**Clostridium difficile infection: the next big thing!**

Tom Riley  
Microbiology & Immunology  
School of Pathology & Laboratory Medicine  
The University of Western Australia  
and  
Division of Microbiology & Infectious Diseases  
PathWest Laboratory Medicine  
Queen Elizabeth II Medical Centre  
Nedlands, WA  
Western Australia

**Risk factors for C. difficile?**

- Exposure to the organism – where?  
- Exposure to antibiotics – clindamycin, then cephalosporins, now fluoroquinolones (outside Australia)  
- Maybe others now?

**Effect of antibiotics on normal flora**

- No antibiotic  
  - Normal flora  
  - No C. difficile

- Antibiotic  
  - C. difficile that is resistant to the antibiotic has a selective advantage

- No antibiotic  
  - Normal flora  
  - No C. difficile

**C. difficile infection**

- Most common cause of infectious diarrhoea in hospital patients
- 2 major virulence factors:  
  - toxin A (an enterotoxin)  
  - toxin B (a cytotoxin)
- 3rd “binary” toxin

**Effect of antibiotics on normal flora**

- No antibiotic  
  - Normal flora  
  - No C. difficile

- Antibiotic  
  - C. difficile that is resistant to the antibiotic has a selective advantage

- No antibiotic  
  - Normal flora  
  - No C. difficile
C. difficile PCR ribotype 027

- More severe disease
- Produces more toxins A and B
- Produces binary toxin
- Fluoroquinolone resistant
- Epidemic spread across North America and UK/Europe from early 2000s
- Numbers dropping in UK/Europe
- Still major issue in USA

Superbug kills one person an hour

Epidemic spread across North America and UK/Europe from early 2000s
Numbers dropping in UK/Europe
Still major issue in USA

Rates in England 2008-11

Comparison of the Burdens of Hospital-Onset, Healthcare Facility-Associated Clostridium difficile Infection and of Healthcare-Associated Infection due to Methicillin-Resistant Staphylococcus aureus in Community Hospitals

Becky A. Miller, MD; Luke F. Chen, MD, MPH; Daniel J. Sexton, MD; Deverick J. Anderson, MD, MPH

We sought to determine the burden of nosocomial C. difficile infection in comparison to other healthcare-associated infections (HAIs) in community hospitals participating in an infection control network. Our data suggest that C. difficile has replaced MRSA as the most common etiology of HAI in community hospitals in the southeastern United States.
Reasons for increase

- Changes in test numbers
  - Some evidence of this
  - Greater awareness
- Changes in testing methods
  - Yes – when and what impact?
- If a real increase then why?
  - Healthcare associated vs community-associated
  - Changes in risk factors???????

Community-acquired CDI

- Not new – just underdiagnosed!
- 19/154 (12%) patients in ED (Brettle et al BMJ 1982)
- 4.7% increasing to 15.9% in patients with prior antibiotic exposure (Riley et al. J Hyg Camb) 1986
- 5.5% (Riley et al. Pathology 1991)
- 10.7% (specific request/history antibiotics Riley et al. Clin Infect Dis 1995)
- Risk factors clearly need exploring
C. difficile PCR ribotype 244

- More severe disease – attributable mortality 30% (Rhoda Stuart)
- Currently community acquired
- Produces more toxins A and B
- Produces binary toxin
- Fluoroquinolone susceptible
- Sept-Oct 2010 ACSQHC snapshot – one isolate
- Now 3rd most common ribotype in Australia ~5%

Relative evolutionary relatedness of five main subgroups and demonstration of microdiversity of subgroups.

C. difficile in pigs

- Early this century outbreaks of CDI in 5d old piglets in USA - high mortality (16%)
- Since 2000, C. difficile the major & most common cause of enteritis in neonatal piglets in USA
- Economic losses
- Pig ribotype 078
- 078 now infecting people in Europe and USA. 5th most common
- ? Food source or environment

Is Clostridium difficile a threat to Australia’s biosecurity?

Thomas W. Viley

Australia can benefit from lessons learned in the epidemic of C. difficile infection in Europe and North America.

MJA Volume 198 Number 12 15 June 2008

Every effort should be made to stop the epidemic C. difficile from becoming established in our production animals. Unfortunately, the mere perception of C. difficile infection as a foodborne disease will damage the industry.

However, if cephalosporin use is driving C. difficile infection in animals overseas, then additional efforts to target cephalosporin use in veterinary medicine may be needed in Australia.

Clostridium difficile infection in Europe: a hospital-based survey

Methods: We set up a network of 16 hospitals in 14 European countries.

Microbiological characteristics

Most frequent PCR ribotype of toxigenic isolates

<table>
<thead>
<tr>
<th>Ribotype</th>
<th>012</th>
<th>008</th>
<th>001</th>
<th>003</th>
<th>004</th>
<th>027</th>
<th>002</th>
<th>017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>46 (38%)</td>
<td>28 (34%)</td>
<td>24 (30%)</td>
<td>23 (28%)</td>
<td>20 (25%)</td>
<td>18 (38%)</td>
<td>17 (21%)</td>
<td>14 (17%)</td>
</tr>
</tbody>
</table>

Courtesy of John Turnidge

Food source or environment
C. difficile

- No C. difficile in chickens – relatively small sample (~60)
  - 4-5 day old chicks
  - 4 weeks old
  - At slaughter – 8 weeks

C. difficile in cattle in Australia

- 2008/9: cattle, 300 carcase washings/gut contents from WA
  - No C. difficile

- 2009/10: 280 faecal samples from eastern Australia
  - 5 positives (1.8%)

- 2012: 100 veal calves, one abattoir in Vic, one abattoir in Q
  - 72% positive in both places

Emerging infections Disease outbreak alert and response

- Slide kindly provided by Pierre Formenty
Contaminated vegetables

- MUSHROOMS!

To summarise the issues

- Major human health problem – now in the community
- Now a major animal health problem (particularly piglets and adult horse)
- Gross contamination of the environment OUTSIDE hospitals
- Contamination of meat in some parts of the world
- Contamination of vegetables (probably through use of animal manure, pig effluent, etc.)
- Australia has a community acquired on-going outbreak
- CDI is a zoonosis
- Will require a One Health approach to resolve

Acknowledgments

NIAMR/CRC
Australian Biosecurity CRC
Australian Pork Ltd
Rural Industries R & D Corporation
Australian Commission on Safety & Quality in Healthcare
WA Department of Health
Meat & Livestock Australia

Collaborations with:
Monash University (Dena Lyras)
Sanger Institute (Trevor Lawley)
LSHTM (Brendan Wren)
Oxford University/PHL (Derrick Crook, David Eyre, Kate Dingle)
University of Leeds (Mark Wilcox)