

Clostridium difficile infection (CDI) in institutional and community settings

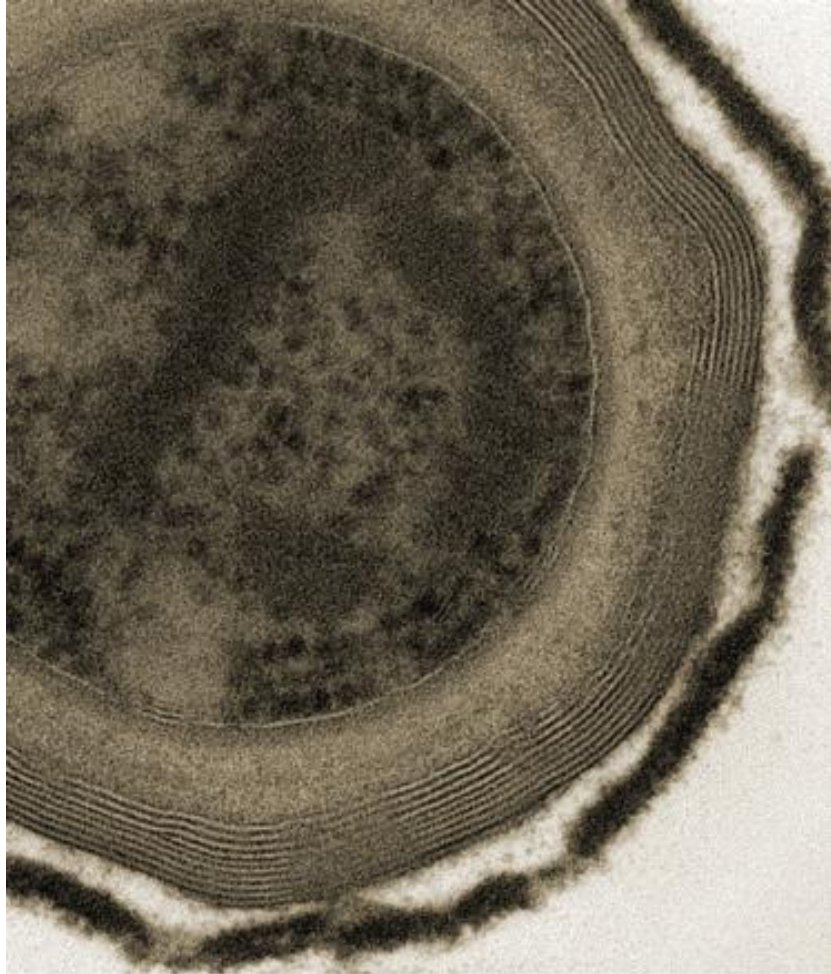
J Scott Weese DVM DVSc DipACVIM



- The bug
- Classical *C. difficile* infection (CDI)
- Hypervirulent CDI
- *C. difficile* in the hospital environment
- Community-associated CDI
- *C. difficile* in the household environment

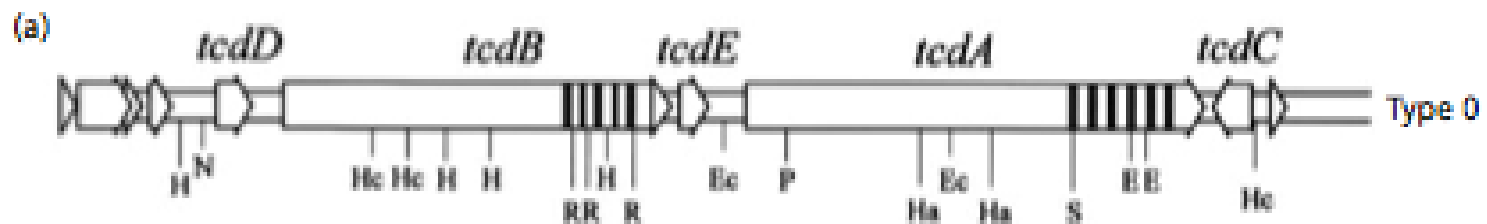
C. difficile

- Gram positive anaerobic sporeforming bacterium first isolated in early 1900's
- Cause of enteric disease in humans and various animal species
- Most commonly diagnosed cause of antimicrobial- and hospital-associated diarrhea in humans



Relevant basics

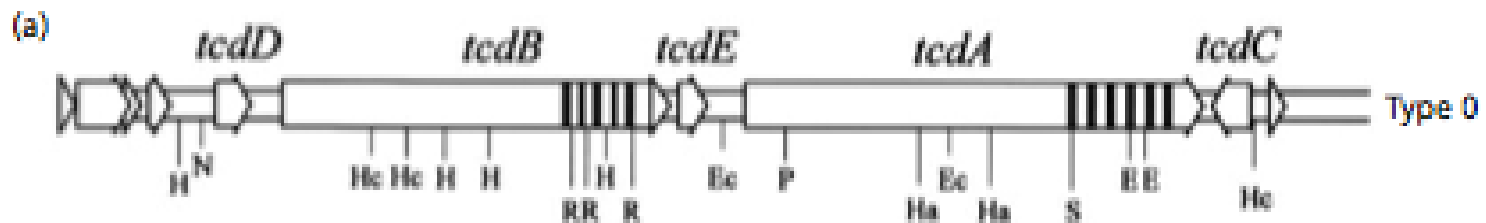
- Three main recognized toxins
 - Toxin A
 - Toxin B
 - CDT (Binary toxin)
 - Varying combinations
 - Likely other toxins



Relevant basics

- Three main recognized toxins
 - Toxin A
 - T
 - C
 -
 - Likely other toxins

It's not just about the toxins!



“Classical CDI”

- >65 y of age
- In hospital or longterm care facility
- Antibiotic exposure
 - +/-Chemotherapeutics, stool softeners...
- Comorbidities

- Overall low severe disease (i.e. ICU stay, colectomy) and mortality rates

Changing Epidemiology

- Increased incidence
 - Lower risk individuals
 - Younger individuals
- Increased severe outcomes
- Increased mortality rates
- Increased relapse rate

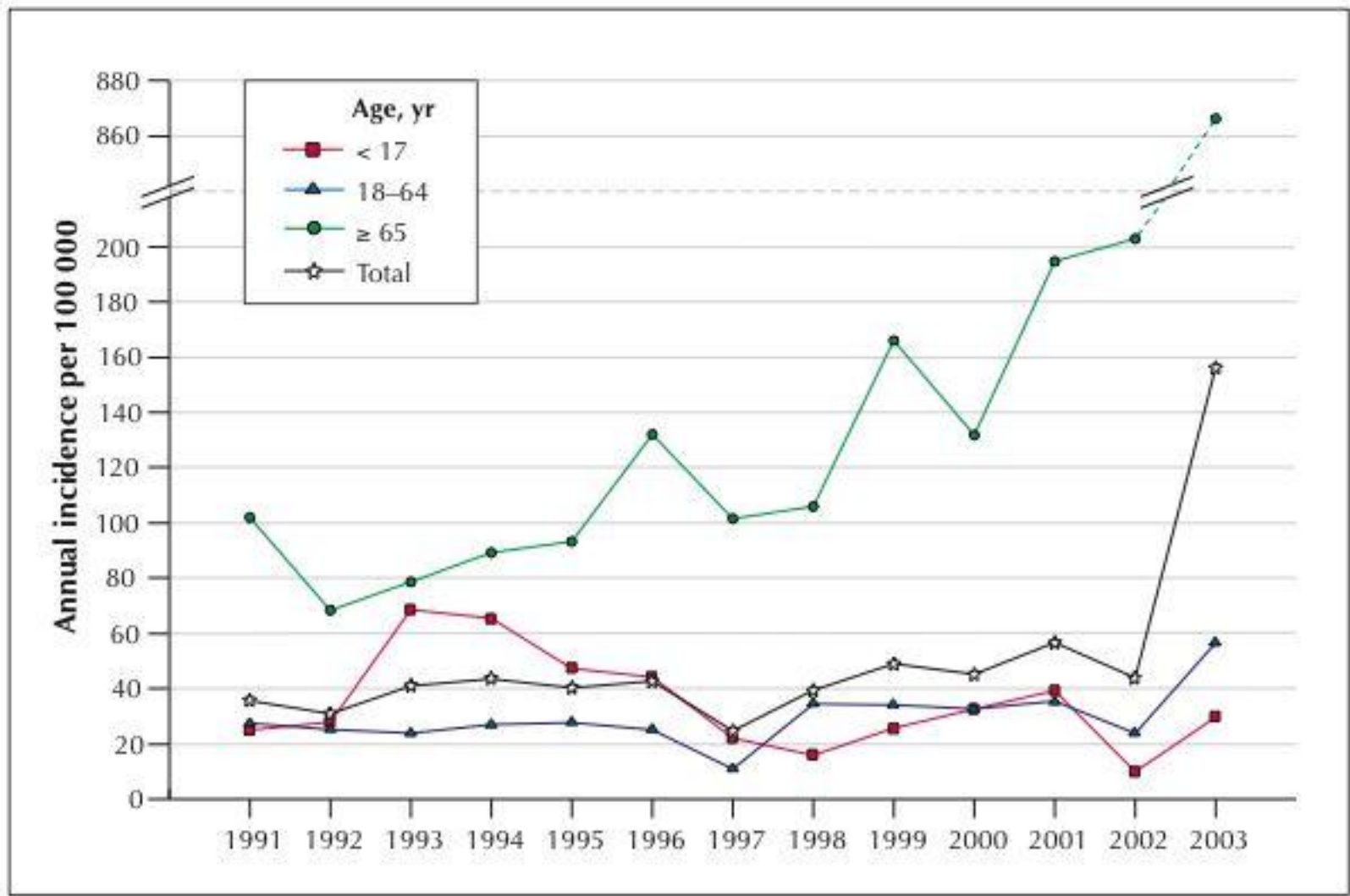


Fig. 1: Annual incidence (per 100 000 population) of *Clostridium difficile*-associated diarrhea (CDAD) in Sherbrooke, Que., 1991–2003.

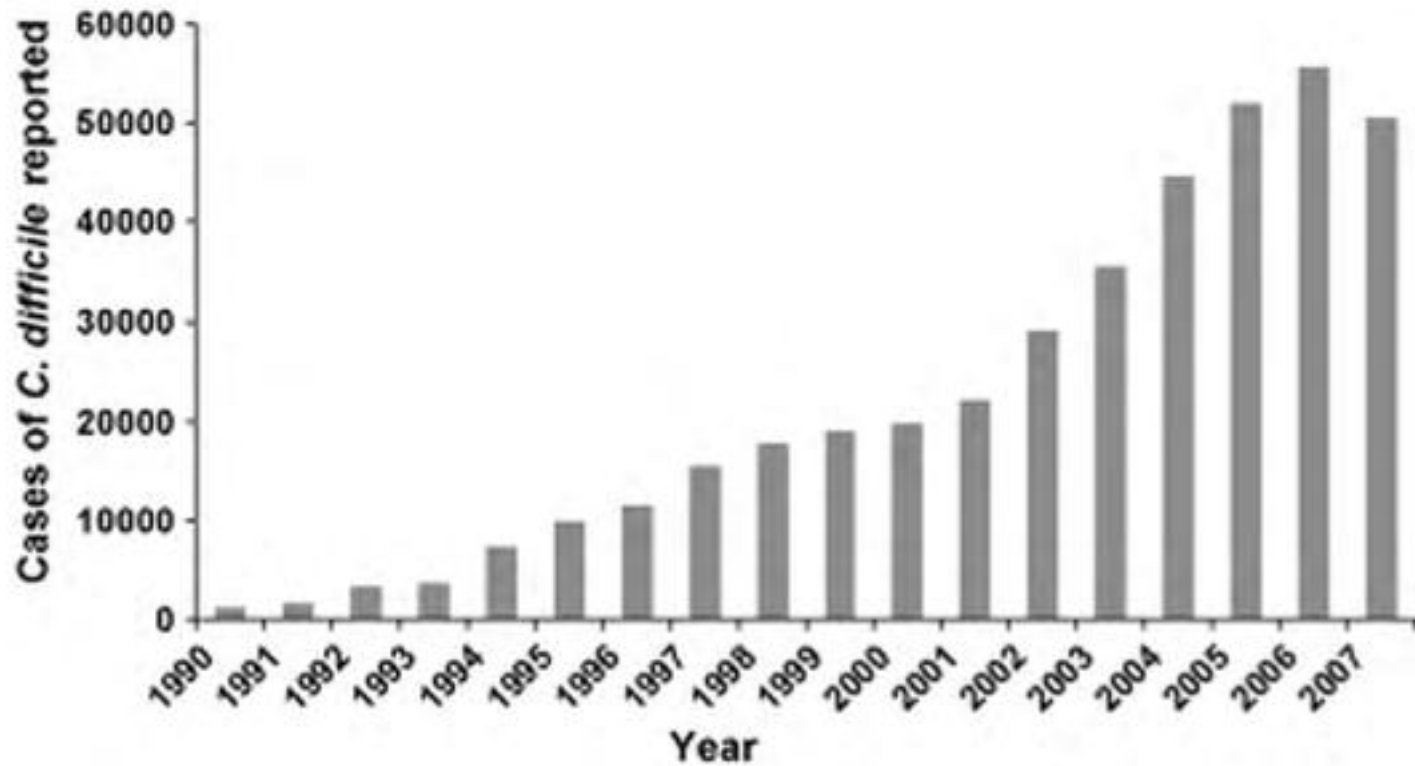


Fig. 1. *C. difficile* incidence figures for England and Wales. Figures from The Health Protection Agency.

***Clostridium difficile* Infections among Hospitalized Children, United States, 1997–2006**

Marya D. Zilberberg, Glenn S. Tillotson, and L. Clifford McDonald

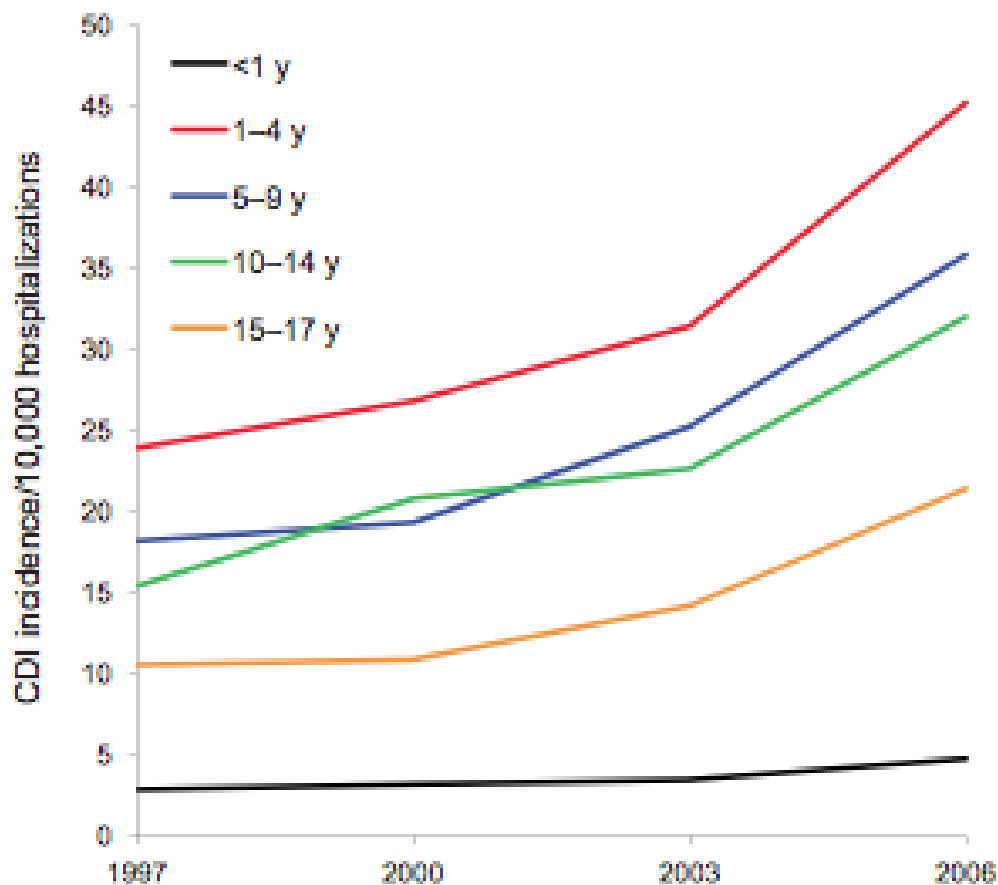
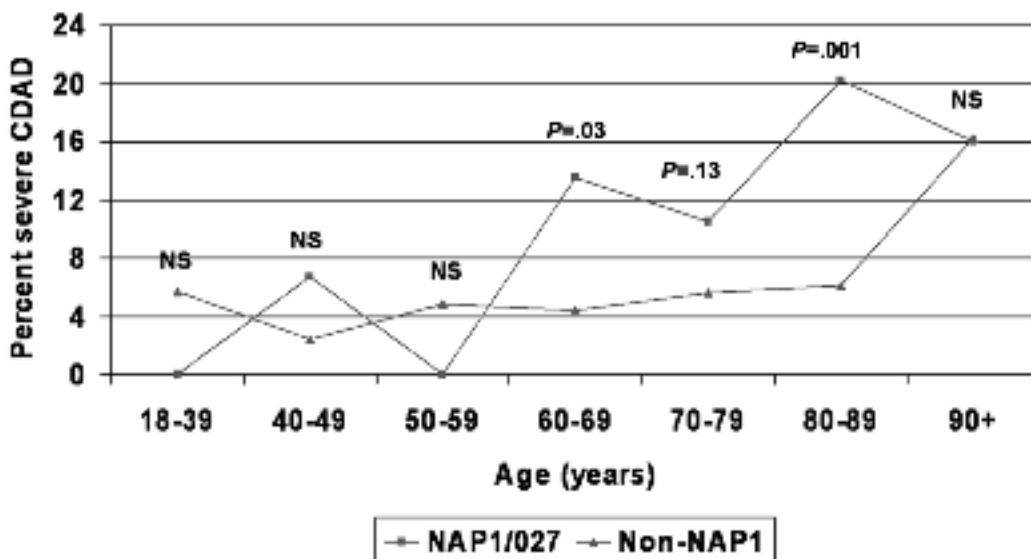
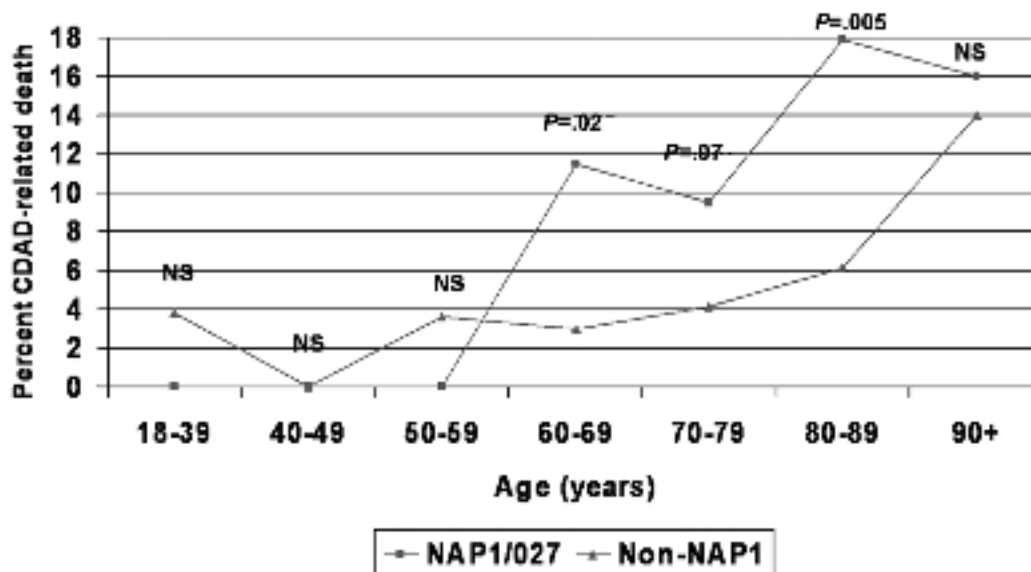


Figure 1. Age-specific incidence of patients with *Clostridium difficile* infection (CDI) per 10,000 hospitalizations, Health Care Utilization Project Kids' and Inpatient Database, United States, 1997–2006.

Health Care–Associated *Clostridium difficile* Infection in Canada: Patient Age and Infecting Strain Type Are Highly Predictive of Severe Outcome and Mortality

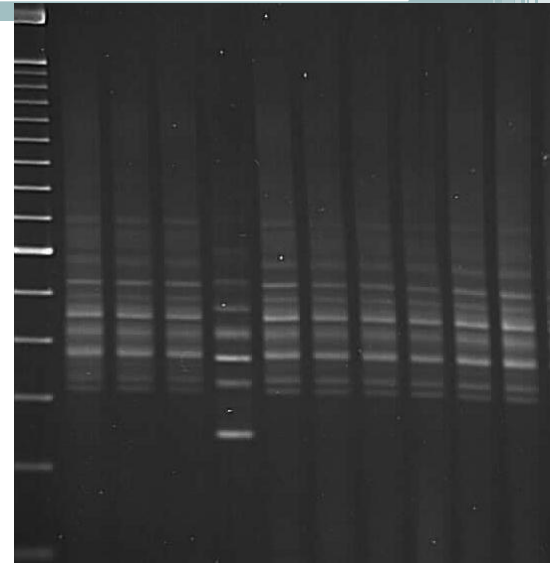
Mark Miller,¹ Denise Gravel,³ Michael Mulvey,⁷ Geoffrey Taylor,⁸ David Boyd,⁷ Andrew Simor,⁴ Michael Gardam,⁵ Allison McGeer,⁶ James Hutchinson,⁹ Dorothy Moore,² and Sharon Kelly,⁵ for the Canadian Nosocomial Infection Surveillance Program*

¹Sir Mortimer B. Davis-Jewish General Hospital and ²Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, ³Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada, Ottawa, and ⁴Sunnybrook Health Sciences Centre, ⁵University Health Network, and ⁶Mount Sinai Hospital, Toronto, Ontario, ⁷National Microbiology Laboratory, Winnipeg, Manitoba, ⁸University of Alberta Hospital, Edmonton, Alberta, and ⁹Health Science Centre, St. John's, Newfoundland

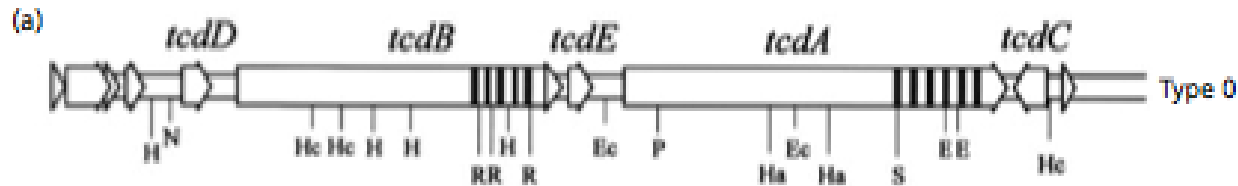


Hypervirulent (HV) CDI

- Ribotype
027/NAP1/BI/Toxinotype III
- Ribotype 078/NAP7/NAP8/ToxinotypeV



What makes HV CDI HV?



- Increased sporulation rate
- Altered surface proteins...increased attachment
- Altered expression of many genes
- Antimicrobial resistance
 - esp. fluoroquinolone resistance
- Response to antimicrobial administration
- Host/pathogen factors

- Don't ask if you have ribotype 027/NAP1 in your hospital....you do

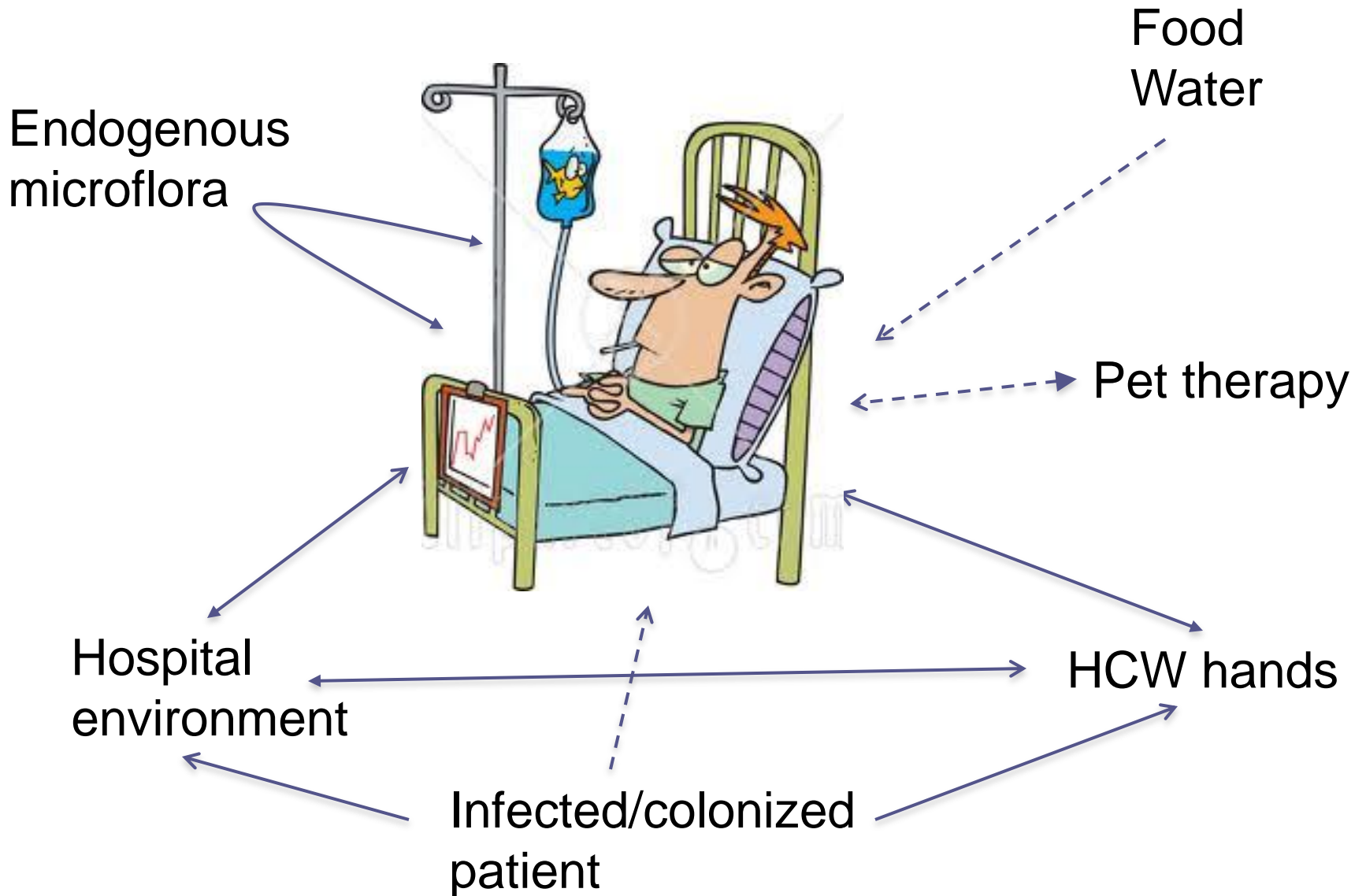
- Presence of a hypervirulent strain does not mean you have or will have an outbreak

Ribotype	Toxin A	Toxin B	CDT	<i>tcdC</i> deletion	<i>tcdC</i> alterations	PFGE*	Toxinotype	# of Regions (/7)	# of isolates	% of isolates
001	+	+	-	-	-	NAP2	0	7	275	25.5
027	+	+	+	18bp	Δ117	NAP1	III	7	209	19.4
N	+	+	+	18bp	Δ117	NAP1	III	5	71	6.6
L	+	+	-	-	-	0042	0	6	63	5.8
017	-	+	-	-	-	0117	VIII	5	58	5.4
A	+	+	+	-	-	0012	IX	7	37	3.4
Y	+	+	+	18bp	Δ117	0098	III	5	36	3.3
S	+	+	-	-	-	0076	0	5	28	2.6
AD	+	+	+	18bp	Δ117	NAP1	III	6	27	2.5
C**	+	+	-	-	-	NAP2	0	6	16	1.5
C**	+	+	+	-	-	0012	IX	3	10	0.9
AK	+	+	-	-	-	NAP6	0	7	25	2.3
D	+	+	-	-	-	NAP2	0	5	21	1.9
F	+	+	-	-	-	0066	0	6	18	1.7
078	+	+	+	39bp	C184T	NAP8	V	5	17	1.6
G	+	+	-	-	-	NAP2	0	5	16	1.5
V	+	+	-	-	-	NAP4	0	5	16	1.5
AC	+	+	-	-	-	NAP2	0	4	15	1.4
H	+	+	-	-	-	0077	XII	1	10	0.9
R	+	+	-	-	-	0046	0	4	10	0.9
U	+	+	-	-	-	00162	0	4	10	0.9
AB	+	+	+	-	-	0047	IX	2	10	0.9

- If you have an institutional outbreak, you almost certainly have a ribotype 027/NAP1 outbreak

- If hypervirulent strains are endemic, what drives outbreaks?
 - Antibiotic use practices?
 - Specific subtypes of strains?
 - Breakdowns in cleaning, disinfection and infection control?
 - Supershedders?
 - Influx of highly susceptible patients?
 - Influx of community cases?
 - Bad luck?





C. difficile in the hospital environment

- Hospital A
 - 0, 0, 2.1, 8.5%
 - Chairs, isolation cart, family room sofa, nursing station counter, isolation gowns, privacy curtain
 - Mix of strains, including 027
- Hospital B
 - 2.3, 1.8, 0, 8.6%
 - Bed rails, chairs, privacy curtain
 - Mix, with many 078 and some 027
- Hospital C
 - 0, 2, 2, 0% (but lots of MRSA....)

- Mixed strains consistent with endemic disease
 - Expect less diversity in outbreaks
 - Seemed to be clustering of strains, probably related to sporadic high-level contamination
- Surprisingly low rates of O27
 - Community hospitals without epidemic disease

- Contaminated sites make sense
 - Fabric
 - Communal surfaces
 - Areas that don't receive as much attention (general room furniture, privacy curtains...)
- No clear relationship with MRSA environmental rates

What is the role of the hospital environment?

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

Netherlands
The Journal of Medicine

CASE REPORT

Sandra Dial, MD, MSc
J. A. C. Delaney, MSc
Alan N. Barkun, MD, MSc
Samy Suissa, PhD

Context Recent reports suggest an increasing occurrence and severity of *Clostridium difficile*-associated disease. We assessed whether the use of gastric acid-suppressive agents is associated with an increased risk in the community.

Objective To determine whether the use of gastric acid-suppressive agents increases the risk of *C difficile*-associated disease in a community population.

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

M.P. Bauer¹, A. Goorhuis², T. Koster³, S.C. Numan-Ruberg¹, E.C. Hagen⁴, S.B. Debast⁵, E.J. Kuijper², J.T. van Dissel¹

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

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Department of Infectious Diseases¹ and Department of Clinical Microbiology,³ Örebro University Hospital, Örebro, and Swedish Institute for Infectious Disease Control, Solna,² Sweden

Community-Acquired *Clostridium difficile* Diarrhea Caused by Binary Toxin, Toxin A, and Toxin B Gene-Positive Isolates in Hungary

Gabriella Terhes,¹ Edit Urbán,¹ József Sóki,¹ Kanjo Abdul Hamid,² and Elisabeth Nagy^{1*}

Department of Clinical Microbiology, Faculty of Medicine, University of Szeged, Szeged,¹ and Central Bacteriological Laboratory, Budapest Institute of the National Public Health and Medical Officer Service, Budapest,² Hungary



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MMWR

Weekly

December 2, 2005 / 54(47);1201-1205

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

- Young age
- Potential for severe disease
- Pregnant women?
- Different risk factors
 - Limited or no antimicrobial exposure
 - Proton pump inhibitors (mixed data)
 - Female gender
 - IBD
 - Contact with children <2y of age
- Community transmission

Wilcox et al 2008, Dial et al 2005/2006

Hypervirulent *Clostridium difficile* Strains in Hospitalized Patients, Canada¹

Michael R. Mulvey, David A. Boyd, Denise Gravel, Jim Hutchinson, Sharon Kelly, Allison McGeer, Dorothy Moore, Andrew Simor, Kathryn N. Suh, Geoff Taylor, J. Scott Weese, Mark Miller, and the Canadian Nosocomial Infection Surveillance Program²

To determine the incidence rate of infections with North American pulsed-field types 7 and 8 (NAP7/NAP8) strains of *Clostridium difficile*, ribotype 078, and toxinotype V strains, we examined data collected for the Canadian Nosocomial Infections Surveillance Program (CNISP) CDI surveillance project during 2004–2008. Incidence of human infections increased from 0.5% in 2004/2005 to 1.6% in 2008.

Emergence of *Clostridium difficile* Infection Due to a New Hypervirulent Strain, Polymerase Chain Reaction Ribotype 078

Abraham Goorhuis,¹ Dennis Bakker,¹ Jeroen Corver,¹ Sylvia B. Debast,³ Celine Harmanus,¹ Daan W. Notermans,² Aldert A. Bergwerff,⁴ Frido W. Dekker,⁵ and Ed J. Kuijper¹

Departments of ¹Medical Microbiology and ²Clinical Epidemiology, Leiden University Medical Center, Leiden, ³Center for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, ⁴Department of Medical Microbiology, Meander Medical Center, Amersfoort, and ⁵Department of Veterinary Medicine, University of Utrecht, Utrecht, The Netherlands

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Letters to the Editor

Clostridium difficile Toxinotype V, Ribotype 078, in Animals and Humans[▽]

Michael R. Mulvey, David A. Boyd, Denise Gravel, Jim Hutchinson, Sharon Kelly, Allison McGeer, Dorothy Moore, Andrew Simor, Kathryn N. Suh, Geoff Taylor, J. Scott Weese, Mark Miller, and the Canadian Nosocomial Infection Surveillance Program

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*

***Clostridium difficile* in Retail Ground Meat, Canada**

Alexander Rodriguez-Palacios,*
Henry R. Staempfli,* Todd Duffield,*
and J. Scott Weese*

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

M. Rupnik

Institute of Public Health Maribor and University of Maribor, Faculty of Medicine, Maribor, Slovenia

Evaluation of *Clostridium difficile* in dogs and the household environment

J. S. WEESE^{1*}, R. FINLEY², R. R. REID-SMITH², N. JANECKO¹
AND J. ROUSSEAU¹

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)

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, $P=0.04$)

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Tainted meats point to superbug C. diff in food

Study finds gut germ in 40 percent of grocery meats; CDC says not to worry



Joe Raedle / Getty Images file

An Arizona researcher found 40 percent of meat products tested from three national chain stores were contaminated with bacteria normally associated with severe hospital infections. Federal health officials, however, say more study is needed to determine whether C. diff is transmitted through food.



Is exposure to *C. difficile* a daily event?



- *C. difficile* from 44/836 (5.3%) of sites in 26/84 (31%) households (Weese et al 2010)

Ribotype	<i>n</i>	Environmental site	Animals (<i>n</i>)
027	8	Pet food bowl (3), kitchen sink (2), kitchen sink tap, kitchen floor, toilet	None
078	5	Fridge shelf (2), kitchen sink, kitchen sink tap, toilet	None
L	5	Toilet (2), kitchen sink, kitchen counter, fridge shelf	Canine (1)
001	5	Kitchen sink, fridge shelf, dog food bowl, toilet, fridge shelf	Canine (4), feline (2)
Y	3	Fridge shelf, vacuum contents, kitchen counter	None
V	2	Kitchen sink tap, dog eating area	Feline (1)
AI	2	Kitchen counter, dog food bowl	Canine (2)
C	1	Kitchen counter	Canine (1)
AA	1	Fridge shelf	None
Q	0	None	Canine (2)

A disease...



a contagious disease...



an epidemic

