



Surveillance for Disease and Sources of Infection: Initiatives at the Federal Level and International

L. Clifford McDonald, MD

Division of Healthcare Quality
Promotion, CDC

SAFER • HEALTHIER • PEOPLE™



Overview

- *Clostridium difficile*
- *Clostridium sordellii*



Clostridium difficile

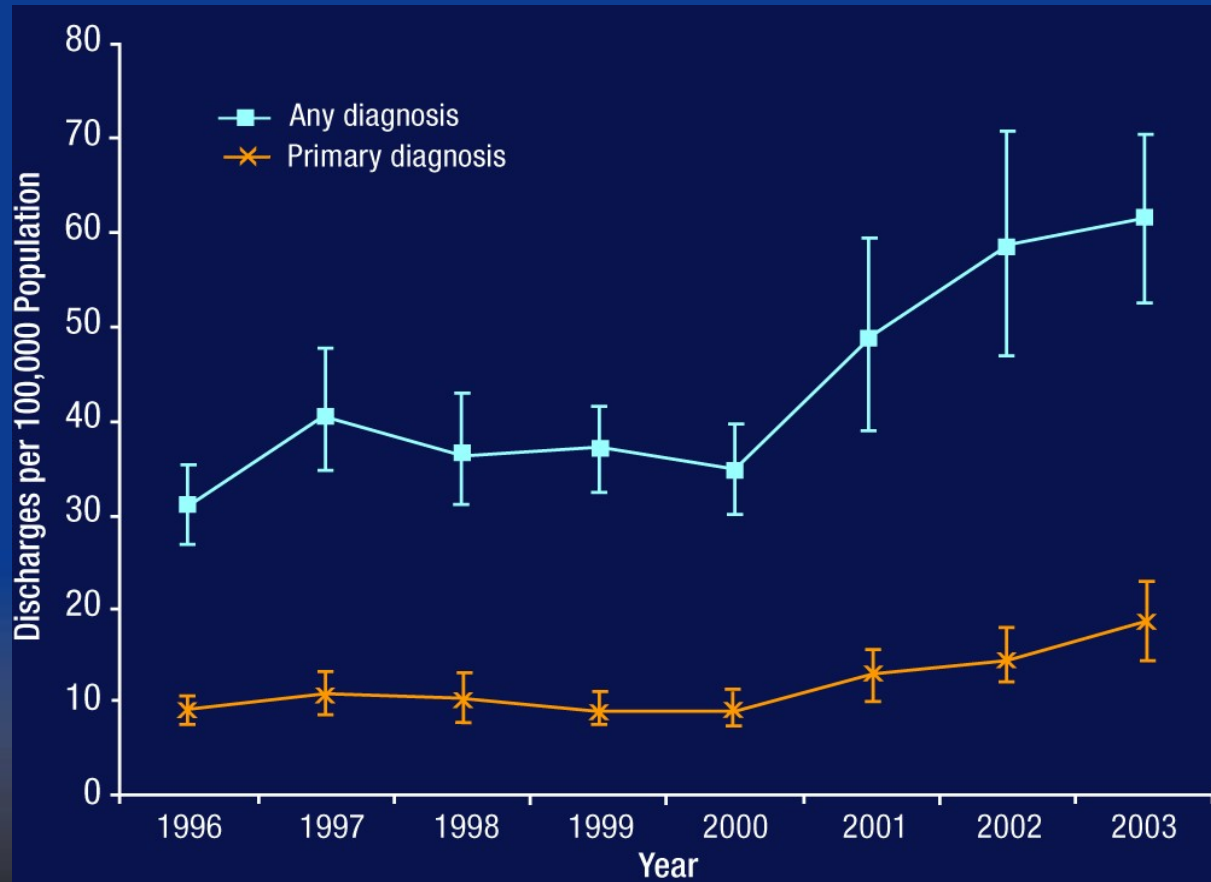
- **Surveillance in healthcare facilities**
- **Community-associated disease**
- **Pregnancy-associated disease**
- **Food-producing animals**



Surveillance for *Clostridium difficile*-associated disease (CDAD)

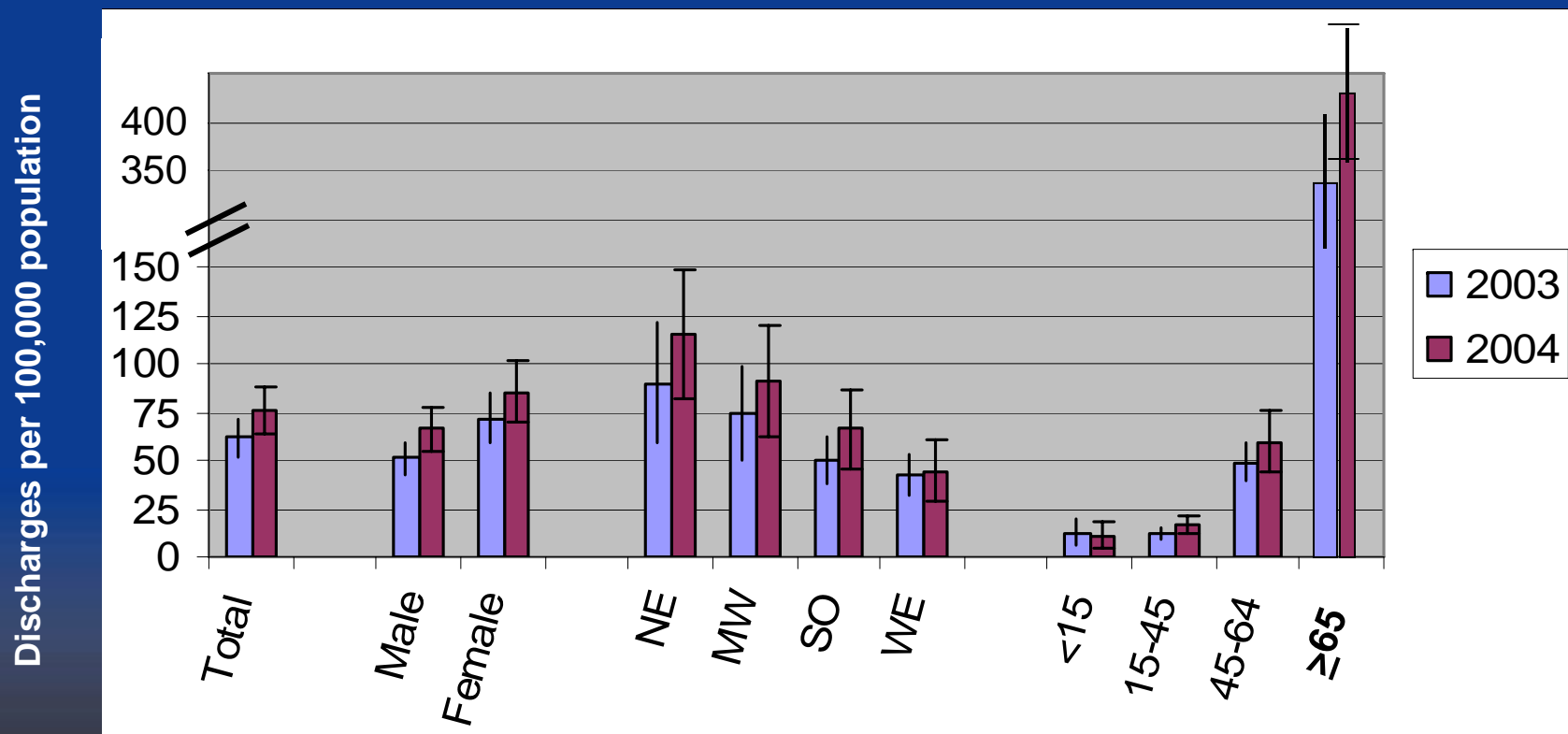
“The majority of *C. difficile* infections are acquired in healthcare facilities”

CDAD Rates in U.S. Hospital Patients Doubled Between 2000 and 2003



McDonald LC, et al. *Emerg Infect Dis.* 2006;12(3): 410-5.

CDAD Rates in U.S. Hospital Patients Increased Another 25% in 2004



Rouphael N, et al. Unpublished data

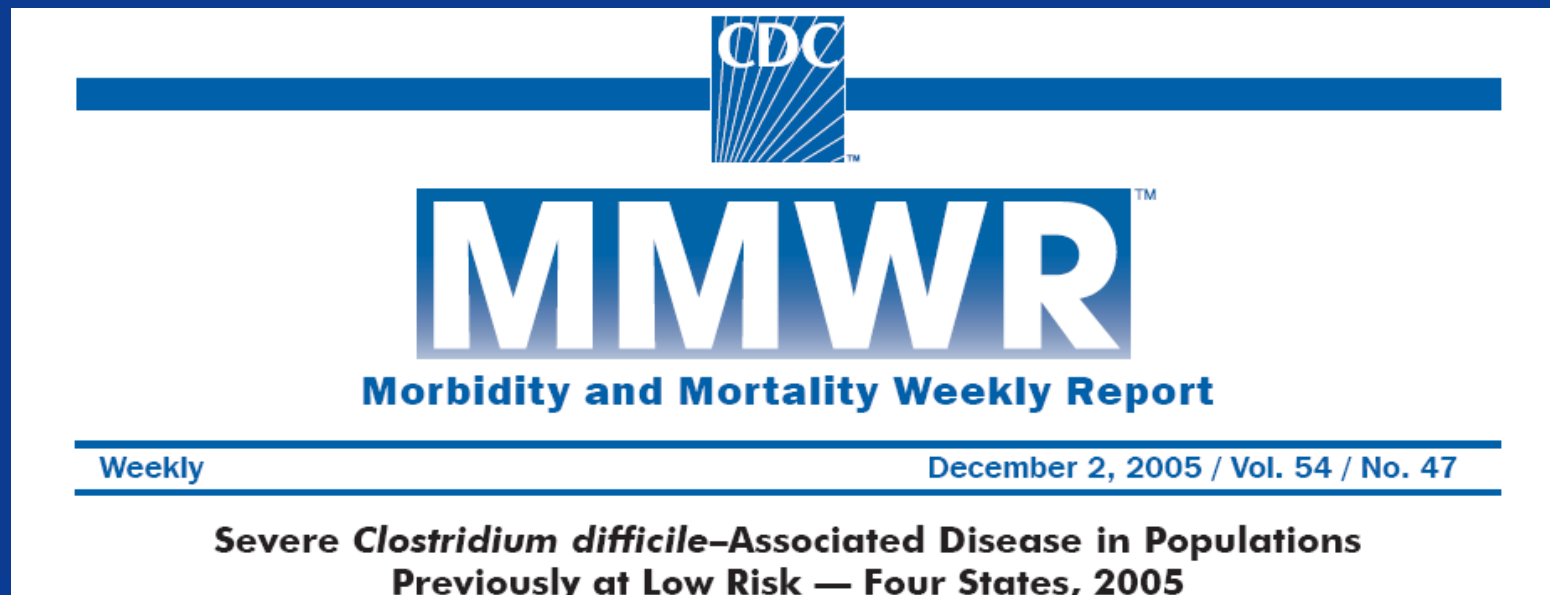
What are Other Countries Doing to Survey CDAD in Hospitals?

- **Quebec, August 2004**
 - Mandatory reporting: acute care hospitals
 - Includes onset \leq 1 month post-discharge
 - Complications including death
- **England, January 2004**
 - Mandatory reporting: all patients \geq 65 y.o.
 - All healthcare facilities in NHS trusts
 - Does not distinguish community vs. healthcare association
- **Canada surveys, 1997 and 2005**
 - Rates and (2005) isolates from sentinel facilities

CDC Priorities to Promote Surveillance of Healthcare-associated CDAD

- **Surveillance recommendations**
 - All facilities should conduct some type of surveillance
 - Definitions and methods
 - Healthcare facilities, networks, state health departments, public reporting initiatives, etc...
- **Study surveillance methods**
 - EpiCenter hospitals
- **National Healthcare Safety Network**
 - Device-associated infections
 - Component for CDAD under early development
 - Individual facility surveillance, networks, public reporting purposes

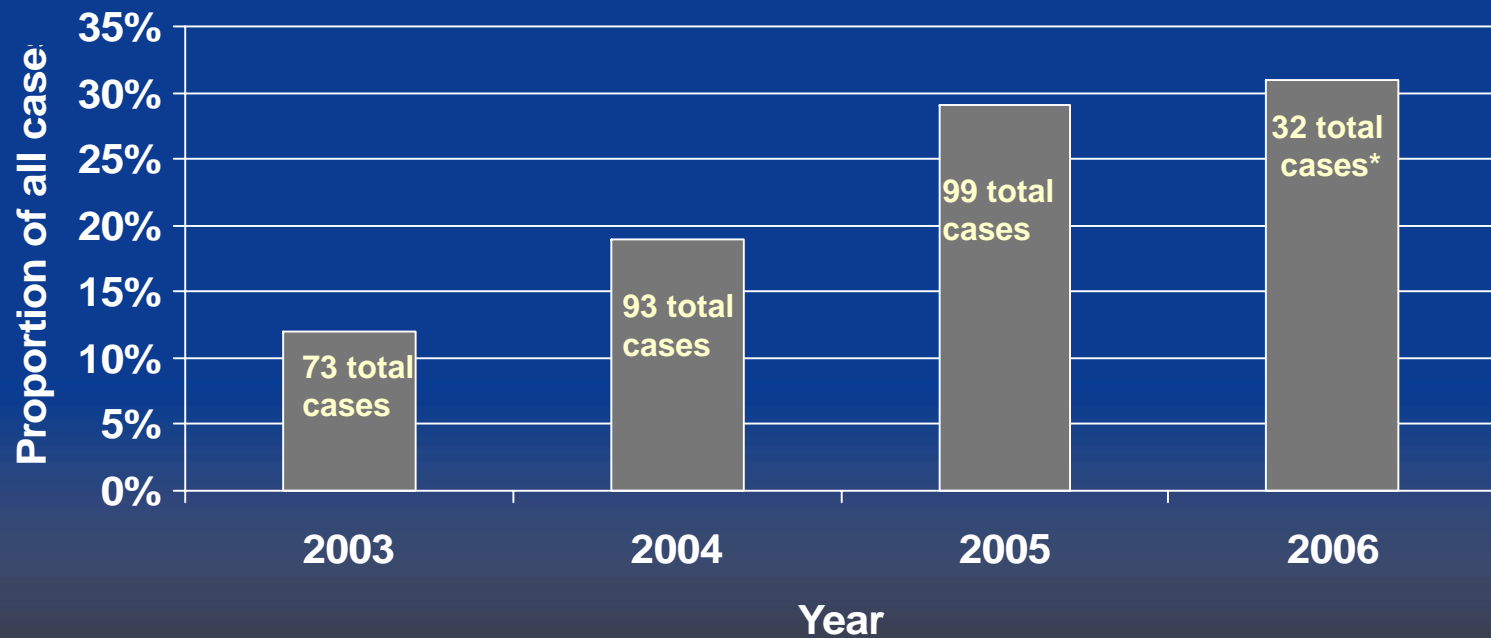
Recent Report of Community-Associated CDAD



- 23 generally healthy persons without recent exposure to healthcare facilities
- Several without recent antimicrobial use

CDC. *MMWR*. 2005;54:1201-1205.

Community-associated CDAD is Increasing, Atlanta VA Hospital



- Through March 31, 2006
- Chi-square for trend: $P < 0.05$

Gaynes, R et al. Unpublished data

Many Patients Developed CDAD without Recent Hospital or Antimicrobial Exposure, Atlanta VA Hospital, 2003-2006

Months since hospitalization	No. of patients	No. (%) <u>without</u> antimicrobial exposure within prior 30 days
>1 to 4 weeks	7	0
1-3 months	4	1 (25)
>3-12 months	6	1 (17)
> 12 months	44	18 (41)
Totals	61	20 (33)

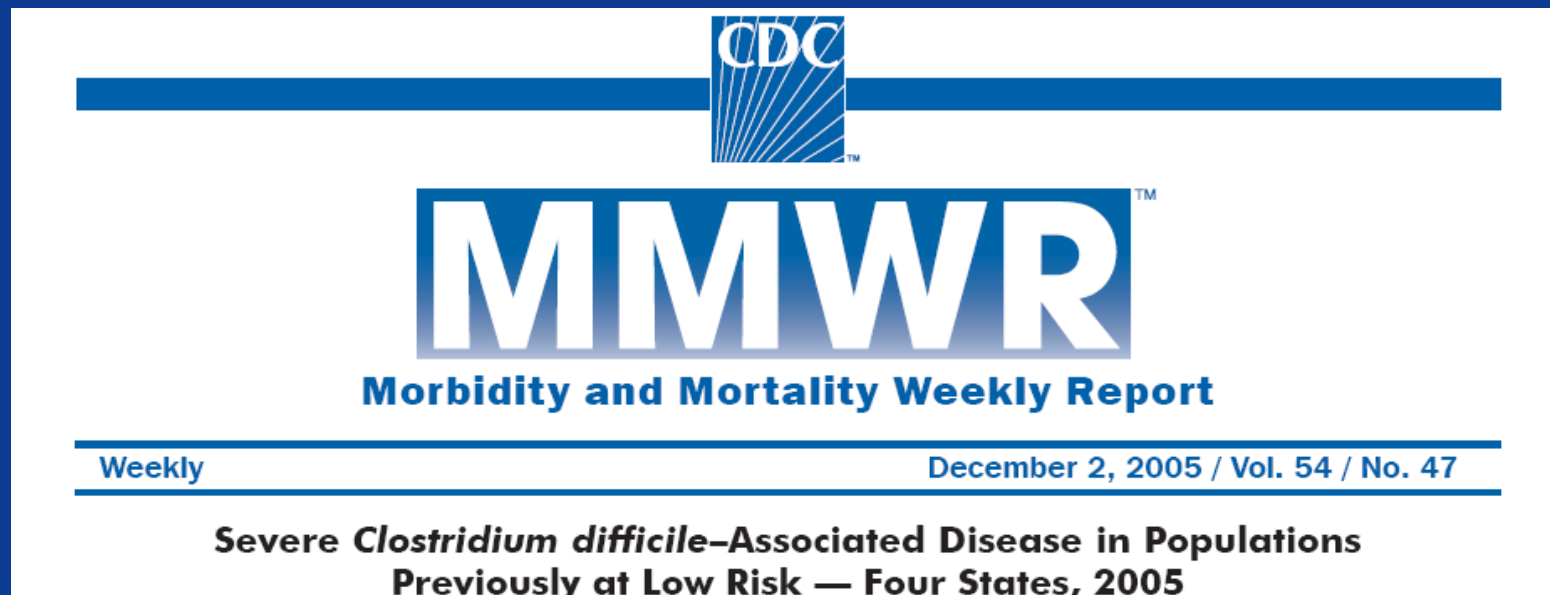
Gaynes, R et al. Unpublished data

Proton Pump Inhibitors (PPIs) Appear to Increase the Risk for CDAD, Atlanta VA Hospital, 2003-2006 (N= 50)

	PPI exposure	No PPI exposure
Antimicrobial exposure	4 (12%)	29 (88 %)
No Antimicrobial exposure	11 (65 %)	6 (35 %)

P<0.0003

Recent Report of Pregnancy-associated CDAD



- 10 cases from four states
- Severe disease in some instances: one death

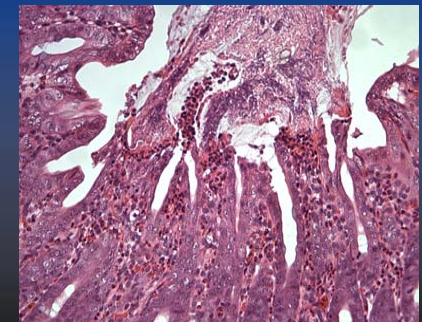
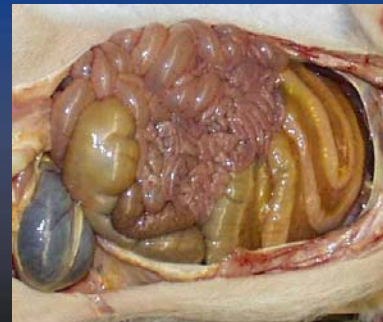
CDC. *MMWR*. 2005;54:1201-1205.

Investigating Additional Cases of Pregnancy-associated CDAD

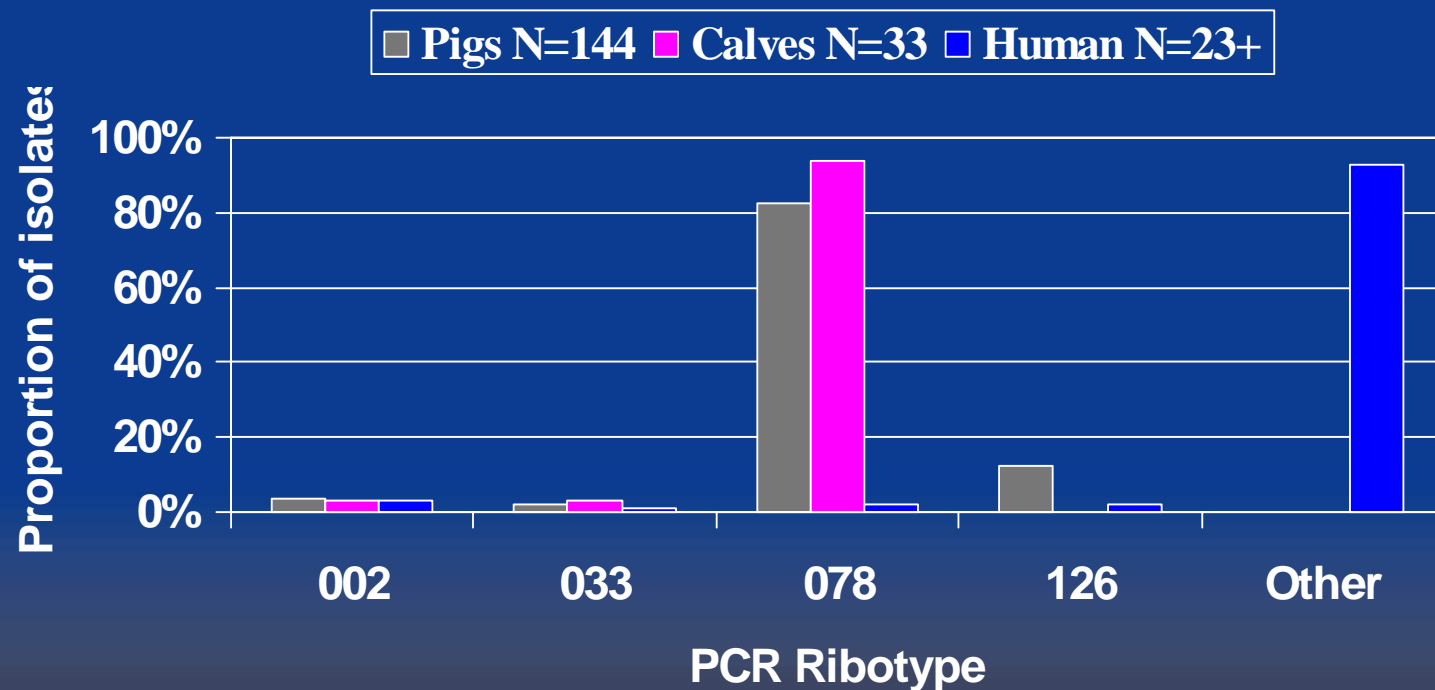
- Emerging Infections Network of the Infectious Diseases Society of America
- 405 ID clinician respondents, 2006
 - 17 (4%) reported having seen cases
 - 23 (6%) were aware of cases
- 48 cases of pregnancy-associated CDAD
 - 14 (29%) occurred prior to delivery
 - 20% developed recurrent disease
 - 3 developed toxic megacolon, 1 fetal loss, 1 maternal death

CDAD is Emerging in Food-Producing Animals

- *C. difficile* long recognized pathogen in horses, rabbits, hamsters, etc
 - Focus on companion animals
- Recent outbreaks in food-producing animals
 - Neonatal pigs
 - Beef and dairy calves
- Associated with high disease rates in affected production facilities



The Strains Infecting Animals are Genetically Different from the Most Common Human Strains



Songer JG et al. Unpublished data

Epidemic Animal Strains Share Certain Characteristics with the Human Epidemic Strain that Could Indicate Increased Virulence

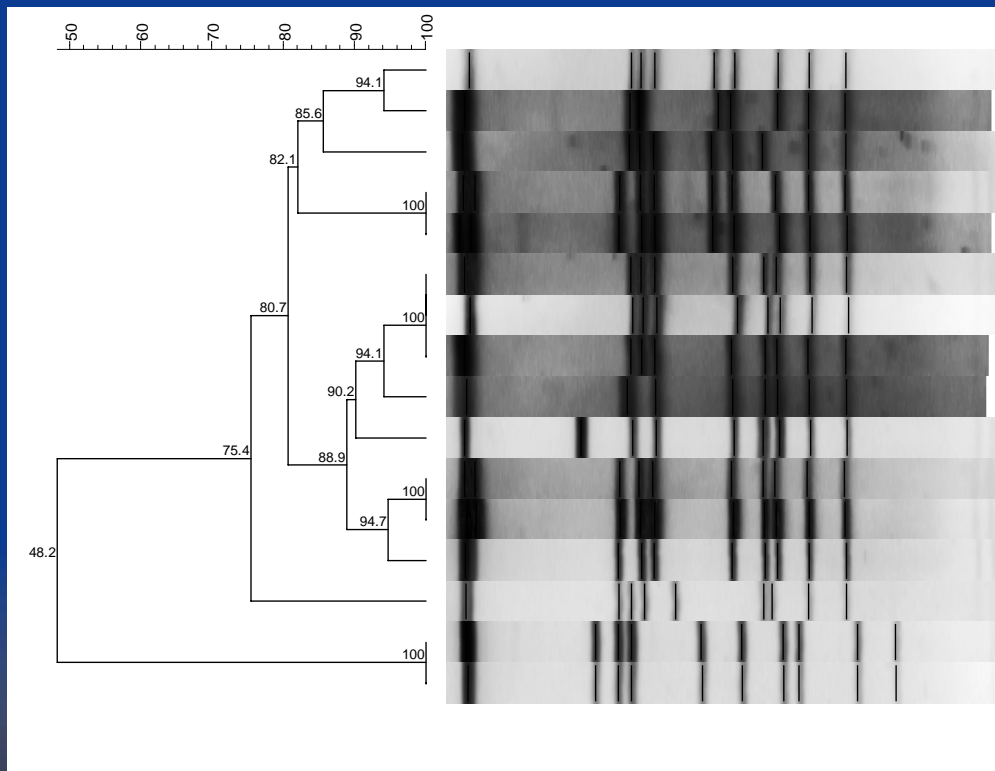
Characteristic	Human Standard Strains	Human Epidemic Strain	Food Animal Epidemic Strain(s)
Toxinotype	0	III	V
PCR Ribotype	001 and others	027	078
PFGE* pattern	< 80% related to NAP1†	NAP1	< 80% related to NAP1†
Binary toxin	—	+	+
Deletion in <i>tcdC</i>	—	18 bp	39 bp

*Pulsed-field gel electrophoresis.

† North American pulsed-field type 1.

Kilgore G, Songer JG, Thompson A, et al. Unpublished data

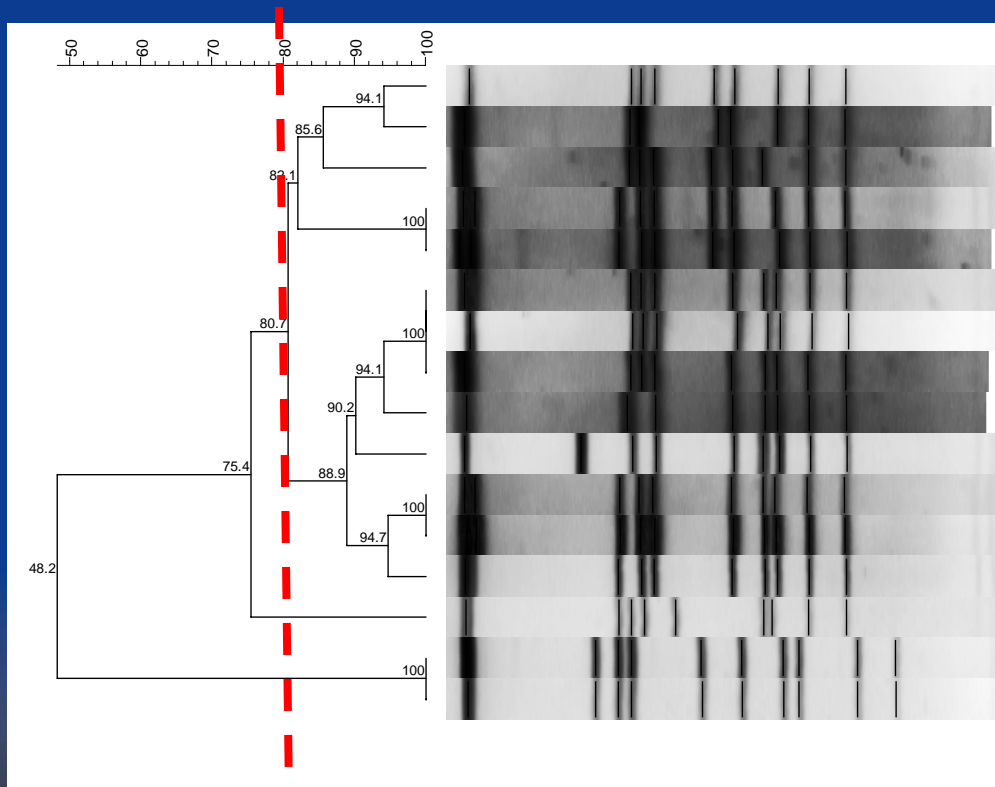
Human CDAD Caused by Strains Similar to Animal Epidemic Strains, 2001-2006



Source	Toxinotype	Binary tox	<i>tcdC</i> del
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Human	V	+	39 bp
Hosp Env	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp

Thompson A, Songer J, et al. Unpublished data

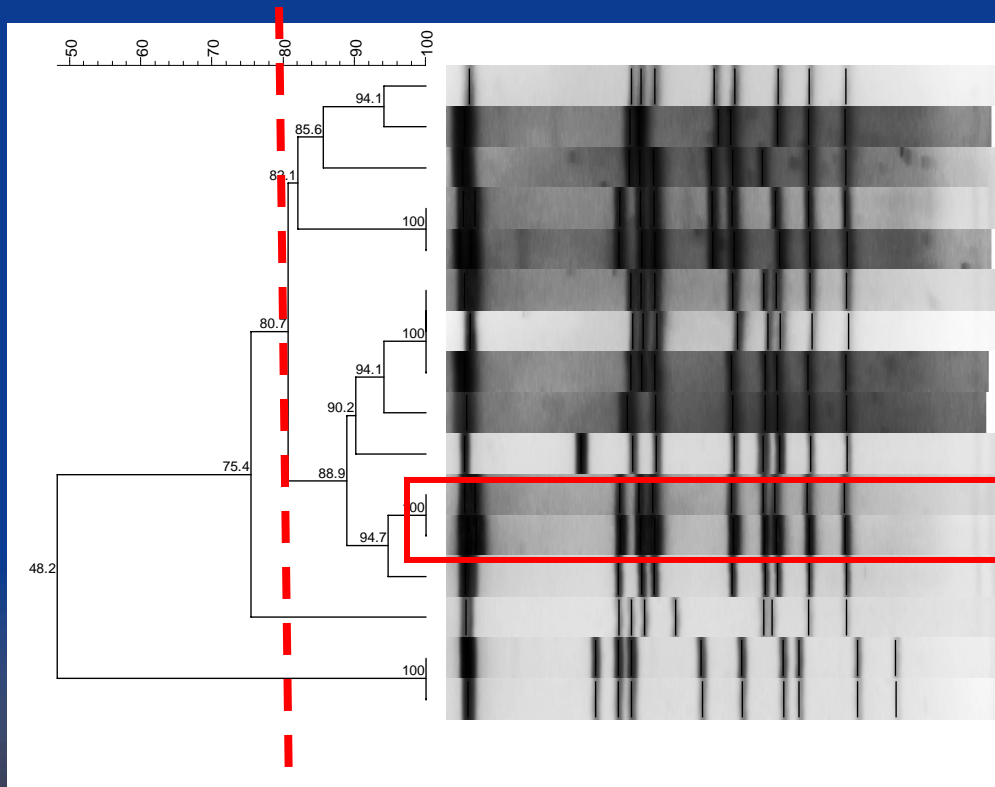
Human CDAD Caused by Strains Similar to Animal Epidemic Strains, 2001-2006



Source	Toxinotype	Binary tox	<i>tcdC</i> del
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Human	V	+	39 bp
Hosp Env	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp

Thompson A, Songer J, et al. Unpublished data

Human CDAD Caused by Strains Similar to Animal Epidemic Strains, 2001-2006



Source	Toxinotype	Binary tox	<i>tcdC</i> del
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Human	V	+	39 bp
Hosp Env	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp

Thompson A, Songer J, et al. Unpublished data

Human CDAD Caused by Animal Epidemic Strains Appear Typical

Characteristic	No. (%) of patients, N=5
Age > 70 years	4 (80)
Significant comorbid disease	4 (80)
Healthcare associated	4 (80)
Antibiotics within 30 days	4 (80)
H2 antagonist within 30 days	2 (40)
PPI within 30 days	1 (20)
Death attributed to CDAD	1 (20)

How Should we Interpret Finding Similar *C. difficile* Strains in Food-Producing Animals and Humans?

Animal Production
Facilities

Toxinotype

V

Animal

-to-

Animal

Ribotype

078

How Should we Interpret Finding Similar *C. difficile* Strains in Food-Producing Animals and Humans?

Animal Production Facilities

Toxinotype
V

Animal
-to-
Animal

Ribotype
078

Healthcare Facilities

Toxinotypes
0, III, others

Patient
-to-
Patient

Ribotypes
001, 027,
others

How Should we Interpret Finding Similar *C. difficile* Strains in Food-Producing Animals and Humans?

Animal Production Facilities

Toxinotype
V
Animal
-to-
Animal

Ribotype
078

Emerging
Community-
Associated
Human
Disease
Responsible
Strains?

Healthcare Facilities

Toxinotypes
0, III, others
Patient
-to-
Patient

Ribotypes
001, 027,
others

How Should we Interpret Finding Similar *C. difficile* Strains in Food-Producing Animals and Humans?

Animal Production
Facilities

Toxinotype
V
Animal
-to-
Animal

Ribotype
078

Healthcare
Facilities

Toxinotypes
0, III, others
Patient
-to-
Patient

Ribotypes
001, 027,
others

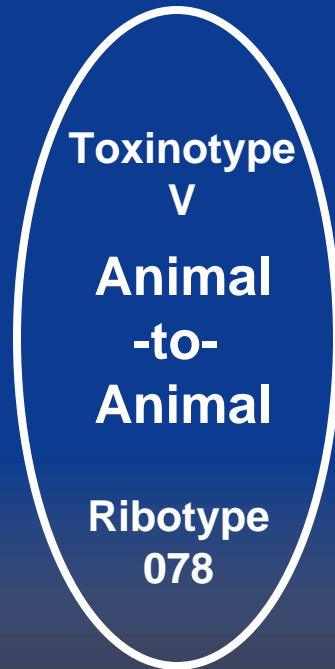
Emerging
Community-
Associated
Human
Disease
Responsible
Strains?

?Environmental Sources?

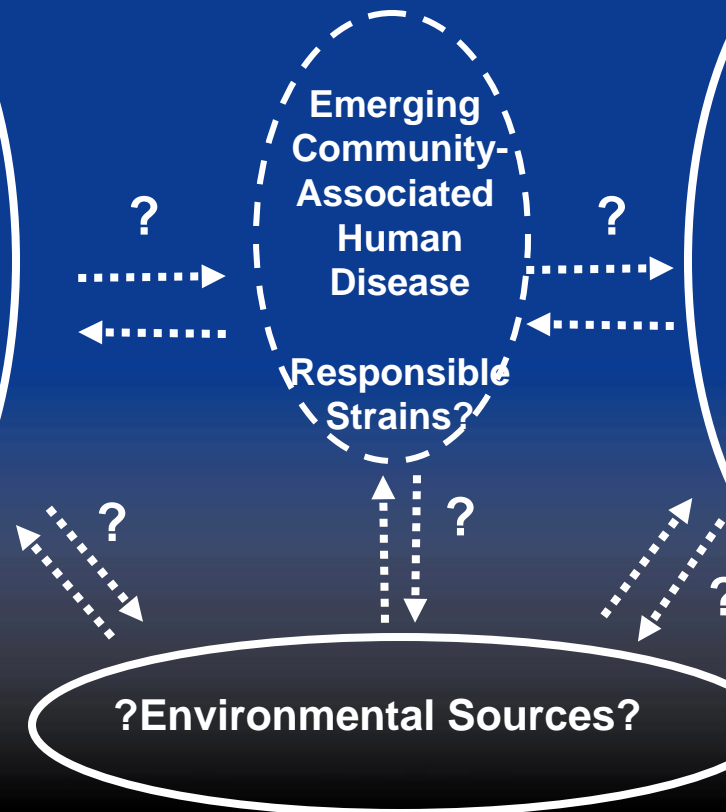
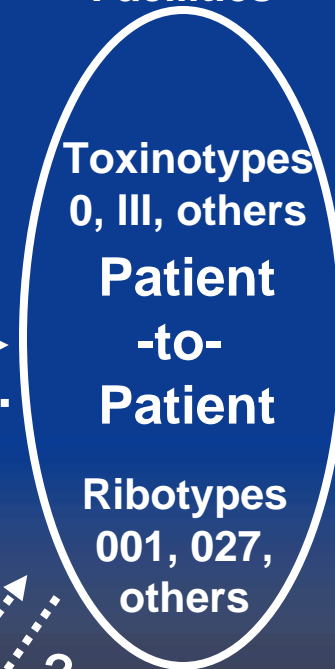


How Should we Interpret Finding Similar *C. difficile* Strains in Food Producing Animals and Humans?

Animal Production
Facilities



Healthcare
Facilities



CDC is Investigating Community-associated CDAD

- Working with an established network
 - Food Net/Emerging Infections Program
 - Pilot studies
 - Obtain isolates from community cases
 - Perform cultures on retail meat samples
 - Ongoing process for other known food borne pathogens
- North Carolina Epi Aid



Clostridium sordellii

- **Additional cases of pregnancy-associated toxic shock-like syndrome**
- **Methods for finding additional cases**
- **Studies of isolates submitted for reference testing**

CDC is Investigating Additional Cases of Pregnancy-associated Toxic Shock-like Syndrome

- **Four additional cases**
 - Medical abortion or miscarriage
 - Aged < 35 years
 - Occurred since 2000
 - Three died

Cases of Toxic Shock-like Syndrome Following Medical Abortion

Case	Region	Weeks gestation	Agents Used	Intra-uterine Infection	<i>Clostridium</i> identified
<i>Previous cases</i>					
5 cases	Western US (4) ¹ , Canada (1) ²	6-10	Mifepristone Misoprostol	Yes	<i>C. sordellii</i>
<i>Additional cases³</i>					
Case A	West	8	Mifepristone Misoprostol	Yes	<i>C. perfringens</i>
Case B	Midwest	19	Misoprostol Laminaria	Yes	<i>C. perfringens</i>
*Case C	West	Unknown	Unknown	No	<i>C. sordellii</i>

¹Fischer M, et al. N Engl J Med. 2005 Dec 1; 353(22): 2352-60.

²Sinave, C. et al. CID. 2002 Dec 1; 35(11): 1441-3.

³Cohen, A., Reagan, S., CDC, IDPA, unpublished data.

*Unable to confirm medical abortion

Cases of Toxic Shock-like Syndrome Following Medical Abortion

Case	Region	Weeks gestation	Agents Used	Intra-uterine Infection	<i>Clostridium</i> identified
<i>Previous cases</i>					
5 cases	Western US (4) ¹ , Canada (1) ²	6-10	Mifepristone Misoprostol	Yes	<i>C. sordellii</i>
<i>Additional cases³</i>					
Case A	West	8	Mifepristone Misoprostol	Yes	<i>C. perfringens</i>
Case B	Midwest	19	Misoprostol Laminaria	Yes	<i>C. perfringens</i>
*Case C	West	Unknown	Unknown	No	<i>C. sordellii</i>

¹Fischer M, et al. N Engl J Med. 2005 Dec 1; 353(22): 2352-60.

²Sinave, C. et al. CID. 2002 Dec 1; 35(11): 1441-3.

³Cohen, A., Reagan, S., CDC, IDPA, unpublished data.

*Unable to confirm medical abortion

Cases of Toxic Shock-Like Syndrome Following Miscarriage

Case	Region	Weeks gestation	Intra-uterine Infection	<i>Clostridium</i> identified
<i>Previous cases¹</i>				
Case 1	Not reported	2 nd trimester	Yes	<i>C. sordellii</i>
Case 2	Not reported	2 nd trimester	Yes	<i>C. sordellii</i> , <i>C. perfringens</i>
<i>Additional case²</i>				
Case A	Midwest	18	Yes	<i>C. sordellii</i>

¹Zane, SB and Berg, CJ. N Engl J Med. 2006 Apr 13; 354(15): 1645-7.

²Cohen, A., Reagan, S., CDC, IDPA, unpublished data



How did CDC Hear About These Cases?



- FDA adverse events monitoring
- State Health Departments
- Academic Partners
- Division of Reproductive Health's Pregnancy Mortality Surveillance System
 - Prevent deaths: monitor trends and identify risk factors
 - Clinical/pathology samples cannot be requested
 - No identifiable information can be published

Searching for Additional Pregnancy-Associated Toxic Shock-like Syndrome in California

321 possible cases in 2000-2003

149 excluded because no autopsy performed

144 excluded based on death certificates

5 excluded based on autopsy reports

5 excluded based on medical records

18 possible cases remain

3 awaiting autopsy reports

6 awaiting medical records

9 awaiting tissue reports

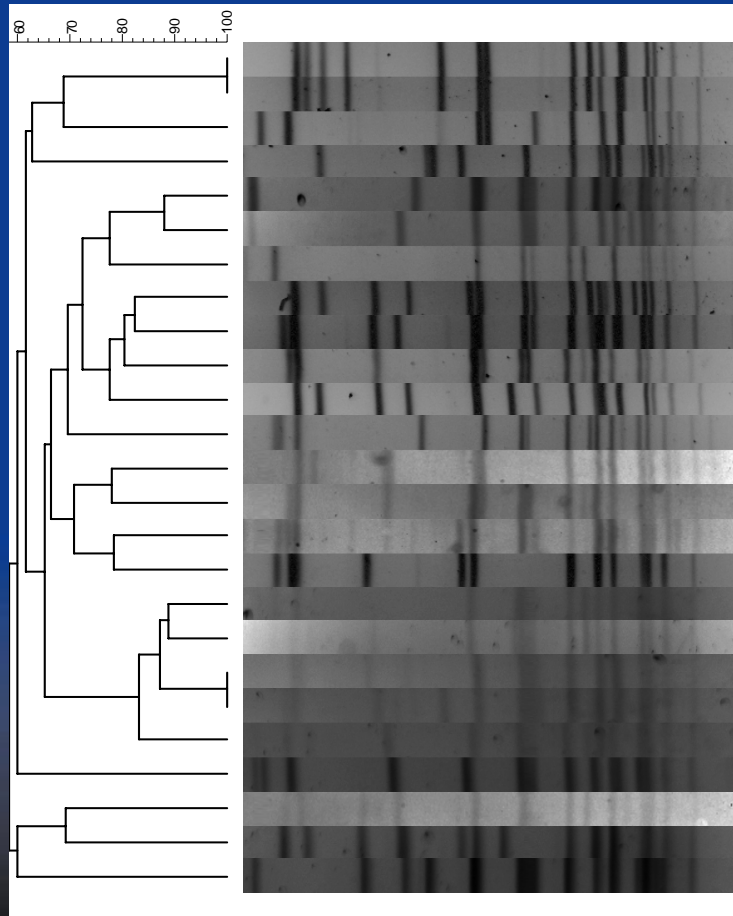
CA Unexplained Deaths Project and Dept of Health Services Maternal and Child Health Branch.
Unpublished data

Only a Minority of Clinical *C. sordellii* Possess Lethal Toxin

	Totals	Year Received at CDC for Testing					
		Not Recorded	1960s	1970s	1980s	1990s	2000-2006
Total no. of isolates	53	6	4	31	1	3	8
No. (%) from animals	5 (9)	0	3 (75)	2 (6)	0	0	0
No. (%) from human blood	11 (21)	0	0	7 (22)	0	2 (66)	3 (38)
No. (%) unknown source	8 (15)	2 (33)	0	1 (3)	1 (100)	1 (33)	3 (38)
No. (%) positive for Lethal toxin by PCR	13 (25)	0	0	8 (26)	0	3 (100)	2 (25)

No Evidence of Epidemic *C. sordellii* Strains

Dice (Opt:1.00%) (Tot:1.0%-1.0%) (H>0.0% S>0.0%) [0.0%-100.0%]
 PFGE H9812 PFGE H9812

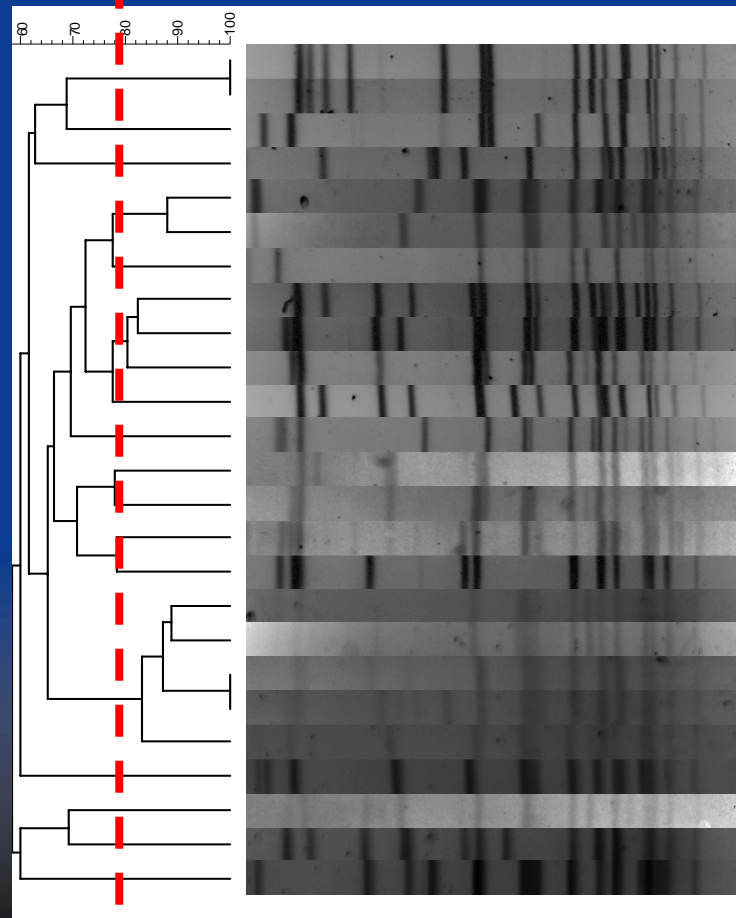


Year	Toxin	State	Source
2005	NEG	CA	unknown
1970	NEG	NC	leg wound
2004	POS	LA	left knee wound
1970	POS	MO	blood
1970	POS	MT	leg wound
1975	POS	Canad	right toe
1974	POS	CA	tissue
1974	POS	PA	trach aspirate
1975	NEG	AR	wound left h
1972	NEG	PA	peritoneal fluid
1975	NEG	CA	blood
1970	NEG	NM	blood
1971	NEG	MI	blood
1991	POS	WA	blood
2002	POS	MN	blood
2002	NEG	ND	blood
2005	NEG	CA	unknown
1975	NEG	TX	abdomen
1973	POS	CA	wound right arm
1973	POS	CA	wound
1973	POS	UT	wound thigh
1974	NEG	MS	foot wound
1975	NEG	NM	blood
1970	NEG	GA	liver
1973	NEG	MT	blood

No Evidence of Epidemic *C. sordellii* Strains



Dice (Opt:1.00%) (Tol:1.0%-1.0%) (H>0.0% S>0.0%) [0.0%-100.0%]
 PFGE H9812 PFGE H9812

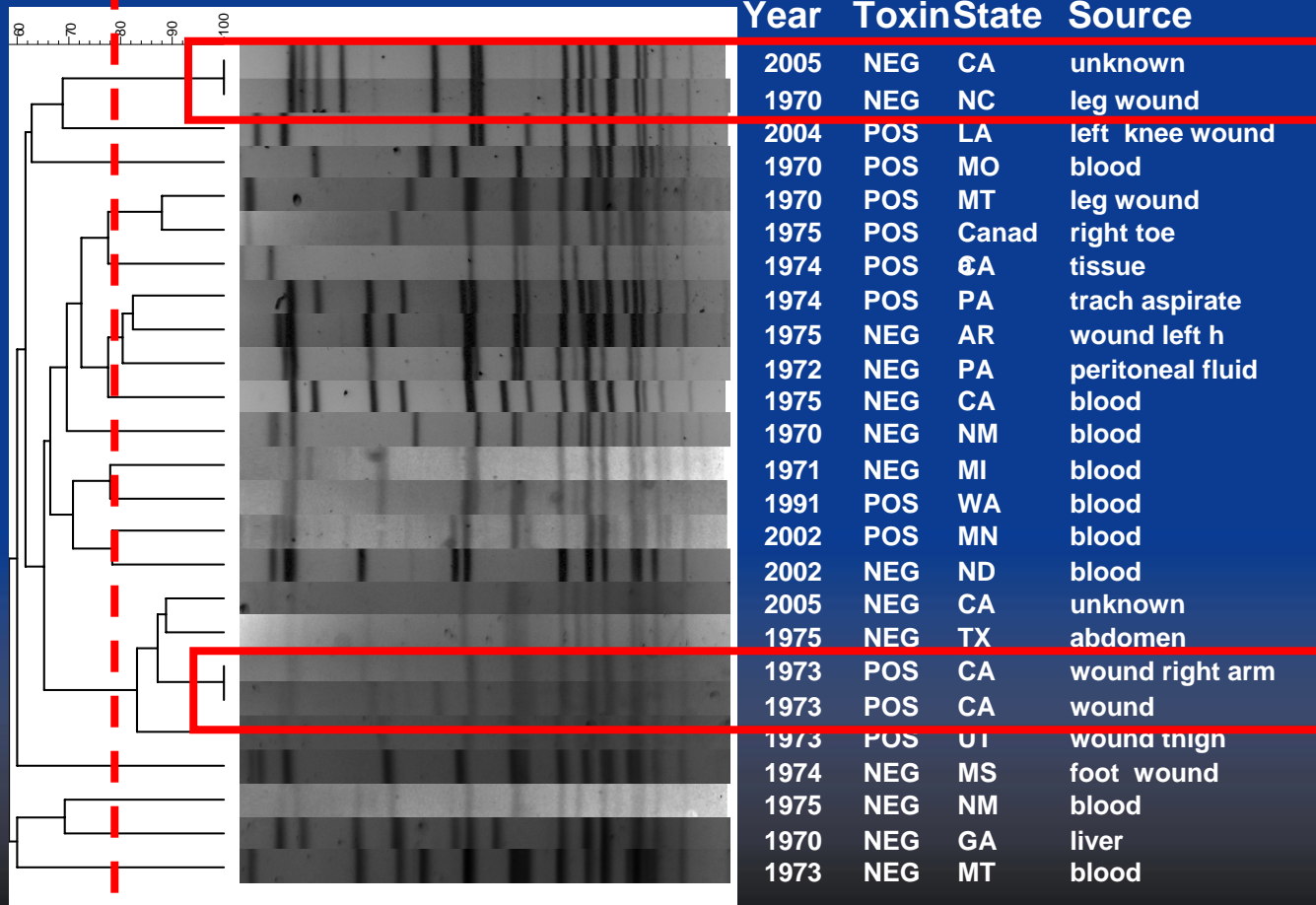


Year	Toxin	State	Source
2005	NEG	CA	unknown
1970	NEG	NC	leg wound
2004	POS	LA	left knee wound
1970	POS	MO	blood
1970	POS	MT	leg wound
1975	POS	Canad	right toe
1974	POS	CA	tissue
1974	POS	PA	trach aspirate
1975	NEG	AR	wound left h
1972	NEG	PA	peritoneal fluid
1975	NEG	CA	blood
1970	NEG	NM	blood
1971	NEG	MI	blood
1991	POS	WA	blood
2002	POS	MN	blood
2002	NEG	ND	blood
2005	NEG	CA	unknown
1975	NEG	TX	abdomen
1973	POS	CA	wound right arm
1973	POS	CA	wound
1973	POS	UT	wound thigh
1974	NEG	MS	foot wound
1975	NEG	NM	blood
1970	NEG	GA	liver
1973	NEG	MT	blood

No Evidence of Epidemic *C. sordellii* Strains



Dice (Opt:1.00%) (Tot:1.0%-1.0%) (H>0.0% S>0.0%) [0.0%-100.0%]
 PFGE H9812 PFGE H9812





Thank You