Hepatic Encephalopathy

Hepatic Encephalopathy

A complex neuropsychiatric syndrome:

- Disturbances in consciousness
- Alteration in personality
- With or without fluctuating neurologic signs, asterixis or flapping tremor
- Distinctive electroencephalographic changes

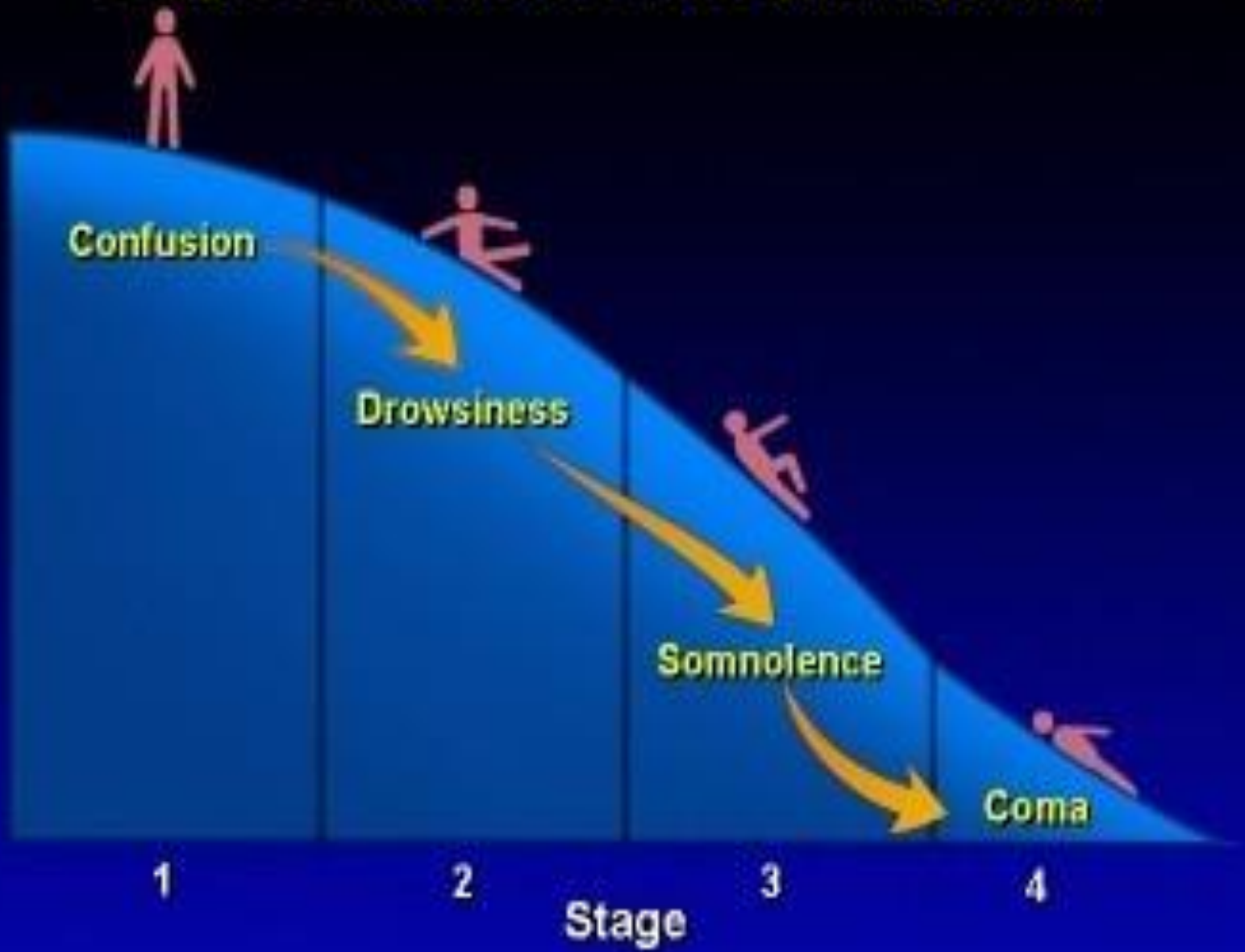
Hepatic Encephalopathy

- May be *acute and reversible* or *chronic and progressive*
- In severe cases, irreversible coma and death may occur
- Acute episodes may recur with variable frequency

Stages of Hepatic Encephalopathy

Stage	Mental state	Neurologic signs
1	Mild confusion: limited attention span, irritability, inverted sleep pattern	Incoordination, tremor, impaired handwriting
2	Drowsiness, personality changes, intermittent disorientation	Asterixis, ataxia, dysarthria
3	Somnolent, gross disorientation, marked confusion, slurred speech	Hyperreflexia, muscle rigidity, Babinski sign
4	Coma	No response to pain, decerebrate posture

Stages of Hepatic Encephalopathy



Hepatic Encephalopathy

World Congress of Gastroenterology, 1998

Table 1 Proposed classification of hepatic encephalopathy (HE)

Type A: HE associated with acute liver failure

Type B: HE associated with portosystemic bypass

Type C: HE associated with chronic liver disease/cirrhosis

- Episodic HE – single or recurrent
- Persistent HE – mild or severe
- Subclinical HE – alternatively minimal HE

Hepatic Encephalopathy

- Signs: **Mental Signs:**
  - Forgetfulness, mild confusion
  - Poor judgment
  - Being extra nervous or excited
  - Not knowing where they are or where they're going
  - Inappropriate behavior or severe personality changes

Hepatic Encephalopathy

- Signs: **Physical Signs:**
  - Breath with a musty or sweet odor
  - Change in sleep patterns
  - Worsening of handwriting or loss of other small hand movements
  - Shaking movements of hands or arms
  - Slurred speech

Epidemiology of HE

- Approximately **5.5** million people in the US have cirrhosis, a major cause of complications and death
- In those with Cirrhosis, the risk of developing hepatic encephalopathy is **20%** per year and at any time about **30 - 45%** of people with cirrhosis exhibit evidence of overt encephalopathy

Hepatic Encephalopathy Precipitants

Excess protein

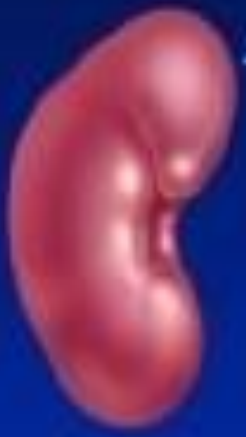
GI bleeding

Sedatives / hypnotics

TIPS

Temp

Infections



Diuretics

Serum K⁺

Plasma volume

Azotemia

Precipitating Factors

- Miscellaneous:
  - Constipation
  - Surgery
  - Hypothyroidism
  - Progressive liver disease

Pathogenesis

- In healthy subjects, nitrogen containing compounds from the intestine, generated by gut bacteria from food are transported by the portal vein to the liver, where 80–90% are metabolized & excreted immediately
- This process is impaired in HE because the hepatocytes are incapable of metabolizing the waste products

Pathogenesis

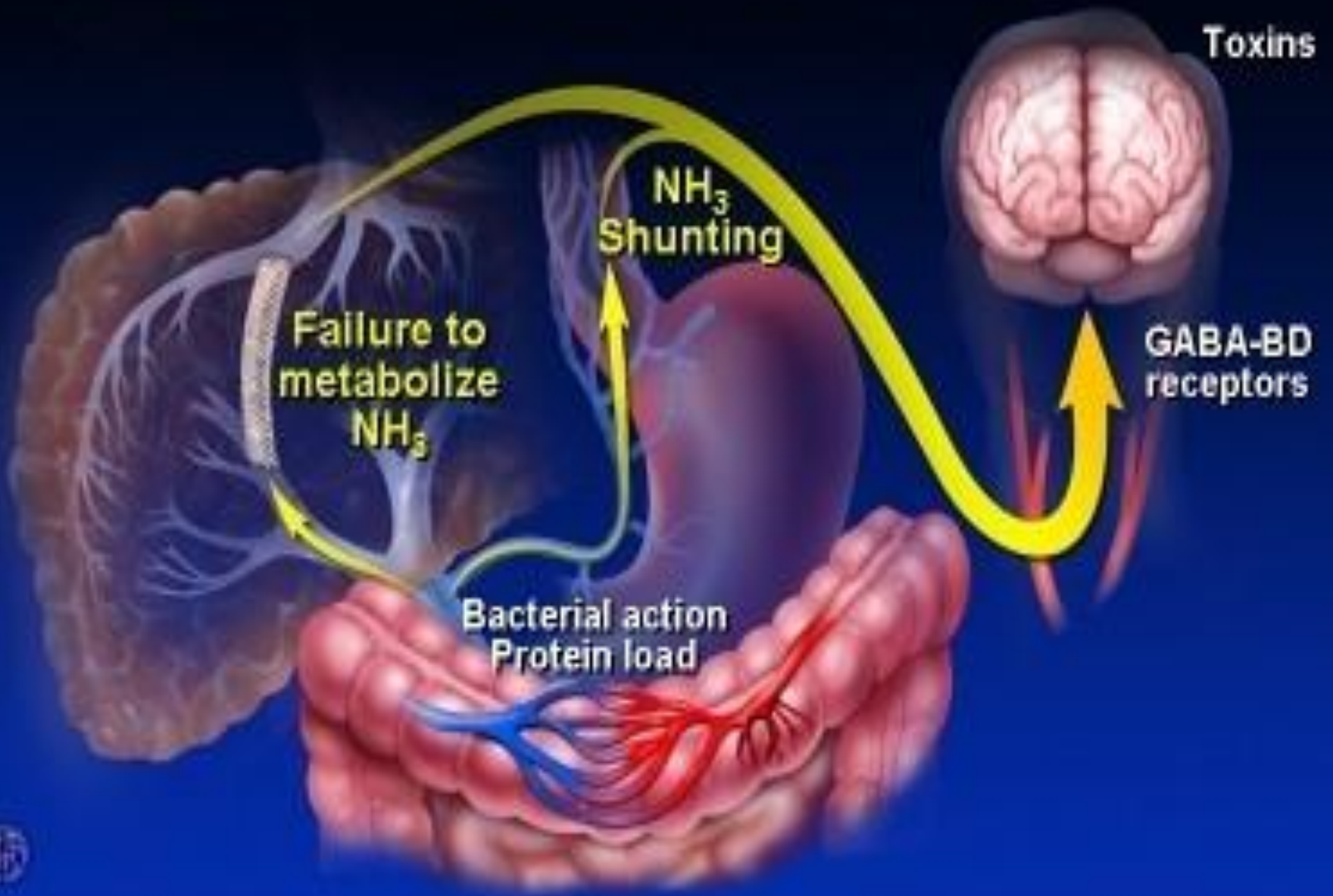
- Other waste products include mercaptans, short-chain fatty acids and phenol
- BDZ like compounds have been detected at increased levels as well as abnormalities in the GABA neurotransmission system
- Dysregulation of the serotonin system
- Depletion of zinc and accumulation of manganese may play a role

Pathogenesis

Ammonia plays a central role

- **Small intestine:** **The degradation of glutamine produce ammonia**
- **Large intestine:** **Breakdown of urea and proteins by normal flora**
- **Muscle:** **Proportion to muscle work**
- **Kidney:** **Ammonia production increases when hypokalemia develops and diuretic therapy is in use**

Hepatic Encephalopathy Pathogenesis



Pathogenesis

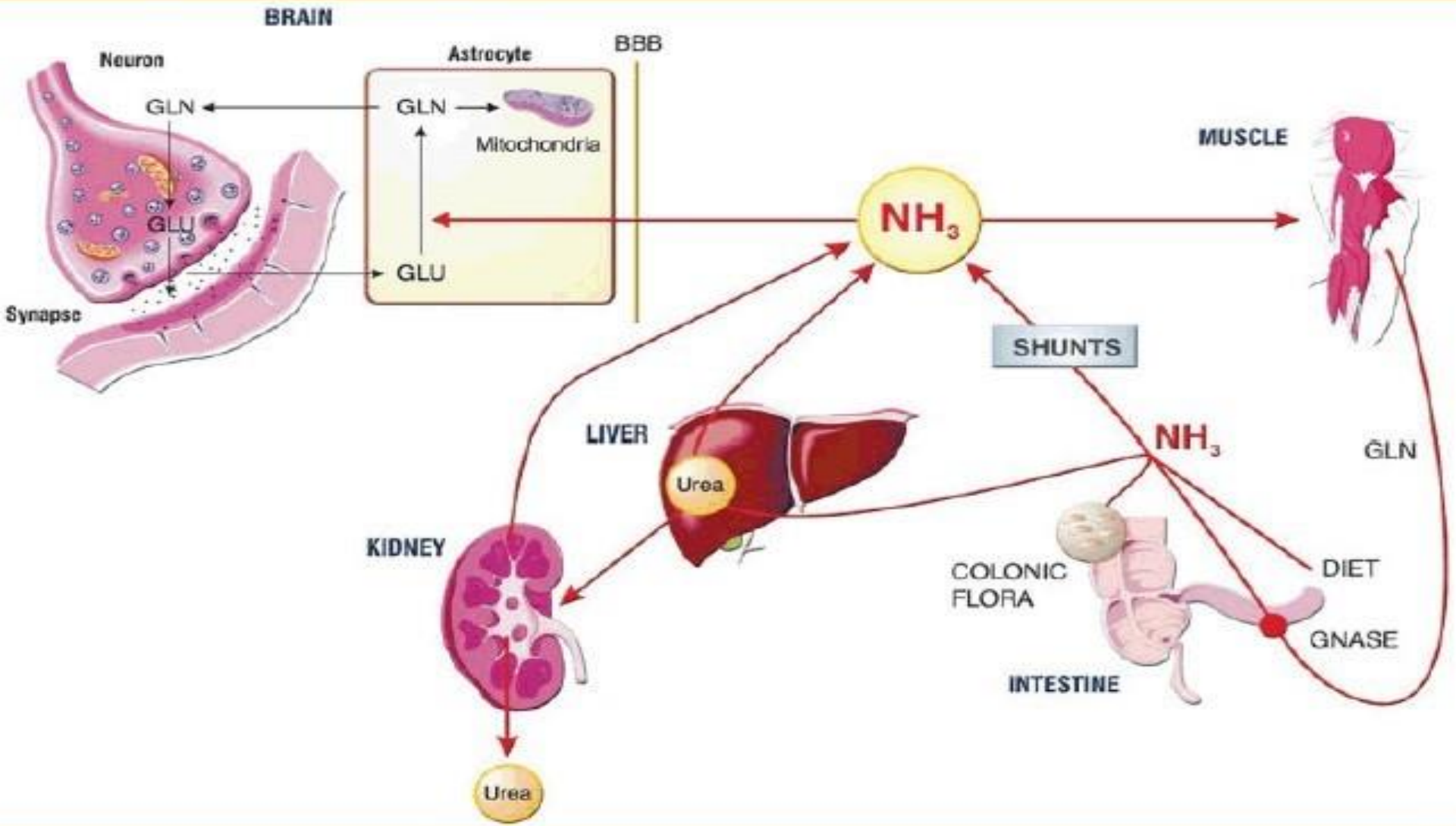
- In case of CLD Ammonia accumulate in the systemic circulation
- Ammonia can cross BBB and metabolized by astrocytes (30% of the brain cell)

Ammonia

Glutamate → **Glutamine**

- Glutamine increases osmotic pressure in astrocytes which become swollen

Pathogenesis



Aims of treatment

- Identification & removal of the underlying precipitating factors
- Reduction of nitrogenous load from gut
- Assessment of the need for long term therapy

Treatment Options

- Nutritional management: Pt. should avoid prolong period of protein restriction
- Bowel cleansing: Mainstay of treatment
- Antibiotics: Therapeutic alternative to laxatives
- Flumazinil: For those who used to take BDZ
- Bromocriptine: May improve extra pyramidal signs

Non-absorbable Disaccharides

- Lactulose and Lactitol
  - Dosage:30g to 60g daily, based on clinical sign and 2 to 4 stools daily
  - Degrade into short-chain organic acids in colon
  - Cannot be hydrolyzed or absorbed in small intestine

Adverse Effects of Disaccharides

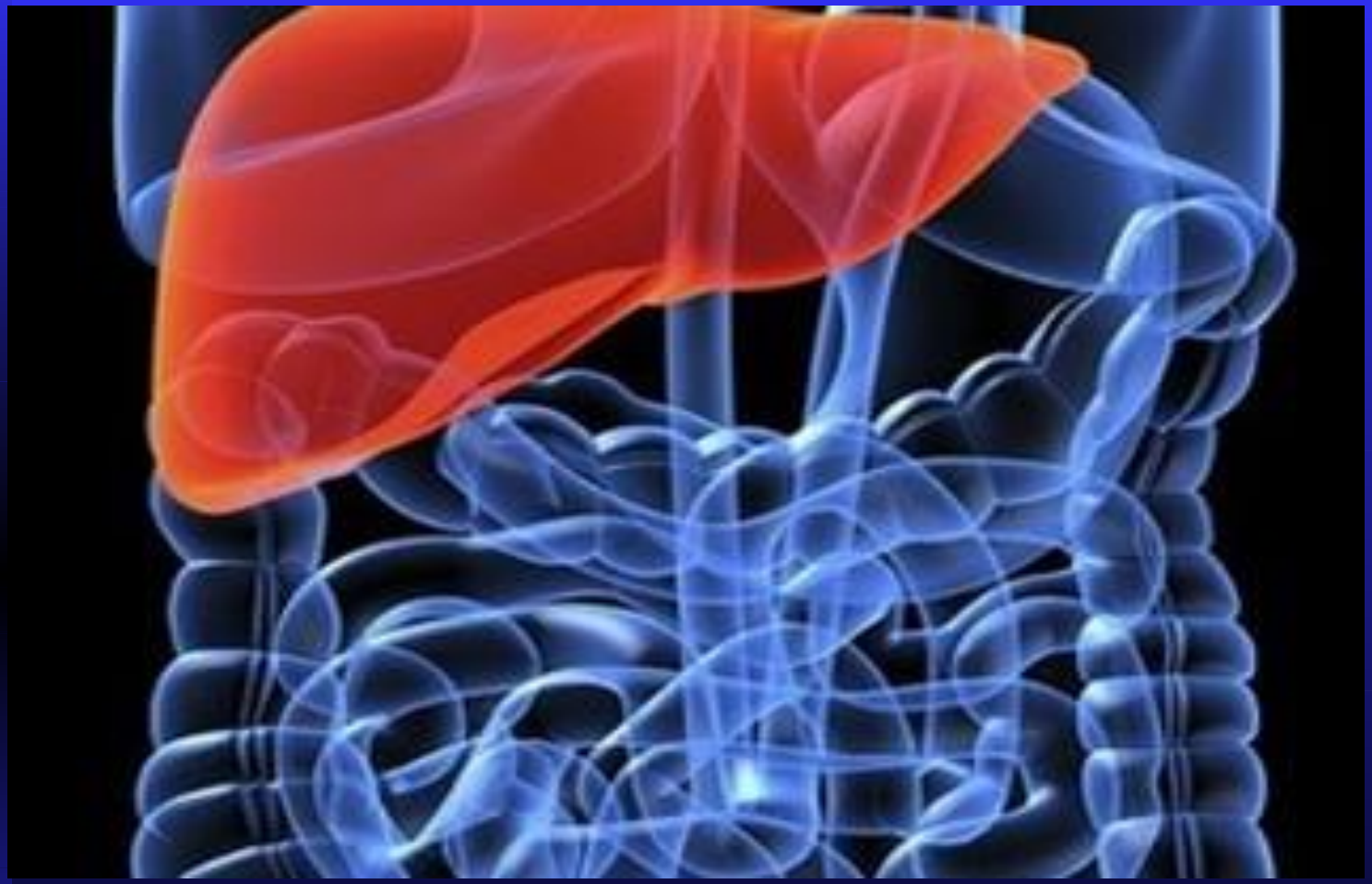
- Flatulence
- Diarrhoea
- Profuse diarrhoea may lead to hypovolemia and electrolyte imbalance --> Aggravate HE

Antibiotics

- **Metronidazole** may be effective in acute situation but its prolong use causes peripheral neuropathy
- **Neomycin** should be avoided due to its severe adverse reactions i.e. ototoxicity, nephrotoxicity
- **Rifaximin** is mainly unabsorbed & well tolerated for long term

References

1. *http://en.wikipedia.org/wiki/Hepatic_encephalopathy*
2. *http://emedicine.medscape.com/Hepatic encephalopathy*
3. *www.liverfoundation.org/aboutheliver/info/hepaticencephalopathy*
4. *N England J Med 2010;362:1071-81*
5. *Aliment. Pharmacol. Thesis. 31 (5): 537–47*
6. *www.xifaxan550.com*



THAT`S ALL !

THANKS ☺