

# Cirrhosis and Its Complications

Dr. Gh.R Rezamand MD

Gastroenterologist

IUMS

# Case 1

- A 55-year-old patient was referred to you due to increased liver enzymes. The tests are as follows. What is the next step?

AST= 73

ALT= 56

ALP= 450

Bil T= 1.7

Bil D= 0.7

INR= 1.1

Plat= 95000

Alb= 3.8

# Etiology

- Drug history
- Alcohol
- Herbal
- Behavior

# Liver fibrosis

## Symptoms

Anorexia

Weight loss

Weakness

Fatigue

Muscle cramps

Easy bruising

Amenorrhea/oligomenorrhea/metrorrhagia (women)

Impotence (men)

Infertility

Decreased libido (men)

Jaundice\*

Dark or "cola-colored" urine\*

Pruritus\*

Hematemesis/melena/hematochezia\*

Abdominal distension\*

Lower extremity edema\*

Confusion or sleep disturbances\*

\* Suggests advanced disease or the development of a major complication.

## Physical examination

Hepatomegaly

Splenomegaly

Spider angiomas/spider telangiectasias

Palmar erythema

Digital clubbing

Hypertrophic osteoarthropathy

Dupuytren's contracture

Muehrcke nails

Terry nails

Parotid gland enlargement (likely due to alcohol use and not cirrhosis per se)

Gynecomastia (men)

Loss of chest or axillary hair (men)

Testicular atrophy (men)

Caput medusa

Cruveilhier-Baumgarten murmur (venous hum heard best with the stethoscope over the epigastrium)

Jaundice\*

Ascites (abdominal distension, shifting dullness, fluid wave)\*

Asterixis\*

Fetor hepaticus\*

\* Suggests advanced disease or the development of a major complication.

## Laboratory tests

Moderately elevated aminotransferases (often with an AST:ALT ratio >1)

Elevated alkaline phosphatase (2 to 3 times the ULN)

Elevated gamma-glutamyl transpeptidase

Thrombocytopenia

Leukopenia/neutropenia

Anemia

Low serum albumin\*

Prolonged prothrombin time/elevated INR\*

Hyperbilirubinemia\*

Hyponatremia\*

Elevated serum creatinine\*

\* Suggests advanced disease or the development of a major complication.

## Imaging tests

Surface nodularity

Increased echogenicity (ultrasound)

Atrophy of the right lobe

Hypertrophy of the caudate or left lobes

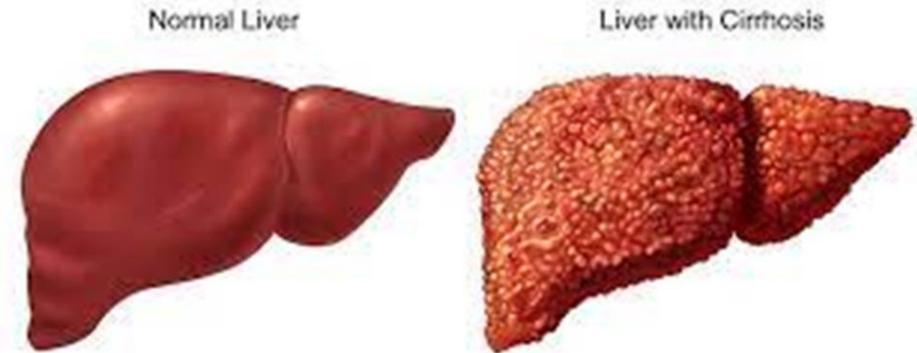
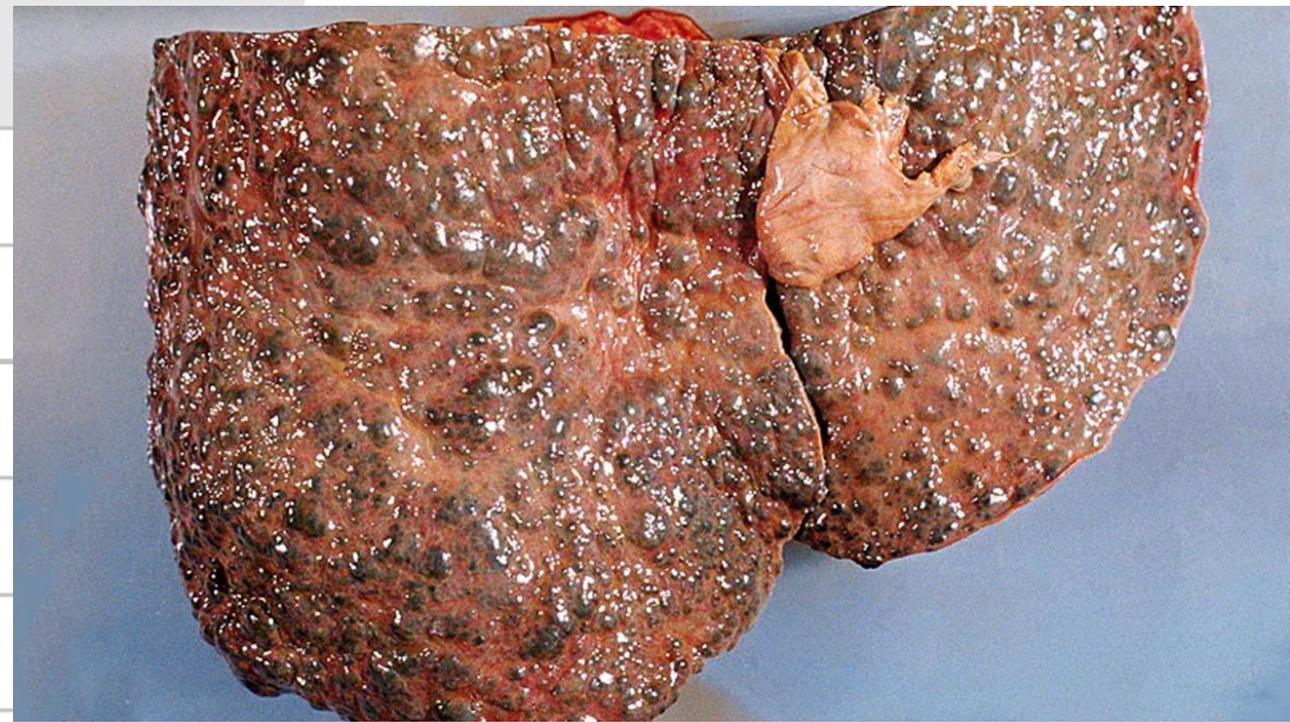
Small, nodular liver\*

Ascites\*

Hepatocellular carcinoma\*

Portal/splenic/superior mesenteric vein thrombosis\*

Portosystemic collaterals\*



\* Suggests advanced disease or the development of a major complication.

# STAGES OF FIBROSIS

1. Histologically (Biopsy)
2. Noninvasive tests

# Noninvasive assessment of hepatic fibrosis

- Serologic tests: eg, FIB-4
- Imaging examinations: Elastography

# Fibrosis-4 (FIB-4) Calculator

Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = \text{[Yellow Oval]}$$

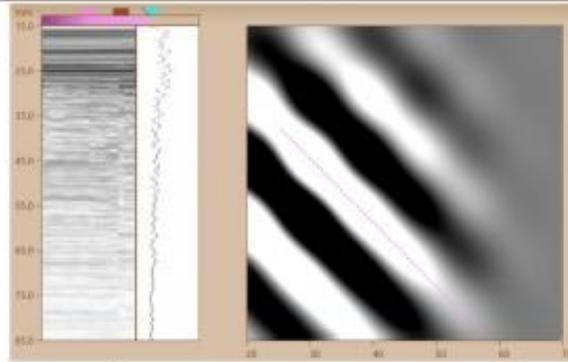
## Interpretation:

Using a lower cutoff value of 1.45, a **FIB-4 score <1.45** had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a **FIB-4 >3.25** would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

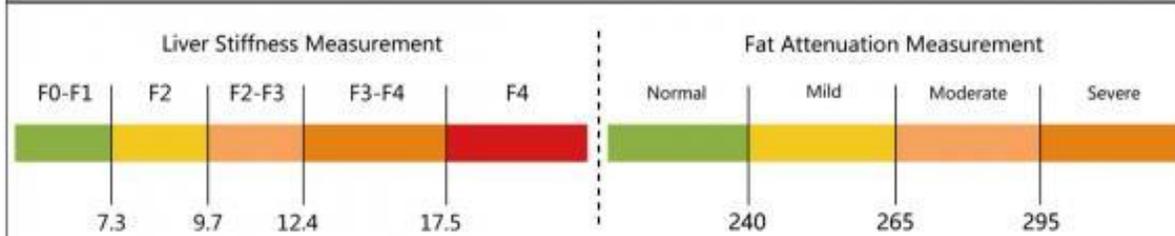
# HISKY MED

## Examination Report

Name	Nikolay Dobromislov	Age/D.O.B.	7/14/1980				
Height(cm)	180	Weight(kg)	82	Gender	M	BMI	25.3
Referring Clinic							
Physician				ID	28022018001		



Stiffness(KPA)		Measurements		UAP(db/m)	
Median	4.3	Success Rate	100.0	Median	244
IQR/Median	16%	Valid/Total	10/10	IQR/Median	1%



For reference only. Please consult your physician for further diagnosis.

Note

# METAVIR score

- Many use five-point scales such as the METAVIR score:
  - F0: No fibrosis
  - F1: Portal fibrosis without septa
  - F2: Few septa
  - F3: Numerous septa without cirrhosis
  - F4: Cirrhosis
- Patients are typically considered to have **significant fibrosis** if their fibrosis score is  $\geq F2$ .

The major goals of managing patients with cirrhosis include

1. Slowing or reversing the progression of liver disease
2. Preventing superimposed insults to the liver
3. Identifying medications that require dose adjustments or should be avoided entirely
4. Managing symptoms and laboratory abnormalities
5. Preventing and treating the complications of cirrhosis
6. Determining the appropriateness and optimal timing for liver transplantation

# ETIOLOGIES AND CLASSIFICATION

- Causing by **chronic**
  - hepatic inflammation
  - cholestasis

## TABLE 344-1 Causes of Cirrhosis

Alcohol

Chronic viral hepatitis

Hepatitis B

Hepatitis C

Autoimmune hepatitis

Nonalcoholic steatohepatitis

Biliary cirrhosis

Primary biliary cholangitis

Primary sclerosing cholangitis

Autoimmune cholangiopathy

Cardiac cirrhosis

Inherited metabolic liver disease

Hemochromatosis

Wilson's disease

$\alpha_1$  Antitrypsin deficiency

Cystic fibrosis

Cryptogenic cirrhosis

# Liver function

- More than 500 vital functions have been identified with the liver
  - **Synthetic** ( albumin, immune factors... )
  - **Regulation** ( blood levels of amino acids, Iron...)
  - **Processing** ( Bilirubin )
  - **Clearance and detoxification** (drugs and other poisonous substances)

# Muscle cramps

- 1) Confirm the muscle cramps are related to cirrhosis
- 2) Check electrolyte levels and replete if low
- 3) Treat with branched-chain amino acids if symptoms persist
- 4) Treat with taurine if symptoms persist
- 5) Treat with vitamin E if symptoms persist

## Common complications of cirrhosis

Variceal hemorrhage
Ascites
Spontaneous bacterial peritonitis
Hepatic encephalopathy
Hepatocellular carcinoma
Hepatorenal syndrome
Hepatopulmonary syndrome
Hepatic hydrothorax
Portopulmonary hypertension
Cirrhotic cardiomyopathy
Portal vein thrombosis

## TABLE 344-2 Complications of Cirrhosis

### Portal hypertension

Gastroesophageal varices

Portal hypertensive gastropathy

Splenomegaly, hypersplenism

Ascites

Spontaneous bacterial peritonitis

### Hepatorenal syndrome

Type 1

Type 2

### Hepatic encephalopathy

### Hepatopulmonary syndrome

### Portopulmonary hypertension

### Malnutrition

### Coagulopathy

Factor deficiency

Fibrinolysis

Thrombocytopenia

### Bone disease

Osteopenia

Osteoporosis

Osteomalacia

### Hematologic abnormalities

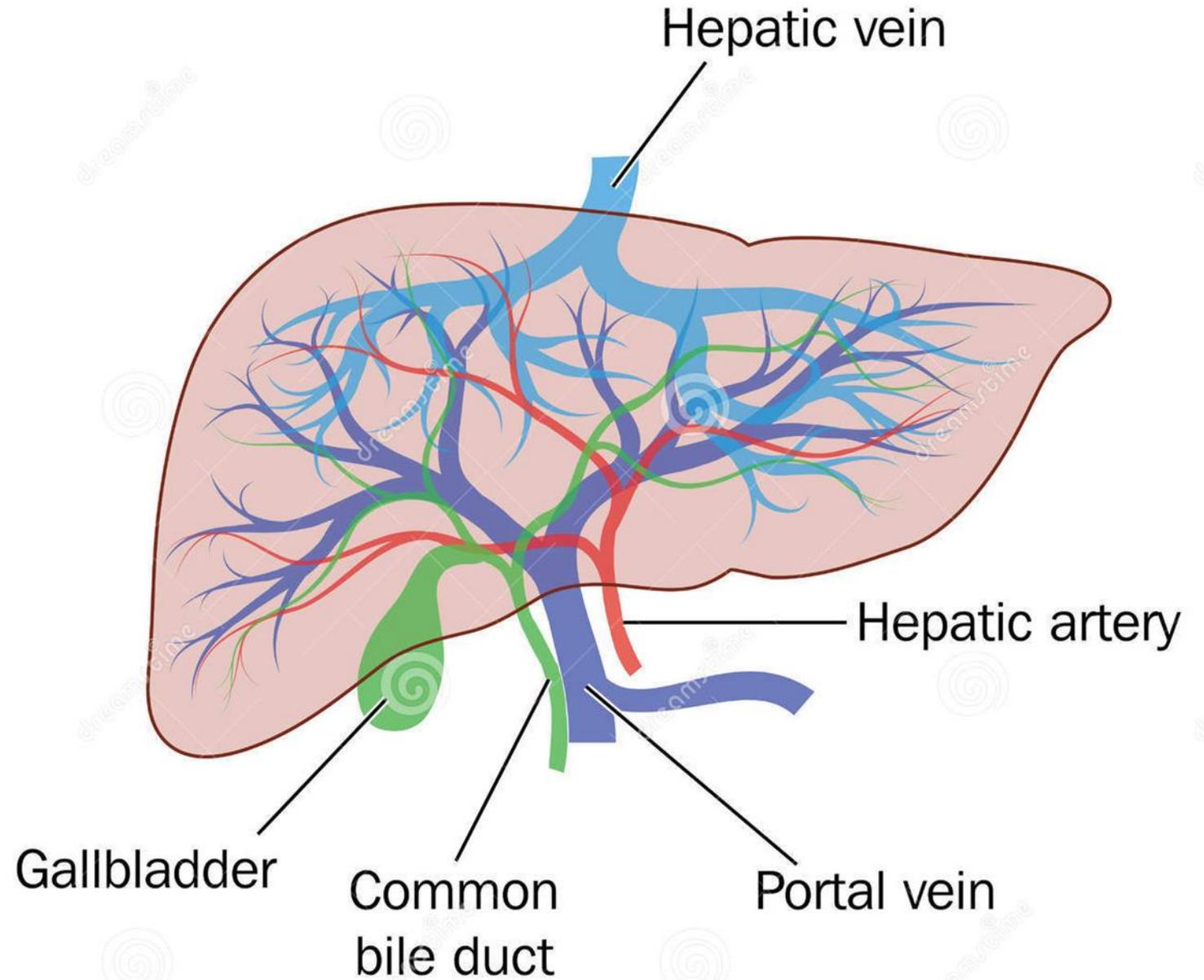
Anemia

Hemolysis

Thrombocytopenia

Neutropenia

# Portal hypertensi



# PORTAL HYPERTENSION

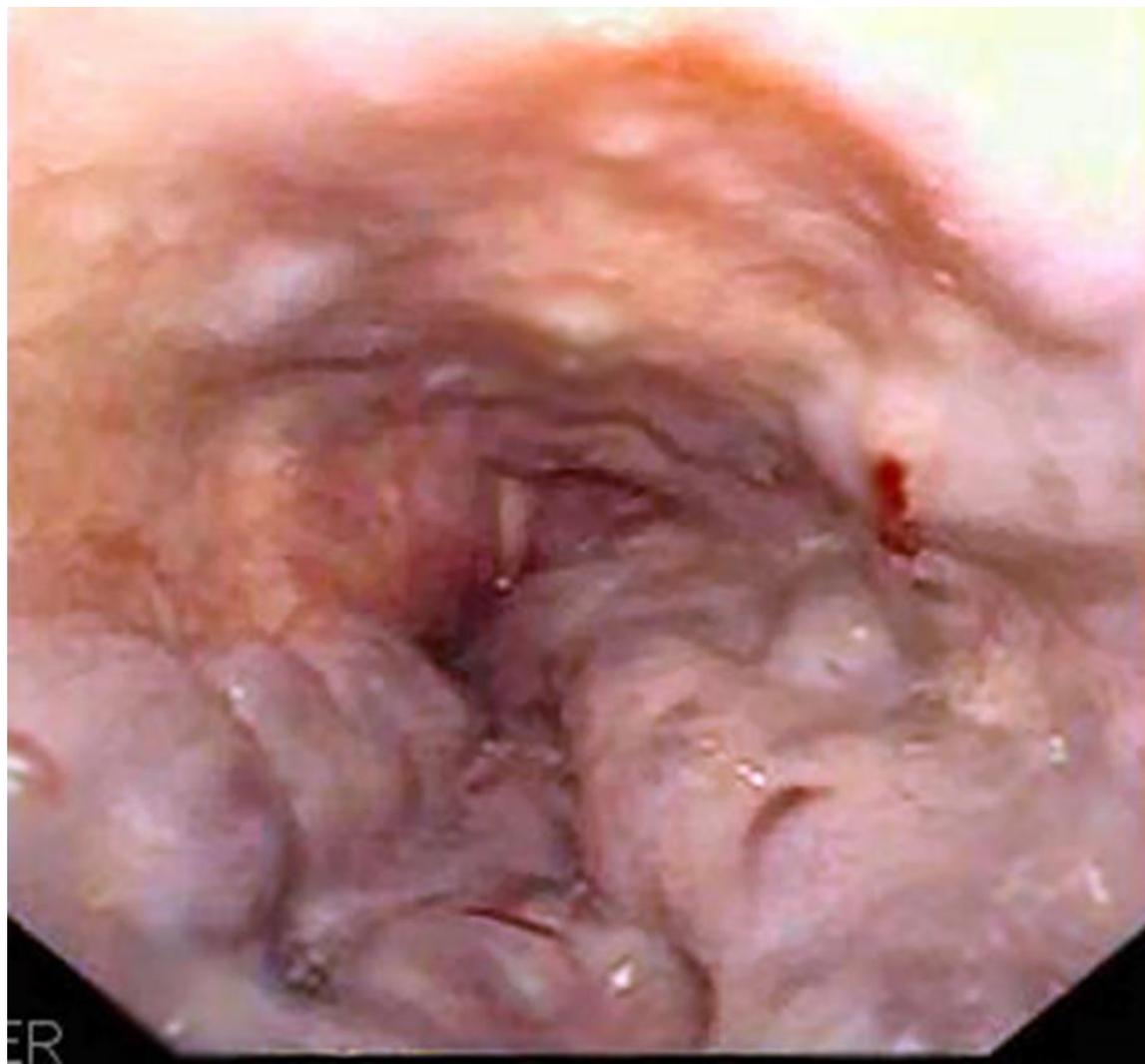
- Portal hypertension is defined as the elevation of the hepatic venous pressure gradient (HVPG) to  $>5$  mmHg
- Major complication if  $HVPG > 10$
- Portal hypertension is **caused by**:
  1. Increased intrahepatic resistance due to cirrhosis, regenerative nodules and microthrombi
  2. Increased splanchnic blood flow secondary to vasodilation

# Varices

# SCREENING FOR VARICES ?

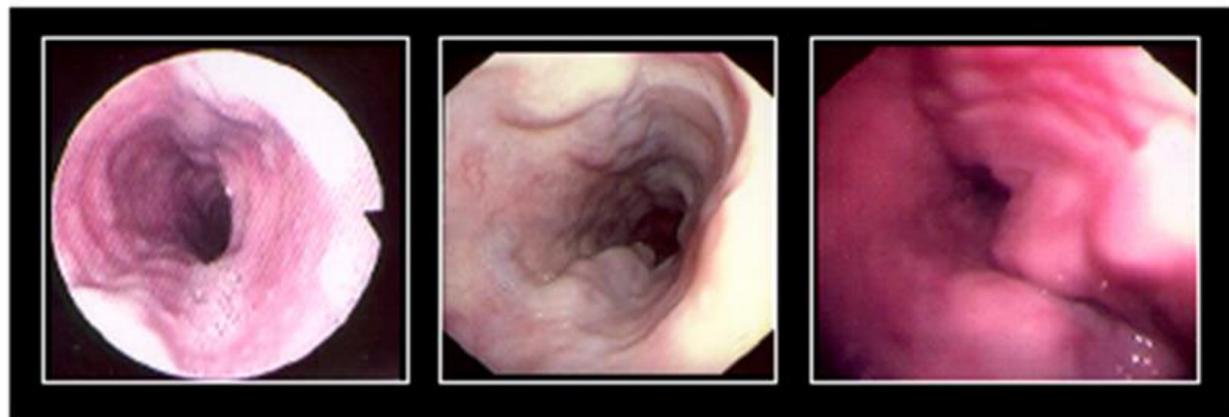
- All patient with cirrhosis
- You can avoid if:
  - Platelet count drops to  $<150,000$
  - and**
  - the liver stiffness increases to  $\geq 20$  kPa

UNC GI



ER

## Size classification of esophageal varices



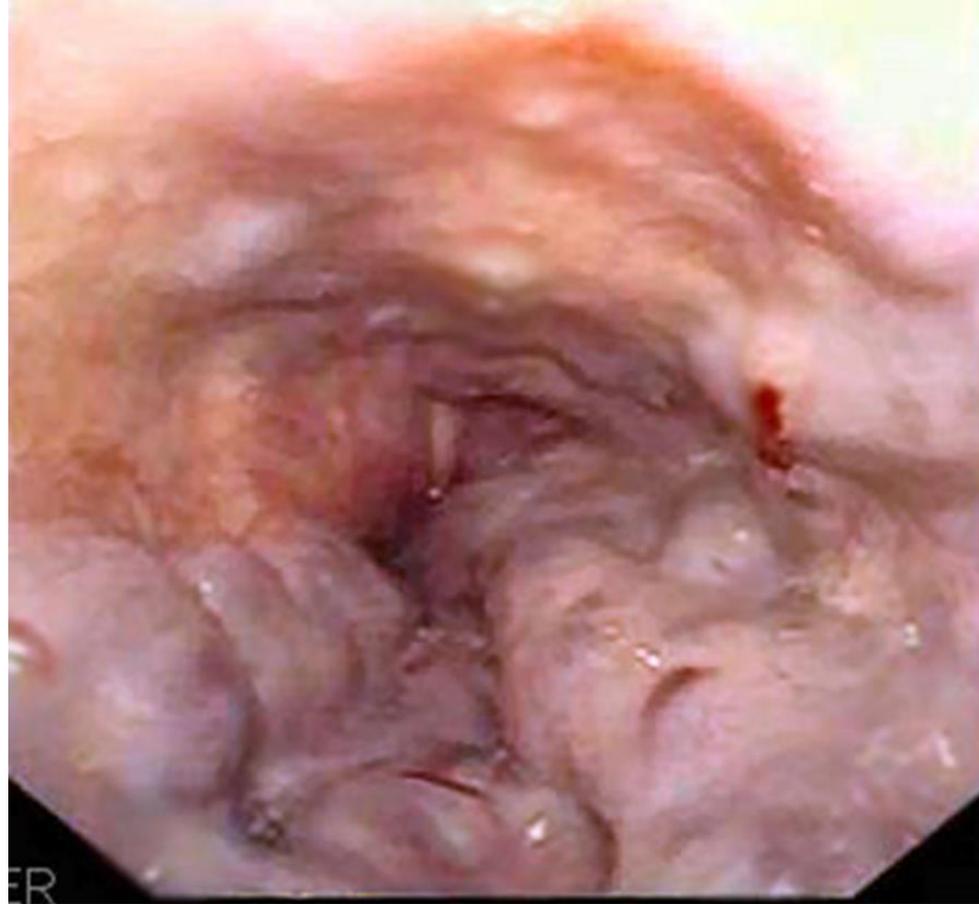
The size of varices, as illustrated in these endoscopic pictures, can be used to estimate the risk of variceal bleeding. The first panel shows small straight varices (F1), the second panel shows enlarged tortuous varices that occupy less than one-third of the lumen (F2), and the third panel shows large coil-shaped varices that occupy more than one-third of the lumen (F3).

---

*Courtesy of Arun Sanyal, MD.*

UpToDate®

Endoscopy shows this image, What is your next step ?



# We give prophylaxis to patients with:

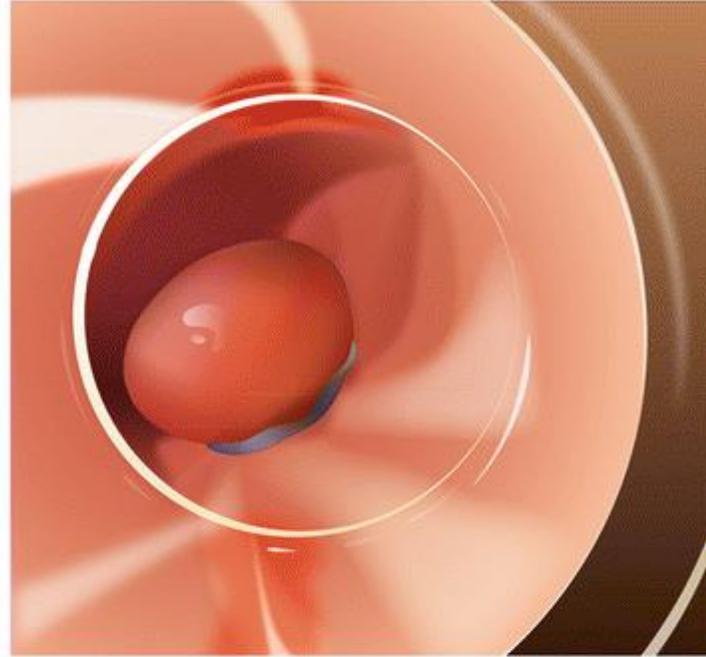
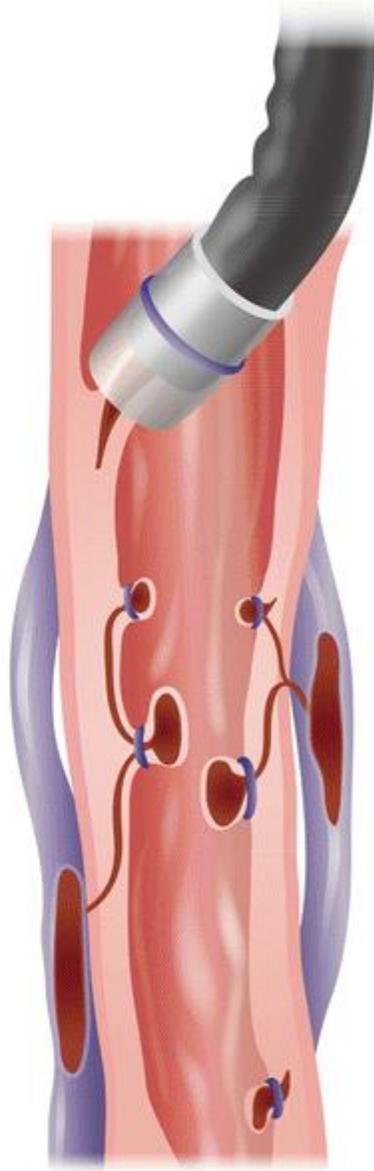
1. Small varices with red signs or Child B or C cirrhosis
2. Medium or large varices

# Primary prophylaxis

- Nonselective beta blockers:
  - Nadolol
  - propranolol

**OR**

- Endoscopic variceal ligation (EVL)



# CASE

- A 46-year-old man with a history of cirrhosis has referred to the emergency room due to hematemesis. What is your next steps ?

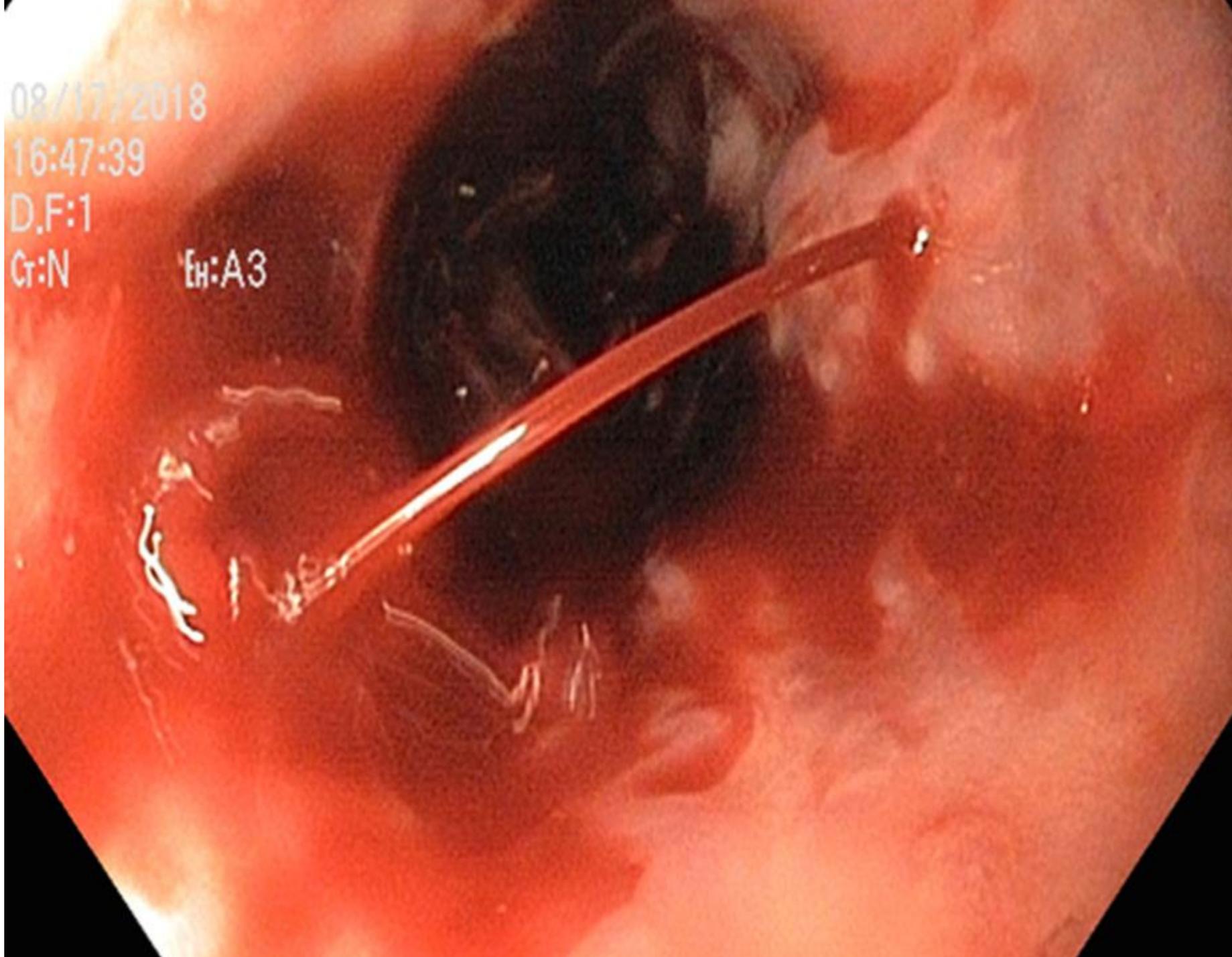
08/17/2018

16:47:39

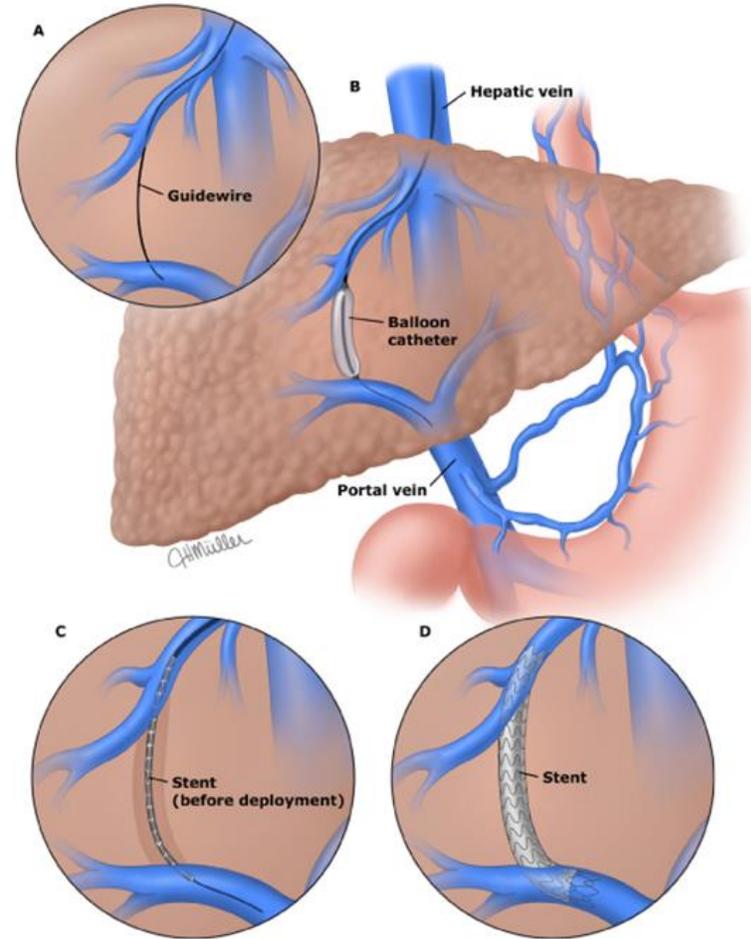
D.F:1

Ct:N

En:A3

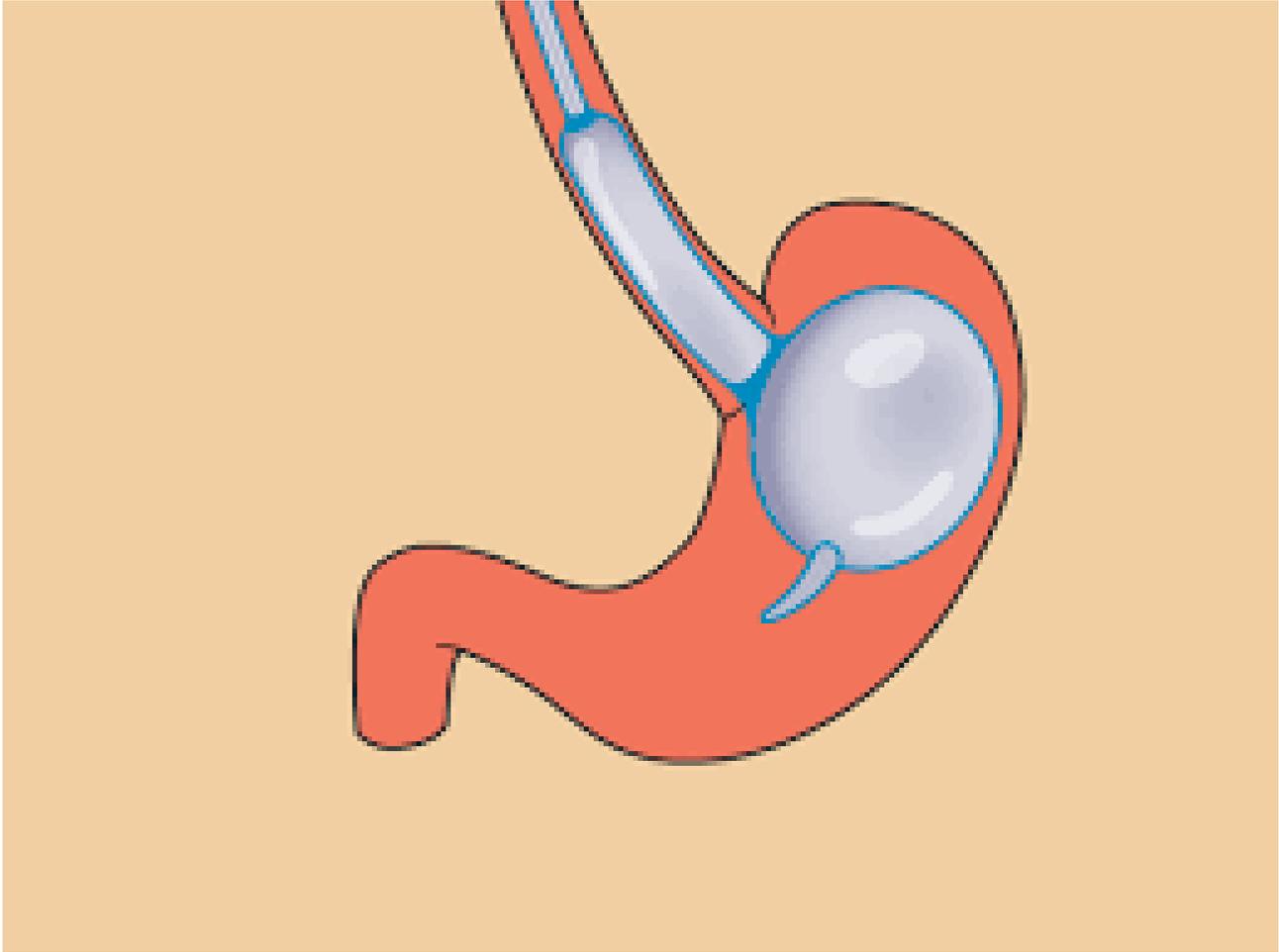


## Transjugular intrahepatic portosystemic shunt



A transjugular intrahepatic portosystemic shunt (TIPS) is created by passing a needle catheter via the transjugular route into the hepatic vein and wedging it there. The needle is then extruded and advanced through the liver parenchyma to the intrahepatic portion of the portal vein and a stent is placed between the portal and hepatic veins. A TIPS functions like side-to-side surgical portacaval shunt, but does not require general anesthesia or major surgery for placement. (A) Passage of a guidewire between the hepatic vein and the portal vein. (B) Inflation of a balloon catheter within the liver to dilate the tract between the hepatic vein and the portal vein. (C) Deployment of the stent. (D) Stent in its final position.



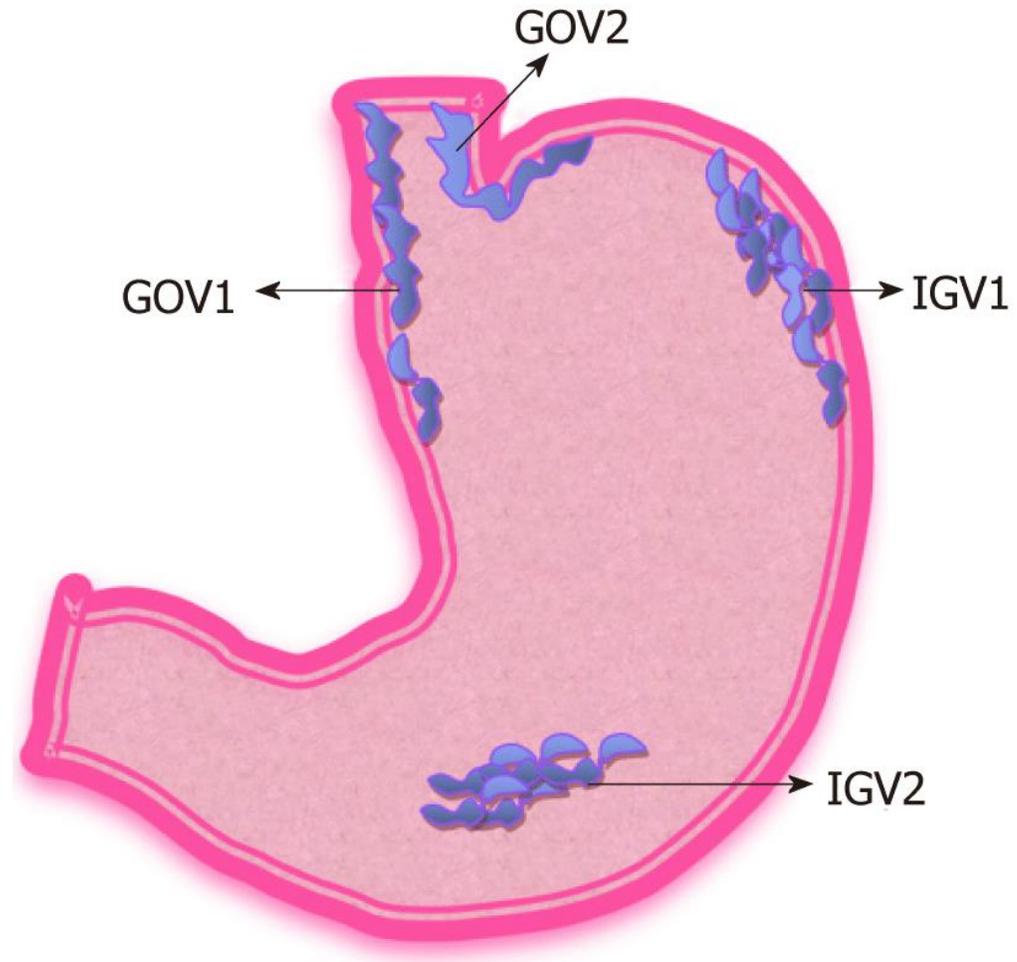


## Pulley Traction Device.



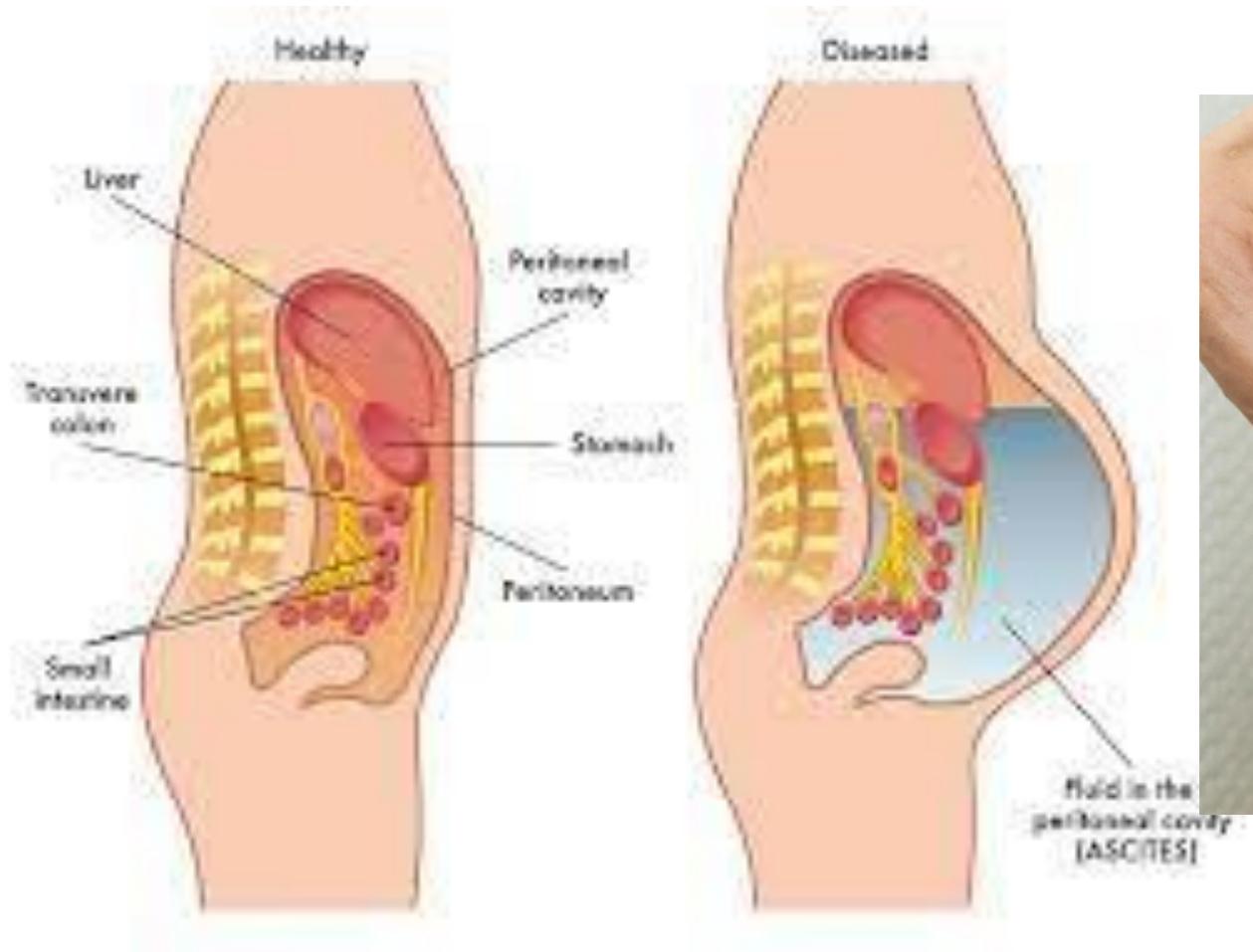
Copyright© [www.gastrotraining.com](http://www.gastrotraining.com). All rights reserved.

# Gastric varices



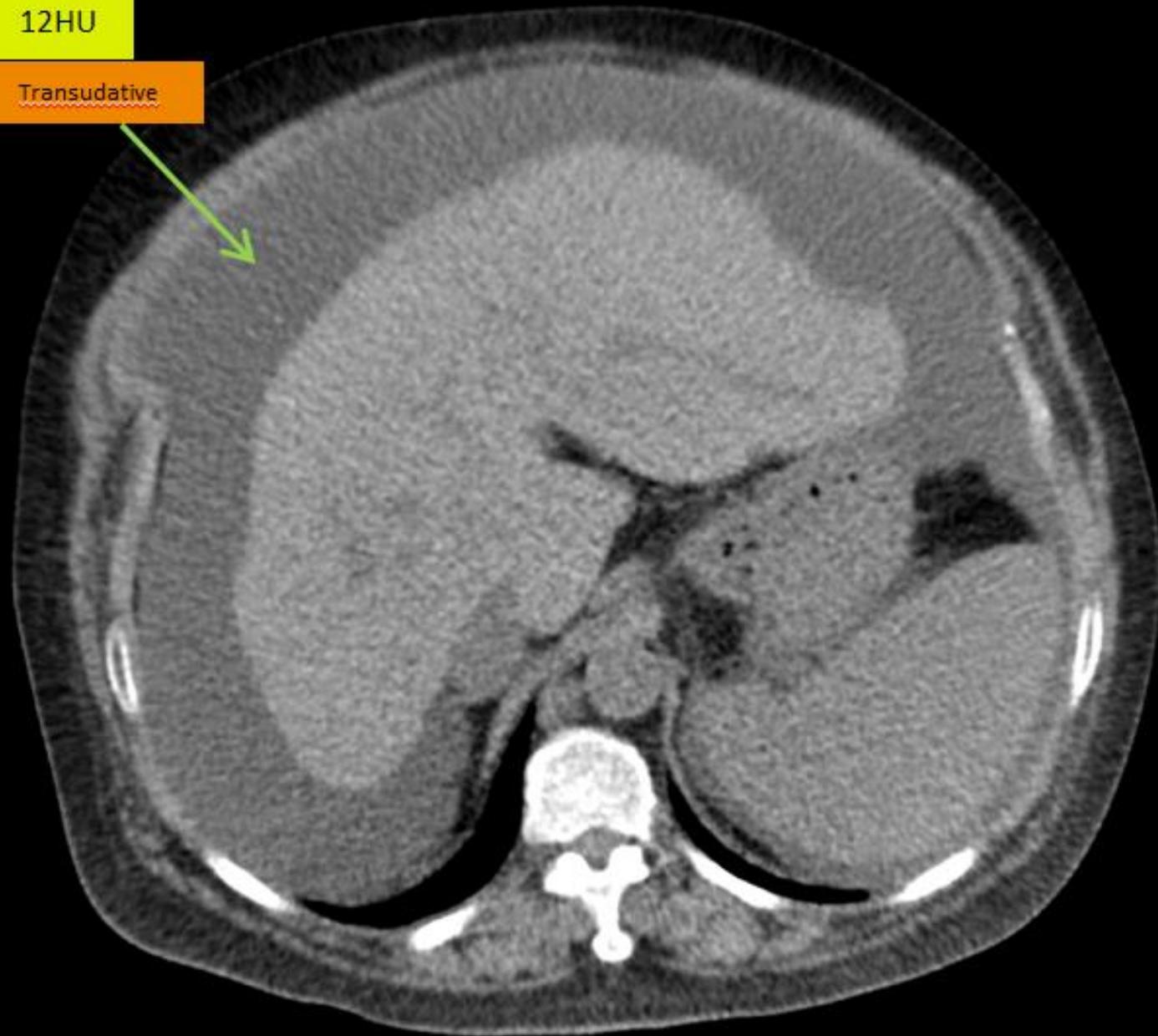
# Case

- A 46 yrs old man was admitted for ascites,
- Andominal distension +
- Andominal pain –
- Sono: Liver was coarse. Moderate free fluid was seen



12HU

Transudative



## Causes of ascites

<b>Cirrhosis</b>	81 percent
<b>Cancer</b>	10 percent
<b>Heart failure</b>	3 percent
<b>Tuberculosis</b>	2 percent
<b>Dialysis</b>	1 percent
<b>Pancreatic disease</b>	1 percent
<b>Other</b>	2 percent

*Data from: Runyon BA, Montano AA, Akriviadis EA, et al. Ann Intern Med 1992; 117:215.*

## Indications for abdominal paracentesis in a patient with ascites

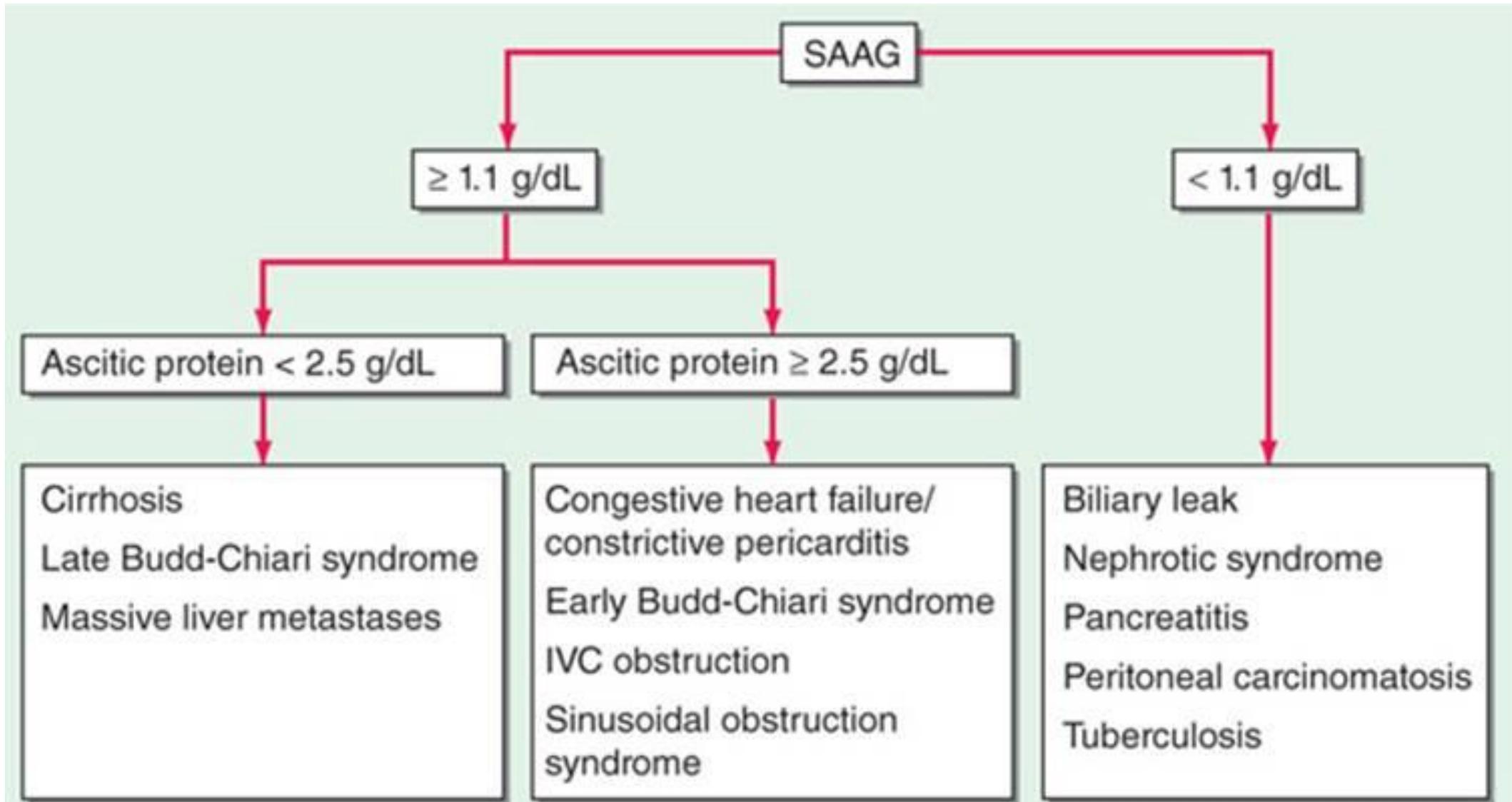
New onset ascites
At the time of each admission to the hospital
Clinical deterioration, either inpatient or outpatient
Fever
Abdominal pain
Abdominal tenderness
Mental status change
Ileus
Hypotension
Laboratory abnormalities that may indicate infection
Peripheral leukocytosis
Acidosis
Worsening of renal function
Gastrointestinal bleeding (a high risk time for infection)

*Reference: Runyon BA, AASLD. Introduction to the revised American Association for the Study of Liver Diseases Practice Guideline management of adult patients with ascites due to cirrhosis 2012. Hepatology 2013; 57:1651.*

## Tests performed on ascitic fluid

<b>Routine tests</b>
Cell count and differential
Albumin concentration
Total protein concentration
<b>Optional tests</b>
Culture in blood culture bottles
Glucose concentration
Lactate dehydrogenase concentration
Gram stain
Amylase concentration
<b>Unusual tests</b>
Tuberculosis smear and culture
Adenosine deaminase activity
Cytology
Triglyceride concentration
Bilirubin concentration
Serum pro-brain natriuretic peptide
Carcinoembryonic antigen (CEA) concentration
Alkaline phosphatase concentration

# Algorithm for the diagnosis of ascites according to the serum-ascites albumin gradient (SAAG)



## Classification of ascites by the serum-to-ascites albumin gradient

High albumin gradient (SAAG $\geq$ 1.1 g/dL)
Cirrhosis
Alcoholic hepatitis
Heart failure
Massive hepatic metastases
Heart failure/constrictive pericarditis
Budd-Chiari syndrome
Portal vein thrombosis
Idiopathic portal fibrosis
Low albumin gradient (SAAG $<$ 1.1 g/dL)
Peritoneal carcinomatosis
Peritoneal tuberculosis
Pancreatitis
Serositis
Nephrotic syndrome

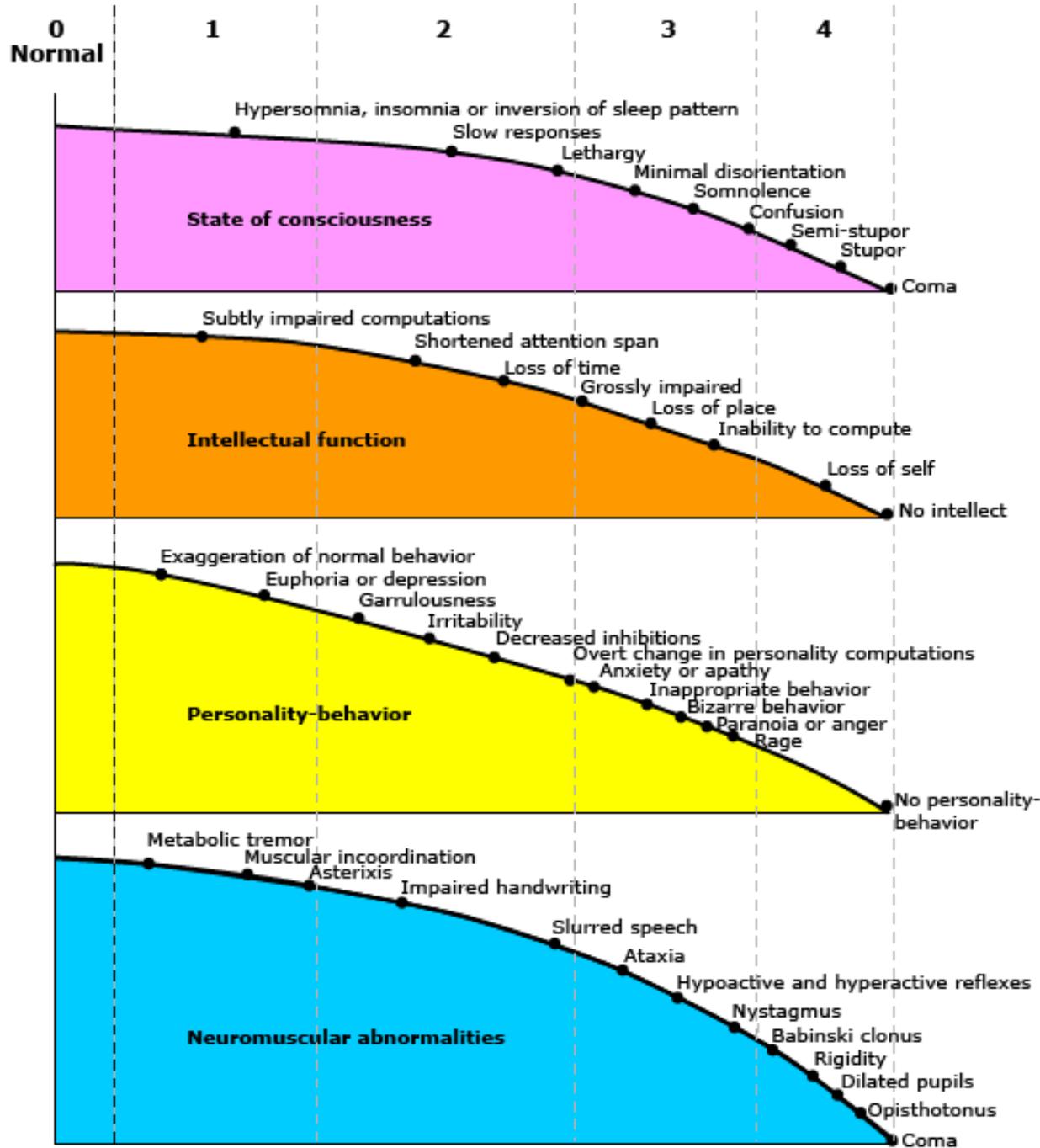
# Case

- A 53 years old man with Hx of cirrhosis was admitted for altered mental status. He was confused.
- BP: 90/60 HR:100 RR: 25 BT: 37.7
- In P/E abdomen was prominent with Mild tenderness but no guarding or rebound tenderness . What is your DD ?

# HEPATIC ENCEPHALOPATHY

- A **serious complication** occurring in the presence of **liver failure**
- Broadly defined as an **alteration in mental status** and **cognitive function**
- **Gut-derived neurotoxins** that are **not removed by the liver** because of **vascular shunting** and **decreased hepatic mass** **reach the brain** and cause the symptoms known as hepatic encephalopathy

### Stages of hepatic encephalopathy



## Precipitants of hepatic encephalopathy in patients with cirrhosis

<b>Drugs</b>
Benzodiazepines
Nonbenzodiazepine hypnotics (eg, zolpidem)
Narcotics
Alcohol
<b>Increased ammonia production, absorption or entry into the brain</b>
Excess dietary intake of protein
Gastrointestinal bleeding
Infection
Electrolyte disturbances such as hypokalemia
Constipation
Metabolic alkalosis
<b>Dehydration</b>
Vomiting
Diarrhea
Hemorrhage
Diuretics
Large volume paracentesis
<b>Portosystemic shunting</b>
Radiographic or surgically placed shunts
Spontaneous shunts
<b>Vascular occlusion</b>
Hepatic vein thrombosis
Portal vein thrombosis
<b>Primary hepatocellular carcinoma</b>

## Efficacy of treatments of hepatic encephalopathy

Rationale	Controlled studies	
	vs lactulose	vs placebo
<b>Ammonia hypothesis</b>		
<b>Decrease in ammoniagenic substrates</b>		
Enemas with lactulose		+
Restriction of dietary protein intake		?
<b>Inhibition of ammonia production</b>		
Antibiotics		
Neomycin, paromomycin, metronidazole	=	ND
Rifaximin	=	+
Vancomycin	=/+	ND
Disaccharides		
Lactulose		?
Lactitol	=	ND
Lactose in lactase deficiency		+
Modification of colonic flora		
Lactobacillus SF 68	=	ND
Correction of hypokalemia	ND	ND
<b>Metabolic ammonia removal</b>		
Ornithine-aspartate		+
Benzoate	=	ND
<b>False neurotransmitter hypothesis</b>		
<b>Branched chain amino acid supplementation</b>		
Modified amino acid solutions (FO80 type)	=	±
"COMA" solutions	ND	ND
Dietary BCAA supplementation		+
<b>Increased dopamine</b>		
L-DOPA, bromocriptine		-
<b>GABA hypothesis</b>		
Flumazenil		+
<b>Other</b>		
Zinc		±

+: superior to control; =: equal to lactulose; -: no effect; ±: conflicting results; ND: not done.

# Spontaneous bacterial peritonitis (SBP)

## Signs and symptoms at the time of diagnosis in 489 patients with spontaneous bacterial peritonitis

Clinical feature	Percent with sign or symptom
Fever	69
Abdominal pain	59
Altered mental status	54
Abdominal tenderness	49
Diarrhea	32
Paralytic ileus	30
Hypotension	21
Hypothermia	17

Data from McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders Company, Philadelphia 1994, p.455.

## **Bacteria isolated from ascitic fluid in 519 patients with spontaneous bacterial peritonitis**

<b>Organism</b>	<b>Percent of isolates</b>
Escherichia coli	43
Klebsiella pneumoniae	11
Streptococcus pneumoniae	9
Other streptococcal species	19
Enterobacteriaceae	4
Staphylococcus	3
Pseudomonas	1
Miscellaneous*	10

\*In some regions of the world, such as Korea, *Aeromonas hydrophila* infection is an important cause of SBP, particularly in warm weather months. Affected patients commonly also have diarrhea. [Choi JP, et al. Clin Infect Dis 2008; 47:67.]

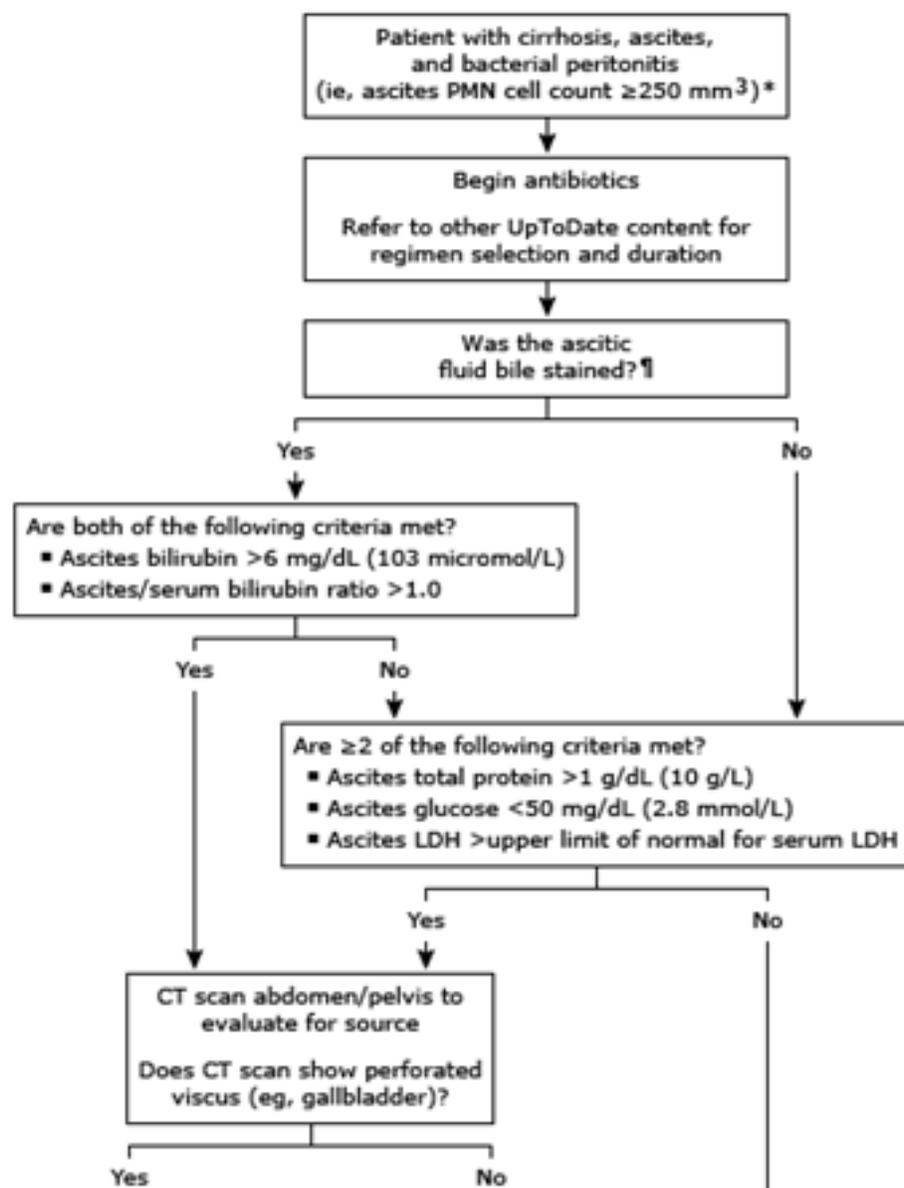
---

*Data from McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders, Philadelphia 1995. p.455.*

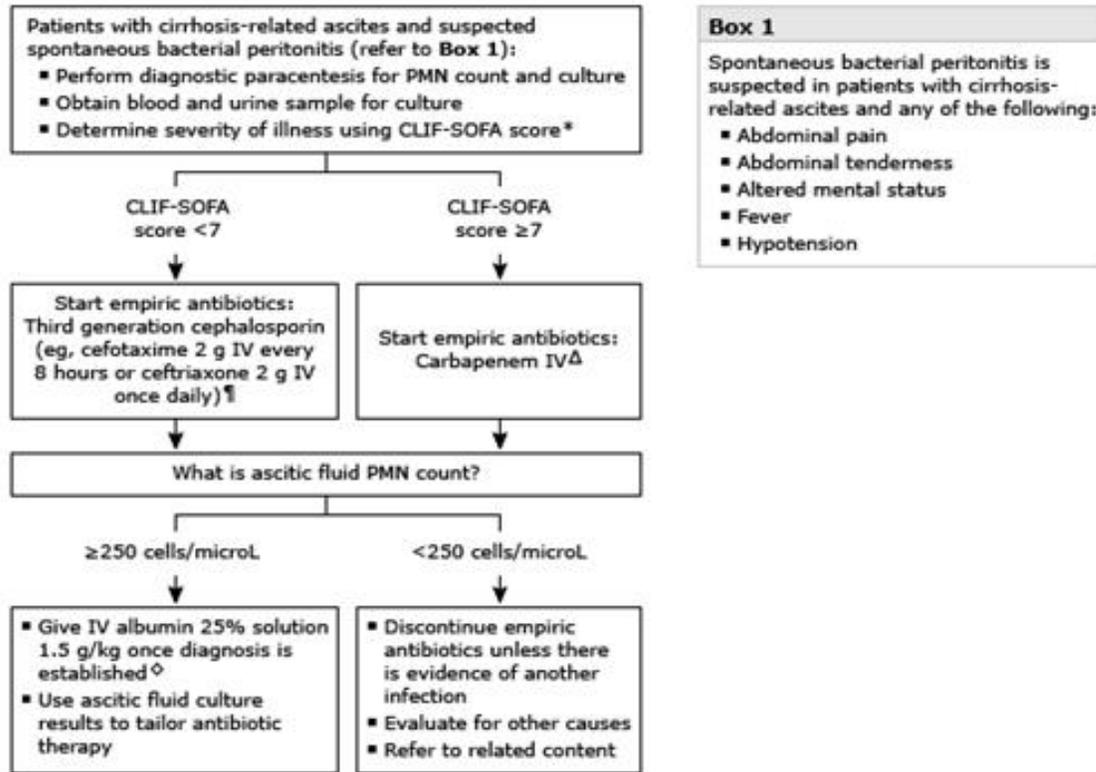
## Tests performed on ascitic fluid

<b>Routine tests</b>
Cell count and differential
Albumin concentration
Total protein concentration
<b>Optional tests</b>
Culture in blood culture bottles
Glucose concentration
Lactate dehydrogenase concentration
Gram stain
Amylase concentration
<b>Unusual tests</b>
Tuberculosis smear and culture
Adenosine deaminase activity
Cytology
Triglyceride concentration
Bilirubin concentration
Serum pro-brain natriuretic peptide
Carcinoembryonic antigen (CEA) concentration
Alkaline phosphatase concentration

## Distinguishing spontaneous from secondary bacterial peritonitis



## Evaluation and initial management for adult patients with suspected spontaneous bacterial peritonitis



Refer to content on management of spontaneous bacterial peritonitis.

# Secondary Bacterial Peritonitis?

- less than 5% of SBP
- 100% mortality if not treated
- Criteria:
  1. Total protein >1 g/dL (10 g/L)
  2. Glucose <50 mg/dL (2.8 mmol/L)
  3. LDH >the upper limit of normal for serum

# Antibiotic prophylaxis

- ●Patients with cirrhosis and gastrointestinal bleeding.
- ●Patients who have had one or more episodes of SBP.
- ●Patients with cirrhosis and ascites if the ascitic fluid protein is  $<1.5$  g/dL (15 g/L) along with either impaired renal function or liver failure. Impaired renal function is defined as a creatinine  $\geq 1.2$  mg/dL (106 micromol/L), a blood urea nitrogen level  $\geq 25$  mg/dL (8.9 mmol/L), or a serum sodium  $\leq 130$  mEq/L (130 mmol/L). Liver failure is defined as a Child-Pugh score  $\geq 9$  and a bilirubin  $\geq 3$  mg/dL (51 micromol/L).
- patients with cirrhosis who are hospitalized for other reasons and have an ascitic protein concentration of less than 1 g/dL (10 g/L)

# Severity of cirrhosis

- Clinicians need to differentiate between:
  1. **Compensated** cirrhosis
  2. **Decompensated** cirrhosis when develop:
    - Ascites
    - Hepatic encephalopathy
    - Variceal bleeding
- **Decompensated cirrhosis** should be considered for **liver transplantation**, particularly if the decompensations are poorly controlled.

# Case

- A 65 yrs old was admitted for Orthopedic department for femoral fracture. Gastroenterology consultation was requested for preoperative evaluation of a patient for elevated liver enzymes,
- Lab: AST: 68 ALT: 54 ALP: 357 Bil: 2.3
-

# HOW SEVERE IS THE CIRRHOSIS?

## 1. Child-Pugh system:

- Class:
  - A = Compensated
  - B
  - C = Decompensated

## 2. Model for End-Stage Liver Disease (MELD) score:

- Score: 6 to 40

# Child pugh score

Parameter	Numerical score		
	1	2	3
Ascites	None	Slight	Moderate to severe
Encephalopathy	None	Slight to moderate	Moderate to severe
Bilirubin (mg/dL)	< 2.0	2-3	> 3.0
Albumin (g/dL)	> 3.5	2.8-3.5	< 2.8
Prothrombin time (prolonged in seconds)	1-3 s	4-6 s	> 6.0

Child's Pugh Class A = 5-6 points; Child's Pugh Class B = 7-9 points;  
Child's Pugh Class C = 10-15 points.

# MELD Score (Model For End-Stage Liver Disease) (12 and older) ☆

Stratifies severity of end-stage liver disease, for transplant planning.

## INSTRUCTIONS

Use in patients  $\geq 12$  years old. Note: As of January 2016, calculation of the MELD has changed. It now includes serum sodium level. See [OPTN's announcement](#).

When to Use ▾

Pearls/Pitfalls ▾

Why Use ▾

Dialysis at least twice in the past week  
Or [CVVHD](#) for  $\geq 24$  hours in the past week

No

Yes

Creatinine

Cr  $> 4.0$  mg/dL is automatically assigned a value of 4.0

Norm: 0.7 - 1.3

mg/dL ⇌

Bilirubin

Norm: 0.3 - 1.9

mg/dL ⇌

INR

Norm: 0.8 - 1.2

Sodium

Norm: 136 - 145

mEq/L ⇌

**Result:**

Please fill out required fields.

# Vaccination

- Patients with cirrhosis are typically vaccinated against:
  1. Hepatitis A
  2. Hepatitis B
  3. Pneumococcal vaccine
  4. Influenza vaccine (yearly)

# Screening

- Screening for varices
  - Patients with cirrhosis should undergo an **upper endoscopy** to look for varices.
- Screening for hepatocellular carcinoma
  - Patients with cirrhosis usually undergo regularly screening for HCC with a periodic **ultrasound** examination and **blood tests**

## ■ Identifying, targeting, and banding esophageal varices

"Esophageal varices form as a result of increased portal pressure, the product of increased portal venous inflow and resistance to outflow from the portal venous system. Portal hypertension is a major complication of chronic liver disease. In cirrhosis, architectural distortion of the liver causes an increase in the intrahepatic vascular resistance."

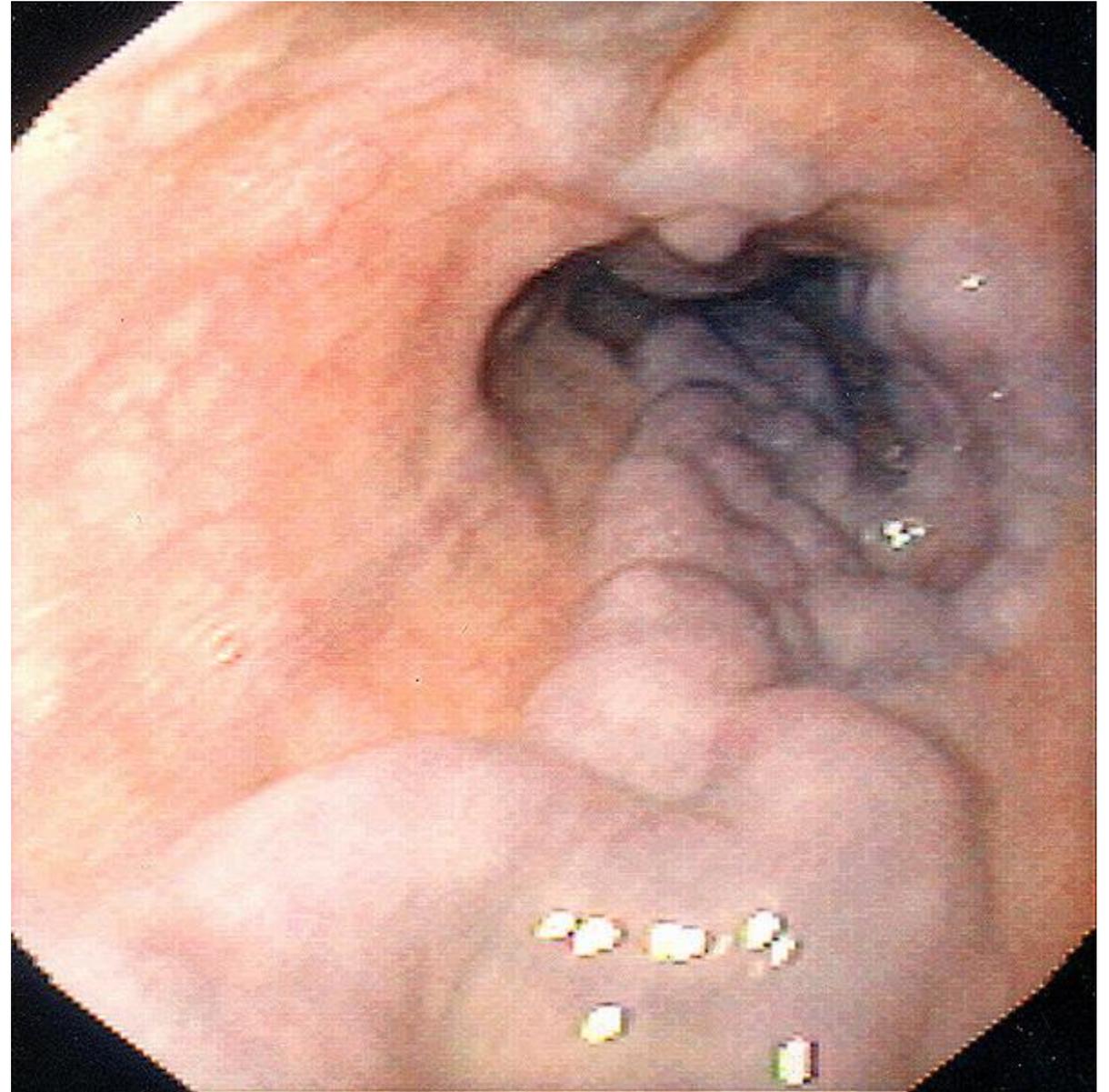
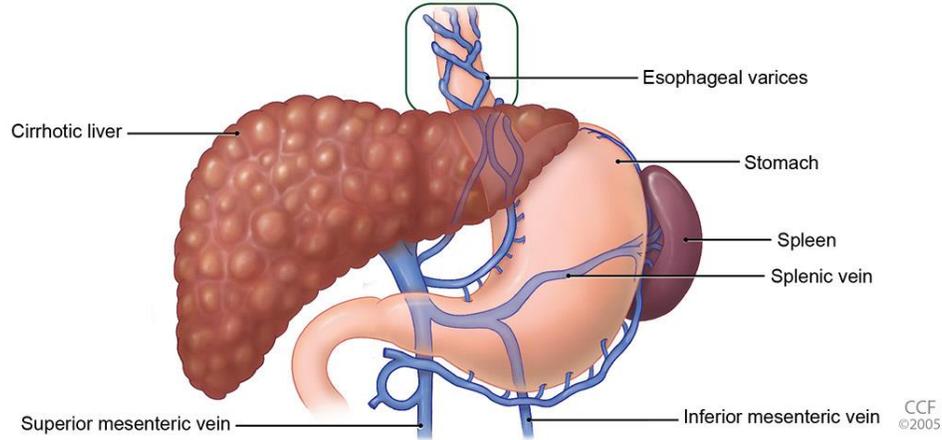
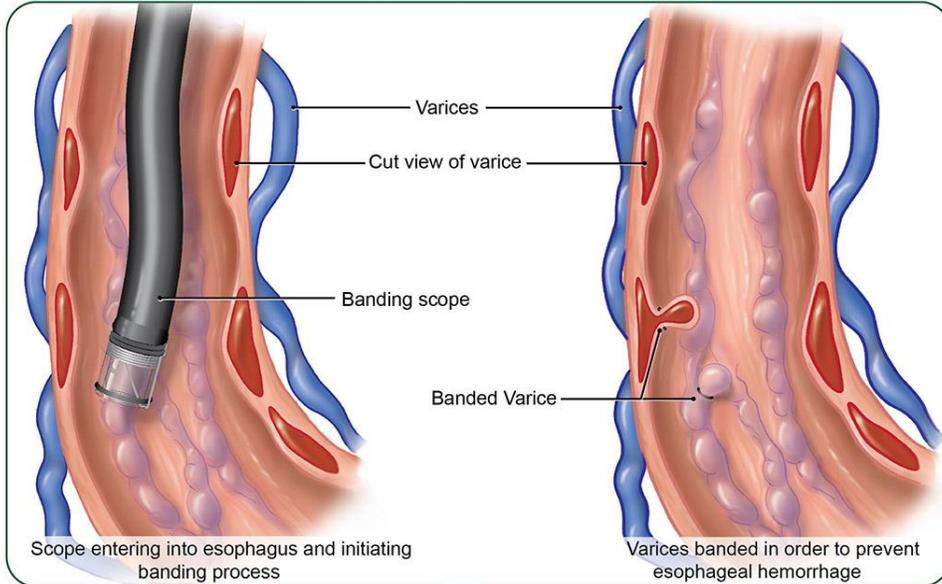
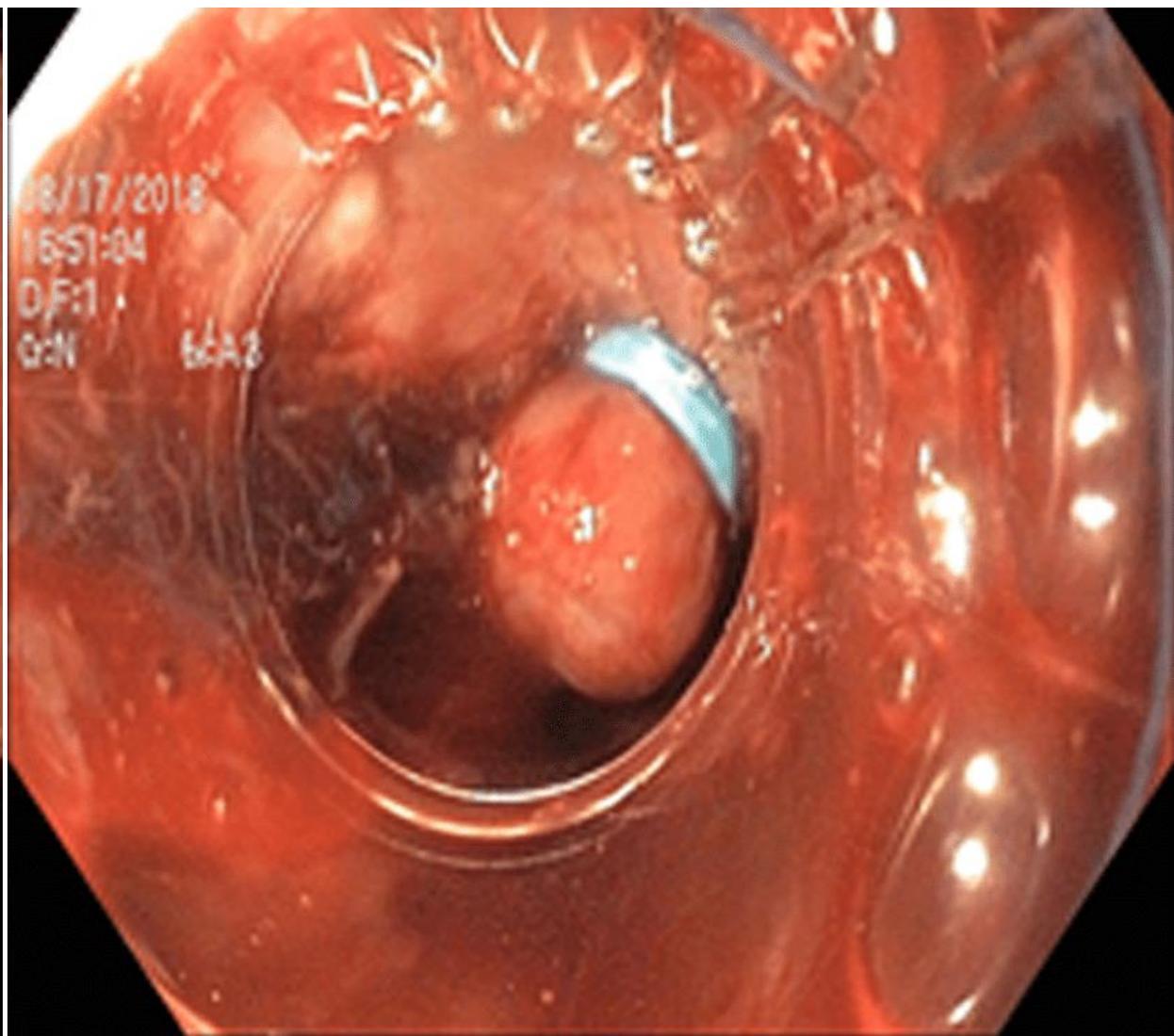
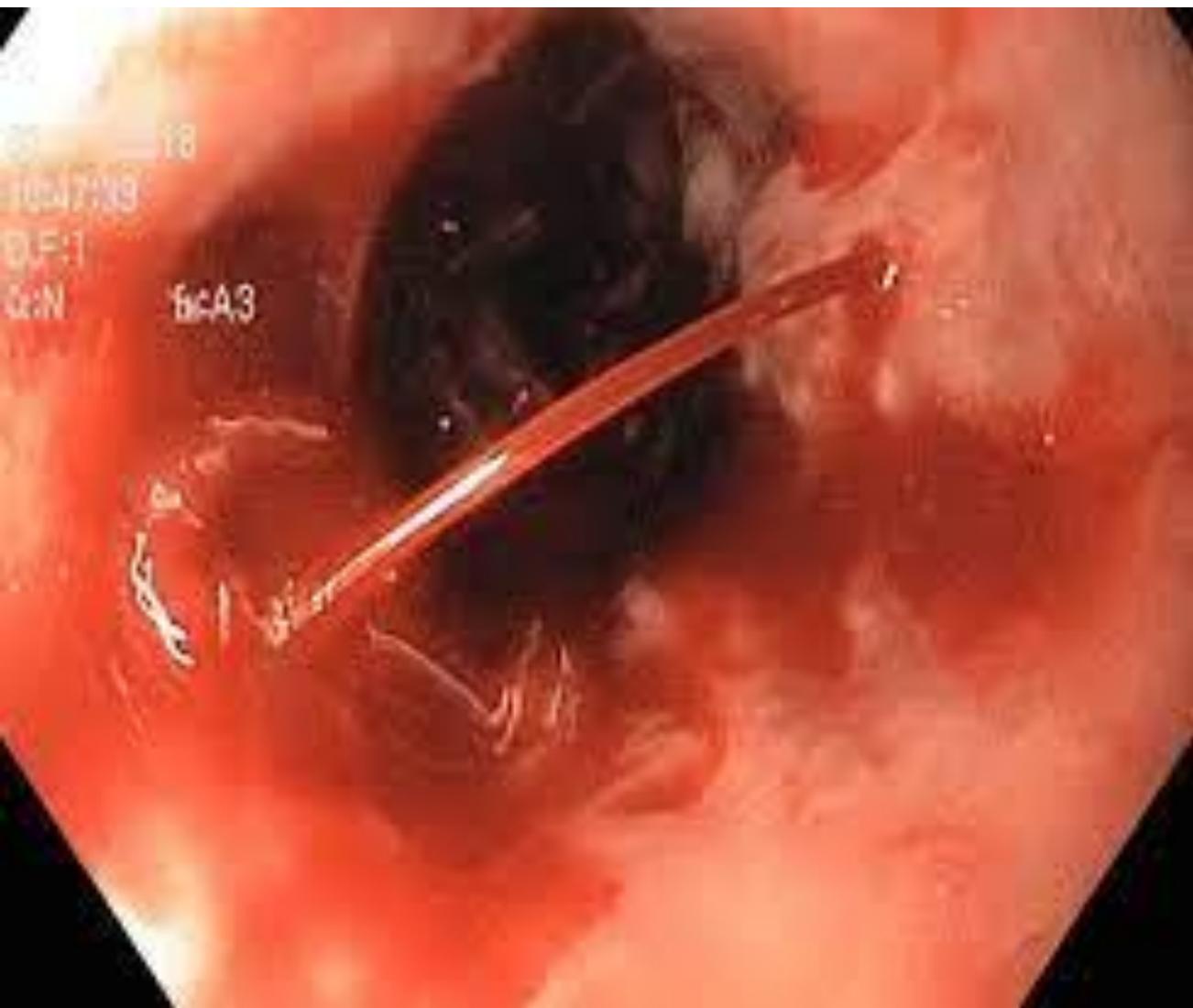
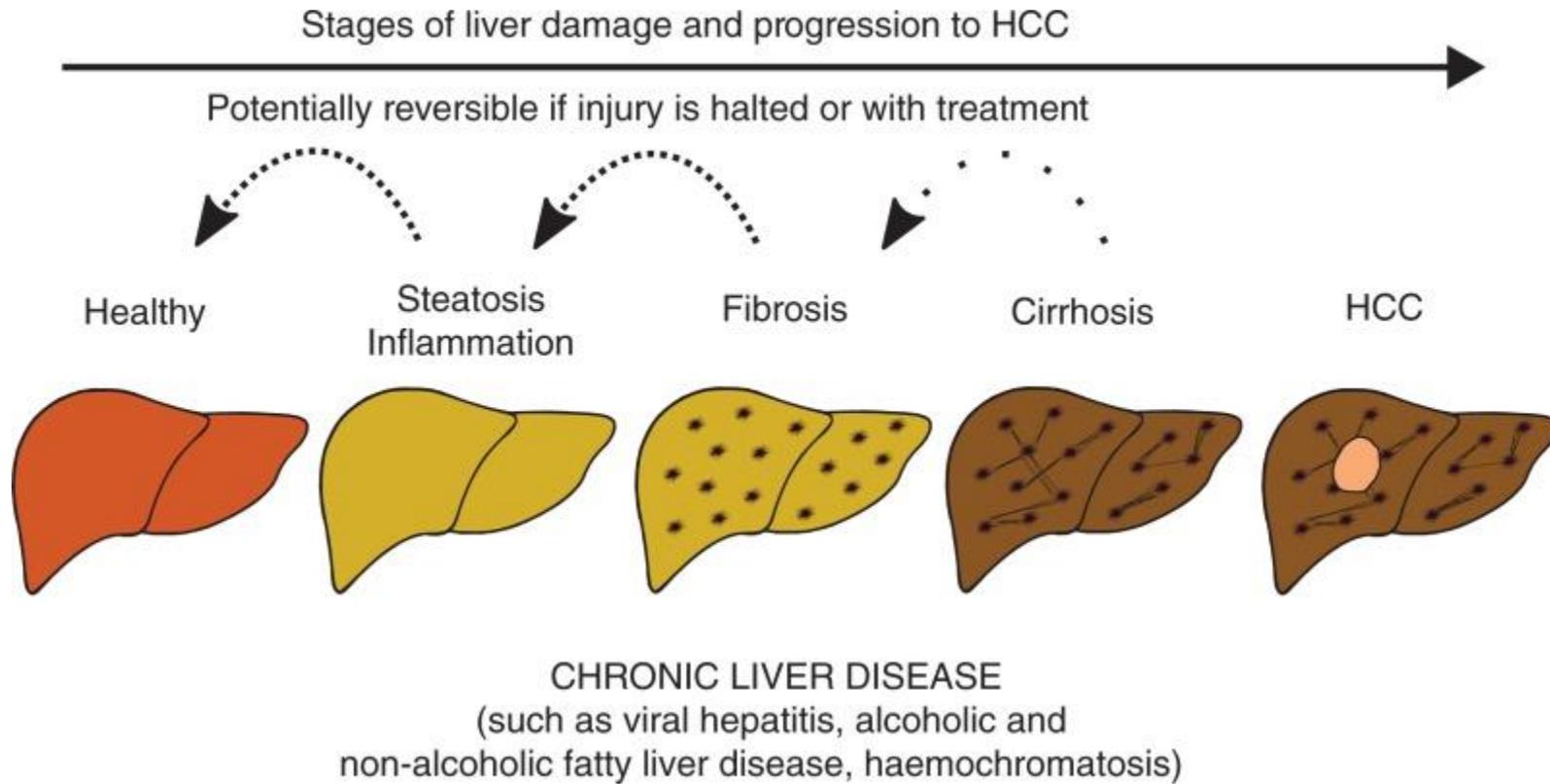


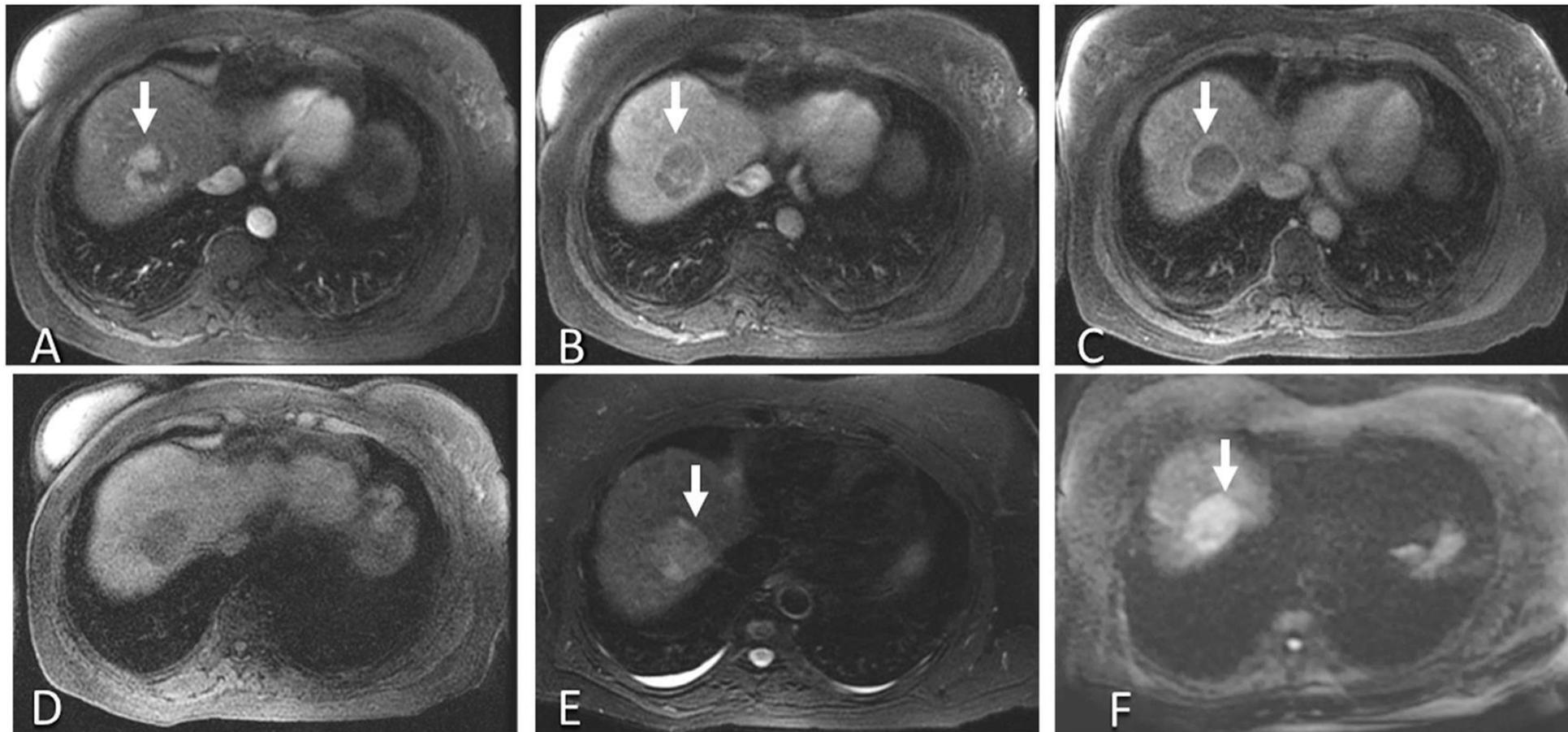
FIGURE 1

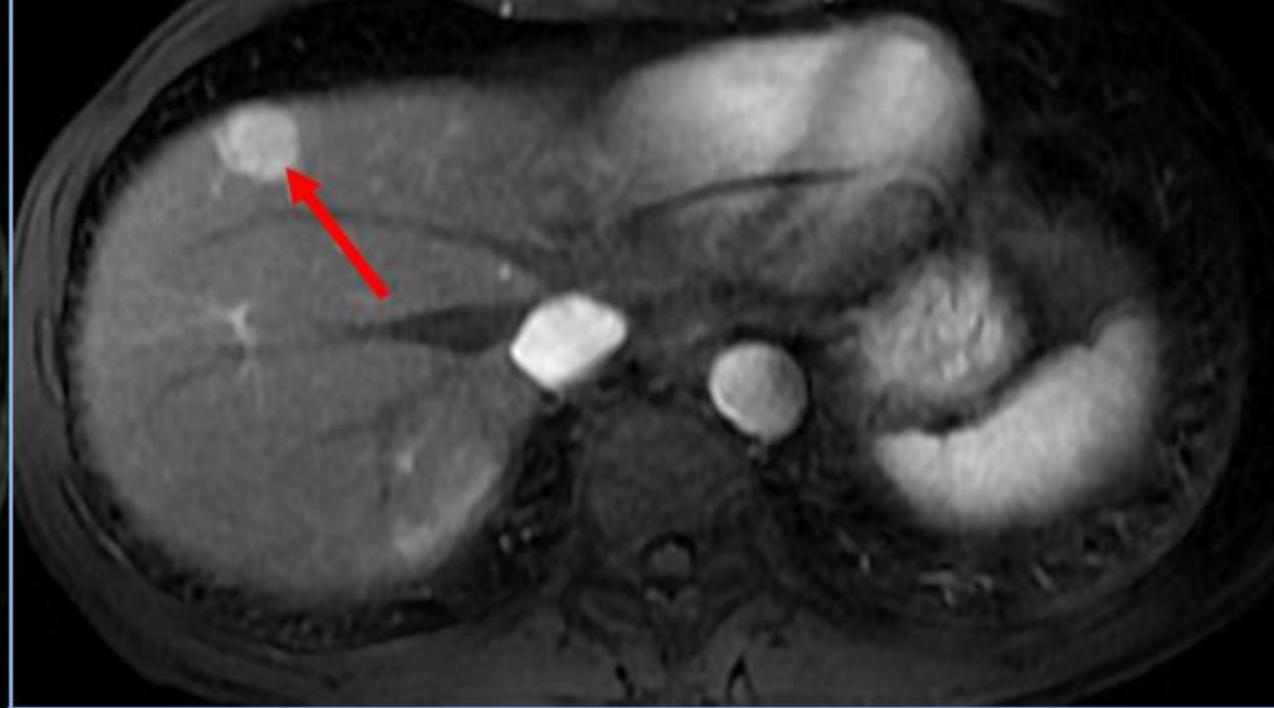


# HCC



# HCC in dynamic liver MRI





# Nutrition

- Patients with advanced liver disease are **commonly malnourished** because:
  - Poor dietary intake
  - Alterations in gut nutrient absorption
  - Alterations in protein metabolism
- **Malnutrition = increased mortality**
- It is important to **maintain nutritional status** with adequate calories and consumption of nutrient-rich foods

# Dietary advice

- **General recommendations** include:
  - Multiple small meals including a late evening snack
  - Total calories of 25–30 kcal per kg of ideal body weight per day
  - Protein 1.2–1.5 g/kg of ideal body weight per day
- Salt restriction for patients who tend to accumulate fluid
- Water restriction if severe hyponatremia (Na <123 or <125)

# Exercise

- Exercise is generally **safe for** patients with **early stage** of cirrhosis
- However, exercise may **increase the risk of variceal bleeding** in patients with **advanced disease** (such as those who have ascites or varices).  
(**Varices Screenig** then **ligation** then exercise)