Clostridioides difficile (Clostridium difficile)

Clostridioides difficile (C. diff), formerly Clostridium difficile, is a Gram positive bacilli of the genus Clostridioides. Recently, the genus Clostridioides was found to be phylogenetically distinct from Clostridium, leading to C. diff's new name. C. diff is an anaerobic, spore forming bacterium. These bacteria are known to cause severe diarrhea and other intestinal disease, usually after the normal gut flora is killed by antibiotics allowing proliferation of C. diff in the gut. C. difficile releases two toxins that can damage the intestine. Toxin A is an enterotoxin that damages the brush border of the gut, and toxin B is a cytotoxin that induces actin depolymerization, leading to damage of the cytoskeletal structure. Together, these toxins are responsible for the inflammation and diarrhea seen in infected patients. C. difficile infections almost always occur after use of broad-spectrum antibiotics like clindamycin or ampicillin, which destroy the normal gut flora and allow C. difficile to proliferate. C. difficile infections result in a pseudomembranous colitis and can also lead to toxic megacolon in extreme cases. Because this bacteria is part of the normal gut flora in many patients, C. difficile infection should be diagnosed via detection of toxins in the stool as opposed to culture. Treatment includes metronidazole and vancomycin. Other treatment options for recurrent disease include the antibiotic fidaxomicin, as well as performing a stool transplant to replenish normal gut flora.



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Characteristics

Gram-Positive
Graham-cracker Positive-angel
This bacteria stains gram-positive, which means that it retains large amounts of the Gram stain due to its high peptidoglycan content in the cell wall.

Bacillus
Rod
These bacteria are rod-shaped.

Anaerobe
Ant-robe
These bacteria prefer to grow in an anaerobic environment.

Clindamycin and Ampicillin
Cleaning-mice and Amp-pencil
Broad spectrum antibiotics and those with significant anaerobic activity, especially clindamycin and ampicillin, are associated with C. difficile infection. This is because these antibiotics destroy normal gut flora, allowing C. difficile to proliferate instead.

Toxin A Enterotoxin
Apple with Toxic-green-glow
Toxin A is an enterotoxin released by C. difficile that damages the brush border of the gut. This toxin can eventually be detected in the stool for diagnosis.

Damages Brush Border of Gut
Damaged toilet Brush
Toxin A is an enterotoxin released by C. difficile that damages the brush border of the gut, leading to malabsorption and severe diarrhea.

Toxin B Cytotoxin
Bee with Side-toe-toxic-green
Toxin B is a cytotoxin released by C. difficile that induces actin depolymerization, leading to damage of the cytoskeletal structure.This toxin can eventually be detected in the stool for diagnosis.

Damages Cytoskeletal Structure
Damaged Cytoskeleton (actin and microtubule filaments) of toilet
Toxin B induces actin depolymerization, leading to damage of the cytoskeletal structure and cell death. This results in significant inflammation within the bowel wall, leading to bleeding and overall gut dysfunction.

Signs and Symptoms

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Diarrhea

Toilet

Watery diarrhea is a common symptom of C. difficile infection. Any patient in the hospital with new onset of severe watery diarrhea after antibiotic use should be evaluated for a C. difficile infection.

Pseudomembranous Colitis

Sumo-man-bra Colon

The toxin production by C. difficile induces significant inflammatory cell invasion into the bowel wall. This inflammation produces pseudomembranes on the bowel lumen which can be seen on gross examination, leading to the term pseudomembranous colitis. Other symptoms include fever, bloody diarrhea, and abdominal pain.

Toxic Megacolon

Mega Colon Character

In severe cases of pseudomembranous colitis, excessive inflammation and loss of gut motility can lead to extreme dilation of the colon. This life-threatening complication is known as toxic megacolon. These patients are at high risk for bowel perforation and shock.

Diagnosis

Detect Toxins in Stool

Test tube with Toxins and Stool

Because this bacteria is part of the normal gut flora in many patients, C. difficile infection should be diagnosed via detection of toxins in the stool as opposed to culture.

Treatment

Metronidazole

Metro-knight

In mild-to-moderate cases, oral metronidazole has good activity against anaerobic bacteria. However, it is no longer recommended as first-line therapy for adults.

Vancomycin

Van-tank-mice

Vancomycin has good gram positive activity and is therefore another option for the treatment of C. difficile infection. It is first line in cases of severe disease, specifically. When used to treat C. difficile, vancomycin is administered orally because intravenous administration does not achieve minimum therapeutic concentration in the gut lumen. Other treatment options for recurrent disease include the antibiotic fidaxomicin, as well as performing a stool transplant to replenish normal gut flora.

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