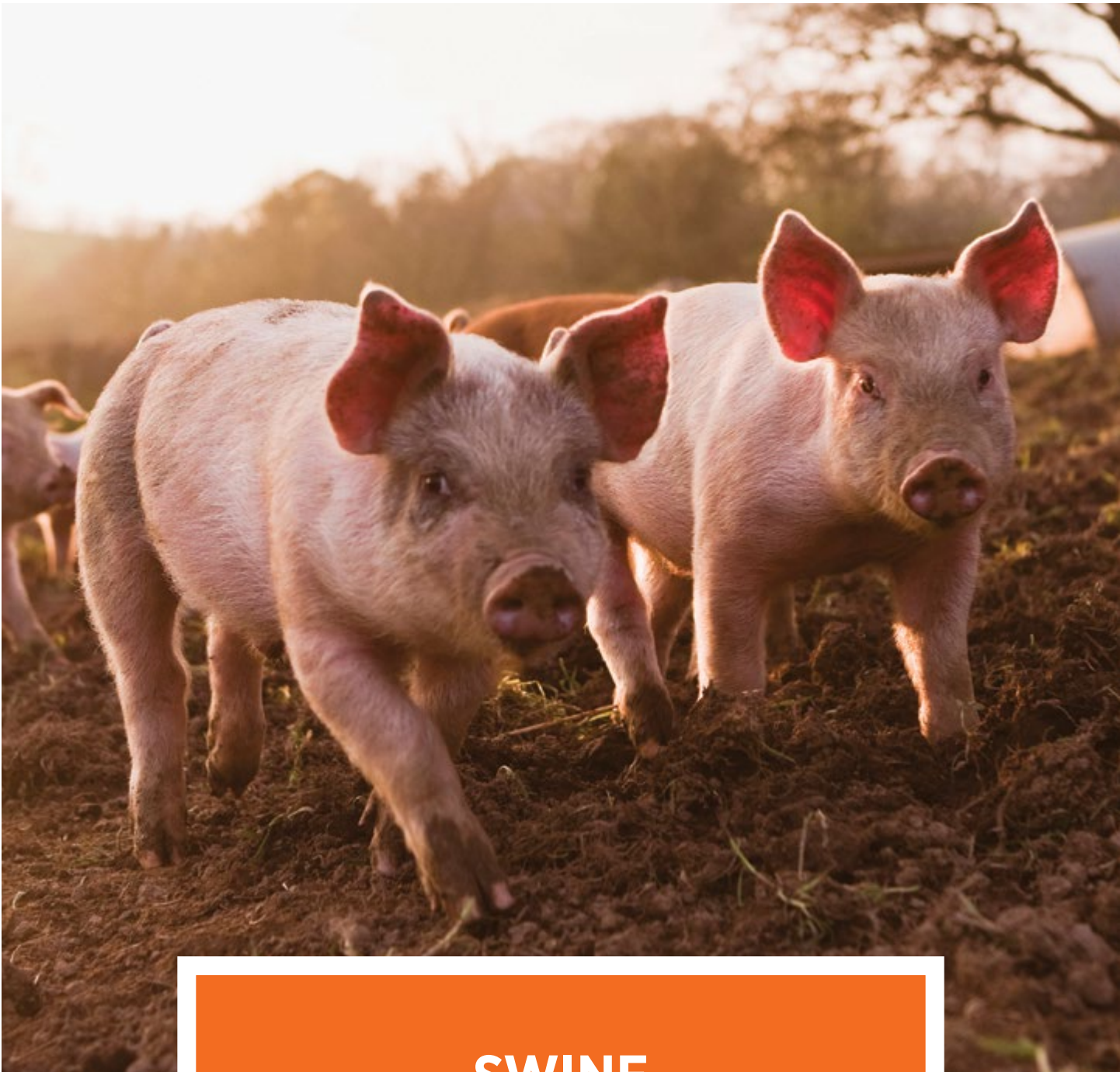


PREVENTION ACTIONS:

Clean housing and correct milking practices are key to the prevention of mastitis in small ruminants.

RESISTANCE PROFILE:

- Resistance to beta-lactams (*mecA* gene), aminoglycosides and tetracyclines have been reported
- If resistance is due to the *mecA* or similar genes that confer resistance to all beta-lactam antimicrobials the number of effective antimicrobials becomes much fewer.
- Resistance to macrolides has been reported in coagulase-negative staphylococci.



SWINE



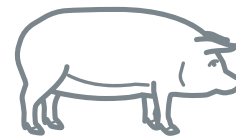
ESCHERICHIA COLI

Escherichia coli (gram negative rods in the family *Enterobacteriaceae*) are normal bacterial flora of the lower intestinal tract of homeothermic animals, including pigs and humans. They can also be found in the environment, where they can remain viable for months. Many variants are commensals that do not cause disease. Particular *E. coli* variants cause a wide range of pathological conditions globally in many animal species. The clinical manifestations in pigs include profuse watery diarrhea with rapid dehydration, acidosis, and death. Rarely, pigs may collapse and die before diarrhea begins. In the pathogenesis of diarrheal diseases, key factors are the presence of fimbriae that mediate attachment to the intestinal epithelium, and genes encoding enterotoxins (classically both heat labile and heat stable toxins) that cause fluid secretion. Genes for both fimbriae and enterotoxins can be transmitted on plasmids, which can also include antimicrobial resistance genes. Adhesion of fimbriae is mediated via intestinal receptors, which are variably present in pigs of different ages, with susceptibility greatest in young animals.

What you need to know

- Outbreaks of neonatal colibacillosis may require immediate treatment including antimicrobials, but attention should be directed to the underlying factors, particularly appropriate vaccination protocols, and environmental conditions and hygiene that may be predisposing to the disease.
- *E. coli* disease occurs predominantly in the vulnerable post-weaning phase. Antimicrobials are commonly required to control and prevent outbreaks, but attention should be given to environmental conditions and dietary factors that may be predisposing to disease.
- In weaned pigs known to be infected with porcine reproductive and respiratory syndrome (PRRS) or influenza viruses that affect feed intake in weaned pigs, preventive antimicrobial use may be necessary to reduce mortality due to secondary infections.

SPECIES:



PREVENTION ACTIONS:

Following the core principles of swine health management is also important, including: not mixing pigs from different sources, adopting all-in/all-out management whenever practical, maintaining good hygiene, and minimizing environmental stresses due to temperature fluctuations and poor ventilation.

RESISTANCE PROFILE:

Resistance has been reported to these antimicrobials:

- Ceftiofur
- Enrofloxacin
- Florfenicol
- Gentamicin
- Neomycin
- Sulfonamides
- Tetracyclines

PASTEURELLA MULTOCIDA

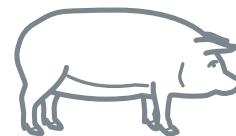
Image credit: Dr. Karen Olsen University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

The family *Pasteurellaceae* (including *Pasteurella*, *Hemophilus* and *Actinobacillus* genera) are the predominant organisms colonizing the palatine tonsil of the pig. All three genera are diverse and include commensal and pathogenic variants. *P. multocida* is a gram-negative rod or coccobacillus which causes diverse clinical manifestations in many domesticated and wild animal species. *P. multocida* is also zoonotic, and is among the most common organisms causing infections from animal bites. Toxigenic variants of *P. multocida* type D have historic importance in pigs as the agent of progressive atrophic rhinitis. This disease has declined in importance in the United States due to the availability of vaccines and improved systems of herd health management. However, *P. multocida* remains an important respiratory pathogen in swine, mostly in association with other respiratory pathogens as part of the porcine respiratory disease complex (PRDC). Isolates from pneumonia lesions are predominantly non-toxigenic type A. Efforts to reproduce disease with *P. multocida* alone are often unsuccessful, indicating the organisms mostly act as secondary pathogens. However, some more virulent variants can be primary causes of pneumonia and pleuritis, notably in Brazil. The pathogenesis of *Pasteurella* infections generally, including in pigs, remains poorly understood.

What you need to know

- *P. multocida* should be expected to occur as a secondary pathogen causing pneumonia during any outbreak of respiratory disease in swine.
- Rapid implementation of appropriate and effective antimicrobial protocols is essential to maintain animal health and welfare in the face of outbreaks or in high-risk groups.
- In weaned pigs known to be infected with PRRS or influenza viruses that predispose to outbreaks, preventive antimicrobial use may be necessary to reduce mortality due to secondary infections such as *P. multocida*.

SPECIES:



PREVENTION ACTIONS:

- *P. multocida* is an opportunistic pathogen that is part of the normal flora of the upper respiratory tract of pigs. Vaccination has been an effective aid in controlling atrophic rhinitis, but not pneumonia in pigs.
- The key to prevention is therefore prevention of prevalent primary respiratory pathogens of pigs, particularly PRRS, influenza and *Mycoplasma hyopneumoniae*.
- Following the core principles of swine health management is also important, including: not mixing pigs from different sources, adopting all-in/all-out management whenever practical, maintaining good hygiene, and minimizing environmental stresses due to temperature fluctuations and poor ventilation.

RESISTANCE PROFILE:

Resistance to these antimicrobials has been reported:

- Tetracyclines
- Enrofloxacin
- Tiamulin

SALMONELLA SPP

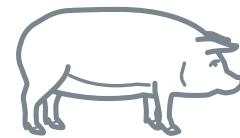
Salmonella enterica serotype Choleraesuis, *Salmonella enterica* serotype Typhimurium, including monophasic variant 4,[5],12:i:-.

Key features of antimicrobial resistance of *Salmonella* in swine and other species are that multiple drug resistance (MDR) is common and that resistance patterns are very often linked to specific serotypes and geographical regions. Overall shifts in observed resistance patterns can therefore be driven by changes in the relative prevalence of specific serotypes (or lineages within serotypes) more so than by patterns of antimicrobial use. Prominent examples include the ACSSuT (Ampicillin – Chloramphenicol – Streptomycin – Sulfonamide – Tetracycline) pattern in *S. Typhimurium* DT104 (and other variants) during the 1990s, and more recently the ASSuT genotype of a monophasic variant 4,[5],12:i:- which appears to be of European origin.

What you need to know

- *Salmonella* are widespread in the environment and in wild and domestic animal populations.
- Multiple serotypes often are present simultaneously in the same herd and within the individual animals.
- Resistance patterns are often serotype related. Antimicrobial susceptibility testing should be performed on isolates from confirmed clinical cases, rather than from pen fecal samples.

SPECIES:



PREVENTION ACTIONS:

- Rodent control.
- Heat treatment of feed to minimize *Salmonella* contamination.
- New approaches in vaccinology, such as vaccines against iron capturing proteins (siderophores) are in development and have some promise for providing broader protection.

RESISTANCE PROFILE:

- Tetracyclines (Chlortetracycline, Oxytetracycline)
- Aminoglycosides (Neomycin, Gentamicin)
- Sulfonamides
- Beta Lactams (Ampicillin)
- Macrolides (Tilmicosin)
- Phenicol (Florfenicol)
- Pleuromutilins (Tiamulin)
- Cephalosporins
- Fluoroquinolones – Quinolone resistance is not of direct concern to swine health, as no fluoroquinolone antimicrobials are approved for treating salmonellosis, and extralabel drug use of this class is illegal. It is included only due to potential concern with respect to human health with emergence of fluoroquinolone resistance, particularly the plasmid mediated *qnr* genes.

STREPTOCOCCUS SUIIS

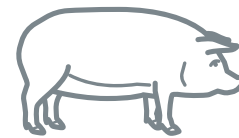
Image credit: University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

Streptococcus suis, a gram-positive coccus, is a component of the normal flora of the oropharynx and nasal cavities of pigs, and is ubiquitous in swine populations. It is also an important opportunistic pathogen of pigs, and a rare (although sometimes severe) zoonotic pathogen. The 29 verified serotypes of *S. suis* are diverse genetically and in pathogenicity. The relative prevalence of different serotypes varies geographically and over time. Although several serotypes of *S. suis* have been isolated from human clinical cases, the majority have been serotype 2. Serotype 2 is among the more common serotypes causing clinical disease in pigs in many countries, but is relatively less common in the United States. Other prevalent serotypes causing clinical disease in swine are serotypes 1, 1/2 (particularly in the United States), 7 and 9. *Streptococcus suis* is also a rare but severe zoonotic pathogen, and occupational.

What you need to know

- *S. suis* is a significant opportunistic pathogen of pigs, particularly after weaning.
- Rapid implementation of appropriate and effective antimicrobial protocols is essential to maintain animal health and welfare in the face of outbreaks or in high-risk groups.
- In weaned pigs known to be infected with PRRS or influenza viruses that predispose to outbreaks, preventive antimicrobial use may be necessary to reduce mortalities from secondary infections such as *S. suis*.

SPECIES:



PREVENTION ACTIONS:

- Elimination of the pathogen is unrealistic as it is normal flora that is acquired early in life, and cross immunity among strains appears to be minimal.
- Following the core principles of swine health management is also important, including: not mixing pigs from different sources, adopting all-in/all-out management whenever practical, maintaining good hygiene, and minimizing environmental stresses due to temperature fluctuations and poor ventilation.

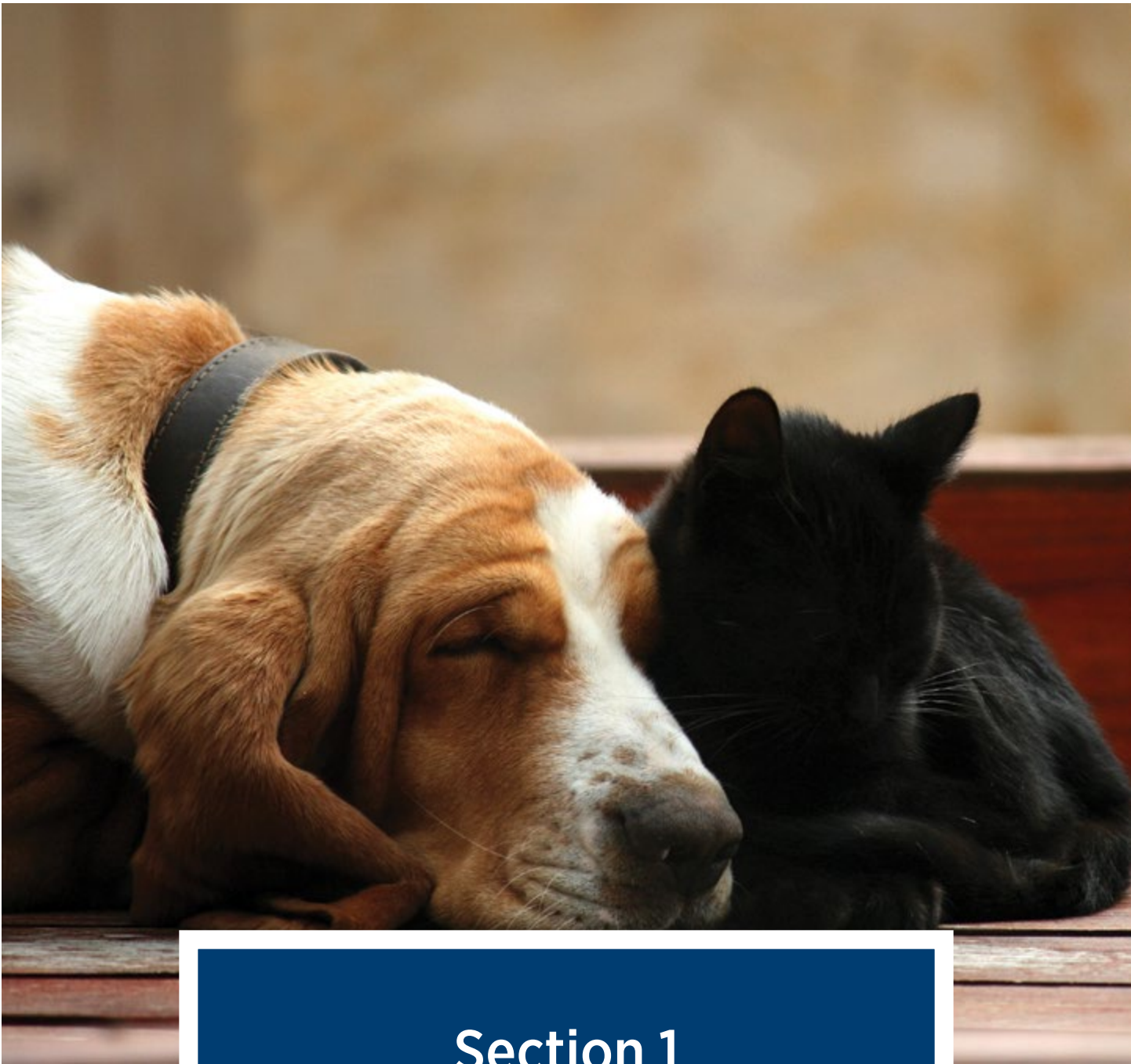
RESISTANCE PROFILE:

- Beta lactams
- Ceftiofur
- Enrofloxacin



AVMA/Committee on Antimicrobials
Antimicrobial resistant pathogens
affecting animal health in the
United States

TECHNICAL APPENDIX



Section 1
DOGS & CATS



1.1 CAMPYLOBACTER JEJUNI

- d. **Transmissibility:** *C. jejuni* can be spread through infected stool, particularly in situations of high animal density (e.g., kennels, pet stores, breeding facilities) and in young animals whose immune systems are not fully developed, are often housed in groups, and who are not yet trained to defecate outdoors. *C. jejuni* can also be spread through ingestion of contaminated raw food, such as chicken, turkey, or unpasteurized dairy products and through cross-contamination of feeding bowls, utensils, and eating areas.
- e. **Availability of effective antimicrobials:** *C. jejuni* has intrinsic resistance to several antimicrobial drugs including bacitracin, novobiocin, rifampin, streptogramin B, trimethoprim, and vancomycin. Further, the lack of susceptibility testing standards for *Campylobacter* is a barrier to understanding acquired resistance patterns.
- f. **Barriers to prevention:** *Campylobacter* can be shed, sometimes commonly, in the feces of healthy animals. There is not an easy or rapid test available to know whether an animal is infected with *C. jejuni*, and currently there are no susceptibility testing standards for *Campylobacter* in dogs and cats.

KEY DATA POINTS

- a. **Clinical impact:** While most infections may be subclinical or mild and self-limiting, pets with *Campylobacter jejuni* infections may develop fever, abdominal pain, diarrhea, and vomiting. At this time, it is unknown whether resistant strains cause more serious problems than susceptible strains.
- b. **Economic impact:** This is unknown.
- c. **Prevalence:** The true prevalence in the animal population is not known. The data available were collected from laboratories, and consequently only represent laboratory submitted samples and are not representative of the general population. In many cases the only reason that the sample was submitted to the laboratory is because the patient did not respond to the first-choice antimicrobial agent. As a result, these data may indicate a higher prevalence of resistance than that observed in the general population. In a United States study, 5% of *Campylobacter* infections were attributed to puppy contact.

IMPACT ON ANIMAL HEALTH:

This is an area that is currently being explored and quantified. The 2016 – 2018 outbreak of *Campylobacter* in puppies being transmitted to people demonstrated how the movement and commingling of dogs across the country coupled with the use of antimicrobials by breeders and pet stores may be contributing to the spread of resistant strains.

CURRENT ACTIONS:

The American Animal Hospital Association (AAHA) and the Ontario Animal Health Network (OAHN) have developed guidelines to control the spread of disease within hospital environments.

RESOURCES:

1. Campagnolo ER, Philipp LM, Long JM, Hanshaw NL. (2018). Pet-associated campylobacteriosis: a persisting public health concern. *Zoonoses Public Health*, 65:304–11. <https://onlinelibrary.wiley.com/doi/full/10.1111/zph.12389>
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3. Damborg, P., Broens, E., Chomel, B., Guenther, S., Pasmans, F., & Wagenaar, J. et al. (2016). Bacterial Zoonoses Transmitted by Household Pets: State-of-the-Art and Future Perspectives for Targeted Research and Policy Actions. *Journal Of Comparative Pathology*, 155(1), S27-S40. doi: 10.1016/j.jcpa.2015.03.004 <https://www.sciencedirect.com/science/article/pii/S0021997515000523?via%3Dihub>
4. Friedman, C. R., Hoekstra, R. M., Samuel, M., Marcus, R., Bender, J., Shiferaw, B., Reddy, S., Desai Ahuja, S., Helfrick, D. L., Hardnett, F., Carter, M., Anderson, B., & Tauxe, R. V. (2004). Risk Factors for Sporadic *Campylobacter* Infection in the United States: A Case-Control Study in FoodNet Sites. *Clinical Infectious Diseases*, 38(s3), S285–S296. <https://doi.org/10.1086/381598>
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7. Pet Industry Joint Advisory Council. (2019). For pet stores and breeders: Pet Industry Joint Advisory Council - Recommendations for Antibiotic Stewardship in Companion Animals. https://pijac.org/sites/default/files/pdfs/PIJACAntibioticStewardship_March2019.pdf
8. Williams, C., Scheftel, J., Elchos, B., Hopkins, S., & Levine, J. (2015). Compendium of Veterinary Standard Precautions for Zoonotic Disease Prevention in Veterinary Personnel: National Association of State Public Health Veterinarians: Veterinary Infection Control Committee 2015. *Journal Of The American Veterinary Medical Association*, 247(11), 1252–1277. doi: 10.2460/javma.247.11.1252 <http://www.nasphv.org/Documents/VeterinaryStandardPrecautions.pdf>



1.2 ENTEROBACTERIALES

Enterobacteriaceae (*Escherichia coli*, *Proteus* spp., *Klebsiella* spp.) and *Acinetobacter* spp.

KEY DATA POINTS:

- a. **Clinical impact:** The clinical outcomes in animals infected with resistant strains of Enterobacteriaceae are the same as outcomes from infections with susceptible strains. All infections, both resistant and susceptible, when left untreated can cause long-term illness, acute sepsis, and other problems. On the other hand, if the infection is managed properly, which may include appropriate antimicrobial agents, these infections can be resolved. Underlying factors predisposing the animal to acquiring the infection still need to be addressed, regardless of what strain of bacteria caused the infection.
- b. **Economic impact:** Unknown. These infections can be successfully treated if the appropriate antimicrobial is selected. Some of the drugs may be more expensive than other common veterinary drugs. Disinfecting and cleaning patient treatment areas and exam rooms in response to healthcare-associated multidrug resistant bacterial infections can add to expenses and disrupt services.
- c. **Prevalence:** The true prevalence in the animal population is not known. However, studies suggest that the prevalence has risen in the last decade. The data available were collected from laboratories, and consequently only represent the laboratory-submitted samples, and are not representative of the general population. In many cases the only reason that the sample was submitted to the laboratory is because the patient did not respond to the first-choice antimicrobial agent. As a result, these data may indicate a higher prevalence of resistance than that in the general population.
- d. **Transmissibility:** Transmission within a household is possible, for example pet-to-pet, people-to-pets, and pets-to-people. Transmission from pets to the environment is possible (for example, in public parks), and pets can be exposed through their diet, for example through raw foods. The significance of these routes of transmission has been insufficiently studied and documented in veterinary medicine.
- e. **Availability of effective antimicrobials:** There are no FDA-approved drugs indicated to treat extended-spectrum beta-lactamases ESBL-producing strains in animals. Some antimicrobial agents approved for animals may be active against ESBL strains; however, this must be confirmed through susceptibility testing. Most (almost all) pathogens in this class are fluoroquinolone resistant. If the strains are fluoroquinolone resistant, there are no oral agents that are consistently effective. Veterinarians may use antimicrobials extra-labelly for these infections based on susceptibility testing, and most of these options are human-label formulations. In these cases, the only agents active will be injectable antimicrobials, which depending on the susceptibility testing, may include amikacin, 3rd-generation cephalosporins (ceftazidime), or carbapenems (usually meropenem). For urinary tract infections, nitrofurantoin might be a suitable choice, but its use is discouraged in patients with chronic kidney disease. In addition, it is uncertain how long it will stay at effective concentrations in veterinary patients.
- f. **Barriers to prevention:** Antimicrobial resistant gram-negative bacterial infections can be difficult to prevent since the source of these infections is not always clear. Antimicrobial use may be a contributing factor in small animals, but no specific drug class has been identified. Therefore, eliminating or restricting certain drug classes is unlikely to prevent the problem.

IMPACT ON ANIMAL HEALTH:

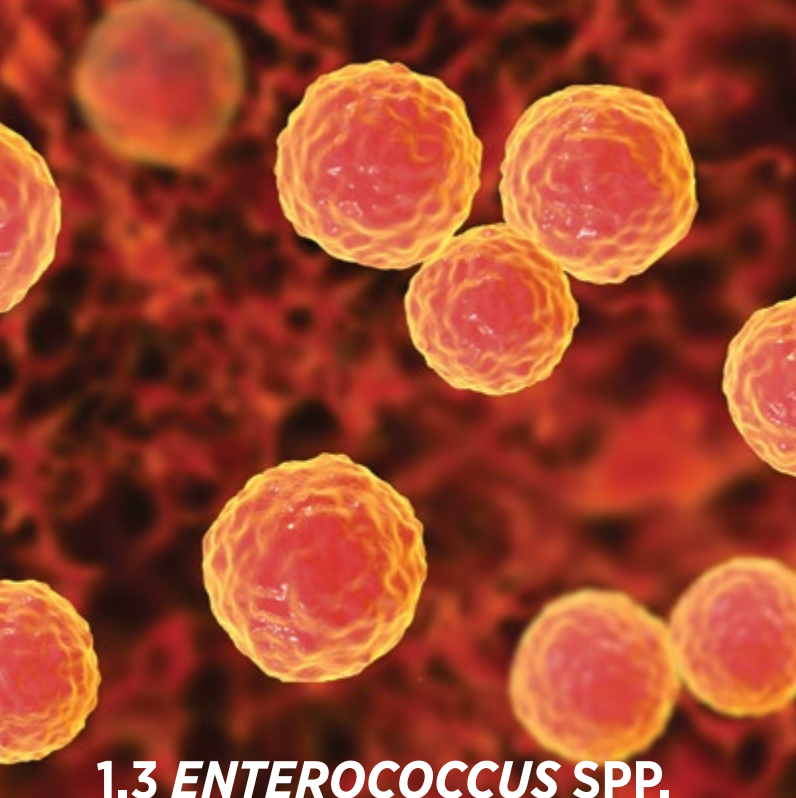
The clinical outcomes in animals infected by antimicrobial-resistant strains of Enterobacteriaceae are the same as those caused by infections from susceptible strains. When left untreated, both resistant and susceptible infections can cause long-term illness, acute sepsis, and other problems. On the other hand, if these infections are managed effectively, which may include appropriate antimicrobials, these infections can be resolved. Underlying factors predisposing the animal to acquiring a clinical infection still need to be addressed, regardless of what strain of bacteria caused the infection. Care should be taken to prevent hospital-acquired infections and to protect patients with weakened immune systems, both due to disease or immunosuppressive medications. There are no current measures in place to combat the threat from drug-resistant strains of these bacteria. There are no national surveillance programs that monitor trends of Enterobacteriaceae and Acinetobacter spp. infection prevalence or incidence. There are no new antimicrobials in development for veterinary medicine to address this threat. There is very little funding available to initiate studies to examine this problem in more depth.

CURRENT ACTIONS:

- The International Society for Companion Animal Infectious Diseases (ISCAID) has developed clinical guidelines to highlight diagnostic and treatment choices for bacterial infections of the skin, respiratory tract and urine, some which are due to Enterobacteriaceae and Acinetobacter spp.
- The American Animal Hospital Association (AAHA) and the Ontario Animal Health Network (OAHN) have developed guidelines to control the spread of disease within hospital environments.

RESOURCES:

1. Cummings, K. J., Aprea, V. A., & Altier, C. (2015). Antimicrobial resistance trends among canine Escherichia coli isolates obtained from clinical samples in the northeastern USA, 2004-2011. *The Canadian veterinary journal = La revue veterinaire canadienne*, 56(4), 393-398. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357913/>
2. Damborg, P., Broens, E., Chomel, B., Guenther, S., Pasmans, F., & Wagenaar, J. et al. (2016). Bacterial Zoonoses Transmitted by Household Pets: State-of-the-Art and Future Perspectives for Targeted Research and Policy Actions. *Journal Of Comparative Pathology*, 155(1), S27-S40. doi: 10.1016/j.jcpa.2015.03.004 <https://www.sciencedirect.com/science/article/pii/S0021997515000523?via%3Dihub>
3. Hillier A., Lloyd D.H., Weese J.S. et al. (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*, 25:163-e43. doi: 10.1111/vde.12118. <https://onlinelibrary.wiley.com/doi/full/10.1111/vde.12118>
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6. Weese, J., Blondeau, J., Boothe, D., Guardabassi, L., Gumley, N., & Papich, M. et al. (2019). International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *The Veterinary Journal*, 247, 8-25. doi: 10.1016/j.tvjl.2019.02.008 <https://www.sciencedirect.com/science/article/pii/S109002331830460X?via%3Dihub>
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1.3 ENTEROCOCCUS SPP.

e. **Availability of effective antimicrobials:** *Enterococcus* spp. are intrinsically resistant to cephalosporins, fluoroquinolones, trimethoprim-sulfonamides, clindamycin, and macrolides (erythromycin or tylosin). In addition, isolates that are resistant to penicillin will be resistant to most antimicrobial drugs included on routine culture and susceptibility test reports. The choice of antimicrobial agent should be made based on culture and susceptibility test reports.

f. **Barriers to prevention:** *Enterococcus* spp. infections can be difficult to prevent due to their environmental persistence and their intrinsic antimicrobial resistance to multiple drug classes. In some cases, these bacteria may not be associated with clinical illness, which means infection control and biosecurity measures (e.g., hand hygiene, cleaning, and disinfection) need to be in place regardless of patient clinical signs.

KEY DATA POINTS

- a. **Clinical impact:** The most notable impact is opportunistic healthcare-acquired infections potentially leading to bacteremia or urinary tract infections.
- b. **Economic impact:** This is unknown. A culture and susceptibility test must be performed to confirm susceptibility, which adds extra expense for the pet owner.
- c. **Prevalence:** The true prevalence in the animal population is not known. The data available were collected from laboratories, and consequently only represent laboratory submitted samples and are not representative of the general population. In many cases the only reason that the sample was submitted to the laboratory is because the patient did not respond to the first-choice antimicrobial agent. As a result, these data may indicate a higher prevalence of resistance than that in the general population.
- d. **Transmissibility:** *Enterococcus* spp. are most commonly spread by contact with contaminated surfaces or human hands. Additionally, prior antimicrobial use is a risk factor for infection.

IMPACT ON ANIMAL HEALTH:

The real impact of drug-resistant *Enterococcus* spp. on animal health remains unknown. These bacteria are often not as pathogenic as other bacteria such as those within the *Enterobacteriaceae*. Antimicrobial-resistant *Enterococcus* can be found in urine in the absence of clinical signs, and the impact on animal health in these cases can be considered low. Likewise, *Enterococcus* can be cultured from wound infections, lungs, and other sites, and the impact is not known. There are no current measures in place to combat the threat from antimicrobial-resistant strains of enterococci and no national surveillance programs to monitor their frequency or trends. Even if an infection caused by drug-resistant *Enterococcus* requires treatment, there are no new antimicrobial agents in the pipeline for veterinary medicine to deal with this threat.

CURRENT ACTIONS:

- The International Society for Companion Animal Infectious Diseases (ISCAID) has developed clinical guidelines to highlight diagnostic and treatment choices for bacterial infections of the skin, respiratory tract and urine, some which are due to *Enterococcus* spp.
- The Ontario Animal Health Network and the American Animal Hospital Association (AAHA) have developed guidelines to control the spread of disease within hospital environments.

RESOURCES:

1. Hillier A., Lloyd D.H., Weese J.S. et al. (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*, 25:163-e43. doi: 10.1111/vde.12118. <https://onlinelibrary.wiley.com/doi/full/10.1111/vde.12118>
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4. Weese, J., Blondeau, J., Boothe, D., Guardabassi, L., Gumley, N., & Papich, M. et al. (2019). International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *The Veterinary Journal*, 247, 8-25. doi: 10.1016/j.tvjl.2019.02.008 <https://www.sciencedirect.com/science/article/pii/S109002331830460X?via%3Dihub>
5. Williams, C., Scheftel, J., Elchos, B., Hopkins, S., & Levine, J. (2015). Compendium of Veterinary Standard Precautions for Zoonotic Disease Prevention in Veterinary Personnel: National Association of State Public Health Veterinarians: Veterinary Infection Control Committee 2015. *Journal Of The American Veterinary Medical Association*, 247(11), 1252-1277. doi: 10.2460/javma.247.11.1252 <http://www.nasphv.org/Documents/VeterinaryStandardPrecautions.pdf>



1.4 PSEUDOMONAS AERUGINOSA

KEY DATA POINTS

- a. **Clinical impact:** The clinical impact is small compared to drug-resistant staphylococci and *Enterobacteriaceae* because of the relatively low prevalence of infection. Drug-resistant *Pseudomonas aeruginosa* is not cultured frequently, except in dermatology cases (mostly from otitis), and occasionally from wound infections, cats with chronic upper respiratory tract infections, and (sometimes) burn wounds. When infections occur that need treatment, a culture and susceptibility test are required. Infections can sometimes be resolved with topical treatment, particularly in the case of ear infections. For systemic infections, treatment may consist of injection of antimicrobial agents based on susceptibility testing.
- b. **Economic impact:** This is unknown. Culture and susceptibility tests add extra expenses for the pet owner. When systemic treatment is indicated, frequent injections may be required, adding to time and cost burden.
- c. **Prevalence:** The true prevalence in the animal population is not known. The data available were collected from laboratories, and consequently only represent laboratory submitted samples and are not representative of the general population. In many cases the only reason that the sample was submitted to the laboratory is because the

patient did not respond to the first-choice antimicrobial agent. As a result, these data may indicate a higher prevalence of resistance than that found in the general population.

- d. **Transmissibility:** *Pseudomonas* is ubiquitous in the environment; therefore, open any wound can become infected. Infections can also be healthcare-acquired through a contaminated environment or fomites. Transmission between animals is not known to be a significant source of infection. There is no evidence that *Pseudomonas* transmits from animals to people.
- e. **Availability of effective antimicrobials:** *Pseudomonas aeruginosa* is intrinsically resistant to many common antimicrobials including most penicillins, most cephalosporins, tetracyclines, trimethoprim-sulfonamides and chloramphenicol. FDA-approved antimicrobials for companion animals, including fluoroquinolones, are not active against resistant strains of *Pseudomonas*. Resistant infections requiring treatment are treated with available topical agents (e.g., ear infections), but if treatment requires systemic therapy, the choices come from this list of human-labeled drugs: amikacin, ceftazidime (anti-pseudomonal cephalosporin), piperacillin-tazobactam, or a carbapenem (usually meropenem). All these agents must be given by injection and should be chosen based on culture and susceptibility test results.
- f. **Barriers to prevention:** Because many of the infections are in the ear, the best prevention is management of the underlying problems (i.e., allergic dermatitis/otitis). *Pseudomonas* is ubiquitous in the environment, and it is difficult to prevent in animals if the environment is optimal for *Pseudomonas* growth. This organism can be found in the hospital environment (e.g., disinfectant washes, soap trays, scrubbing solutions, and other moist environments and biofilms). Therefore, steps to minimize exposure from these sources should be considered if a hospital has a persistent problem.

IMPACT ON ANIMAL HEALTH:

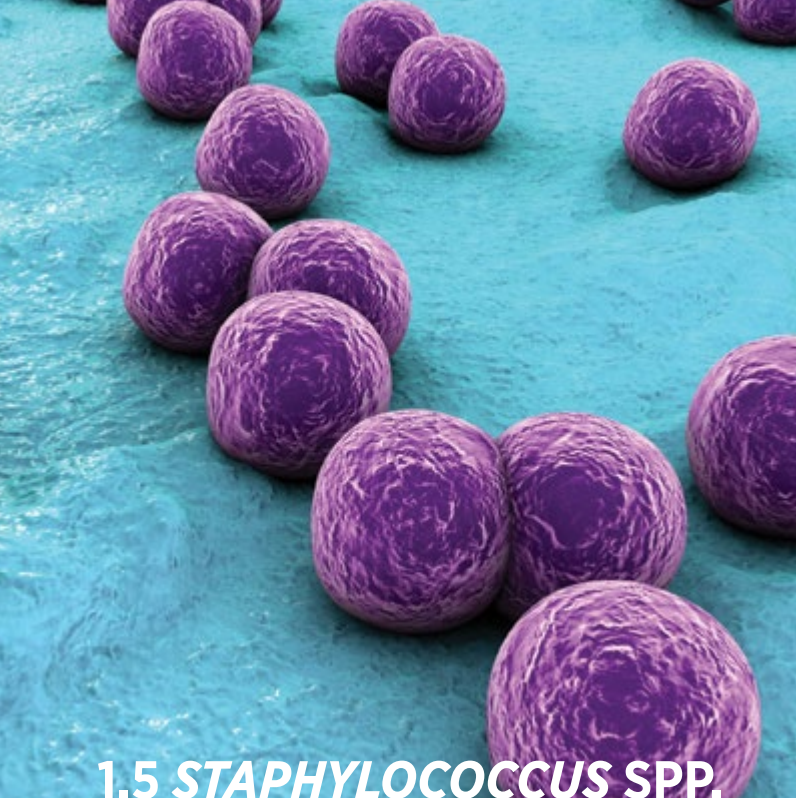
When these antimicrobial drug-resistant *Pseudomonas* infections occur and treatment is indicated, they may require injectable antimicrobials, such as ceftazidime, meropenem, piperacillin-tazobactam, and amikacin (amikacin should be used in combination). These agents can be difficult for some pet owners to administer. If the infection is not treated with the appropriate antimicrobials, it can become chronic, and more difficult to resolve.

CURRENT ACTIONS:

- The International Society for Companion Animal Infectious Diseases (ISCAID) has developed clinical guidelines to highlight diagnostic and treatment choices for bacterial infections of the skin and respiratory tract, some which are due to *Pseudomonas* spp.
- The American Animal Hospital Association (AAHA) and the Ontario Animal Health Network (OAHN) have developed guidelines to control the spread of disease within hospital environments.

RESOURCES:

1. Hillier A., Lloyd D.H., Weese J.S. et al. (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*, 25:163-e43. doi: 10.1111/vde.12118. <https://onlinelibrary.wiley.com/doi/full/10.1111/vde.12118>
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3. Weese, J., Blondeau, J., Boothe, D., Guardabassi, L., Gumley, N., & Papich, M. et al. (2019). International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *The Veterinary Journal*, 247, 8-25. doi: 10.1016/j.tvjl.2019.02.008 <https://www.sciencedirect.com/science/article/pii/S109002331830460X?via%3Dihub>
4. Williams, C., Scheftel, J., Elchos, B., Hopkins, S., & Levine, J. (2015). Compendium of Veterinary Standard Precautions for Zoonotic Disease Prevention in Veterinary Personnel: National Association of State Public Health Veterinarians: Veterinary Infection Control Committee 2015. *Journal of The American Veterinary Medical Association*, 247(11), 1252-1277. doi: 10.2460/javma.247.11.1252 <http://www.nasphv.org/Documents/VeterinaryStandardPrecautions.pdf>



KEY DATA POINTS

- a. **Clinical impact:** Resistant staphylococci are no more virulent than their susceptible counterparts; however, they can be difficult to treat. When methicillin-resistant strains are recognized, few FDA-approved antimicrobials are available for treatment. If topical agents are not feasible, systemic agents active against methicillin-resistant *S. pseudintermedius* (MRSP) usually come from this list: chloramphenicol, rifampin, nitrofurantoin (cystitis only), and sometimes doxycycline or minocycline. These agents are listed as 2nd- or 3rd-tier by the International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for treating superficial bacterial folliculitis in dogs. A culture and susceptibility test must be performed to confirm susceptibility to these, or another agent. Some treatments require monitoring of liver enzymes, kidney parameters, or a complete blood count for proper treatment monitoring, which adds further expense.
- b. **Economic impact:** The economic impact of treating MRSP is currently unknown. These infections can usually be successfully treated if the appropriate antimicrobial is identified and used. Culturing and susceptibility testing incur additional costs to the pet owner. Some effective antimicrobial agents may be more expensive than other common veterinary agents and may require monitoring, adding to the cost of care.

- c. **Prevalence:** The true prevalence in the animal population is not known. The data available were collected from laboratories, and consequently only represent the laboratory-submitted samples and are not representative of the general population. In many cases the only reason that the sample was submitted to the laboratory is because the patient did not respond to the first-choice antimicrobial agent. As a result, these data may indicate a higher prevalence of resistance than that observed in the general population.
- d. **Transmissibility:** Transmission may occur directly from dog to dog, or indirectly by people transferring the infection from dog to dog (e.g., by hand exposure in a hospital). This organism is carried on the dog's skin, nose, and perineum; therefore, licking (one dog to another) is a potential route of transmission. There is little evidence that transmission of MRSP from animals to people causes clinical infection in people except for isolated case reports.
- e. **Availability of effective antimicrobials:** Treatment options are available. In some cases, topical treatments can be effective. When systemic antimicrobial agents are indicated, there are agents available for treatment (oral tablets, capsules, or injectable agents). These include human-labeled drugs that are not approved for use in animals but can still be used legally according to the AMDUCA extralabel drug use legislation.
- f. **Barriers to prevention:** Infection control policies in hospitals can be effective preventive methods. Infection control measures can include identification and isolation of patients with drug-resistant infections, simple hygiene measures (hand washing or use of hand disinfectant stations, etc.), and limiting the exposure to other animals in the hospital. Adherence to these policies can be a barrier to prevention when not implemented or if compliance is lacking.

IMPACT ON ANIMAL HEALTH:

The best way to prevent MRSP infections is patient management to reduce *Staphylococcus* infection. Since most cases of *Staphylococcus* infection in dogs result from an underlying problem (e.g., skin parasites or atopic/allergic dermatitis), diagnosing and treating the underlying condition(s) is vital to ensure resolution of infection. In addition, promoting infection control, biosecurity and hygiene both in homes and in veterinary hospitals can help prevent direct or indirect (e.g., clippers) transmission.

CURRENT ACTIONS:


- The International Society for Companion Animal Infectious Diseases (ISCAID) has developed clinical guidelines to highlight diagnostic and treatment choices for bacterial infections of the skin, respiratory tract and urine, some which are due to *Staphylococcus* spp.
- The American Animal Hospital Association (AAHA) and the Ontario Animal Health Network (OAHN) have developed guidelines to control the spread of disease within hospital environments.

RESOURCES:

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Section 2
CATTLE

A close-up photograph of a petri dish containing a red agar medium. Several white, circular bacterial colonies of varying sizes are visible, some appearing as distinct points and others as larger, more confluent patches.

2.1 MANNHEIMIA HAEMOLYTICA, PASTEURELLA MULTOCIDA, HISTOPHILUS SOMNI

Image Credit: Dr Karen Olsen University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

KEY DATA POINTS

- a. **Clinical impact:** Bovine Respiratory Disease (BRD) is the most important disease of beef cattle and affects multiple industry segments including cow/calf, stocker, and feedlot. BRD is the leading cause of death in beef calves three weeks of age and older. Morbidity is high in outbreaks, and mortality can be high if treatment is not rapid or the result of a treatment failure. BRD is the leading cause of death in weaned dairy calves and the second most common cause of death in preweaned dairy calves. These pathogens cause severe, fibrinous bronchopneumonia in affected cattle. Clinical and physical examination findings of depression, inappetence, increased respiratory rate and effort, and fever can rapidly progress to recumbency and death if not treated with effective antimicrobial therapy early in the disease course. While infection with *M. haemolytica*, *P. multocida*, and/or *H. somni* lead to the pathology characteristic of BRD, other factors related to host immunity and herd management also contribute to susceptibility.
- b. **Economic impact:** The economic impact of BRD is considerable given the costs incurred from mortality, prevention, control, and treatment strategies and production losses. A large-scale analysis of feedlot data determined that the net return for an animal treated one time for BRD was \$13 less than an animal that was never diagnosed with BRD. Animals treated three or more times for BRD returned approximately \$75 per head less than animals not affected by BRD. Estimated losses for the entire U.S. cattle industry are upward of \$4 billion annually.
- c. **Prevalence:** According to the USDA NAHMS, respiratory disease impacts approximately 20%, 16%, and 3.8% of preweaned dairy heifers, feedlot cattle and unweaned beef calves, respectively, annually in the United States. One multi-year observational study reported annual BRD morbidity ranging from 5 to 44%. Mortality rates from BRD also vary considerably by production class but estimates range from 1 to 5% of the at-risk population. Surveys of fatal feedlot BRD cases have identified *M. haemolytica*, *P. multocida*, and *H. somni* in 10%-27% of cases sampled. When live cattle with clinical signs of BRD were tested by respiratory sampling before antimicrobial treatment, *M. haemolytica* was identified in 12% - 31% of cattle, *P. multocida* in 55% - 68%, and *H. somni* in 12% - 25% (Allen et al., 1991; Timsit et al., 2017). In surveys of dairy calves with clinical signs of BRD, rates of identification from respiratory samples obtained from live calves before antimicrobial treatment were 16% for *M. haemolytica*, 53% - 59% for *P. multocida*, and 0% - 13% for *H. somni*.
- d. **Transmissibility:** *M. haemolytica*, *P. multocida*, and *H. somni* are members of the normal flora of the upper respiratory tract, and it is believed that many BRD cases result from opportunistic infection of the lung by endogenous normal flora. However, a modified live, genetically modified *M. haemolytica* given by intranasal administration to cattle was shown to transmit to in-contact non-vaccinated cattle, indicating that *M. haemolytica* can be transmitted horizontally among cattle. The degree to which horizontally transmitted *M. haemolytica*, *P. multocida*, or *H. somni* contribute to BRD, relative to that induced by endogenous bacteria, has not been assessed.
- e. **Availability of effective antimicrobials:** Multiple classes of antimicrobials are approved in the United States for the treatment or control of bovine respiratory disease associated with *M. haemolytica*, *P. multocida*, and *H. somni*. However, isolates of *M. haemolytica* have been found that possess an integrative-conjugative element (ICE) that carries up to 12 antimicrobial resistance genes. This same ICE has been shown to transfer to other BRD pathogens. Although multidrug resistance (MDR) encoded by ICE has been reported in *M. haemolytica*, *P. multocida*, and *H. somni*, the degree to which this MDR leads to treatment failure in cattle treated for BRD is not clear. To date very

little research has compared treatment response rates in cattle with MDR *M. haemolytica*, *P. multocida*, and/or *H. somni* to response rates in cattle with susceptible infections. In a report describing data from 16 clinical trials testing the efficacy of the antimicrobial tilmicosin for BRD therapy, the difference in response rate for cattle that had a resistant isolate of *M. haemolytica* or *P. multocida* identified by deep nasal swab prior to treatment was not statistically significantly different than response rates for cattle with susceptible isolates (McClary et al., 2011). However, the prevalence of tilmicosin resistance in the sampled cattle was quite low (0.8% for *M. haemolytica* and 6.9% for *P. multocida*). Some veterinarians and producers have expressed concerns about poor treatment response rates in groups of cattle from which MDR *M. haemolytica* or *P. multocida* have been isolated; however, in such cases, cattle have usually been sampled only after treatment with one or more antimicrobials, making it difficult to differentiate whether MDR is a cause of or a result of treatment failure. Research comparing treatment response rates in cattle with MDR infections before treatment to those in cattle with susceptible infections is needed to provide evidence-based recommendations regarding the impact of AMR on BRD treatment response rates.

f. **Barriers to prevention:** Bovine respiratory disease (BRD) has a multifactorial etiology and develops as a result of complex interactions between environmental factors, host factors, and pathogens. Environmental factors (e.g., weaning, transport, commingling, crowding, inclement weather, dust, and inadequate ventilation) serve as stressors that adversely affect the immune and nonimmune defense mechanisms of the host. In addition, certain environmental factors (e.g., crowding and inadequate ventilation) can enhance the transmission of infectious agents among animals. Nutritional status can also affect host susceptibility. Many infectious agents have been associated with BRD. Viral pathogens may alter the animal's defense mechanisms, allowing colonization of the lower respiratory tract by bacteria. (Merck Veterinary Manual, BRD Complex) Thus, the main barrier to preventing the spread of the impact of these organisms is the system of cattle marketing in the United States, in which a relatively large proportion of cattle from multiple sources are commingled and transported at times when they are most immunologically susceptible to infection with respiratory pathogens. The current marketing system does not provide adequate financial incentives for cattle producers to undertake time consuming and relatively costly practices that have been shown to decrease rates of BRD in cattle by modifying environmental factors such as vaccination timing and weaning well in advance of shipment.

RESOURCES:

1. Cernicchiaro N, White BJ, Renter DG, Babcock AH. 2013. Evaluation of economic and performance outcomes associated with the number of treatments after an initial diagnosis of bovine respiratory disease in commercial feeder cattle. *AJVR*, 74.
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3. Kelly AP, Janzen ED. 1986. A review of morbidity and mortality rates and disease occurrence in North American feedlot cattle. *Can Vet J*, 27.
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2.2 MORAXELLA BOVOCULI AND MORAXELLA BOVIS

Image Credit: Dr. Kristin Clothier UC Davis College of Veterinary Medicine

- d. **Transmissibility:** The pathogen is carried in the nasopharynx and ocular conjunctiva of healthy cattle where it is spread to susceptible animals through direct contact or through vectors such as face flies. Strain diversity is high with multiple serotypes and genotypes of both *M. bovis* and *M. bovoculi* having been characterized.
- e. **Availability of effective antimicrobials:** Tetracyclines (oxytetracycline) and macrolides (tulathromycin) are the only two approved therapies for treatment of IBK caused by *M. bovis*. Other antimicrobials have shown varying degrees of clinical efficacy (florfenicol, for example) but lack label indications.
- f. **Barriers to prevention:** Prevention strategies include vaccination, fly control, and eye patches and coverings. However, affected animals are typically calves that are managed in remote pastures, therefore access to animals for prevention and treatment can be challenging. Existing vaccines (for either *M. bovis*, *M. bovoculi*, or both) have also demonstrated limited efficacy in numerous field trials and randomized clinical trials.

KEY DATA POINTS

- a. **Clinical impact:** Infectious bovine keratoconjunctivitis (IBK) also known as “pinkeye” is endemic in U.S. beef herds with extremely high morbidity. Estimated herd level prevalence is approximately 50% and within herd prevalence of 8-10%. IBK causes ocular pain, damages vision, and may cause corneal scarring. Clinical data on impacts in dairy cattle are not available, but IBK is a challenge in this market segment as well.
- b. **Economic impact:** Estimates of economic impact are in the \$100 plus million USD. Reduced weaning weights in affected animals are estimated to be 15.9 kg/head and adverse effects on carcass traits in affected animals have been reported.
- c. **Prevalence:** IBK has been identified as a significant problem in numerous beef herds with producers ranking it as the third highest animal health challenge in a recent survey, with 12.5% of producers indicating it was the most significant challenge (Martin, 2019). National Animal Health Monitoring System (USDA NAHMS) survey data indicates that pinkeye is the most frequently reported disease in breeding females and second most reported in calves greater than 3 weeks of age.

DATA VISUAL:

Strain Count	IBK Signs	Collection location	Identified after the discovery of genotype 2	Prevalence of full or partial antibiotic resistance element in genotype 1	Prevalence of repeats-in-toxin in genotype 1	Genotype
110	+	Nebraska, USA	No	7.27%	88.18%	1
73	+	21 other U.S. States	No	19.18%	79.45%	1
6	-	University of Nebraska	No	0.00%	33.33%	1
57	-	US Meat Animal Research Center	Yes	0%	58.06%	1 and 2

<https://doi.org/10.1371/journal.pone.0209113.t001>

This table from Dickey et al. (2018) highlights that almost 20% of *Moraxella bovoculi* strains isolated outside of Nebraska contained full or partial islands of antimicrobial resistance genes, containing up to ten co-located resistance genes and has been shown to confer resistance *in vitro* to nearly all antimicrobials used for IBK therapy.

IMPACT ON ANIMAL HEALTH:



Images courtesy of J. Dustin Loy

RESOURCES:

1. O'Connor AM, Brace S, Gould S, Dewell R, Engelken T. A randomized clinical trial evaluating a farm-of-origin autogenous *Moraxella bovis* vaccine to control infectious bovine keratoconjunctivitis (pinkeye) in beef cattle. *J Vet Intern Med.* 2011 Nov-Dec;25(6):1447-53. doi: 10.1111/j.1939-1676.2011.00803.x. Epub 2011 Oct 7.
2. O'Connor A, Cooper V, Censi L, Meyer E, Kneipp M, Dewell G. A 2-year randomized blinded controlled trial of a conditionally licensed *Moraxella bovoculi* vaccine to aid in prevention of infectious bovine keratoconjunctivitis in Angus beef calves. *Journal of Veterinary Medicine Internal Medicine* 12 October 2019 <https://doi.org/10.1111/jvim.15633>



Section 3
CHICKENS & TURKEYS



3.1 *ESCHERICHIA COLI* (BROILER CHICKENS)

KEY DATA POINTS

- a. **Clinical impact:** The severity of clinical signs, mortality and duration of the disease are variable and exacerbated by the primary pathogen and stressful husbandry practices including poor ventilation, improper environmental temperature and increased ammonia levels due to wet litter conditions.
- b. **Economic impact:** Colibacillosis is often considered the most common infectious bacterial disease of poultry. When considered in their entirety, *Escherichia coli* infections are responsible for significant economic losses in the poultry industry. Categories of economic losses include morbidity leading to decreased growth rate and feed conversion efficiency, increased mortality, increased condemnations (both whole bird and parts) at processing and cost of therapeutic antimicrobial treatments.
- c. **Prevalence:** *E. coli* is a ubiquitous opportunistic pathogen in broiler populations. There are no available data on the true disease incidence of *E. coli* infections in broilers. However, general polyserositis due to *E. coli* ranked seventh out of seventeen (7/17) of the disease-related issues that broiler production veterinarians faced in 2019, an increase in importance from 2018 when it was ranked twelfth out of seventeen (12/17) (2, 3).
- d. **Transmissibility:** *E. coli* infections of hatchery origin are easily transmitted between actively hatching/newly hatched chicks inside the hatching cabinet and may also be transmitted from infected to uninfected embryos via *in ovo* vaccination procedures. Increased measures to reduce contamination of hatching eggs with fecal matter, not incubating floor eggs, keeping hatching eggs dry and possible steps to sanitize hatching eggs properly will reduce incidence of *E. coli* omphalitis. After 7 days of age, transmission of *E. coli* infections occurs readily between broilers within a poultry house and occasionally to uninfected broilers located in adjacent poultry houses. Increased biosecurity measures to prevent introduction of primary respiratory pathogens such as infectious bronchitis virus, Newcastle virus or immune-depressive viruses like Marek's Disease virus, infectious bursal disease virus and infectious anemia virus and reductions of environmental stressors such as increased dust and ammonia levels from inadequate ventilation rates may reduce or limit transmission between houses and farms.
- e. **Availability of effective antimicrobials:** Gentamicin may be effectively used in the hatchery to prevent disease associated with *E. coli* omphalitis (yolk sac infection) and to decrease mortality in the first week of life. The label for injectable gentamicin sulfate for use in broiler chickens states that it is recommended for the prevention of early mortality in day-old chickens associated with *Escherichia coli*, *Salmonella* Typhimurium and *Pseudomonas aeruginosa* susceptible to gentamicin sulfate. In the broiler hatcheries, gentamicin is normally administered *in ovo*, which is an extra-label administration and with the recent emphasis on antimicrobial stewardship, most hatcheries have discontinued its use and have concentrated their efforts on good cleaning and disinfection. In broilers greater than 7 days of age, sulfonamides, tetracycline and streptomycin all are approximately 50% effective in therapeutically treating diseases associated with *E. coli* in broilers (4). Water-soluble antimicrobials are more commonly used for therapeutic purposes in broiler chickens because sick birds may stop eating but often continue to drink water (5). Further, therapeutic intervention through the water can often be accomplished more quickly than the feed.
- f. **Barriers to prevention:** The major barrier to prevention of secondary *E. coli* infections in broilers is the lack of efficacious vaccines, together with inadequate vaccinal control of the primary viral respiratory pathogen infectious bronchitis virus (IBV), and at times also Newcastle disease (NDV) or the immune-depressive diseases like Marek's Disease, infectious bursal disease, infectious anemia and hemorrhagic enteritis which predispose to *E. coli* infections. Elimination of the pathogen is unrealistic as it is part of the normal flora that is acquired early in life.

RESOURCES:

1. Nolan LK, Vaillancourt JP, Barbieri NL, Logue CM. Colibacillosis. In: Swayne DE, editor. *Diseases of Poultry*. 2020. 14th Edition, Wiley-Blackwell. p. 770-830.
2. Scott Gustin, DVM, (Personal communication), Presenter of AVBP Current Diseases of Concern at 123rd Annual Meeting of the United States Animal Health Association October 23 – 30, 2019 – Providence, RI
3. Burlison M. Broiler Industry Report. *Proceedings of the 122nd Annual Meeting of the United States Animal Health Association*. 2019;122:320-326. Accessed at: https://www.usaha.org/upload/Proceedings/2018_Proceedings_v2_Comb_FINAL.pdf
4. Roth, Nataliya et al. "The application of antibiotics in broiler production and the resulting antibiotic resistance in *Escherichia coli*: A global overview." *Poultry Science* vol. 98,4 (2019): 1791-1804. doi:10.3382/ps/pey539 Accessed here: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6414035/pdf/pey539.pdf>
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6. Merck Veterinary Manual accessed here: <https://www.merckvetmanual.com/poultry/colibacillosis/colibacillosis-in-poultry>



3.2 ESCHERICHIA COLI (LAYER CHICKENS)

KEY DATA POINTS

- a. **Clinical impact:** The severity of clinical signs, mortality and duration of the disease are variable and exacerbated by the primary pathogen and stressful husbandry practices including poor ventilation, improper environmental temperature and increased ammonia levels due to wet litter conditions.
- b. **Economic impact:** Colibacillosis is often considered the most common infectious bacterial disease of poultry. When considered in their entirety, *Escherichia coli* infections are responsible for significant economic losses in the poultry industry. The main economic loss of *E. coli* in layer production comes from mortality, especially early in lay and post peak. For a flock going to 100 weeks single cycle, a bird that dies at 30 weeks from peritonitis could lose over 400 eggs. At \$0.06 per egg, this is \$24 in revenue per bird. A flock of 100,000 birds with 4% mortality due to peritonitis could lose almost \$100,000 in potential revenue.
- c. **Prevalence:** *E. coli* is a ubiquitous pathogen that impacts almost every layer flock to varying degrees. The Association of Veterinarians in Egg Production (AVEP) ranked *E. coli* as the #1 concern in caged layers and #2 concern for cage free layers. (2)
- d. **Transmissibility:** *E. coli* infections of hatchery origin are easily transmitted between actively hatching/newly hatched chicks inside the hatching cabinet and may also be transmitted from infected to uninfected chicks via day old vaccination procedures. Increased measures to reduce contamination of hatching eggs with fecal matter, not incubating floor eggs, keeping hatching eggs dry and possible steps to sanitize hatching eggs properly will reduce incidence of *E. coli* omphalitis. After 7 days of age, transmission of *E. coli* infections occurs readily between pullets within a poultry house and occasionally to uninfected pullets located in adjacent poultry houses. Increased biosecurity measures to prevent introduction of primary respiratory pathogens such as infectious bronchitis virus, Newcastle virus or immune-depressive viruses like Marek's Disease virus, infectious bursal disease virus and infectious anemia virus and reductions of environmental stressors such as increased dust and ammonia levels from inadequate ventilation rates may reduce or limit transmission between houses and farms.
- e. **Availability of effective antimicrobials:** Gentamicin may be effectively used in the hatchery to prevent disease associated with *E. coli* omphalitis (yolk sac infection) and to decrease mortality in the first week of life. The label for injectable gentamicin sulfate for use in layer chickens states that it is recommended for the prevention of early mortality in day-old chickens associated with *Escherichia coli*, *Salmonella* Typhimurium and *Pseudomonas aeruginosa* susceptible to gentamicin sulfate. In the layer hatcheries, gentamicin is normally administered to day old females, however, with the recent emphasis on antimicrobial stewardship, most hatcheries have discontinued its use and have concentrated their efforts on good cleaning and disinfection. Sulfonamides, tetracycline and streptomycin all are approximately 50% effective in therapeutically treating diseases associated with *E. coli* in layers. Pullets are most commonly treated through the feed and for layers the only option is treatment through the feed. The delay in time from diagnosis to a new batch of feed with antimicrobials can be critical to stop the outbreak. The lack of approved water antimicrobials with a zero-day egg withdrawal is a challenge.
- f. **Barriers to prevention:** The major barrier to prevention of *E. coli* infections in layers is the lack of efficacious vaccines, together with inadequate vaccinal control of the primary viral respiratory pathogen infectious bronchitis virus (IBV), and at times also Newcastle disease (NDV), or immune-depressive viruses like Marek's Disease virus, infectious bursal disease virus and infectious anemia which predispose to *E. coli* infections. Elimination of the pathogen is unrealistic as it is part of the normal flora that is acquired early in life.

RESOURCES:

1. Nolan LK, Vaillancourt JP, Barbieri NL, Logue CM. Colibacillosis. In: Swayne DE, editor. *Diseases of Poultry*. 2020. 14th Edition, Wiley-Blackwell. p. 770-830.
2. Eric Gingerich, DVM, (Personal communication), Presenter of AVEP Current Diseases of Concern at 123rd Annual Meeting of the United States Animal Health Association October 23 – 30, 2019 – Providence, RI
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3.3 ESCHERICHIA COLI (TURKEYS)

KEY DATA POINTS

- a. **Clinical impact:** Common conditions/pathologies caused by avian pathogenic *Escherichia coli* (APEC) include colisepticemia, air sacculitis, peritonitis, osteomyelitis/synovitis and omphalitis/yolk sac infection. Typically, APEC infections are secondary to other stressors such as viral infection or environmental stress. When antimicrobials are used for therapy in affected flocks, mortality can be limited to 1-2%. If there is not a therapeutic option, mortality can commonly exceed 10%. Even without treatment, infection tends to resolve once the underlying cause(s) is addressed (i.e. seroconversion to viral infection or adjustment to barn conditions).
- b. **Economic impact:** Colibacillosis is often considered the most common infectious bacterial disease of poultry. When considered in their entirety, *E. coli* infections are responsible for significant economic losses in the poultry industry. Categories of economic losses include morbidity leading to decreased growth rate and feed conversion efficiency, increased mortality, increased condemnations (both whole bird and parts) at processing and cost of therapeutic antimicrobial treatments.

- c. **Prevalence:** In an annual survey, colibacillosis was ranked as the #2 health issue that turkey veterinarians faced in 2016, 2017 and 2018 (3,4).
- d. **Transmissibility:** APEC are typically present in the birds' environment. APEC infections are usually secondary to other stressors such as viral infection or environmental stress. Providing proper vaccination for common viral diseases (e.g. Newcastle disease and Hemorrhagic Enteritis) and appropriate barn conditions, especially temperature and air quality, will help to minimize the incidence of colibacillosis.
- e. **Availability of effective antimicrobials:** APEC has variable sensitivity to oxytetracycline, sulfonamides, and spectinomycin. Identification of the underlying stressor is critical. Once a stressor is identified and addressed, morbidity and mortality should subside.
- f. **Barriers to prevention:** Effective viral vaccines are critical. Specifically, the vaccines against Newcastle disease and Hemorrhagic Enteritis can help reduce the likelihood of secondary infections caused by APEC. Well trained animal husbandry personnel are critical to minimize environmental stresses. Commercial *E. coli* vaccines can be beneficial.

RESOURCES:

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2. Merck Veterinary Manual: Colibacillosis in Poultry accessed here: <https://www.merckvetmanual.com/poultry/colibacillosis/colibacillosis-in-poultry>
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4. Clark, SR and V. Ahlmeyer. Turkey Industry Report. *Proceedings of the 121st Annual Meeting of the United States Animal Health Association*. 2018;121:394-407.

3.4 ORNITHOBACTERIUM RHINOTRACHEALE

Image credit: Dr Karen Olsen University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

(Turkeys)

KEY DATA POINTS

- a. **Clinical impact:** *Ornithobacterium rhinotracheale* (ORT) typically causes severe pneumonia, pleuritis and airsacculitis in older birds (>8 weeks of age). The severity of clinical signs, mortality and duration of the disease are extremely variable and are exacerbated by poor air quality and suboptimal barn management. Infection can result in significant losses especially if the strain is resistant to available therapeutic options. Antimicrobials are used for therapy in affected flocks and when used typically contain the losses to <5%. If there are no viable therapeutic options, losses can easily exceed 15%.
- b. **Economic impact:** The economic impact of ORT, which is largely due to mortality, can be severe if older, close to market-age flocks are infected. Even where there is a viable antibiotic based on sensitivity, there are times when treatment is not an option due to withdrawal requirements prior to sending the affected flock to slaughter. Further, ORT infection can lead to significant economic losses caused by diminished growth rate, higher feed conversion ratio, increased mortality and slower processing line speeds and higher condemnation rates at the processing plant. In turkey breeders ORT infection can cause significant economic losses due to decreased production of hatching eggs.

- c. **Prevalence:** In an annual survey, ORT was ranked as the #3 health issue that turkey veterinarians faced in 2017 and 2018 (2,3).
- d. **Transmissibility:** ORT spreads primarily by horizontal transmission through direct contact with infected birds or indirect contact with aerosols or contaminated drinking water. Contaminated people and equipment can also serve as mechanical carriers of the pathogen. Vertical transmission has been hypothesized (4,5). *O. rhinotracheale* can survive longer at lower environmental temperatures (6 days at 22°C and at least 150 days at -12°C). This may be the reason that occurrence of the disease is more common during the winter. Proper water sanitation can minimize the severity and spread. Vaccination is limited and results are varied (toxoids, bacterins). Bacterin use is limited to turkey breeders. No commercial vaccine is approved. Limited application of controlled exposure efforts on individual flocks have shown value.
- e. **Availability of effective antimicrobials:** *O. rhinotracheale* has variable sensitivity to oxytetracycline, sulfonamides and penicillin. Treatment for complicating secondary infections such as colisepticemia might also be necessary. Supportive care should include addressing any air quality issues (ammonia, excessive humidity), warming up affected barn to increase bird comfort, and applying consistent water sanitation along with routine cleaning of drinkers. Water soluble guaifenesin may help clear mucus.
- f. **Barriers to prevention:** No commercial vaccine is approved for this widespread disease in the turkey industry. Understanding of the antigenic epitopes and cross protection between serotypes of ORT is limited and needs to be better understood in order to identify the characteristics a good vaccine candidate(s) require(s). Biosecurity is critical for preventing ORT infections. Proper water sanitation can minimize the severity and spread of *O. rhinotracheale*. Limited application of controlled exposure efforts on individual flocks have shown value.

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3. Clark, SR and V. Ahlmeyer. *Turkey Industry Report. Proceedings of the 121st Annual Meeting of the United States Animal Health Association*. 2018;121:394-407.
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3.5 PASTEURELLA MULTOCIDA

(Turkeys)

KEY DATA POINTS

- a. **Clinical impact:** Fowl cholera (*Pasteurella multocida* infection) lesions include pneumonia and airsacculitis. Birds may also develop ambulatory issues due to osteomyelitis and/or synovitis. Neurologic signs such as torticollis can also be present in affected flocks. Virulence of the pathogen can be highly variable, ranging from subtle lesions with low to moderate rates of mortality to acute forms of the disease with little gross pathology and significant losses.
- b. **Economic impact:** The economic impact due to mortality associated with Fowl Cholera can be severe, especially with *P. multocida* strains that have no therapeutic options. Infection is not self-limiting, so in flocks experiencing an outbreak, given enough time, mortality can be severe. Early marketing of an affected flock might be an option; however, this strategy results in additional economic losses due to marketing younger and lighter weight turkeys.
- c. **Prevalence:** In an annual survey, Fowl Cholera ranked #10 out of 36 priority health issues that turkey veterinarians faced in 2018 (3), an increase from a #16 ranking in 2017 (4).
- d. **Transmissibility:** Biosecurity is critical in preventing exposure to *P. multocida*. Control of domestic animals (especially cats) and peri-domestic animals (skunks,

rodents) around turkey barns is critical. A modified-live vaccine is available but use needs to be carefully managed as the vaccine itself can cause disease.

- e. **Availability of effective antimicrobials:** *P. multocida* has variable sensitivity to oxytetracycline, sulfonamides and penicillin. Early marketing of affected flocks should be considered.
- f. **Barriers to prevention:** The commercially available live Fowl Cholera vaccines can cause moderate to severe disease in turkeys. Live vaccines can induce mortality that cannot be easily differentiated from field challenge. Sequencing of the organism from lesions is required to determine if disease was induced by field exposure or vaccination. Adequate rodenticide rotations are important to reduce rodent pressure around turkey barns as well as biosecurity programs that prohibit domestic species, especially cats, from being on the farm. Feral cats are a specific concern.

RESOURCES:

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3. Clark SR and V. Ahlmeyer V. Turkey Industry Report. *Proceedings of the 122nd Annual Meeting of the United States Animal Health Association*. 2019;122:334-349.
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Section 4
EQUINE



4.1 ENTEROBACTERIACEAE

(*Escherichia coli*, *Proteus* spp., *Enterobacter* spp., *Klebsiella* spp.)

KEY DATA POINTS

- a. **Clinical impact:** Both resistant and susceptible strains of *Enterobacteriaceae* can cause equine infections including peritonitis (particularly associated with gastric rupture and perforation), osteomyelitis, synovitis, and cystitis as well as ocular, uterine, and wound infections. There is no evidence available to show that severity of infection or virulence is worse with antimicrobial-resistant strains compared to wild-type strains, but there may be delayed treatment if resistant strains are implicated.
- b. **Prevalence:** The true prevalence of antimicrobial-resistant strains in the equine population is not known. The data available comes from studies – small surveys usually – in which data was collected from laboratories. These reports only represent the samples submitted to a laboratory, not the general population. In many cases, the only reason that the sample was submitted to the laboratory is because the patient did not respond to the first-choice antimicrobial agent. Therefore, there may be selection bias in the reports of resistance from these isolates.
- c. **Transmissibility:** In people, these pathogens are transmitted by direct person-to-person contact and can be ingested from contact with environment, water, or food that has been contaminated with fecal material. Transmission

between horses is similarly possible, and hospital-acquired infections have been documented. Horses can also be a source of human infections primarily through contact with feces.

- d. **Availability of effective antimicrobials:** There are no FDA-approved antimicrobials for horses that are active against MDR *Enterobacteriaceae*. Therefore, legal extralabel use of animal or human drugs may be needed for treatment. Because the susceptibility profile can be unpredictable, clinicians are encouraged to perform culture and susceptibility testing to identify appropriate agents for treatment. However, a lack of susceptibility testing standards for many antibacterial agents for horses is a barrier to effectively identify the most appropriate treatment. The agents that are generally the most active against these bacteria are aminoglycosides (amikacin, gentamicin), piperacillin-tazobactam, or a carbapenem (meropenem). Occasionally, some may be susceptible to fluoroquinolones (e.g., enrofloxacin), but this is unlikely. Use of carbapenems should be considered a last-choice antibiotic and reserved for severe and broadly multi-drug resistant infections.
- e. **Barriers to prevention:** Strategies to prevent ESBL and other MDR strains of *Enterobacteriaceae* are not different in horses, than other animals or humans. General pathogen control within a hospital setting is recommended including regular removal of feces from stalls and maintenance of effective hygienic protocols, instating proper biosecurity for horses with gastrointestinal disease, identification and isolation of patients with drug-resistant infections, and regular hand-washing practices implemented by employees. One study reported the lack of ease of cleaning equine hospital facilities compared to small animal facilities is a common barrier to preventing these bacteria from contaminating the environment. ESBL strains of bacteria can persist in hay and bedding material for an extended period and this may serve as a risk factor for acquisition of MDR pathogens.
- f. **Risk factors:** Hospitalization is likely a risk factor due to the potential for hospital-acquired infection from contaminated environments. Previous antimicrobial use also likely contributes. Frequent use of ceftiofur (3rd generation cephalosporin) is likely a factor, but this has not been proven.

RESOURCES:

1. Ahmed, M. O., et al. (2010). ; Antimicrobial resistance in equine fecal *Escherichia coli* isolates from North West England. *Ann Clin Microbiol Antimicrob* 9: 12.
2. Damborg, P., Broens, E., Chomel, B., Guenther, S., Pasmans, F., & Wagenaar, J. et al. (2016). Bacterial Zoonoses Transmitted by Household Pets: State-of-the-Art and Future Perspectives for Targeted Research and Policy Actions. *Journal Of Comparative Pathology*, 155(1), S27-S40. doi: 10.1016/j.jcpa.2015.03.004 <https://www.sciencedirect.com/science/article/pii/S0021997515000523?via%3Dihub>
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7. van Spijk JN, Schmitt S, Schoster A. Infections caused by multidrug-resistant bacteria in an equine hospital (2012–2015). *Equine Veterinary Education*. 2017.
8. Walther B, Lubke-Becker A, Stamm I, Gehlen H, Barton AK, Janssen T, Weiler LH, Geunther S. Suspected nosocomial infections with multi-drug resistant *E. coli*, including extended-spectrum beta-lactamase (ESBL)-producing strains, in an equine clinic. *Berl Munch Tierarztl Wochenschr*. 2014 Nov-Dec; 127(11-12): 421-427.



4.2 PSEUDOMONAS AERUGINOSA

KEY DATA POINTS

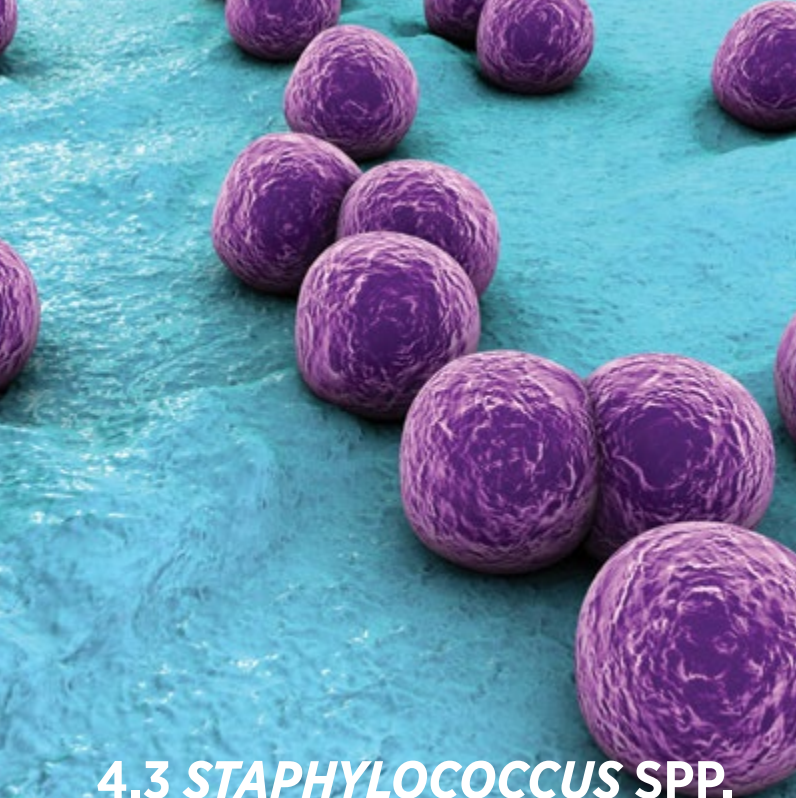
- a. **Clinical impact:** Both susceptible and resistant strains of *Pseudomonas* can cause a wide range of infections. In horses, infections are primarily linked to ocular or respiratory systems. Respiratory infections are typically advanced and associated with multiple pathogens or severe lesions such as abscesses in the lungs. Infections of surgical sites and open wounds are also possible, because contact with the pathogen in the environment is common. Outbreaks of endometritis due to *P. aeruginosa* have been documented, potentially due to venereal transmission of the pathogen.
- b. **Prevalence:** The prevalence of antimicrobial-resistant strains of *P. aeruginosa* in the equine population is not known. The data available come from studies of samples sent to laboratories and do not represent the general population, as many times samples are only submitted to the laboratory when the patient does not respond to the first-choice antimicrobial agent. Therefore, sampling bias may affect these results.
- c. **Transmissibility:** Transmission is usually due to contact with the pathogen in the environment. Because this organism is ubiquitous in nature, open wounds are susceptible to infection. The pathogen often colonizes the respiratory tract

or is present on the skin, and therefore this allows for the possibility of opportunistic infections due to a wide range of potential primary causes.

- d. **Availability of effective antimicrobials:** There are no FDA-approved antimicrobials for horses that are active against resistant strains of *P. aeruginosa*. Occasionally some strains may be susceptible to a fluoroquinolone such as enrofloxacin. Most isolates are susceptible to amikacin. In some instances, a human-labeled drug such as a carbapenem (usually meropenem) has been used. However, this should be considered a last-choice antibiotic and reserved for severe and broadly multi-drug resistant infections. If treatment can be accomplished with local infusions, or topically delivered agents, this may resolve some infections and avoid systemic administration of antimicrobials.
- e. **Barriers to prevention:** *P. aeruginosa* is ubiquitous in the environment, especially in areas that are regularly wet or poorly ventilated. Healthy animals are also often carriers of the pathogen in their respiratory tract which can facilitate transmission. Keeping the environment relatively clean and dry should be a priority for hospitals, but it is likely to be overtly challenging if not impossible to eliminate this pathogen from any animal housing facility. Surgical sites and open wounds should also remain covered to prevent contamination with environmental debris.

RESOURCES:

1. European Medicines Agency. 15 January 2015 EMA/CVMP/AWP/401740/2013 Committee for Medicinal Products for Veterinary Use (CVMP) Reflection paper on the risk of antimicrobial resistance transfer from companion animals. (https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-risk-antimicrobial-resistance-transfer-companion-animals_en.pdf)
2. Johns IC, Adams EL. Trends in antimicrobial resistance in equine bacterial isolates: 1999–2012. *Veterinary Record*. 2015 Jan 27;vetrec-2014.
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4.3 STAPHYLOCOCCUS SPP.

Staphylococcus aureus

KEY DATA POINTS

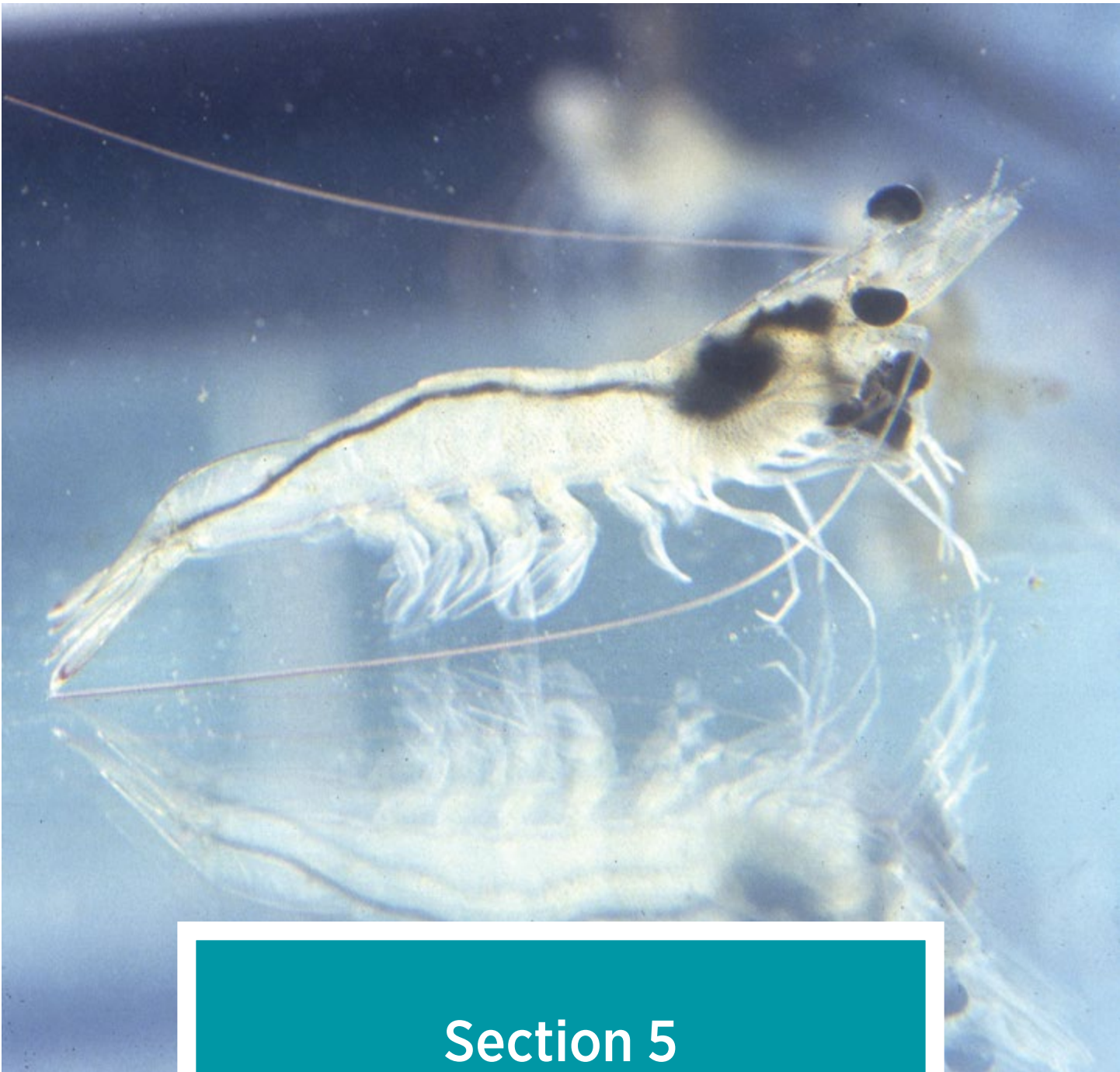
- a. **Clinical impact:** Equine infections with methicillin-resistant *Staphylococcus aureus* (MRSA) and other resistant *Staphylococcus* spp. can cause a broad range of clinical presentations. Dermatitis, cellulitis, bacteremia, septic arthritis, osteomyelitis, metritis, and pneumonia have all been reported. Staphylococcal infections associated with surgical sites, intravenous catheters, and surgical implants have also occurred in horses. Patients may present for veterinary care with a range of complaints including colic, lameness, hernia, incision exudation, or wounds that are caused by both methicillin-susceptible strains and resistant strains. It is also relatively common for horses to carry this pathogen within their nasal passages, on skin, or in the intestinal tract and demonstrate no clinical signs. There is no evidence that severity of infection or virulence is worse with antimicrobial-resistant strains compared to wild-type strains. In general, staphylococcal infections have a good prognosis for treatment despite resistance, with over 80% of patients surviving to discharge. Patients with staphylococcal pneumonia or wound infections require longer hospitalization in order to provide necessary supportive care or additional surgery when warranted.
- b. **Prevalence:** The true prevalence in the animal population is not known. There are scattered reports, mostly from

investigators at universities who have collected samples, but this does not represent the general population. In many cases, samples are submitted for culture and sensitivity to laboratories because the patients did not respond to the first-choice antimicrobial agent; therefore, there may be sampling bias. One multi-center study of over 115 equine patients diagnosed with MRSA demonstrated resistance most commonly to tetracyclines (92%), gentamicin (84%), trimethoprim-sulfamethoxazole (71%) and erythromycin (63%).

- c. **Transmissibility:** MRSA can be transmitted between horses and can also be transmitted from horses to people and vice versa when in close contact. However, zoonotic transmission is rare. Veterinarians and those with occupational exposure have a higher than average rate of colonization with equine-related strains of MRSA.
- d. **Availability of effective antimicrobials:** Treatment options are available. Some strains may be susceptible to trimethoprim-sulfonamides, which are approved for horses, but the determination of susceptibility is based on the human breakpoint for trimethoprim-sulfamethoxazole, and it is undetermined if this can be used to interpret susceptibility for equine isolates. MRSA isolates may be variably susceptible to other antimicrobial agents, such as chloramphenicol, fluoroquinolones, amikacin, and macrolides, but this should be confirmed with susceptibility testing. Testing standards are not available for chloramphenicol and macrolides in horses; therefore, data on its activity are difficult to interpret. Some options for antimicrobial therapy are human-labeled drugs that are not approved for use in animals such as vancomycin and rifampin. These can be used legally according to the Animal Medicinal Drug Use Clarification Act (AMDUCA) extra-label use legislation. Lack of susceptibility testing standards for many antibacterial agents in horses is a barrier for effective treatment.
- e. **Barriers to prevention:** Failure to enforce or properly implement these policies can be a barrier to preventing infection. Similarly, lack of compliance to instated infection control policies amongst hospital or clinic staff can also make infection control challenging. Risk factors: In one study, risk factors for MRSA colonization of horses included previous infection, presence of colonized horses on the same farm, admission to the neonatal intensive care unit, and admission to a hospital service other than the surgical service. Prior antimicrobial administration has also been associated with colonization of MRSA.

RESOURCES:

1. Adams, R., et al. (2018). An epidemiologic study of antimicrobial resistance of *Staphylococcus* species isolated from equine samples submitted to a diagnostic laboratory. *BMC Vet Res* 14(1): 42.
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Section 5
FISH & SHRIMP



5.1 AEROMONAS SPP.

A. salmonicida, *A. hydrophila*

KEY DATA POINTS

a. Clinical impact:

- *Aeromonas* spp. has a worldwide presence.
- Virulent *A. hydrophila* can have a mortality rate as high as 20-30% in near market-sized fish.
- *A. salmonicida* is an obligate pathogen. It is associated with salmonid aquaculture, but an atypical *A. salmonicida* causes diseases in warmwater and marine fish species. In young susceptible salmonids, mortalities can approach 85%.

b. Economic impact: Limited information is available. Since 2009, a virulent *A. hydrophila* strain has caused the loss of approximately 3 million pounds of near market-sized catfish annually in the southeastern U.S. catfish aquaculture industry.

c. Prevalence:

- Virulent *A. hydrophila* outbreaks have occurred annually in warm weather months in the southeastern United States.
- *A. salmonicida* outbreaks occur when temperatures are above 8°C. The latent form can reside in fish without clinical signs or lesions. Shedding is unpredictable with outbreaks reported sporadically.

d. Transmissibility:

- *A. hydrophila* is a ubiquitous pathogen that can be found in most aquatic environments. Outbreaks are typically opportunistic or secondary to a stress event, thus one of the minimizing factors for outbreaks is limiting stress.
- *A. salmonicida* can enter aquatic facilities through upstream reservoir hosts that shed bacteria into the affluent water. Predators that prey on fish can also inadvertently bring infected fish into aquatic facilities or water sources. Horizontal transmission is the main mode of transmission with vertical transmission suspected. The bacteria typically invade its host through gills, skin, and/or wounds. If strict biosecurity practices or sanitation protocols are not followed, there are higher risks for outbreaks.

e. Availability of effective antimicrobials: Although FDA has approved the use of three antimicrobials for *Aeromonas* spp. (*A. salmonicida*-florfenicol and ormetoprim/sulfadimethoxine, *A. liquefaciens* (*hydrophila*) - oxytetracycline dihydrate). *Aeromonas* spp. have shown multidrug resistance to tetracyclines and trimethoprim-sulfamethoxazole. Additionally, antimicrobial resistance that extends beyond the FDA aquaculture-approved antimicrobials has been reported in foreign countries.

f. Barriers to prevention:

- Since *A. hydrophila* is ubiquitous in the aquatic environment and is a natural inhabitant of the gastrointestinal tract of fish, eliminating the bacteria is nearly impossible.
- *A. salmonicida* can be found in most regions with salmonid aquaculture. The bacteria has been found in wild fish populations and other non-salmonid species can act as reservoirs.
- Asymptomatic carriers of the latent form of *A. salmonicida* can shed bacteria.
- Birds, mammals, amphibians, and reptiles can transport *Aeromonas* spp. into aquaculture facilities.

CURRENT ACTIONS:

- United States Fish and Wildlife Service (USFWS) Aquatic Animal Drug Approval Partnership has made a reference guide available for the FDA-approved use of antimicrobials for their labeled indication. This guide specifically lists the antimicrobial and the bacteria for its intended use.
- The FDA Center for Veterinary Medicine (CVM) has issued regulations that require the use of a Veterinary Feed Directive (VFD) to help ensure that medicated feeds containing medically important antimicrobials are used judiciously.

WHAT READERS CAN DO:

- a. Maintain optimal water parameters, ideal husbandry conditions, quarantine new fish arrivals, practice strict biosecurity protocols, treating effluent water with ultraviolet light or ozone to prevent or minimize outbreaks.
- b. Incorporate strict biosecurity protocols and strong sanitation practices when possible.
- c. For *Aeromonas* spp. outbreaks, culture, identify, and use the appropriate antimicrobial after sensitivity testing as prescribed by a veterinarian.
- d. Prevent predators such as birds, otters, and raccoons from bringing infected fish onto facilities.
- e. If a population within a facility has been identified as positive, culling the population would remove a potential reservoir for *A. salmonicida* since surviving fish can act as latent carriers.
- f. Using vaccines can minimize the likelihood of an *A. salmonicida* outbreak.
- g. Feeding probiotics may help to minimize outbreaks with *A. hydrophila*.

RESOURCES:

1. Aquatic Animal Drug Approval Partnership <https://www.fws.gov/fisheries/aadap/home.htm>
2. American Fisheries Society <https://units.fisheries.org/fhs/fish-health-section-blue-book-2016/section-1-diagnostic/>
3. FDA Approved Aquaculture Drugs <https://www.fda.gov/animal-veterinary/aquaculture/approved-aquaculture-drugs>
4. Veterinary Feed Directive (VFD) <https://www.fda.gov/animal-veterinary/development-approval-process/veterinary-feed-directive-vfd>



5.2 EDWARDSIELLA SPP.

Image credit: Dr. Esteban Soto U C Davis College of Veterinary Medicine

E. ictaluri and *E. piscicida*

KEY DATA POINTS

a. **Clinical impact:** In catfish, the disease enteric septicemia is caused by *Edwardsiella ictaluri*, and a clinically similar disease is caused by *E. piscicida*. Left untreated, the mortality in commercial catfish fingerling ponds is ~60%. For hybrid catfish which are reported to be less susceptible to the effects of *Edwardsiella* spp., the reported mortality is approximately 40% for untreated fish. Similar clinical signs and lesions were reported in zebrafish and in tilapia.

b. **Economic impact:**

- U.S. catfish are an important domestic product with an estimated economic value of \$1 billion in total economic impact. In the catfish farming industry, bacterial disease outbreaks have caused significant losses in production. With mortality rates up to 60%, the potential economic loss is great.
- Zebrafish: High economic impact because of the contamination of valuable genetic stocks with *E. ictaluri* resulting in high morbidity and mortality and the potential for a carrier state in survivors with a subsequent loss of valuable research animals and experimental data.
- Tilapia are not a large domestic fish crop in the United States; these are primarily imported. Experimental challenges indicate the losses can approach 50-100% (Soto et al., 2012).

c. **Prevalence:**

- Enteric septicemia of catfish (caused by either *E. ictaluri* or disease caused by *E. piscicida*) is endemic in the U.S. catfish industry. Outbreaks typically occur when pond temperatures range from 22-26° C.
- In 2011, *E. ictaluri* was first reported as causing naturally occurring epizootics in laboratory populations of zebrafish.

d. **Transmissibility:** *E. ictaluri* is an obligate pathogen that does not persist in the environment for long periods. It is transmitted from fish to fish by close contact, cannibalism, by water, or fecal/oral transmission.

e. **Availability of effective antimicrobials:** Ormetoprim/sulfadimethoxine and florfenicol medicated feeds are approved by the FDA for use in the control of mortality associated with *E. ictaluri*. Oxytetracycline (the only other antimicrobial approved for use in fishes in the United States) can be used in an extra-label fashion (on orders from a licensed veterinarian) if ormetoprim/sulfadimethoxine and florfenicol are not available. Breakpoints are not formally established for *E. ictaluri* or *E. piscicida* by Clinical and Laboratory Standards Institute (CLSI). Values that determine susceptibility, intermediate susceptibility, or resistance are determined by individual laboratories to assess the performance of antimicrobials in their region. However, resistance to all three of these antimicrobials has been reported (see specific references just below). Resistance genes have been found on transferable plasmids in pathogenic species of *Edwardsiella* spp. These are thought to play a major role in the transmission of antimicrobial resistance determinants in the aquatic environment. In 2009, a florfenicol resistant *E. ictaluri* was identified that also had multi-drug resistant MDR (Plasmid pM07-1) for chloramphenicol, tetracycline, streptomycin, ampicillin, amoxicillin-clavulanic acid, ceftiofur, and ceftiofuran. Plasmid pM07-1 confers decreased susceptibility to all three antimicrobial drugs that are currently approved for aquaculture use in the United States. In 2015, Griffin et al. reported that isolates of *E. ictaluri* in tilapia had an apparent resistance to sulfonamides. The *sul* genes are reported to be associated with sulfonamide resistance in other bacterial species of fishes.

f. **Barriers to prevention:**

- Up until a few years ago there was not an effective vaccine for *E. ictaluri* in catfish. There is still no effective vaccine for *E. piscicida*.
- Elimination of the pathogens is unrealistic because it is endemic in catfish ponds.

- High intensity production environments such as crowding (foodfish production under intensive-culture environments [e.g. ~10,000 hybrid catfish/acre]), competition for feed, poor water quality, predators, etc., contribute to development of disease. Stress can cause carriers to shed the bacteria.
- For zebrafish, there are no vaccines or FDA approved antimicrobials for use in the treatment of infection in the United States. In the past, researchers have taken formulations approved for use in terrestrial animals (e.g.

Nuflor (florfenicol) in cattle) and mixed it with zebrafish feed with oil to coat it and used this to medicate infected fish. There are no commercial facilities that manufacture medicated zebrafish food.

- There are illegal unapproved antimicrobials that are on the market via the internet and pet shops where fish owners can buy medicated feeds. Uninformed users may not use antimicrobials that the bacteria are susceptible to or for the correct dosage/duration which can lead to resistance.

DATA VISUAL:

Organism	<i>E. ictaluri</i>	<i>E. piscicida</i>
# Tested	190	47
Sulfadimethoxine/ormetoprim % (R)	1 (0.5)	0
Oxytetracycline %(R)	2 (1.1)*	0
Oxytetracycline %(I)	0	0
Florfenicol %(R)	0	0
Sulfadimethoxine/ormetoprim & Oxytetracycline (I) %	1 (0.5)	0
Sulfadimethoxine/ormetoprim & Florfenicol (R)	0	0
Oxytetracycline (R) & Florfenicol (I)	74 (38.9)*	3 (6.4)
Oxytetracycline (R) & Florfenicol (R)	9 (4.7)*	0
All 3 antimicrobials Oxytetracycline (R), Sulfadimethoxine/ormetoprim (I), and Florfenicol (I)%	1 (0.5)	0

MSU CVM Aquatic Diagnostic Laboratory in Stoneville, MS. 2018 Annual Case Summary. Incidence of Antimicrobial intermediate susceptibility and resistance in *Edwardsiella ictaluri* and *Edwardsiella piscicida*

IMPACT ON ANIMAL HEALTH:


Left untreated the mortality associated with *E. ictaluri* in catfish is approximately 60% in channel catfish fingerlings and approximately 40% in hybrid catfish fingerlings. If treated with florfenicol medicated feed according to the label claim, the survival in channel fingerlings is 60% and in hybrid fingerlings is 70%. If there were dissemination of the pM07-1 plasmid, it could leave the veterinarian and farmer with no approved options to treat *Edwardsiella* outbreaks in U.S. farm raised catfish because this plasmid confers resistance to all three approved antimicrobials for use in fish.

CURRENT ACTIONS:

The aquaculture industry is supporting the early adoption of FDA CVM's Five-Year Plan for Supporting Antimicrobial Stewardship in Veterinary Settings to remove unapproved or illegally marketed antimicrobials from over the counter and online sales.

RESOURCES:

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2. Hawke J, Kent M, Rogge M, Baumgartner W Wiles J Shelley J Savolainen, Wagner R (2013) Edwardsieliosis caused by *Edwardsiella ictaluri* in laboratory populations of Zebrafish *Danio rerio*. *Journal of Aquatic Animal Health* 25(3):171-183.
3. Reichley SR, Ware C, Steadman J, Gaunt PS, Garcia JC, et al. Comparative Phenotypic and Genotypic Analysis of *Edwardsiella* Isolates from Different Hosts and Geographic Origins, with Emphasis on Isolates Formerly Classified as *E. tarda*, and Evaluation of Diagnostic Methods (2017). *Journal of Clinical Microbiology*. 55 (12): 3466-3491.
4. Welch TJ, Evenhuis J, White DG, McDermott PF, Harbottle H, Miller RA, Griffin M and Wise D (2009) IncA/C plasmid-mediated florfenicol resistance in the catfish pathogen *Edwardsiella ictaluri*. *Antimicrob Agents Chemother* 53:845-846.
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12. AVMA (2019) *Judicious Therapeutic Use of Antimicrobials in Aquatic Animal Medicine*. Available: <https://www.avma.org/KB/Policies/Pages/Judicious-Use-of-Antimicrobials-for-Treatment-of-Aquatic-Animals-by-Veterinarians.aspx>



5.3 FLAVOBACTERIUM PSYCHROPHILUM

Image credit: Dr. Esteban Soto U C Davis College of Veterinary Medicine

KEY DATA POINTS

- a. **Clinical impact:** *Flavobacterium psychrophilum* is ubiquitous in cold freshwater ecosystems. The bacteria is the causative agent of Bacterial Cold-Water Disease (BCWD), which is also known as rainbow trout fry syndrome (RTFS) in Europe. BCWD affects a wide range of cold-water fish species but is most significant in wild and cultured salmonids like coho and rainbow trout. Induction of clinical disease is associated with decreasing water temperature. BCWD occurs at water temperatures below 16°C and becomes significantly more serious at temperatures below 10°C. Because of their small size, young fish (fingerling and smaller) and fry are most significantly affected, and mass mortalities associated with BCWD can occur very quickly in younger age classes. The “classic” presentation of BCWD manifests as open, ulcerative lesions on the body surface of affected fish associated with listlessness, exophthalmia, coelomic distention, and gill pallor. Infection is typically first noted as fraying of the dorsal and adipose fins and skin roughening that progress to necrosis of infection sites. Ulcerations most frequently appear on the lateral aspects of the peduncle but can be seen anywhere on the body. External lesions are associated with extensive internal pathology, including bacterial colonization, necrosis, and inflammation in spleen, liver, and kidneys. Septicemia often results in bacteria localizing to the muscle, bone, and dermis causing necrotic myositis and cephalic osteochondritis, which can affect fish chronically even after resolution of the initial BCWD signs. Antimicrobial therapy can reduce losses associated with *F. psychrophilum*.
- b. **Economic impact:** *F. psychrophilum* infection is responsible for the loss of tens of millions of dollars worldwide annually by causing mortality and filet damage in cultured and farmed salmon and trout.
- c. **Prevalence:** The prevalence of *F. psychrophilum* in North American aquaculture and stock enhancement is unknown but the organism and associated disease is distributed worldwide in cold-water culture environments. The organism is ubiquitous in cold freshwater ecosystems, and, although case reports in cultured and wild fish have been published, the incidence of diseases has not been studied.
- d. **Transmissibility:** Bacterial shedding by infected fish is highly dependent upon water temperature. Epizootics commonly occur when water temperatures range between 4 -10° C. Dead and moribund fish shed significantly more bacteria than sub-clinically infected fish. Vertical transmission has been documented in coho salmon and rainbow trout. Oral transmission has not been demonstrated.
- e. **Availability of effective antimicrobials:** Florfenicol (Aquaflor®) and oxytetracycline (Terramycin 200®) are currently approved by the FDA for treatment of disease associated with *F. psychrophilum* in salmonids.
- f. **Barriers to prevention:** Vaccination has not been successful against *F. psychrophilum*, owing to the vast genetic diversity of the bacteria. Eradication of the pathogen from the environment is not feasible due to its ubiquitous distribution. Fish culture environments often present an ideal situation for disease transmission because of increased stocking density, increased fish stressors, and concentration of the pathogen (i.e. shedding from dead and moribund fish).

IMPACT ON ANIMAL HEALTH:

F. psychrophilum infection has been responsible for massive die offs of coho salmon and rainbow trout in hatchery and culture settings. Individual fish that survive acute infection may suffer from the chronic effects of the infection, such as myositis and osteochondritis, which may result in enhanced susceptibility to further bacterial, viral, or parasitic infection and reduced growth.

CURRENT ACTIONS:

Laboratory work is ongoing at several universities, extension centers, and fish culture institutions worldwide to develop a viable vaccine against BCWD. Individual fish culture centers work to improve and enact best practices that minimize the concentration of *F. psychrophilum* in culture systems and reduce risk factors associated with disease induction (i.e. overstocking, environmental stressors, etc.).

RESOURCES:

1. *Bacterial Coldwater Disease* https://www.adfg.alaska.gov/static/species/disease/pdfs/fishdiseases/bacterial_coldwater_disease.pdf
2. *Coldwater Disease* http://www.glfsc.org/pubs/SpecialPubs/sp83_2/pdf/chap22.pdf
3. *Invasive Species Compendium: Coldwater Disease* <https://www.cabi.org/isc/datasheet/87862>
4. *Bacterial Coldwater Disease* <https://agriflivedn.tamu.edu/fisheries/files/2013/09/WRAC-Publication-Bacterial-Coldwater-Disease.pdf>



5.4 VIBRIO PARAHAEMOLYTICUS

SPECIES FOR WHICH THIS PATHOGEN IS A CONCERN:

Vibrio parahaemolyticus is generally considered to be more problematic in penaeid shrimp (susceptible species include *Litopenaeus vannamei*, *Penaeus monodon*, *Penaeus chinensis*, and *Macrobrachium rosenbergii*).

KEY DATA POINTS

a. **Clinical impact:** In cultured shrimp, acute hepatopancreatic necrosis disease (AHPND) is caused by certain strains of *V. parahaemolyticus* (having acquired a plasmid that encodes deadly binary toxins). Susceptible species include *Litopenaeus vannamei* (Pacific white shrimp), *Penaeus monodon* (black tiger shrimp), *Penaeus chinensis* (Chinese white shrimp); more recently, AHPND was detected in *Macrobrachium rosenbergii* (freshwater prawn). AHPND is characterized by sudden, mass mortalities (up to 100%), usually within 30-35 days of stocking post-larvae or juveniles in grow-out ponds. Clinical signs include slightly expanded chromatophores, lethargy, softening of the shell, muscular pallor, erratic swimming, empty GI tract (stomach and midgut), hepatopancreatic discoloration, atrophy, and altered consistency (aqueous to rubbery). *V. parahaemolyticus* has been identified as the bacterial

agent causing tail rot disease in *Amphiprion sebae* (sebae clownfish). Clinical signs include hemorrhage associated with edges of tail fin, erythema at fin bases, skin ulcers with red margins, lethargy, erratic swimming behavior, and inappetence. 100% mortality was observed within 6 days of intramuscular inoculation under experimental/laboratory conditions.

- b. **Economic impact:** Shrimp is an important economic seafood product with high demand and economic value. World aquaculture shrimp production in 2012 was estimated at more than 4 million tons, valued at approximately \$17 billion USD. With mortality rates up to 100%, the potential economic loss due to AHPND is great. In 2017, the first confirmed outbreak of AHPND in the United States occurred at three different Texas shrimp farms. Production decreased to less than 40% of what it was the year prior.
- c. **Prevalence:** AHPND in the United States was first reported in 2017, when three different shrimp farms in Texas were affected. There have been no reports in the United States since then.
- d. **Transmissibility:** *V. parahaemolyticus* is transmitted by immersion/cohabitation in an environment (i.e., water) where the agent is present and via an oral route.
- e. **Availability of effective antimicrobials:** One study investigated antimicrobial resistance in 350 *V. parahaemolyticus* strains isolated from water and sediment samples collected along the southeastern United States Atlantic coast. Resistance to amoxicillin, ampicillin, apramycin, cephalothin, penicillin, and streptomycin was prevalent across strains. Fewer isolates were resistant to amikacin, gentamicin, nalidixic acid, sulfa agents, and trimethoprim. Notably, 84 isolates (25%) demonstrated multidrug resistance to 10 or more antimicrobials.
- f. **Barriers to prevention:**
- Exportation of shrimp and shrimp feed; the movement of susceptible animals (common in shrimp aquaculture) increases the risk of disease spread.
 - High intensity production environments, where stressors such as crowding, competition for feed, poor water quality, etc., contribute to development of disease.
 - Lack of vaccines and FDA-approved antimicrobials for use in cultured shrimp make prevention and treatment of infection difficult in the United States.

IMPACT ON ANIMAL HEALTH:

During June 2017, three *P. vannamei* farms in Cameron County, TX, experienced outbreaks from *V. parahaemolyticus*. Below is a summary of the investigation and response.

- a. The farm was placed under quarantine and all animals were harvested.
- b. Cleaning and disinfection of the affected premises (including all equipment) was completed. In addition, all farm ponds and ditches were dried and disinfected.
- c. Environmental samples and surveillance of the control area were negative for AHPND.
- d. As a precaution, additional surveillance and requirements prior to restocking were carried out by TWPD through the Texas Shrimp Inspection Program.
- e. The AHPND event was considered resolved as of 12/26/2017.

CURRENT ACTIONS:

AHPND is an OIE reportable disease. USDA surveils imported shrimp following standards detailed in the OIE Aquatic Animal Health Code (Chapter 9.1: Acute Hepatopancreatic Necrosis Disease), which may include quarantine of imported animals for an indefinite period of time and/or testing for *V. parahaemolyticus* depending on the status of the country of origin. In addition, USDA routinely refuses entry of shrimp for reasons related to banned antimicrobial residues.

RESOURCES:

1. OIE – World Organization for Animal Health. *Manual of Diagnostic Tests for Aquatic Animals (the Aquatic Manual)*. Chapter 2.2.1: Acute Hepatopancreatic Necrosis Disease https://www.oie.int/fileadmin/Home/eng/Health_standards/aahm/current/chapitre_ahpnd.pdf
2. OIE – World Organization for Animal Health. *Aquatic Animal Health Code (the Aquatic Code)*. Chapter 9.1: Acute Hepatopancreatic Necrosis Disease https://www.oie.int/fileadmin/Home/eng/Health_standards/aahc/current/chapitre_ahpnd.pdf
3. Southern Regional Aquaculture Center (SRAC). *Biosecurity in Aquaculture, Part 1: An Overview*. <http://fisheries.tamu.edu/files/2013/09/SRAC-Publication-No.-4707-Biosecurity-in-Aquaculture-Part-1-An-Overview.pdf>
4. Food and Agriculture Organization of the United Nations. *Biosecurity in Aquaculture: Philippines*. <http://www.fao.org/fishery/static/news/MultistakeholderConsultation/Item7.pdf>
5. NOAA Fisheries: *Fisheries of the United States, 2017* <https://www.fisheries.noaa.gov/national/fisheries-united-states-2017>
6. Southern Shrimp Alliance: *Antimicrobials and Additives* <https://www.shrimpalliance.com/category/antibiotics>
7. Centers for Disease Control and Prevention: *Vibrio Species Causing Vibriosis* <https://www.cdc.gov/vibrio/index.html>

RESOURCES:

1. Anjay SCD, Kumar A, Kaushik P, Kurmi B. (2014). Occurrence of *Vibrio parahaemolyticus* in marine fish and shellfish. *Indian Journal of Geo-Marine Sciences*, 43, 887-890.
2. Asok A, Arshad E, Jasmin C, Somnath Pai S, Bright Singh IS, Mohandas A, Anas A. (2012). Reducing *Vibrio* load in *Artemia nauplii* using antimicrobial photodynamic therapy: a promising strategy to reduce antibiotic application in shrimp larviculture. *Microbial Biotechnology*, 5, 59-68.
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6. García-Aljaro C, Riera-Heredia J, Blanch AR. (2014). Antimicrobial resistance and presence of the SXT mobile element in *Vibrio* spp. isolated from aquaculture facilities. *New Microbiology*, 37, 339-346.
7. Joshi J, Srisala J, Truong VH, Chen IT, Nuangsaeng B, Suthienkul O, Lo CF, Flegel TW, Sritunyalucksana K, Thitamadee S. (2014). Variation in *Vibrio parahaemolyticus* isolates from a single Thai shrimp farm experiencing an outbreak of acute hepatopancreatic necrosis disease (AHPND). *Aquaculture*, 428, 297-302.
8. Lai HC, Ng TH, Ando M, Lee CT, Chen IT, Chuang JC, Mavichak R, Chang SH, Yeh MD, Chiang YA, Takeyama H. (2015). Pathogenesis of acute hepatopancreatic necrosis disease (AHPND) in shrimp. *Fish & Shellfish Immunology*, 47, 1006-1014.
9. Lee CT, Chen IT, Yang YT, Ko TP, Huang YT, Huang JY, Huang MF, Lin SJ, Chen CY, Lin SS, Lightner DV. (2015). The opportunistic marine pathogen *Vibrio parahaemolyticus* becomes virulent by acquiring a plasmid that expresses a deadly toxin. *Proceedings of the National Academy of Sciences*, 112, 10798-10803.
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5.5 VIBRIO VULNIFICUS

KEY DATA POINTS

- a. **Clinical impact:** *Vibrio vulnificus* is considered a ubiquitous organism in brackish and marine environments. It has been associated with disease outbreaks in multiple fish species, but particularly in eels and tilapia. In fish, it typically causes acute mortalities associated with septicemia, behavioral changes (lethargy), ulcerative and hemorrhagic skin and gill lesions, splenomegaly, and severe hemorrhagic lesions in the liver.
- b. **Prevalence:** The prevalence of *V. vulnificus* in U.S. aquaculture is unknown. The organism is a ubiquitous organism of brackish and marine environments, and although case reports in cultured and feral fish have been made, the incidence of diseases has not been studied. Worldwide, cultured eels appear particularly susceptible to infection and diseases.
- c. **Transmissibility:** In laboratory-controlled challenges, immersion, and oral routes of exposure have been demonstrated as potential routes of entry to fish. The gills have been suggested by several authors as the main portal of entry to eels. The virulence of the isolates is highly variable and environmental conditions like salinity and

temperature are reported as important factors to consider as virulence of the isolates also are dependent on them.

- d. **Availability of effective antimicrobials:** There are currently no FDA-approved antimicrobials for use in cultured fish destined for human consumption infected with *V. vulnificus*. Extra-label use of florfenicol, oxytetracycline and sulfadimethoxine/ormetoprim can be an option (at discretion of veterinarian) if the veterinarian has evidence of susceptibility of the strain to the drug.
- e. **Barriers to prevention:** Vaccines and immunostimulants have been reported in the literature for the prevention of *V. vulnificus* infections. However, due to the tremendous serological and genetic diversity of this species, variable responses can be expected.

CURRENT ACTIONS:

Most of the data available on *V. vulnificus* in the United States comes from human infections after ingesting raw oysters. Additional case reports have associated skin injury caused by fish spines with local and disseminated diseases in human patients.

RESOURCES:

1. CDC *Vibrio* Species Causing Vibriosis <https://www.cdc.gov/vibrio/index.html>
2. CDC *Vibrio vulnificus* & Wounds <https://www.cdc.gov/disasters/disease/vibriofaq.html>
3. Ina-Salwany, M.Y., Al-saari, N., Mohamad, A., Mursidi, F.-A., Mohd-Aris, A., Amal, M.N.A., Kasai, H., Mino, S., Sawabe, T. and Zamri-Saad, M. (2019), *Vibriosis in Fish: A Review on Disease Development and Prevention*. *J Aquat Anim Health*, 31: 3-22. doi:10.1002/aah.10045



Section 6 **SHEEP & GOATS**



6.1 CAMPYLOBACTER JEJUNI

KEY DATA POINTS

- a. **Clinical impact:** *C. jejuni* is mostly considered to be a cause of abortion in sheep flocks and less commonly a cause of ileitis, enteritis, or infertility. Tetracycline-resistant strains of *C. jejuni* have been reported to be extensive in the United States. The vast majority have been found to be a single genetic clone. Outbreaks of 10-40% of pregnant sheep aborting in late gestation can occur with little warning in flocks with new infections; enzootic levels of disease may be lower at 5 to 7%. This makes this disease particularly impactful on an affected flock. Biosecurity precautions may only partially protect the flock from infection. The organism may be introduced to the flock by sheep that excrete the bacteria in their feces or possibly by carrion eating birds such as crows and seagulls. While goat herds can experience abortion from this agent, it is not commonly reported.
- b. **Economic impact:** USDA surveys from 2011 of sheep producers provide estimates of impact. Flocks reported that 43.8% experienced abortion at some level. While 73.8% of flocks did not know the cause of abortion, among the approximately 25% of cases for which a cause was identified, campylobacteriosis was the second most commonly reported cause (6.6%).

- c. **Prevalence:** Campylobacteriosis is a high prevalence zoonotic and foodborne disease in humans in the United States; however, risk of infection from small ruminants is not fully known. *C. jejuni* is commonly shed in the feces of sheep. A study that followed sheep in 48 flocks in Ontario, Canada found a high prevalence of *C. jejuni* in the feces (70/138 pooled fecal samples). Some of these isolates were resistant to important antimicrobials: 39.4% to tetracycline, 4.2% to ciprofloxacin and nalidixic acid, and 0.7% to telithromycin. A study conducted by APHIS in the United States in 2011 found that *Campylobacter* spp. were isolated from 19.7% of sheep fecal samples; 80.4% of typed isolates were *C. jejuni*. In those isolates, antimicrobial resistance to tetracycline was reported in 62.6% with nalidixic acid, ciprofloxacin, and erythromycin following at 6.2%, 6.0%, and 0.5%, respectively. The clone SA appears to be highly resistant to tetracyclines, and it is speculated that use of chlortetracycline in the feed to control *Campylobacter* abortion in sheep may have selected for this resistant clone. This clone has also been identified in human cases in the United States, either as sporadic cases or as outbreaks, and is usually associated with consumption of raw milk.
- d. **Transmissibility:** Animal-to-animal transmission is usually through contamination of feed or grazing in areas contaminated feces. Animal-to-human transmission may be through contamination of food. Given the prevalence of this organism in human foodborne illness, transmission appears relatively common.
- e. **Availability of effective antimicrobials:** Vaccines are available with variable levels of protection. However, veterinarians are often faced with trying to slow an abortion outbreak, in which case, antimicrobials are used. Traditionally *C. jejuni* abortion was controlled using a chlortetracycline feed additive in the United States. This made treatment of a flock during an abortion outbreak easy, particularly in animals out on pasture. Injection of multiple animals in a pasture setting can be challenging. However, the clone SA currently isolated from many sheep abortion cases has been found to be highly resistant to tetracyclines as it very commonly carries the *tet(O)* gene. A study published in 2014 compared U.S. isolates to those from the U.K. Of U.S. isolates obtained after 2006, 100% were the genetic clone ST-8 and were very resistant to tetracycline with an MIC₉₀ of > 64 ug/mL. These same isolates were mostly susceptible to ciprofloxacin, gentamicin, and nalidixic acid (3.03% resistant), or were 100% susceptible to azithromycin, clindamycin, erythromycin, florfenicol, and telithromycin. These

antimicrobials would need to be administered parenterally, some are illegal to use extra-label in food producing animals, and none are approved for use in sheep or goats. The effectiveness of injectable products has also not been well-established, although preliminary studies suggest injectable macrolides may be effective.

- f. **Barriers to prevention:** Immunity can develop in affected ewes but is not lifelong. Vaccination may be effective, but cross-protection may not always occur between the field strain and vaccine strain. There is also no cross-protection with vaccines containing other *Campylobacter* species, such as *C. fetus*. Given how common *C. jejuni* is cultured from ovine feces, it is unlikely that screening of new introductions for being a *C. jejuni* carrier could be practically done.

CURRENT ACTIONS:

Research is ongoing, but more is needed on developing an effective vaccine so that antimicrobials no longer need to be used in an outbreak situation or to control on-going infection in a flock.

RESOURCES

1. Sahin O, Plummer PJ, Jordan DM, et al. Emergence of a tetracycline-resistant *Campylobacter jejuni* clone associated with outbreaks of ovine abortion in the United States. *Journal of clinical microbiology* 2008;46:1663-1671.
2. Wu Z, Sippy R, Sahin O, et al. Genetic diversity and antimicrobial susceptibility of *Campylobacter jejuni* isolates associated with sheep abortion in the United States and Great Britain. *Journal of clinical microbiology* 2014;52:1853-1861.
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6.2 STAPHYLOCOCCUS AUREUS

KEY DATA POINTS

- a. **Clinical impact:** Clinical mastitis due to *Staphylococcus aureus* can lead to decreased milk production, loss of one or both glands, and death loss in sheep and goats, so antimicrobial therapy can reduce production loss and mortality.
- b. **Economic impact:** The economic impact is unknown in the United States, but the production losses associated with subclinical mastitis can be significant. The economic impact would include loss of milk production in the current and potentially later lactations, the cost of antimicrobial therapy, and the cost of discarding milk after treatment. A very small number of goat and sheep dairies routinely perform antimicrobial susceptibility testing, but there are no standardized breakpoints for prediction of clinical success in small ruminant mastitis. Therefore, the likelihood is that the presence of resistant bacteria will not be immediately recognized as *in vitro* resistance but instead as non-responsive infections. This may then lead to additional rounds of treatment or re-treatment with an alternative antimicrobial drug, which can result in additional drug costs and additional milk loss.
- c. **Prevalence:** In 2007, USDA estimated approximately 218,000 goats on operations with 10 or more goats, representing approximately 5,700 farms (3). These operations reported an incidence of clinical mastitis of

2.8% of animals and 30.7% of operations in the most recent USDA survey in 2009 (3). This represents an estimated 7,000 animals with clinical mastitis every year. Estimates of *S. aureus* incidence in sheep and goats in the United States have not been extensively reported, but one report estimated prevalence in goats at 5% at kidding and 10% at 40 days-in-milk (4). In sheep, prevalence was estimated at 33.3% at lambing and 7.1% 40 days after lambing.(4)

The prevalence of resistance is unknown, and there are limited published data on small ruminant bacterial antimicrobial susceptibility. Data below represent samples from only one region of the United States, so the true prevalence of resistance is unknown.

Table X: Antimicrobial resistance of isolates from milk samples from sheep and goats in 2018-2019 from the California Animal Health & Food Safety Laboratory System

	% Resistant*		Breakpoint for resistance
	<i>Staphylococcus aureus</i> (n=24)	<i>Staphylococcus</i> sp. coag-negative (n= 46)	
Ampicillin	17%	13%	>= 0.5
Penicillin-novobiocin	0	6.5%	>= 4/8
Cephalothin	0	6.5%	>= 8
Erythromycin	4%	11%	>= 8
Oxacillin	0	6.5%	>= 4
Penicillin	21%	6.5%	>= 2
Tetracycline	13%	6.5%	>= 1
Pirlimycin	4%	11%	>= 4
Ceftiofur	0	4.3%	>= 8

*Testing was performed according to the Clinical and Laboratory Standards Institute (CLSI) VET08, "Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals. 4th ed." using the Trek Sensititre Mastitis Plate format. Interpretations were extrapolated from bovine mastitis (penicillin-novobiocin, pirlimycin, ceftiofur), equine (penicillin) canine (cephalothin) and general veterinary (ampicillin, erythromycin, tetracycline) criteria.

- d. **Transmissibility:** *S. aureus* is considered a contagious pathogen and can be transmitted via milking equipment, milkers' hands, and other fomites. Although the incidence of methicillin-resistant staphylococci (MRSA) remains relatively low in most regions, because *S. aureus* can be zoonotic and the methicillin resistance gene has been

shown to be transmissible to other bacteria, the presence of resistance is a concern.

- e. **Availability of effective antimicrobials:** Because dairy cows are also commonly affected with clinical mastitis, there are several antimicrobial drug products available globally that are often used extra-label to treat mastitis in sheep and goats. Many of these products are intramammary preparations. However, if the resistance is due to the *mecA* or similar genes that confer resistance to all beta-lactam antimicrobials, the number of effective antimicrobials becomes much fewer. Other drugs available as intramammary products in the United States likely to be effective include pirlimycin and erythromycin, and in other countries, tetracycline, streptomycin, and other drugs may be options.
- f. **Barriers to prevention:** Vaccines for sheep or goats for this pathogen are not universally available, although a product appears to have been recently approved by USDA CVB and is not yet commercially available. (<https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/veterinary-biologics/product-summaries/vet-label-data/cbcd97a9-77d4-40b9-9e97-cf990cc2eeb1>) Efficacy of this product was sufficient to receive a new CVB approval, although other products have failed to demonstrate efficacy.

RESOURCES:

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2. Smith MC, Sherman DM. Mammary Gland and Milk Production In: Smith MC, Sherman DM, eds. *Goat Medicine*, 2nd edition. Ames, IA: Wiley-Blackwell, 2009;647-689.
3. USDA. *Goat 2009, Part II: Reference of Goat Health and Marketing Management Practices in the United States, 2009* In: USDA-APHIS-VS C, ed. Fort Collins, CO, 2011;1-104.
4. McDougall S, Pankey W, Delaney C, et al. Prevalence and incidence of subclinical mastitis in goats and dairy ewes in Vermont, USA. *Small Ruminant Research* 2002;46:115-121.
5. Kautz FM, Nickerson SC, Ely LO. Use of a staphylococcal vaccine to reduce prevalence of mastitis and lower somatic cell counts in a registered Saanen dairy goat herd. *Research in veterinary science* 2014;97:18-19
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IMPACT ON ANIMAL HEALTH:

Resistant infections can be more difficult to treat and may not be immediately recognized as *in vitro* resistance but instead as non-responsive infections. This may then lead to additional rounds of treatment or re-treatment with an alternative antimicrobial drug, which can result in significant production loss in affected herds.

WHAT IS BEING DONE TO ADDRESS THIS PROBLEM:

Given the prevalence of *S. aureus* mastitis in the United States and other countries, it would be prudent to continue investigation of *S. aureus* typing, public health risks, and resistance gene characterization.



6.3 COAGULASE-NEGATIVE STAPHYLOCOCCI

KEY DATA POINTS

- a. **Clinical impact:** In 2007, USDA estimated approximately 218,000 goats on operations with 10 or more goats, representing approximately 5,700 farms (1). These operations reported an incidence of clinical mastitis of 2.8% of animals and 30.7% of operations in the most recent USDA survey in 2009 (1). This represents an estimated 7,000 animals with mastitis every year. The prevalence of coagulase-negative staphylococci across herds is unknown; therefore, the clinical impact of this pathogen in herds is also unknown. Prevalence in one study was estimated at 87.5% at kidding and 66.7% at 40 days in milk in goats, and 66.7% at lambing and 78.6% at 40 days after lambing (2).
- b. **Economic impact:** The economic impact is unknown in the United States, but the production losses associated with subclinical mastitis can be significant (3-5). The economic impact would include loss of milk production in the current and potentially later lactations, the cost of antimicrobial therapy, and the cost of discarding milk after treatment. A very small number of goat and sheep dairies routinely perform antimicrobial susceptibility testing, and there are no standardized breakpoints for prediction of

clinical success in small ruminant mastitis. Therefore, the likelihood is that the presence of resistant bacteria will not be immediately recognized as *in vitro* resistance, but as non-responsive infections. This may then lead to additional rounds of treatment or re-treatment with an alternative antimicrobial drug, which can result in additional drug costs and additional milk loss.

- c. **Prevalence:** The prevalence of resistance in coagulase-negative *Staphylococcus* isolates from sheep and goats in the United States is unknown. However, reports from other areas of the world include prevalence estimates of up to 50% in some settings, although most reports suggest a range of 0-10% prevalence (Table X).
- d. **Transmissibility:** Although the prevalence of methicillin-resistant staphylococci remains relatively low in most regions, because the methicillin resistance gene has been shown to be transmissible to other bacteria, the presence of resistance is a concern.
- e. **Availability of effective antimicrobials:** Beta-lactam antimicrobial drugs are the most commonly used drugs for mastitis in small ruminants. Particularly in goats, intramammary administration of products approved for dairy cows are commonly used to treat mastitis, and the majority of intramammary products in the United States are beta-lactam drugs: amoxicillin, cloxacillin, hetacillin, penicillin (in combination with novobiocin), cephalirin, and ceftiofur.
- f. **Barriers to prevention:** No effective mastitis vaccines for small ruminants are available in the United States.

CURRENT ACTIONS:

Several studies regarding mastitis prevention have been conducted; however, additional information and research regarding prevention through vaccines or technological advances in milking equipment may be valuable to preventing mastitis and the need for antimicrobial use.

RESOURCES:

1. USDA. *Goat 2009, Part II: Reference of Goat Health and Marketing Management Practices in the United States, 2009* In: USDA-APHIS-VS C, ed. Fort Collins, CO, 2011;1-104.
2. McDougall S, Pankey W, Delaney C, et al. Prevalence and incidence of subclinical mastitis in goats and dairy ewes in Vermont, USA. *Small Ruminant Research* 2002;46:115-121.
3. Barron-Bravo OG, Gutierrez-Chavez AJ, Angel-Sahagun CA, et al. Losses in milk yield, fat and protein contents according to different levels of somatic cell count in dairy goats. *Small Ruminant Research* 2013;113:421-431.
4. Koop G, van Werven T, Schuiling HJ, et al. The effect of subclinical mastitis on milk yield in dairy goats. *Journal of dairy science* 2010;93:5809-5817.
5. Gosselin VB, Dufour S, Calcutt MJ, et al. Staphylococcal intramammary infection dynamics and the relationship with milk quality parameters in dairy goats over the dry period. *Journal of dairy science* 2019;102:4332-4340.
6. Macori G, Giacinti G, Bellio A, et al. Molecular Epidemiology of Methicillin-Resistant and Methicillin-Susceptible *Staphylococcus aureus* in the Ovine Dairy Chain and in Farm-Related Humans. *Toxins (Basel)* 2017;9.
7. Giacinti G, Carfora V, Caprioli A, et al. Prevalence and characterization of methicillin-resistant *Staphylococcus aureus* carrying *mecA* or *mecC* and methicillin-susceptible *Staphylococcus aureus* in dairy sheep farms in central Italy. *Journal of dairy science* 2017;100:7857-7863.
8. Gosselin, VB, Dufour, S, Middleton, JR. Association between species-specific staphylococcal intramammary infections and milk somatic cell score over time in dairy goats. *Prev Vet Med* 2020;174:104815.
9. Wang, M, Want, T, Guan, Y, et al. The preparation and therapeutic roles of scFv-Fc antibody against *Staphylococcus aureus* infection to control bovine mastitis. *Appl Microbiol Biotechnol* 2019;103:1073-1712.



Section 7
SWINE



7.1 ESCHERICHIA COLI

KEY DATA POINTS

a. **Clinical impact:** *Escherichia coli* is a major cause of swine disease globally. There are three major clinical manifestations associated with intestinal disease, while extraintestinal manifestations including septicemia and urinary tract infections tend to be sporadic and of secondary importance. The presence of the pathogen per se in a herd is not sufficient to cause disease, and management and environmental factors are important for control and prevention. The major syndromes in pigs are neonatal colibacillosis in pigs up to 5 days old, and post weaning colibacillosis and edema disease, which occur predominantly in the nursery phase between 21 and 56 days of age. Although the bacteria are normally present in the large intestine, clinical disease is associated with colonization of the small intestine. The variants associated with neonatal colibacillosis (non-hemolytic; predominantly fimbriae F4, F5, F6, F41; heat stable toxin STa most common) tend to be distinct from those causing disease in weaned pigs (hemolytic; fimbriae F4, F18; heat labile and heat stable enterotoxins, and shiga toxins in edema disease). The predominant shiga-toxin causing edema disease in pigs is Stx2e which damages endothelial cells in many tissues including the brain, gastric sub-mucosa,

small intestine, eyelids and colonic mesentery where edema may be evident. The Stx2e shiga-toxin is extremely rare in human cases of hemolytic-uremic syndrome.

- b. **Economic impact:** Historically, neonatal colibacillosis was among the most important diseases of pigs globally. It has decreased in importance due to improved herd health management, particularly the use of prefarrowing vaccination of sows to induce colostral and milk antibodies to prevalent strains. However, due to the endemic nature of the pathogen, neonatal colibacillosis can occur in any herd where problems of management or failures in immune management exist. In contrast, post-weaning diarrhea and edema disease of weaned pigs continue to be important problems in modern production and antimicrobial use is commonly required to treat and control these diseases in pigs. The need to prevent and control enteric disease in weaned pigs is one of the major constraints on efforts to raise pigs without antimicrobials.
- c. **Prevalence:** *E. coli* are ubiquitous as commensal flora of swine, and are therefore present in all herds. The incidence of disease is highly variable and a function of both the virulence of strains present and the management and environmental factors that predispose to disease. High morbidity and mortality can occur in affected groups of pigs. Shiga-toxin producing strains of *E. coli* causing edema disease may also harbor enterotoxin genes, thus edema disease and diarrhea can occur concurrently.
- d. **Transmissibility:** As the organisms are endemic in herds as normal flora, exposure occurs in the first hours after birth. Fecal-oral transmission is the predominant mode of transmission. Maternal immunity transferred by colostral IgG and IgA in milk are important protective factors for suckling pigs. The risk of disease is a function of the virulence and toxin producing capacity of strains present in herds. In the post weaning environment, fecal-oral transmission of pathogenic strains being shed by infected pigs can lead to outbreaks.

e. **Availability of effective antimicrobials:** A broad range of antimicrobials have label claims in the United States for colibacillosis in swine, with options for injectable, water, and feed administration. These include aminoglycosides (gentamicin, neomycin), and tetracyclines (chlortetracycline, oxytetracycline, tetracycline), enrofloxacin and sulfamezathine. Injectable aminoglycosides should not be administered to pigs after 3 days of age due to the risk of residues. Selection of the appropriate drug and route(s) of administration is dependent on the epidemiologic scenario including the age of pigs involved. Both the clinical history on a farm and antimicrobial susceptibility testing are important considerations in antimicrobial selection.

f. **Barriers to prevention:** The major obstacle to prevention is that *E. coli* is an opportunistic pathogen that is part of the normal flora of the lower intestinal tract of pigs. Vaccination of sows has been highly effective in reducing neonatal colibacillosis, but not for post-weaning disease which occurs when antibodies in milk have been withdrawn and colostrum antibodies are declining. Factors that limit feed intake in the early post weaning period, including concurrent diseases (e.g., PRRS, influenza) and feed quality may predispose to outbreaks.

DATA VISUAL:

Susceptibility profiles (reported as % susceptible) for *E. coli* and hemolytic *E. coli* at ISU VDL in 2018

<https://vetmed.iastate.edu/sites/default/files/VDL/pdf/Susceptibility-Porcine-2018.pdf>

Antibiotic	<i>E. coli</i>	H <i>E. coli</i>
Ampicillin	28% (634)	23%(1807)
Ceftiofur	52%(629)	75%(1805)
Chlortetracycline	20% (390)	12%(1086)
Clindamycin	0% (631)	0%(1804)
Enrofloxacin	70% (634)	70%(1807)
Florfenicol	15%(629)	22%(1804)
Gentamicin	80% (634)	60%(1807)
Neomycin	79% (629)	60%(1804)
Oxytetracycline	19% (390)	11%(1086)
Penicillin	0% (631)	0%(1805)
Spectinomycin	34% (629)	26%(1804)
Sulfadimethoxine	51%(629)	33%(1804)
Tetracycline	18%(244)	10%(721)
Tiamulin	0%(629)	0%(1804)
Tildipirosin	NI	NI
Tilmicosin	0%(629)	0%(1804)
“Timethoprim/ Sulfamethoxazole”	77%(624)	69%(1807)
Tulathromycin	NI	NI
“Tylosin (Tartrate/Base)”	NI	NI

RESOURCES:

1. <https://vetmed.iastate.edu/vdpam/FSVD/swine/index-diseases/Ecoli-diarrhea>
2. <https://www.merckvetmanual.com/generalized-conditions/edema-disease/overview-of-edema-disease>



7.2 PASTEURELLA MULTOCIDA

Image credit: Dr. Karen Olsen University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

KEY DATA POINTS

- a. **Clinical impact:** Uncomplicated respiratory disease attributable to a single pathogen is the exception in modern swine production. Following the successful control of progressive atrophic rhinitis in the United States, most of the clinical impact of *Pasteurella multocida* is attributable to its role as a secondary pathogen in pneumonias initiated by other respiratory pathogens including *Mycoplasma hyopneumoniae*, PRRS and influenza viruses. Antimicrobial use is often necessary to treat outbreaks of respiratory disease to reduce the morbidity and mortality due to secondary bacterial pneumonias, particularly *P. multocida*. Incidence is highest in growing pigs, although outbreaks in sows have been reported rarely.
- b. **Economic impact:** Because *P. multocida* is ubiquitous in swine populations, and respiratory disease initiated by various pathogens is highly prevalent, it is likely that the economic impact of the organism as a secondary agent is substantial. However, no data are available that quantify this.
- c. **Transmissibility:** The epidemiology of *P. multocida* is not well understood. As the organisms are endemic in herds as normal flora, exposure occurs early in life. Direct nose to nose contact is thought to be the primary means of transmission among pigs. Within herd studies indicate that particular variants become predominant in individual herds.

Mixing pigs from multiple sources increases the likelihood of acquiring more virulent isolates.

- d. **Availability of effective antimicrobials:** A broad range of antimicrobials have label claims in the United States for *P. multocida* in swine, with options for injectable, water, and in feed administration. These include ceftiofur, tylosin, tilmicosin, chlortetracycline, oxytetracycline, enrofloxacin, florfenicol, tylvalosin, tulathromycin, and sulfamezathine. Because of the wide variability in incidence and severity of respiratory disease outbreaks in swine, selection of the appropriate drug and route(s) of administration is dependent on the epidemiologic scenario including the age of pigs and range of agents involved. Both the clinical history on a farm and antimicrobial susceptibility testing are important considerations in antimicrobial selection. An analysis of susceptibility patterns of *P. multocida* from swine from 2006 to 2016 indicates that the prevalence of resistance remains less than 5% for all antimicrobials tested apart from tetracyclines. The data indicated a modest increase in resistance to tetracyclines over the period studied, but no apparent trend to increase for the other antimicrobials tested. Multiple drug resistance in *P. multocida* in swine still appears to be uncommon and broad options for treatment remain available. However, resistance to tetracyclines should be anticipated to occur most commonly, and susceptibility testing is important for establishing protocols for treatment, control and prevention of secondary bacterial pneumonias caused by *P. multocida*.
- e. **Barriers to prevention:** The major obstacle to prevention is that *P. multocida* is an opportunistic pathogen that is part of the normal flora of the upper respiratory tract of pigs. Vaccination has been an effective aid in controlling atrophic rhinitis, but not pneumonia in pigs. The key to prevention is therefore prevention of prevalent primary respiratory pathogens of pigs, particularly PRRS, influenza and *M. hyopneumoniae*. Following the core principles of swine health management is also important, including not mixing pigs from different sources, adopting all-in/all-out management whenever practical, maintaining good hygiene, and minimizing environmental stresses due to temperature fluctuations and poor ventilation.

DATA VISUAL:

Susceptibility patterns (reported as % susceptible) of *Pasteurella multocida* types A and D at ISU VDL in 2018

<https://vdl.iastate.edu/sites/default/files/VDL/pdf/Susceptibility-Porcine-2018.pdf>

Antibiotic	PMul A	PMul D
Ampicillin	100%(95)	100%(56)
Ceftiofur	100%(95)	100%(56)
Chlortetracycline	97%(30)	100%(21)
Clindamycin	0%(95)	0%(56)
Enrofloxacin	100%(95)	100%(56)
Florfenicol	100%(95)	100%(56)
Gentamicin	99%(95)	100%(56)
Neomycin	98%(95)	100%(56)
Oxytetracycline	43%(30)	57%(21)
Penicillin	89%(95)	91%(56)
Spectinomycin	74%(95)	61%(56)
Sulfadimethoxine	52%(95)	52%(56)
Tetracycline	85%(65)	66%(35)
Tiamulin	78%(95)	16%(56)
Tildipirosin	98%(65)	97%(35)
Tilmicosin	98%(95)	55%(56)
Timethoprim/ Sulfamethoxazole	25%(95)	38%(56)
Tulathromycin	28%(95)	38%(56)
Tylosin (Tartrate/Base)	0%(95)	0%(56)

RESOURCES:

1. Oliveira Filho JX, et al. (2019) Pathogenic variability among *Pasteurella multocida* type A isolates from Brazilian pig farms. *BMC Vet Res.* 14:244.
2. Hayer SS et al. (2020) Prevalence and time trend analysis of antimicrobial resistance in respiratory bacterial pathogens collected from diseased pigs in USA between 2006-2016. *Res Vet Sci.* 128:135-144.\



7.3 SALMONELLA

Salmonella enterica serotype Choleraesuis, *Salmonella enterica* serotype Typhimurium, including monophasic variant 4,[5],12:i:-.

KEY DATA POINTS

In swine, salmonellosis has two distinct clinical presentations with different underlying pathophysiology. The host adapted *Salmonella enterica* serotype Choleraesuis is an invasive pathogen causing acute systemic disease including septicemia, pneumonia, hepatitis, and skin discoloration, with enteritis an inconsistent feature of the syndrome. In contrast, clinical infections with non-host-adapted serotypes (predominantly *Salmonella enterica* serotype Typhimurium, with others rarely causing disease) are typically limited to enterocolitis. Although *Salmonella enterica* serotype Choleraesuis is highly pathogenic in humans, infections are very rare. In contrast, *Salmonella enterica* serotype Typhimurium is among the most prevalent serotypes causing human salmonellosis worldwide, and has been associated with many different food vehicles, including pork products.

It is important to note that asymptomatic colonization of pigs with *Salmonella* occurs commonly in the alimentary tract and associated lymph nodes, but clinical salmonellosis occurs only sporadically. Consequently, definitive diagnosis requires demonstration of pathologic lesions in addition to culture of the organisms. Although all age groups are susceptible, disease occurs predominantly in weaned and growing pigs.

- a. **Clinical impact:** In the past, *Salmonella enterica* serotype Choleraesuis was a major pathogen of swine. However, the advent of effective vaccines has greatly reduced the impact of the disease, and vaccination is the core measure for controlling this pathogen. Although *Salmonella enterica* serotype Typhimurium is less pathogenic, it is a more prevalent pathogen in most swine producing countries and can be a serious problem in individual herds. Vaccines can also be effective in reducing the clinical impact of *Salmonella enterica* serotype Typhimurium disease.
- b. **Economic impact:** There is minimal information available on the economic impact of clinical salmonellosis in pigs in the United States. Reduction of the impact of *Salmonella enterica* serotype Choleraesuis by vaccination has been substantial.
- c. **Prevalence:** *Salmonella* generically can be considered ubiquitous in swine herds, and national surveys of growing pigs indicate a prevalence of asymptomatic fecal shedding of the order of 5 – 10% of animals. By comparison, outbreaks of clinical disease are sporadic, and there are no data on their incidence at herd level.
- d. **Transmissibility:** *Salmonella* transmission is predominantly fecal-oral, though infection via the respiratory tract may also occur, particularly with *Salmonella enterica* serotype Choleraesuis. There is evidence that the infectious dose is much lower via the respiratory route than via ingestion. *Salmonella* are durable bacteria with the ability to persist for months to years in the environment. Non-host-adapted serotypes have broad host ranges, and collectively may be considered ubiquitous. It is therefore difficult to exclude *Salmonella* from herds in the long term. Although efforts to produce ‘*Salmonella* free’ pigs have been pursued for decades, these have been motivated by human health concerns, with any reduction in swine disease being a secondary benefit. Although such programs in Norway, Sweden, and Finland have been deemed successful, they are expensive to maintain and may only be feasible in countries at high latitudes. In these programs, control of *Salmonella* in feed is a core activity. However, the serotypes of primary concern to swine health tend to be relatively uncommon among isolates from feed, and benefits to swine health from *Salmonella* control in feed have not been clearly shown.

e. **Availability of effective antimicrobials:** Due to the diversity of antimicrobial resistance phenotypes occurring in *Salmonella*, including the potential for multi-drug resistance (MDR), choices for treatment need to be based on antimicrobial susceptibility testing rather than generic guidelines. Given that clinical salmonellosis due to non-host-adapted serotypes may be considered a secondary disease, investigation of likely predisposing factors is of primary importance, and treatment with antimicrobials should be used only temporarily to reduce losses in outbreaks. However, there is little evidence implicating specific factors being responsible for predisposing to outbreaks of disease, beyond general recommendations regarding good management, and hygiene.

f. **Barriers to prevention:** Absolute exclusion of *Salmonella* from most herds is difficult to achieve in the long term. As *Salmonella* are common in many raw feed ingredients, prevention of introduction via feed is challenging. Most common interventions are heat treatment (e.g., pelleting) of feed or inclusion of organic acids (formic acids), but these approaches do not reliably eliminate risks of introduction into herds. Immunity to *Salmonella* is considered serotype specific, although some cross protection among related serotypes (e.g., within serogroups) that share common antigens is likely. Live vaccines appear to stimulate better immunity than killed vaccines. New approaches in vaccinology, such as vaccines against iron capturing proteins (siderophores) are in development and have some promise for providing broader protection.

A close-up photograph of a petri dish containing a red agar medium. Numerous small, white, circular bacterial colonies are visible, scattered across the surface. The colonies appear to be arranged in some patterns, possibly from a streak or spread plate. The background is dark, making the red agar and white colonies stand out.

7.4 STREPTOCOCCUS SUIS

Image credit: University of Minnesota Veterinary Diagnostic Laboratory, Bacteriology Section

KEY DATA POINTS

- a. **Clinical impact:** *Streptococcus suis* emerged to become a significant pathogen of pigs globally around the 1970's. Although all age-groups can be affected, outbreaks of clinical disease occur most commonly in weaned pigs and are rare in late finishing pigs and adults. Acute neurological disease and septicemia are the hallmarks of the infection associated with meningitis, polyserositis, arthritis, and endocarditis. This clinical pattern of acute septicemia and meningitis is similar in swine and human infections. Both individual cases and outbreaks occur sporadically, and the clinical impact can be highly variable over time within sites. Concurrent infections, particularly PRRS infection, and other stressful events can predispose to outbreaks. The clinical course is also highly variable, ranging from sudden death without premonitory signs in peracute infections, to chronic infections involving poor appetite, lameness and endocarditis. The attack rate is generally less than 5%, but much higher rates of mortality (20 – 30%) can occur if outbreaks are not promptly treated.
- b. **Economic impact:** Although *S. suis* is universally recognized as a premier swine pathogen, systematic data on its overall economic impact are not available. However, due to the rapid onset of disease and potential for high mortality in the absence of treatment, timely and appropriate use of antimicrobials to control outbreaks is essential.
- c. **Prevalence:** *S. suis* is ubiquitous in swine populations, but the incidence of clinical disease is highly variable both within and among herds. Sporadic individual cases (<0.5% cumulative incidence) contribute to endemic mortality in weaned pigs and may go undiagnosed. Charting mortality can be a sensitive tool for rapid detection of outbreaks of neurological disease, enabling prompt herd treatment with antimicrobials to prevent high morbidity and mortality.
- d. **Transmissibility:** *S. suis* are normal flora in the upper respiratory and genital tract of pigs. Exposure and colonization of neonatal pigs occurs very early in life. The factors that contribute to systemic invasion and disease in individual pigs, and to outbreaks in herds, are not well understood. However, the pathogenicity of particular strains and the occurrence of stress due to concurrent disease or environmental factors are important. Effective generic *S. suis* vaccines have not proven successful, and outcomes of autogenous vaccine use are highly variable. There is some promise that vaccine efficacy may be improved through use of whole genome sequencing.
- e. **Availability of effective antimicrobials:** As with most streptococci, beta lactam antimicrobials (e.g., penicillin, ampicillin, amoxicillin) have long been successfully employed to treat, control and prevent cases of *S. suis* infection in pigs globally. However, in the United States, none of these antimicrobials have label claims for *S. suis*, therefore they must be prescribed in accordance with AMDUCA for extralabel use. In the United States, both ceftiofur (cephalosporin, therefore also a beta lactam antimicrobial) and enrofloxacin (fluoroquinolone) products have label claims for *S. suis* infections by injection. However, given that both these classes are categorized as critically important for human medicine by the FDA, and have restrictions on extralabel use (illegal in the case of fluoroquinolones), they should be avoided as empirical treatments. Where injectable treatment is indicated, extralabel use of older beta lactam drugs should be considered in the absence of

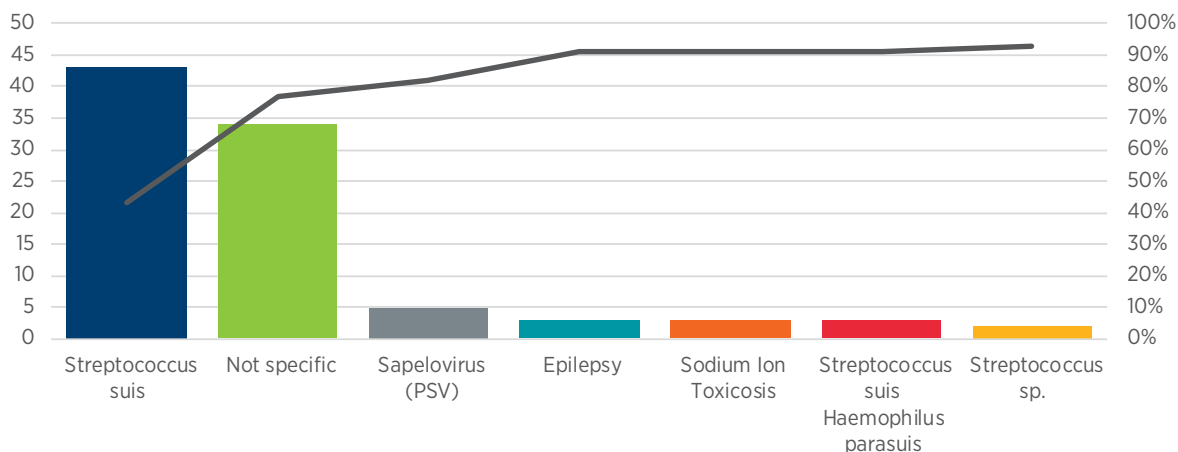
evidence of lack of efficacy. Antimicrobials with label claims for administration in water for *S. suis* are florfenicol and tylvalosin. Susceptibility patterns of *S. suis* appear to have been relatively stable in the United States over decades, with relatively low prevalence of resistance (<10%) for most antimicrobials tested apart from tetracyclines¹. Notably, the prevalence of resistance to penicillin was 6.9% (albeit with some evidence for increased resistance in the latter years) over 10 years (2006 – 2016), despite widespread use of this antimicrobial in swine for decades. Selection of antimicrobials should be guided by clinical history and susceptibility testing of isolates obtained from systemic sites (e.g., brain, liver, spleen).

f. **Barriers to prevention:** The major barrier to prevention of *S. suis* infections is the lack of reliable vaccines, together with the challenge of controlling PRRS and influenza A viruses in the U.S. swine industry, which predispose to outbreaks. Elimination of the pathogen is unrealistic as it is normal flora that is acquired early in life, and cross immunity among strains appears to be minimal. Following the core principles of swine health management is also important, including: not mixing pigs from different sources, adopting all-in/all-out management whenever practical, maintaining good hygiene, and minimizing environmental stresses due to temperature fluctuations and poor ventilation.

DATA VISUAL:

Chart illustrates the significance of *S. suis* as the major cause of neurological disease in pigs in the United States (data from Swine Disease Reporting System <https://www.swinehealth.org/wp-content/uploads/2020/01/SHIC-109-DSDMR-1-6-2020.pdf>)

NERVOUS DISEASE DIAGNOSIS



RESOURCES:

1. Hayer SS et al. (2020) Prevalence and time trend analysis of antimicrobial resistance in respiratory bacterial pathogens collected from diseased pigs in USA between 2006-2016. *Res Vet Sci.* 128:135-144.
2. <https://www.merckvetmanual.com/generalized-conditions/streptococcal-infections-in-pigs/streptococcus-suis-infection>
3. <https://www.chp.gov.hk/en/healthtopics/content/24/3648.html>