**Clostridium difficile in the Community: Food for Thought**

**Prof. Tom Riley,**

**A Webber Training Teleclass**

Hosted by Jane Barnett
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April 17, 2013

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**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

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**Toxin A & toxin B**

- Large structurally and functionally related proteins
- Genes are contained on a 19.6-kB Pathogenicity Locus (PaLoc) which is absent in non-toxigenic strains
- Majority of pathogenic strains produce both toxins which affect actin cytoskeleton
- Polymorphisms in the PaLoc can affect toxin production - toxin A-negative, toxin B-positive strains

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**Binary toxin**

- Additional toxin produce by 2-5% of isolates
- Consists of two component proteins, the genes for which are contained within the CDT locus on the chromosome
- Actin-specific ADP-ribosyltransferase
- Unknown significance in disease, but associated with increased severity of diarrhoea

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**Cytopathic effects**

**Cellular Morphology**
- Cell-rounding
- Detachment from extracellular matrix

**Cellular Processes**
- Activation of caspases → apoptosis
- Decrease in integrity of light-cell junctions
- Inflammatory response
  - Release of cytokines & chemokines
  - Production of reactive oxygen intermediates

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**Histological effects**

- Massive inflammatory response
- Recruitment of polymorphonuclear neutrophils to area
- Increase in epithelial permeability

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**Risk factors for getting C. difficile?**

- Exposure to the organism – how much?
- Exposure to antibiotics – clindamycin, then cephalosporins, now fluoroquinolones
- Maybe others now?

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**Effect of antibiotics on normal flora**


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**Investigation**

Investigation into outbreaks of *Clostridium difficile* at Stoke Mandeville Hospital, Buckinghamshire Hospitals NHS Trust

July 2004

[Link to investigation document]

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**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**

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

We sought to determine the burdens of nosocomial *Clostridium 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 HAIs in community hospitals in the southeastern United States.


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**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
- Three clusters in Australia since 2009

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**CDI in Australia**

- Not a notifiable infection
- But mandatory reporting by hospitals since 2010
- Reporting of “hospital identified” cases of CDI

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**Fig. 2** Incidence of *Clostridium difficile*-associated diarrhea at SCGH 1983-92

**Cephalosporin use SCGH, 1983-92**

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**C. difficile: monthly episodes 1993-2000**

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** aggregate *Clostridium difficile* infection rates Western Australia**

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**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??????

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**Community acquired CDI**

- C. difficile was the most common enteric pathogen detected.
- Most patients had only mild to moderate diarrhoea.
- In the majority of patients the diarrhoea was protracted.
- 80-85% of patients had received antimicrobial agents in the 3 months preceding onset of diarrhoea.
- Most treated successfully with metronidazole.

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**Community acquired CDI**

- This is not new!
- Very much under-diagnosed for years
- C. difficile is ubiquitous
- Many sources in the community
- All animals get colonised at birth incl. humans
- But – generally requires exposure to an infectious dose AND prior gut insult
- Risk factors need further investigation

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The Epidemiology of Community-Acquired Clostridium difficile Infection: A Population-Based Study

- What is current knowledge?
  - Clostridium difficile infection is increasing worldwide with hospitalization and antibiotic exposure as the most common risk factors.
  - The epidemiology and characteristics of community-acquired Clostridium difficile infection are not well defined.
- What is new here?
  - A major proportion of Clostridium difficile infection patients is community-acquired.
  - These patients are younger, often lack traditional risk factors, and have less severe disease than patients with hospital-acquired infection.


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Contact with infants <2 years old significantly associated with CDI


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CDI cases identified at Metro Non-Tertiary Hospitals 2010-2011

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**C. difficile PCR ribotype 244**

- More severe disease – attributable mortality 30% (Dr Rhonda Stuart)
- Currently community acquired
- Produces more toxins A and B
- Produces binary toxin, tcdC mutation at pos.117
- Fluoroquinolone susceptible
- Putative 027 with GeneXpert
- Sept-Oct 2010 ACSQHC snapshot – one isolate
- 2011/12 3rd most common ribotype ~5%

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Early this century outbreaks of CDI in 5-d 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, 3rd most common
? Food source or environment


Clostridium difficile infection in Europe: a hospital-based survey

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**C. difficile in cattle in Australia**
- 2008/9: adult cattle, 151 carcass washings and 151 gut contents from WA
  - No C. difficile
- 2009/10: 280 faecal samples from adults E Australia
  - 5 positives (1.8%)
- 2012: 360 <7 day old veal calves, several abattoirs in Vic and Queensland (4% in 2-6 month old calves)
  - 56% positive

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**Contaminated vegetables**
- Al Salfi and Brazier. The distribution of *Clostridium difficile* in the environment of South Wales. J Med Microbiol 1996; 45: 133-7.(7/300 [2.3%] positive)

**MUSHROOMS!**

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**Our 1st theory**
- Contaminated Australian meat or vegetables
- Driven by flu season plus antibiotics
- But can’t find RT 244 in any animals!
- Doesn’t account for all the increase
- RT 244 comes from North America

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**Ribotype 251**
- 2nd major new RT emerged in Australia
- Similar to RT 244
- Community acquired, severe disease
- Binary toxin positive but no *tcdC* deletion or mutation
- There no putative 027 with GeneXpert
- Groups with 027 by PFGE
- Cluster found in USA along with a cluster of 244

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**Our 2nd theory**

- Contaminated food imported from North America
- 96% of Australian food locally produced
- A seasonality of RT 244 infections
- Exactly the same problem occurring in NZ with the same food importation patterns as Australia
- But probably endemic local food-borne disease also

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**Animal/human connections**

- Ribotype 126
- Ribotype 127 - cattle
- Ribotype 033
- Ribotype 237 - pigs
- Ribotype ??? – horses
- Many other new ribotypes from animals: usually binary toxin positive, that are starting to appear in humans

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**To summarise the issues**

- Major new human health problem in Australia (and NZ) – community CDI
- Need to find the source/reservoir
- Need to prevent establishment of RTs 244/251 in hospitals
- Now a major animal health problem (pigs/horses)
- Gross contamination of the environment OUTSIDE hospitals - probable contamination of food
- CDI is a zoonosis
- Will require a One Health approach to resolve

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18 April  **LEADERSHIP IN INFECTION PREVENTION AND CONTROL**
Speaker: Martin Kiernan, Southport & Ormskirk Hospital NHS Trust

29 April  **(Denver Russell Memorial Teleclass) ROLE OF SURFACES IN DISEASE TRANSMISSION: DOES ENHANCED DISINFECTION REDUCE TRANSMISSION?**
Speaker: Prof. Bill Rutala, University of North Carolina

06 May  **(Free WHO Teleclass … Europe) SPECIAL LECTURE FOR MAY 5**
Speaker: Prof. Didier Pittet, World Health Organization, Geneva

09 May  **SURVEILLANCE OF HEALTHCARE ASSOCIATED INFECTION IN ACUTE CARE SETTINGS**
Speaker: Teresa Horan, Rollins School of Public Health, Emory University

16 May  **WHAT’S NEW IN TECHNOLOGIC INNOVATIONS FOR THE PREVENTION OF INTRAVASCULAR CATHETER ASSOCIATED BLOODSTREAM INFECTION**

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