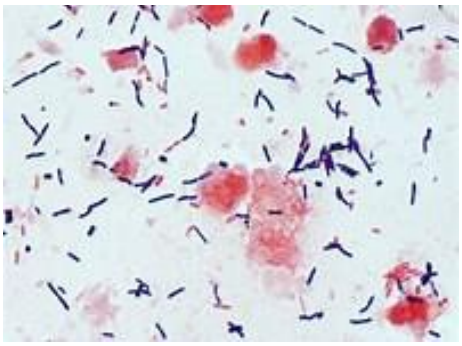
STANDARD DEVIATIONS: Dys(gusting)biosis

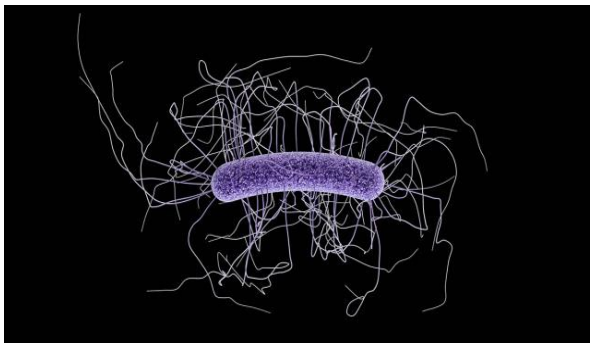
Dear diagnosticians,

Laboratory testing can be a shi++y job, literally. One disorder that we see way too much of is the diarrheal complications from toxicity in *Clostridioides difficile* infections (CDI). Estimated to cause ~250,000 hospitalizations a year in the U.S., CDI will be a lethal diagnosis for nearly 15,000 people in 2019. Most deaths will occur in patients over 65 years who have been hospitalized for other complications and **acquire the disease during their stay**. One in 11 die within a month of diagnosis. The CDC has classified C difficile as an **Urgent Drug-Related Threat** to U.S. patients. Why it is not a reportable disease is a mystery.

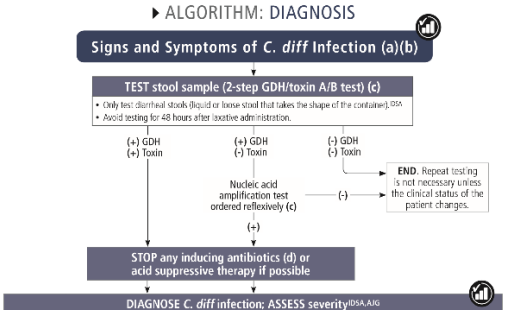
This is a story about how organisms can be opportunistic and how biosafety can be an important player in controlling outbreak. We'll take a gander at the bug and its etiology, the importance of antibiotic stewardship, treatment, and prevention.

Clostridioides are anaerobic, motile, Gram-positive spore forming bacteria. Its vegetative cells are rod shaped, pleomorphic, and occur in pairs or short chains. Under the microscope, they appear as long, irregular (often drumstick- or spindle-shaped) cells with a bulge at their terminal ends (forms subterminal spores).





It grows well on blood agar, anaerobically, and is catalase negative. Two toxins are produced: enterotoxin A and cytotoxin B. The enterotoxin disrupts the intestinal mucosa and the cytotoxin affects cell structure. Classic culture can take up to 5 days but rapid tests for GDH antigen and the toxin B gene (tcdB) are quick and specific and have become the go-to assays.



Most hospitalized cases of CDI occur in patients taking antibiotics. This is the classic case of a bug coming into its own by evolving resistance genes that allow it to proliferate when normal flora is decimated by antibiotic therapy for another problem. Ordinary strains of *C. diff* produce two toxins, called toxins A and B, but the new, worrisome hypervirulent strains produce up to 16 times more toxin A and 23 times more toxin B. The PFGE identified ribotype 027 is the major hypervirulent strain that has become a terror in North America. This species is responsible for a **400% increase in CDI incidence from 2000-2007**. It is enterotoxin A (-) and cytotoxin B (+). Other clades are emerging.

The elderly, immune-suppressed, and people having certain medical procedures are the most common **hospital-acquired infections (HAIs).** Onset presents with diarrhea (duh), fever, nausea, and malaise. Three or more unformed stools in 24 hr. is a tell-tale presentation, as well as the mucoid type diarrhea seen. In the normal bowel, the plethora of bacteria present keep the
C. diff population in check; when that balance is tipped in favor of an AMR *C. diff*, the toxin(s) accumulate to, well, toxic levels. The mucus lining of the intestine is compromised and can evolve into a septic peritonitis. The big issues tend to arise from dehydration, hypotensive responsive and renal failure. This is **dysbiosis**.

Ironically, the treatment for CDI is antibiotics. Vancomycin is the current drug of choice to treat CDI. It's fluoroquinolones and cephalosporin that the organism has developed resistance to, and which leads to the opportunistic growth when those are on board. Halting the initial antibiotic is also a critical first step.

Fecal transplant has become an alternative for patients who don't respond to vancomycin. It reverses the imbalance of microbiota. The discovery of super-donors and investigation of dietary supplements are promising therapies.

Our 2017 data indicate that **Utah saw 600 hospital-onset infections**. We reported 10% more *C. difficile* in acute care here than the national average. Two hospitals had statistically fewer infections (McKay Dee and Promise) but **5 exceeded the national baseline** (Jordan Valley West Valley campus, LDS, Primary Children's, University of Utah, and Utah Valley Regional).

Antibiotic stewardship, a buzzword for our response to the AMR crisis (and it is a crisis), plays a fundamental role in prevention. By judicious use of drug therapies, physicians can reduce the CDI incidence. Up to 50% of antibiotic prescriptions are either inappropriate or unnecessary.

C. difficile spores are hardy and can live outside the human body for a very long time and may be found on things in the environment such as bed linens, bed rails, bathroom fixtures, medical equipment, and, of course, specimen containers and their nasty contents. CDI can spread from person-to-person on contaminated equipment and on the hands of doctors, nurses, other healthcare workers (hint, hint), and visitors.

So, this is where my biosafety preaching gets loud and obnoxious....

Hand hygiene and disinfection are the two most important things we can do to prevent the spread of CDI within our facilities. Isolation and the PPE barrier we create with stringent glove and gown use around CDI patients aim to reduce HAI. That's just common sense and good practice. Hand hygiene before and after any patient contact is key.

As healthy laboratorians, we aren't really the susceptible hosts that get CDI. But if you are taking antibiotics, if you are immune-suppressed, and if you handle specimens that may be spore bearing, the risk of infection or transmission exists. This organism is a poster child for good old biosafety awareness.

Have a great week and be safe,

Bryan

p.s. Taxonomy changed in 2016, from *Clostridium* to *Clostridioides*. The mystery behind its exclusion from the reportable disease list is being plumbed. Any guesses?

References:

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