Standard Operating Procedure

Acute overt Hepatic encephalopathy

Special Region (1)

University Of Medicine

Version 2.0

Effective date: 29th January 2026

Review date: 29th January 2028

Approved by: Internal medicine Unit

1) Introduction

The joint American-European guidelines[1] define hepatic encephalopathy as "a brain dysfunction caused by liver insufficiency and/or portosystemic shunts."

Thirty percent to 45% of cirrhotic patients could be affected by overt hepatic encephalopathy (OHE)[2].

2) Pathophysiology

Exact mechanism is unclear; possible factors involved include neurotoxins (particularly ammonia), impaired neurotransmission due to metabolic alterations, changes in brain energy metabolism, systemic inflammation, and alterations in the blood-brain barrier.

3) Clinical Features

The clinical presentation of OHE ranges from asterixis to coma. The most frequent/typical symptoms of OHE are asterixis, which is the first manifestation of OHE, and psychomotor slowing[3].

Most patients have already featured of chronic liver insufficiency features and decompensated cirrhosis (fetor hepaticus, jaundice, spider naevi, leukonychia, clubbed nails, gynecomastia, Dupuytren's contracture, palmar erythema, ascites, spontaneous bacterial peritonitis, leg edema, etc., …).

Check for anemia, jaundice, hematemesis and melaena (Do PR examination for patients with suspected upper GI bleeding).

Examine for Hepatomegaly (? hepatocellular carcinoma/ acute on chronic liver disease) and splenomegaly (enlarged in portal hypertension).

Check for possible underlying liver disease.

- Spider naevi are florid in alcoholic cirrhosis, Dupuytren's contracture and parotic enlargement are more noted in alcoholic cirrhosis. Hepatomegaly is commonly encountered in acute on chronic alcoholic liver disease.

- Tattoo marks may be seen in patients with underlying hepatitis B infection and hepatitis C infection.
- Injection marks are commonly found in IVDU patients.

4) Diagnosis classification and severity of Hepatic encephalopathy (West Haven criteria)

- Minimal (covert): psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change
- Grade 1 (covert): trivial lack of awareness, sleep rhythm alterations, shortened attention span, impaired addition or subtraction, euphoria or anxiety
- Grade 2 (overt): lethargy or apathy, disorientation for time, obvious personality change, inappropriate behavior, dyspraxia, asterixis
- Grade 3 (overt): somnolence to semi-stupor, unresponsive to stimuli, confused, gross disorientation, bizarre behavior
- Grade 4 (overt): Coma

Note

Commonly encountered clinical features and Hepatic encephalopathy are Asterixis (Flapping tremor)– grade 2, Confused – grade 3, and Coma – grade -4.

Diagnosis of hepatic encephalopathy should be written as type (A or B or C), (episodic or persistent), (covert or overt) hepatic encephalopathy, with precipitation factor (s).

E.g., type C episodic, overt hepatic encephalopathy precipitated by Hypokalemia.

<u>Types of encephalopathies</u>

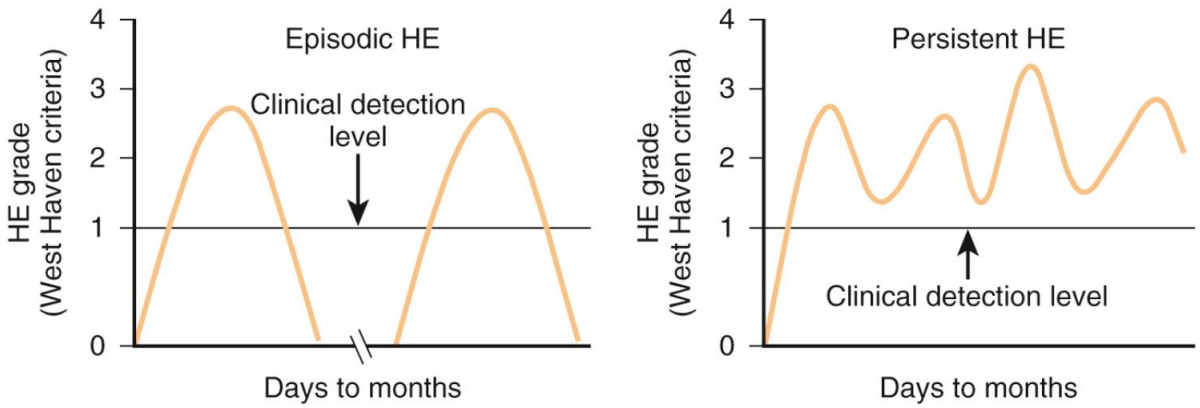
Type A – Hepatic encephalopathy due to acute liver failure

Type B – Hepatic encephalopathy due to bypass (e.g. shunt procedure)

Type C - Hepatic encephalopathy due to cirrhosis

Over or covert hepatic encephalopathies are classified by West-Heaven Criteria.

Episodic or persistent hepatic encephalopathies can be evaluated as the following figures:



5) Investigation

- Investigation for baseline: CP (auto), creatinine, electrolytes, absolute neutrophil count in ascites fluid, urine analysis, AFP and ultrasound for hepatocellular carcinoma screening if not done 3 months ago
- Serum ammonia level : Although it can support the diagnosis of hepatic encephalopathy, alternative diagnosis should be considered if suspected patient has normal ammonia level.
- Investigation for underlying liver diseases: HBs ag, HCV ab
- Investigation for Child-Pugh Grading: Serum albumin, serum bilirubin, prothrombin time

6) Management

Hepatic encephalopathy is a **potentially** reversible toxic–metabolic encephalopathy, similar to metabolic encephalopathy due to transient hypoglycemia and drug-induced encephalopathy from narcotic overdose, provided the precipitating cause is promptly recognized and treated.

Management is meant to treat the precipitation factors for hepatic encephalopathy and to treat the hepatic encephalopathy itself.

Correct common precipitating factors

- Sepsis (SBP, UTI , . . .)
- Hypoglycemia
- Alcohol and Drugs (opioid, sedatives, Gabapentin, pregabalin, ...)
- Upper GI bleeding
- Electrolytes imbalance (hypokalemia . . . . .)
- Excessive Fluid loss due to over diuresis or abdominal paracentesis

Nutrition

Patients may require a short-term protein-restricted diet after HE is diagnosed but should not continue protein restriction indefinitely, because malnutrition and sarcopenia are risk factors for HE. The recommended daily protein intake is 1.2 to 1.5 g/kg/day.

Lactulose

Lactulose is recommended first line for the management of episodic overt HE.

Dose

Oral: 20-30 g (30-45 mL) orally every 2 hours until laxative effect, then 30 to 45 mL (20 to 30 g) PO 3 to 4 times daily. Adjust dose every 1 to 2 days to produce 2 to 3 soft stools/day

Per rectal: 300 mL diluted with 700 mL water and given as rectal enema, retain for 30-60 minutes, may be repeated every 4-6 hours.

Rifaximin

Rifaximin should be considered in patients with persistent symptoms despite treatment with lactulose or those who cannot tolerate lactulose. It is recommended as add-on therapy for episodic overt HE to prevent recurrences. Rifaximin is typically added to, rather than substituted for, lactulose.

Add rifaximin if hepatic encephalopathy does not well respond to lactulose treatment after 12-24 hours despite adequate stool frequency.

Add rifaximin **earlier** if[4,5,6]:

- Grade III–IV HE
- Recurrent HE history (if patient has the history suggestive of covert hepatic encephalopathy)

- ICU admission

Dose

550 mg orally twice daily

Intravenous LOLA (L-ornithine L – aspartate)

This pharmacotherapy is used as an additional drug rather than monotherapy for overt Hepatic encephalopathy[5].

Dose

20 G per day in 250 ml of 5 % DW over 4 hours for 7 days in patients who do not respond to conventional treatment.

40 G per day may be used in more severe hepatic encephalopathy.

Contraindication

Serum creatinine - > 3 mg/dl

Oral branch chain amino acid (oral BCAA)

It may be used as nutritional adjunct in malnourished patients and not for first line treatment for overt hepatic encephalopathy or prevent recurrent hepatic encephalopathy.

Secondary prevention

Start treatment after 1 episode of acute overt HE to reduce relapses and hospitalization.

Treatment options:

- Lactulose – 6 months
- Rifaximin – 6 months
- Lactulose + rifaximin – 6 months

7) Prognosis and Patient information

Risk of recurrent HE after 1st episode of overt HE –

- 1 year survival after acute overt HE - 42% 1-year survival

- 3-year survival after acute overt HE - 23% 3-year survival

Patient and caregiver relatives nearby should understand liver cirrhosis is an irreversible disease and it is time to consider going for liver transplant. They should also know the survival of the patient according to Child- Pugh Classification described below.

Child-Pugh Classification and 1-year survival rate

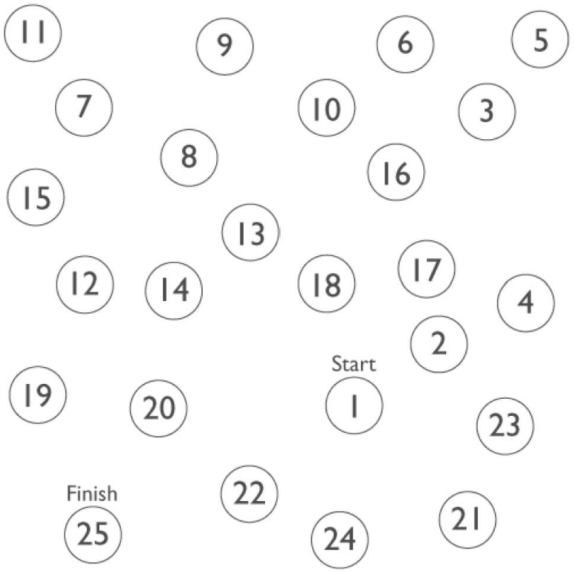
Variable	Points		
	1	2	3
Encephalopathy	None	Stage I–II	Stage III–IV
Ascites	Absent	Controlled	Refractory
Bilirubin (mg/dL)	<2	2–3	>3
Albumin (g/L)	>35	28–35	<28
Prothrombin time (seconds)	<4	4–6	>6
Sum of points	5–6	7–9	10–15
Stage	A	B	C
1-year survival rate (%)	95	80	44

8) How to assess minimal Hepatic encephalopathy

Minimal hepatic encephalopathy (covert HE) is necessary to diagnose just before patients get discharge after improving overt hepatic encephalopathy.

Number connecting test is used to diagnose minimal hepatic encephalopathy. Stroop application on Google play store or apple store can also be used to screen for minimal hepatic encephalopathy.

Number connecting test



Interpretation

≤ 30–40 sec	Normal
> 40–60 sec	Suggestive of Minimal HE
> 60 sec or errors	Abnormal - likely Minimal HE
Unable to complete	Strongly abnormal - strongly Minimal HE

9) References

1. Vilstrup H., Amodio P., Bajaj J., et al.: Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatol Baltim Md 2014; 60 (2): pp. 715-735.
2. Ferenci P., Lockwood A., Mullen K., et al.: Hepatic encephalopathy-definition, nomenclature, diagnosis, and quantification: final report of the working party at the

11th World Congresses of Gastroenterology, Vienna, 1998 . Hepatology 2002; 35 (3): pp. 716-721.
3. Harris M.K., Elliott D., Schwendimann R.N., et al.: Neurologic presentations of hepatic disease . Neurol Clin 2010; 28 (1): pp. 89-105.
4. Vilstrup H, et al.**Hepatic Encephalopathy in Chronic Liver Disease: Practice Guideline** *Hepatology*. 2014;60(2):715–735.
5. EASL Clinical Practice Guidelines on Hepatic Encephalopathy *Journal of Hepatology*. 2022;77(3):807–824.
6. Sharma P, et al. **Management of overt hepatic encephalopathy** *Clinical Liver Disease*. 2020.

Version (1) First Edited by kelvin on 20th May 2025.

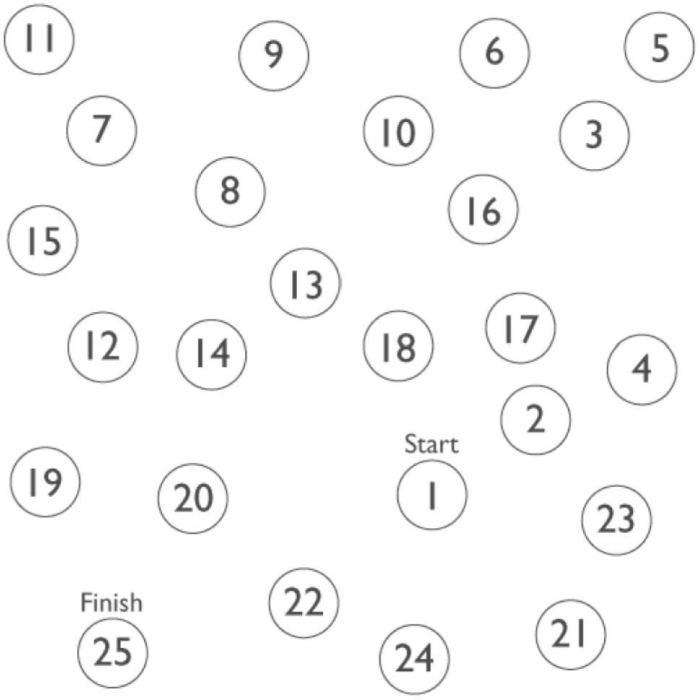
Version (2) Edited by Dr Kelvin on 29th Jan 2026.

Review date – February 2027.

Special region (1) , Union of Myanmar

10) Supplementary tools

1. Number connecting test – A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