Complications of Cirrhosis

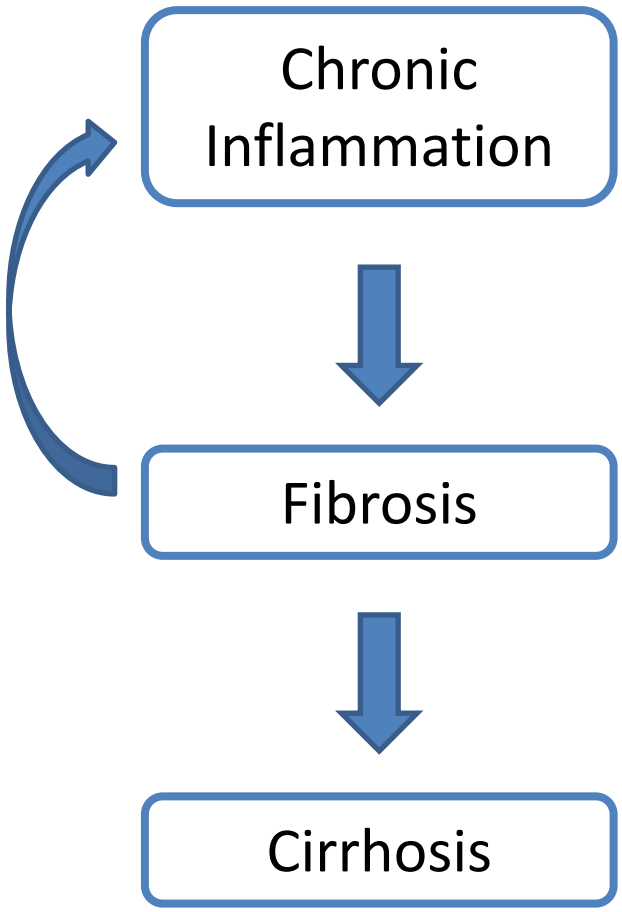
Causes of Cirrhosis

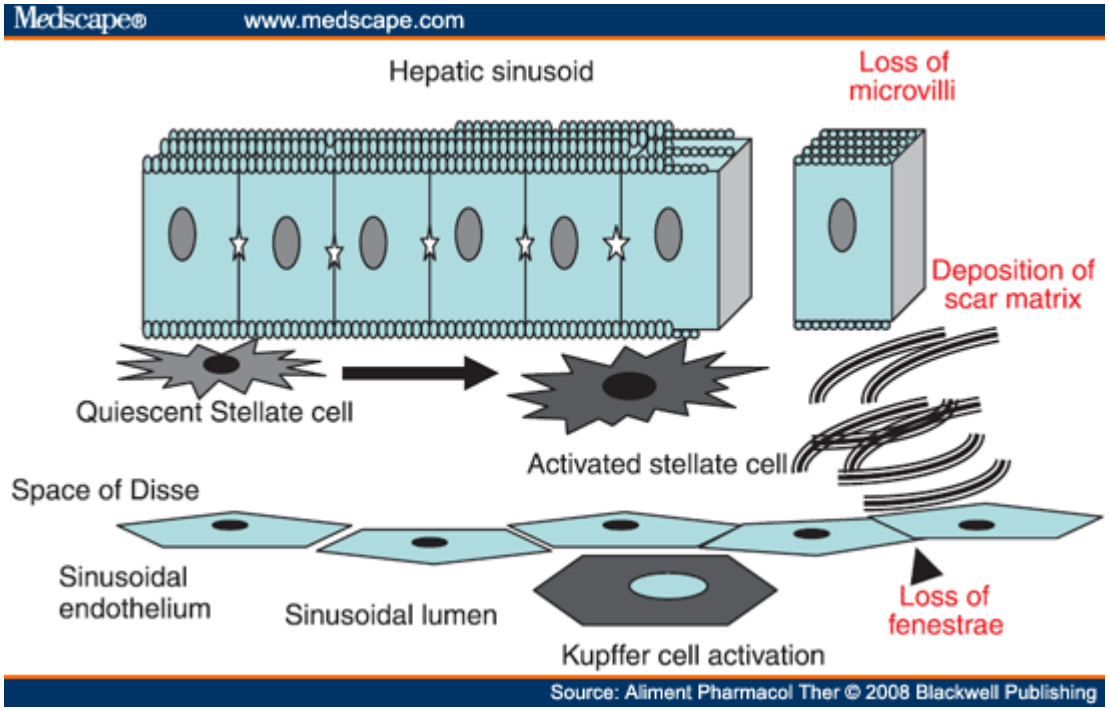
- Alcohol

- Chronic Viral Hepatitis (B/C)
- Haemochromatosis
- Autoimmune Hepatitis
- NAFLD/NASH
- Primary Biliary Cirrhosis
- Primary Sclerosing Cholangitis

- α1-AT deficiency
- Drugs

Pathophysiology of Cirrhosis





Cirrhosis is a histological diagnosis :
"advanced diffuse hepatic fibrosis with nodular regeneration"

Diagnosis of Cirrhosis

Difficulty is distinguishing between chronic non-cirrhotic liver disease and compensated cirrhosis.

- History
  - Risk factors
  - Family history
- Examination
  - Signs of chronic liver disease
  - Evidence of portal hypertension

Diagnosis of Cirrhosis

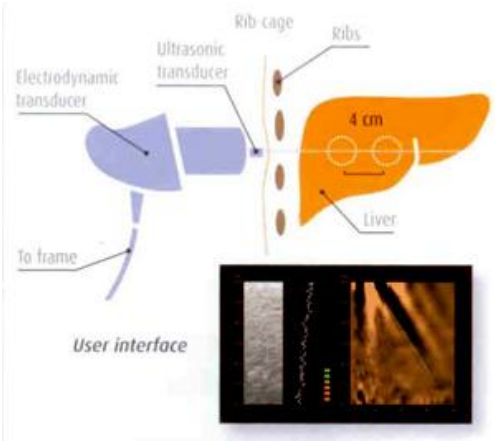
- Blood tests
  - LFTs may be normal
  - ↑Bilirubin, ↑PT, ↓Alb suggest synthetic dysfunction
  - 'Liver screen' to indentify cause

- Imaging
  - US/CT may suggest cirrhosis (nodular liver, enlarged caudate lobe, coarse texture)
  - ~25% of cases missed on US

Diagnosis of Cirrhosis

- Liver Biopsy
  - Gold standard
  - Not without risk
  - Will it change management?

- Fibroscan



- Serological markers of fibrosis
  - Hyaluronic Acid
  - Procollagen III NP
  - TIMP-1
  - King's Score

Compensated & Decompensated Cirrhosis

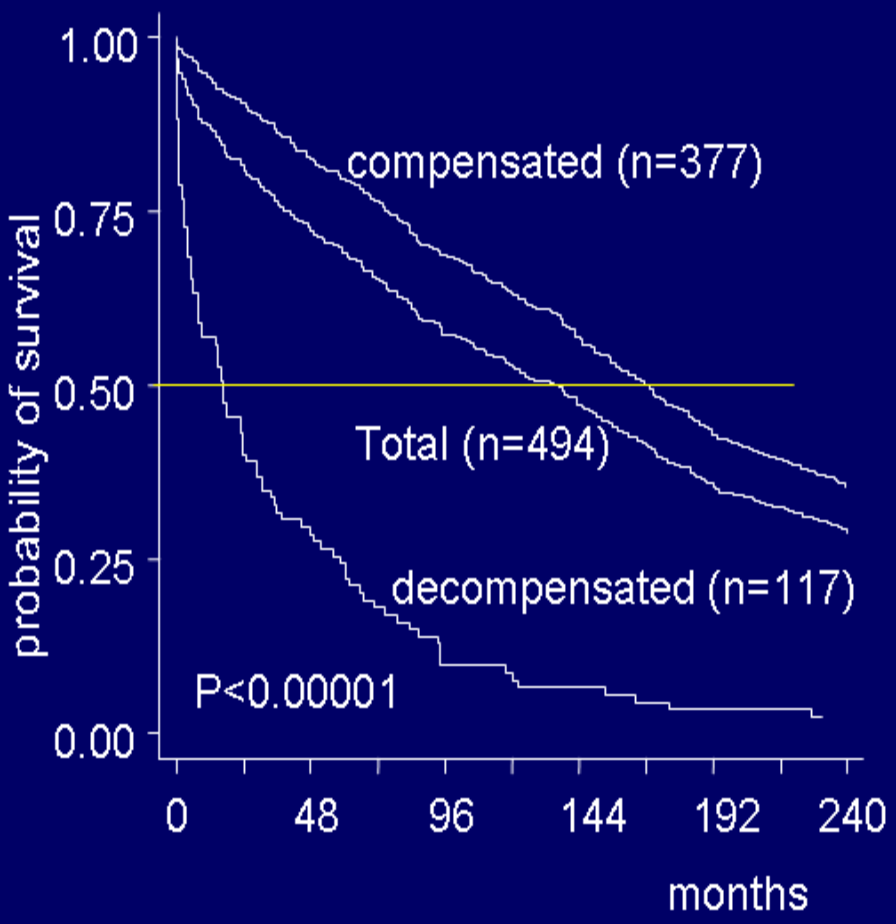
Compensated

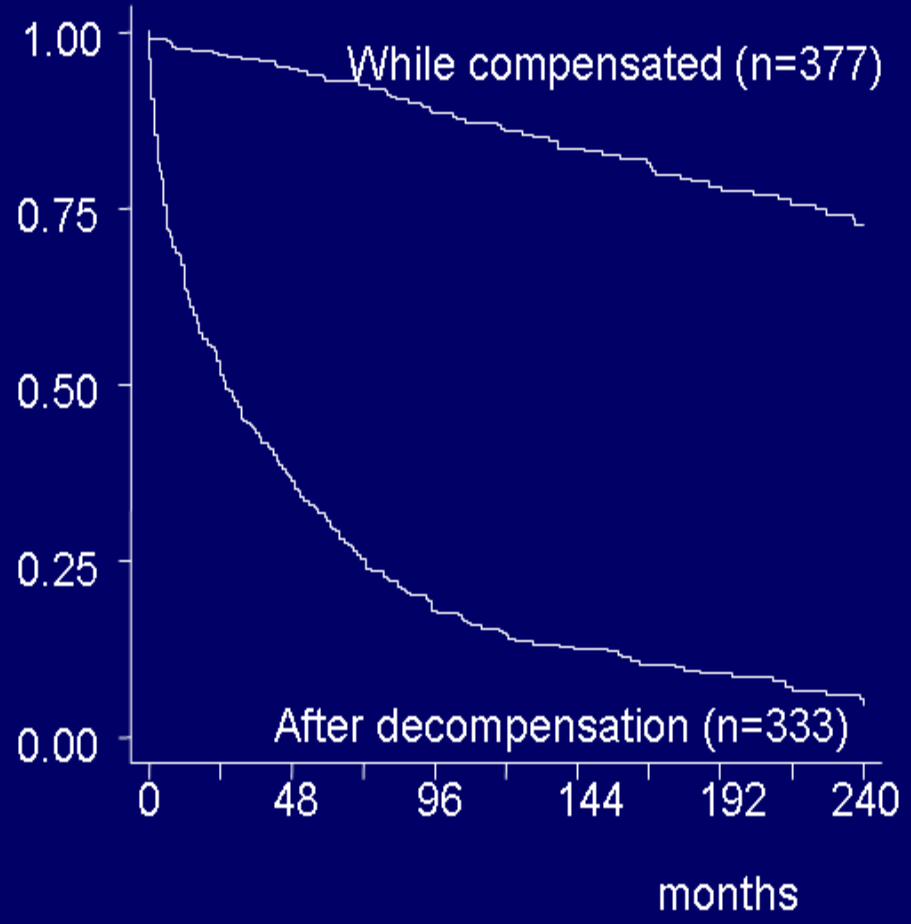
- Good synthetic function
- No ascites
- No encephalopathy
- No jaundice
- +/- varices

Decompensated

- Characterised by development of one or more of….
  - Ascites
  - Encephalopathy
  - Variceal Haemorrhage

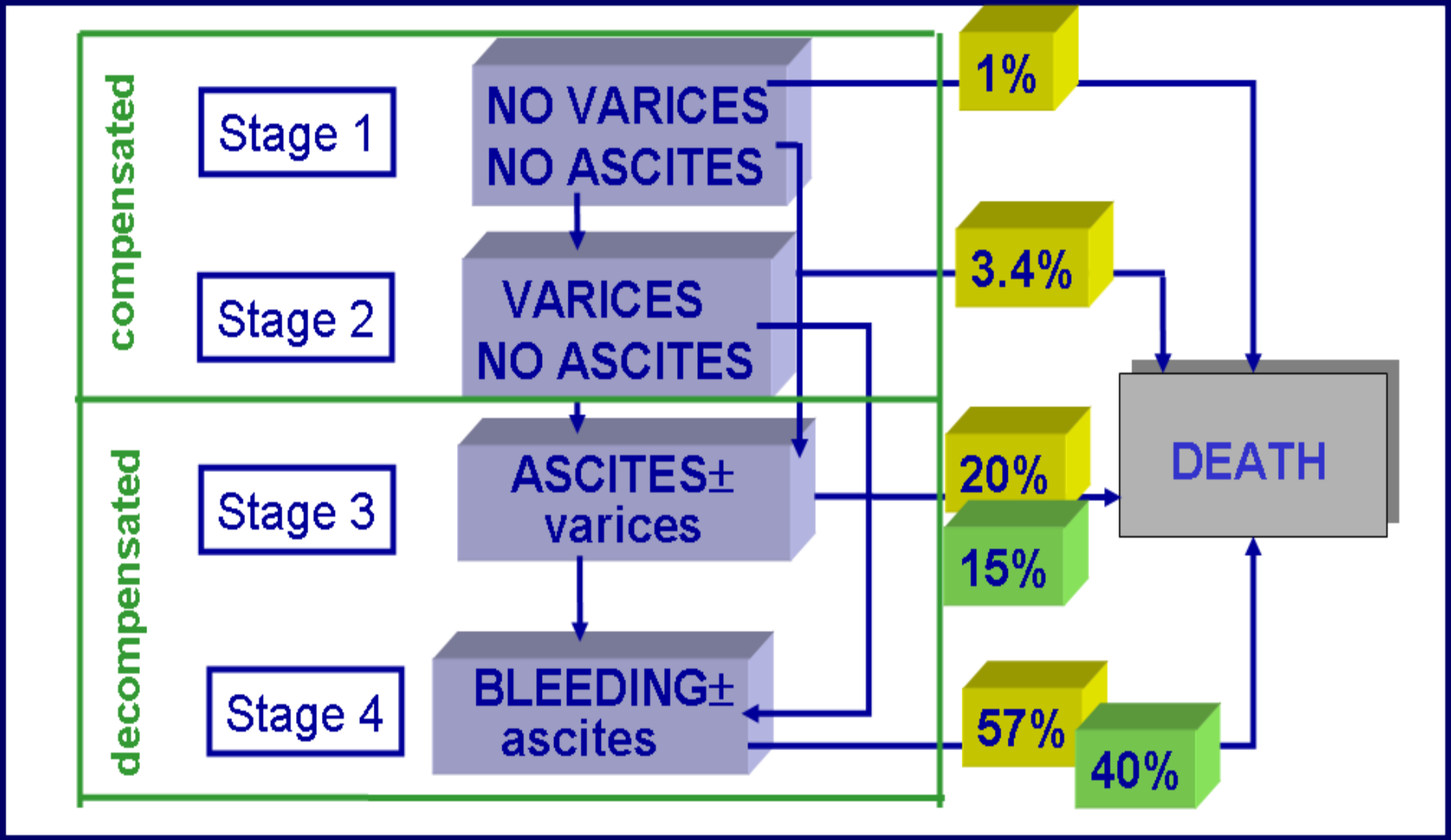
Survival of cirrhosis according to stages
25-years inception cohort study of 494 patients





D'Amico G. Gastroenterology 2001; 120: A2

Clinical stages of cirrhosis
One year outcome probability from cohort studies



D'Amico G, Dig Dis Sci 1986; 31: 468-75
D'Amico G. Gastroenterology 2001; 120: A2.

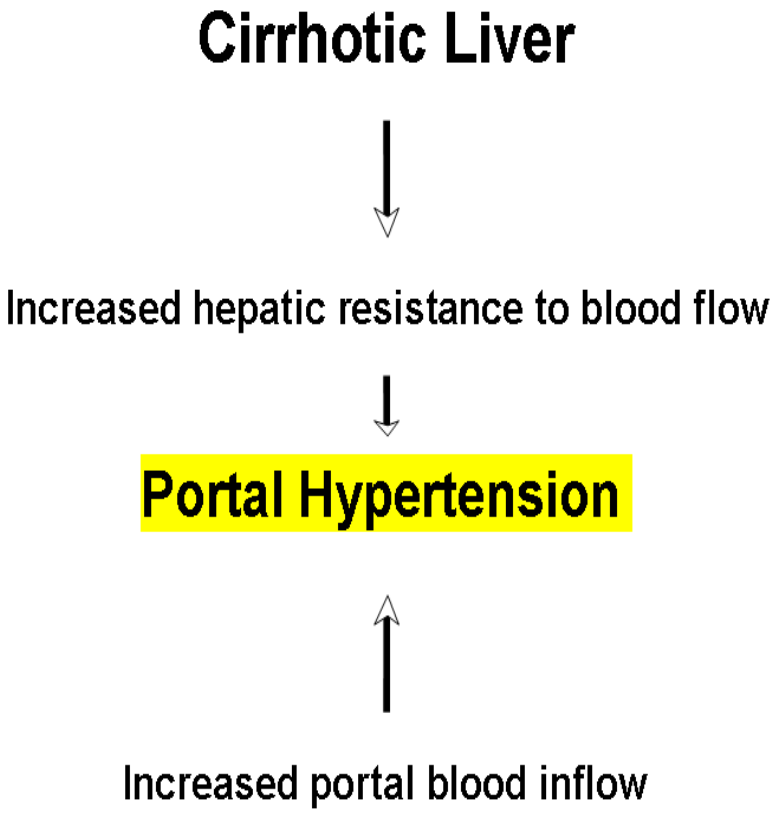
Planas R. Clin Gastro Hepa 2006;4:1385-94
Stokkeland K. Hepatology 2006;43:500-505
El-Serag Am J Gastro 2000;95:3566 –73

Complications of Cirrhosis

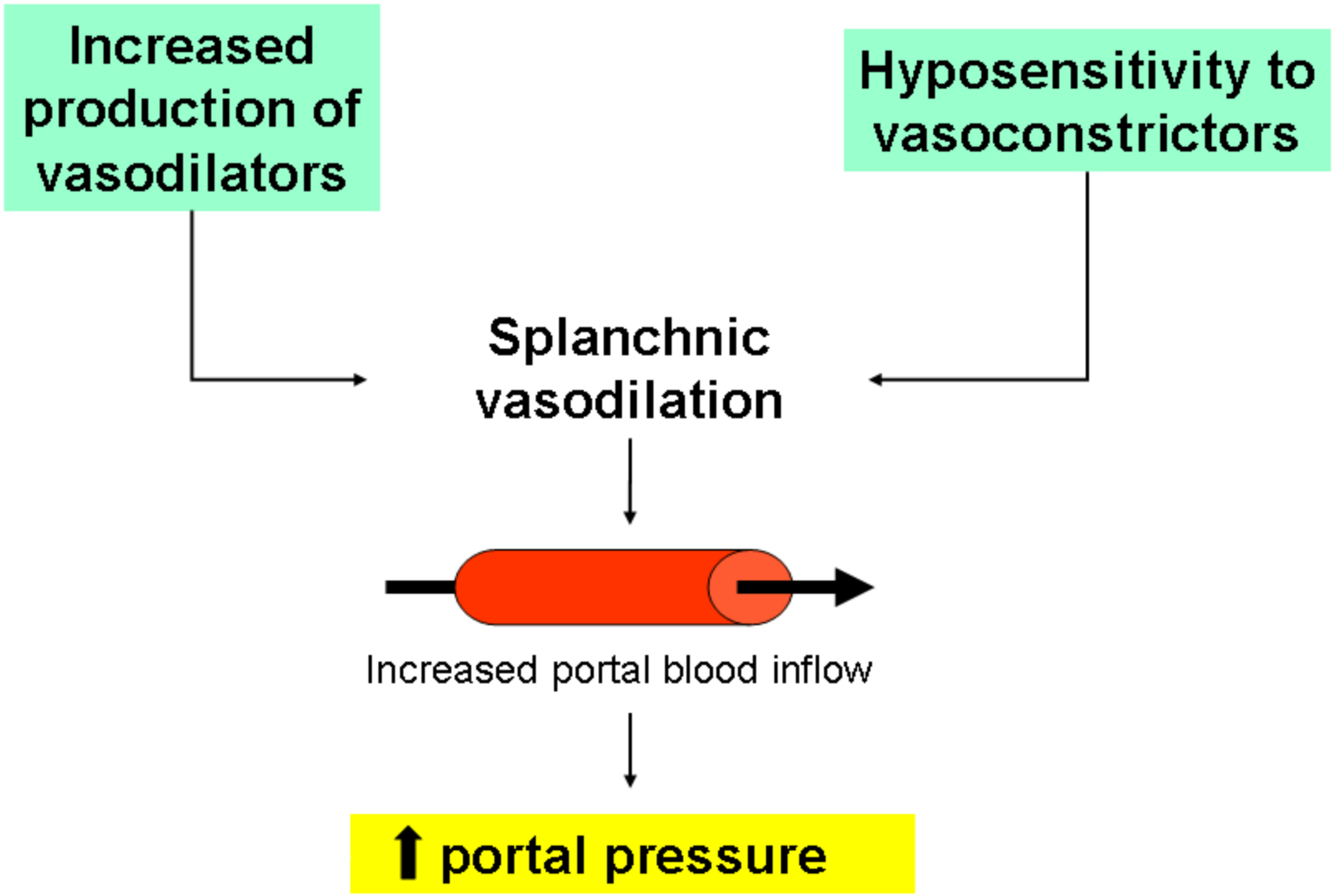
- Variceal Haemorrhage
- Hepatic Encephalopathy
- Ascites
- Spontaneous Bacterial Peritionitis
- Hepato-Renal Syndrome

- Management of patients with cirrhosis

Variceal Haemorrhage



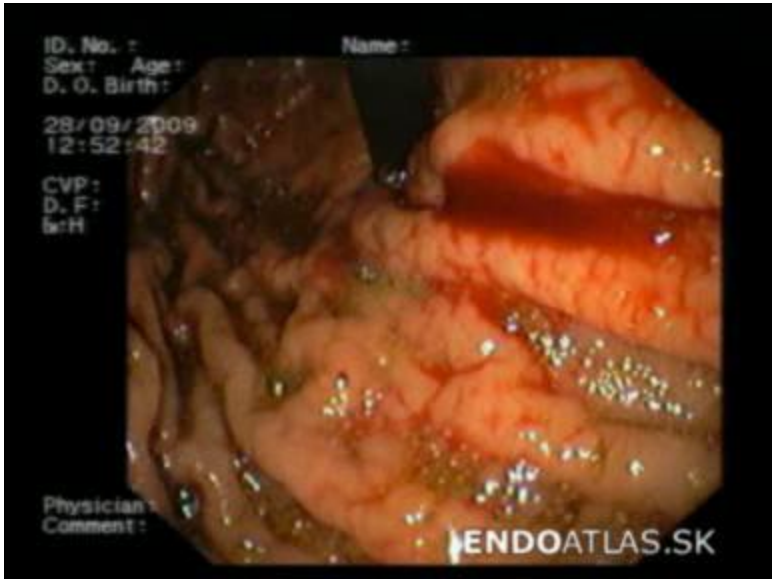
Mechanisms of splanchnic arteriolar vasodilation in cirrhosis



Variceal Haemorrhage - treatment

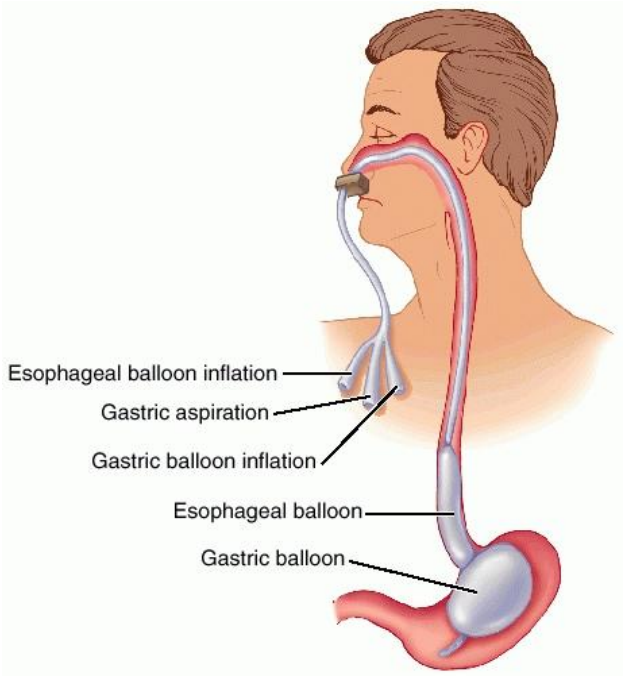
- Control of bleeding
  - Drugs
    - Terlipressin/Somatostatin/Octreotide
  - Endoscopic therapy
    - Endoscopic band-ligation
- Antibiotics
  - Bleeding precipiated by infection in 40-50%
  - High risk of bacteraemia/sepsis following bleed
- Haematological support
  - Blood, FFP

Variceal banding

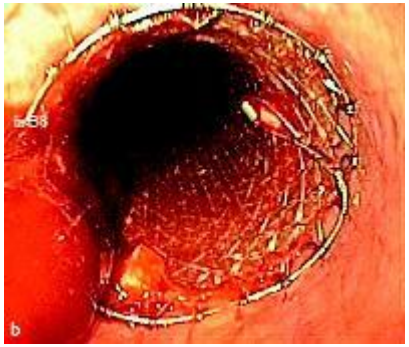


Variceal Haemorrhage

- If EBL fails…
  - Sengstaken Blakemore tube
    - Not definitive
    - 24h maximum

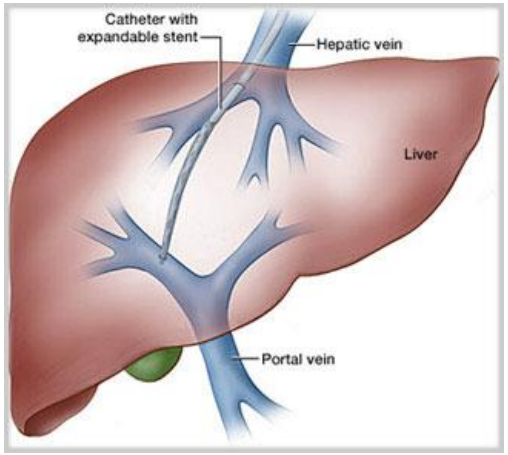


  - Danis Stent



Variceal Haemorrhage

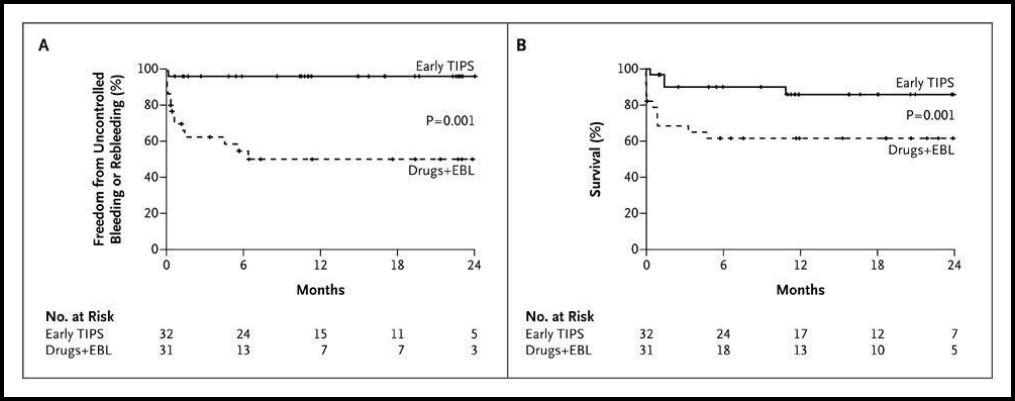
- TIPS (Transjugular Intrahepatic Portosystemic Shunt)



  - Previously rescue treatment after failure of endoscopic therapy

Early use of TIPS

Actuarial Probability of the Primary Composite End Point and of Survival, According to Treatment Group



Garcia-Pagan J et al. N Engl J Med 2010;362:2370-2379

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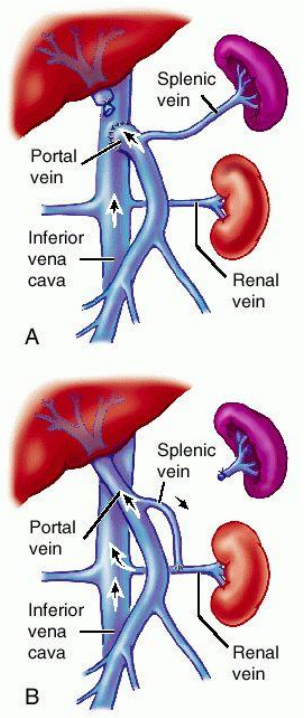
Variceal Haemorrhage - prevention

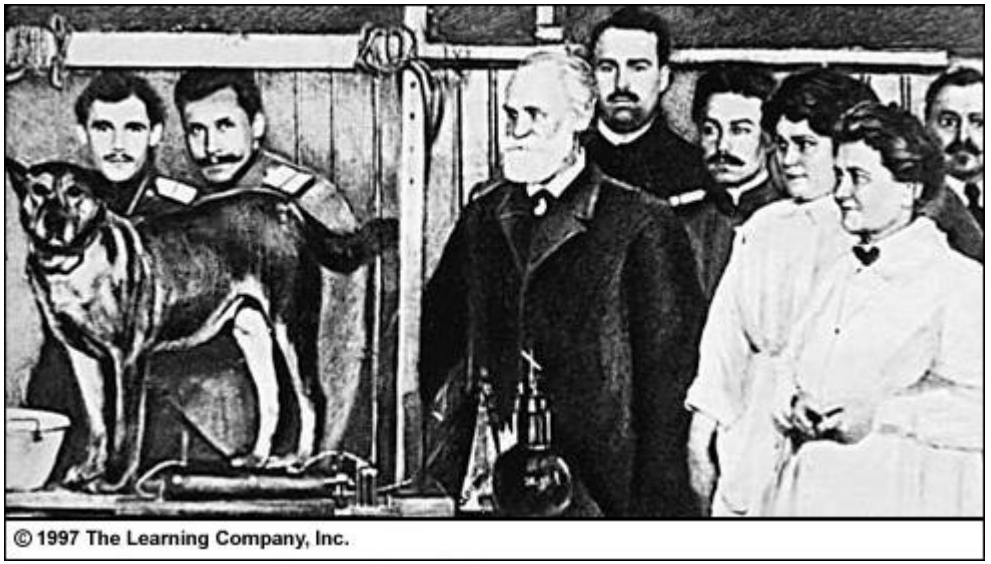
- Non-selective β-blockers (Propanolol)
- Serial banding programme

Hepatic Encephalopathy

Hepatic Encephalopathy

- First described by Pavlov in dogs with surgical porto-caval shunt
  - ‘Meat Intoxication’
  - Recognised link to raised Ammonia



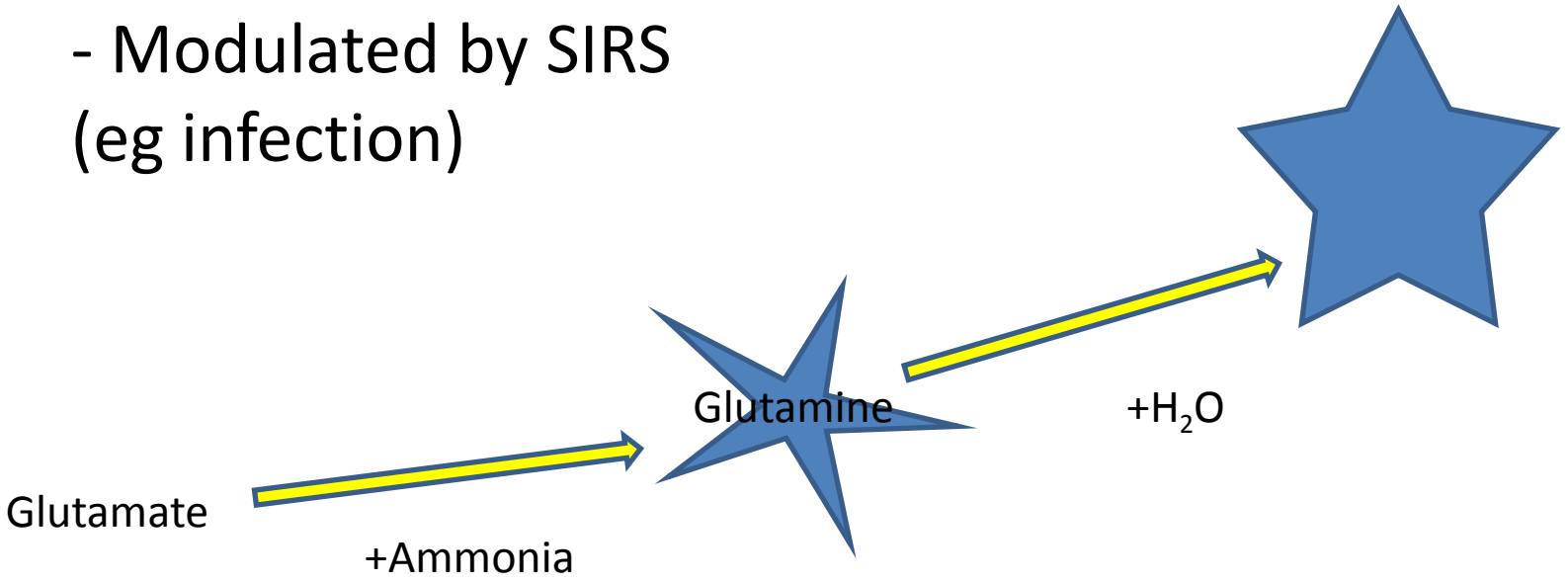


Hepatic Encephalopathy

- Neuropsychiatric disturbances in patients with significant liver dysfuntion
- Clinical diagnosis characterised by
  - Flapping tremor (Asterixis)
  - Fetor hepatis
- West Haven Grading
  1. Impaired higher functions, normal conciousness
  2. Disorentation, personality change
  3. Confusion, gross disorientation, increased somnolence
  4. Coma

Encephalopathy - pathophysiology

- Astrocyte Swelling
  - Modulated by SIRS (eg infection)



- Clinical correlation with ammonia levels is poor

Encephalopathy - precipitants

- Additional liver insult (alcohol, viral infection)

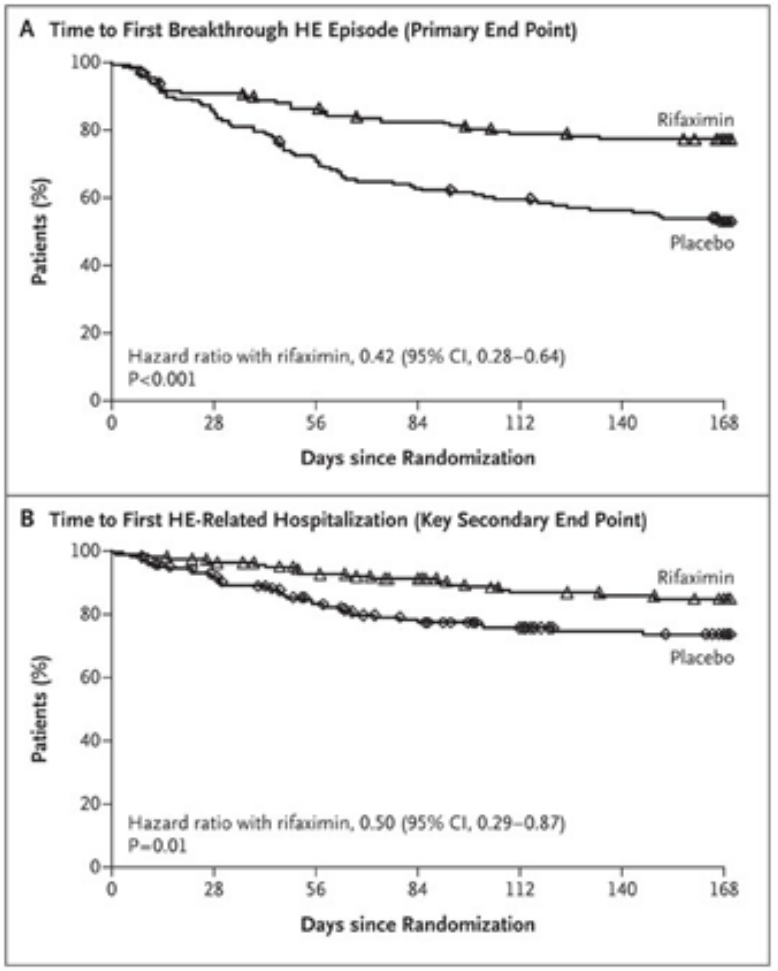
- Infection
- GI Bleeding
- Dehydration
- Constipation
- Drugs (eg opiates)
- Large protein meal

Encephalopathy - treatment

- Treat underlying cause (bleeding, infection)
- Stop offending drugs
- Hydration
- Lactulose
  - Alters colonic pH and increases transit
  - Large doses eg 30ml tds
  - Aim for 3 soft stools per day

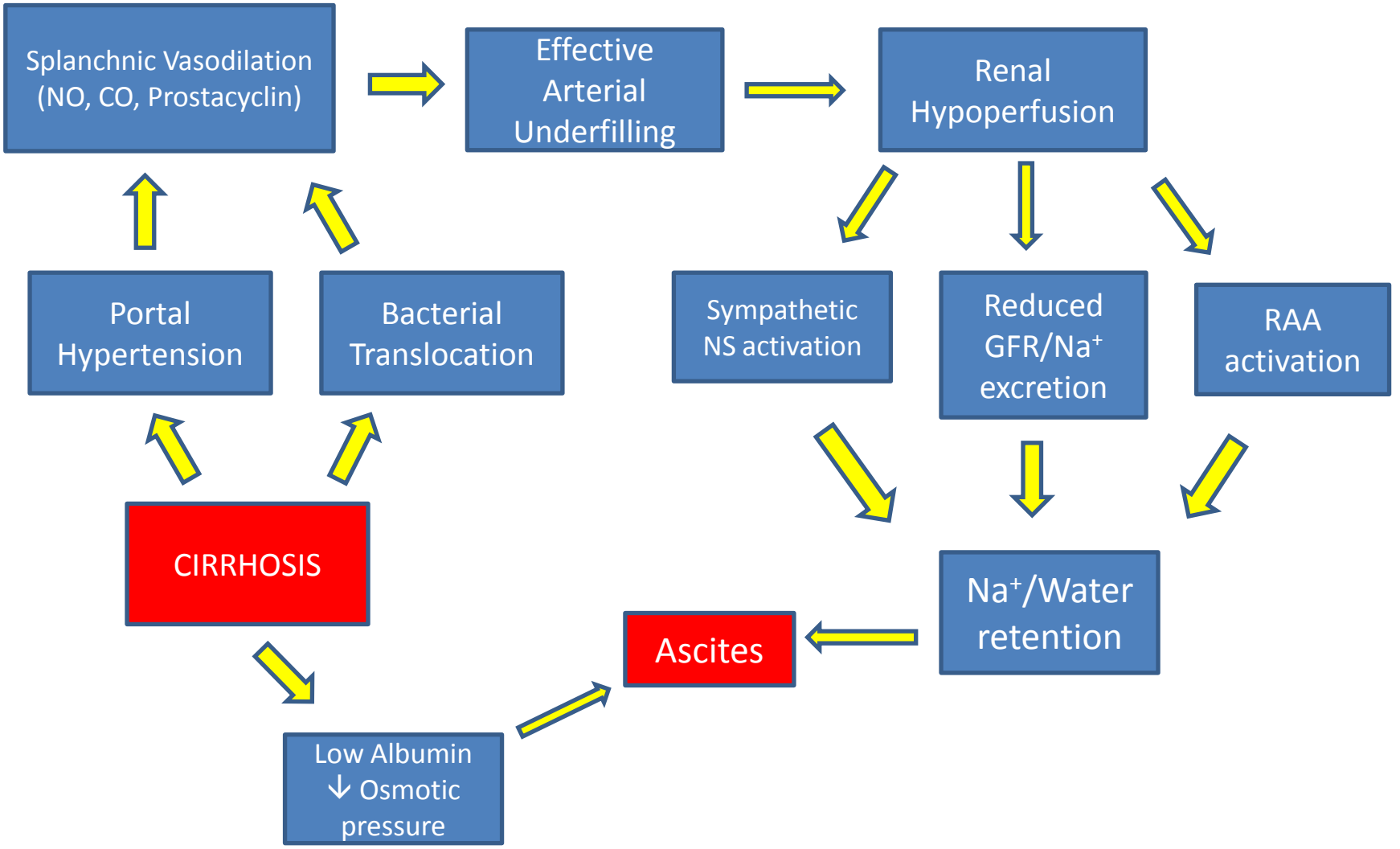
Encephalopathy - treatment

- Rifaximin
  - Non-absorbable antibiotic



Ascites

Ascites in cirrhosis - pathogenesis



Ascites - investigations

- Diagnostic Tap
  - Albumin
    - SAAG (Serum Alb g/L – Ascitic Alb g/L)
      - < 11 g/L = Malignancy, Pancreatitis, TB
      - ≥ 11 g/L = Cirrhosis, Heart failure, Low protein states
    - White Cell count
      - Should be performed within 24h of admission
      - >250 neut/mm^3 or >500 total wcc/mm^3 diagnostic of SBP
    - Culture in BC bottles

Management of ascites in cirrhosis

- Bed rest NOT recommended

- Dietary Salt restriction – no-added salt diet (5.2g/day)
- Water restriction – controversial

- Diuretics
  - Spironolactone 100-400mg/day
  - Frusemide 40-160mg/day
  - Aim to reduce weight by 0.5kg/day if no oedema (daily weights)

Large Volume Paracentesis

- Safe & Effective
- More effective, fewer complications and shorter hospital stay vs Diuretics

- Use for
  - Large volume ascites
  - Refractory ascites (not responding to max diuretic Rx)

Spontaneous Bacteria Peritonitis (SBP)

Spontaneous Bacterial Peritonitis

- 15% of cirrhotic patients with ascites admitted to hospital have SBP
- Mortality ~20%
- Frequently asymptomatic
- Presentations
  - Abdo pain, Fever, Encephalopthy, ARF, Sepsis

- **All patients with cirrhosis and ascites should have a diagnostic tap performed on admission.**

Gram-negative bacilli that cause SBP ‘translocate’ from the intestinal lumen

Mechanisms of Intestinal Bacterial Translocation Are Poorly Understood

Alterations	Proposed Mechanisms
Intestinal bacterial overgrowth	Dysmotility, delayed transit time, nutrition?
Intestinal permeability	Mucosal hypoxia, acidosis, ATP depletion, NO, LPS, TNF
Impaired Immunity	Impaired chemotaxis, migration, phagocytic function, complement deficiency.

Spontaneous Bacterial Peritonitis 2

- Mainly *E Coli, Streps, Enterococci*
- Broad spectrum antibiotics
  - Previously Cefotaxime (high *C Diff* risk)
  - Augmentin or Ciprofloxacin

- Albumin in SBP
  - Jury still out
  - Certainly give if any renal dysfunction
    - 1.5g/kg day 1
    - 1g/kg day 3

- Don’t forget antibiotic prophylaxis (Norfloxacin 400mg od)
  - Reduced recurrence from from 68% to 20%

Hepato-renal Syndrome (HRS)

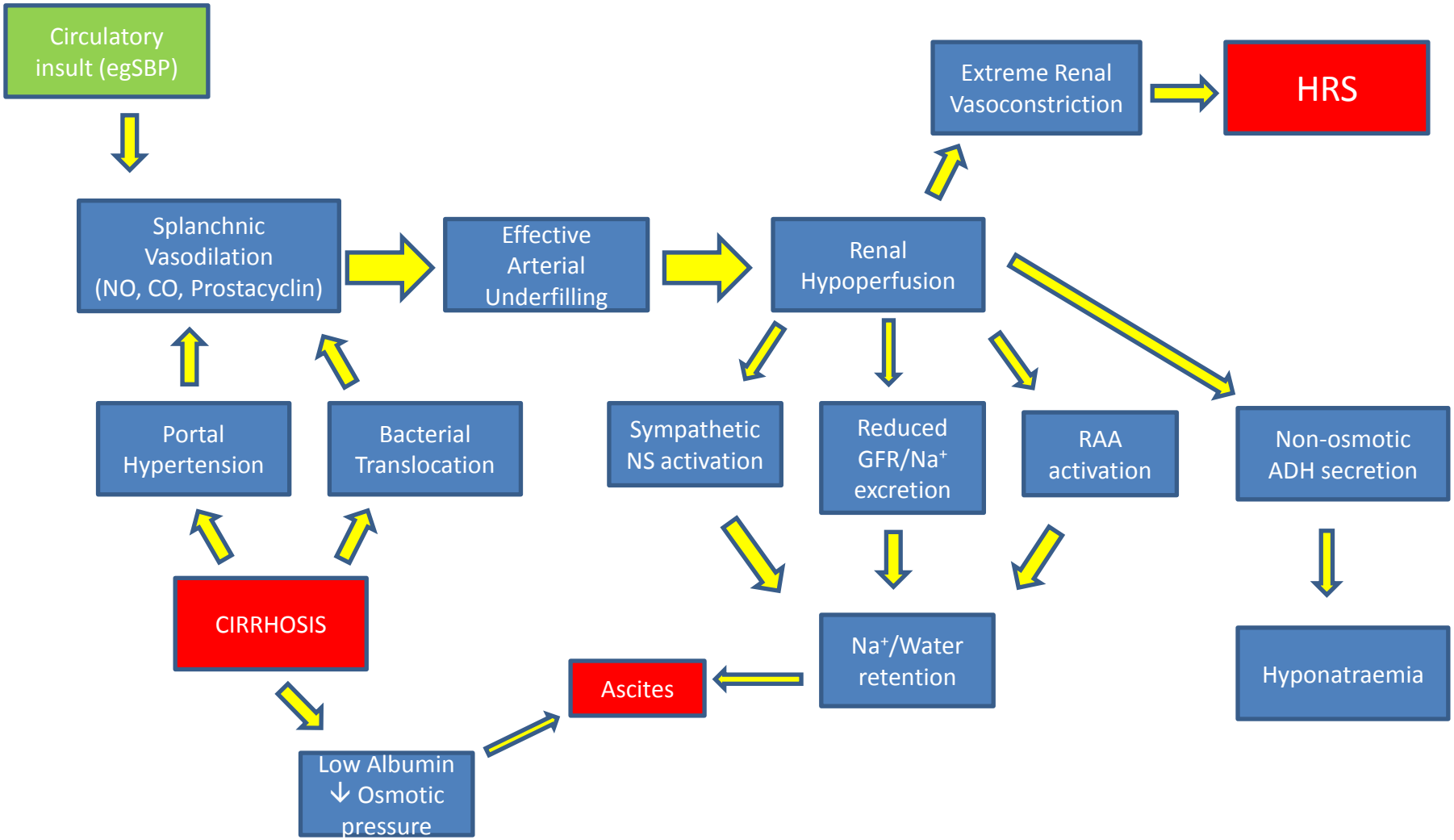
HRS - Definition

- "*occurrence of renal failure in a patient with advanced liver disease in the absence of an identifiable cause of renal failure*"
- Essentially a diagnosis of exclusion
- Very high mortality > 50% at 1 month

HRS - Definition

- International Ascites Club criteria
  - Cirrhosis with ascites
  - Absence of shock
  - Cr >133
  - Absence of hypovolaemia
    - No diuretics for 2/7
    - Volume expansion with Albumin 1g/kg
  - No recent nephrotoxic drugs
  - Absence of parenchymal renal disease
    - <0.5g day proteinuria
    - No microhaematuria
    - Normal Renal USS

HRS - pathogenesis



HRS - Treatment

- Terlipressin/Octreotide
  - Splanchnic vasoconstriction
  - Divert blood to systemic circulation
- IV Albumin
  - Improve renal perfusion

Management of Cirrhotic patients

- Majority of cases managed the same as any unwell general medical patient
- Dehydration/Hypovolaemia
  - Volume expansion (Csytalloid/Colloid)
  - Albumin only in certain situations (Drainage, HRS, ?SBP)
- Seek and treat sepsis
  - Low threshold for antibiotics
  - Don’t forget SBP
- Nutrition/Vitamins