Goal. The goals of this lesson are to provide an overview of the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) joint clinical guidelines for *Clostridium difficile* infection in adults, and to review the 2014 IDSA/SHEA practice recommendations regarding strategies in prevention of *Clostridium difficile* infection.

Objectives. At the completion of this activity, the participant will be able to:

1. define hospital-acquired and community-acquired *Clostridium difficile* infection;
2. recognize risk factors and clinical presentation of *Clostridium difficile* infection;
3. list strategies for prevention of *Clostridium difficile* infection; and
4. demonstrate an understanding of pharmacologic agents and treatment regimens used for *Clostridium difficile* infection, as recommended in IDSA/SHEA guidelines.

Background

*Clostridium difficile* infection (CDI) is one of the most commonly-reported causes of hospital-associated illness. According to the Centers for Disease Control and Prevention (CDC), *C. difficile* accounted for nearly half a million infections among United States adults in 2011. Based on data obtained from U.S. death certificates, CDI is the leading cause of gastroenteritis-associated death. In 2011, approximately 29,000 patients died within 30 days of initial CDI diagnosis — half of the deaths were directly attributed to CDI and a quarter were community-acquired cases.

Hospital-acquired CDI is defined as symptom onset and positive stool culture three or more days after hospital admission.

The incidence of *C. difficile* infection among hospitalized patients is widely variable from year to year, but has generally increased. Nearly 15 cases per 1000 hospital discharges were treated for CDI. Hospital-acquired CDI more than quadruples the cost of hospitalizations and increases hospital length of stay from 2.8 to 5.5 days, increasing annual expenditures by about $1.5 billion in the United States. In 2008, the attributable costs of inpatient CDI were estimated to be between $3,000 and $15,000 per episode. As a result, significant financial burden is placed on the healthcare system, with excess healthcare costs to acute care facilities alone upwards of $4.8 billion annually.

Although a majority of CDI cases are hospital-acquired, an increase in the incidence of community-acquired CDI cases has been observed over the past 10 years. CDI has been reported with increasing frequency within the community and nursing homes, indicating that prevention of CDI should extend beyond the hospital setting. Community-acquired *C. difficile* infection is defined as disease onset in a patient who had no history of an overnight stay in a healthcare facility within 12 weeks prior to infection. This definition, however, does not rule out acquisition from a healthcare facility. Community-acquired CDI generally occurs in younger patients who have had no clear antimicrobial exposure or other known risk factors; therefore, community-acquired CDI is associated with lower morbidity and mortality rates. However, up to 40 percent of patients with community-acquired CDI require hospitalization, and recurrence rates are similar among both patient populations.

As some of the most trusted healthcare professionals in the United States, pharmacists have an opportunity to play an important role in prevention and treatment of CDI. Recognition of signs and symptoms of CDI, knowledge of risk factors for developing or worsening CDI, and knowledge of medications associated with CDI treatment may help improve how antibiotics are prescribed in both hospital and community settings. Pharmacists may
also play a role by educating other healthcare professionals about the most appropriate therapies based on disease severity and patient characteristics.

There are three major guidelines for the diagnosis and treatment of CDI. The Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) and the American College of Gastroenterology (ACG), and the European Society for Clinical Microbiology each have their own set of guidelines. The intent of this lesson is to educate pharmacists about appropriate CDI management in accordance with IDSA/SHEA guidelines.

**Etiology & Pathogenesis**

*C. difficile* is an anaerobic gram-positive, spore-forming, toxin-producing bacillus which is non-invasive and colonizes the large intestine. The organism itself is noninvasive; thus, infection outside of the colon is extremely rare. The majority of anaerobic infections arise from endogenous sources. However, many clostridial infections are caused by exposure to organisms from exogenous sources. Its ability to produce spores explains how *C. difficile* can be acquired from the environment. Infection is transmitted among humans via the fecal-oral route via spores which are resistant to heat, acid, and many antibiotics. *C. difficile* spores are abundant in healthcare facilities and may also be found in the environment and food supply, allowing for both nosocomial and community transmission.

Clinical expression of CDI is influenced by virulence of the infecting strain and the host immunologic response. Signs and symptoms of CDI are mediated by the production of two protein exotoxins (TcdA and TcdB) that cause colitis. TcdA and TcdB cause diarrhea by inactivation of specific enzymes in the large intestine which leads to colonic cell (epithelial cell of the large intestine) death, loss of function of the intestinal barrier, and inflammation of the colon. Imbalance of the normal flora within the intestine, often by administration of certain pharmacologic agents, produces an environment which facilitates *C. difficile* growth and subsequent infection in susceptible patients.

Hospitals began reporting significant increases in severe CDI cases to CDC in the early 2000s. Researchers discovered a more virulent strain and named it BI/NAP1/027. This strain is characterized by high fluoroquinolone resistance, effective sporulation, markedly high toxin production, and a mortality rate three times higher than other *C. difficile* strains. Some studies have found that the BI/NAP1/027 strain produces more TcdA and TcdB toxins in vitro and may also produce more spores. Fluoroquinolone resistance is attributed to the production of a third toxin — binary toxin. In the United States, the prevalence of the BI/NAP1/027 strain averages approximately 25 to 35 percent of CDI cases.

**Risk Factors**

Risk factors for development of CDI are summarized in Table 1. The single most important risk factor for acquiring CDI is antimicrobial use. One study reported that 96 percent of patients with symptomatic CDI had received antimicrobials within the 14 days before the onset of diarrhea. The same study further observed that all patients with symptomatic CDI had received an antimicrobial within the previous three months. Healthcare providers should inquire about past antimicrobial usage within at least the past eight weeks prior to presentation. Ampicillin, amoxicillin, cephalosporins, clindamycin, and fluoroquinolones are most frequently associated with CDI; however, it is important to note that any antimicrobial agent may disrupt the normal flora in the colon and lead to infection. The risk of CDI with a particular antimicrobial agent is dependent on concentrations achieved in the gut, effects on normal intestinal flora, and the agent’s activity against *C. difficile*.

A patient’s CDI risk increases with the administration of multiple antimicrobial agents and with prolonged duration of antimicrobial therapy.

Patients aged 65 years or older are at increased risk of developing CDI, likely due to increased exposure to healthcare facilities and decreased immune function. In 2011, CDC reported greater than 80 percent of deaths associated with CDI occurred among Americans aged 65 years or older. Patients who have comorbid disease states such as inflammatory bowel disease or renal disease and those who have feeding tubes or have undergone surgery to manipulate the gastrointestinal tract are also at increased risk of developing or acquiring CDI. Additionally, immunocompromised patients such as those with active cancer, HIV patients, and solid-organ transplant recipients are at increased risk of acquiring CDI.

The role of gastric acid-suppressing agents such as histamine-2 receptor antagonists (e.g., ranitidine, famotidine) and proton pump inhibitors (e.g., omeprazole, pantoprazole) in the development of CDI remains controversial. Theoretically, suppression of gastric acid would cause an increase in gastric pH, allowing potentially pathogenic organisms to reach the colon. However, *C. difficile* spores are acid-resistant and are able to remain viable at gastric pH. Some studies have reported an increased risk of infection associated with acid suppression while other stud-

<table>
<thead>
<tr>
<th>Table 1 Risk factors for <em>C. difficile</em> infection</th>
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<tbody>
<tr>
<td>• Exposure to antibiotics</td>
</tr>
<tr>
<td>• Age ≥65 years</td>
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<tr>
<td>• Comorbid disease states</td>
</tr>
<tr>
<td>• Exposure to acid-suppressing agents</td>
</tr>
<tr>
<td>• Exposure to <em>C. difficile</em> in healthcare setting</td>
</tr>
<tr>
<td>• Immunosuppression</td>
</tr>
<tr>
<td>• Manipulation of the GI system</td>
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</tbody>
</table>
ies, after adjusting for comorbid
disease states, have not demon-
strated such an increase. Current
guidelines do not suggest discon-
tinuation of gastric acid-suppressing
therapy.

Clinical Presentation & Diagnosis
Several studies have illustrated
that 50 percent or more of hospital
patients colonized by *C. difficile* are
symptomless carriers. Symptoms
usually begin soon after coloniza-
tion, with a median time to onset of
two to three days. General symp-
toms of CDI may include fever,
clamping, abdominal discomfort,
and peripheral leukocytosis.

While some patients with CDI
may be asymptomatic, a majority of
patients present with foul-smelling,
watery diarrhea and pseudomem-
branous colitis, which may lead to
complications such as toxic megaco-
lon (an acute, toxic colitis associat-
ed with dilation of the colon), ileus,
hypotension, sepsis, or death. *C. difficile*-associated diarrhea may be
accompanied by passage of mucus
or occult blood; however, melena
(black, tarry stools) and hemato-
chezia (passage of bloody stools)
are rare. Manifestations outside of
the intestine, such as bacteremia,
are very rare. Patients with severe
disease may present with abdomi-
nal pain and distension, but with
minimal to no diarrhea.

Diagnosis is based on both
clinical presentation and laborato-
ry parameters. IDSA/SHEA defines
CDI as the occurrence of three or
more unformed stools in 24 hours
or less, plus a positive stool test for
toxigenic *C. difficile* or its toxins,
TcdA or TcdB, or the presence of
pseudomembranous colitis dem-
onstrated through colonoscopic or
histopathologic findings. Labora-
tory tests for *C. difficile* or toxins
should be performed exclusively
on stools of patients with diarrhea.
CDI is classified into four catego-
ries based on disease severity.

Table 2 summarizes the criteria for
each classification of severity based
on the guidelines.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Mild to moderate</td>
<td>WBC ≤15,000 cells/mcL AND SCR &lt;1.5x baseline</td>
</tr>
<tr>
<td>Severe</td>
<td>WBC ≥15,000 cells/mcL OR SCR ≥1.5x baseline</td>
</tr>
<tr>
<td>Severe complicated</td>
<td>CDI associated with hypotension, shock, ileus, or megacolon</td>
</tr>
<tr>
<td>Recurrent</td>
<td>CDI that occurs within 8 weeks of therapy completion</td>
</tr>
</tbody>
</table>

Prevention
As with most infections, early de-
tection allows for early treatment
and infection control. Pharmacists
across various practice settings can
promote preventative strategies for
*C. difficile* infection by educating
patients, caregivers, and health-
care workers about compliance
with proper hand hygiene, contact
precautions, and antimicrobial
stewardship.

Strict adherence to universal
precautions and handwashing is
imperative to reduce transmission.
*C. difficile* spores are resistant to
alcohol; therefore, alcohol-based
antisepsics are ineffective and
proper handwashing technique
should be utilized. Hands should be
washed thoroughly with soap and
running water. When available,
disposable instruments should be
utilized. Patients should be placed
in private rooms to prevent further
disease transmission. Barrier pre-
cautions such as gloves and gowns
should be worn in the presence
of patients with known CDI and
should be continually worn at least
until diarrhea resolves. Patients
and household contacts should be
counseled to wash hands with soap
and running water after using
the bathroom and before eating.
Additionally, cleaning kitchen and
bathroom surfaces with 1:10 part
bleach to water solution, until diar-
rrhea resolves, is recommended.

Because antimicrobial use is
strongly associated with develop-
ment of CDI, antimicrobial stew-
dardship programs may be designed
to reduce risks by promoting judi-
cious use of antimicrobial agents.
Pharmacists should be mindful of
high-risk patients, such as those
with recent antimicrobial use or
hospitalizations. Pharmacists may
also help minimize exposure and
ensure that appropriate healthcare
personnel are informed when a *C.
difficile* test has yielded positive
results, allowing for initiation of
optimal therapy and necessary
precautions.

Probiotics have been suggested
as a way to reduce development of
CDI. Advocates of this theory rea-
son that probiotics may prevent *C.
difficile* overgrowth during a course of
antibiotic therapy. While there is
moderate evidence that two probi-
otics, *Lactobacillus* (Culturelle®)
and *Saccharomyces boulardii*
(Florastor®), reduce the incidence
of antimicrobial-associated diar-
rrhea, there is insufficient data to
justify widespread use of probiotics
in prevention of CDI. Additional
problems with commercially avail-
able probiotic products include
their lack of standardization, varia-
tions in bacterial counts, and the
potential of inducing bacteremia
or fungemia. Currently, both the
IDSA/SHEA and the ACG guide-
lines recommend against the use
of probiotics in preventing primary
*C. difficile* infection, citing the need
for larger trials to demonstrate
beneficial outcomes.

Pharmacologic Therapy
Treatment of *C. difficile* infection is
based on several factors. Whether
the infection is the initial incident
or a recurrence, specific patient
characteristics, and the severity of
infection should all be considered
when determining appropriate
therapy. IDSA/SHEA lists three
Factors that may indicate a severe or complicated course: advanced age, peak white blood cell count, and peak serum creatinine. Increased age likely reflects senescence (the process of growing old) in the immune response, leukocytosis likely reflects the severity of colon inflammation, and an elevated serum creatinine level may be indicative of poor fluid status or inadequate renal perfusion.

Three main outcomes should be considered upon determination of appropriate pharmacologic therapy: time to symptom resolution, recurrence after initial symptom resolution, and the frequency of major complications (e.g., death within 30 days of CDI diagnosis, shock, toxic megacolon, colonic perforation, emergency colectomy, or admission to the intensive care unit).

Once CDI is suspected, offending antimicrobial agent(s) should be discontinued immediately, when appropriate. Use of antimitotic agents should be avoided, as they may mask symptoms and precipitate toxic megacolon. Prospective trials have not compared regimens with durations greater than 10 days. However, many clinicians recognize that some patients may have a slower response to treatment and will require targeted antimicrobial therapy specific for CDI for a longer duration (e.g., 14 days). Metronidazole (Flagyl) and vancomycin (Vancocin) are the two first-line antimicrobial agents used most frequently in North America. A third agent, fidaxomicin (Dificid), was approved for the treatment of CDI in May 2011. While metronidazole is widely used in the treatment of CDI, vancomycin and fidaxomicin are currently the only two antimicrobial agents that carry FDA-approvals for the treatment of *C. difficile*-associated diarrhea (CDAD). Table 3 summarizes common antimicrobial agents used in CDI treatment and common adverse effects.

**Metronidazole.** Metronidazole is the drug of choice for an initial episode of mild to moderate CDI. It is an antiprotozoal agent with an off-label indication for the treatment of CDAD. It can be administered either orally or intravenously. Dosing for metronidazole in the treatment of CDAD is 500 mg PO (or IV) every 8 hours for 10 to 14 days. Oral metronidazole is nearly 100 percent bioavailable; thus, upon administration, oral metronidazole is rapidly and almost completely absorbed, with only 6 to 15 percent of the drug excreted in stool. Fecal concentrations of metronidazole likely reflect its secretion in the colon, and its concentration decreases quickly after CDI treatment is initiated. Metronidazole is undetectable in the stool of asymptomatic *C. difficile* carriers. As a result, there is little justification for metronidazole courses greater than 14 days, especially if diarrhea has resolved. Historically, metronidazole resistance in CDAD has been rare.

Patients receiving metronidazole therapy should be counseled regarding drug-drug interactions, drug-food interactions, and common adverse reactions. Metronidazole should not be prescribed for patients on certain antineoplastic agents, antiretrovirals, and other QT-prolonging agents due to contraindication. Effects of warfarin (Coumadin) may be enhanced by concomitant administration with metronidazole; therefore, patients taking warfarin should be counseled to contact the provider who manages their anticoagulation therapy for appropriate dose adjustments and monitoring. Those who are already on QT-prolonging agents (e.g., antipsychotics, antiarrhythmics, tricyclic antidepressants) should be prescribed alternative therapy, as addition of metronidazole may potentially cause life-threatening arrhythmias and torsades de pointes. Patients who have taken disulfiram (Antabuse) within the past two weeks prior to being prescribed metronidazole should also use alternate therapy. The combination of metronidazole and disulfiram may cause a serious adverse reaction, with symptoms such as skin flushing, tachycardia, dyspnea, nausea, vomiting, throbbing headache, visual disturbance, mental confusion, orthostatic hypotension, and circulatory collapse. Lastly, the use of alcohol or propylene glycol-containing products while taking metronidazole is

**Table 3**

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose</th>
<th>Route/Frequency</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fidaxomicin (Dificid)</td>
<td>200 mg</td>
<td>PO q12h</td>
<td>GI upset, hypersensitivity reactions, GI hemorrhage, anemia, neutropenia</td>
</tr>
<tr>
<td>Metronidazole (Flagyl)</td>
<td>500 mg</td>
<td>IV/PO q8h</td>
<td>GI upset, metallic taste, headache, peripheral neuropathy, vaginitis, disulfiram-like reaction with alcohol</td>
</tr>
<tr>
<td>Vancomycin (Vancocin)</td>
<td>125 mg or 500 mg†</td>
<td>PO/PR† q6h†</td>
<td>GI upset, bad taste, headache, peripheral edema</td>
</tr>
</tbody>
</table>

†High-dose vancomycin and rectal retention enema should be reserved for treatment of severe, complicated cases.

‡Pulsed vancomycin regimen using varying dosing schedules may be utilized in treatment of recurrent CDI.

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common antimicrobials used in treatment of CDI
Contraindicated due to the potential to develop a disulfiram-like reaction. Patients taking metronidazole should be advised to refrain from alcohol or propylene glycol-containing products during their treatment and for three days after treatment ends.

Common adverse reactions of metronidazole include headache, nausea, and metallic taste. Additionally, infections such as candidiasis and vaginitis may occur. Many prescribers will prescribe a one-time fluconazole (Diflucan) regimen while patients are taking metronidazole. Patients may also be advised to increase their consumption of live bacterial culture-containing products, such as yogurt or a probiotic, to help prevent infection secondary to metronidazole administration.

**Vancomycin.** Vancomycin is a first-line antimicrobial agent that has received FDA approval for the treatment of CDAD. It is important to note that only the oral preparation of vancomycin is indicated for treatment of CDAD. Intravenous vancomycin is ineffective, as it is not excreted into the colon. While IDSA/SHEA guidelines include the option of a vancomycin retention enema, the rectal route of administration is off-label. Several studies have reported vancomycin as superior to metronidazole in cases of severe *C. difficile*. Depending on disease severity, oral vancomycin may be administered as 125 mg or 500 mg PO four times daily for 10 to 14 days. In contrast to metronidazole, oral vancomycin is poorly absorbed. Fecal concentrations following oral administration reach very high levels and are maintained throughout the duration of therapy. Due to its poor absorption, orally administered vancomycin has relatively no risk of systemic toxicity. IDSA/SHEA guidelines reserve vancomycin retention enemas for cases of severe, complicated disease in patients with abdominal distention, ileus, or toxic megacolon. Retention enemas are administered as 500 mg rectally every six hours, and should be concurrently administered with oral vancomycin with or without intravenous metronidazole.

Therapeutic effects of oral vancomycin may be diminished by concurrent administration with bile acid sequestrants or anion-binding resins (e.g., cholestyramine, colestipol). Patients required to take both of these agents should be counseled to separate doses by at least two hours. Common adverse reactions of vancomycin include abdominal pain, fatigue, headache, nausea, peripheral edema, and vomiting. When administered as an oral solution, patients have reported a persistent foul, salty, rancid, or metallic taste sensation.

**Fidaxomicin.** Fidaxomicin is an antimicrobial agent belonging to the macrolide class and is indicated for the treatment of mild to moderate *C. difficile* infection. Fidaxomicin received FDA approval in May 2011 on the basis of two randomized, controlled trials comparing it to vancomycin. In both published phase III trials, fidaxomicin demonstrated non-inferiority to vancomycin for clinical response at the end of therapy and at 25 days post therapy. Further analyses suggested that fidaxomicin is superior to vancomycin, as evidenced by fewer recurrences at 25 days after therapy. This superiority, however, was only observed with initial infections not caused by the more virulent BI/NAP1/027 *C. difficile* strain. Given the short duration of these trials, limited data, and relatively high cost, fidaxomicin may be appropriate for patients with recurrent CDI or as initial therapy in patients at high risk of developing recurrent CDI, though parameters for its appropriate use are still being defined.

Fidaxomicin undergoes minimal systemic absorption; hence, there are no manufacturer recommendations for dosage adjustments in cases of renal or hepatic dysfunction. The most commonly reported adverse effects of fidaxomicin include nausea, GI hemorrhage, abdominal pain, vomiting, anemia, and neutropenia.

Alternative Agents. Several agents indicated for use in other infectious disease states are being studied as alternatives to metronidazole and vancomycin for treatment of CDI. These other agents have shown some activity against *C. difficile*, but are not recommended by current guidelines.

The significance of toxin production in the pathophysiology of CDI has incited the consideration of anion-binding resins as a potential alternative to antimicrobial therapy. Although they are not effective as primary care for CDI, cholestyramine (Questran) and colestipol (Colestid) may be advantageous due to their ability to bind *C. difficile* toxins without altering normal flora in the colon. Limiting alteration of normal colonic flora may allow for more rapid regeneration of flora damaged by CDI. Anion-binding resins may offer benefit as adjunctive therapy for recurrent infection. Suggested regimens are colestipol 5 g every 12 hours or cholestyramine 4 g three to four times daily for seven to 14 days, usually with oral vancomycin. Tolevamer is a *C. difficile* toxin-binding resin developed specifically for CDI. Preliminary studies with tolevamer have shown promising results; however, subsequent large trials have found it to be inferior to both vancomycin and metronidazole as primary therapy. Because resins bind oral vancomycin in the gut, patients should be advised to space therapies at least two hours apart.

Small case studies have suggested that sequential therapy with vancomycin and then rifaximin (Xifaxan) may be effective in treating recurrent CDI. In one small study, eight women with recurrent CDI received a two-week course of rifaximin, immediately after completing their last course of vancomycin. Seven patients had no further recurrence of infection. Due to the small sample size of this study, however, conclusions cannot be extrapolated to a larger population. The mechanism by which rifaximin acts in treating CDI has not been elucidated. Furthermore,
rifamycin exposure prior to development of CDI is a risk factor for rifampin-resistant *C. difficile* infection. Since rifaximin is a structural analog of rifampin, this effectively limits the use of rifaximin for treatment of CDI in any patient with prior exposure to rifamycin agents such as rifampin, rifabutin, and rifapentine.

Adjunctive use of monoclonal antibodies against *C. difficile* toxin has been observed to reduce the recurrence rate of CDI. Bezlotoxumab (Zinplava) is a monoclonal antibody that binds to TcdB and received FDA approval in 2016 for secondary prevention of CDI in patients at high risk for recurrence, including patients over 65 years of age and those with a prior history of CDI. Two randomized trials which included more than 2500 patients demonstrated that use of bezlotoxumab in conjunction with standard oral antibiotic therapy was associated with a considerably lesser rate of recurrent infection in comparison to oral antibiotic therapy alone. Still, a number of unresolved concerns remain before developing guidance with respect to placement of bezlotoxumab in relation to other treatment approaches, including identifying patients who are most likely to benefit, as well as cost-effectiveness analyses.

Lastly, intravenous immune globulin (IVIG), which contains *C. difficile* antitoxin, has been used in some patients with relapsing or severe *C. difficile* colitis. While case reports proposing that IVIG may be a useful addition to antibiotic therapy for refractory CDI are available, a retrospective review of 18 patients who received IVIG demonstrated no significant difference in clinical outcomes compared with 18 matched control cases.

**Treatment Modality**

The IDSA/SHEA guidelines for the management of CDI recommend oral metronidazole for an initial mild or moderate episode and oral vancomycin for an initial severe episode. The ACG guidelines further elaborate that if a patient is not responsive to metronidazole therapy within five to seven days of initiation, then the patient should be switched to oral vancomycin. The combination of IV metronidazole plus high-dose oral (or via nasogastric tube) vancomycin, with consideration for rectal instillation of vancomycin in cases of complete ileus, is recommended for an initial severe, complicated episode. Treatment regimens discussed in the IDSA/SHEA guidelines are summarized in Table 4.

**Summary**

*Clostridium difficile* infection causes a significant burden on the healthcare system. Not only does CDI limit resources in terms of equipment and personnel, but it also limits monetary resources, with inpatient cost estimates of $3,000 to $15,000 per episode. In the early 2000s, an increasingly virulent *C. difficile* strain was initially observed. This strain, termed BI/NAP1/027, occurs in 25 to 35 percent of patients with CDI. The BI/NAP1/027 strain was recognized for its high fluoroquinolone resistance, high *C. difficile* toxin production, effective sporulation, and a mortality rate three times greater than other strains of CDI. *Clostridium difficile* infection is one of the most commonly reported...
hospital-acquired infections. Recent studies, however, have reported an increased observance of community-acquired CDI. *C. difficile* itself is a spore-forming pathogen, rendering the body’s natural defense system and many antimicrobial agents ineffective. Recent antimicrobial usage and exposure are the two most likely items to cause the development of CDI. Patients aged 65 and older, immunocompromised patients, patients who have undergone manipulation of the GI tract, and those with comorbid disease states are at higher risk of developing CDI. While some studies have suggested the use of gastric acid-suppressing agents may factor into CDI development, there is currently not enough evidence to recommend the discontinuation of gastric acid-suppressing therapy as a means of prevention.

Patients may be asymptomatic carriers, but the majority of patients present with foul-smelling, watery diarrhea and pseudomembranous colitis, which may lead to complications such as toxic megacolon, ileus, hypotension, sepsis, or death.

IDSA/SHEA guidelines for treatment of CDI recommend prevention of horizontal transmission of CDI by implementing control measures such as hand hygiene, contact precautions, use of private rooms, and environmental cleaning and disinfection. Hands must be washed with soap and running water, as alcohol-based antiseptics do not effectively kill *C. difficile* spores. Healthcare personnel and caregivers are advised to wear disposable gloves and gowns when in contact with a CDI patient. Private rooms with a dedicated commode help limit disease transmission. The use of disposable tools, when available, is also recommended. Development of an antimicrobial stewardship program to promote judicious antimicrobial usage should further help reduce CDI rates. For several years, the administration of probiotics has been advocated as a preventative measure of CDI; however, data on the benefits of probiotics are limited. Additionally, the lack of standardization of commercially available probiotic products and the possibility of inducing bacteremia or fungemia limit their utility.

IDSA/SHEA lists age, peak white blood cell count, and peak serum creatinine as three factors that may indicate a severe or complicated course. Antimicrobial treatment regimens are based on disease severity and whether CDI is an initial occurrence or a recurrent infection. Metronidazole and oral vancomycin are the cornerstones of CDI treatment. A newer agent, fidaxomicin, is indicated in the treatment of mild to moderate CDI; however, its exact role in CDI treatment has yet to be determined. Several other agents (e.g., anion-binding resins, bezlotoxumab, IVIG, and rifaximin) have been used in small studies to determine their roles in the treatment of CDI. Due to the small sample sizes, these alternative agents are not currently recommended for routine use in treating CDI. Duration of therapy is generally 10 days, but 14-day duration in patients who respond slowly to therapy is not uncommon.

Pharmacists play an important role in the prevention of *C. difficile* infection. Pharmacists may educate patients and healthcare personnel about risk factors for CDI. Furthermore, they may emphasize appropriate infection control strategies and antimicrobial stewardship practices. Pharmacists may also play a role in CDI treatment by assisting clinicians in selecting the most appropriate antimicrobial regimen based on disease severity and patient-specific characteristics. Lastly, pharmacists should counsel patients with regard to potential adverse effects, drug-drug and drug-food interactions associated with antimicrobial agents used in treating CDI.
continuing education quiz

Prevention and Treatment of C. difficile: A Review of IDSA/SHEA Guidelines

1. Hospital-acquired C. difficile infection is defined as:
   a. symptom onset and positive stool culture less than three days after hospital admission.
   b. symptom onset and positive stool culture three or more days after hospital admission.
   c. symptom onset and positive stool culture at any point after hospital admission.

2. Community-acquired C. difficile infection (CDI) is defined as:
   a. disease onset in patient with no history of overnight stay in a healthcare facility within 12 weeks prior to infection.
   b. disease onset in outpatient exposed to C. difficile at home.
   c. disease onset three or more days after a hospital admission.

3. All of the following statements are true EXCEPT:
   a. C. difficile is an anaerobic gram-positive, spore-forming, toxin-producing bacillus.
   b. CDI is transmitted among humans via the fecal-oral route.
   c. CDI is common outside of the large colon.

4. Fluoroquinolone resistance is attributed to production of:
   a. TcdA.
   b. TcdB.
   c. binary toxin.

5. All of the following are risk factors for the development of CDI EXCEPT:
   a. persons aged 55 or older.
   b. exposure to antibiotics.
   c. immunosuppression.

6. Current guidelines suggest discontinuation of gastric acid-suppressing therapy for patients with CDI.
   a. True
   b. False

7. All of the following are common signs or symptoms of CDI EXCEPT:
   a. fever.
   b. foul-smelling diarrhea.
   c. hematochezia.

Completely fill in the lettered box corresponding to your answer.

1. [a] [b] [c]  2. [a] [b] [c]  3. [a] [b] [c]  4. [a] [b] [c]  5. [a] [b] [c]  6. [a] [b] [c]  7. [a] [b] [c]  8. [a] [b] [c]  9. [a] [b] [c]  10. [a] [b] [c]  11. [a] [b] [c]  12. [a] [b] [c]  13. [a] [b] [c]  14. [a] [b] [c]  15. [a] [b] [c]

☐ I am enclosing $5 for this quiz made payable to: Ohio Pharmacists Association.

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1. Rate this lesson:   (Excellent) 5 4 3 2 1 (Poor)
2. Did it meet each of its objectives? ☑ yes ☐ no
   If no, list any unmet__
3. Was the content balanced and without commercial bias? ☑ yes ☐ no If no, why?__
4. Did the program meet your educational/practice needs? ☑ yes ☐ no
5. How long did it take you to read this lesson and complete the quiz? ________________
6. Comments/future topics welcome.

To receive CPE credit, your quiz must be received no later than July 15, 2020. A passing grade of 80% must be attained. CPE credit for successfully completed quizzes will be uploaded to the CPE Monitor. CPE statements of credit can be printed from the CPE Monitor website. Send inquiries to opa@ohiopharmacists.org.

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