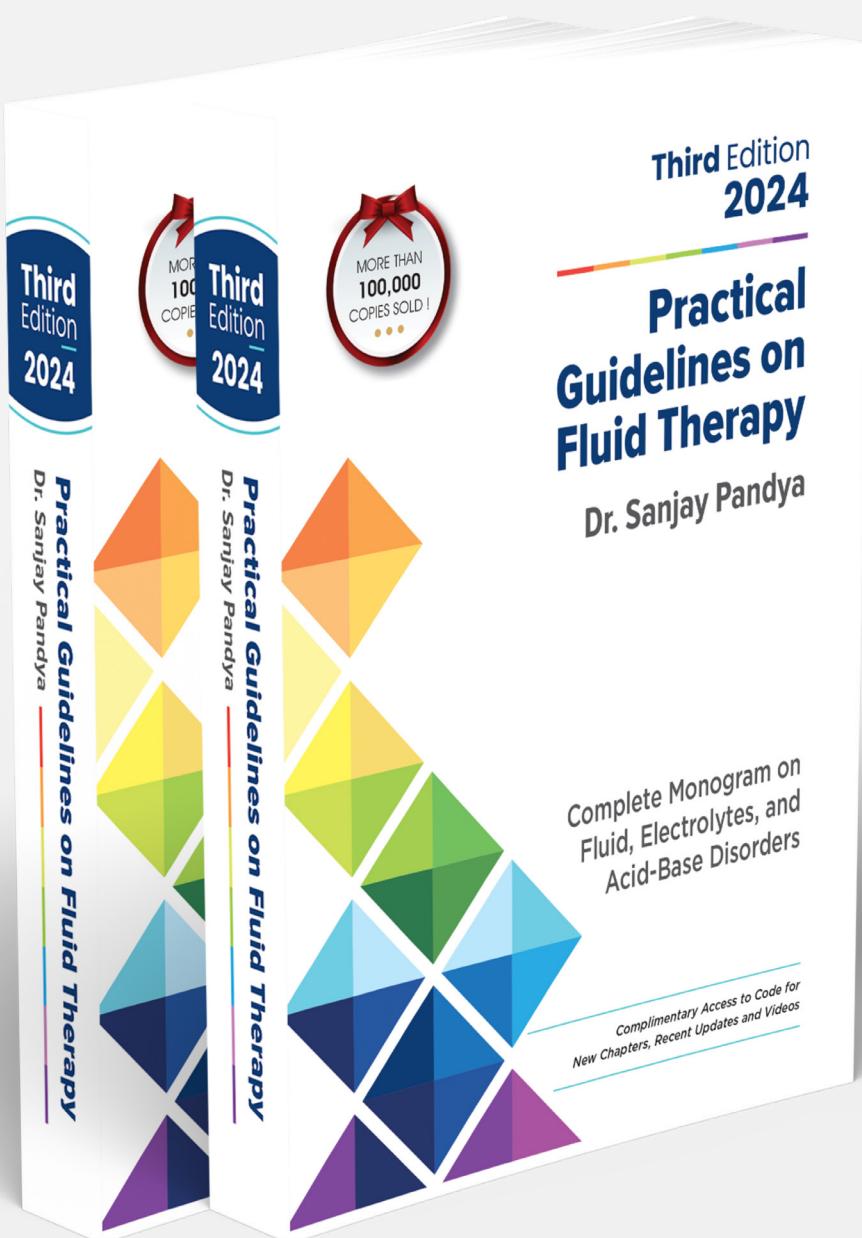




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## Chapter 36:

### Hepatic Encephalopathy



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# 36 | Hepatic Encephalopathy

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Hepatic encephalopathy (HE) is a potentially reversible condition characterized by a spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma, which occurs as one of the many complications of decompensated liver disease or portosystemic shunting [1]. About 30 to 45% of patients with cirrhosis develop overt hepatic encephalopathy [2], which is associated with significant morbidity, mortality, high healthcare cost, and a huge burden on patients and their caregivers [3, 4].

## PATHOPHYSIOLOGY

The pathophysiology of HE is poorly understood, it is often multifactorial, and different abnormalities may be present at the same time, leading to the development of HE [5].

The various pathogenetic mechanisms proposed in the development of HE are [5, 6]:

- Neurotoxins (Ammonia, benzodiazepines, benzodiazepine-like compounds such as gamma-aminobutyric acid, and manganese deposition within the basal ganglia).
- Alteration in neurotransmission due to increased GABA - neurotransmitters and serotonin activity in HE.
- False neurotransmitters such as tyramine, octopamine, and beta-phenylethanolamines may compete with the normal catecholamine neurotransmitters.
- Altered brain energy due to impaired hepatic gluconeogenesis in the terminal stages of liver failure.
- The systemic inflammatory response may exacerbate the harmful effects of hyperammonaemia on the brain [7].
- Alterations of the blood-brain barrier contribute to an increased influx of varieties of neurotoxic substances into the brain, which may contribute to HE.

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### 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. *Hepatology*. 2014;60(2):715–35.
2. Romero-Gómez M, Boza F, García-Valdecasas MS, et al. Subclinical hepatic encephalopathy predicts the development of overt hepatic encephalopathy. *Am J Gastroenterol* 2001;96(9):2718–23.
3. Kabaria S, Dalal I, Gupta K, et al. Hepatic Encephalopathy: A Review. *EMJ Hepatol*. 2021;9(1):89–97.
4. Garcia-Martinez R, Diaz-Ruiz R, Poncela M. Management of Hepatic Encephalopathy Associated with Advanced Liver Disease. *Clin Drug Investig*. 2022;42(Suppl 1):5–13.
5. Elwir S, Rahimi RS. Hepatic Encephalopathy: An Update on the Pathophysiology and Therapeutic Options. *J Clin Transl Hepatol*. 2017;5(2):142–151.
6. Ferenci P. Hepatic encephalopathy. *Gastroenterol Rep (Oxf)*. 2017;5(2):138–147.
7. Shawcross DL, Davies NA, Williams R, et al. Systemic inflammatory response exacerbates the neuropsychological effects of induced hyperammonaemia in cirrhosis. *J Hepatol*. 2004;40(2):247–54.
8. Jaffe A, Lim JK, Jakab SS. Pathophysiology of Hepatic Encephalopathy. *Clin Liver Dis*. 2020;24(2):175–188.
9. Häussinger D, Dhiman RK, Felipo V, et al. Hepatic encephalopathy. *Nat Rev Dis Primers*. 2022;8(1):43.
10. Montagnese S, Russo FP, Amodio P, et al. Hepatic encephalopathy 2018: A clinical practice guideline by the Italian Association for the Study of the Liver (AISF). *Dig Liver Dis*. 2019;51(2):190–205.
11. Hasan LZ, Wu GY. Novel Agents in the Management of Hepatic Encephalopathy: A Review. *J Clin Transl Hepatol*. 2021;9(5):749–759.
12. Bajaj JS, O'Leary JG, Lai JC, et al. Acute-on-Chronic Liver Failure Clinical Guidelines. *Am J Gastroenterol*. 2022;117(2):225–252.
13. Hoilat GJ, Suhail FK, Adhami T, et al. Evidence-based approach to management of hepatic encephalopathy in adults. *World J Hepatol* 2022;14(4):670–681.
14. Maharshi S, Sharma BC, Sachdeva S, et al. Efficacy of nutritional therapy for patients with cirrhosis and minimal hepatic encephalopathy in a randomized trial. *Clin Gastroenterol Hepatol* 2016;14(3):454–460.e3.
15. Faccioli J, Nardelli S, Gioia S, et al. Nutrition Assessment and Management in Patients with Cirrhosis and Cognitive Impairment: A Comprehensive Review of Literature. *J. Clin. Med.* 2022;11(10):2842.
16. Amodio P, Berneur C, Butterworth R, et al. The nutritional management of hepatic encephalopathy in patients with cirrhosis: International Society for Hepatic Encephalopathy and Nitrogen Metabolism Consensus. *Hepatology* 2013;58(1):325–36.
17. Córdoba J, López-Hellín J, Planas M, et al. Normal protein diet for episodic hepatic encephalopathy: results of a randomized study. *J Hepatol*. 2004;41(1):38–43.
18. Maharshi S, Sharma BC, Srivastava S. Malnutrition in cirrhosis increases morbidity and mortality. *J Gastroenterol Hepatol*. 2015;30(10):1507–13.
19. Plauth M, Bernal W, Dasarathy S, et al. ESPEN guideline on clinical nutrition in liver disease. *Clin Nutr*. 2019;38(2):485–521.
20. Bianchi GP, Marchesini G, Fabbri A, et al. Vegetable versus animal protein diet in cirrhotic patients with chronic encephalopathy. A randomized cross-over comparison. *J Intern Med*. 1993;233(5):385–92.
21. Merli M, Iebba V, Giusto M. What is new about diet in hepatic encephalopathy. *Metab Brain Dis*. 2016;31(6):1289–1294.
22. Tsien CD, McCullough AJ, Dasarathy S. Late evening snack: exploiting a period of anabolic opportunity in cirrhosis. *J Gastroenterol Hepatol*. 2012;27(3):430–41.
23. Gluud LL, Dam G, Les I, et al. Branched-chain amino acids for people with hepatic encephalopathy. *Cochrane Database Syst Rev*. 2017;2017(5):CD001939.
24. Katayama K, Kawaguchi T, Shiraishi K, et al. The Prevalence and Implication of Zinc Deficiency in Patients With Chronic Liver Disease. *J Clin Med Res*. 2018;10(5):437–444.
25. Silva M, Gomes S, Peixoto A, et al. Nutrition in Chronic Liver Disease. *GE Port J Gastroenterol*. 2015;22(6):268–276.

- 
26. Loomba V, Pawar G, Dhar KL, et al. Serum zinc levels in hepatic encephalopathy. *Indian J Gastroenterol.* 1995;14(2):51–53.
27. Takuma Y, Nouso K, Makino Y, et al. Clinical trial: oral zinc in hepatic encephalopathy. *Aliment Pharmacol Ther.* 2010;32(9):1080–90.
28. Chavez-Tapia NC, Cesar-Arce A, Barrientos-Gutiérrez T, et al. A systematic review and meta-analysis of the use of oral zinc in the treatment of hepatic encephalopathy. *Nutr J.* 2013;12:74.
29. Shen YC, Chang YH, Fang CJ, et al. Zinc supplementation in patients with cirrhosis and hepatic encephalopathy: a systematic review and meta-analysis. *Nutr J.* 2019;18(1):34.
30. Fallahzadeh MA, Rahimi RS. Hepatic Encephalopathy and Nutrition Influences: A Narrative Review. *Nutr Clin Pract.* 2020;35(1):36–48.
31. Hung TH, Tseng CW, Tsai CC, et al. Prognosis of hypoglycemia episode in cirrhotic patients during hospitalization. *BMC Gastroenterol.* 2021;21(1):319.
32. Scheiner B, Lindner G, Reiberger T, et al. Acid-base disorders in liver disease. *J Hepatol.* 2017;67(5):1062–1073.
33. Jiménez JV, Carrillo-Pérez DL, Rosado-Canto R, et al. Electrolyte and Acid-Base Disturbances in End-Stage Liver Disease: A Physiopathological Approach. *Dig Dis Sci.* 2017;62(8):1855–1871.
34. Musso CG, Juarez R, Glasscock RJ. Water, electrolyte, acid-base, and trace elements alterations in cirrhotic patients. *Int Urol Nephrol.* 2018;50(1):81–89.
35. Katopodis P, Pappas EM, Katopodis KP. Acid-base abnormalities and liver dysfunction. *Ann Hepatol.* 2022;27(2):100675.
36. Mikkelsen ACD, Thomsen KL, Vilstrup H, et al. Potassium deficiency decreases the capacity for urea synthesis and markedly increases ammonia in rats. *Am J Physiol Gastrointest Liver Physiol.* 2021;320(4):G474–G483.
37. Zavagli G, Ricci G, Bader G, et al. The importance of the highest normokalemia in the treatment of early hepatic encephalopathy. *Miner Electrolyte Metab.* 1993;19(6):362–7.
38. European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. *J Hepatol.* 2018;69(2):406–460.
39. Fortune B, Cardenas A. Ascites, refractory ascites and hyponatremia in cirrhosis. *Gastroenterol Rep (Oxf).* 2017;5(2):104–112.
40. Alukal JJ, John S, Thuluvath PJ. Hyponatremia in Cirrhosis: An Update. *Am J Gastroenterol.* 2020;115(11):1775–85.
41. Sharma BC, Sharma P, Agrawal A, et al. Secondary prophylaxis of hepatic encephalopathy: an open-label randomized controlled trial of lactulose versus placebo. *Gastroenterology.* 2009;137(3):885–91, 891.e1.
42. Gluud LL, Vilstrup H, Morgan MY. Non-absorbable disaccharides vs placebo/no intervention and lactulose vs lactitol for the prevention and treatment of hepatic encephalopathy in people with cirrhosis. *Cochrane Database Syst Rev.* 2016;4:CD003044.
43. Morgan MY, Hawley KE, Stambuk D. Lactitol versus lactulose in the treatment of chronic hepatic encephalopathy. A double-blind, randomised, cross-over study. *J Hepatol.* 1987;4(2):236–44.
44. Bass N, Mullen K, Sanyal A, et al. Rifaximin treatment in HE. *N Engl J Med.* 2010;362(12):1071–1081.
45. Sanyal A, Younossi ZM, Bass NM, et al. Randomised clinical trial: rifaximin improves health-related quality of life in cirrhotic patients with hepatic encephalopathy - a double-blind placebo-controlled study. *Aliment Pharmacol Ther.* 2011;34(8):853–61.
46. Eltawil KM, Laryea M, Peltkian K, et al. Rifaximin vs. conventional oral therapy for hepatic encephalopathy: a meta-analysis. *World J Gastroenterol.* 2012;18(8):767–77.
47. Kimer N, Krag A, Møller S, et al. Systematic review with meta-analysis: the effects of rifaximin in hepatic encephalopathy. *Aliment Pharmacol Ther.* 2014;40(2):123–32.
48. Bajaj JS, Barrett AC, Bortey E, et al. Prolonged remission from hepatic encephalopathy with rifaximin: results of a placebo crossover analysis. *Aliment Pharmacol Ther.* 2015;41(1):39–45.
49. Patel VC, Lee S, McPhail MJW, et al. Rifaximin- $\alpha$  reduces gut-derived inflammation and mucin degradation in cirrhosis and encephalopathy: RIFSYS randomised controlled trial. *J Hepatol.* 2022;76(2):332–342.
50. Sharma BC, Sharma P, Lunia MK, et al. A randomized, double-blind, controlled trial comparing rifaximin plus lactulose with lactulose alone in treatment of overt hepatic encephalopathy. *Am J Gastroenterol.* 2013;108(9):1458–1463.
51. Hudson M, Schuchmann M. Long-term management of hepatic encephalopathy with lactulose and/or rifaximin: a review of the evidence. *Eur J Gastroenterol Hepatol.* 2019;31(4):434–450.
52. Wang Z, Chu P, Wang W. Combination of rifaximin and lactulose improves clinical efficacy and mortality in patients with hepatic encephalopathy. *Drug Des Devel Ther.* 2018;13:1–11.
53. Fu J, Gao Y, Shi L. Combination therapy with rifaximin and lactulose in hepatic encephalopathy: A systematic review and meta-analysis. *PLoS ONE.* 2022;17(4):e0267647.

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