Clostridium Difficile Update

Transmission, Prevention, Treatment
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C. Diff Colitis

- History
  - Described in 1935 by Hall and O’Toole
  - Named the “Difficult Clostridium”
  - Found to colonize healthy newborns
  - Found to be toxigenic
  - 1978 C diff. Toxin found in the stool of patients with antibiotic associated diarrhea

Epidemiology of C diff

- Prevalence of asymptomatic colonization 7-50% of adult inpatients in acute care
- 5-7% among adults in long term care
- Risk of colonization increases during hospitalization
Changing Epidemiology of C. diff

- Estimated 500,000 cases of C diff/year in US
- Estimated 15,000-20,000 deaths/year
- Community C diff 7.6 cases/100,000 person years
- 35% have had no antibiotics within 42 days

Nature. 2009;7;526-36

Pathogenesis of C. diff

- A “two hit” phenomenon
  - Colonization with C diff
  - Alteration of gut flora with antibiotics

Critical Care 2008, 12:203
C diff Outbreaks

Three Factors Implicated
- Increased production of Toxins A and B
- Flooroquinolone resistance
- Production of a binary toxin

Toxin Production in Epidemic Strains of C diff

Pathogenesis of C diff

Pathogenesis of C diff
Risk Factors for C diff

- Advanced age
- Duration of hospitalization
- Exposure to antibiotics
- Chemotherapy
- HIV
- GI surgery
- Acid suppression

Clinical Manifestations of C diff

- Range from asymptomatic to fulminant disease
- Diarrhea
- Fever
- Abdominal pain
- Leukocytosis
- May have abdominal pain/distention without diarrhea in advanced disease

Clinical Manifestations of C diff

- Incubation period from acquisition of C diff to CDI is short (median 2-3 days)
- Patients may remain at risk for C diff for 3 months or longer after they have stopped antibiotics

Diagnosis of C difficile Infection

- Testing should be performed only on diarrheal stool, unless ileus due to C diff is suspected
- Only a single specimen needed for testing
- PCR testing is rapid, sensitive and specific
- EIA testing for C diff toxin A and B is rapid but less sensitive
- Repeat testing during the same episode of diarrhea is discouraged
- No “test of cure”
Transmission of C diff

Factors Associated with Increased Shedding of C diff

- Diarrhea
- Fecal incontinence
- High concentrations of organisms in the stool
- “super shedders”

Environment as a Source of Transmission of C difficile

- C diff is commonly isolated from the hands of health care providers
- The frequency of positive hand cultures is strongly correlated to the level of environmental contamination
  - Hands 0% when Environment 0-25%
  - Hands 8% when Environment 26-50%
  - Hands 36% when Environment >50%

- Acquisition of spores on gloved hands occurred as frequently after contact with environmental surfaces as after contact with skin sites (50% vs 50%)
- Prior room occupant with C diff is a significant risk factor for C diff acquisition (11% vs 5%)

Environmental Sources of C difficile

- Electronic thermometers
- Blood pressure cuffs
- Bedside commodes
- Stethoscopes

What Makes C diff Different From Other Bacteria?

Infection Control Measures for C diff Infection

- Gowns and gloves for contact with patients
- Wash hands with soap and water
- Private room or cohort patients with private commode
- Chlorine containing cleaning agents, terminal cleaning of rooms
- Antibiotic restraint
Special Approach to Prevent C diff Transmission

• Expedite identification and isolation of patients
• Prolong duration of contact precautions
• Improve bathing to reduce the burden of spores on skin
• Daily disinfection of high-touch surfaces during C diff treatment
• Use more sensitive diagnostic tests

Cleaning of High Touch Surfaces Daily

Environmental Cleaning to Control C diff

CDC, SHEA, IDSA all recommend use of a 1:10 dilution of sodium hypochlorite for environmental disinfection in outbreak settings of C diff

UV Light and C diff

Use of UV Light to Control C diff

- Numerous retrospective studies funded by industry
- Recent prospective study looking at environmental cultures
Use of UV Light to Control C diff

![Graph showing the use of UV light to control C diff](image)

Hand Hygiene for C diff

- C diff in its spore form is highly resistant to killing by alcohol
- Spores can be physically removed by soap and water
- Several studies have documented reduction in C diff rates by improvement in hand washing compliance

C diff on Hands of HCWs

- Compared hand contamination
  - 66 HCW caring for patients with CDI
  - 44 HCW controls
  - Monitored for 8 weeks
- Results
  - C diff spores on 24% of samples of hands from HCWs caring for CDI patients
  - No spores on hands of control HCWs
- Nursing assistants had highest rates
- Most of HCWs used gloves for patient contact

Summary of Prevention Measures

**Core Measures**
- Contact Precautions for duration of illness
- Hand hygiene in compliance with CDC/WHO
- Cleaning and disinfection of equipment and environment
- Laboratory-based alert system
- CDI surveillance
- Education

**Supplemental Measures**
- Prolonged duration of Contact Precautions*
- Presumptive isolation
- Evaluate and optimize testing
- Soap and water for HH upon exiting CDI room
- Universal glove use on units with high CDI rates*
- Bleach for environmental disinfection
- Antimicrobial stewardship program

* Not included in CDC/HICPAC 2007 Guideline for Isolation Precautions

Clostridium Difficile Treatment and Transmission
Margaret Hagan, MD

Family Medicine Winter Symposium
December 5, 2014


Measures to Improve C diff Rates

- Analyze rates
- Form a multidisciplinary performance improvement team
  - Environmental cleaning
  - Proper PPE
  - Hand washing
  - Antibiotic stewardship

Treatment of C diff Infection

- Metronidazole
- Vancomycin
- Fidaxomicin
- Probiotics
- Immunoglobulin
- Fecal Transplant
Treatment of C diff Infection

- Metronidazole is the drug of choice
  - 500mg tid for 10-14 days
- Vancomycin drug of choice for severe infection
  - 125-500mg qid for 10-14 days
  - Tapering schedule for recurrent infections
- Severe/Complicated C diff
  Vancomycin 500mg po q 6 hours and
  Metronidazole 500mg IV q 8 hours

Metronidazole vs Vancomycin

![Bar chart comparing response rates of Vancomycin and Metronidazole]

Fidaxomicin vs Vancomycin

- A multicenter, prospective, randomized, placebo controlled trial
- 629 patients enrolled at 52 sites
- No difference in cure rates
- Treatment with Fidaxomicin associated with lower rate of recurrence (15.4 vs 25.3%)
- Cost issues

Treatment of C diff Infection

- Vancomycin enema
- Fecal transplant
- Colectomy

Infection Control and Hospital Epidemiology, Vol. 31, No. 5 (May 2010), pp. 431-455


Fecal Transplantation

• Treating *Clostridium difficile* Infection With Fecal Microbiota Transplantation
  • Obtain donor stool from a relative
  • Screen donor for C diff
  • Mix donor stool with tap water to make a solution
  • Instill as an enema to the patient
• Via Christi has a protocol for FMT
• Requires specific consent form

_Clin Gastro and Hepatol._, December 2011.9(12) 1044-1049

Probiotics in the Treatment of C diff

• Current C diff guidelines do not recommend use of probiotics
• Cochrane review 2008 reviewed 4 studies and found a statistically significant benefit in only one small study
• More recent studies of multi-strain probiotics show promise
Role of Immunotherapy in the Treatment of C diff

- Inability to mount an immune response appears to make patient susceptible to recurrent infections
- Favorable outcomes with use of IgG for recurrent infections
- No randomized controlled trials
- Vaccine for C diff is being studied

Immune Response to C diff

- Check IgG level on patients with severe or recurrent C diff
- Give a one-time dose of IVIG to patients with low IgG
Role of Antibiotic Stewardship in Controlling C diff

- Use of antibiotics is associated with increase in C diff rates
- Certain antibiotics are associated with higher C diff rates (floroquinolones)
- Several studies have shown reductions in C diff rates with effective antimicrobial management programs