The Epidemiology of *Clostridium difficile*

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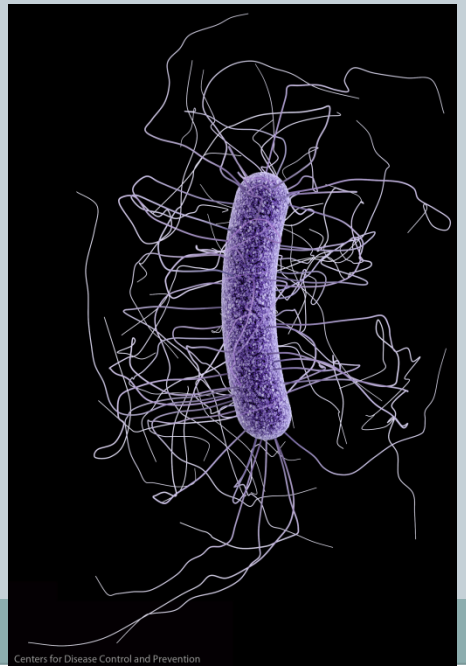


Some history first

- *Clostridium difficile*, a spore-forming gram-positive (i.e., thick cell wall) anaerobic bacillus, was initially detected in the fecal flora of healthy newborns in 1935.

- *C. diff* was thought to be nonpathogenic until 1978, when Bartlett et al identified *C. diff* as the source of cytotoxin in the stools of patients with colitis, a disorder frequently associated with antimicrobial use

Bartlett JG, Chang TW, Gurwith M, Gorbach SL, Onderdonk AB. Antibiotic-associated pseudomembranous colitis due to toxin-producing clostridia. N Engl J Med 1978;298:531-4.

Role of antibiotics

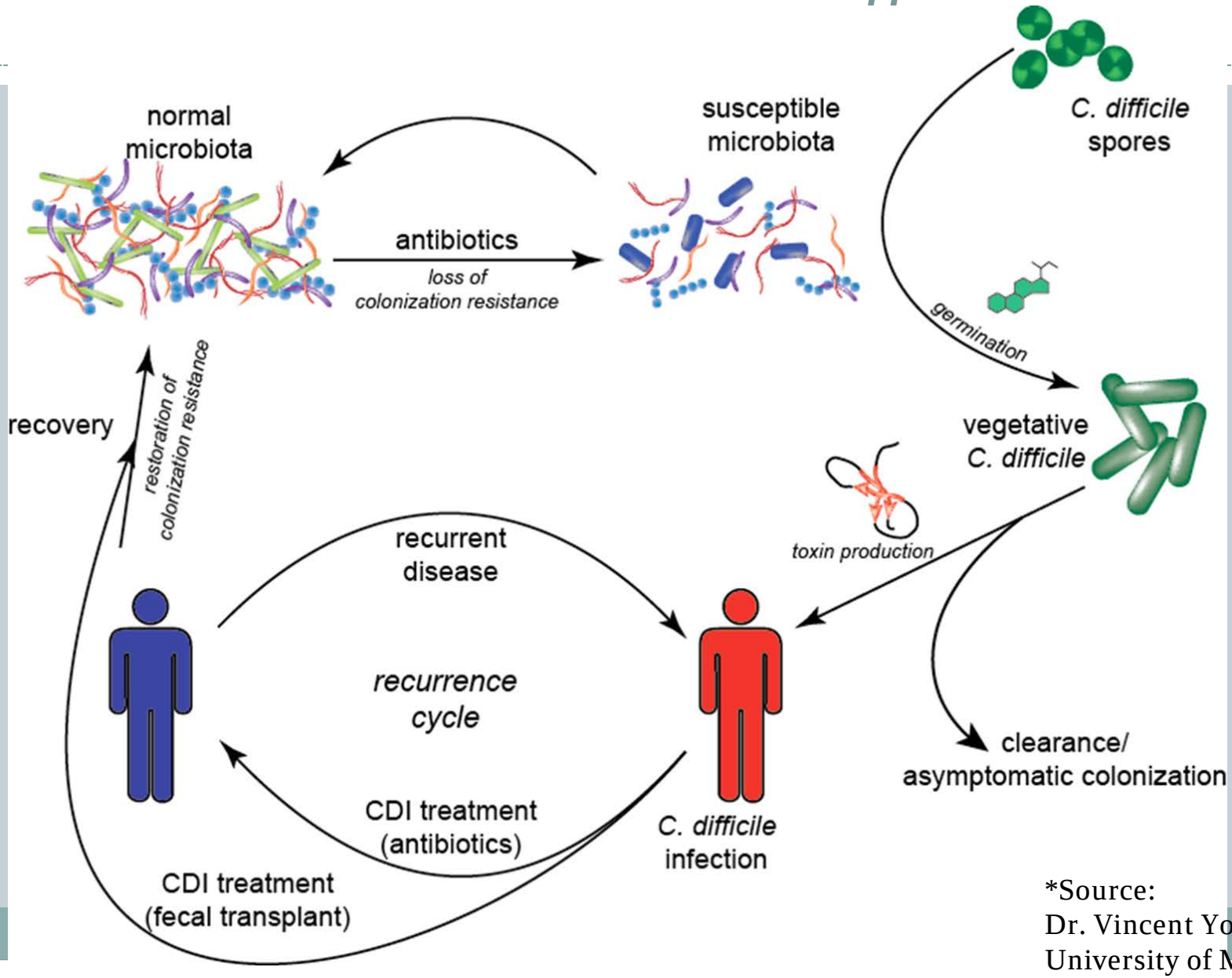
- Intestines contain millions of bacteria, many of which help protect your body from infection.
- When you take an antibiotic to treat an infection, the drug can destroy some of the normal, helpful bacteria as well as the bacteria causing the illness.
- Without enough healthy bacteria, C. difficile can quickly grow out of control. The antibiotics that most often lead to C. difficile infections include fluoroquinolones, cephalosporins, clindamycin and penicillins.

Microbial Diversity

- Microbial diversity is important to gut health and overall health
  - Confers stability and resistance to pathogens
  - Any disruption or deviation of microbial diversity could lead to bacterial colonization by new organisms (like *C. diff)*

- Antibiotics seriously disrupt the biodiversity of our gut microbiome (i.e., the sum of all organisms in our gut and their interactions)

Normal microbiome to *C. diff* infection



*Source:
Dr. Vincent Young
University of Michigan

C. Diff symptoms

- **Clostridium difficile** colitis (inflammation of the large intestine) resulting from infection with **Clostridium difficile**, a type of spore-forming bacteria. It causes an infectious diarrhea called **C. difficile** diarrhea.

- Once established, *C. diff* can produce toxins that attack the lining of the intestine. The toxins destroy cells and produce patches (plaques) of inflammatory cells and decaying cellular debris inside the colon and cause watery diarrhea.

C. Diff activity

- Because *C. difficile* is shed in feces, any surface or device that becomes contaminated with feces can serve as a reservoir for *C. difficile* spores.

- *C. difficile* spores resist desiccation (i.e., drying and dying) for months and can persist on hard surfaces for as long as **5 months**.

Spread of *C. diff*

- People can get infected if they touch surfaces contaminated with feces, and then touch their mouth.
- Healthcare workers can **spread** the bacteria to their patients if their hands are contaminated.
- At risk of getting *C. difficile* infection if you have an illness that requires prolonged use of antibiotics. The elderly are at greatest risk. Treatment of initial CDI is with antibiotics.

Prevention of *C. diff*

- **Hand-washing.** Health care workers should practice good hand hygiene before and after treating each person in their care. In the event of a C. diff outbreak, **using soap and warm water is a better choice for hand hygiene, because alcohol-based hand sanitizers do not effectively destroy C. diff spores.** Visitors also should wash their hands with soap and warm water before and after leaving the room or using the bathroom.

- **Contact precautions.** People who are hospitalized with C. diff have a **private room, and if not available, share a room with someone who has the same illness**. Hospital staff and visitors wear **disposable gloves and gowns while in the room.**

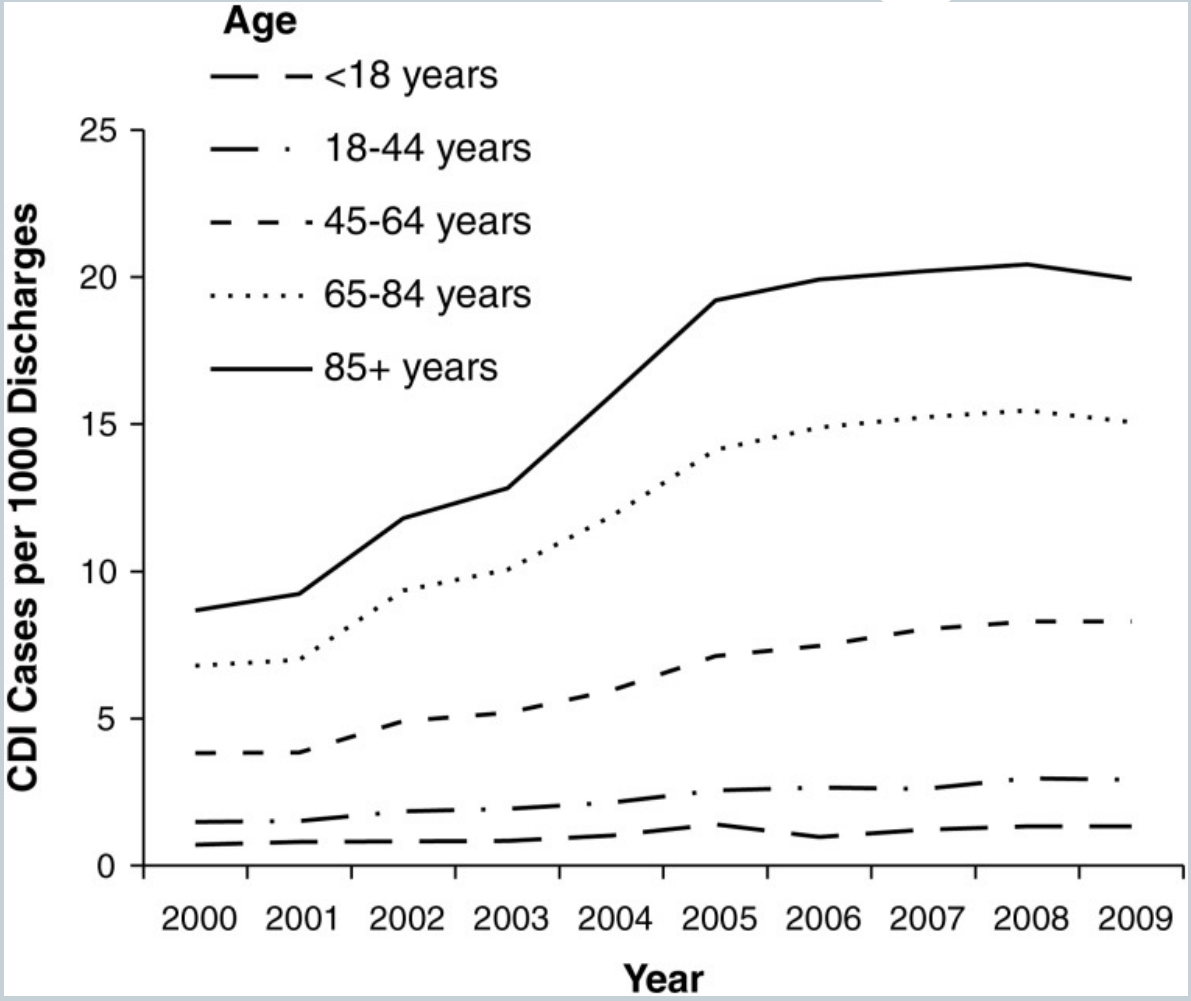
- **Thorough cleaning.** In any setting, **all surfaces should be carefully disinfected with a product that contains chlorine bleach.** C. diff spores can survive routine cleaning products that don't contain bleach.

- **Avoid unnecessary use of antibiotics.** Antibiotics are sometimes prescribed for viral illnesses that aren't helped by these drugs. Take a wait-and-see attitude with simple ailments. If you do need an antibiotic, ask your doctor to prescribe one that has a narrow range and that you take for the shortest time possible.

Epidemiology of *C. diff*

- Each year, more than a half million people get sick from C. difficile
- In recent years, C. difficile infections (CDI) have become more frequent, severe and difficult to treat.
- Increases in CDI incidence have been largely attributed to the emergence of a previously rare and more virulent strain, BI/NAP1/027.

Epidemiology of *C. diff*



Discharge rate for Clostridium difficile infection from US short-stay hospitals by age

Clin Infect Dis. 2012 Aug;55 Suppl 2:S65-70. doi: 10.1093/cid/cis319.
Current status of Clostridium difficile infection epidemiology.
Lessa FC, Gould CV, McDonald LC.

Epidemiology of *C. diff*

- Elderly hospitalized patients receiving antibiotics remain the main group at risk of infection, and have the greatest associated mortality.
- However, recent evidence shows an increased incidence of CDI in younger populations with no previous contact either with the hospital or with antibiotics.
- The incidence of CDI in other groups, previously considered at low risk, such as children and pregnant women, has increased.

Epidemiology of *C. diff*

- *Clostridium difficile* infection is one of the most common health care-associated infections
- Up to 40% of patients suffer from recurrence of *C. diff* infection following standard antibiotic therapy
- Ironically, *C. diff* infections are usually treated with additionally antibiotics (e.g., metronidazole, vancomycin, fidaxomicin)

Treatment for recurrent *C. diff* infection

- Recently, fecal microbiota transplantation (FMT) has been successfully used to treat recurrent *C. difficile* infection.

A different kind of transplantation

The New York Times

January 16, 2013

When Pills Fail, This, er, Option Provides a Cure

By DENISE GRADY

The treatment may sound ap

Mar 10 2013

Hope floats: Fecal transplants cure >90% of recurrent C. difficile (RCT, NEJM)

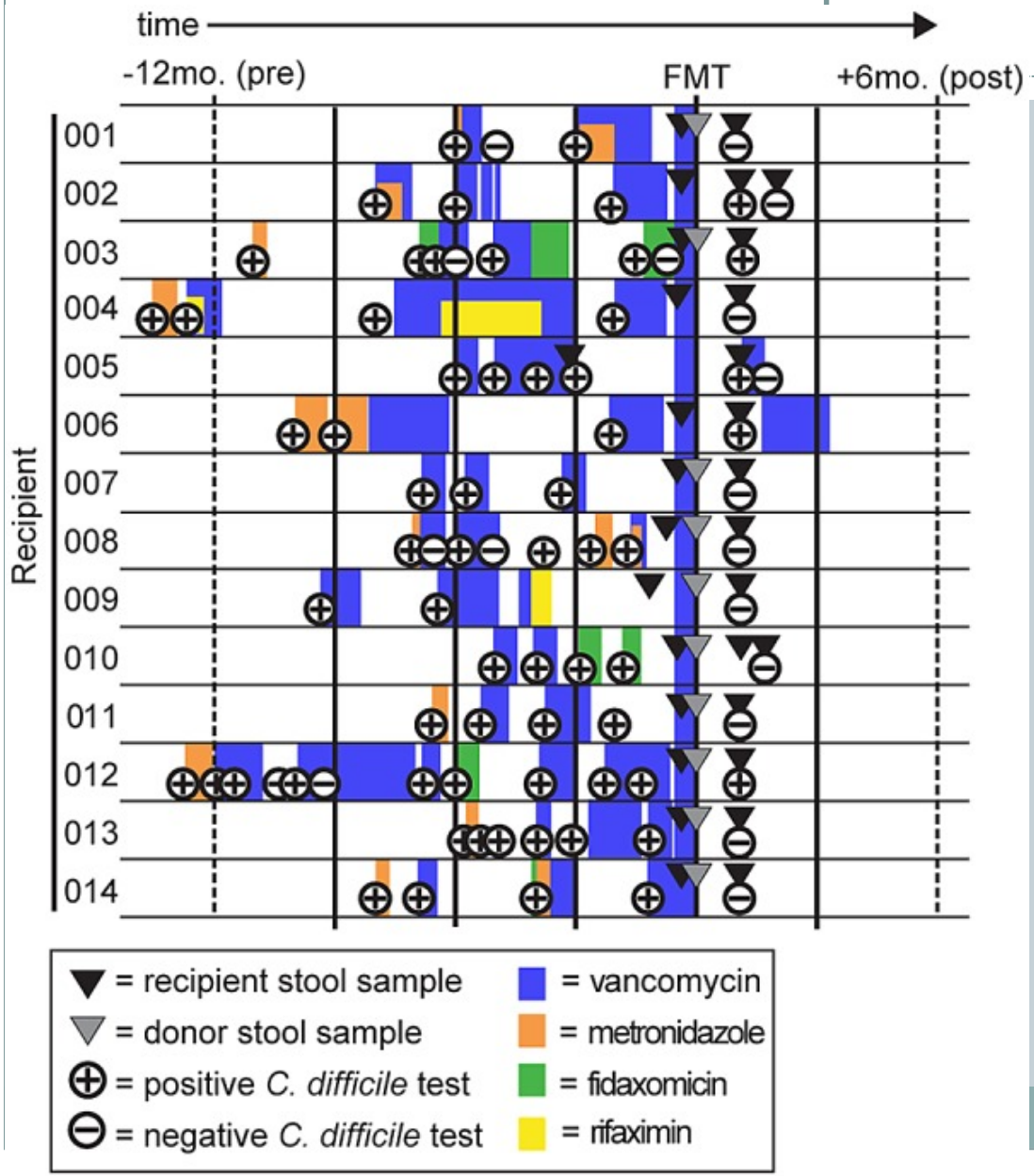
GI and Nutrition, Infectious Disease and Sepsis, N Engl J Med, Randomized Controlled Trials

Add comments

Fecal Transplants Cure *C. difficile* Infections, When Drugs Can't

Antibiotics are what cause *Clostridium difficile* infection to emerge in the first place, so it's perhaps no surprise that the usual treatment — more antibiotics — often fails. From 15-25% of patients with *C. difficile* are not permanently cured by their initial treatment with metronidazole, and among those whose *C. diff* colitis relapses, a long road of misery often awaits. Only 60% are cured after a first recurrence, with the rest requiring prolonged courses of vancomycin; in a significant proportion of patients, *C. difficile* persists even despite extended drug treatment. Some of these poor souls eventually undergo total colectomy — a brutal treatment for what is theoretically a curable infection.

Recovery of the Gut Microbiome following Fecal Microbiota Transplantation



**Since 12 participants remained asymptomatic throughout study contact, we consider this FMT study to have an 86% success rate.

**The fecal microbiota of recipients following transplantation was more diverse and more similar to the donor profile than the microbiota prior to transplantation.

Source: Recovery of the gut microbiome following fecal microbiota transplantation. *Mbio*
Seekatz AM, Aas J, Gessert CE, Rubin TA, Saman DM, Bakken JS, Young VB.

All recurrent *C. diff* treatment options

- Antibiotics (typically vancomycin)
  - For a first recurrence, the effectiveness of antibiotic therapy is around **60 percent and further declines** with each subsequent recurrence.
- Fecal microbiota transplant
  - Research has shown FMT has a success rate higher than **90 percent** for treating C. difficile infections. One small, randomized, controlled trial stopped early because the results were so positive, with a 94 percent success rate overall.
- Probiotics
  - A yeast called Saccharomyces boulardii, in conjunction with antibiotics, might help prevent further recurrent C. difficile infections. Benefits have not been conclusively demonstrated, and not all probiotics have the same effects. Few side-effects; not much research on safety yet.

Final thoughts

- Best way to prevent CDI is to reduce unnecessary antibiotic usage
- Prevention through stewardship is the answer