

Decompensated Cirrhosis for Hospitalist and Internists

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Learning Objectives

- *Identify and manage the main complications of cirrhosis.*
- *Review indications for TIPS and appropriate timing for transplantation request.*
- *Formulate a long-term management plan decompensated cirrhosis including HCC surveillance and esophageal variceal screening*

Our Case

57 y.o. woman presents to the ED with hematemesis

She has been sick for two days with vague RUQ pain and low-grade fever (38.4°C)

BP 80/40, HR 110, Sat' s 92% on RA

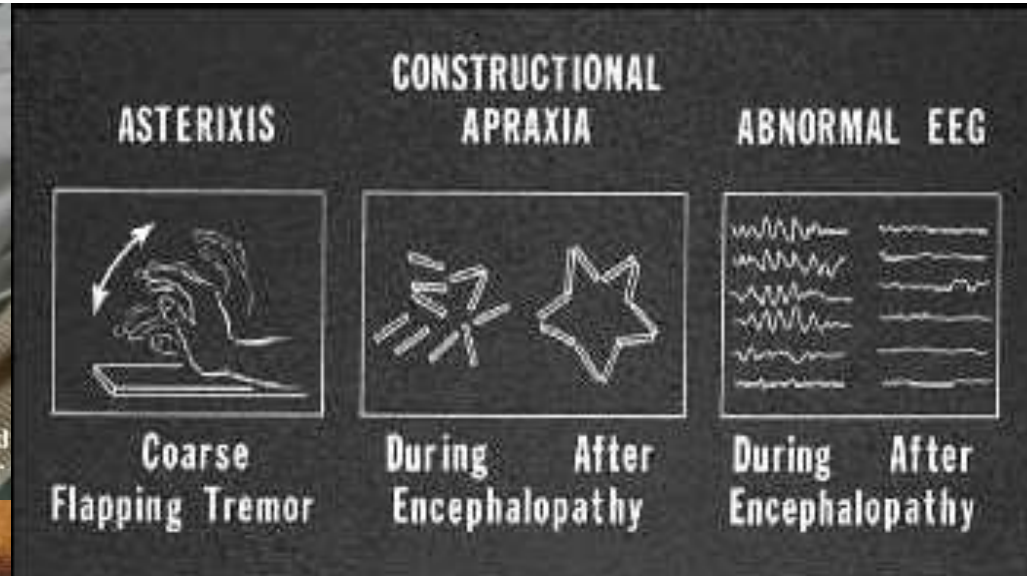
Alert. Scleral icterus. 5 spider Nevi on face and upper chest, palmar erythema, dullness at the flanks. Abdomen soft, non-tender. Palpable, tender liver.

What Is/Are Your Next Step(s)?

1. ABC' s ALWAYS!
2. IV access (1 or 2 bore' s) and administer crystalloid or colloid solution (aim for BP systolic 90 mmHg)
3. IV pantoprazole 80 mg, then 8 mg/h
4. Octreotide 50 mcg iv then 50 mcg/h
5. Correct INR (if > 2.2), platelets (if $< 50,000$)
6. IV antibiotics (cefotaxime 2gm q12h)
7. Transfuse only if hemoglobin < 70 g/L



Hepatic “Alarm” Signs



All Hospitalized Patients with Liver Disease Should Be Classified

Liver Failure

- a. Hyperacute
- b. Acute
- c. Subacute

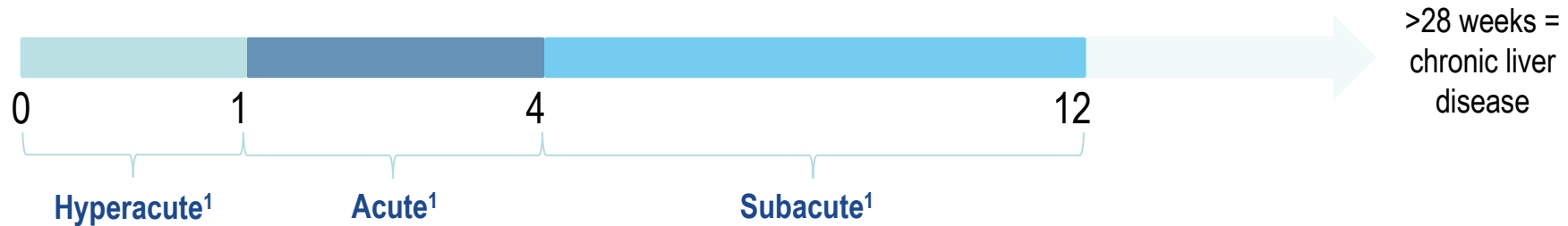
Cirrhosis

- a. Compensated
- b. Decompensated

Acute-on-Chronic Liver Failure Syndrome

Sub-Classifications of Liver Failure

Weeks from development of jaundice to development of HE¹



+++	++	+	Severity of coagulopathy ²
+	++	+++	Severity of jaundice ²
++	++	+/-	Degree of intracranial hypertension ²
Good	Moderate	Poor	Chance of spontaneous recovery ²
Paracetamol HAV, HEV	HBV	Non-paracetamol drug-induced	Typical cause ²

+++ High severity; ++ Medium severity; + Low severity; +/- Present or absent

O'Grady JG, et al. Lancet 1993;342:273-5; 2. Bernal W, et al. Lancet 2010;376:190-201; EASL CPG ALF. J Hepatol 2017;66:1047-81

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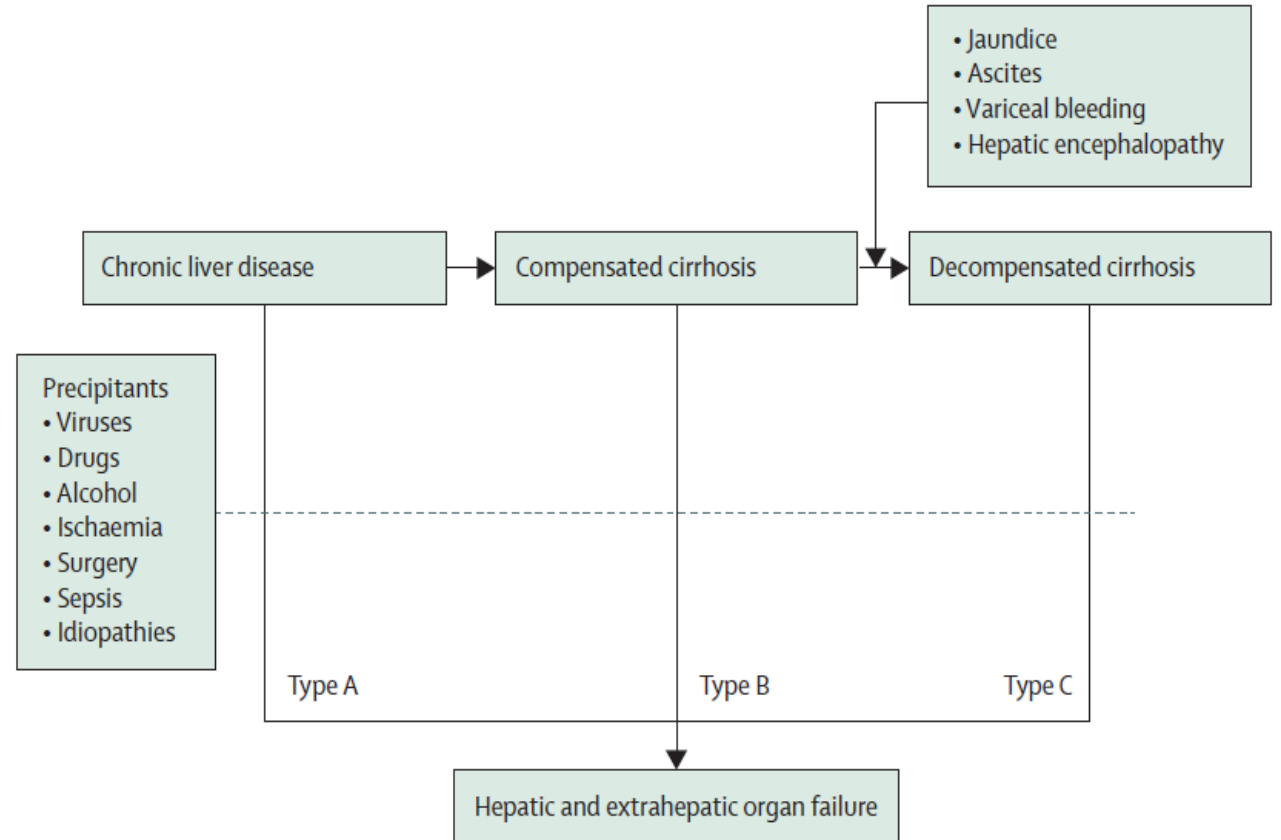
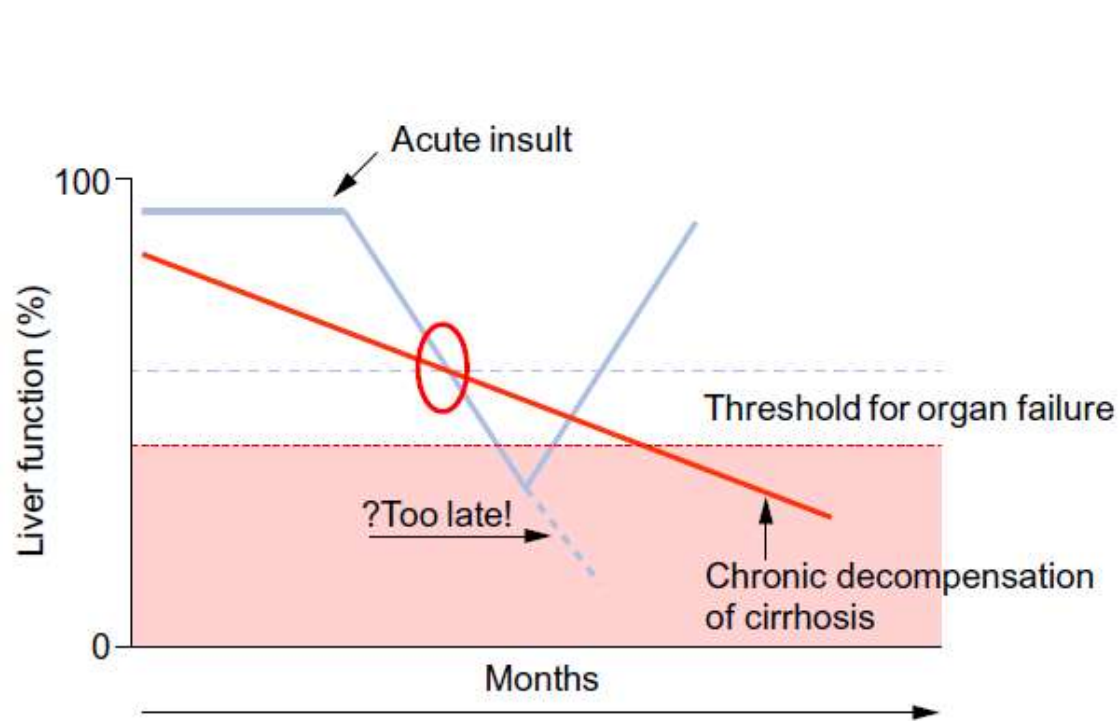
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Acute-on-Chronic Liver Failure Syndrome

Acute-On-Chronic Liver Failure Syndrome



William Bernal, Rajiv Jalan, Alberto Quaglia, Kenneth Simpson, Julia Wendon, Andrew Burroughs
 Lancet 2015; 386: 1576-87

Acute on Chronic Liver Failure Consortium Organ Failure Score

	Score=1	Score=2	Score=3
Liver (bilirubin)	<103 µmol/L	104–206 µmol/L	>206 µmol/L
Kidney (creatinine)	<175 µmol/L	176–310 µmol/L	>310 µmol/L or renal replacement
Brain grade (West-Haven)	0	1–2	3–4
Coagulation (international normalised ratio)	<2.0	2.0–2.4	≥2.5
Circulation (mean arterial pressure)	≥70 mm/Hg	<70 mm/Hg	Vasopressors
Respiratory:			
PaO ₂ /FiO ₂	>300	201–300	≤200
SpO ₂ /FiO ₂	>357	215–357	≤214

Values at study enrolment. A score of 3 is the definition of organ failure for each system, except for the kidney, for which a score of 2 or more is the definition. PaO₂=partial pressure of oxygen. FiO₂=fraction of inspired oxygen. SpO₂=peripheral capillary oxygen saturation. Source: Jalan and colleagues, 2015.²¹

All Hospitalized Patients with Liver Disease Should Be Classified

Liver Failure

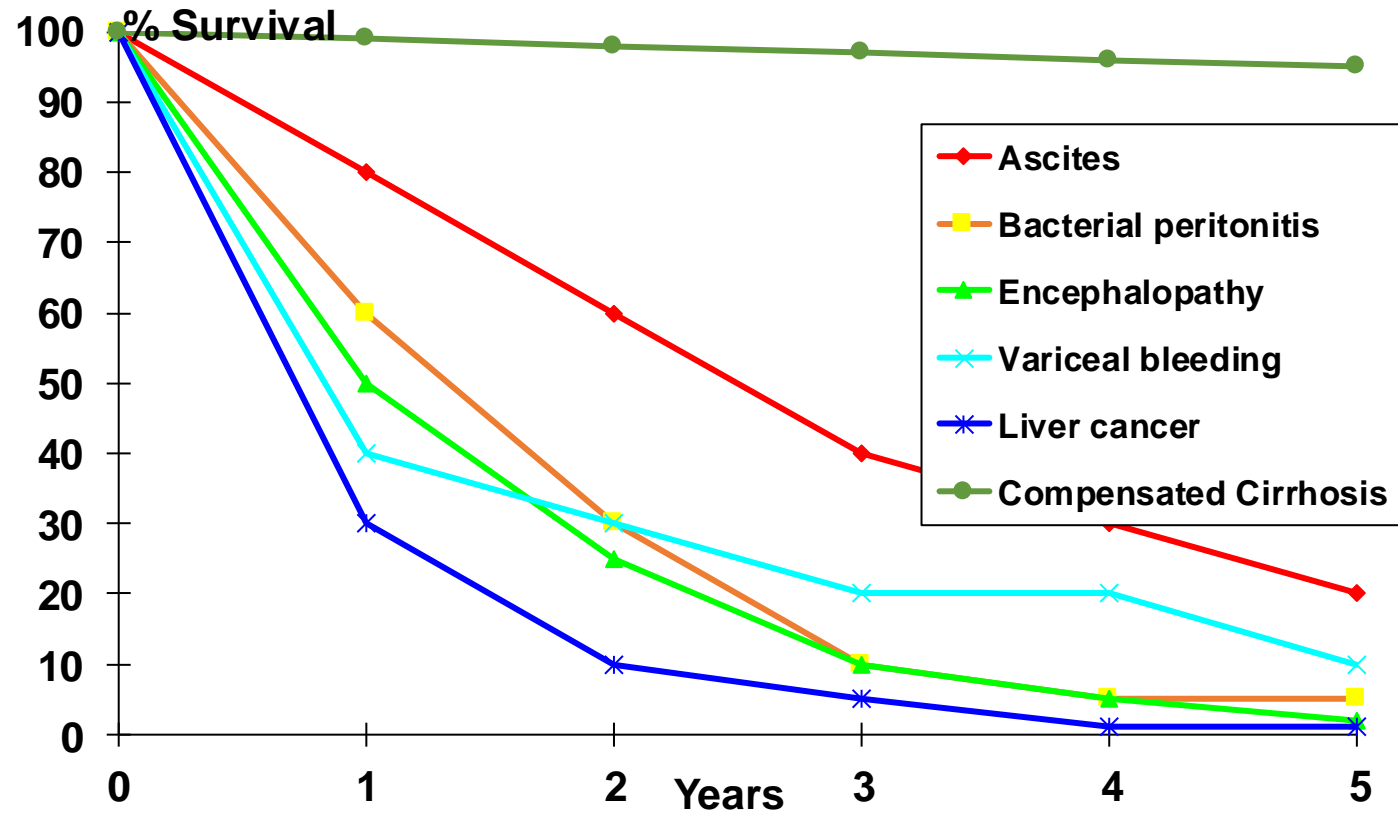
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Cirrhosis

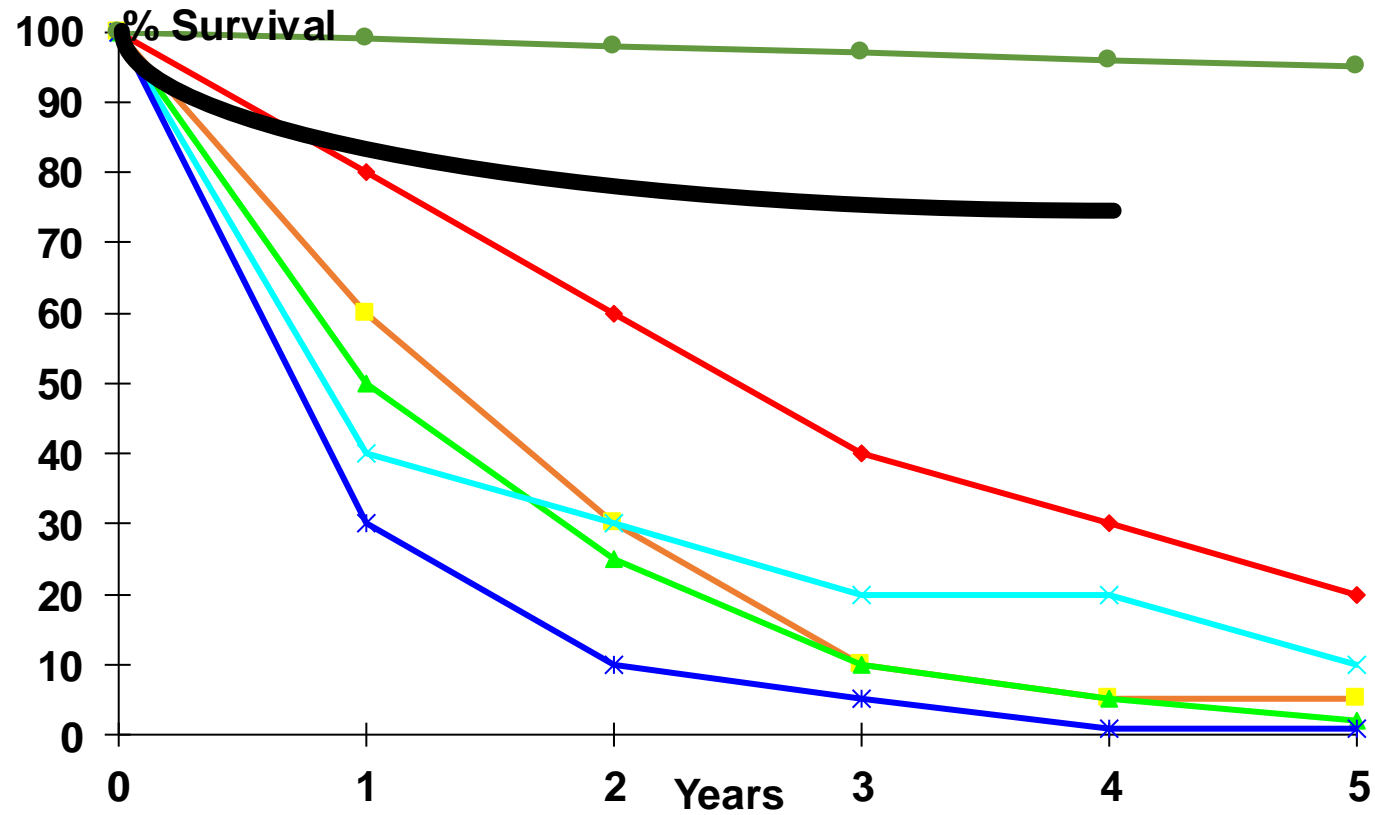
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Acute-on-Chronic Liver Failure Syndrome

Why Decompensation Matters



Why Decompensation Matters



Back to Our Case

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Alert. Scleral icterus. 5 spider Nevi on face and upper chest, palmar erythema, dullness at the flanks. Abdomen soft, non-tender. Palpable, tender liver.

Initial Laboratory Test Results

WBC' s 16, Hgb 104 (MCV 106), plts. 70

ALT 90

AST 200

GGT 400

ALP 190

T. Bili 86

INR 2

Albumin 24

Urea 16; Cr 100

Severity of Hepatic Dysfunction

Child-Pugh classification of severity of liver disease

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/liter)	2-3 mg/dL (34.2 to 51.3 micromol/liter)	>3 mg/dL (>51.3 micromol/liter)
Albumin	>3.5 g/dL (35 g/liter)	2.8-3.5 g/dL (28 to 35 g/liter)	<2.8 g/dL (<28 g/liter)
Prothrombin time			
Seconds over control	<4	4-6	>6
INR	<1.7	1.7-2.3	>2.3
Encephalopathy	None	Grade 1-2	Grade 3-4

MELD Score

(Based on INR, total bilirubin and creatinine, +/- serum sodium)

Provides 3-month risk for mortality

Next Day Patient Has Upper Endoscopy

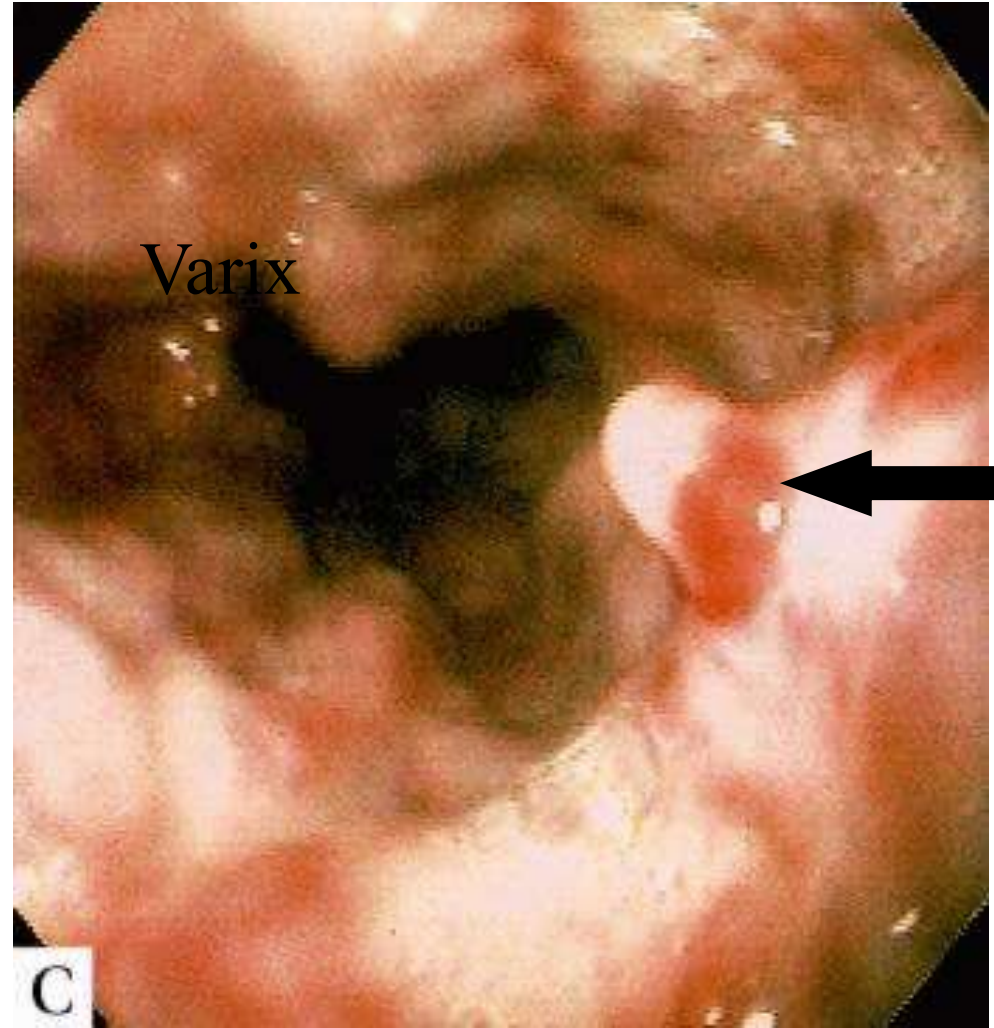
Patient found to have a two columns of grade 3 varices, one with several high-risk stigmata

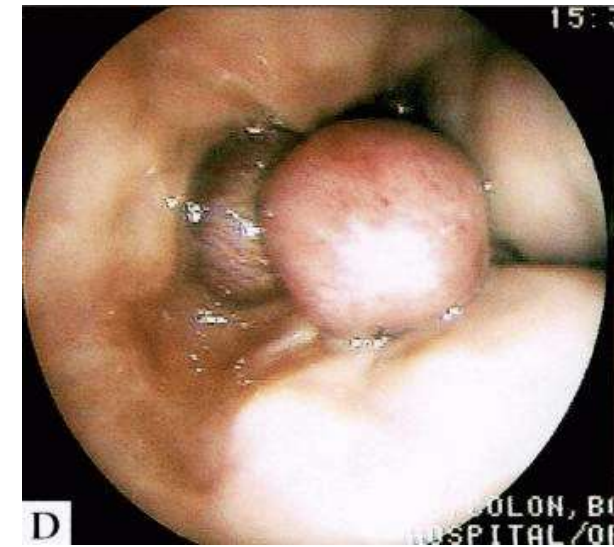
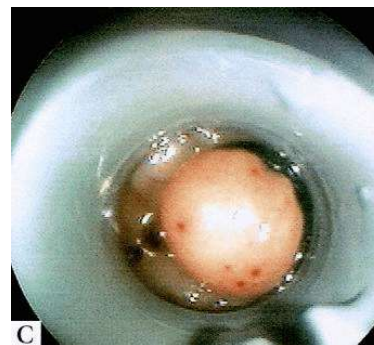
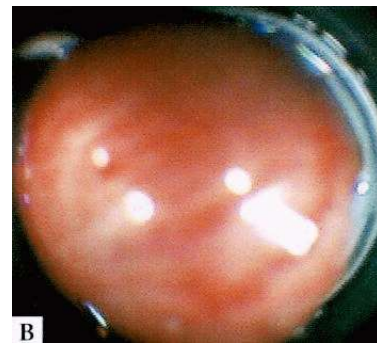
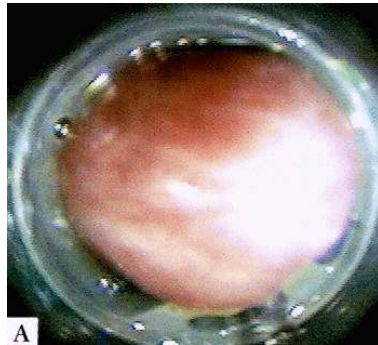
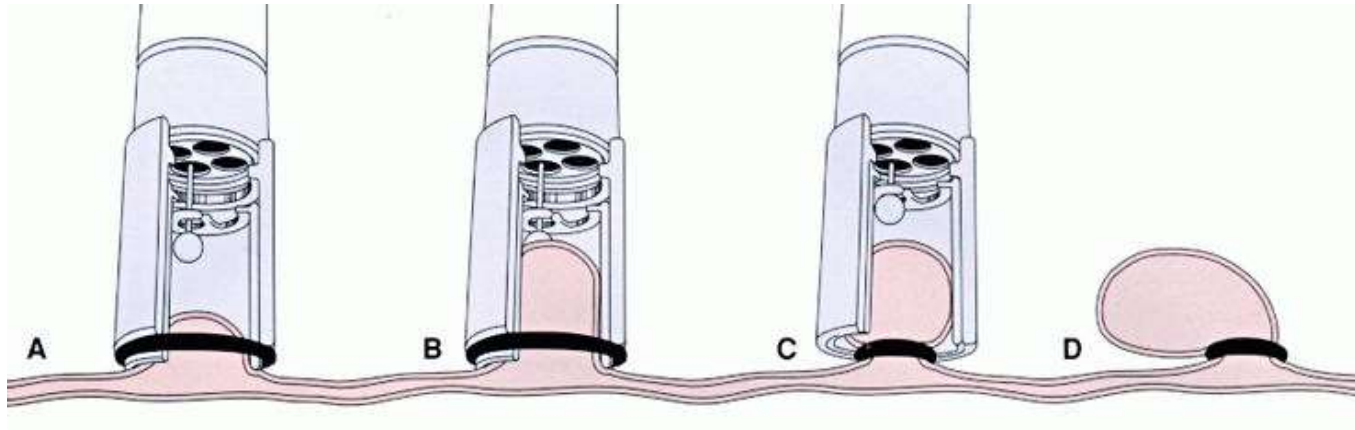
Treated successfully with band ligation

PPI infusion continued for 72 hours

Octreotide continued for 5 days

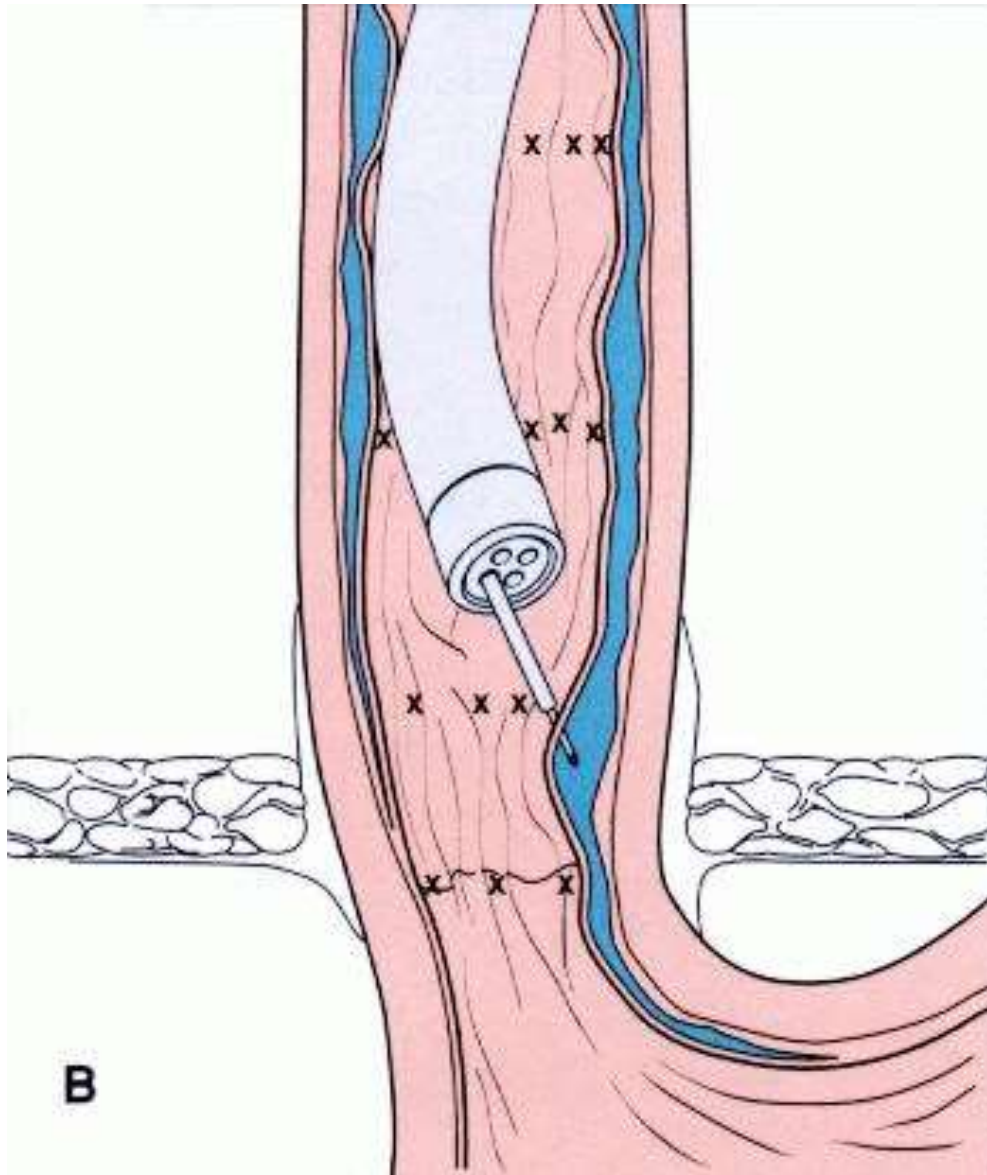
Propranolol (10-20 mg BID) started post endoscopy as secondary prophylaxis



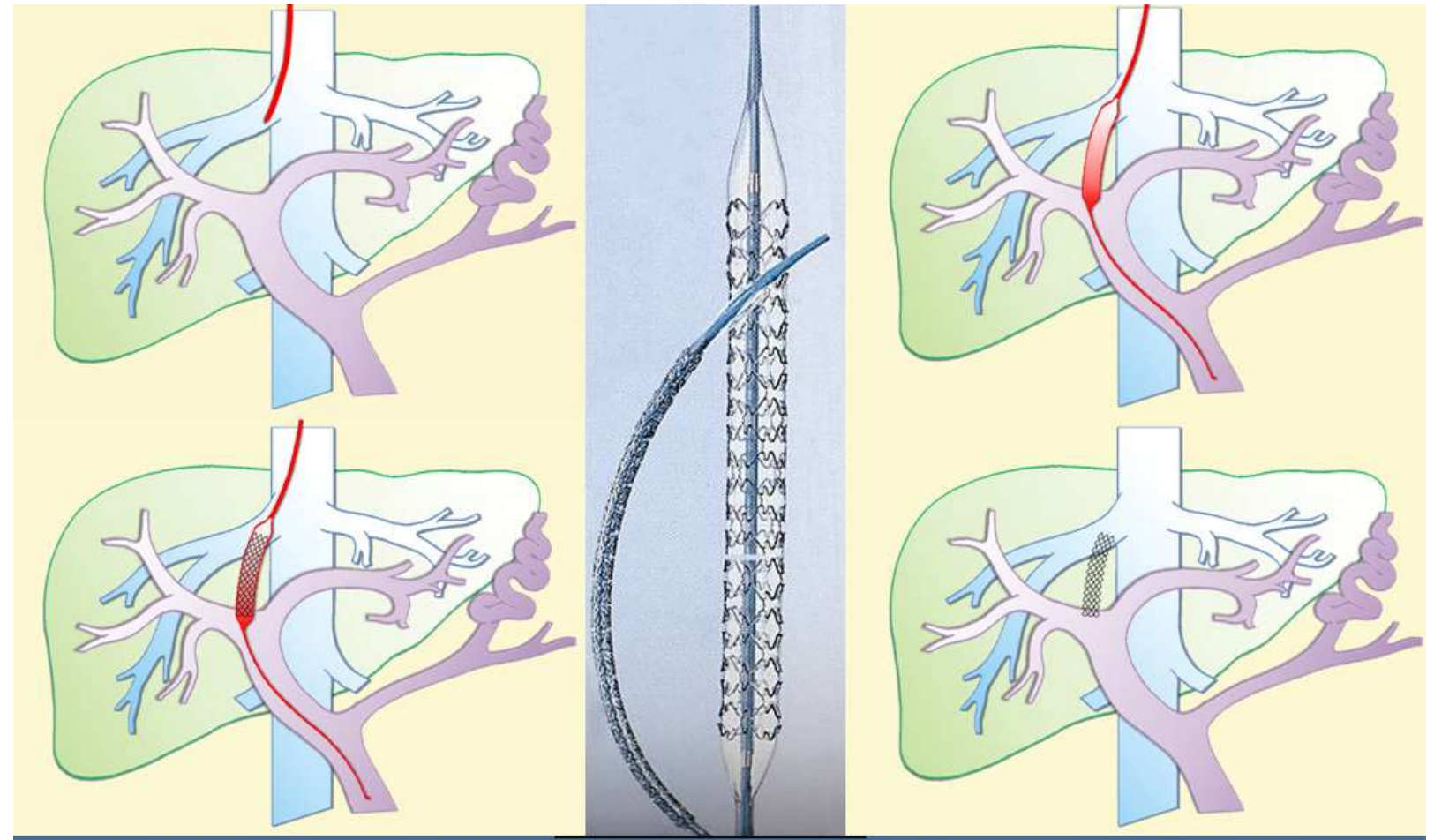
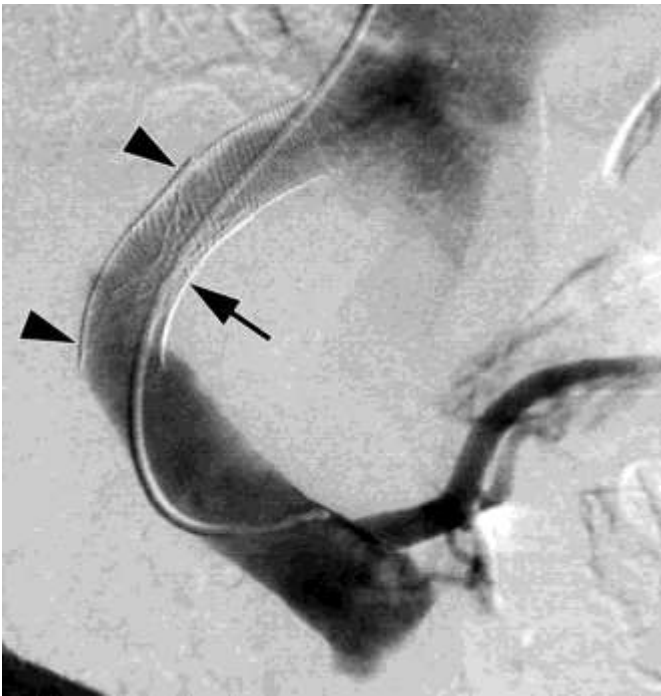
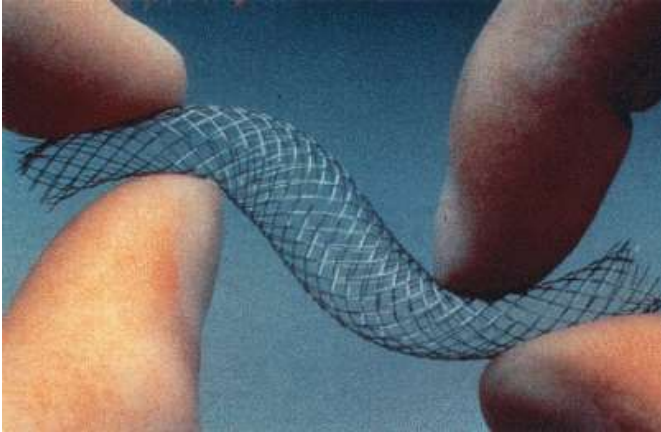


Endoscopic Variceal Ligation

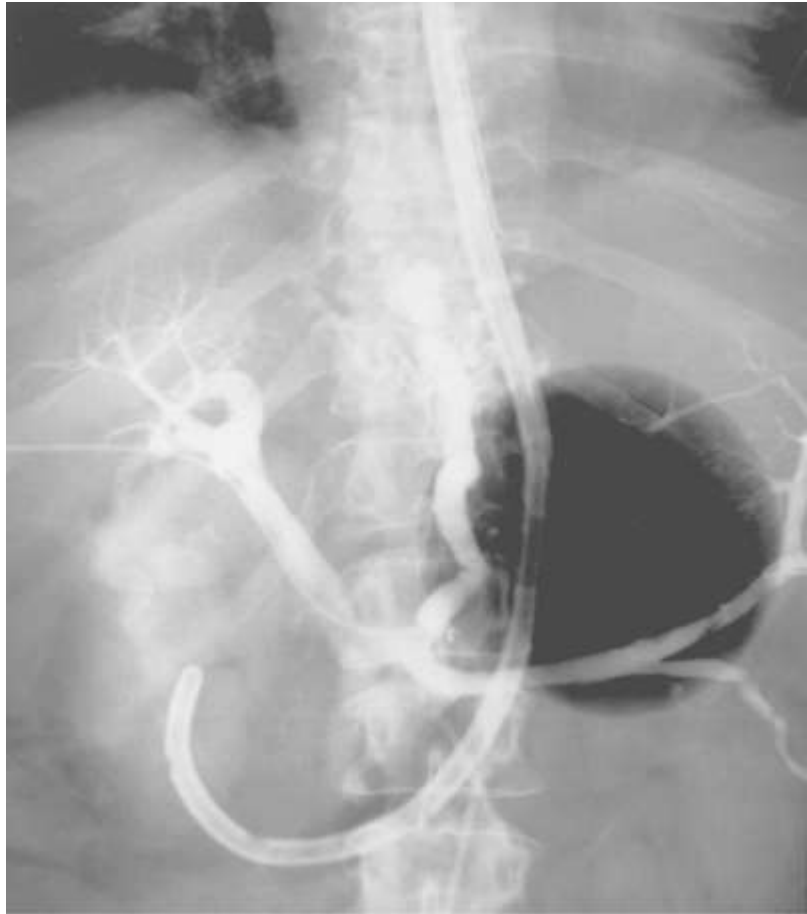
Sclerotherapy



TIPS Insertion



Linton-Nachlas Gastric Balloon For Esophageal Varices



Management of Esophageal Varices

- Patients with advanced portal hypertension (platelet count < 100) are more likely to have large varices
- All patients with platelet count < 150 or hepatic stiffness > 20 KPa should be screened for presence of varices (primary prophylaxis)
- Start Propranolol 10 BID or Nadolol 20 mg OD or Carvedilol 3.125 (for hypertensive patients) are appropriate for prevention of bleeding from varices – titrate to HR 60/min
- Octreotide 50 ug bolus and then 50 ug/hr IV drip for 2-5 days
- Do not over resuscitate
- Correct coagulopathy before transfusions (patients can handle hemoglobin down to 70g/L)



More History After Patient Is Stabilized

20-year history of drinking 4 oz
of vodka per day

Drinking heavier over past
week to celebrate her
birthday

History is otherwise
unremarkable

HCV-Ab (-), HBsAg (-), HFE
gene test (pending)



Alcoholic Hepatitis with/without Cirrhosis

Clinical and pathological criteria

Fever, RUQ pain, anorexia, jaundice are typical

Biopsy shows neutrophil infiltration, necrosis, Mallory bodies

Treatment is supportive (nutrition), possible Prednisolone after risk/complications for alcohol withdrawal managed

Best to confirm diagnosis and estimate prognosis by liver biopsy for severe disease

Glasgow Alcoholic Hepatitis Score

Score given	1	2	3
Age	<50	≥50	–
WCC ($10^9/l$)	<15	≥15	–
Urea (mmol/l)	<5	≥5	–
PT ratio or INR	<1.5	1.5–2.0	>2.0
Bilirubin ($\mu\text{mol/l}$)	<125	125–250	>250

GAHS > 9: poor prognosis

Consider prednisolone 32mg po OD if no contraindications

But 7-days later calculate Lille Score to stop or continue prednisone for 4 wks

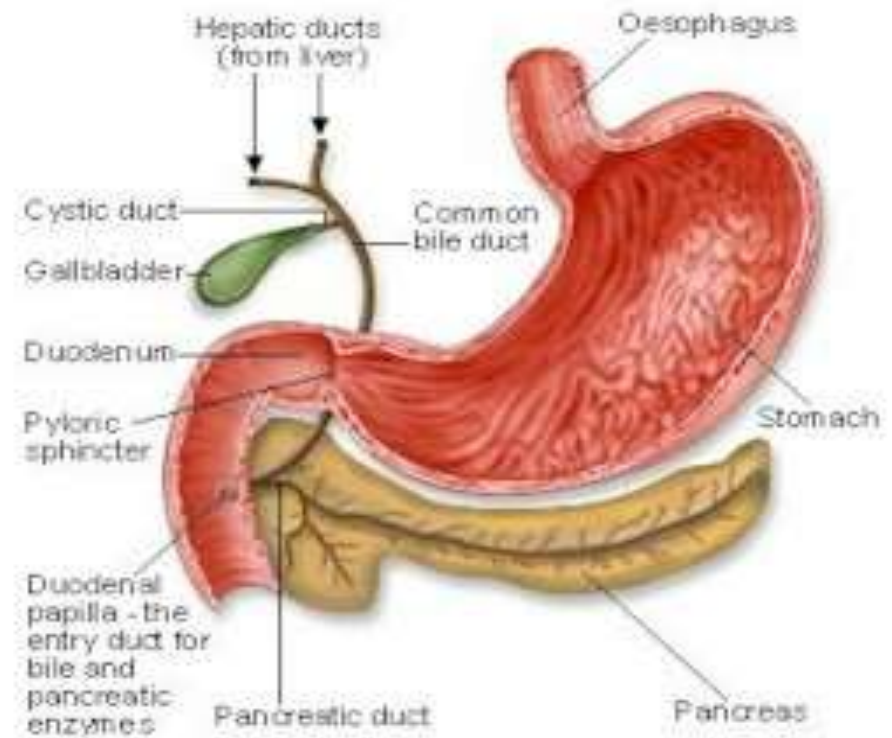


Back to Our Case

Our patient has GAHS 8 and
a week later is down to 6

Treat with nutrition

Several days later nurses
say she is confused and
worried about hepatic
encephalopathy



Find Precipitants For Encephalopathy

Infection

Gastrointestinal bleeding

Medical noncompliance

Medication—sedatives, narcotics, other

Electrolyte disturbances

Portosystemic shunting

 Transjugular intrahepatic portosystemic shunt

 Spontaneous

Dehydration

Excessive protein load

Constipation

Worsening liver function

Classification of Hepatic Encephalopathy

Grade 1	Constructional apraxia Poor memory – number connection test Agitation/ irritability Reversed sleep pattern
Grade 2	Lethargy, disorientation Asterixis
Grade 3	Drowsy, reduced conscious level
Grade 4	Coma

- Do not limit protein intake, may encourage vegetable-based proteins and dairy products

Treatment of Hepatic Encephalopathy

Empiric

1. Lactulose 15 - 30 cc' s q1h until wake up
 - Alternative PEG 3353 (restoralax/laxaday)
 - If comatose: use lactulose retention enema with 300 cc in 700 cc water
2. Rifaximin 550mg po BID
 - Flagyl or Metronidazole IV or PO 250mg q12h
3. Raise head of bed > 30 degrees in hyperacute liver failure to avoid brain edema
4. Sodium benzoate in rare cases

Specific

Treat the underlying cause



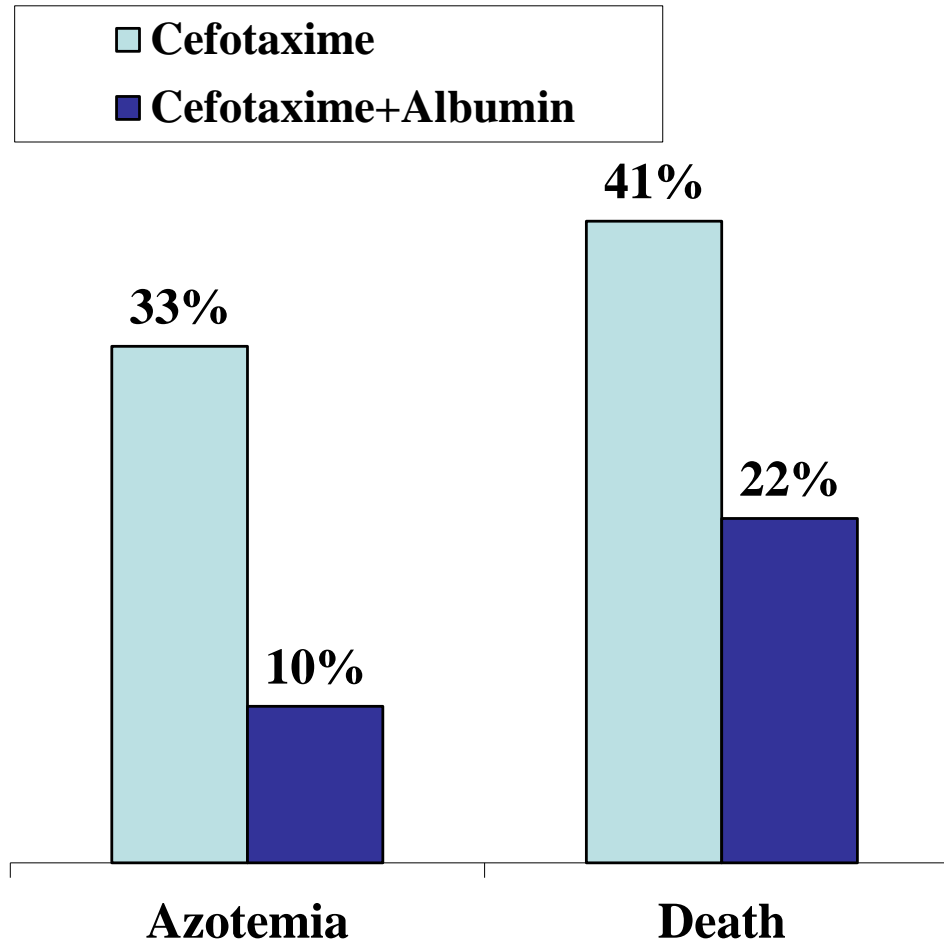
Back to Our Case

Our patient had been given
Dimenhydrinate and
Lorazepam

To rule out infection,
paracentesis was
performed: WBC's 600,
80% neutrophils



Albumin Infusion in Presence of SBP is Necessary



Albumin infusion 1.5 g/Kg on day-1 and then 1.5 g/Kg on day-3

Cefotaxime 1g q 8 hrs
or 2g q12 hrs

N Engl J Med. 1999 Aug 5;341(6):403-9

Interpretation of Serum to Ascites Albumin Gradient?

SAAG > 11 g/L

High JVP

Congestive heart failure, constrictive pericarditis (cardiac ascites)

Low JVP

Cirrhosis, alcoholic hepatitis, fulminant hepatic failure

Budd - Chiari syndrome (hepatic vein thrombosis) or veno occlusive disease

Myxoedema

Massive liver metastasis



Interpretation of Serum to Ascites Albumin Gradient?

SAAG < 11 g/L

Exudate (high protein, high LDH)

Peritoneal carcinomatosis

Tuberculosis, peritonitis

Pancreatic ascites

Transudate (low protein, low LDH)

Nephrotic syndrome

Malnutrition

Protein-losing enteropathy



Ascites Management



- Dietary sodium restriction < 80 mEq/d or $< 1,500$ mg/d (avoid Na in IV fluids)
- Paracentesis (at least diagnostic)
- Start potassium sparing diuretics (spironolactone 50 mg po OD; or amiloride 10 mg po OD). Add furosemide 40mg q 2d or OD for rapid results or if patient hyponatremic
- For hyponatremia, limit free water intake and don't give Na infusion except in severe cases (Na < 115 mEq/L)
- Don't worry about mild hypo- or hyper-kalemia
- Consider TIPS or Transplantation in patients requiring frequent therapeutic paracentesis



Investigations to Help Identify Patients for HCC Surveillance

On Labs

- FIB-4 Score (based on age, AST, ALT, platelet count) greater than 3.0

On imaging

- Nodular liver on U/S, CT or MRI with Splenomegaly
- Elastography (Fibroscan) with high liver stiffness >15 KPa or high hepatic stiffness on MRE >4.5KPa

On histology/pathology

- Cirrhosis on histology or CSP > 12mmHg
- Nodular and shrunken liver on laparoscopy

Cheat Sheet To Identify Causes

Cause	Test (result)	Therapy
Alcohol	MCV (↑)	Abstinence
HBV + delta virus infection	HBsAg (+), HBV-DNA(+) HDV-RNA (+)	Nucleoside (lamivudine, entecavir); or Nucleotide (tenofovir) analogs
HCV infection	HCV-RNA (+)	After discharge: Direct Acting Antiviral Agents
Primary biliary cirrhosis	Alkaline phosphatase (↑) AMA (+)	Ursodeoxycholic acid or Obeticholic acid (for non-responders)
Autoimmune hepatitis	ANA (+), ASMA (+) Immunoglobulin-G (↑)	Prednisone, azathioprine
Hemochromatosis	HFE gene mutation	Phlebotomy
Wilson's disease	Ceruloplasmin (↓)	D-penicillamine, zinc
NAFLD/NASH	Glucose (↑) Triglycerides (↑)	Low-calorie diet, physical activity, insulin- sensitizer drugs (metformin) or insulin

Any Other Questions



#CoffeeGoodForLiver

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[@LiverSensible](#)

Diagnostic Criteria for Hepatorenal Syndrome

MAJOR

Chronic or acute liver disease with advanced hepatic failure
and portal hypertension

Creatinine > 1.5 mg/dL or 24-hour creatinine clearance < 40 mL/min

Absence of shock, ongoing infection, use of nephrotoxic
drugs, gastrointestinal or renal fluid losses > 500 g/d or
 > 1000 g/d in the setting of edema

Urine protein < 500 mg/dL

No ultrasonographic evidence of primary renal disease

No sustained improvement in renal function after hydration

MINOR

Urine sodium < 10 mEq/L

Urine osmolality $>$ plasma osmolality

Urine red blood cells < 50 per high power field

Urine output < 500 mL/d

Serum sodium < 130 mEq/L

Use MDRD (6-point) for eGFR

Diagnostic Criteria for Hepatopulmonary Syndrome

Variable	Criterion
Oxygenation defect	Partial pressure of oxygen <80 mm Hg or alveolar–arterial oxygen gradient ≥ 15 mm Hg while breathing ambient air
Pulmonary vascular dilatation	Positive findings on contrast-enhanced echocardiography or abnormal uptake in the brain (>6%) with radioactive lung-perfusion scanning
Liver disease	Portal hypertension (most common) with or without cirrhosis
Degree of severity†	
Mild	Alveolar–arterial oxygen gradient ≥ 15 mm Hg, partial pressure of oxygen ≥ 80 mm Hg
Moderate	Alveolar–arterial oxygen gradient ≥ 15 mm Hg, partial pressure of oxygen ≥ 60 to <80 mm Hg
Severe	Alveolar–arterial oxygen gradient ≥ 15 mm Hg, partial pressure of oxygen ≥ 50 to <60 mm Hg
Very severe	Alveolar–arterial oxygen gradient ≥ 15 mm Hg, partial pressure of oxygen <50 mm Hg (<300 mm Hg while the patient is breathing 100% oxygen)

N ENGL J MED 358;22 WWW.NEJM.ORG MAY 29, 2008

Diagnostic Criteria for Portopulmonary Hypertension

Clinical portal hypertension with or without significant chronic liver disease

Mean pulmonary artery pressure (mPAP) >25 mmHg at rest

Mean pulmonary capillary wedge pressure (mPCWP) <15 mmHg

Pulmonary vascular resistance (PVR) >240 dyne/sec/cm⁻⁵ (3.0 Wood Units)

[Ann Thorac Med. 2010 Jan-Mar; 5\(1\): 5-9.](#)

Diagnostic Criteria for Cirrhotic Cardiomyopathy

Proposal of diagnostic criteria for cirrhotic cardiomyopathy agreed upon at the 2005 World Congress of Gastroenterology in Montreal (10). There are suggestions (not included in this table) to improve these criteria considering dysfunction of right ventricle (15), biventricular diastolic dysfunction at rest, large left and right atria, higher systolic pulmonary arterial pressure and left ventricular mass (16) and evaluate systolic function assessment using tissue strain imaging (17).

Systolic dysfunction

Resting ejection fraction <55%
Blunted increase in cardiac output with exercise or pharmacological stimuli

Diastolic dysfunction

Early diastolic atrial filling ratio (E/A ratio) <1.0 (age corrected)
Deceleration time (DT) >200 ms
Prolonged isovolumetric relaxation time >80 ms

Supportive criteria

Electrophysiological abnormalities (prolongation of QT)
Abnormal chronotropic response
Electromechanical uncoupling
Enlarged left atrium
Increased myocardial mass
Increased brain natriuretic peptide and pro-peptide
Increased troponin I

[Braz J Med Biol Res. 2019; 52\(2\): e7809.](#)

CAGE questionnaire

1. Have you ever felt like you should **CUT** down on your drinking?
2. Have people **ANNOYED** you by criticizing your drinking?
3. Have you ever felt bad or **GUILTY** about your drinking?
4. Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (**EYE OPENER**)?

CAGE Score	Likelihood ratio
0	0.14
1	1.5
2	4.5
3	13.2
4	101

Ewing, et al. Detecting alcoholism: the CAGE questionnaire. JAMA. 1984;252:1905-1907.
Kitchens, JM. Does this patient have an alcohol problem?. JAMA. 1994;272:1782-7

Predicting Relapse After Discharge

TABLE 2. Final proportional hazards model

Variable	Freq.	Coeff.	Exp.(coeff.)*	Coeff./SE
Duration of heavy drinking		0.3228	1.3810	2.2718
< 11 years = 0	75			
11–25 years = 1	98			
> 25 years = 2	82			
Daily drinking (ml alcohol)		0.5129	1.6701	3.1486
< 150 = 0	50			
150–305 = 1	79			
> 305 = 2	126			
Previous alcoholism treatment		0.6290	1.8758	2.1506
No = 0	76			
Yes = 1	179			

* Exp_e (coeff.) = relative risk (RR) of readmission for a patient with a value > 0 over a patient with a value of 0.

Pharmacological Management Of Alcohol Dependence

Naltrexone (ReVia)

Acts as an opiate agonist; decreases heavy drinking by blocking endogenous opioids, a process that attenuates craving and the reinforcing effects of alcohol

Initial dose, 12.5 mg daily or 25 mg daily; therapeutic dose, 50 mg daily

Acamprosate (Campral)†

Increases abstinence by stabilizing activity in the glutamate system, which is affected by long-term heavy consumption

666 mg 3 times a day

Disulfiram (Antabuse)

Blocks aldehyde dehydrogenase; blockade allows acetaldehyde to accumulate with alcohol consumption, causing unpleasant symptoms (e.g., flushing, headache, vomiting, dyspnea, confusion)

Initial dose, 250 mg daily; therapeutic dose, 500 mg daily

My Routine: If HAR > 3 start Naloxone 25mg every 2days for a week then 25mg daily, then 50mg daily

Predicting Need for Liver Transplantation

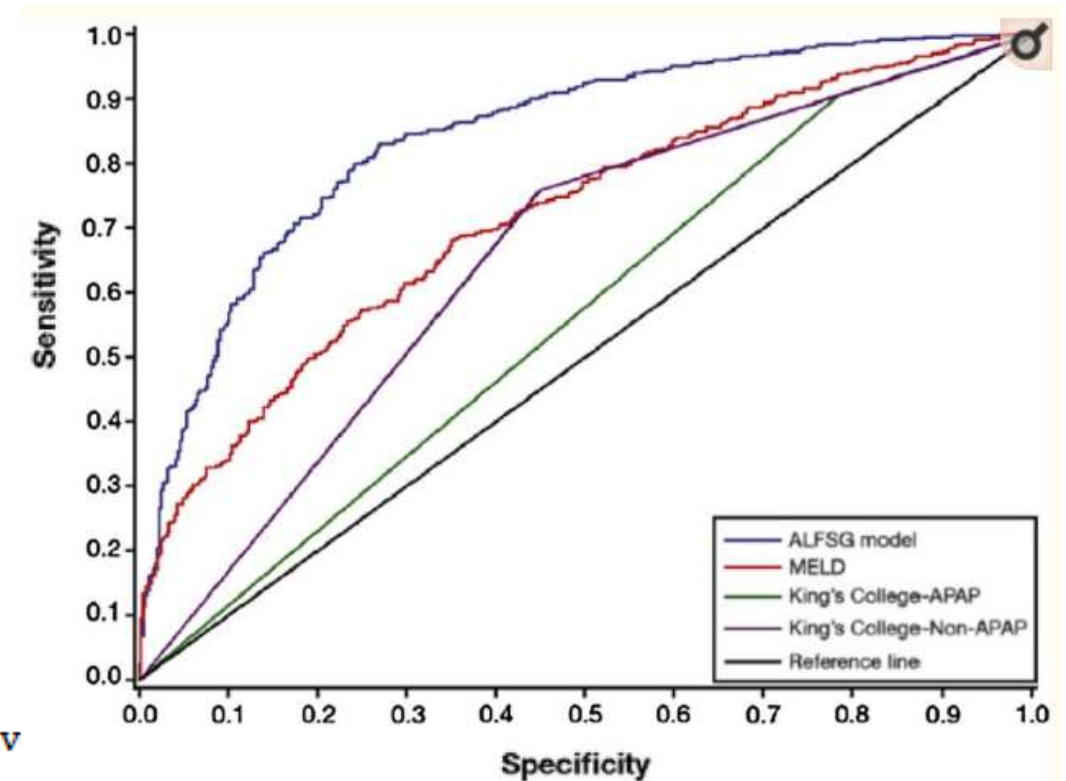
Table 4: Kings College Hospital criteria for liver transplantation in acute liver failure

Paracetamol (acetaminophen) overdose

- pH <7.3 (irrespective of encephalopathy)
- Or all of the following:
- Grade III-IV encephalopathy
 - Creatinine >300umol/litre
 - Prothrombin time >100 seconds (INR >6.5)

Non-paracetamol aetiology

- Prothrombin time >100 seconds
- Or any 3 of the following:
- Age <10 years or >40 years
 - Prothrombin time >50 seconds
 - Bilirubin >300umol/litre
 - Time from jaundice to encephalopathy >2 days
 - Non-A, non-B hepatitis, halothane or drug-induced acute liv



Exclusion Criteria for Liver Transplant Listing

Absolute contraindications:

- Advanced cardiac disease – unstable CAD, severe (right or left) heart failure
- Cancer/malignancy outside the liver
- Frailty with poor functional status, limited mobility and/or dementia
- Irreversible brain damage
- Misuse of prescribed or non-prescribed drugs
- Multi-system failure not correctable by liver transplantation
- Persistent extrahepatic infections despite medical management (e.g. non-healing diabetic ulcers)
- Ongoing alcohol and/or substance use within last six months in patients with addiction history
- Severe obesity (**BMI > 45**) or malnutrition (**BMI < 18**)
- Severe progressive pulmonary disease including severe pulmonary hypertension
- Severe, unstable psychiatric disorders (e.g. recent suicide attempt, or severe, poorly controlled depression and/or mania)
- Unable or not committed to adhere to medical treatments (e.g. medications, appointments, tests)

Relative contraindications:

- Ongoing tobacco use and unwilling to quit
- Inability to achieve accessible, available and stable social support 24/7
- Extrahepatic cancers within the past 2 – 5 years
- Refusal of all blood products and blood component transfusions
- Obesity with **BMI > 40**

Source

