Pseudomembranous Colitis (C. Diff. Colitis) — Causes and Diagnosis

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Pseudomembranous colitis, also referred to as clostridium difficile infection or colitis, is a potential complication of recent antibiotic use. Students should be aware of its causes, consequences and management.

Definition of Pseudomembranous Colitis

Pseudomembranous colitis refers to inflammation of the colon (colitis) due to infection with the Clostridium difficile bacteria. The colitis is characterized by pseudomembranes, which can be seen macroscopically and microscopically, hence the name. Pseudomembranous colitis occurs when there is disruption to the normal bowel flora of the gut with the use of antibiotics.

Epidemiology of Pseudomembranous Colitis
Spread of pseudomembranous colitis

The first case of clostridium difficile colitis was reported in 1978. Its incidence and severity has been increasing, and now, it is the most common hospital acquired (nosocomial) diarrheal illness. There are approximately 3 million cases of pseudomembranous colitis each year in the United States.

Clostridium difficile is a commensal gut bacteria, present in about 5-15 % of normal healthy adults, and up to 57 % of patients in hospitals and long-term facilities. The spores of C. difficile are present in nature and in environments like hospitals and nursing homes. Advanced age is one major risk factor for developing pseudomembranous colitis.

Etiology of Pseudomembranous Colitis

Causes of pseudomembranous colitis

Pseudomembranous colitis most commonly arises due to the use of broad-spectrum antibiotics, leading to infection with clostridium difficile. Clostridium difficile (C. difficile) is a gram-positive, anaerobic, rod-shaped bacteria (bacillus) that produces spores. Antibiotics can disrupt/kill the natural gut flora, allowing clostridium difficile to proliferate. The most commonly implicated antibiotics include ampicillin, cephalosporins (2nd and 3rd generations), fluoroquinolones and clindamycin.

Pathology and Pathophysiology of Pseudomembranous Colitis

Exposure to broad-spectrum antibiotics disrupts the normal flora of the bowel, predisposing the individual to infection. When the individual is then colonized with a toxigenic strain of clostridium difficile, infection may arise.
In the colon, clostridium difficile proliferates and produces two exotoxins, called **toxins A (an enterotoxin) and B (a cytotoxin)**. These exotoxins are responsible for the adverse effects that take place. They induce inflammation in the colon, causing increased vascular permeability. Pseudomembranes are formed, and consist of inflammatory cells including neutrophils along with cellular debris, fibrin and mucin. Macroscopically, the pseudomembranes appear as **white or yellow plaques** that adhere to the underlying inflamed colonic mucosa. Of the two exotoxins that produce tissue damage, toxin A is the most responsible as it induces the tissue damage, while toxin B helps perpetuate the damage once the mucosa is already injured.

The development of clinical disease depends on a person’s immune system and the toxigenic potential of the clostridium difficile strain. Otherwise an individual may become an asymptomatic carrier, in which case there is usually no toxin production.

### Symptoms of Pseudomembranous Colitis

**Signs of pseudomembranous colitis**

Signs and symptoms of pseudomembranous colitis are **usually apparent 4 to 9 days following commencement of antibiotics**. But it can develop as early as after 2 days or up to 8 weeks after antibiotic use.

#### General symptoms

- **Diarrhea**
- Abdominal pain and tenderness
- Fever
- Nausea and vomiting

**Diarrhea** is one of the key clinical features of pseudomembranous colitis, and can vary in its severity. It is usually a **high-volume, watery, foul-smelling diarrhea, and rarely is bloody**. However, if diarrhea is absent this may herald a serious complication such a paralytic ileus or toxic megacolon.

**Abdominal pain** also varies in its severity, and can be **colicky** in nature; however, it may be absent in some cases. Patients may also have an accompanying **fever**, while **nausea and vomiting** uncommonly occurs.

In cases of **fulminant colitis**, the patient may have **severe abdominal pain and**
tenderness. They may also display **signs of shock** including hypotension and tachycardia.

## Diagnosis of Pseudomembranous Colitis

Diagnosis of pseudomembranous colitis can be made with **history and physical exam**. Other tests, such as the ones listed below may be helpful, but are not necessary for diagnosis.

### Blood tests

Patients with pseudomembranous colitis usually have a **raised white cell count (WCC)**, but this is not a specific or sensitive finding for the disease. In cases of fulminant colitis, WCC may be significantly high.

### Stool tests

Stool tests play a key role in the diagnosis of this condition. Stool samples in a patient are generally positive for the presence of leukocytes. Specific stool tests to detect clostridium difficile include a **stool cytotoxin tissue culture assay**, a **stool immunoassay for toxins A and B**, a **stool PCR test**, and a **stool glutamate dehydrogenase**.

Treatment for pseudomembranous colitis should not be delayed by waiting for stool test results. In other words, a positive stool test is **not** needed for diagnosis.

### Radiology

An **abdominal x-ray** may be done in cases where there is abdominal distension to detect **colonic wall thickening, air in the bowel and the degree of dilatation**.

An **abdominal CT scan** may be considered in patients with severe disease, displaying signs of complications, such as absent bowel sounds, worsening abdominal pain and/or abdominal distension. A CT scan may reveal **colonic wall thickening, dilatation of the bowel, ascites or bowel perforation**.

### Additional tests
A sigmoidoscopy or colonoscopy may reveal evidence of pseudomembranous colitis with characteristic pseudomembrane formation and ulcerations. These investigations may be performed when there is treatment failure or when there is suspicion of other causes for the patient’s presentation. A biopsy may be performed too.

**Differential Diagnoses of Pseudomembranous Colitis**

- Antibiotic associated diarrhea (causes diarrhea with the presence of nausea and absence of fever; negative clostridium difficile toxin tests)
- Gastroenteritis (viral or bacteria; history of consumption of contaminated foods, recent travel, or infectious contacts)
- Ischemic colitis (bloody diarrhea)
- *Inflammatory bowel disease* (chronic diarrhea; extraintestinal features may be present)

**Therapy of Pseudomembranous Colitis**

**Medical therapy of pseudomembranous colitis**

The patient’s antibiotics should be withdrawn. If the patient requires the antibiotics, a substitute should be used that is not associated with causing pseudomembranous colitis. The antibiotics ampicillin, clindamycin, 2nd and 3rd generation cephalosporins and fluoroquinolones should be avoided.

Clostridium difficile infection is usually treated with either *metronidazole* or *vancomycin* is used to treat it. Mild to moderate infections can be treated with metronidazole for 10 days, while severe infections are treated with vancomycin. Combination therapy may be used in complicated cases.

**Supportive care measures** are important as well. Patients’ fluid status and electrolytes should be monitored closely and kept stable. It is also necessary to practice infection control with the use of barrier precautions and hand hygiene.
Recurrent *C. difficile* infection occurs in approximately 20% of patients. Treatment options for patients with recurrent infection include *vancomycin* and *fecal microbiota transplant (FMT)* (also known as stool transplant). FMT can be done endoscopically or via nasogastric tube and the goal is to restore the normal healthy intestinal bacteria.

**Progression and Prognosis of Pseudomembranous Colitis**

Pseudomembranous colitis is especially dangerous in older patients or those who are immunocompromised. In outbreaks of the disease, mortality rates can reach up to 6.9%. Fortunately, most patients generally recover.

Cases of fulminant colitis, though uncommon, carry a high risk of mortality (35-80%). Risk factors for the development of fulminant colitis include inflammatory bowel disease, a significantly elevated white cell count and recent gastrointestinal surgery.

Recurrent disease occurs in 15-30% of patients after treatment. This may be due to relapse of the infection or re-infection with a new strain of *C. difficile*.

**Review Questions**

The correct answers can be found below the references.

1. **Which of the following antibiotics may be used to treat pseudomembranous colitis?**
   - A. Clindamycin
   - B. Amoxicillin
   - C. Vancomycin
   - D. Cephalexin

2. **In what setting are rates of *Clostridium difficile* colonization the highest?**
   - A. The community
   - B. Childcare facilities
   - C. Hospitals
   - D. Hotels

3. **Which of the following is the most important finding for diagnosing pseudomembranous colitis?**
   - A. Stool test showing leukocytes
   - B. Stool test showing toxins A and B of *C. difficile*
   - C. Stool test showing glutamate dehydrogenase
   - D. Stool test showing pseudomembranes

**References**


Correct answers: 1C, 2C, 3B

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