Chapter 42
Approach to *Clostridioides Difficile* (*C. Difficile*) Infection in the ICU

42.1 Introduction

Clostridioides difficile infection (CDI) is a significant cause of healthcare-associated infections, ranging from mild diarrhea to life-threatening colitis. CDI typically occurs after antibiotic use, which disrupts the normal gut microbiota, allowing *C. difficile* to proliferate. Early and accurate identification of CDI severity is critical for effective management and to prevent complications. Management of CDI is guided by clinical severity, with treatments tailored for non-severe, severe, or fulminant presentations. Recurrent infections are common, requiring specific protocols for effective treatment. Recent updates in the management of CDI emphasize newer agents like fidaxomicin and adjunctive therapies such as bezlotoxumab, offering better outcomes in preventing recurrences [1–3] [Ref: Algorithm 42.1].

42.2 Initial Evaluation

The initial step in managing CDI involves assessing the severity of the infection to guide treatment:

- Non-severe CDI: Defined by a white blood cell count (WBC) ≤15,000 cells/μL and serum creatinine (Cr) <1.5 mg/dL. Patients typically present with diarrhea but without systemic toxicity.
- Severe CDI: Characterized by WBC >15,000 cells/μL or serum creatinine ≥1.5 mg/dL. These patients have a higher risk of complications, warranting more intensive treatment.
- Fulminant CDI: The most critical form, marked by hypotension, shock, ileus, or megacolon. Patients often require a combination of oral and intravenous (IV) treatments and may need ICU care.

S. B. Mishra et al., *Mastering ICU Care*,
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42.3 Non-severe CDI: First-Line Treatment

The primary goal in treating non-severe CDI is to eradicate the infection while minimizing the risk of recurrence. Updated guidelines highlight:

- Fidaxomicin (200 mg orally twice daily for 10 days) is preferred over vancomycin due to a lower risk of recurrence.
- Vancomycin (125 mg orally four times daily for 10 days) remains a suitable alternative, particularly when fidaxomicin is unavailable.
- Metronidazole (500 mg orally three times daily for 10 days) is reserved as an alternative when neither fidaxomicin nor vancomycin is available, though it is less effective, especially in recurrent cases.

42.4 Severe CDI: First-Line Treatment

For severe CDI, therapy aims to control bacterial overgrowth while closely monitoring for systemic complications:

- Fidaxomicin (200 mg orally twice daily for 10 days) is preferred due to better outcomes in preventing recurrences.
- Vancomycin (125 mg orally four times daily for 10 days) is a viable alternative when fidaxomicin is not feasible.
- Adjunctive bezlotoxumab should be added for primary CDI if other risk factors for recurrence (age $\geq$ 65 years, immunocompromised host) or if an episode of CDI in the last 6 months is present.
- Treatment should be accompanied by close monitoring of hydration status, potential complications, and prompt adjustments in therapy based on the patient's clinical response.

42.5 Fulminant CDI: First-Line Treatment

Managing fulminant CDI requires aggressive intervention to reduce morbidity and mortality:

- Vancomycin (500 mg orally or via nasogastric tube four times daily) is recommended, with consideration for rectal vancomycin (500 mg in 100 mL of normal saline every 6 hours) if the patient has ileus.

And

Intravenous metronidazole (500 mg every 8 hours) is added to ensure systemic coverage, particularly when oral delivery is compromised.

- As per ESCIMD guidelines, IV tigecycline 100 mg loading then 50 mg 12 hourly can also be used as an alternative regimen.
- This regimen is essential to ensure the medication reaches the colon effectively, even in the presence of intestinal paralysis.

42.6 Recurrent CDI

Recurrence is a common challenge in CDI, affecting about 20–30% of cases. Management strategies are adjusted based on previous treatments:

First Recurrence:

- If previously treated with metronidazole, transition to vancomycin (125 mg orally four times daily for 10 days).
- If vancomycin was used initially, switch to fidaxomicin (200 mg orally twice daily for 10 days).
- A vancomycin taper and pulse regimen can also be used, gradually reducing the dose over weeks to enhance the suppression of *C. difficile*, and adjunctive bezlotoxumab should be given if prior episode is present in the last 6 months.

Second or Subsequent Recurrences:

- Use vancomycin in a tapered and pulsed regimen, such as 125 mg four times daily for 10–14 days, then gradually tapering over 2–8 weeks. Adjunctive bezlotoxumab should be added if prior episode is present in the last 6 months.
- Fidaxomicin remains a viable option if not previously utilized.
- For patients with multiple recurrences, fecal microbiota transplantation (FMT) is recommended, restoring normal gut flora and reducing recurrence risk.

42.7 Adjunctive Therapies

Several adjunctive measures can support recovery and reduce recurrence risk:

- Bezlotoxumab: A monoclonal antibody targeting *C. difficile* toxin B, it is considered for patients at high risk of recurrence (e.g., those aged ≥65, immunocom-

promised). It is administered as a single IV dose of 10 mg/kg during antibiotic therapy. However, caution is advised for patients with congestive heart failure due to potential risks.

- Stopping the inciting antibiotic: Discontinuing unnecessary antibiotics helps restore gut microbiota, reducing the risk of recurrence.
- Avoiding anti-motility agents (e.g., loperamide): These can slow the clearance of the bacteria and increase the risk of toxic megacolon.
- Maintaining adequate hydration and electrolyte balance: Addressing dehydration and electrolyte disturbances from diarrhea is critical.
- Infection control: Contact precautions, hand hygiene, and isolation are vital to prevent the spread of CDI in healthcare settings.

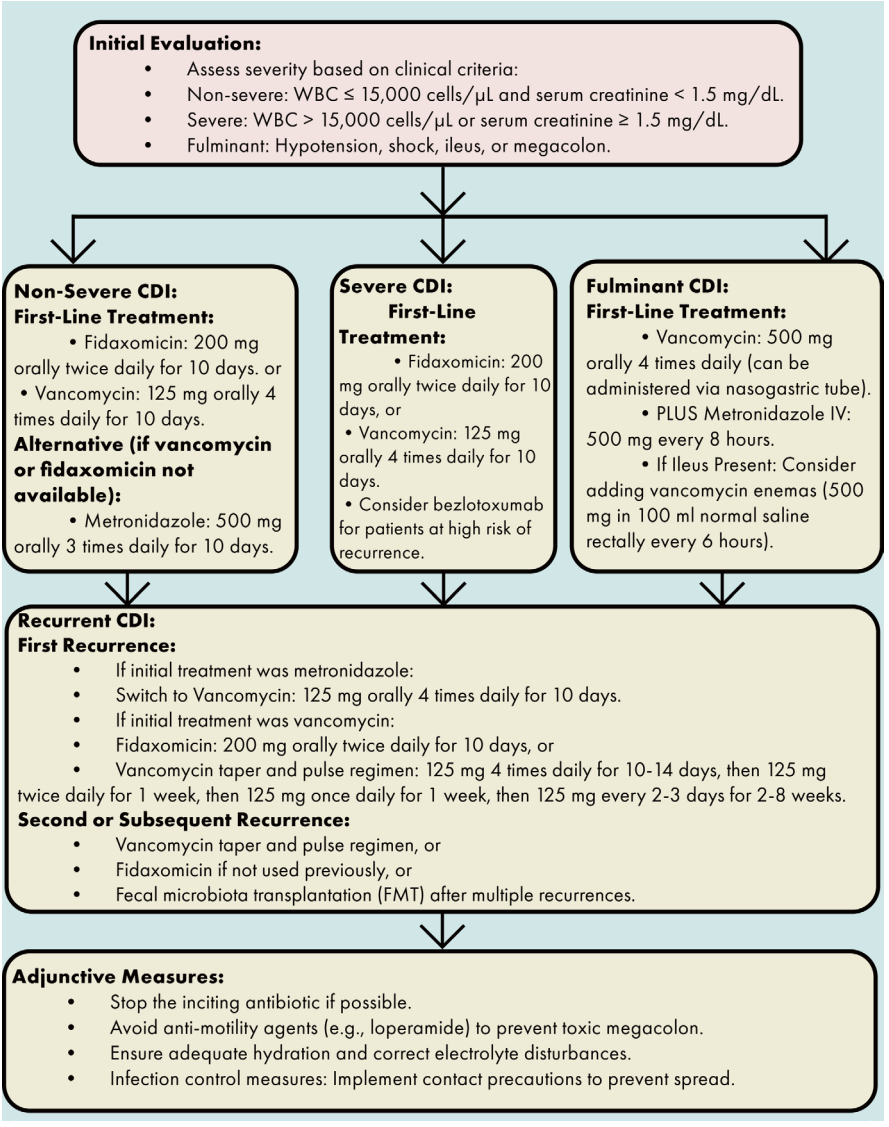
42.8 Early Diagnosis

Accurate and timely diagnosis is fundamental in CDI management. Implementing a multistep testing algorithm—such as using glutamate dehydrogenase (GDH) and toxin assays or a combination of nucleic acid amplification tests (NAATs)—ensures that patients with clinically significant CDI are appropriately identified and treated. This approach helps reduce the risk of overtreatment and improves patient outcomes.

42.9 Conclusion

Management of *Clostridioides difficile* infection (CDI) is tailored to clinical severity, with a focus on preventing complications like recurrence, fulminant colitis, or toxic megacolon. Updated guidelines favor fidaxomicin over vancomycin for its lower recurrence rates, with metronidazole as an alternative in resource-limited settings. In cases of recurrence, strategies such as vancomycin taper regimens or fecal microbiota transplantation provide effective options. Early recognition and appropriate treatment are key to reducing CDI-related morbidity and mortality. Adherence to current guidelines, particularly in using newer therapeutic options and adjunctive measures, ensures improved outcomes in managing this challenging condition.

Algorithm 42.1: Approach to *Clostridioides difficile* (*C. Difficile*) infection in the ICU



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