Chapter 43
Approach to Hepatic Encephalopathy in the ICU

43.1 Introduction

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome that arises from liver dysfunction, typically associated with cirrhosis. It can present with a range of symptoms, from subtle cognitive changes to deep coma. Up to 30–50% of patients with cirrhosis will develop some form of HE during their lifetime, significantly affecting one-year mortality rates. Early recognition and targeted management are essential to prevent complications and improve patient outcomes.

The pathophysiology of HE involves the buildup of neurotoxins like ammonia and manganese due to impaired liver detoxification and portosystemic shunting. These toxins cross the blood-brain barrier, leading to astrocyte swelling, changes in neurotransmitter levels, and brain edema. Understanding these mechanisms helps guide treatment strategies, focusing on reducing neurotoxic burden and stabilizing neurological function [1, 2] [Ref: Algorithm 43.1].

43.2 Assess if the Patient's Airway Is Compromised

- Severe cases of HE, especially those resulting from acute liver failure, can lead to cerebral edema, increasing intracranial pressure and potentially causing brainstem compression. Early airway protection is critical, particularly in patients with fulminant liver failure, to prevent hypoxia and secondary brain injury. Intubation should be considered for patients with significantly impaired consciousness (e.g., low Glasgow Coma Scale score).
- The use of sedatives should be minimized, as they can exacerbate encephalopathy. If sedation is necessary, it is advisable to use agents with minimal hepatic metabolism, such as propofol [3].

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43.3 Staging

43.3.1 West Haven Criteria [4]

- **Grade 1:** Characterized by a lack of awareness, euphoria or anxiety, reduced attention span, and difficulty with simple tasks such as addition or subtraction.
- **Grade 2:** Marked by lethargy or apathy, slight disorientation to time, place, or person, personality changes, inappropriate behavior, and the presence of a flapping tremor (asterixis).
- **Grade 3:** The patient is somnolent to semi-stuporous but still responsive to verbal stimuli, with significant confusion and marked disorientation.
- **Grade 4:** Represents coma, with no response to verbal commands and complete unresponsiveness.

This classification helps guide clinical management and monitor disease progression.

43.3.2 Classification Based on the Underlying Cause [4]

Type A (Acute): Associated with acute liver failure, this form of HE often presents rapidly and is commonly linked with cerebral edema and increased intracranial pressure.

Type B (Bypass): Occurs due to portal-systemic shunting in the absence of intrinsic liver disease. The shunt allows toxins to bypass the liver, leading to neuropsychiatric symptoms.

Type C (Cirrhosis): Seen in patients with chronic liver disease or cirrhosis. It is further categorized into:

- **Episodic:** Intermittent episodes triggered by precipitating factors.
- **Persistent:** Chronic, ongoing symptoms of encephalopathy.
- **Minimal (or Covert):** Subtle cognitive and psychomotor deficits without overt clinical signs, often requiring specialized testing for diagnosis.

This classification aids in identifying the etiology and tailoring appropriate treatment strategies.

43.3.3 Overt HE

This refers to clinically apparent episodes of neuropsychiatric dysfunction. It can be **episodic**, occurring as isolated events, or **recurrent**, defined as more than one episode within a six-month period.

43.3.4 Persistent HE

In this form, patients do not return to their baseline neuropsychiatric status between episodes. Symptoms are continuous or fluctuate without complete resolution, indicating a chronic impairment in cognitive and neurological function.

43.4 Presence of Precipitating Factors

- Identifying and managing precipitating factors is crucial, as they can often trigger or worsen HE. Common precipitating factors include infections (e.g., spontaneous bacterial peritonitis), electrolyte imbalances such as hyponatremia, renal failure, and the excessive use of diuretics, gastrointestinal bleeding, medicine noncompliance, dehydration (due to diarrhea, vomiting, fluid restriction), alcohol consumption, and use of sedatives or specific analgesics. Targeted management of these factors can significantly improve patient outcomes.
- Diagnostic workup should include cultures, serum electrolytes, blood urea nitrogen (BUN) levels, and ammonia levels, although ammonia levels may not always directly correlate with the severity of HE [5, 6].

43.5 Focus on General Supportive Care and Continue Evaluation

- Supportive care is essential for stabilizing patients with HE. This includes maintaining adequate caloric intake (35–40 kcal/kg/day) and protein intake (1.2–1.5 g/kg/day) to prevent catabolism. Contrary to earlier beliefs, protein restriction is not recommended due to the risk of malnutrition; instead, a balanced diet with a higher vegetable protein content is preferable. Small meals or liquid nutritional supplements evenly distributed throughout the day and a late-night snack should be offered.
- Ongoing evaluation should include monitoring neurological status and conducting further tests, such as cultures or imaging, to identify other contributing factors to encephalopathy.

43.6 If the Patient Is Not Responding to Lactulose, Consider Rifaximin or Alternative Therapies

- Lactulose is a cornerstone of HE therapy due to its ability to lower systemic ammonia. It promotes conversion of ammonia (NH_3) into ammonium (NH_3^+) in the gut by acidifying the colon, which also inhibits ammonia-producing bacterial

strains. Additionally, lactulose increases colonic motility, reducing the duration available for ammonia reabsorption, and supports nitrogen excretion by acting osmotically. Dose: 30 ml 3–4 times /day. Enema can also be given if there is inadequate response or there is intolerance to oral/enteral feed. Target 2–4 soft/loose stools per day.

Rifaximin enhances treatment by decreasing the population of gut flora that produce ammonia. It acts locally in the gut without systemic absorption and inhibits bacterial RNA synthesis, thus further lowering neurotoxin production. Dose: 550 mg twice daily or 400 mg thrice daily.

- Alternatives like L-ornithine L-aspartate (LOLA) may be considered to further reduce ammonia levels in patients not responding to lactulose and rifaximin. Emerging therapies, such as fecal microbiota transplants, are also being explored for managing refractory cases of HE.

43.7 If the Patient Still Does Not Respond, Reevaluate for Other Complications

- When standard therapy fails, it is essential to reassess for other potential complications or underlying conditions. Persistent HE may indicate the presence of intracranial pathologies, such as subdural hematoma or stroke, which can mimic or worsen encephalopathy.
- In such cases, advanced imaging like MRI or CT scans, along with EEG, can help identify conditions such as non-convulsive status epilepticus. Additionally, evaluate the need for adjusting or closing a transjugular intrahepatic portosystemic shunt (TIPS) if it is contributing to persistent HE [7]

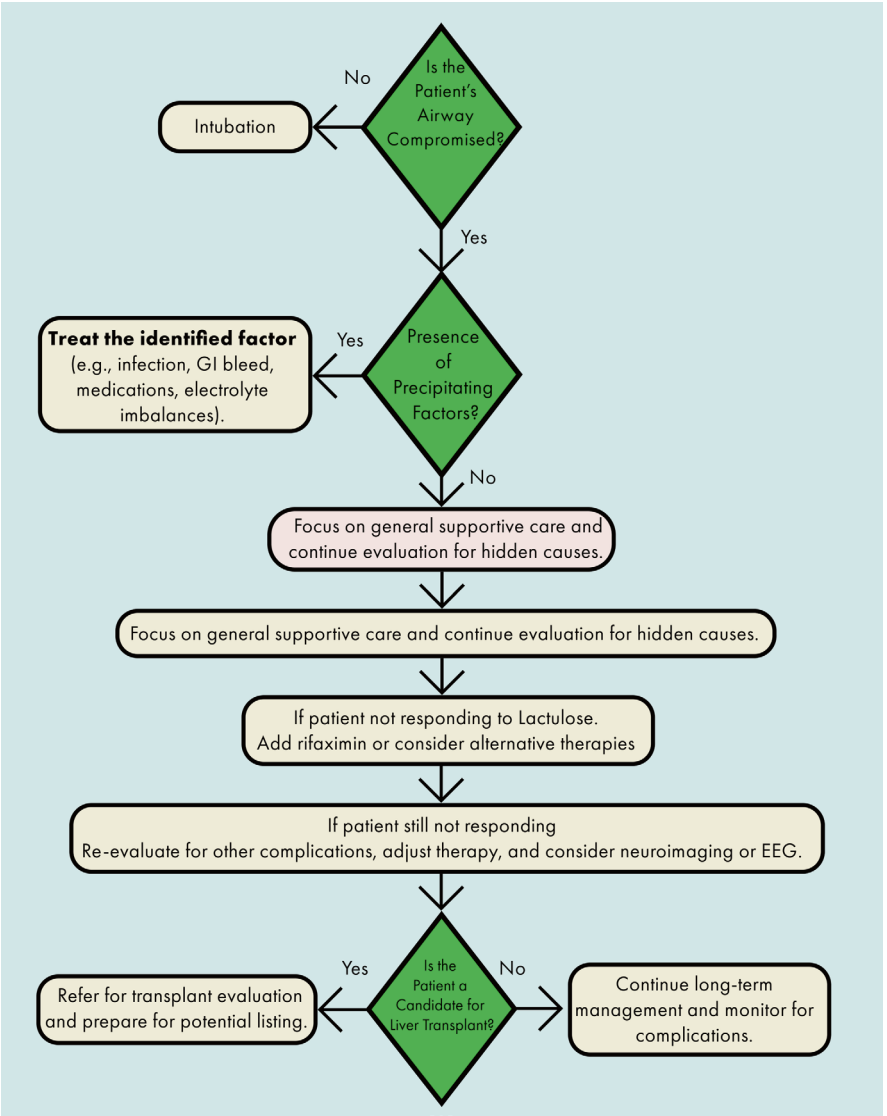
43.8 Is the Patient a Candidate for Liver Transplant?

- In individuals experiencing frequent or treatment-resistant episodes of hepatic encephalopathy, liver transplantation offers a curative approach by correcting the primary hepatic insufficiency. The MELD score plays a pivotal role in determining transplant candidacy by evaluating disease severity.
- Timely consultation with a transplant center is crucial when medical therapy fails to yield adequate results, as delayed referrals may adversely affect prognosis. Alongside clinical eligibility, factors such as daily functioning and overall quality of life should be weighed, considering the profound burden HE imposes on patients.

43.9 Conclusion

Managing hepatic encephalopathy requires a structured approach that includes stabilizing the patient, identifying and treating precipitating factors, and considering advanced treatments such as liver transplantation. Preventing recurrence is a key focus, with secondary prophylaxis using lactulose and rifaximin playing an important role in reducing future episodes. A multidisciplinary approach, involving hepatologists, dietitians, and neurologists, ensures comprehensive care for patients with HE. Individualized care plans and timely interventions are essential to improving outcomes for this complex condition.

Algorithm 43.1: Approach to hepatic encephalopathy in the ICU



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