Clostridium difficile 027, A Southern Hemisphere Perspective
Dr. David Hammer, Medlab South, New Zealand
A Webber Training Teleclass

THE PRESS 6 July 2006

Errors cost 30% of health budget

Total Annual Cost of Nosocomial Infection
- USA  US$ 7 000 000 000
- UK  £ 1 000 000 000
- NZ  NZD 136 000 000

C. difficile – more than just a little diarrhoea …
- 7 – 64% mortality rate
- US $1 000 000 000 / year
- EU €300 000 000 / year
- UK £2000 (extra cost per case)
  and 10 day increase in length of stay
- > 43 000 cases reported in UK 2004
  (2000 x 43000 = £86 000 000)

Declaration of personal interest
- Harry (an elderly family friend)
- Routine shoulder operation – UK NHS
- Acquired C. difficile
- Died in hospital
- Undignified and painful death
- Personal interest in preventing further such tragedies

Epidemiology
- Up to 50% neonates → < 3% 2 year olds
- Isolated in 3% of healthy adults who usually have high antibody levels to toxin A
- Mostly acquired from environment
  - Lower incidence single vs double rooms
  - Possible food sources in studies on meat
- Person to person spread well documented
  - 60% HCW’s hands (in those caring for carriers)
- Occasionally endogenous
- Sexual transmission described

Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com
**Clostridium difficile 027, A Southern Hemisphere Perspective**

*Dr. David Hammer, Medlab South, New Zealand*

*A Webber Training Teleclass*

---

**Not just patients**

- Documented infections in
  - HCWs
  - Lab workers

**Why don’t people get C difficile?**

- Protective factors
  - IgG
  - Non-toxigenic carriage protective
  - Bowel flora ($10^{12}$ bacteria/g stool)
    - Bacterial interference
    - Bowel flora changes with age
    - Bowel flora can be affected by antibiotics, chemo or surgery
- Neonates
  - high colonisation but low disease
  - probable lack of toxin receptors

---

**The Bug**

- Gram positive anaerobic bacillus
- Spores

**Pathogenicity of C. difficile**

- Spores
  - Tough outer layers enable prolonged and tenacious environmental survival
- Toxins
  - A number of poisons produced by the bacterium wreak havoc on human tissue

---

**The Bacterial Spore**

**Implications of spores**

- Potentially survive for decades in the environment
- Difficult to eradicate without extreme measures (eg. bleach or autoclave)

---

Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com
**Toxins**

- *C. difficile* disease is toxin based
- Toxin A (enterotoxin)
  - Also causes inflammatory response
- Toxin B (cytotoxin) 10 x more toxic than A!
- Both damage cytoskeleton
- Binary toxin attacks actin filaments in cell causing cell death

**Toxins Genes**

![Toxins Genes Diagram](image)

**Colonic disease**

![Colonic disease Image](image)

1. Cytolysis and separation of epithelium

**Clinical manifestations**

- Usually within 5 – 10 days of antibiotics
- 2/3 Asymptomatic
- Profuse watery diarrhoea (± blood)
- 50% have fever & ↑ WBC
- 1/3 abdominal pains
- Rarely
  - bacteraemia
  - osteomyelitis
  - splenic abscess
- Reactive arthritis described

**Complications**

- Perforation/ Acute abdomen
  - mimics appendicitis
- Toxic megacolon
  - mimics Inflammatory Bowel Disease
  - 64% mortality
- Beware the 'known colitic' patient!

**Diagnosis of *C. difficile***

Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com
Diagnosis - Culture

- The ‘difficult’ bacterium
- Non-haemolytic, yellow-white ground-glass colonies with rhizoid margins
- p-cresol (horse manure) odour
- Fluoresces chartreuse under UV
- CCFA media – selective but
  - not sensitive for spores (unless bile salts added)
  - non-specific (25% non-toxigenic strains)

Diagnosis – other modalities

- Neutralisation assay
  - Culture and neutralisation of toxins
  - Gold standard but slow & expensive
- ELISA
  - sensitivity 64 – 94%; specificity 75 – 100%
  - Issues with detection of A- B+ strains in older systems
- PCR only recently available for direct diagnosis
- Endoscopy reserved for special situations

The ‘new’ outbreak strain

- Restriction endonuclease analysis BI/ PFGE NAP1, toxintype III, Ribotype 027
- Originally described in 1994
- Historically rare (5%)
  - Past, sensitive to F/Qs (gati- & moxifloxacin)
  - Current epidemic isolates all resistant to F/Qs

027 pathogenesis

- Toxins: A + B + binary toxin + deletion tcdC
- Toxin levels ± 20 x higher than standard strains
  - More virulent
- Increased sporulation
  - Better spread

Toxin & spore production

Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com
**US**
- New strain identified in US since 2001
- CDC data showed a rise of 26% in discharge diagnosis of *C. difficile* between 2000 and 2001

**Canada**
- Identified in 2002 – 2003
- Epidemic detected because of increased colectomies!
  - Quebec: 1995 3.6/10 000 pt days
  - 2005 >15/10 000 pt days
- Death in 22/132 cases of epidemic strain vs 0/25 infected with other strains

**UK**
- Incidence of CDAD doubled between 2001 and 2004
- National incidence of 678/100 000 in people over 75
- 43 672 cases of *C. difficile* in 2004
  - notification now mandatory

**027 in the EU and beyond**
- 2005
  - Netherlands
- 2006
  - Austria, Denmark, France, Switzerland, Scotland
- 2007
  - Belgium, Germany, Ireland, Norway, Spain, Japan
- 2008
  - Sweden

**New Zealand/ Oceania**
- Current situation
  - Anecdotally *C. difficile* is not a major problem
- But
  - NOT a notifiable disease
  - No co-ordinated screening program
  - No 027 specific surveillance
- It’s just a matter of time before it arrives!
- Are we ready for it?
  - Probably not

**Treatment**
- Stop offending antibiotic cures ± 20%
- Supportive therapy
  - Fluids and electrolytes
- Avoid antiperistaltic agents
  - These may make disease worse
- Do not treat asymptomatic carriers

---

Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com
Antibiotic Therapy – Metronidazole

• Oral metronidazole
  – Cheap
  – Recommended for first line use in mild disease
• IV metronidazole
  – some efficacy in NBM patients

Antibiotic Therapy – Vancomycin

• Oral vancomycin
  – Very expensive
  – Recommended for first line use in severe disease
  • WBC > 20,000/ml
  • Creatinine > 200 micromol/L
  • Age > 70
  – use 2nd line in mild disease

Antibiotic Therapy

• Both metronidazole & vancomycin have
  – ≥ 90% cure
  – ≥ 15% relapse
  – Some in vitro resistance described
  – Possible risk of increased VRE

Other treatments

• Limited data available for
  – Teicoplanin
  – Rifamycins
  – Fusidic acid
  – Bacitracin
  – Nitazoxanide
• Anion-exchange resins
• Intravenous Immunoglobulins
  – Very expensive
  – Successful case reports
• Stool infusions reported successful
  – the domain of the desperate!

Recurrence

• Well-described
• May be multiple
• Up to 50% are different strain
  – Resistance is NOT usually a feature
• Re-treat with initial antibiotic used
  – May try tapering/ pulsed doses to eradicate germinating spores
• Role of probiotics is uncertain
  – Saccharomyces boulardii & Clostridium coccoides show some potential
  – No convincing evidence yet
  – Risk of nosocomial disease in immune compromised

Prevention & Control

Incorporating standard precautions

Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com
Case management

- Contact/ Enteric isolation of cases
  - Own toilet
- Gloves
- Gowns
  - Especially dealing with soiled material

Hand hygiene

- Good handwashing technique essential
  - Washing is the preferred method of hand hygiene in the setting of *C. difficile*
- NB – Alcohol does not kill spores!
- However, no studies have shown increased infections in units with use of alcohol hand rub

Environmental factors

- Good bed: toilet ratios
- Environmental disinfection is vital
  - Hypochlorites, peracetic acid, peroxide
  - CDC recommends hypochlorites
  - Adequate cleaning job necessary
- Non-isolation areas also important
- Potential for increased sporulation with
  - Non-sporicidal agents
  - Diluted concentrations of sporicides
  - Disinfectant vaporisers being tested
  - Cleaning of bed pans a problem

Caveat emptor

- Beware of claims of increased efficacy of alcohol or chlorhexidine hand disinfectants against *C. difficile* as these are based on vegetative form, not spores
- Same caution should be applied to some claims concerning environmental disinfectants!

Identifying at risk patients

- Age, comorbidities, antibiotics, PPIs
- Waterlow score >20 could be used to identify high risk patients
  - Sensitivity 70%
  - Specificity 95%

Patient hygiene

- Growing evidence of carriage of *C. difficile* on skin of asymptomatic and symptomatic patients (even after symptom resolution)
- Raises the question of the role of patient cleaning

Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com
# Rationalise antibiotic use
- Well documented association with CDAD &
  - Clindamycin
  - Cephalosporins
  - Fluoroquinolones
- Generally believed that 50% of antibiotics are unnecessary
- Some studies show reduced *C. difficile* infection rates with better antibiotic stewardship

CID 2007 Sept; Suppl 2:S112-21

# SHEA/ IDSA guidelines
- [www.shea-online.org/evidence-based-guidelines.cfm](http://www.shea-online.org/evidence-based-guidelines.cfm)
- Contact precautions
- Proper environmental cleaning
- Hand hygiene
- Lab based notification system
- Surveillance of CDI rates
- Education of clinicians, management, patients & visitors
- Antimicrobial stewardship

# Experimental work
- Vaccine under development

# In Conclusion
- The Infection Control message remains the same:
  
  “Wash your hands, you sinners…”
  
  - James 4:8

- Perhaps there are too many saints in healthcare?

# Hosted by Jane Barnett
jane@webbertraining.com
www.webbertraining.com