Recommendations for the Development of New Hospital Guidelines due to the Effects of Antibiotics on *Clostridium difficile* Colitis

Megan Kohsel
What is *Clostridium difficile*?

- Gram-positive, anaerobic, spore forming
- Ability to produce exotoxins
- Naturally present in approx. 5% of populations microbiota
- It becomes pathogenic when *C. difficile* exploits an uninhabited niche
**C. difficile** virulence factors

- Attachment of the bacterium to the mucin and cells lining colon
- Damage occurs due to toxins and a yellowish layer forms on surface of the colon
- Damage causes an inflammatory response
- Pseudomembrane forms
C. difficile toxins

- Two large AB-type toxins
  - TcdA
  - TcdB
- TcdA
  - Mucosal cells become unable to control fluid movement
  - Slower working than TcdB
- TcdB
  - Collapses the actin cytoskeleton of the tissue cells
  - Some strains only produce TcdB
TcdA Mechanism

- Stimulation leads to cytokines and other inflammatory proteins
- Attraction of neutrophils
- Results in mucosal-cell destruction
- Fluid movement is not able to be controlled
- Pathway for TcdB to enter
- Targets G proteins
  - Responsible for many regulatory functions in mammals
TcdB Mechanism

- Damages the tissue on the underside of the mucosal membrane and intestinal wall.

- Extensive damage can lead to LPS or bacteria from colon to enter into the bloodstream and cause septic shock.
How *C. difficile* may be transmitted

- Survival through spores
  - Can survive for up to 5 months
  - Sanitization is important
- Transmitted by:
  - Environmental surface contamination
  - Staff or infected patients carrying it around on their hands
Symptoms

- **Mild to Moderate**
  - Watery diarrhea three or more times a day
  - Mild abdominal cramping and tenderness

- **Severe**
  - A few of the symptoms include:
    - Watery diarrhea ten to fifteen times a day
    - Severe abdominal cramping and pain
    - A stay in an intensive care unit
    - Endoscopic examination showing the presence of pseudomembranes
Antibiotic Risk Factors

- 96% of people received antibiotics within the last 14 days of their first symptoms
- All had received antibiotics with the last 3 months
- Fluoroquinolones
  - Associated with a higher risk
- Important because many people are taking antibiotics
  - Ex. Acne antibiotics
- Increased antibiotics associated with new hypervirulent strain BI/NAP1/027
Diagnostic Testing

- Best specimen for testing is watery, loose, or unformed stool
- Cell Cytotoxicity Assay
- Enzyme Immunoassay
- Culture
- Glutamate dehydrogenase
- Polymerase Chain Reaction
Current Treatment Options

- Antibiotics
  - Metronidazole
  - Vancomycin
  - Fidaxomicin (Dificid)
- Colectomy
  - Used in severe cases
- Fecal Microbiota transplantation
Fecal Microbiota Transplantation (FMT)

- Process of delivering stool from a healthy donor to a patient
- Routes of administration
  - Enema
  - Colonoscopy
  - Upper GI tract via ingestion
- Preferred due to decrease in probability of a relapse occurring
- Goal: Help the body reestablish its normal microbiota
  - Bacteriodetes and Firmicutes
- Administration: mix fecal matter with nonbacteriostatic saline solution and then strain or blend to remove unwanted particulate
- Good option for people with compromised immune systems
- 83% - 90% efficiency
Why \textit{C. difficile} Is a Concern

- Increasing resistance of patients to antibiotics
- Costing approximately $3.2 billion annually
- Many people today are taking antibiotics for many things making them susceptible
Solutions

- Education
  - Physicians
  - Patients
- Prevention of Transmission
  - Handwashing, gloves, gown
- Hospital Layout
  - Single rooms or patients with *C. difficile* in same room
- Hospital Cleaning Staff Responsibilities
  - Sporocidals, 1:10 dilution of concentrated sodium hyperchlorite (bleach)
Solutions continued...

- FMT in a Pill
  - Reduction of transmission through instruments
- Continued Care Practices
  - Bringing hospital guidelines to the home of the patient
- Further Development of Care
  - Research to gain a better understanding
Conclusion

- It is a disease that can be controlled
  - Education
  - Understanding of risks associated with antibiotics
  - Maintaining a clean environment
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Cruz, M. P. "Fidaxomicin (Dificid), a Novel Oral Macrocyclic Antibacterial Agent For the Treatment of Clostridium difficile-Associated Diarrhea in Adults." *Pharmacy & Therapeutics* 37.5 (2012): 278-81.


