Drugs, Bugs and Pugs:
Antimicrobial Resistance in Pets and the People That Love Them

Stephen Cole VMD, MS, DACVM

Assistant Professor of Microbiology

University of Pennsylvania, School of Veterinary Medicine

Outline

- Carbapenem-resistant Enterobacterales
- ESBL-producing Enterobacterales
- MRSA
- Extensively-drug resistant *Campylobacter*
- VRE
- C. difficile
- Antifungal resistant organisms

Samantha

- 13 YO FS Great Dane
- Hx: Megaesophagus
- Lethargic w/ obvious increased respiratory rate & effort
- Notable PE Findings: T-104.2 F and crackles in cranioventral thorax on auscultation.
- Radiographs suggestive of aspiration pneumonia
- Hospitalized in ICU and begin empiric antimicrobial therapy with IV ampicillin/enrofloxacin

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Samantha- Day 4

- **Initial Culture result**
  - **Beta hemolytic *Streptococcus***
- **No clinical or radiographic improvement noted.**
- **Re-anesthetized for additional endotracheal wash for culture.**
- **Empirically switched to clindamycin and ceftazidime.**

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Samantha- Day 6

2nd Culture Results:

Sensitivity Analysis	Escherichia coli	
Amikacin	<=2	S
Amoxicillin/K Clavulanate	>=32	R
Ampicillin	>=32	R
Cefalexin	>=8	R
Chloramphenicol	>=64	R
Enrofloxacin	>=4	R
Gentamicin	8	R
Imipenem	4	R
Marbofloxacin	>=4	R
Penicillin		
Piperacillin	>=128	R
Tetracycline	>=16	R
Tobramycin	>=16	R
Trimethoprim/Sulfamethoxazole	>=320	R
Vancomycin		

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Bruno

- 10 YO MC Rottweiler admitted on same day as Samantha
- Housed in ICU following adrenalectomy (pheochromocytoma).
- Following surgery had persistent fever and dyspnea despite antimicrobial therapy.
- Culture of lung tissue yields:

Sensitivity Analysis	Escherichia coli	
Amikacin	<=2	S
Amoxicillin/K Clavulanate	>=32	R
Ampicillin	>=32	R
Cefalexin	>=8	R
Chloramphenicol	>=64	R
Enrofloxacin	>=4	R
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Imipenem	4	R
Marbofloxacin	>=4	R
Penicillin		
Piperacillin	>=128	R
Tetracycline	>=16	R
Tobramycin	>=16	R
Trimethoprim/Sulfamethoxazole	>=320	R
Vancomycin		

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Della

- 9 YO FS Beagle mix presented to cardiology service for recheck following pacemaker placement and ICU stay.
- Suffered AKI during procedure from prolonged anesthesia (suspected).
- Urinalysis recheck revealed +++ bacterial rods.

Culture yields:

Sensitivity Analysis	Escherichia coli	
Amikacin	<=2	S
Amoxicillin/K Clavulanate	>=32	R
Ampicillin	>=32	R
Cefalexin	>=8	R
Chloramphenicol	>=64	R
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Tetracycline	>=16	R
Tobramycin	>=16	R
Trimethoprim/Sulfamethoxazole	>=320	R
Vancomycin		

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- 10 YO FS Poodle with history of laryngeal paralysis presented to IM service for recheck following hospitalization for aspiration pneumonia.
- Static clinical signs with radiographic progression.
- Anesthetized for endotracheal wash for culture.

Sensitivity Analysis	Escherichia coli	
Amikacin	<=2	S
Amoxicillin/K Clavulanate	>=32	R
Ampicillin	>=32	R
Cefalexin	>=8	R
Chloramphenicol	>=64	R
Enrofloxacin	>=4	R
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Penicillin		
Piperacillin	>=128	R
Tetracycline	>=16	R
Tobramycin	>=16	R
Trimethoprim/Sulfamethoxazole	>=320	R
Vancomycin		

Talia

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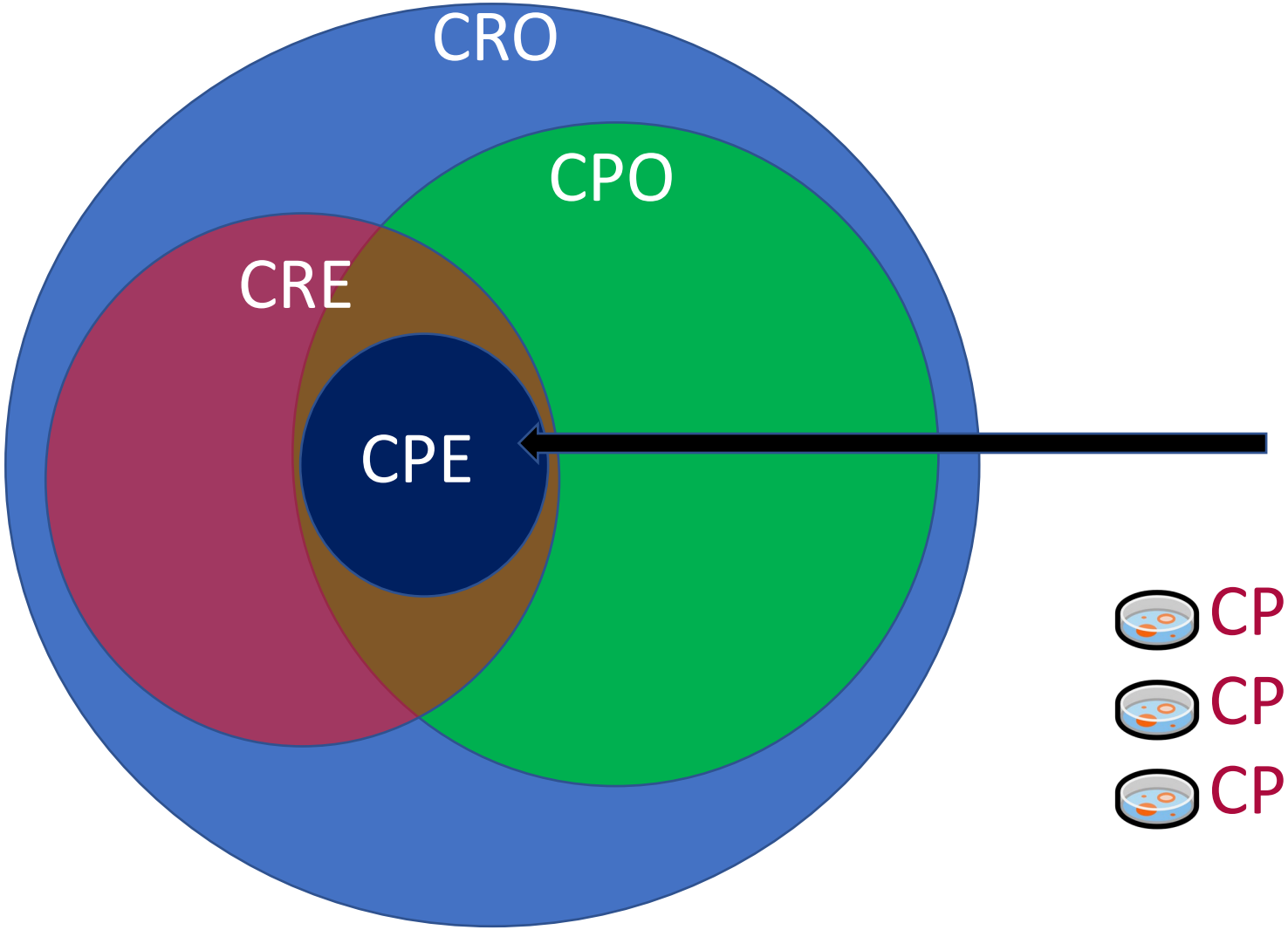
What are CP-CRE?

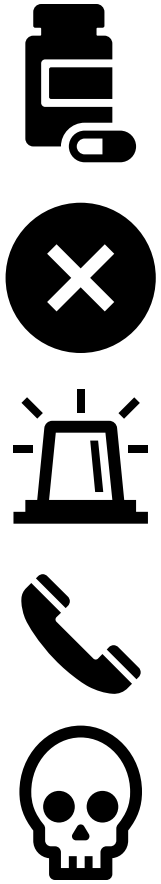


Gram Negative bacteria that are resistant to a carbapenem drug (ertapenem, imipenem, meropenem)

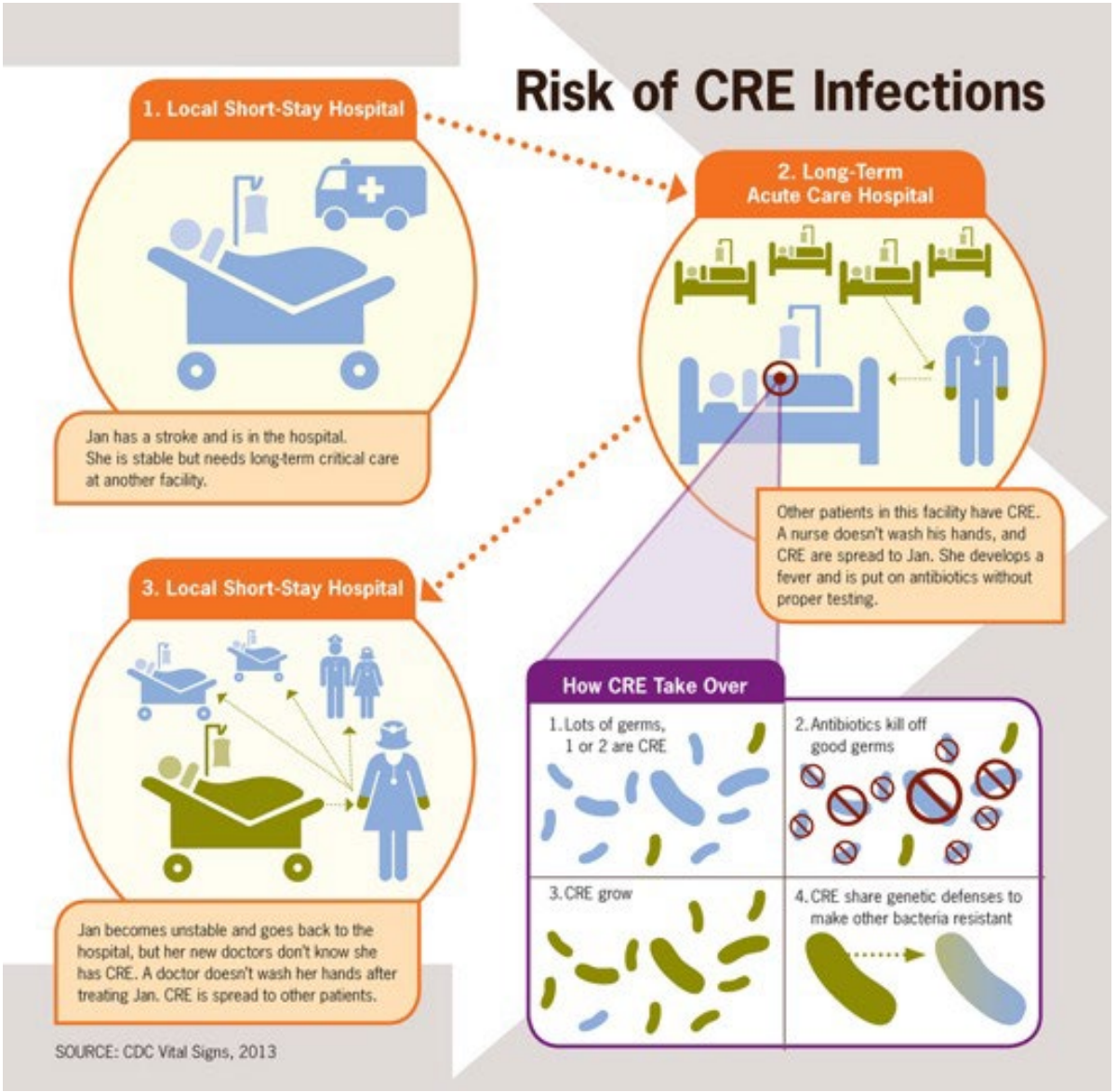
- CP-CR- *Escherichia coli*
- CP-CR- *Klebsiella pneumoniae*
- CP-CR- *Enterobacter cloacae*

Why do CPE Matter?

- **Carbapenems are a drug of last-resort for the treatment of multi-drug resistant Gram-negative infections.**
- **Typically resistant to MOST/ALL of the antimicrobials that would be used to treat infections.**
- **Considered one of the most URGENT threat with regards to AMR bacteria by CDC.**
- **Reportable in many jurisdictions.**
- **Deadly- Mortality rates can range from 60-90% in bacteremic patients.**

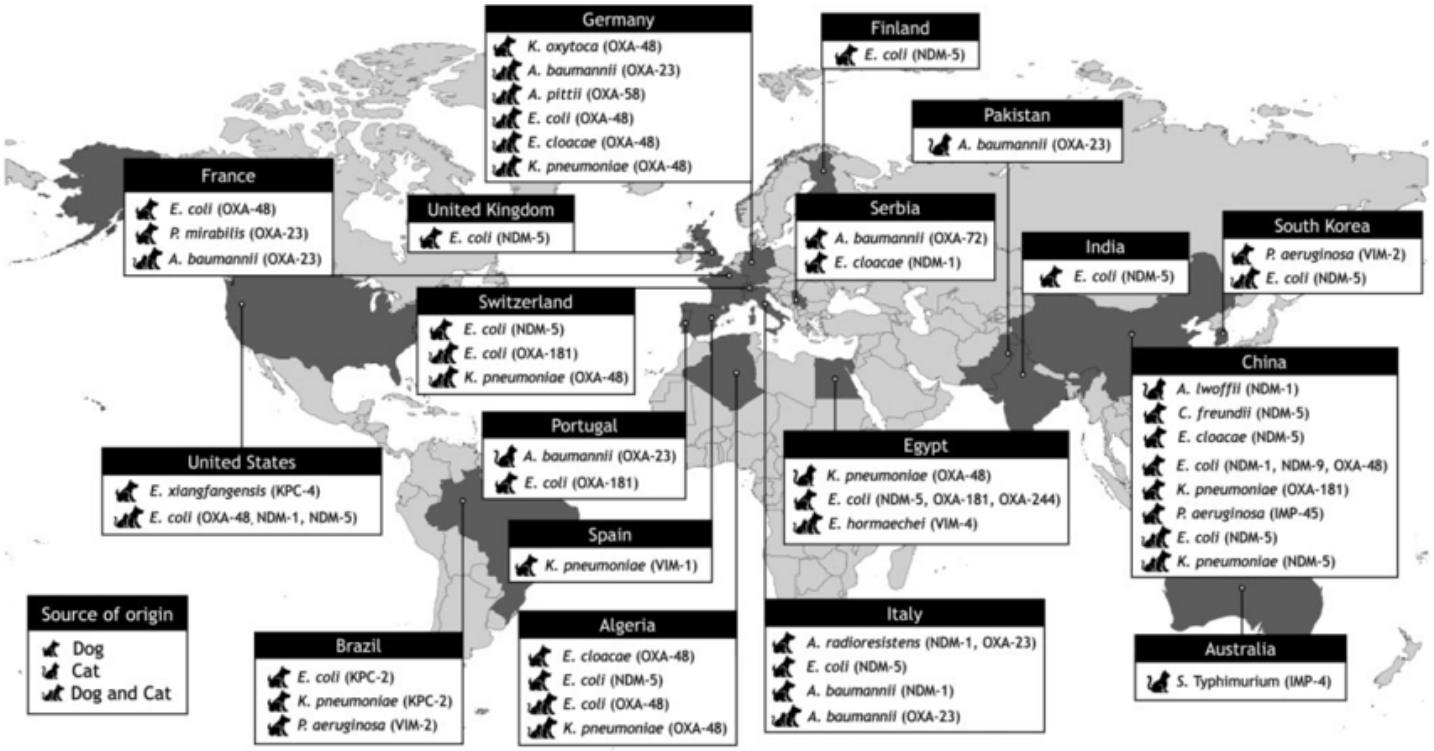


Human Medicine- Primarily Hospital Acquired Infection (HAI)

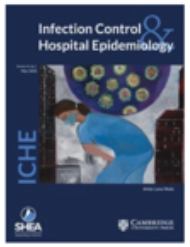


CP-CRE have been reported rapidly and globally in animals

- *Sellera 2021*



Outbreaks will happen in veterinary facilities



Infection Control & Hospital Epidemiology

An Outbreak of New Delhi Metallo--Lactamase-5 (blaNDM-5)–Producing *Escherichia coli* in Companion Animals in the United States

Published online by Cambridge University Press: **02 November 2020**

Shelley C. Rankin and Stephen D. Cole

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CIDRAP Center for Infectious Disease Research and Policy

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FEATURED NEWS TOPICS Novel Coronavirus Ebola MERS-CoV Chronic Wasting Disease

US veterinary hospital faces rare antibiotic-resistant E coli

Filed Under: Antimicrobial Stewardship; NDM-1

Chris Dall I News Reporter I CIDRAP News I Jan 10, 2020

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On Apr 1, 2019, Shelley Rankin, PhD, the chief of clinical microbiology at the University of Pennsylvania's School of Veterinary Medicine, got a surprising notification from the US Food and Drug Administration (FDA).

Kerkez / iStock

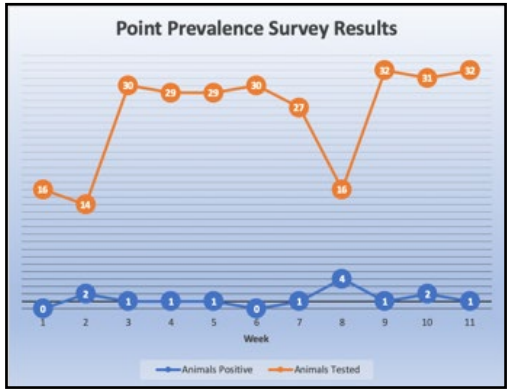
Four times a year, Rankin and her colleagues at PennVet ship off bacterial isolates from the school's veterinary hospitals to the FDA's Veterinary Laboratory Information and Response Network (Vet-LIRN). PennVet is among a network of veterinary labs across the country that submits animal isolates for antibiotic resistance surveillance and whole-genome sequencing.

The notification Rankin received from Vet-LIRN that day regarded a set of isolates submitted at the end of 2018. Among the isolates was a sample of carbapenem-resistant *Escherichia coli* from one of a handful of sick cats and dogs treated at PennVet's Ryan Veterinary Hospital in July and August of 2018.

Since none of the animals had previously been treated with carbapenems, a last-resort antibiotic, Rankin and her colleagues suspected that Vet-LIRN might find a carbapenem-resistance gene in the *E coli* isolate. But it wasn't the gene they expected to find.

'Brand new' vet medicine finding

In Philadelphia's numerous human hospitals, Rankin explained, there's a reasonably high prevalence of



Clinical Epidemiology Study

TABLE 1

Comparisons of Clinical Exposures of Carbapenem-Resistant *Escherichia coli* Case and Control Patients

Type of Clinical Exposure	Cases (n = 15), n (%)	Controls (n = 30), n (%)	Odds Ratio	95% Confidence Interval	*P* Value
Services					
Anesthesia	11 (73.3)	8 (26.7)	12.79	1.59–102.90	.017*
Surgery	8 (53.3)	6 (20.0)	4.0	1.03–15.60	.046*
Intensive care unit	7 (46.7)	4 (13.3)	6.97	0.81–60.20	.076
Cardiology	4 (26.7)	3 (10.0)	5.26	0.55–50.02	.15
Radiology	11 (73.3)	19 (63.3)	1.52	0.42–5.57	.53
Emergency	9 (60.0)	19 (63.3)	0.74	0.11–4.90	.75
Internal medicine	4 (26.7)	10 (33.3)	0.76	0.21–2.74	.67
Dermatology	1 (6.7)	1 (3.3)	2	0.13–31.98	.62
Procedures					
Endotracheal intubation	11 (73.3)	10 (33.3)	10	1.23–81.47	.03*
IV catheterization	6 (40.0)	9 (30.0)	1.88	0.39–8.92	.42
Insertion of medical device	11 (73.3)	15 (50.0)	3.7	0.72–18.97	.12
Computed tomography scan	3 (20.0)	3 (10.0)	2.38	0.38–14.97	.36
Medications					
Glucocorticoids	6 (40.0)	5 (16.7)	3.14	0.76–13.00	.12
Antibiotic use	11 (73.3)	19 (63.3)	2.17	0.36–12.94	.4

Lavigne SH, Cole SD, Daidone C, Rankin SC. Risk Factors for the Acquisition of a blaNDM-5 Carbapenem-Resistant Escherichia coli in a Veterinary Hospital. J Am Anim Hosp Assoc. 2021 May 26;57(3).

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Antimicrobial Stewardship

Sensitivity Analysis	Escherichia coli	
Amikacin	<=2	S
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Tetracycline	>=16	R
Tobramycin	>=16	R
Trimethoprim/Sulfamethoxazole	>=320	R
Vancomycin		

JSAP JOURNAL OF SMALL ANIMAL PRACTICE
BSAVA BRITISH SMALL ANIMAL VETERINARY ASSOCIATION

ORIGINAL ARTICLE

Carbapenem prescribing at a veterinary teaching hospital before an outbreak of carbapenem-resistant *Escherichia coli*

S. D. Cole, D. Perez-Bonilla, A. Hallowell, L. E. Redding

First published: 08 March 2022 | https://doi.org/10.1111/jsap.13481

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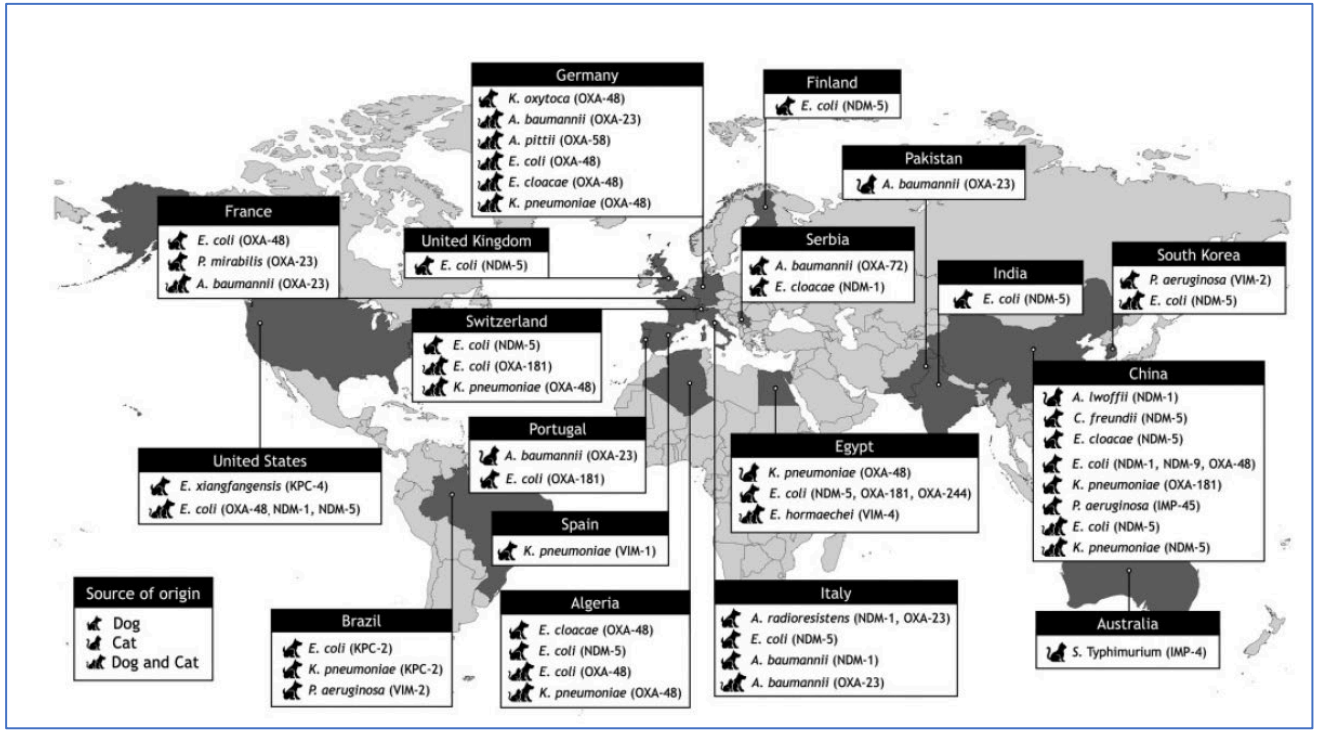
CPO's in Companion Animals



Sellera FP, Da Silva LCBA, Lincopan N. Rapid spread of critical priority carbapenemase-producing pathogens in companion animals: a One Health challenge for a post-pandemic world. J Antimicrob Chemother. 2021 Aug 12;76(9):2225-2229.

Sharing more than friendship – transmission of NDM-5 ST167 and CTX-M-9 ST69 *Escherichia coli* between dogs and humans in a family, Finland, 2015

Thomas Grönthal[1], Monica Österblad[2,3], Marjut Eklund[1], Jari Jalava[3], Suvi Nykäsenoja[4], Katariina Pekkanen[4], Merja Rantala[1]
1. Faculty of Veterinary Medicine, University of Helsinki, Helsinki, Finland
2. Sydspetsens miljöhälsa, Hangö, Finland
3. National Institute for Health and Welfare, Turku, Finland
4. Food Safety Authority Evira, Helsinki, Finland

Correspondence: Thomas Grönthal (thomas.gronthal@helsinki.fi)

Volume 75, Issue 3
March 2020

JOURNAL ARTICLE

Employees of Swiss veterinary clinics colonized with epidemic clones of carbapenemase-producing *Escherichia coli* FREE

Andrea Endimiani ✉, Michael Brilhante, Odette J Bernasconi, Vincent Perreten, Janne S Schmidt, Valentina Dazio, Aurélien Nigg, Stefanie Gobeli Brawand, Stefan P Kuster, Simone Schuller ... Show more
Author Notes

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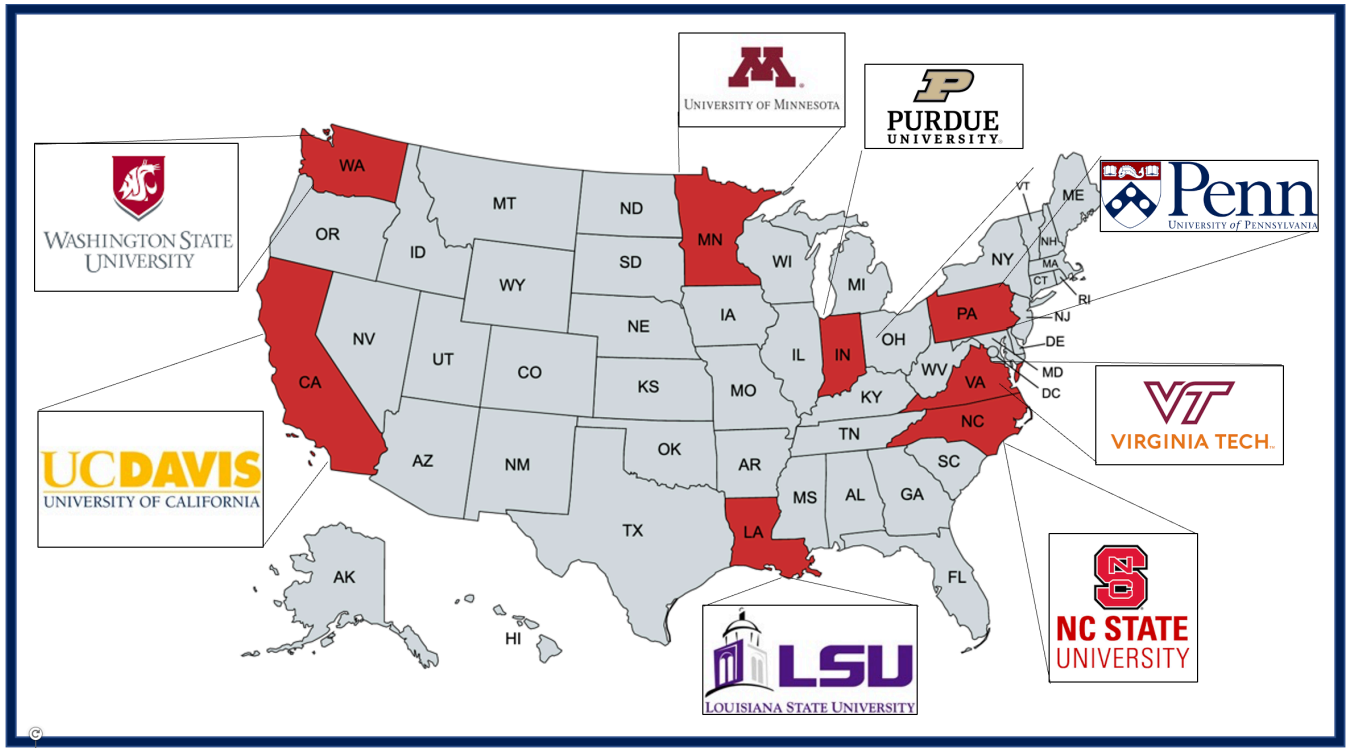
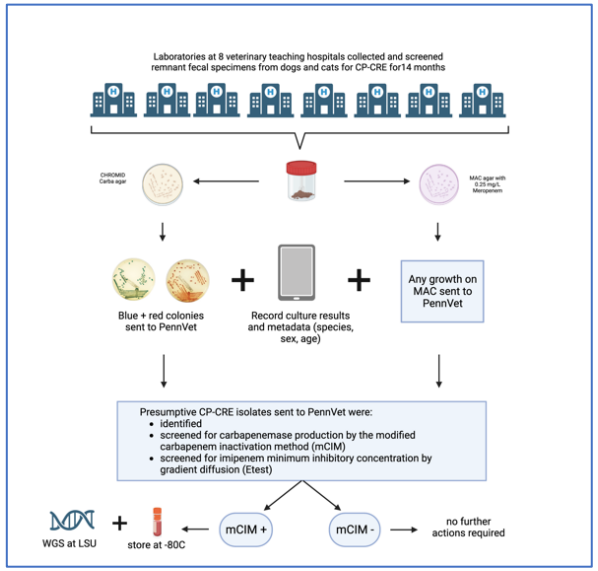
How Prevalent are CPE?





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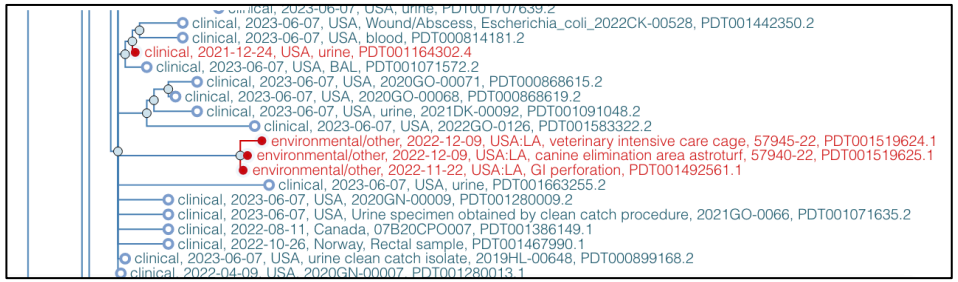
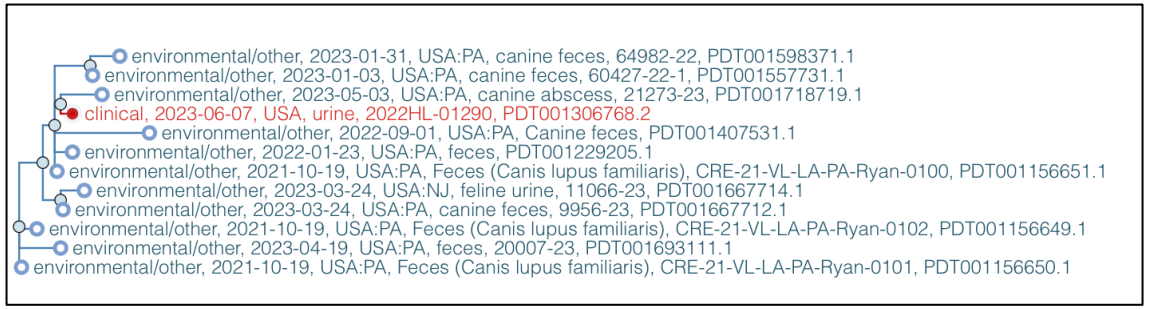
Whole Genome Sequencing Reveals ‘One Health’ Clusters

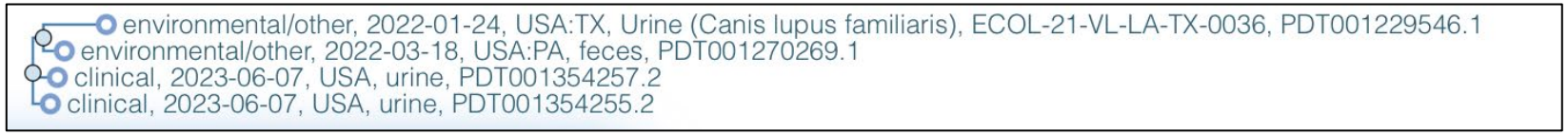


Louisiana
13 SNPs

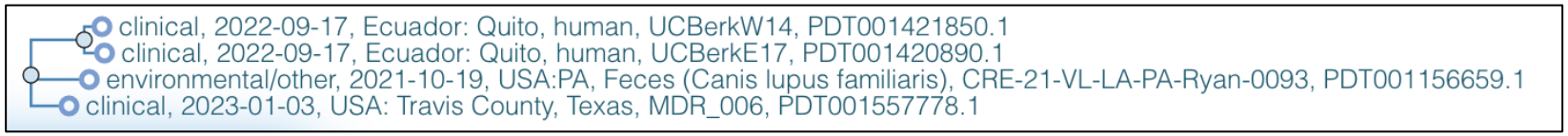
???/Minnesota
15 SNPs



NY/NJ/PA
3 SNPs

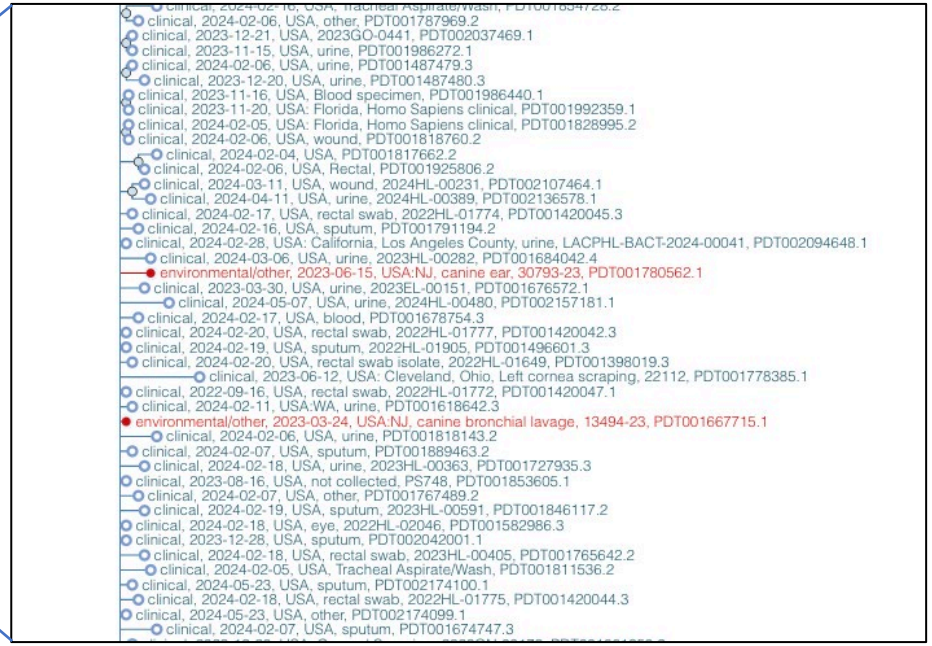


MI/TX/PA
14 SNPs



Equador/PA
38 SNPs

CRPA in Dogs One Health Investigation



VIM-GES-CRPA

NJ Health New Jersey Department of Health

NJCDS New Jersey Communicable Disease Service

CANINE CASES OF EXTENSIVELY-DRUG-RESISTANT PSEUDOMONAS AERUGINOSA LINKED TO MULTISTATE OUTBREAK ASSOCIATED WITH ARTIFICIAL TEARS
Guidance

Date: August 8, 2023

Public Health Message Type: ☐ Alert ☒ Advisory ☐ Update ☐ Information

Intended Audience: ☒ All public health partners ☐ Healthcare providers ☐ Infection preventionists ☒ Local health departments ☐ Schools/child care centers ☐ ACOs ☒ Animal health professionals ☒ Other: Animal Health Diagnostic Laboratories

Key Points or Updates:

(1) A rare strain of carbapenem resistant *Pseudomonas aeruginosa* (CRPA) has been isolated from two canine patients at a New Jersey veterinary facility. The strain is associated with a multi-state outbreak in humans linked to EzriCare Artificial Tears, Delsam Pharma Artificial Tears, and Delsam Pharma Artificial Ointment.

HEALTHWATCH

Superbug from human eye drops outbreak spread to dogs

CBS NEWS HEALTH WATCH

By Alexander Tin
Edited By Paula Cohen
Updated on: April 26, 2024 / 2:19 PM EDT / CBS News

Massachusetts Investigation

A known cluster of 3 people in MA with no known epidemiologic connection.

environmental/other, 2023-01-31, USA:MA, environmental surface, 3256-23, PDT001598368.1
clinical, 2023-06-07, USA, urine, PDT001708644.2
clinical, 2023-09-29, USA, urine, PDT001908887.1
environmental/other, 2023-11-20, USA:MA, canine feces, 43121-23, PDT001993464.1
environmental/other, 2023-11-20, USA:MA, canine feces, 43133-23, PDT001993468.1
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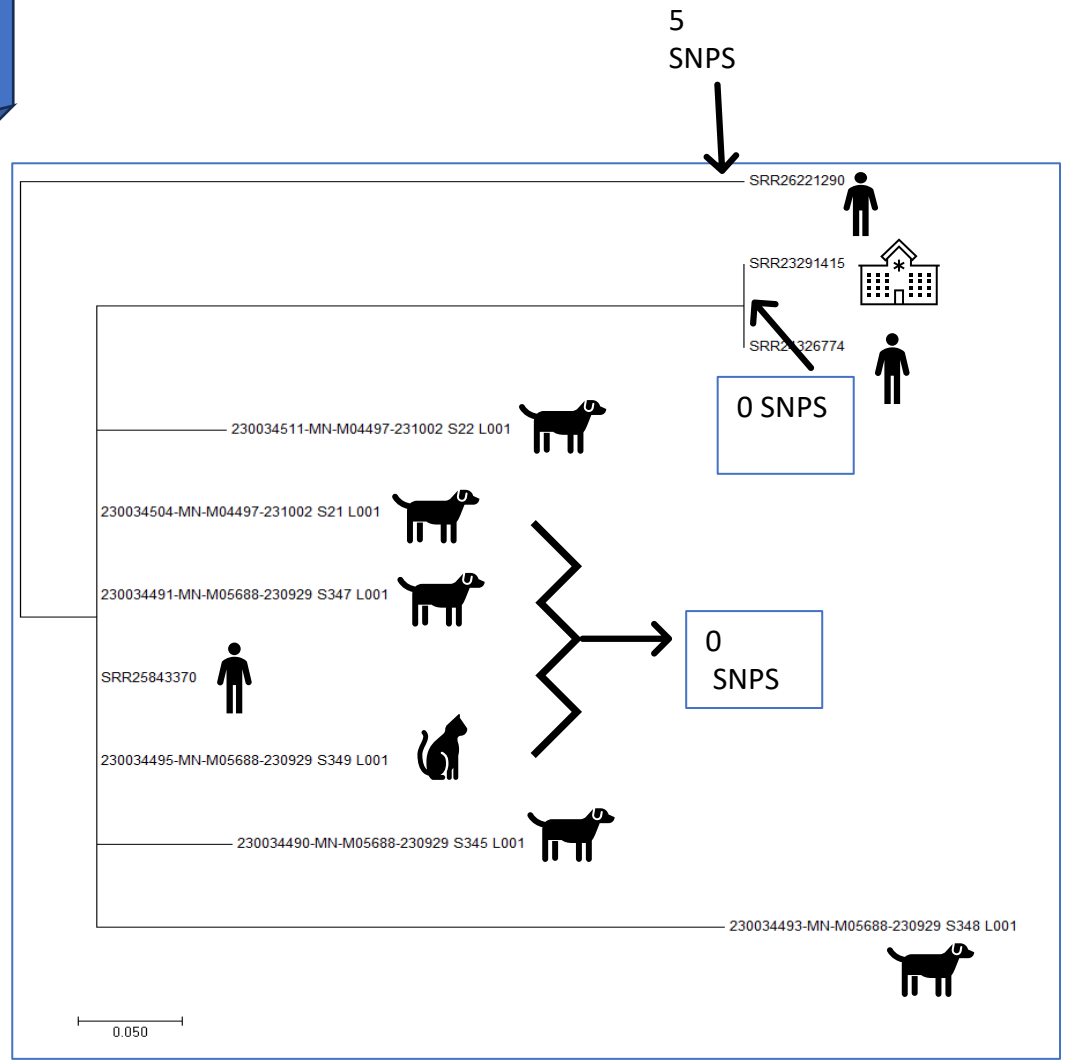
environmental/other, 2023-11-20, USA:MA, canine feces, 47218-23, PDT001993472.1
clinical, 2023-08-31, USA, rectal, PDT001870137.1
environmental/other, 2023-11-20, USA:MA, canine feces, 43130-23, PDT001993466.1
environmental/other, 2023-11-20, USA:MA, feline feces, 47213-23, PDT001993463.1

-	1	5	1	1	2	5	5	1	6
1	-	4	0	0	1	4	4	0	5
5	4	-	4	4	5	8	8	4	9
1	0	4	-	0	1	4	4	0	5
1	0	4	0	-	1	4	4	0	5
2	1	5	1	1	-	5	5	1	6
5	4	8	4	4	5	-	0	4	9
5	4	8	4	4	5	0	-	4	9
1	0	4	0	0	1	4	4	-	5
6	5	9	5	5	6	9	9	5	-



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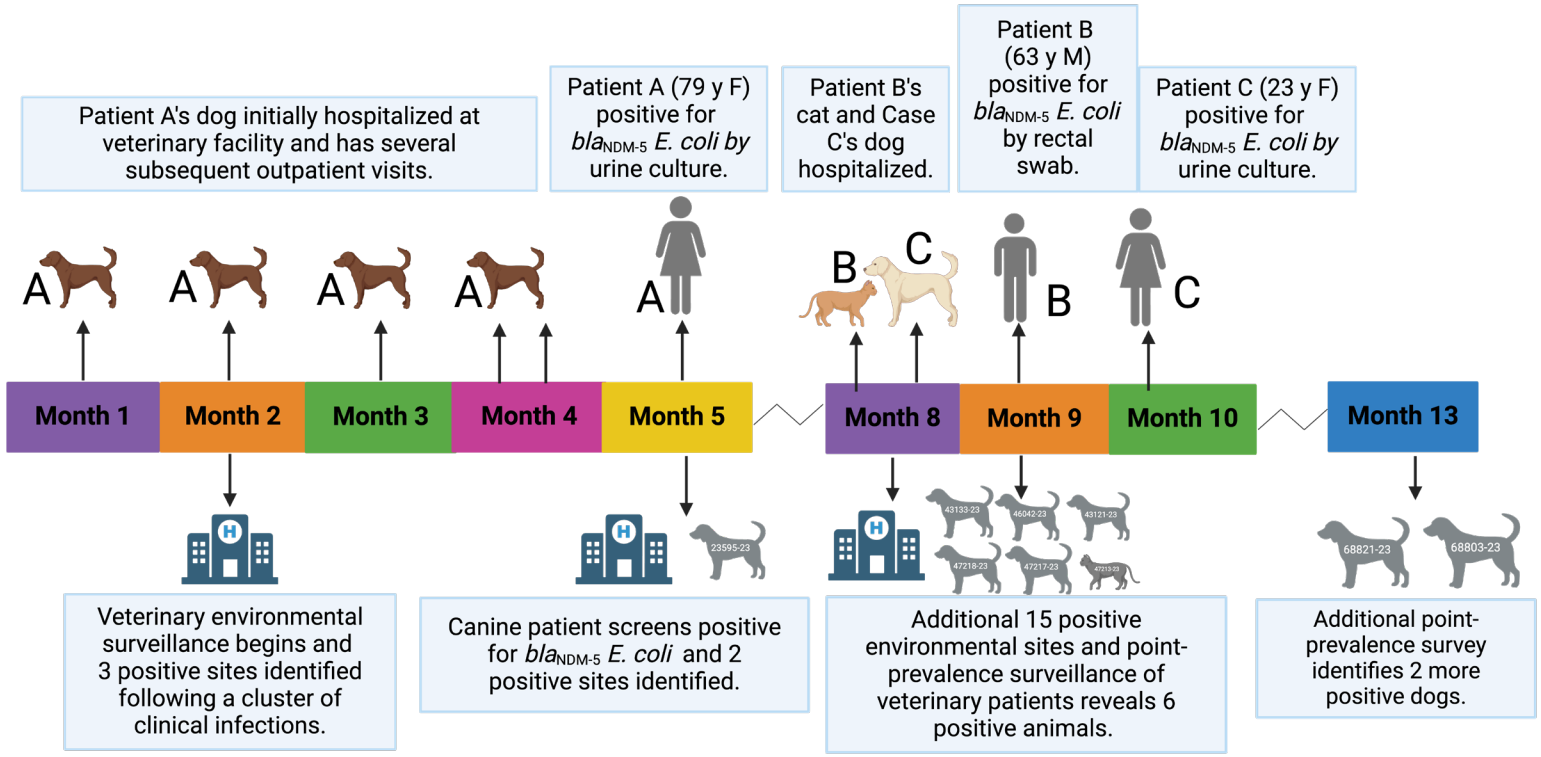
Interview Results

- Before interview determined all 3 people lived in the same county (same as Vet Hospital with outbreak).
- All 3 people had pets who had been seen at the same referral veterinary hospital with ongoing outbreak.



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- MRSA
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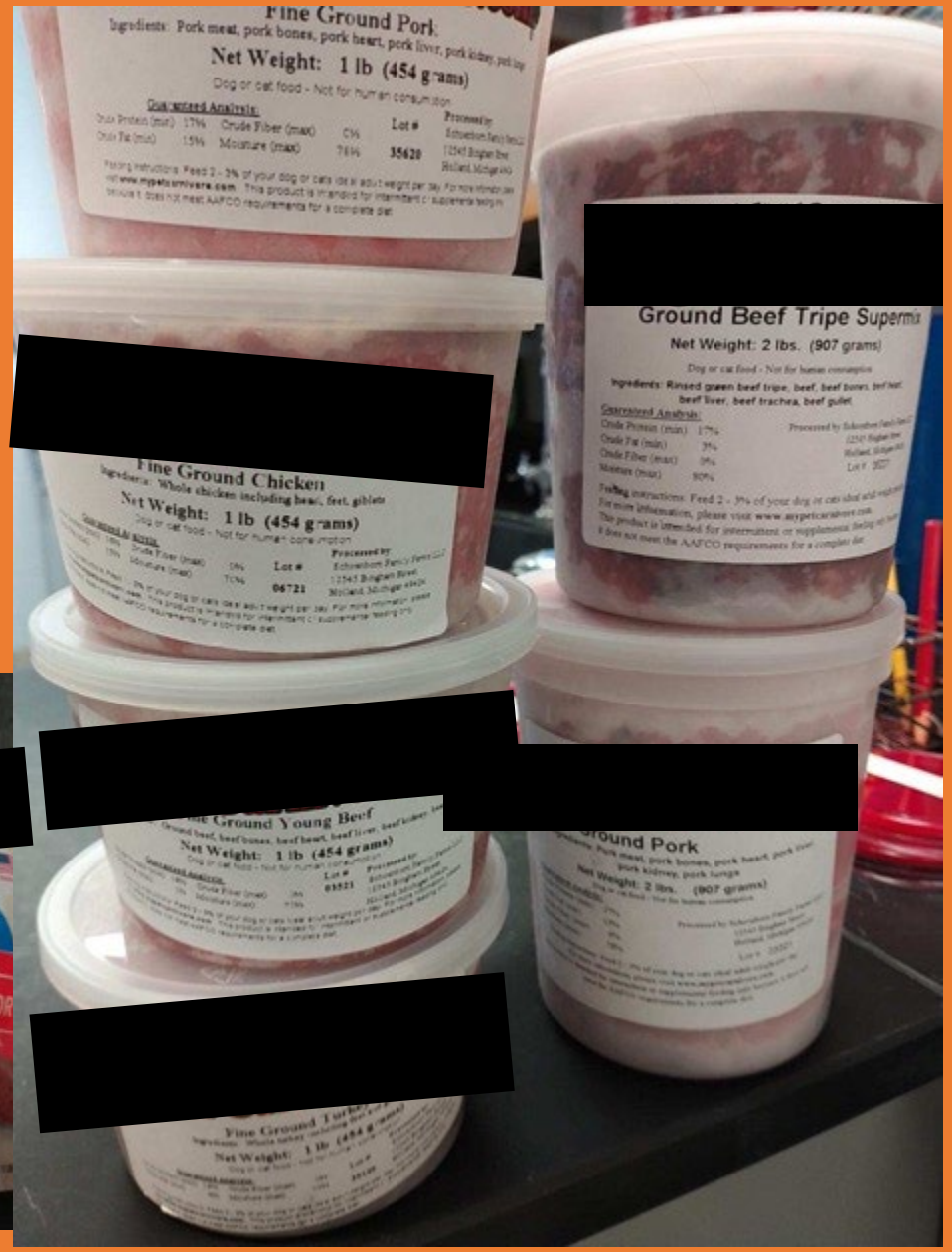
- VRE
- C. difficile
- Antifungal resistant organisms

ESBL in Pets

- 6.8% colonization rate globally based 128 studies
- Outcomes of infections/clinical relevance are poorly described in veterinary medicine.
- Range of clinical disease and severity seen at Ryan Vet Hospital (UPenn).
- May drive the use of carbapenems in veterinary medicine.
- Hx of Abx and Raw Food Diets are Risk Factor

- 200 products
- 61 brands/companies
- 102 frozen/98 freeze-dried
- 20 suppliers



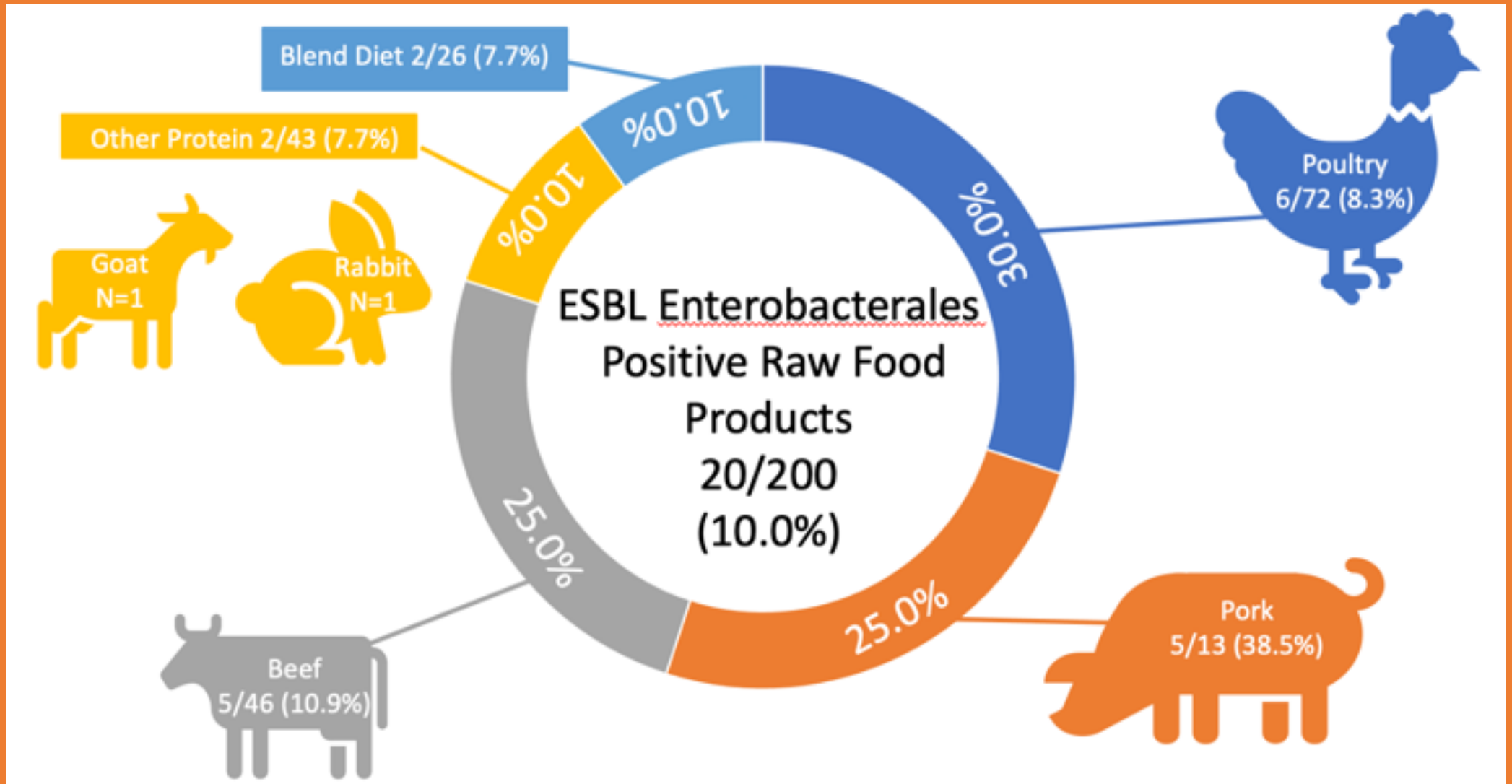


Figure 4. Proportion of positive food products by protein source (inner ring) and proportion of positive samples by protein source (animal icons and bars)

Outline

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Methicillin Resistant *Staphylococcus aureus*

Daily Mail, Monday, Aug

nquiry after scientists claim hundreds of animals have been infected

Could you get MRSA bug from your pet?

By **Beth Hale**

MINISTERS have launched an nquiry into the spread of MRSA o animals following reports of a harp rise in the number of pets nfected.

The Department for Environment, Food and Rural Affairs has set up a committee to investigate the extent to which the deadly superbug has nfiltrated vets' surgeries.

There are fears that the antibiotic-esistant infection could be transferred between pets and their owners – or even nter the food chain if livestock are car-ying the bug.

MRSA – methicillin-resistant staphylo-coccus aureus – is carried harmlessly by one in three humans but can prove fatal n the elderly, newborn babies and those with a weakened immune system.

About 5,000 hospital patients die from it very year.

The bug was first documented in an animal in 1999 but the extent to which it has spread is unclear.

Small-scale studies have suggested that up to 10 per cent of dogs carry MRSA and the British Veterinary Association has been reporting between ten and 12 cases a year of animals being infected.

However, scientists at an Idexx veterinary research laboratory recently alerted the Government after encountering 310 cases of MRSA in animals over the past two and a half years.

Members of the new committee will include actress Jill Moss, who has led a campaign to raise awareness of the risks of MRSA n pets after her dog Bella became the UK's first recorded canine victim of the bacteria.

Bella, a ten-year-old white samoyed, suffered blood poisoning, pneumonia and organ failure caused by MRSA after an operation a year ago on a torn ligament. She had been injured chasing a squirrel near Miss Moss's home in Edgware, North-West London. Her wound became infected a week after surgery and despite a further operation, she had to be put down.

Since then, an eight-year-old alsatian called Connell is also known to have died from MRSA, along with at least one cat and several rabbits and guinea pigs.

Miss Moss, who has appeared in TV shows such as The Bill and EastEnders, said: 'I never in my wildest dreams thought Bella might contract MRSA. If it had been diagnosed earlier she might still be here.

'The real problem is that vets are reluctant to admit they have a problem in their surgeries. They blame the owners but often they are operating in conditions that aren't good enough.'

Miss Moss, 34, said the committee, which will include several health professionals, will look at how to stop MRSA escalating in animals and help to establish the best advice for vets.

It is not known what, if any, danger MRSA in animals poses to humans. The veterinary association urges vets to take similar precautions to hospitals but points out there have been no recorded cases of MRSA being passed from animals to humans and it is highly unlikely the bug could enter the food chain.

Doctors could discover if a patient has MRSA in two hours using a new test.

At present, it takes at least two days to confirm whether a patient has been infected – a dela can prove fatal.

Tony Blair revealed detai pilot scheme in a letter to t ily of 21-year-old James Wo who contracted MRSA hospital for a knee operati

Victim: Bella with owner Jill Moss

MRSA – Human to Animal

MR *S. pseudintermedius*

- Clinically equivalent disease to MSSP- **DIFFERENT FROM MRSA**
- **Not accurate to say "The MRSA of dogs"**
- Methicillin-resistance rates are higher in *S. schleiferi*

How common is MRSA in Dogs and Cats?

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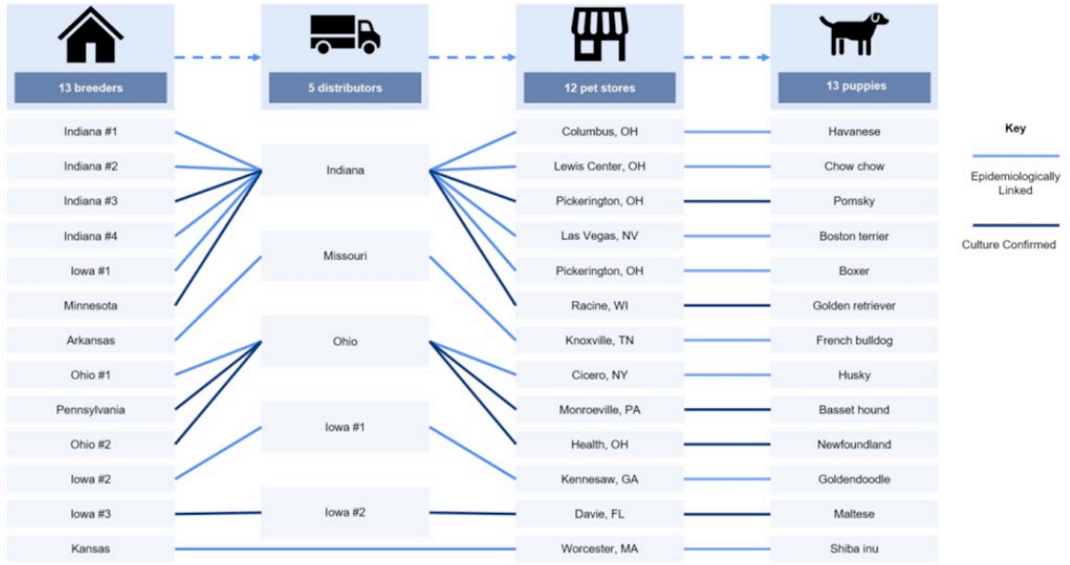


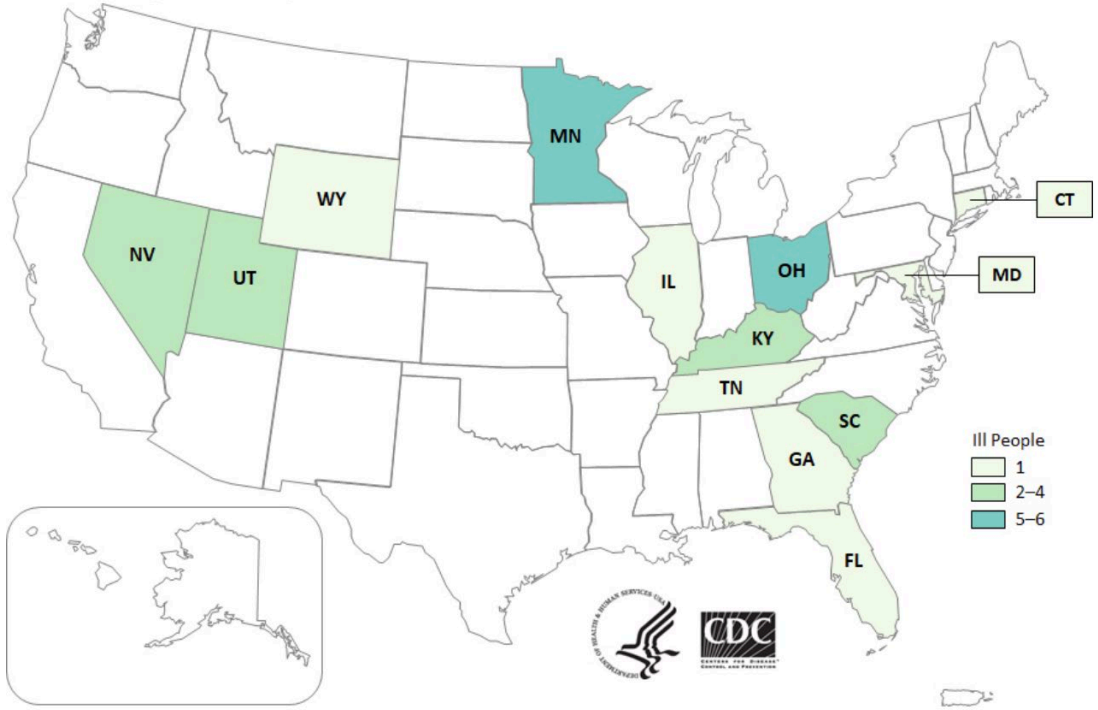
JAVMA news

November 01, 2021

Pet store puppies remain a source of drug-resistant Campylobacter

Report suggests thousands of people likely sickened in decadelong problem

People infected with the outbreak strains, by state of residence, as of December 11, 2019 (n=30)



Outline

- Carbapenem-resistant Enterobacterales
- ESBL-producing Enterobacterales
- MRSA
- Extensively-drug resistant *Campylobacter*
- VRE
- C. difficile
- Antifungal resistant organisms

Vancomycin Resistant *Enterococcus* in Animals

E faecalis and *E faecium* are among the most common organisms isolated from companion animal clinical specimens.

Our laboratory has never seen a VREF. Vancomycin rarely used.

Reports in the literature are common in surveillance studies.

antibiotics

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Prevalence of Vancomycin-Resistant *Enterococcus* (VRE) in Companion Animals: The First Meta-Analysis and Systematic Review

by Yusuf Wada [1,2], Ahmad Adebayo Irekeola [1,3], Engku Nur Syafirah E.A.R. [1], Wardah Yusof [1], Lee Lih Huey [1], Suwaiba Ladan Muhammad [4], Azian Harun [1,5], Chan Yean Yean [1] and Abdul Rahman Zaidah [1,5,*]

1 Department of Medical Microbiology and Parasitology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian 16150, Malaysia

2 Department of Zoology, Faculty of Life Sciences, Ahmadu Bello University, Zaria 810107, Nigeria

3 Microbiology Unit, Department of Biological Sciences, College of Natural and Applied Sciences, Summit University, Offa PMB 4412, Kwara State, Nigeria

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- High variability amongst prevalence studies (22 studies included)
- Estimated pooled prevalence of 14.6% (18.6% in dogs)
- Most recent in USA (2012) from resident cats in Vet hospitals – single cat with a *E. faecalis* non-transferable *vanB* gene.

Prevalence of VRE?

Outline

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Clostridiodes difficile in Animals

- Role in canine and feline diarrhea is poorly characterized.
- Neonates seem most likely to be colonized in several studies.
- Living with owners given antibiotics and immunocompromised owners are risk factors for shedding.
- Horses typically have livestock associated ribotypes, Cats and Dogs with human ribotypes.

Outline

- Carbapenem-resistant Enterobacterales
- ESBL-producing Enterobacterales
- MRSA
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- VRE
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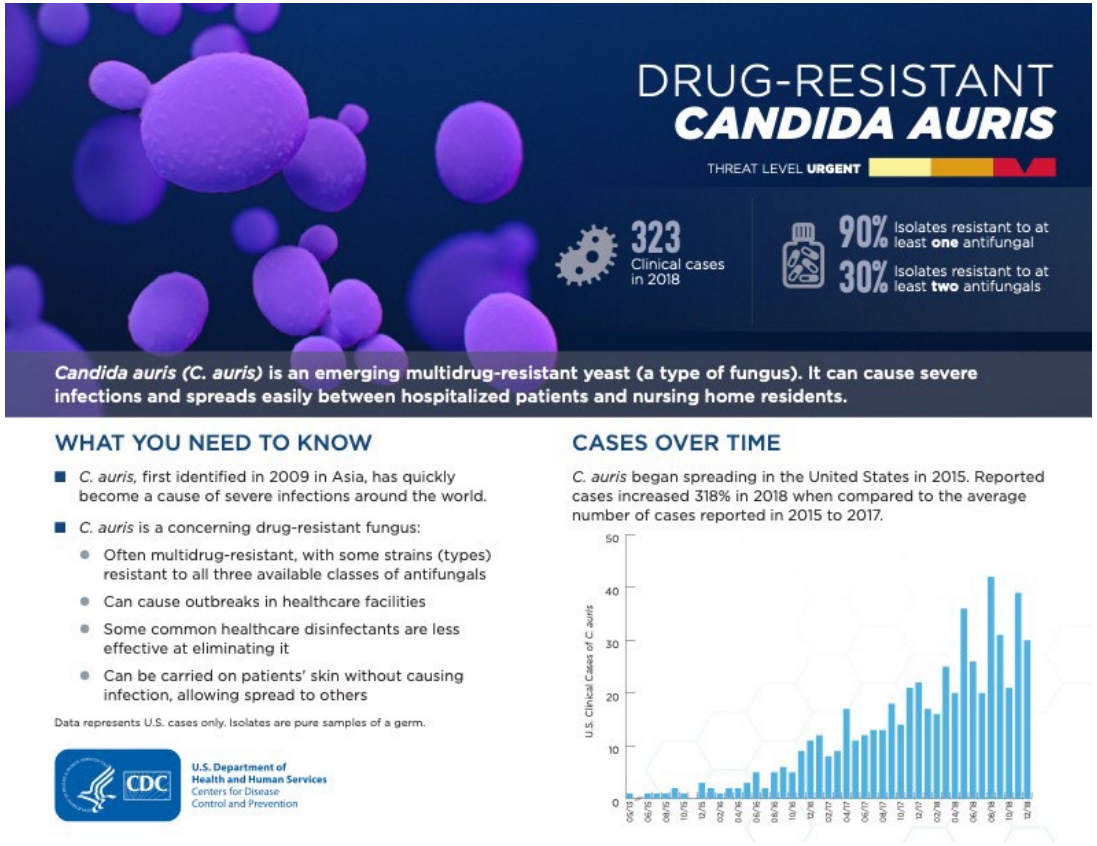
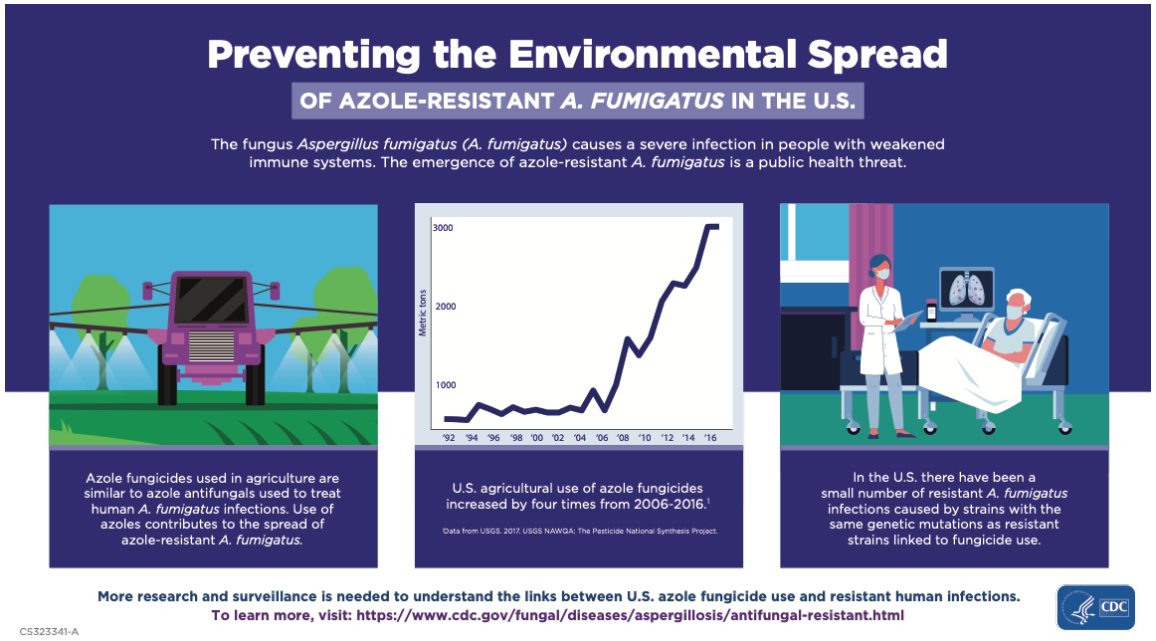
Antifungal Resistant Pathogens





Final thoughts

Why Does It Matter?

- Potentially important reservoir for community transmission of CPOs

- Pet care is an important and growing industry

- Pets help us live happier and healthier lives
  - Physical activity
  - Social connection
  - Maintain Routine
  - Companionship

- Americans live closely and intimately with our pets

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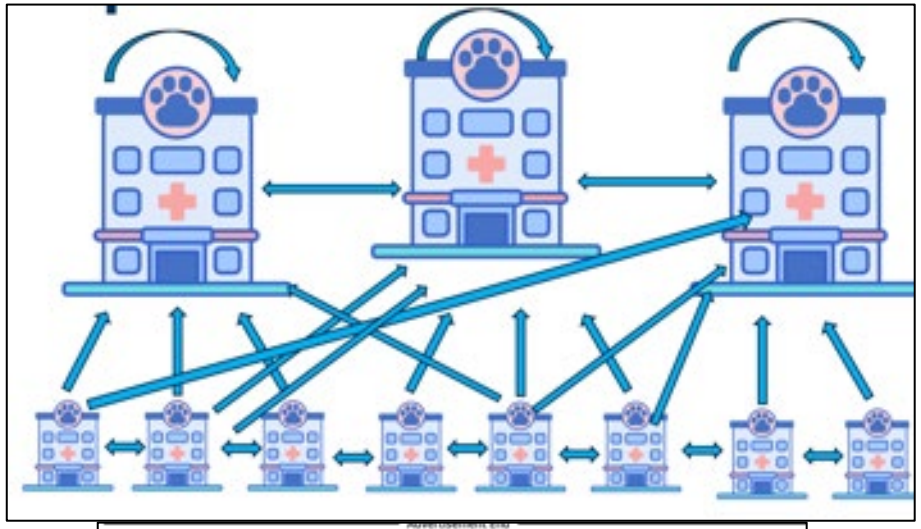
Challenges in Vet Med

- Overall awareness of veterinarians
- Infection prevention (and resources for it) has not grown with the size of complex veterinary referral networks
    - Haenni et al. 2022
        - ESBL/AmpC/CRE
            - Admission 4.8% (6/125)
            - Discharge 24.8% (31/125)
    - Dazzio et al. 2021
        - 28.3% of animals became colonized with an MDRO during hospitalization
- Veterinary laboratories may not always test carbapenems/test for carbapenemases and flag/report results



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A Survey of Current Activities and Technologies Used to Detect Carbapenem Resistance in Bacteria Isolated from Companion Animals at Veterinary Diagnostic Laboratories —United States, 2020

Michelle A. Waltenburg [a], Alicia Shugart [b], John Dustin Loy [c], Deepanker Tewari [d], Shuping Zhang [e], Stephen D. Cole [f], CRO Veterinary Diagnostic Laboratory Investigation Group, Maroya Spalding Walters [b], Megin Nichols [a]

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