Is *Clostridium difficile* a zoonotic and foodborne pathogen?

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Use of Gastric Acid–Suppressive Agents and the Risk of Community-Acquired *Clostridium difficile*–Associated Disease

Community-onset *Clostridium difficile*-associated diarrhoea not associated with antibiotic usage

Two case reports with review of the changing epidemiology of *Clostridium difficile*-associated diarrhoea

Molecular Epidemiology of Hospital-Associated and Community-Acquired *Clostridium difficile* Infection in a Swedish County

CDC MMWR Weekly

Severe *Clostridium difficile*--Associated Disease in Populations Previously at Low Risk --- Four States, 2005

What does *C. diff* do?

- Horses
  - Often severe (fatal) enterocolitis
  - Common, less serious disease in foals
  - Duodenitis/proximal jejunitis
- Dogs/cats
  - Typically mild/moderate diarrhea
- Pigs
  - Severe enteric disease but only in 1-7d old piglets
- Hamsters, cattle…

- If *C. difficile* can infect or colonize so many different species, can it move between species?
- Are animals a source of human infection?
- Are humans a source of animal infection?
- Is food a potential source of *C. diff*?

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Is *Clostridium difficile*-associated infection a potentially zoonotic and foodborne disease?

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Dogs

Country	Population	Prevalence	Ref
Australia	Hospital inpatients	40%	Riley et al 1991
Switzerland	Puppies: 1st 10 weeks Dams Healthy dogs >3 months	94% 43% 1.4%	Perrin et al 1993
US	Shelter dogs Hospital inpatients	0% 18%	Struble et al 1994
Switzerland	Puppies Adult dogs	46/100 dog-months 0%	Buogo et al 1995
UK	Healthy dogs	10%	Al-Saif and Brazier 1996
Canada	Healthy dogs	0%	Weese et al 2001
Canada	Vet hospital admission	9%	Clooten et al, 2008
Canada	Hospital therapy dogs	58%	Lefebvre et al 2006

Hospital Visitation Dogs

- *C. difficile* acquisition by
  - 28% of hospital visitation vs 15% controls (P=0.025)
- Risk factors
  - Healthcare contact: OR 2.2 (1.4-3.5)
  - Visitation of children: OR 3.5 (2.4-4.2)
  - Antimicrobial treatment of someone in the house: OR 2.2 (1.3-3.6)
- Nested case-control study
  - Licked patients: OR 2.9 (1.04-8.1)
  - Sat on beds: OR 2.9 (1.1-7.5)
  - Ate feces: OR 0.12 (0.01-0.88)

Lefebvre et al 2008

Cats

Country	Population	Prevalence	Ref
UK	Veterinary clinics	30%	Borriello et al 1983
	Healthy cats	9%	Weber et al 1989
Australia	Veterinary clinic	38%	Riley et al 1991
UK	Healthy cats	2%	Al-Saif and Brazier 1996
US	Inpatients	9.4%	Madewell et al 1999
Canada	Healthy cats, 5 samples	2.9%*	Weese et al, 2010

Community pets

- *C. difficile* isolated from 14/139 (10%) dogs and 3/14 cats (21%)
  - Only 1/5 daily samples in all but 1
- Risk factors: dogs
  - Living with immunocompromised person (OR 7.9, *P*=0.02)
  - Allowed to run freely in parks (OR 0.3, *P*=0.04)

Weese et al, 2010

Horses

Country	Population	Prevalence	Reference
Sweden	Normal horses	0%	Baverud et al 1997
Canada	Healthy adults	0.4% (1/255)	Weese et al 2001
Canada	Healthy foals	0%	Weese et al 2001
Canada	Healthy race horses	9.7% (33/340)	Medina et al, 2010
Sweden	Healthy foals <14d of age Healthy foals >1 month Non-diarrheic foals tx with ery/rif	29% 1% 44%	Baverud et al 2003

Antimicrobials

- Antimicrobials are risk factors for *C. difficile* shedding in dogs and horses (Clooten et al 2007, Lefebvre et al 2008, Baverud et al 2008, Gustafsson et al 2006) and *C. diff* can be acquired in veterinary hospitals (Madewell 2001, Weese 2001,2004,2006, Clooten 2006)

  ...but, the majority of animals shedding *C. difficile* do not have a history of recent antimicrobial exposure or hospitalization (Weese et al 2001/2006/2010, Clooten et al 2007)

Typing

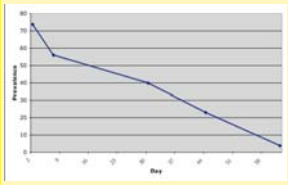
- Isolates from animals indistinguishable from CDI patient isolates (Weese et al 2010, Lefebvre et al 2006, Arroyo et al 2006, Keel et al 2006)
  - Dogs and cats
    - Ribotype 001/NAP2 most common
    - Ribotype 027/NAP1 present but uncommon
  - Horses
    - Ribotype 001/027
    - More toxin variants, esp. toxin A-/B+ (ribotype 017)
    - Some ribotype 078/NAP7,8/toxinotypeV

Transmission from Companion Animals??

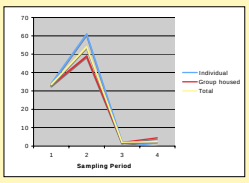
- Inadequate objective study
- Anecdotal evidence *suggesting* intra-household transmission
  - Concurrent detection of *C. difficile* toxins and/or organism from people and pets in households
  - Both isolates rarely available for typing
  - Direction of transmission impossible to discern
- Better evidence suggesting human-animal transmission?

Food animals

Species	Country	Prevalence	Ref
Bovine	Canada	15%	Rodriguez 2006
	US	25% (diarrheic)	Hammitt 2007
	Austria	4.5%	Indra 2009
	Canada	49% (cumulative)	Weese 2009
	Slovenia	2%	Pirs 2008
Pigs	Austria	3.3%	Indra 2009
	Slovenia	52%	Pirs 2008
	Canada	95% (cumulative)	Weese 2009
Chickens	Slovenia	62%	Zidaric 2008
	Zimbabwe	17.4%	Simango 2006
	Zimbabwe	29%	Simango 2008
	Austria	3.4%	Indra 2009



Piglets



Veal calves

Food animal types

Species	Country	Ribotype 078/TT V	Ribotype 027/NAP1/TT III	Human	Ref
Bovine	Canada	26%	12%	100%	Rodriguez 2006
	US	94%	0	97%	Keel 2007
	Canada	65%	0% (1%)	100%	Costa 2009
	Canada	94%	0%	100%	Weese in press
Chickens	Slovenia	0	0	?	Zidaric 2008
Pigs	US	83%	0	98%	Keel 2007
	Slovenia	0 (77%)	0	?	Pirs 2008
	Canada	94%	0	100%	Weese 2009

Food animal types

Species	Country	Ribotype 078/TT V	Ribotype 027/NAP1/TT III	Human	Ref
Bovine	Canada	26%	12%	55%	Rodriguez 2006
	Canada	94%	0	100%	Weese 2009

Toxinotype V *Clostridium difficile* in Humans and Food Animals

Michael A. Jhung,* Angela D. Thompson,* George E. Killgore,* Walter E. Zukowski,† Glenn Songer,‡ Michael Warny,§ Stuart Johnson,†¶ Dale N. Gerding,†¶ L. Clifford McDonald,* and Brandi M. Limbago*

- Netherlands: increase in 078 in human CDI from 3-13% from 2003-2008 (Goorhuis 2008)
  - Younger
  - More frequently CA-CDI
  - MLVA identified overlapping human and porcine clonal complexes
- Increases in human CDI caused by TT V strains in various regions of Europe (Rupnik 2008)
- Pig and human 078 isolates genetically related by MLVA (deBast 2009)

C. difficile in food

Product	Region	Prevalence	Ref
Beef, veal	Canada	20%	Rodriguez 2007
Various	US	Beef: 42%, Pork 41%, Turkey: 44%	Songer 2009
Beef, veal	Canada	Beef, 6.7%: veal 4.6%	Rodriguez 2009
Pork	Canada	2%	Metcalf et al,2010
Chicken	Canada	15%	Weese et al, 2010
Beef, pork	Canada	12% each	Weese et al 2009
Beef, pork, chicken	Austria	0%	Indra 2009
Vegetables	Wales	2.4%	Al Saif 1996
Ready-to-eat salad	Scotland	7.5%	Bakri 2009
Vegetables	Canada	6%	Metcalf et al, unpublished data

Types

Study	Product	078 (TT V)	027 (TT III)	Human
Rodriguez et al 2007	Ground beef and veal	0%	0% (67%)	(100%)
Songer et al 2009	Various	73%	27%	100%
Rodriguez et al 2009	Beef, veal	0%	0% (27%)	100%
Weese et al, 2009	Pork, beef	79%	7.1% (11%)	100%
Weese et al, 2009	Chicken	96%	0%	100%
Metcalf et al, 2010	Pork	0%	43% (57%)	100%

	Toxinotype V		Toxinotype III	
	Animal	Meat	Animal	Meat
Bovine	26% (Can) 65% (Can) 94% (US)	0% (Can) 0% (Can) 86% (Can) 73% (US)	12% (Can) 1% (Can) 0% (US)	67% (Can) 27% (Can) 7.1% (Can) 23% (US)
Porcine	94% (Can) 83% (US) 77% (Slov)	0% (Can) 71% (Can) 67% (US)	0% (Can) 0% (US) 0% (Slov)	14% (Can) 57% (Can) 33% (US)
Chicken	0% (Slov)	96% (Can)	0% (Slov)	0% (Can)
Turkey		100% (US)		0% (US)
Processed*		59% (US)		41% (US)

*Summer sausage, chorizo, braunschweiger, pork sausage

- Sources: meat
  - Animal gastrointestinal tract
  - Healthy muscle tissue
  - Slaughterhouse environment
  - Processing environment
  - Hands of personnel
- Sources: vegetables
  - Manure, soil
  - Processing environment
  - Hands of personnel

How much is there?

- Ground pork
  - 71% (10/14) of positive samples only on enrichment (detection threshold ≤ 10 CFU/g)
- Ground beef
  - 71% (10/14) of positive samples only on enrichment
- Quantifiable samples
  - 20 spores/g: 5 samples
  - 60 spores/g: 1 sample
  - 120 spores/g: 1 sample
  - 240 spores/g: 1 sample

Weese et al 2009

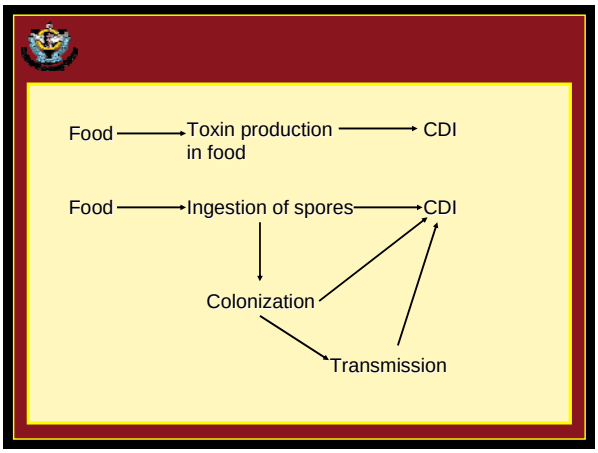
Stick it in

International Food Safety Network

Is *C. difficile* a foodborne pathogen?

Food → Toxin production in food → CDI

Food → Ingestion of spores → CDI



Household Environment

- C. difficile isolated from 44/836 (5.3%) sites in 26/84 (31%) households
  - Most common ribotype
    - 027/NAP1 (25%)
  - 2 most common
    - Ribotype 078
    - Ribotype 001/NAP2
    - Another toxinotype 0 strain
  - Animal vs human vs food sources??

Weese et al 2010

Site	Prevalence	Site	Prevalence
Toilet	9/83 (11%)	Dog eating area	4/84 (4.8%)
Dog food bowl	6/84 (7.1%)	Kitchen sink taps	4/84 (4.8%)
Refrigerator	6/84 (7.1%)	Main entryway	2/84 (2.4%)
Kitchen sink	6/84 (7.1%)	Floor	2/81 (2.4%)
Kitchen counter	4/84 (4.8%)	Vacuum bag contents	1/81 (1.2%)


Is exposure to C. difficile a daily event?


The End