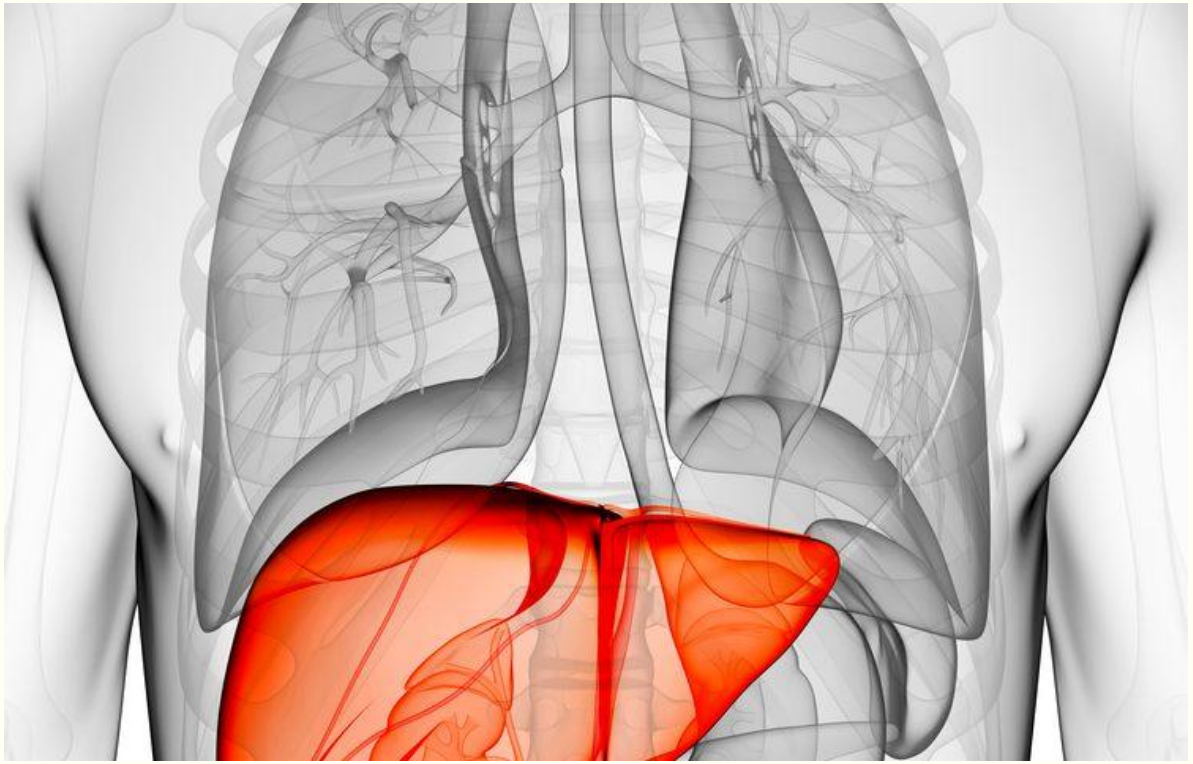
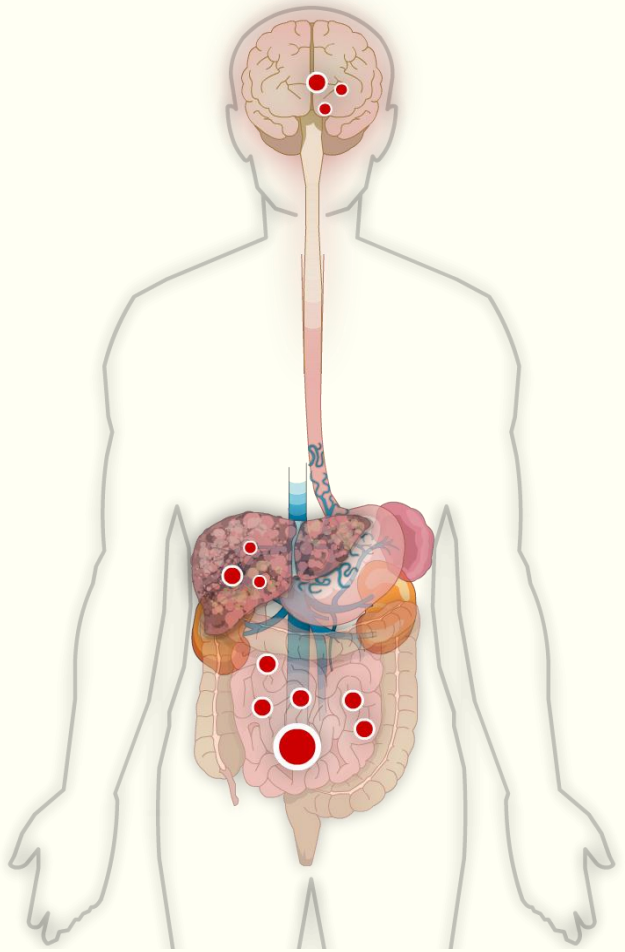
HEPATIC ENCEPHALOPATHY



Mevlana Ömeroğlu, Md
HSU Regional Training and Research Hospital
Erzurum 2018

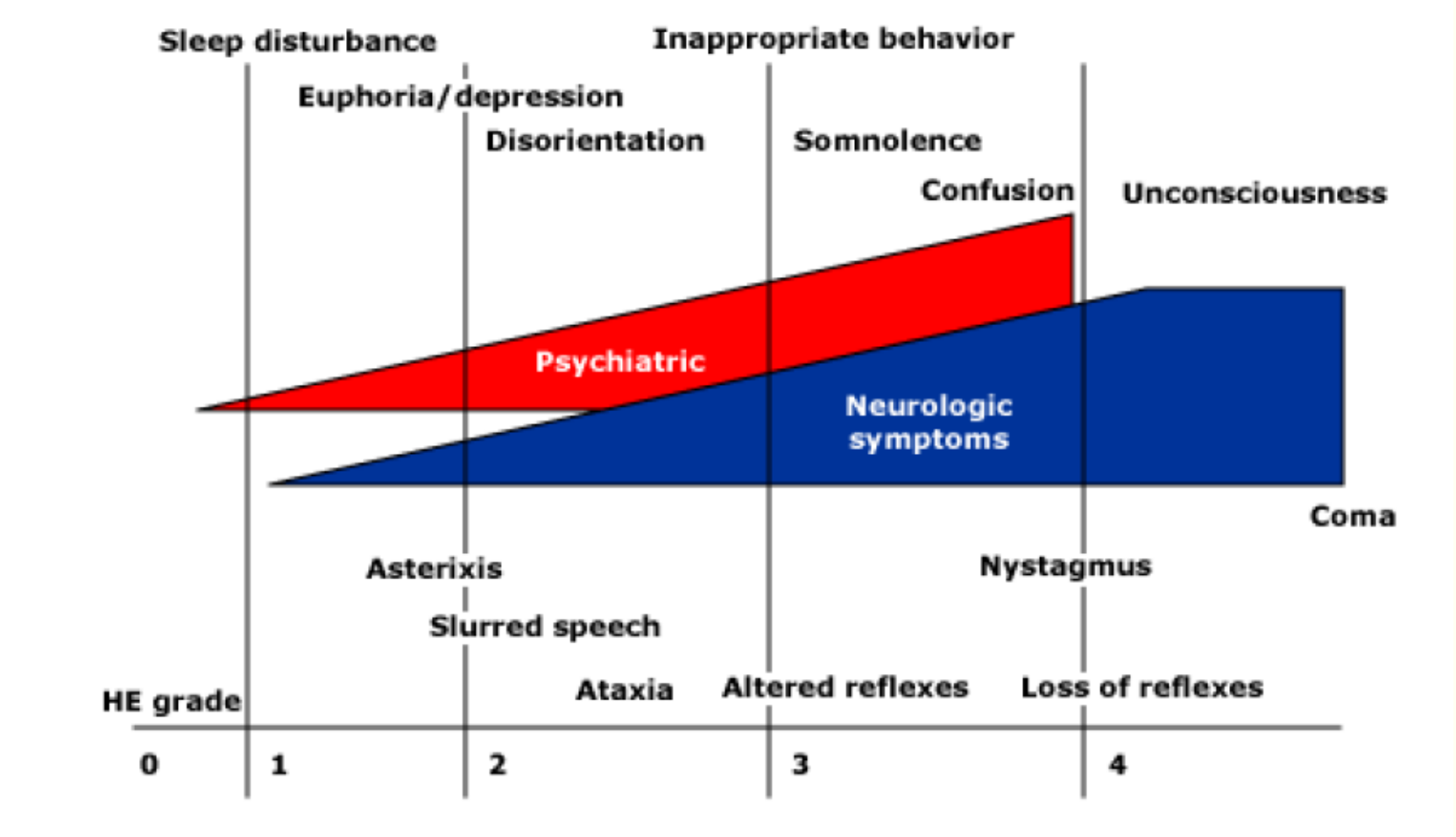
Hepatic Encephalopathy

- A reversible neuropyschiatric abnormalities
  - Cognitive deficit
  - Neuromusculer impairment



Romero-Gómez M, Boza F, García-Valdecasas MS, García E, Aguilar-Reina J. Subclinical hepatic encephalopathy predicts the development of overt hepatic encephalopathy. Am J Gastroenterol. 2001 Sep;96(9):2718-23. PubMed PMID: 11569701

Hepatic Encephalopathy



TYPES	UNDERLYİNG DİSEASE
Type A	**A**kut Liver Failure
Type B	Portal Systemic **B**ypass with no İntrinsic Hepatocellular Disease
Type C	**C**irrhosis with Portal Hypertension

Frederick RT. Current concepts in the pathophysiology and management of hepatic encephalopathy. Gastroenterol Hepatol (N Y). 2011 Apr;7(4):222-33. PubMed PMID: 21857820; PubMed Central PMCID: PMC3127024.

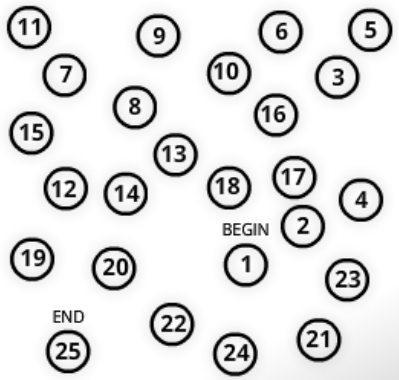
	Level of Consciousness	Neuropsychiatric Symptoms	Neurological Symptoms	
0	Normal	Impairments only measurable with psychometric tests	None "Minimal HE"	Covert HE
1	Slight mental slowing	Euphoria/dysphoria irritability and anxiety, shortened attention span	Fine motor skills affected	
2	Increased fatigue, apathy or lethargy	Slight personality disorder, slight disorientation to time and place.	Flapping tremor, ataxia, slurred speech	Overt HE
3	Somnolence	Aggression, marked disorientation to time and place.	Rigour, clonus, asterixis	
4	Coma	-		

COVERT

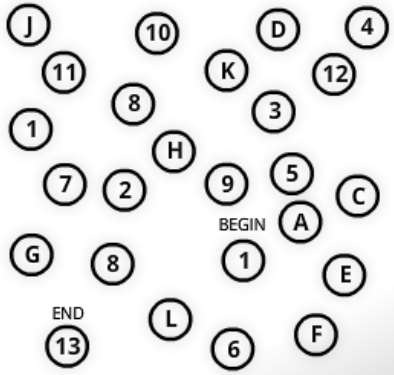
OVERT

Simple clinical

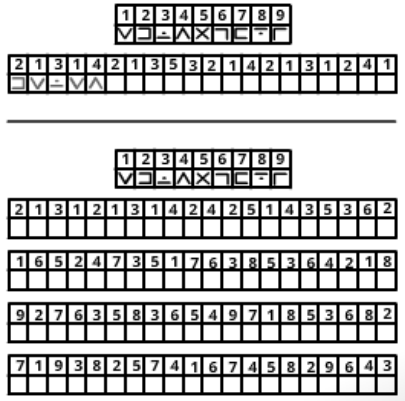
NCT-A



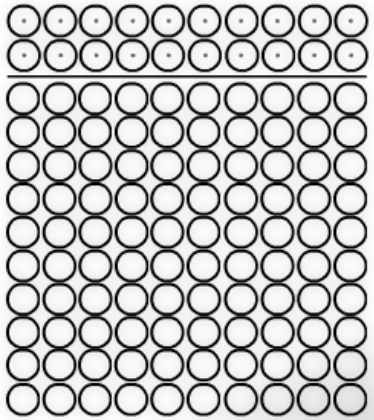
NCT-B



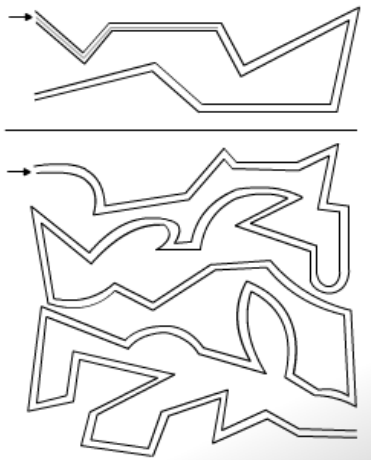
DST



SERIAL DOTTING



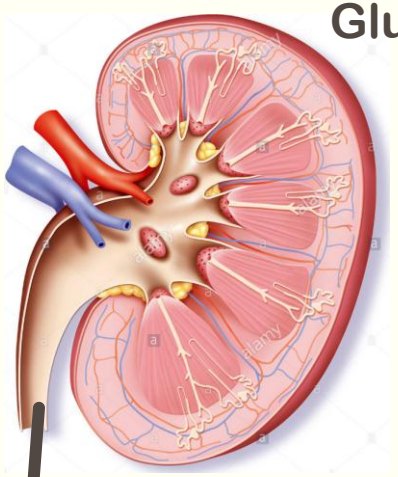
LINE DRAWING



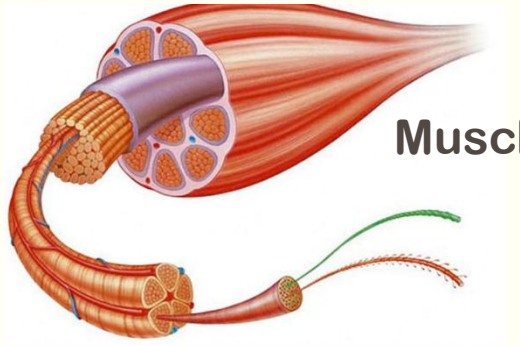
Cognitive Function

COMA

Glutaminase

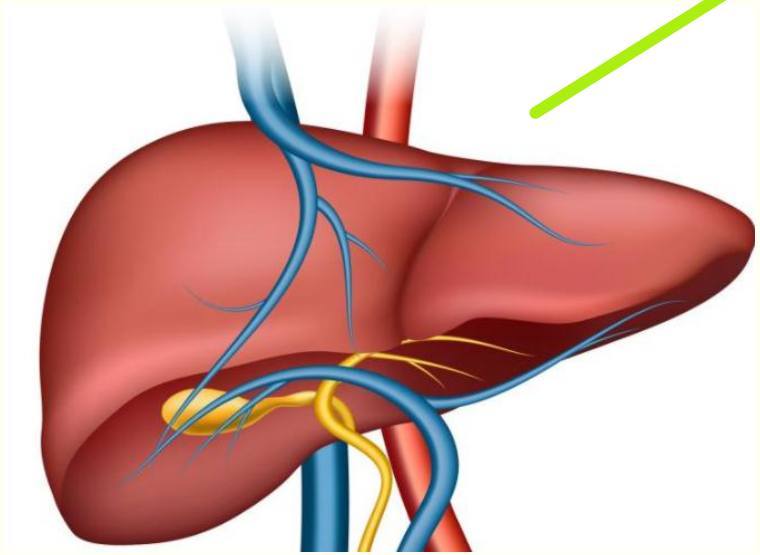


Urea

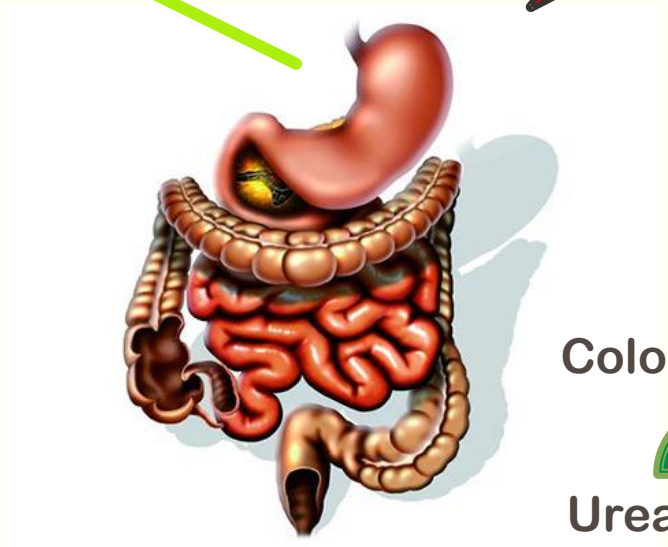


Muscle protein

NH3

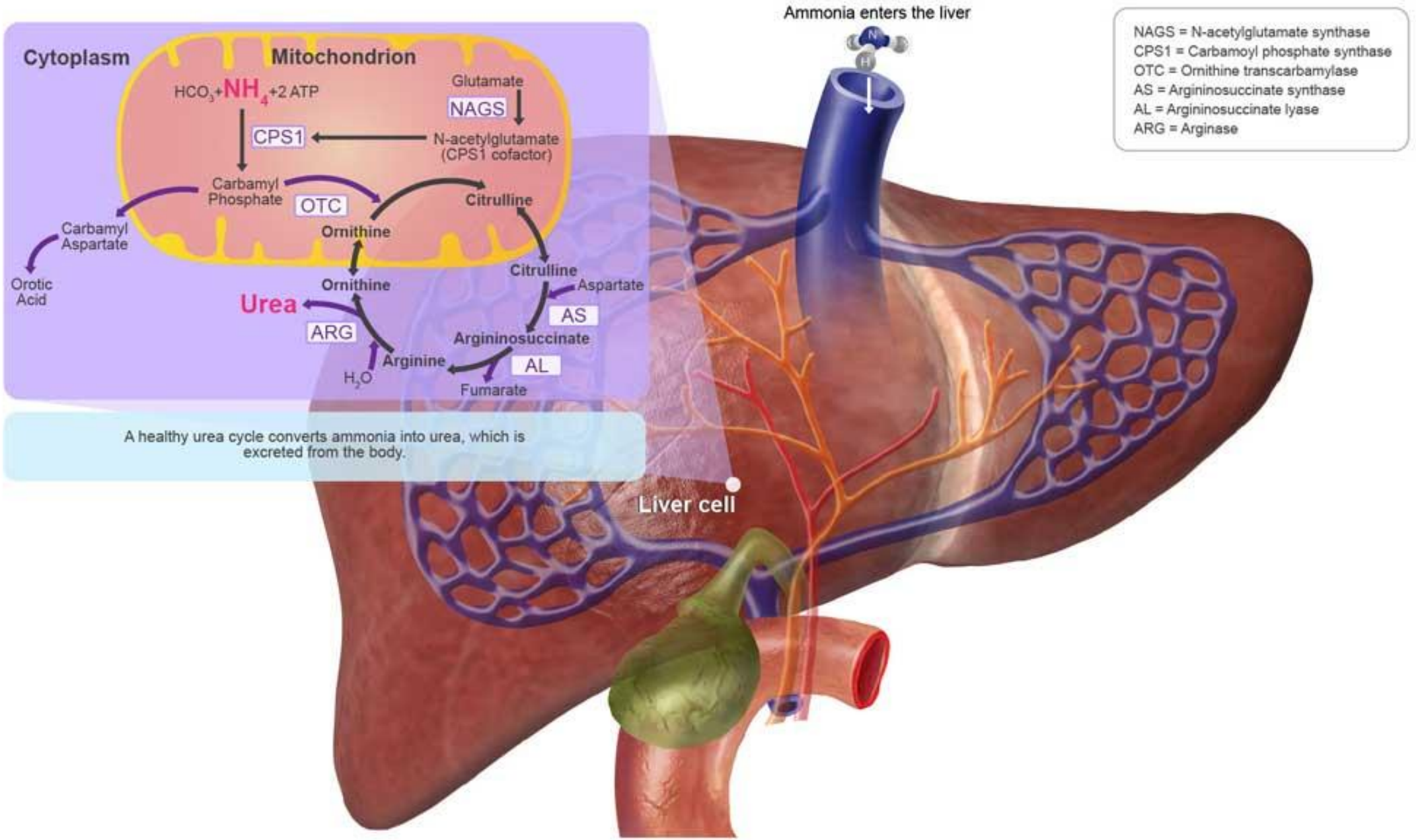


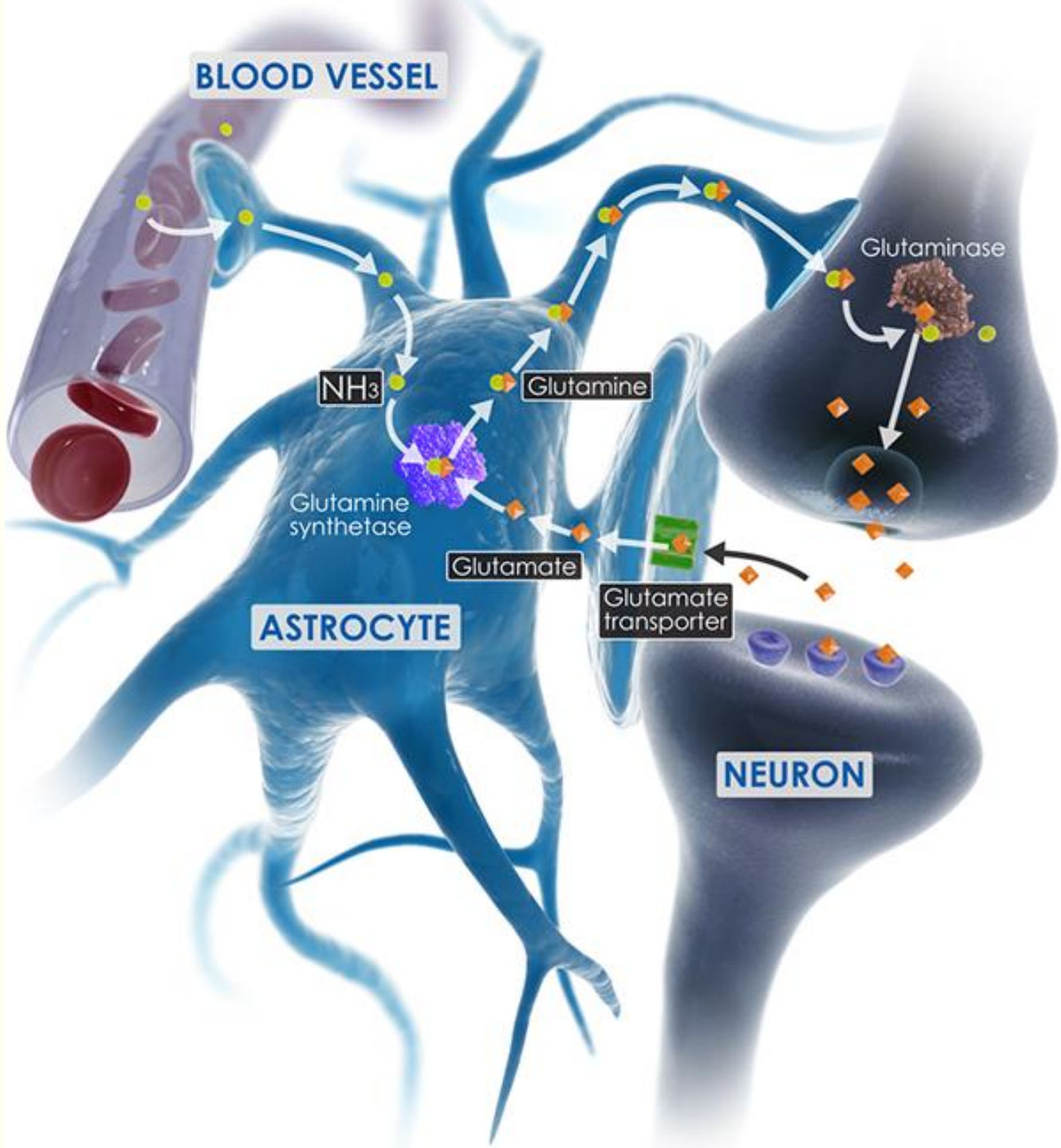
Dietary protein

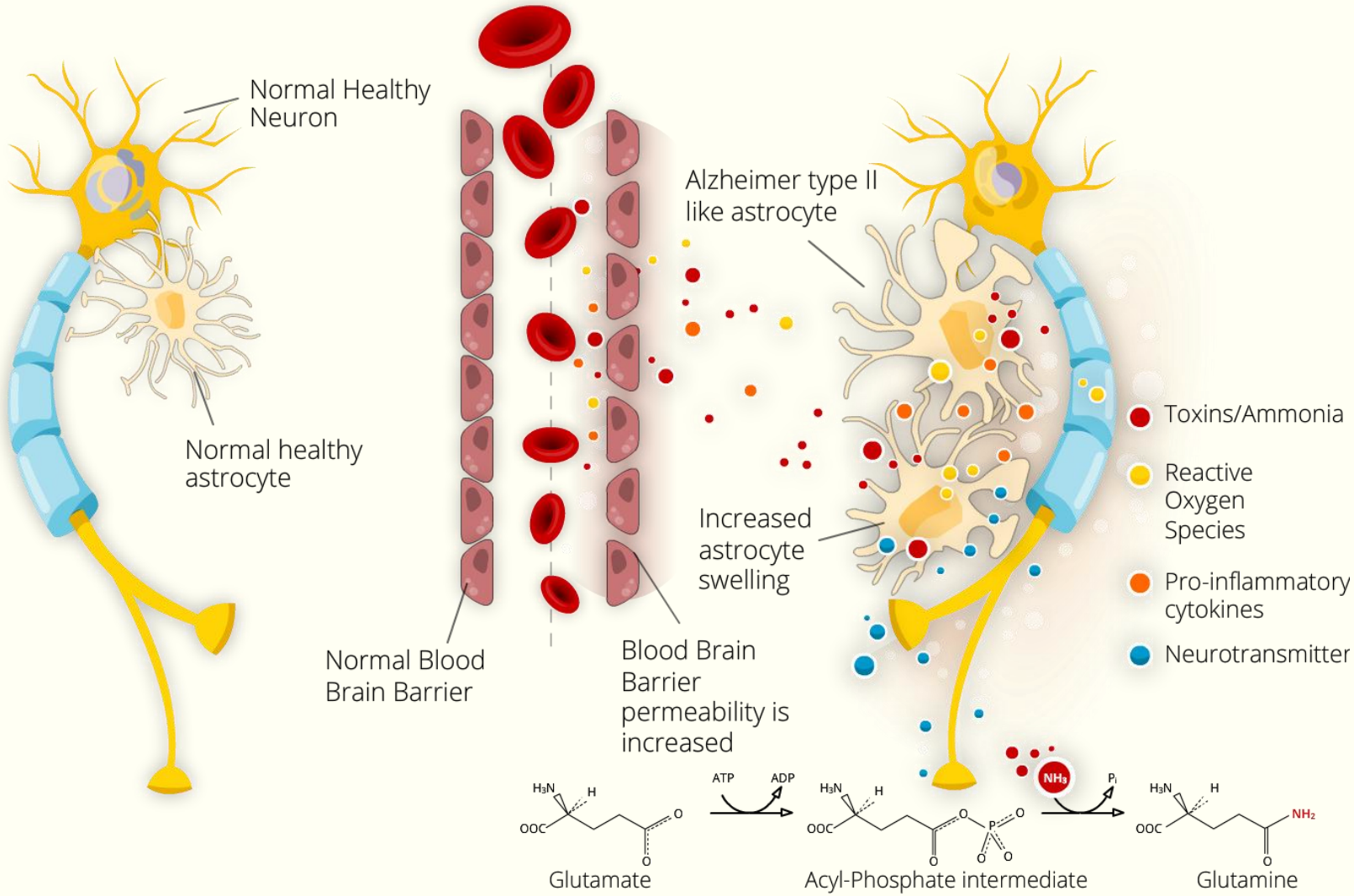


Colonic bacteria

Urea Ammonia


Cytoplasm
Mitochondrion
HCO_3+NH_4+2 ATP
Glutamate
NAGS
CPS1
N-acetylglutamate
(CPS1 cofactor)
Carbamyl
Phosphate
OTC
Citrulline
Carbamyl
Aspartate
Ornithine
Orotic
Acid
Citrulline
Aspartate
Ornithine
Urea
AS
ARG
Argininosuccinate
Arginine
AL
H_2O
Fumarate
A healthy urea cycle converts ammonia into urea, which is excreted from the body.
Ammonia enters the liver
Liver cell
NAGS = N-acetylglutamate synthase
CPS1 = Carbamoyl phosphate synthase
OTC = Ornithine transcarbamylase
AS = Argininosuccinate synthase
AL = Argininosuccinate lyase
ARG = Arginase

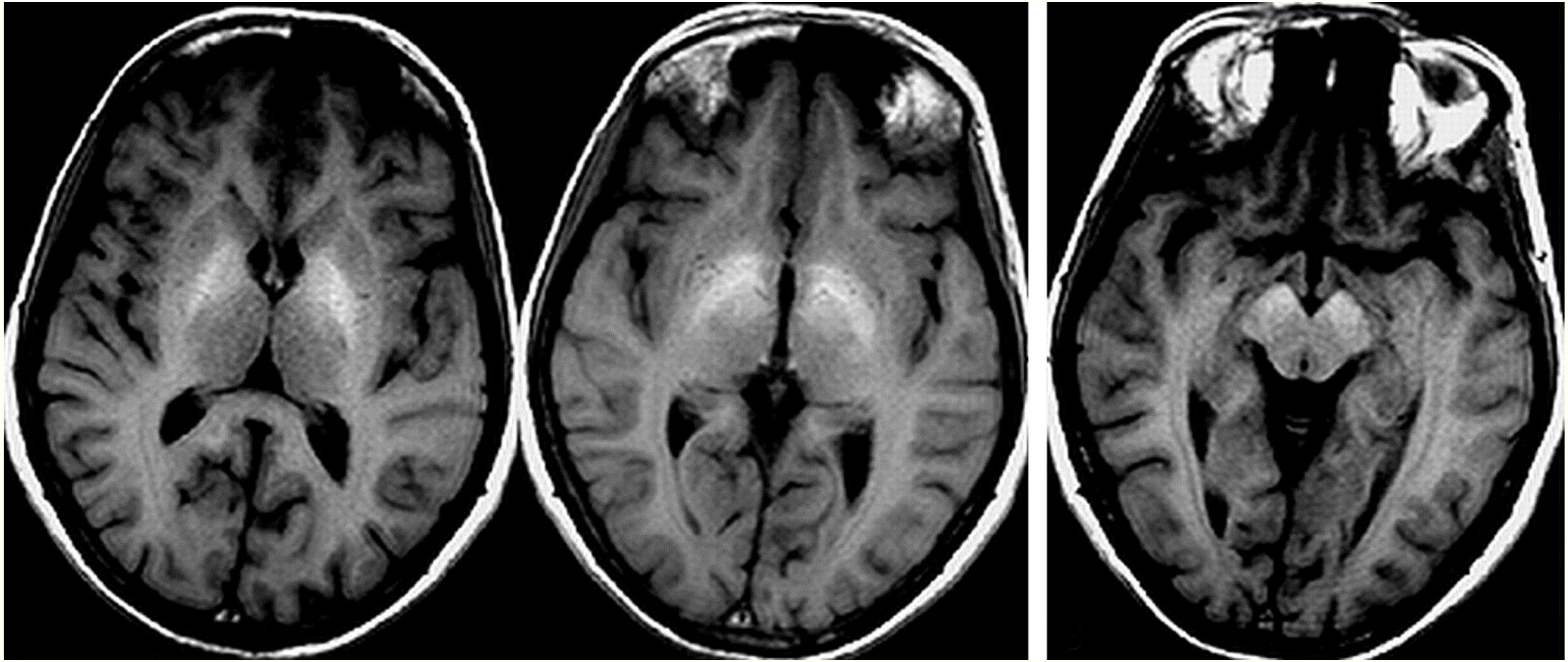

BLOOD VESSEL
Glutaminase
NH3
Glutamine
Glutamine synthetase
Glutamate
Glutamate transporter
ASTROCYTE
NEURON

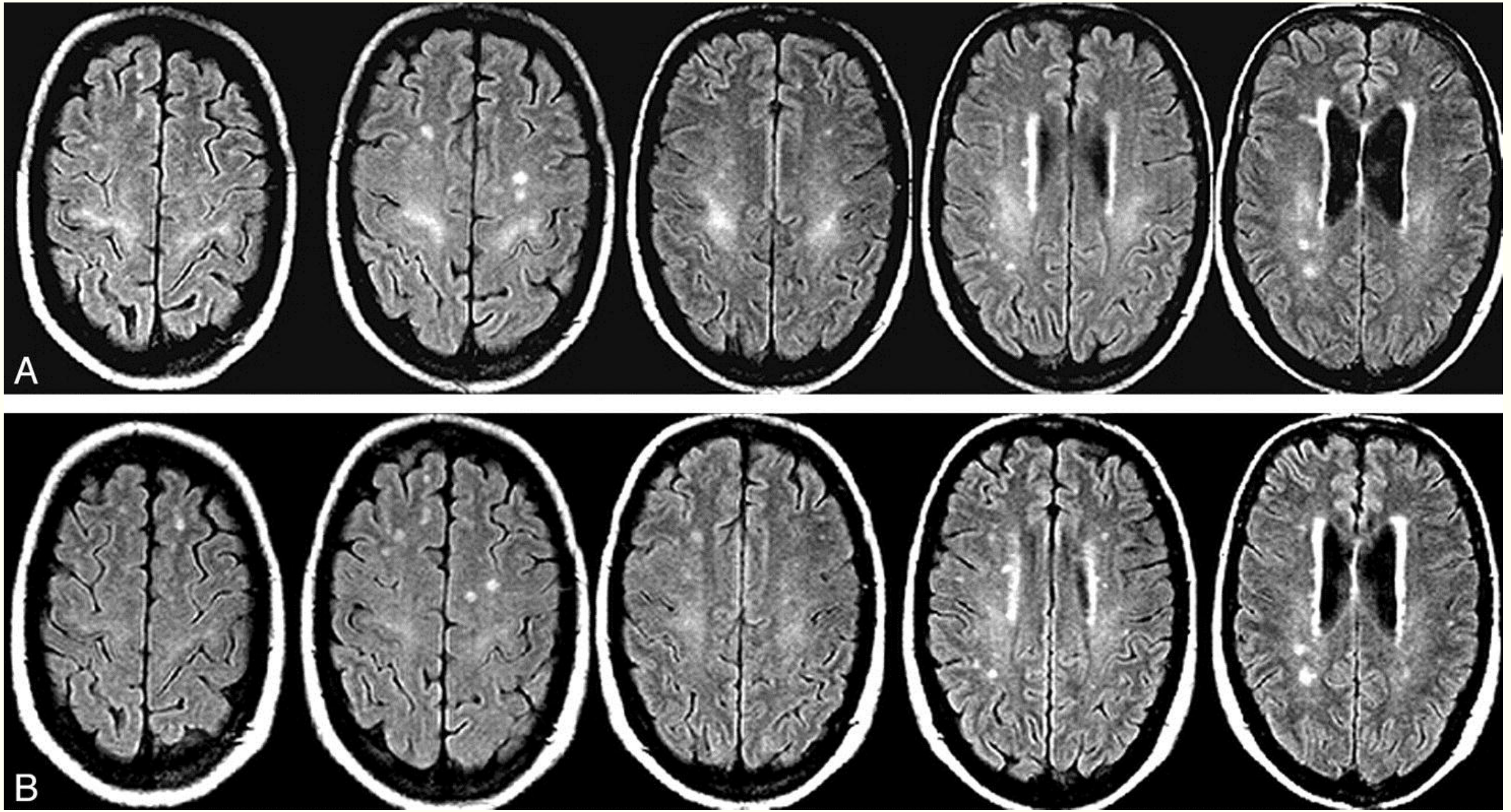


M. D. Norenberg, "The role of astrocytes in hepatic encephalopathy," Neurochemical Pathology. Vol. 6, no. 1-2, pp. 13–33, 1987. R. F. Butterworth, "Altered glial-neuronal crosstalk: cornerstone in the pathogenesis of hepatic encephalopathy," Neurochemistry International. Vol. 57, no. 4, pp. 383–388, 2010.

Diagnose

- History and physical examination
- Laboratory tests
- Exclusion
- Radiologic imaging
- Psychometric tests




A
B

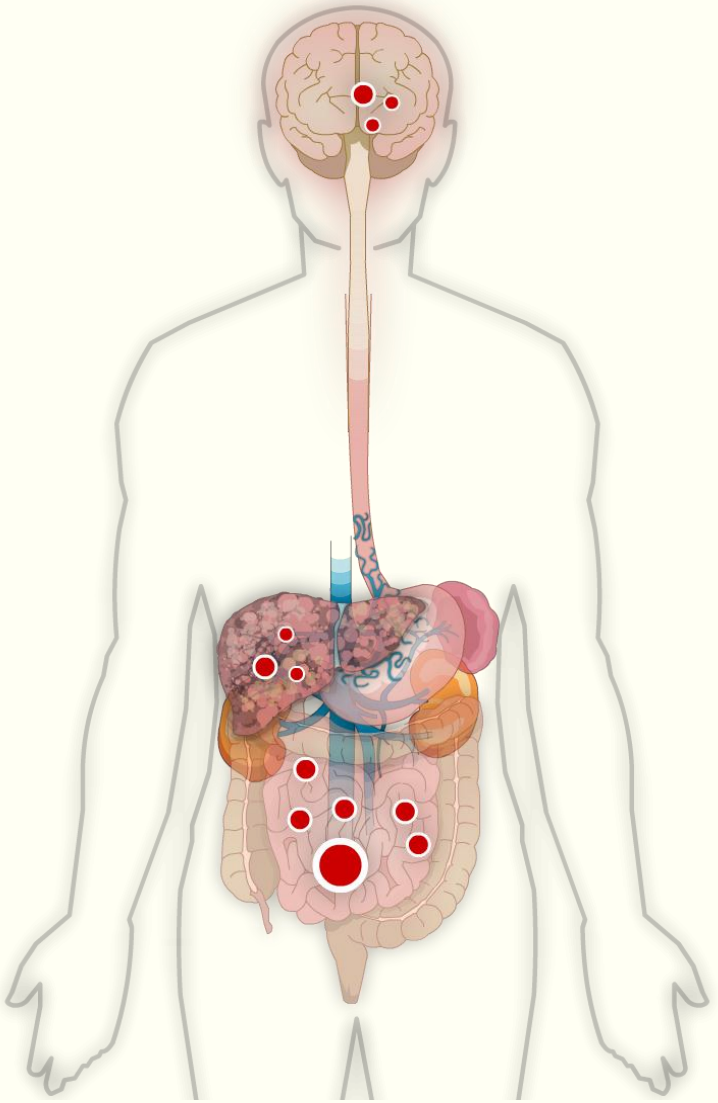
Treatment

- Triage
- Nutritional support
- Dehidration
- Electrolyte abnormalities
- Safe environment
- Falls

Acute Treatment

- Identification and correction precipitating factors
  - Gastrointestinal bleeding
  - Infection (SBP or UTI)
  - Hypokalemia and/or Metabic alkalosis
  - Renal failure
  - Hypovolemia
  - Hypoxia
  - Sedative
  - Hypoglycemia
  - Constipation
  - Hepatocellular carcinoma and/or vascular occlusion

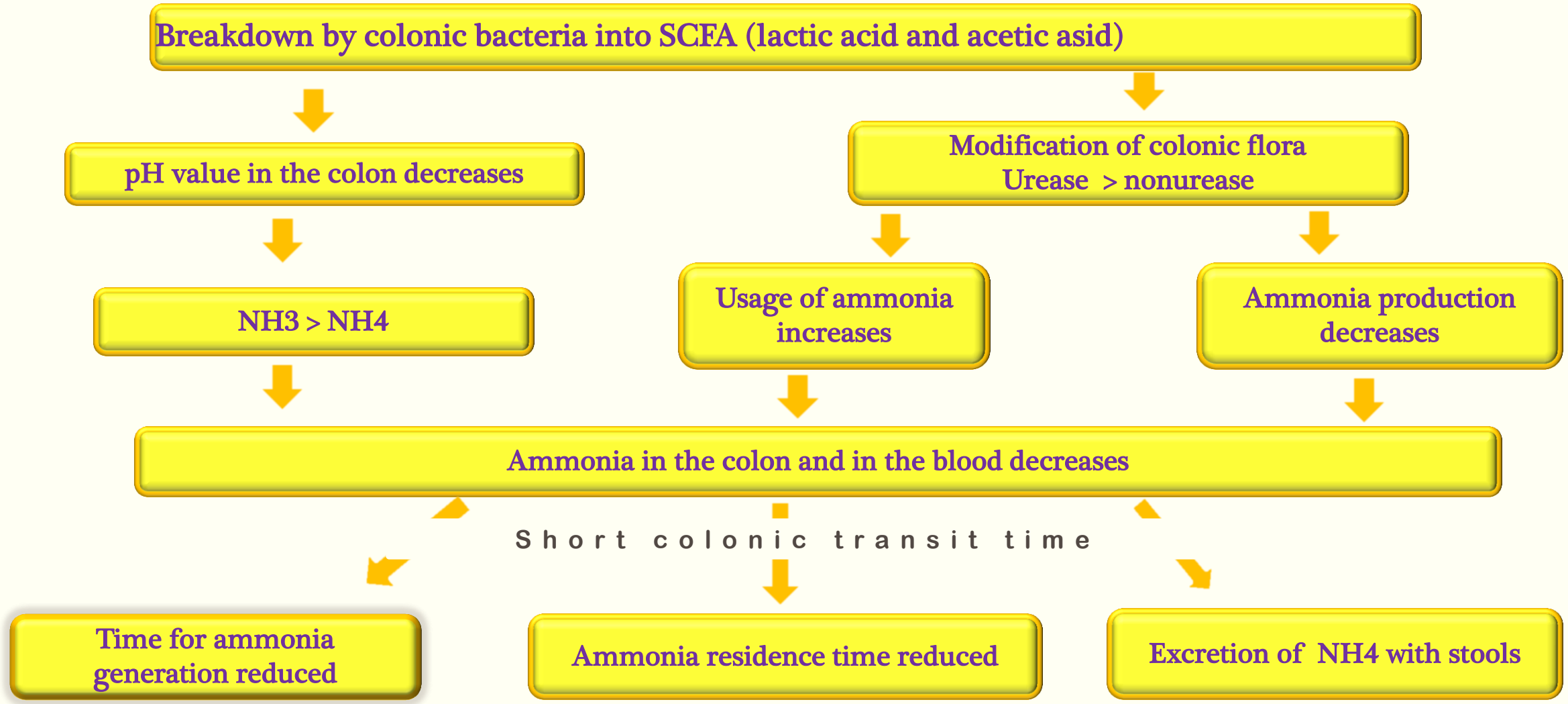
- Measures to lower blood ammonia concentration



Acute Treatment

- **Lactulose**
  - 30 to 45 mL (20 to 30 g) two or four times, 1 to 3 L of a 20 percent solution as enema
- **Lactilol**
  - 67-100 g powder diluated 100 mL of water
- Rifaximin
  - 3 x 400 mg orally or 2 x 550 mg
- Neomycin
  - 3 x 500 mg daily or 2 x 1 g
- Vancomycin
- Metronidazol

Acute Treatment



[Intervention Review]

Non-absorbable disaccharides versus placebo/no intervention and lactulose versus lactitol for the prevention and treatment of hepatic encephalopathy in people with cirrhosis

Lise Lotte Gluud[1], Hendrik Vilstrup[2], Marsha Y Morgan[3]

[1]Gastrounit, Medical Division, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark. [2]Department of Hepatology and Gastroenterology, Aarhus Kommunehospital, Aarhus C, Denmark. [3]UCL Institute for Liver & Digestive Health, Division of Medicine, Royal Free Campus, University College London, London, UK

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Editorial group: Cochrane Hepato-Biliary Group.
Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 4, 2016.
Review content assessed as up-to-date: 19 October 2015.

Citation: Gluud LL, Vilstrup H, Morgan MY. Non-absorbable disaccharides versus placebo/no intervention and lactulose versus lactitol for the prevention and treatment of hepatic encephalopathy in people with cirrhosis. *Cochrane Database of Systematic Reviews* 2016, Issue 4. Art. No.: CD003044. DOI: 10.1002/14651858.CD003044.pub3.

Main results

We included 38 RCTs with a total of 1828 participants. Eight RCTs had a low risk of bias in the assessment of mortality. All trials had a high risk of bias in the assessment of the remaining outcomes. Random-effects meta-analysis showed a beneficial effect of non-absorbable disaccharides versus placebo/no intervention on mortality when including all RCTs with extractable data (RR 0.59, 95% CI 0.40 to 0.87; 1487 participants; 24 RCTs; I^2 = 0%; *moderate quality evidence*) and in the eight RCTs with a low risk of bias (RR 0.63, 95% CI 0.41 to 0.97; 705 participants). The Trial Sequential Analysis with the relative risk reduction (RRR) reduced to 30% confirmed the findings when including all RCTs, but not when including only RCTs with a low risk of bias or when we reduced the RRR to 22%. Compared with placebo/no intervention, the non-absorbable disaccharides were associated with beneficial effects on hepatic encephalopathy (RR 0.58, 95% CI 0.50 to 0.69; 1415 participants; 22 RCTs; I^2 = 32%; *moderate quality evidence*). Additional analyses showed that non-absorbable disaccharides can help to reduce serious adverse events associated with the underlying liver disease including liver failure, hepatorenal syndrome, and variceal bleeding (RR 0.47, 95% CI 0.36 to 0.60; 1487 participants; 24 RCTs; I^2 = 0%; *moderate quality evidence*). We confirmed the results in Trial Sequential Analysis. Tests for subgroup differences showed no statistical differences between RCTs evaluating prevention, overt, or minimal hepatic encephalopathy. The evaluation of secondary outcomes showed a potential beneficial effect of the non-absorbable disaccharides on quality of life, but we were not able to include the data in an overall meta-analysis (*very low quality evidence*). Non-absorbable disaccharides were associated with non-serious (mainly gastrointestinal) adverse events (*very low quality evidence*). None of the RCTs comparing lactulose versus lactitol evaluated quality of life. The review found no differences between lactulose and lactitol for the remaining outcomes (*very low quality evidence*).

Rifaximin versus nonabsorbable disaccharides in the management of hepatic encephalopathy: a meta-analysis

Qian Jiang[a], Xue-Hua Jiang[a], Ming-Hua Zheng[c], Liu-Ming Jiang[d], Yong-Ping Chen[c] and Li Wang[b]

Objective To compare the positive and negative effects of rifaximin and nonabsorbable disaccharides in patients with hepatic encephalopathy.

Methods We used the method recommended by The Cochrane Collaboration to perform a meta-analysis of comparative randomized trials of rifaximin and nonabsorbable disaccharides.

Results Seven randomized controlled trials were identified, but only five trials involving 264 patients met all the inclusion criteria. There was no significant difference between rifaximin and nonabsorbable disaccharides on improvement in patients with hepatic encephalopathy [relative risk (RR) 1.08; 95% confidence interval (CI), 0.85–1.38; $P=0.53$]. RR was 0.98 (95% CI: 0.85–1.13; $P=0.74$) for acute hepatic encephalopathy in 157 patients and 0.87 (95% CI: 0.40–1.88; $P=0.72$) for chronic hepatic encephalopathy in 96 patients, respectively. There was no significant difference between rifaximin and nonabsorbable disaccharides on diarrhea (RR=0.90; 95% CI: 0.17–4.70; $P=0.90$). However, a significant difference in favor of rifaximin on abdominal pain (RR=0.28; 95% CI: 0.08–0.95; $P=0.04$) was identified.

Conclusion Rifaximin is not superior to nonabsorbable disaccharides for acute or chronic hepatic encephalopathy in the long-term or short-term treatment except that it may be better tolerated. Further studies on larger populations are required to provide more sufficient evidence for assessment of the use of rifaximin. *Eur J Gastroenterol Hepatol* 20:1064–1070

European Journal of Gastroenterology & Hepatology 2008, **20:**1064–1070

Keywords: hepatic encephalopathy, meta-analysis, nonabsorbable disaccharides, rifaximin

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- ✓ Polyetilene glycol
- ✓ Acarbose
- ✓ Sodium benzoate
- ✓ Flumazenil
- ✓ Zinc
- ✓ Melatonin

- Coagulopathy .. !!!

THANK YOU..