The Need for Antimicrobial Stewardship in the Commercial Pet Industry

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What is Stewardship?

- Stewardship implies a process of caring and responsible management

- Prevent multidrug resistant bacteria in veterinary and human medicine, and in the environment

- Need to apply stewardship efficiently and economically to the use of antimicrobial drugs so that we can preserve and extend their efficacy
Fact: It’s Hard to Sell Prevention!
CDC Antimicrobial Stewardship Activities

- Set national goals to improve antibiotic use.» Cut inappropriate prescribing practices by 50% in doctors’ office and 20% in hospitals.

- Implement effective stewardship programs using CDC’s Core Elements and recommendations in doctors’ offices, hospitals, and nursing homes, integrated with sepsis early recognition programs.

- Support collaboration to develop and evaluate stewardship activities.

- Provide data about antibiotic use and trends to better understand prescribing practices. For example:» Expand and use CDC’s National Healthcare Safety Network (NHSN) data to guide improvement of antibiotic use in hospitals.» Better understand differences in prescribing patterns in doctors’ offices by states and develop strategies for improvement.

- Expand State HAI/AR Prevention Programs to help implement best practices around improving antibiotic prescribing.

- Support early recognition of sepsis. Heighten public awareness to prevent sepsis and its complications, and to improve antibiotic use.
Antibiotic Resistance (AR) Solutions Initiative

Resistance to important antibiotics for human health is increasing.
In the U.S., an estimated 400,000 people are sickened with resistant *Campylobacter* or *Salmonella* every year.

How will CDC’s Solutions Initiative fight foodborne infections?

- **Detect and describe resistant bacteria rapidly.**
  Increase state laboratory capacity to rapidly uncover foodborne drug-resistant bacteria, including *Campylobacter* and *Salmonella*, using whole genome sequencing (WGS).

- **Find outbreaks faster by increasing lab testing.**
  Test every *Salmonella* isolate for drug resistance.

- **Improve health outcomes.**
  With increased lab capacity, track and investigate life-threatening *Salmonella* infections to prevent outbreaks and provide rapid response.

- **Promote responsible antibiotic use in food-producing animals.**
  Ensure practicing veterinarians have the tools, information, and training to prevent drug resistance by promoting responsible use of antibiotics.
What happens when we don’t practice stewardship?
Puppies Linked To Bacterial Infection Outbreak Across 12 States

Puppies, like this one with Miley Cyrus, can be cute. But take proper precautions when handling them. [+]

Puppy dog eyes can be adorable. Puppy love can be sweet. Puppy dog bloody diarrhea, not so much.
Background: *Campylobacter jejuni* Characteristics

- Gram-negative, microaerophilic
- Difficult to grow in culture
- Infection usually from consumption of contaminated food or water
- Infection also through contact with infected animals
Background: Human *Campylobacter* Infection

- CDC estimates 1.3 million people are affected each year in the U.S.
- Severe diarrhea, can be hemorrhagic
- Incubation: 2 to 5 days
- Duration: approximately 7 days
- Complications
  - Immune-mediated arthritis
  - Irritable bowel syndrome
  - Guillain-Barré syndrome
Background: *Campylobacter* Antibiotic Resistance

- Most treatment for *Campylobacter* infection is supportive
- Fluoroquinolone and macrolide antibiotics are first-line choice
- Increasing resistance since 1997
  - Fluoroquinolone
    - 27%
  - Macrolide
    - 2%
Background: *Campylobacter* in Dogs

- Dogs can be healthy carriers of *Campylobacter*
- Dogs in crowded conditions are more likely to be infected
- Clinical infection occurs more frequently in puppies (<12 month of age)
- Dogs with suspected *Campylobacter* infection are usually treated supportively
  - In severe cases antibiotics are selected empirically
Outbreak Investigation Objectives

1. Identify additional human illnesses
2. Determine the source of Campylobacter infections
3. Develop recommendations
Results: Descriptive Epidemiology

- 113 cases from 17 states
  - 38 (34%) of cases identified by WGS
- Reported and estimated illness onset dates (n=106): 1/12/16–1/7/18
- 99% (104/105) report puppy exposure
- 87% (89/102) report Retail Chain P exposure from 12 states
  - 25 (23%) employees
- 10 cases without exposure to Retail Chain P report exposure to another pet store
Results: Patient Demographics and Outcomes

Age range
(n = 110)

<1 year
27 years
Median
86 years
Results: Patient Demographics and Outcomes

Age range (n = 110)
- <1 year
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Median

Sex (n = 111)
- Female 69 (63%)
-
Results: Patient Demographics and Outcomes

Age range (n = 110)
- <1 year
- 27 years
- Median
- 86 years

Sex (n = 111)
- Female 69 (63%)

Hospitalized (n = 104)
- 23 (22%)
Results: People with *Campylobacter* Infection Linked to Retail Chain P Puppies, by State of Residence, (n=113)
Results: People with *Campylobacter* Infection Linked to Retail Chain P Puppies, by Date of Illness Onset, (n=111)
Overview: Objective 2

Determine the source of *Campylobacter* infection

1. Identify puppies carrying outbreak strains by sampling puppies in stores

2. Use information from puppy records to conduct traceback
Methods: Laboratory Testing
Methods: Laboratory Testing

Polymerase Chain Reaction (PCR)

Culture
Methods: Laboratory Testing

Polymerase Chain Reaction (PCR) → Culture → Whole Genome Sequencing
Methods: Laboratory Testing

Polymerase Chain Reaction (PCR) → Culture → Whole Genome Sequencing → Antibiotic Resistance
Methods: Laboratory Testing

211 samples

- Polymerase Chain Reaction (PCR)

21 *Campylobacter jejuni* positive

- Culture

18 *Campylobacter*

- Whole Genome Sequencing

10 related to the outbreak

- Antibiotic Resistance

10 isolates
Whole Genome Sequencing: *Campylobacter jejuni* Isolates

10

38

Created by Hysen Drogu from the Noun Project
Antibiotic Susceptibility Testing

Predicted resistant/resistant

Predicted susceptible/susceptible

Puppy

Human
Antibiotic Resistance Summary

- Observed in all three sub-clades
- Observed in human and puppy isolates
- Predicted resistance and antibiotic susceptibility testing correlated well

Where is multidrug resistance coming from?
Indication for Antibiotics Administered to 141 Puppies

- None: 5%
- Prophylaxis only: 55%
- Treatment and prophylaxis: 38%
- Treatment only: 1%
<table>
<thead>
<tr>
<th>Antibiotic Class</th>
<th>Number of Days Administered</th>
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<tbody>
<tr>
<td>Nitroimidazoles</td>
<td>997</td>
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<tr>
<td>Sulfa drugs</td>
<td>620</td>
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<tr>
<td>Tetracyclines</td>
<td>422</td>
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<tr>
<td>Macrolides</td>
<td>253</td>
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<td>Quinolones</td>
<td>111</td>
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<td>Penicillins</td>
<td>67</td>
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<td>37</td>
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<td>Aminoglycosides</td>
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<td>Cephalosporins</td>
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<td>Lincosamide</td>
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Need for Stewardship

- Antibiotics such as azithromycin (Zithromax) or erythromycin can shorten the duration of symptoms if it’s given nearly in the illness. Azithromycin (Zithromax) 5 mg/lb daily for 5 days then every 5 days for three treatments.
- Erythromycin is currently unavailable.
- Cephalexin at 15 mg/lb twice daily has also been used successfully.
- Tylan at 10mg/lb given twice a day can be given orally or mixed in the water, using it as the only water source.
- You need to keep them on the medication for a minimum of 21 days to clear Campylobacter - we don’t want to create carriers by stopping treatment too early.
- Baytril has been effective, but fluoroquinolones are contraindicated due to the cartilage damage that may occur with long term use in neonates. Avoid using Baytril in puppies and never use it longer than one week in neonates.
- Chloramphenicol has been used effectively in humans, but has not been reliable in dogs.

Campylobacteriosis - Frustrating and Costly to Deal With!

Campylobacteriosis is an infectious diarrheal disease that is found in both animals and people. Campylobacter can be found in 20 to 30% of dogs or cats with diarrhea, and 10% of the normal dogs or cats in an infected cattery kennel or hospital intake kennel. It’s also referred to as “Stool Scour” since it’s very common in show dogs.

Transmission to neonates is through infected feces and through contaminated food and water. The bacteria are shed in the feces of infected and asymptomatic carriers - many chickens, turkeys, and birds are infected but show no signs of illness. It can also easily be spread through an infected water source or container, especially chicken. Puppies or kittens under six months of age are the most susceptible. Dogs can over 6 months are quite resistant to diarrhea, but they may become asymptomatic carriers, which keeps the organism in the cattery or kennel.

Clinical Pictures:
Neonates can develop diarrhea and enteritis in the weaning period. Clinical signs may vary from mild to severe, depending on the stage of the neonate - you may see loose feces, watery diarrhea or bloody mucoid diarrhea. Unlike many viral infections, puppies and kittens generally do not have a fever, vomit or lose their appetite. This helps you distinguish Campylobacteriosis from Parvovirus.

Treatment:
There are many different treatments that are available with varying amounts of success. You should talk to your veterinarian to find the best option for your dog. You need to keep them on the medication for at least 21 days to clear Campylobacter - we don’t want to cause carriers by stopping treatment too early.

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• Cephalexin at 15 mg/lb twice daily has also been used successfully.
• Tylan at 10mg/lb given once a day can be given orally or mixed in the water, using it as the only water source.
• You need to keep them on the medication for a minimum of 21 days to clear Campylobacter - we don’t want to cause carriers by stopping treatment too early.
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• Chloramphenicol has been used effectively in humans, but has not been reliable in dogs.

Whole kennel treatment:
We need to remember there are carriers in the kennel or cattery that are leading the bacteria to the neonate. In treating the whole kennel, we can target the asymptomatic carriers and eliminate the bacteria out of the kennel.
• Tetracycline in the water can be used with adults, but not the puppies or neonate mothers in the last trimester. Tetracycline should not be used in puppies and kittens because of tooth staining.
• Tylan or LZ 50 can be used in the water or drinking bowls. Both can be used in a self medicator for automatic waterers systems or added to water bowls.

By understanding the disease and eliminating it from the adult carriers we can control most cases in future puppies or kittens - the goal is to treat in the next litter!
Whole kennel treatment—CDC Does NOT


- We need to remember there are carriers in the kennel or cattery that are seeding the bacteria to the neonate. In treating the whole kennel, we can target the asymptomatic carriers and eliminate the bacteria out of the kennel.
- Tetracycline in the water can be used with adults, but not the babies or pregnant mothers in the last trimester.
- Tetracycline should not be used in puppies and kittens because of teeth staining.
- Tylan or LS 50 can be used in the nursery or whelping area. Both can be used in a self medicater for automatic watering systems or added to water bowls.
Antimicrobial Stewardship Definition and Core Principles

Antimicrobial Stewardship for Veterinarians Defined

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.

Core Principles of Antimicrobial Stewardship in Veterinary Medicine

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, respecting the client’s available resources.
Traceback: Routes of Distribution

Culture confirmed, tested in store

PCR, tested in store

Epidemiologic link to case

Breeder

Breeder

Breeder

Distributors
Traceback: Routes of Distribution

Culture confirmed, tested in store

PCR, tested in store

Epidemiologic link to case

8 Distributors

25 Breeders
# Recommendations

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Communication with New Puppy Owners

- Exam
- Vaccinations
- Ask questions
- Diet
- Training
- De-worming
- Zoonotic Disease?
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Conclusions

- Large, multistate *Campylobacter* illness outbreak linked to dogs
- No single source of infection, but likely disseminated throughout the industry
- Outbreak strain is resistant to common first-line antibiotics used to treat *Campylobacter* infections
- Highlights antibiotic resistance and the need for ongoing antibiotic stewardship
Poopy Puppies Poisoning People

By Bruce Clark on October 30, 2017

POSTED IN FOODBORNE ILLNESS OUTBREAKS

- CDC, several states, and the U.S. Department of Agriculture’s Animal and Plant Health Inspection Service (USDA-APHIS) are investigating a multistate outbreak of multidrug-resistant *Campylobacter* infections.

- *Campylobacter* bacteria isolated from clinical samples from people sickened in this outbreak were found to be resistant to commonly recommended, first-line antibiotics. This antibiotic resistance means it may be difficult to treat infections with the outbreak strain with the antibiotics usually prescribed for *Campylobacter* infections.
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
References