

# Approach to Ascites

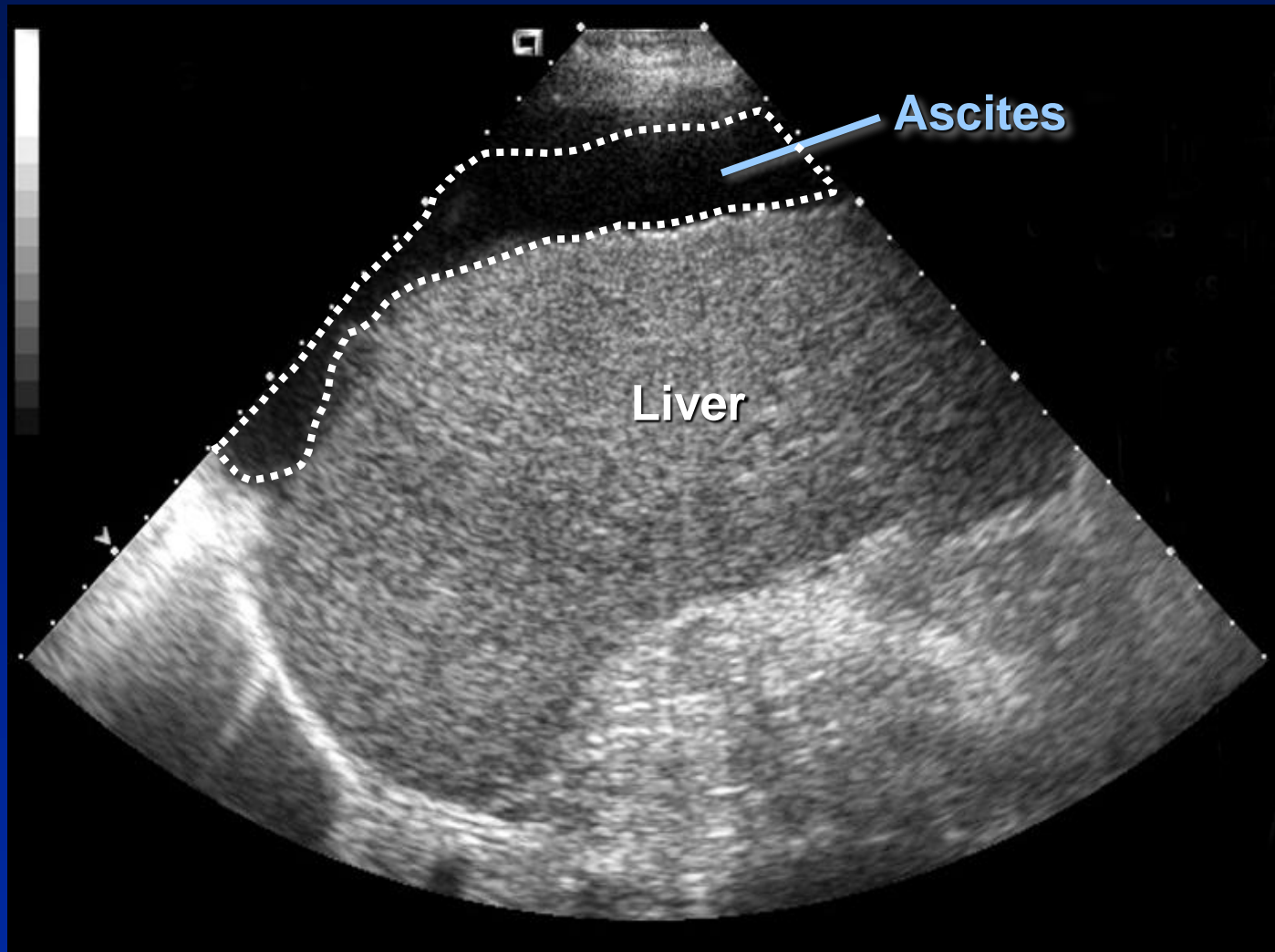
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Division of Hepatology,  
University of Miami.

- 62 year old man referred with abdominal distension.
- Remote icteric illness during college
- Describes himself as social drinker

- P/E mild muscle wasting, BP 110/70, Pulse 90/minute, afebrile
- Mild flank distension, diminished liver span with splenic dullness ? Shifting dullness, no fluid wave

- Initial Labs: Bilirubin 1.9 mgs/dl, AST 70, ALT 23, alk phos 135, platelet count 110 k, INR 1.2
- Ultrasound performed

# Ultrasound is the Most Sensitive Method to Detect Ascites



# Ascites

Initial workup

# Diagnostic Paracentesis

## Indications

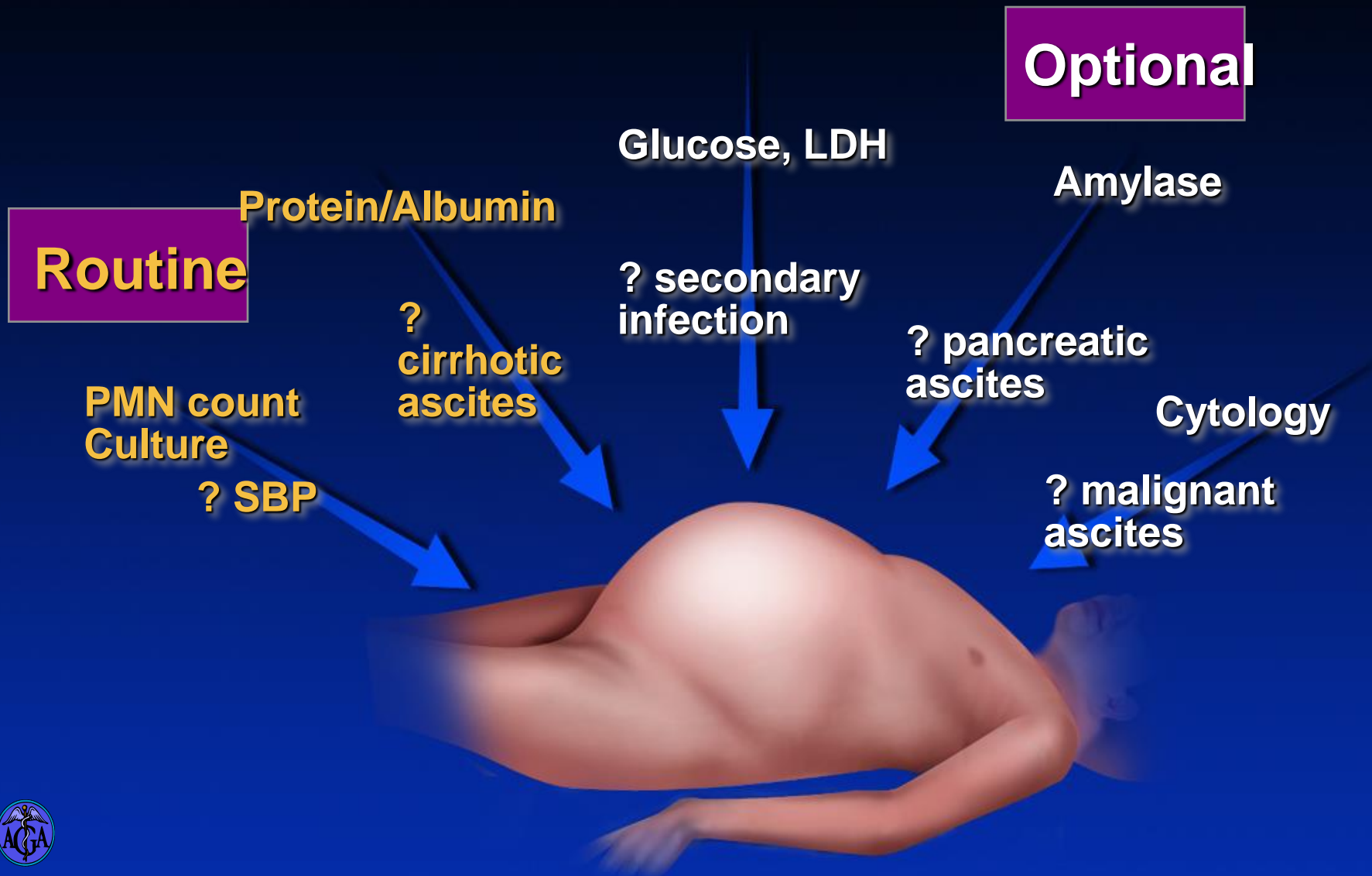
- New-onset ascites
- Admission to hospital
- Symptoms/signs of SBP
- Renal dysfunction
- Unexplained encephalopathy

## Contraindication

- <sup>S</sup>None



# Initial Workup of Ascites Diagnostic Paracentesis

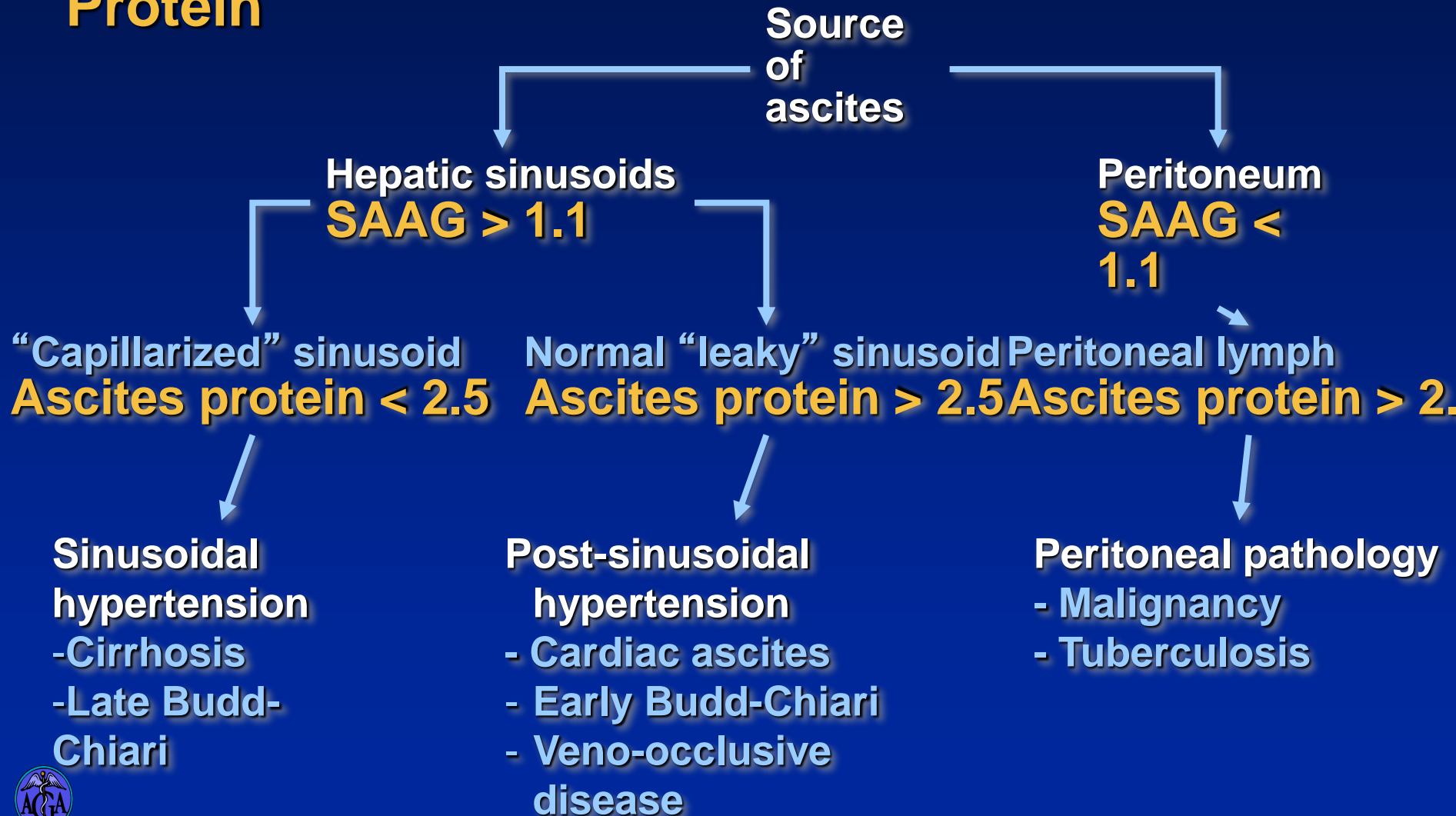




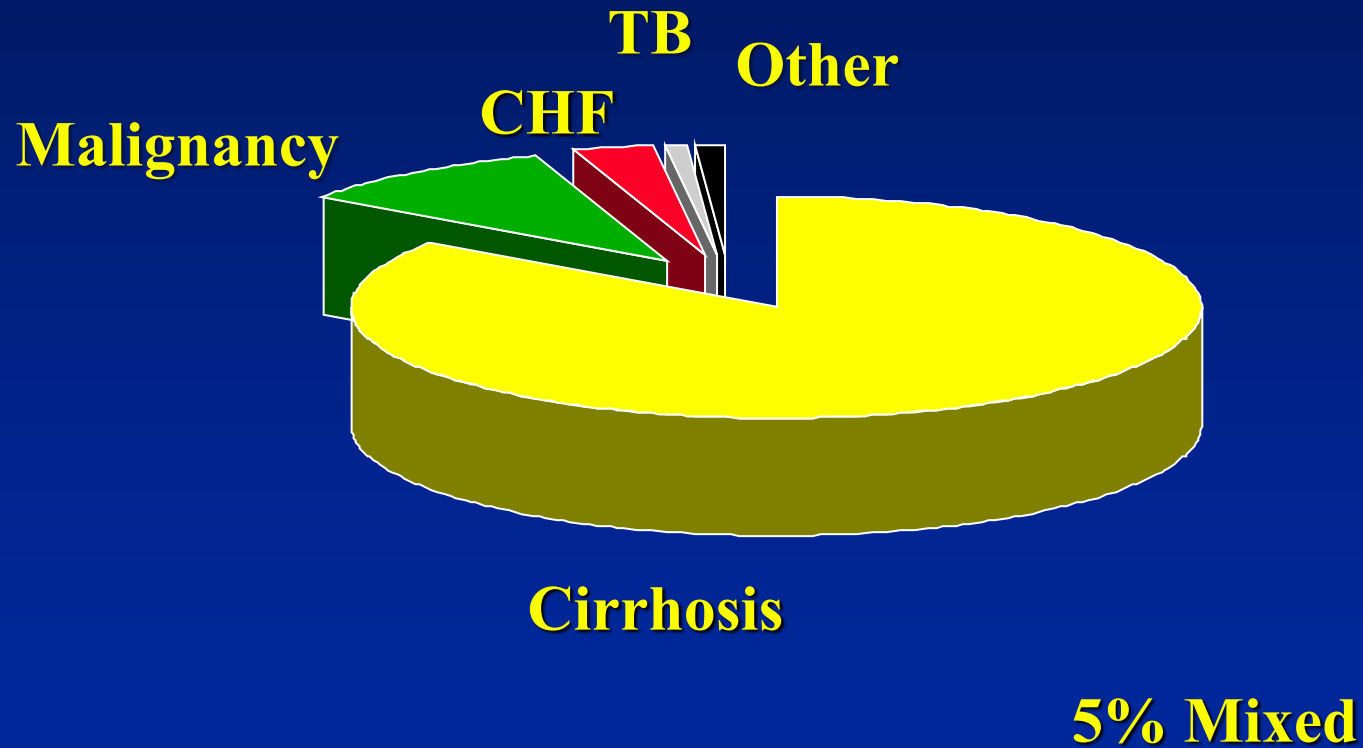
# Ascites Fluid Analysis: Mandatory Tests

- Cell count
  - WBC & RBC
  - Purple top tube
- Serum albumin - ascites albumin gradient (SAAG)
  - Terms exudate & transudate
    - Should no longer be used
    - Apply to only pleural effusions
- Cultures
  - 10-20 ml in blood culture bottles

# Ascites Can Be Characterized by Serum-Ascites Albumin Gradient (SAAG) and Ascites Protein



# Etiology of Ascites



# Ascites Fluid Analysis: Optional Tests

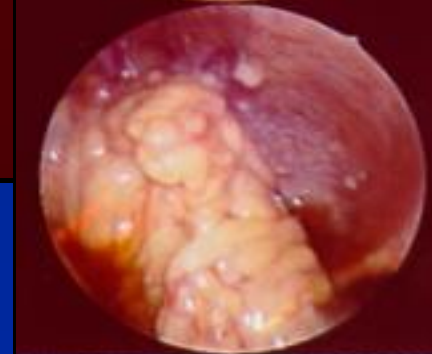
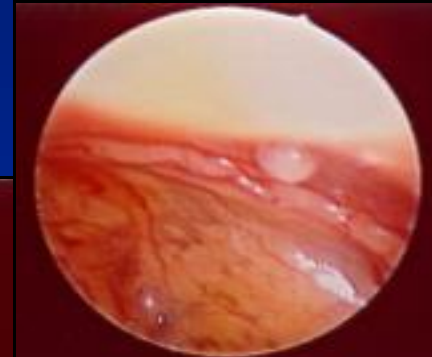
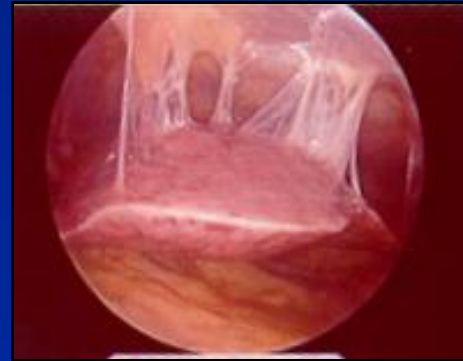
- Infected ascites
  - Total protein, LDH & glucose
  - Gram stain
    - To R/O free perforation of the gut
    - Not for SBP (10% sensitive)
- Milky ascites
  - TG > 200 mg/ml
  - Occasionally high WBC count
- Malignant ascites
  - LDH (ascites > serum)
  - Cytology

# Ascites Classification: High Gradients

- Serum albumin - ascites albumin (SAAG)  $> 1.1$
- Portal hypertension present (90-95%)
- Causes
  - Liver
    - Cirrhosis
    - Very severe, acute hepatitis
    - Cancer: massive liver mets
  - Venous
    - Budd-Chiari syndrome
    - Veno-occlusive disease
    - Portal vein thrombosis
  - Cardiac (R-CHF, constrictive pericarditis)

# Ascites Classification: Low Gradients

- Serum albumin - ascites albumin (SAAG) < 1.1 g/dL
- Causes (every other organ in the abdomen)
  - Perforated gastric ulcer
  - Ruptured gallbladder / biliary leak
  - Infarcted bowel
  - Pancreatitis
  - Renal
    - Nephrotic syndrome
    - Ruptured urinary bladder
  - Peritoneum
    - Infectious
    - Cancer



- 62 year old man with ascites
- Ascites tapped: albumin 1.1 g/dl, wbc < 250, serum albumin 3.1 g/ dl
- SAAG: 2 consistent with portal hypertension
- HCV antibody positive, : diagnosis cirrhosis

# Ascites

Initial management



# Management of Uncomplicated Ascites

**Definition:** Ascites responsive to diuretics in the absence of infection and renal dysfunction

## Sodium restriction

- Effective in 10-20% of cases
- Predictors of response: mild or moderate ascites, Urine Na excretion > 50 mEq/day

## Diuretics

- Should be spironolactone-based
- A progressive schedule (spironolactone → furosemide) requires fewer dose adjustments than a combined therapy (spironolactone + furosemide)



# Definition and Types of Refractory Ascites

Occurs in ~10% of cirrhotic patients

- **Diuretic-intractable ascites 80%**

Therapeutic doses of diuretics cannot be achieved because of diuretic-induced complications

- **Diuretic-resistant ascites 20%**

No response to maximal diuretic therapy (400 mg spironolactone + 160 mg furosemide/day)



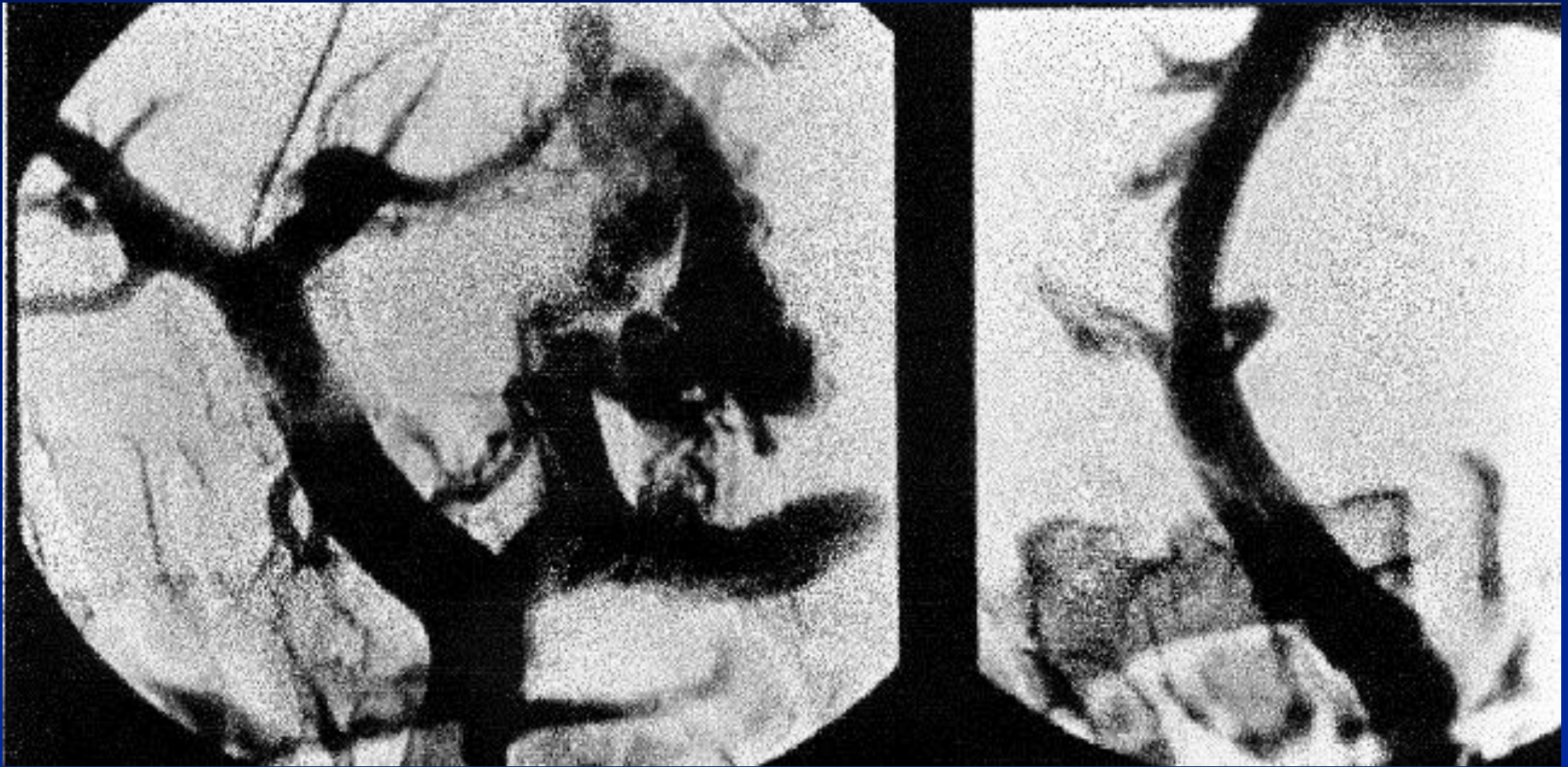
# Ascites

Beyond diuretics

# Ascites: Other Options

- Repeated Large Volume Paracentesis: inconvenient, if required < every 2 weeks suggests non-compliance with salt and fluid restriction
- TIPS: used to manage ascites, recurrent variceal hemorrhage, hepatic hydrothorax etc. May worsen liver disease

# TIPS Blood Flow Changes



# Compared to LVP, TIPS Reduces Ascites Recurrence But Increases Risk of Encephalopathy

	LVP (n=35)	TIPS (n=35)	p
Recurrent ascites	11.7 ± 2.7*	3.6 ± 1.7	0.003
TIPS obstruction	-	40%	-
Grade 3-4 PSE	0.5 ± 0.02	1.1 ± 0.02	0.02
Death	51%	57%	ns

\* Episodes/patient



# Ascites: Other Options

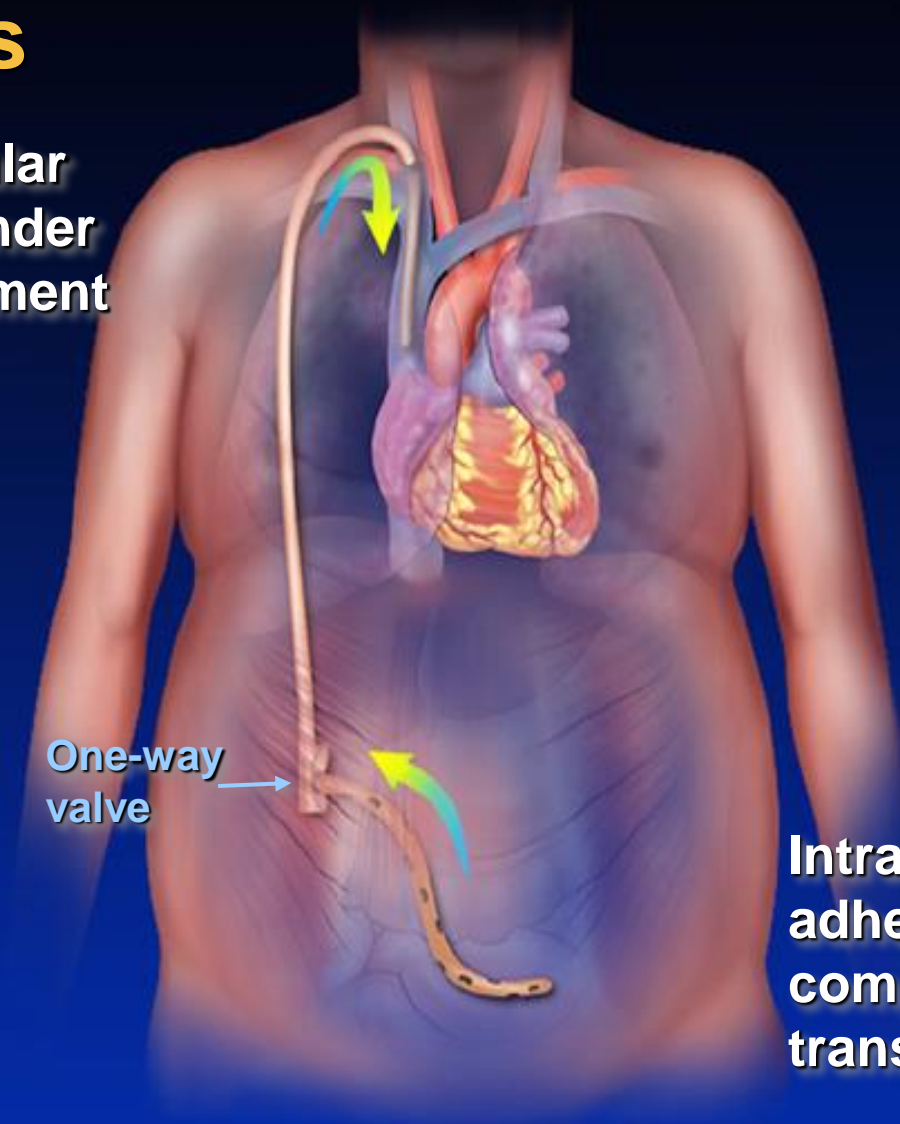
- Peritoneovenous shunt: largely replaced by TIPS
- Pleurx catheter; left in situ, used in malignant ascites

# Peritoneo-Venous Shunt (PVS) is Useful in the Treatment of Refractory Ascites

Use of jugular vein will hinder TIPS placement

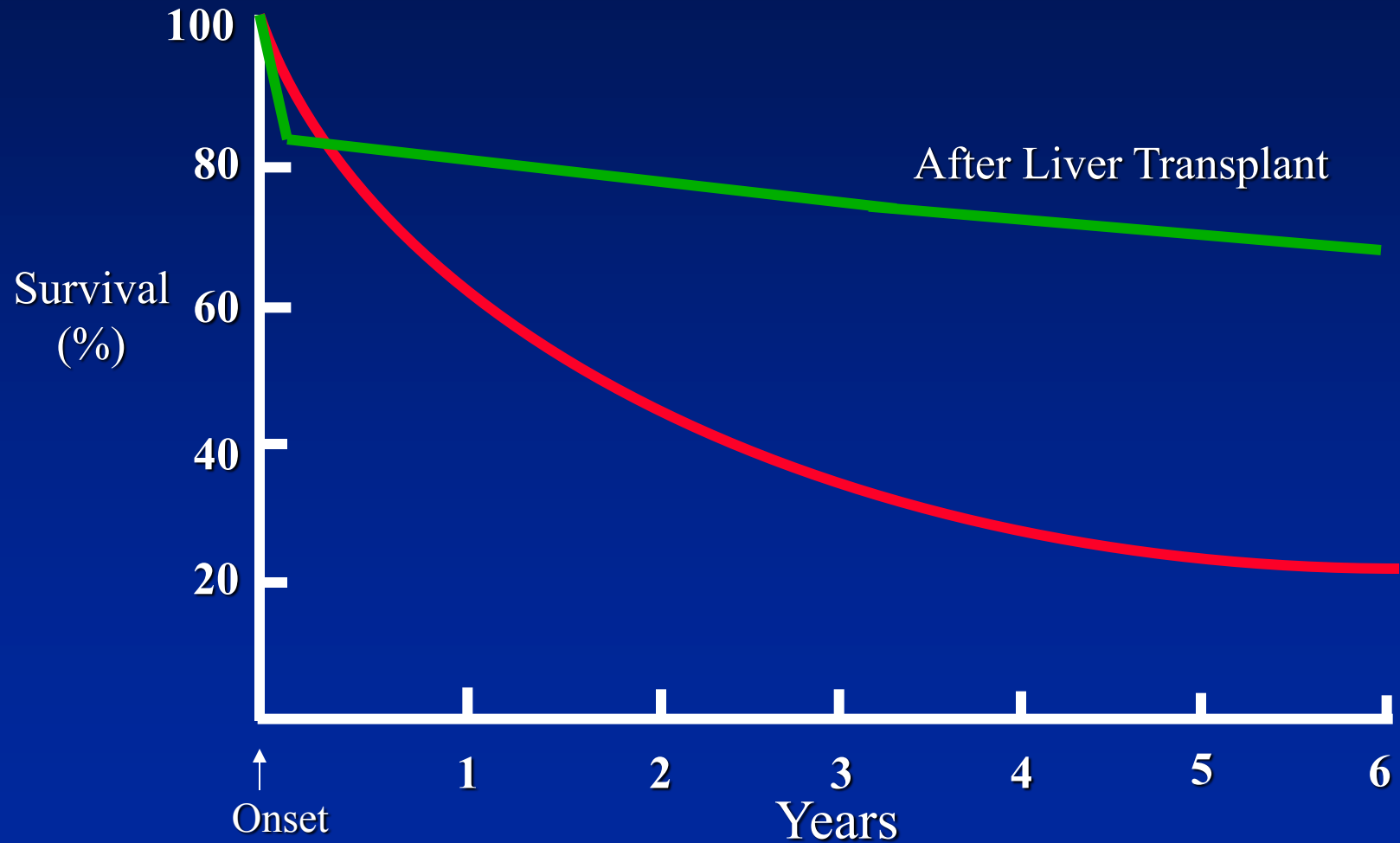
One-way valve

Intraabdominal adhesions may complicate liver transplant surgery





# Ascites: Survival & OLT



# Cirrhosis

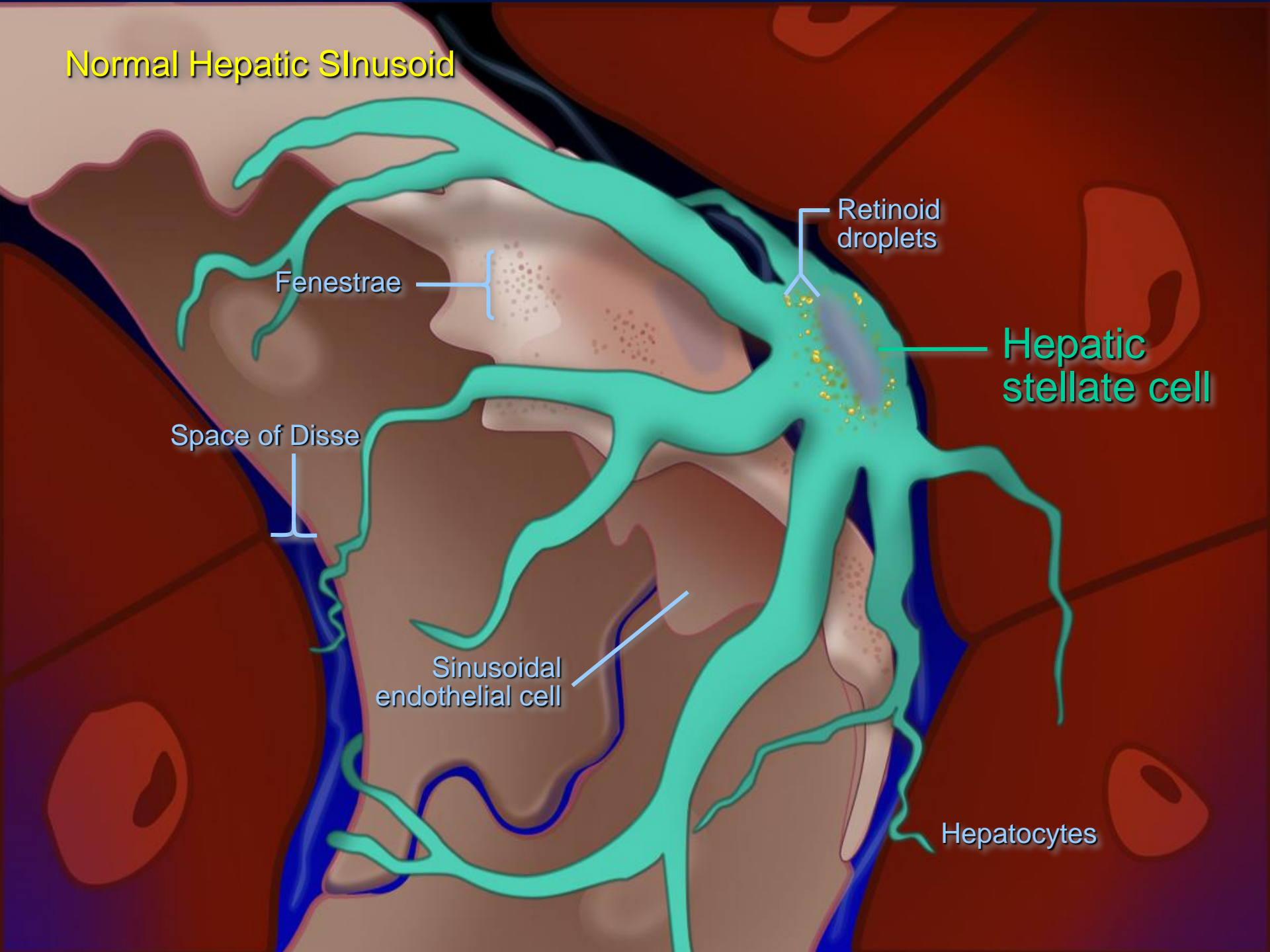
Background



Regenerative  
nodule

Fibrosis

# Normal Hepatic Sinusoid



Fenestrae

Retinoid droplets

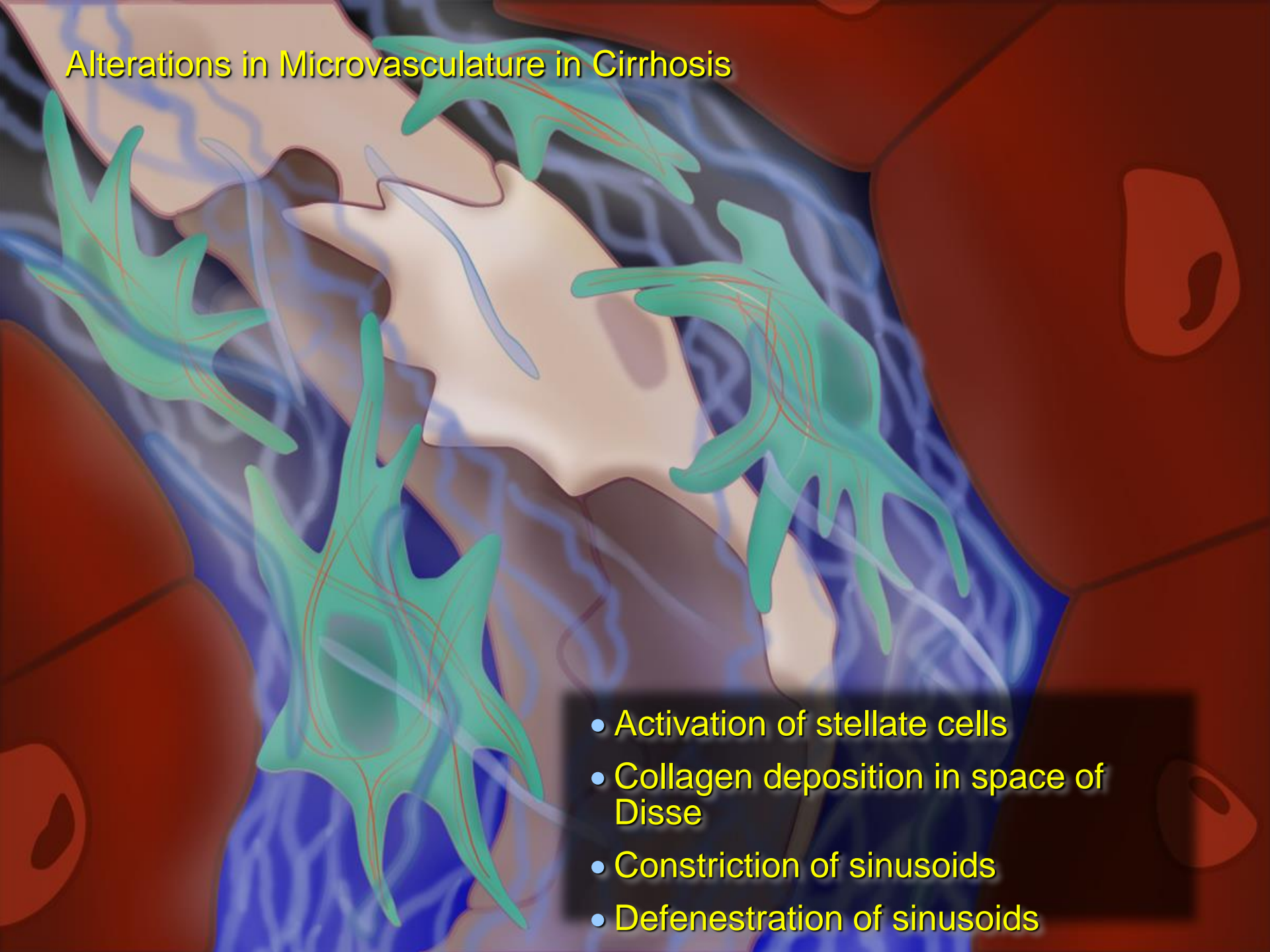
Hepatic stellate cell

Space of Disse

Sinusoidal endothelial cell

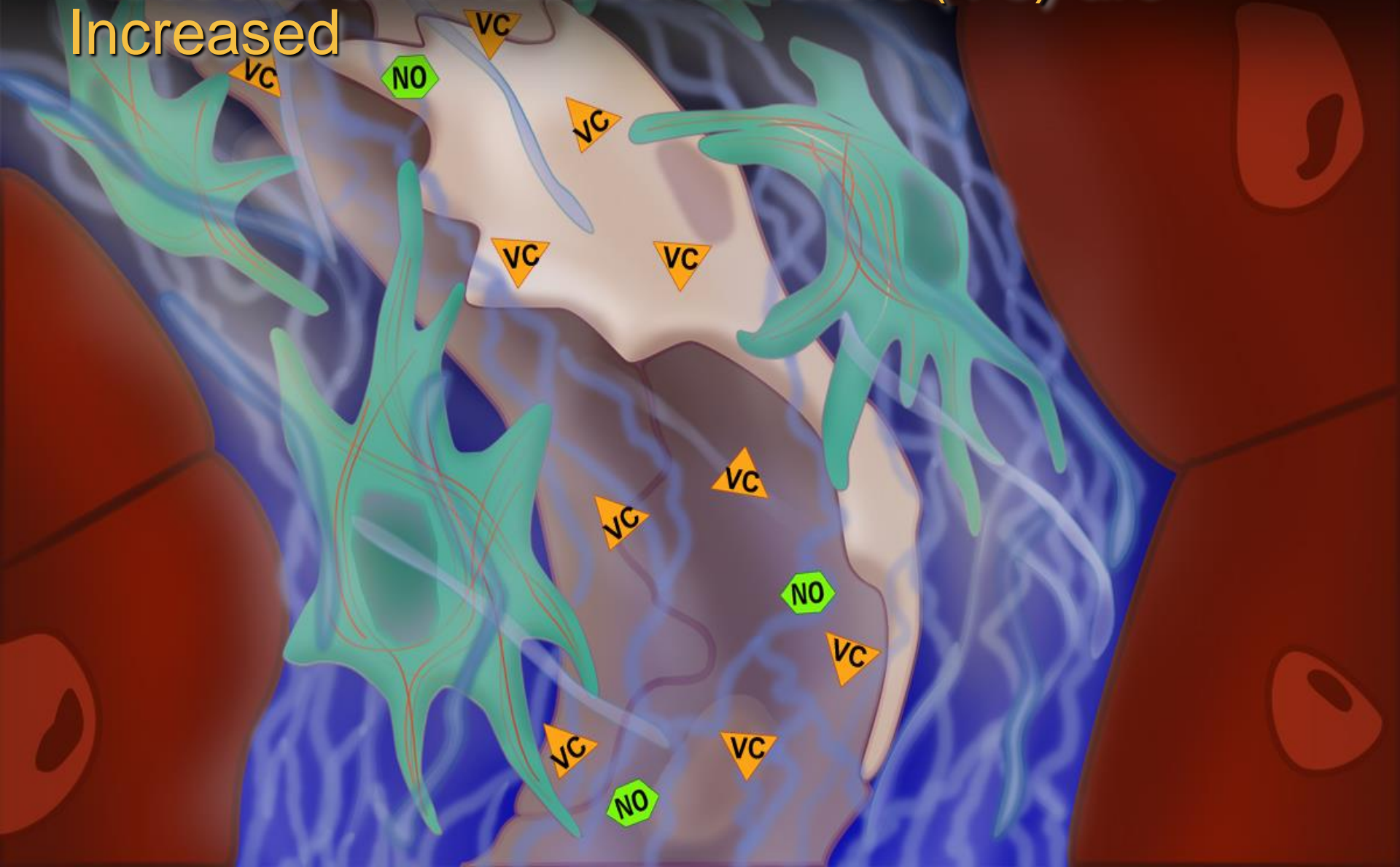
Hepatocytes

## Alterations in Microvasculature in Cirrhosis



- Activation of stellate cells
- Collagen deposition in space of Disse
- Constriction of sinusoids
- Defenestration of sinusoids

In Cirrhosis, Nitric Oxide (NO) Activity is Reduced and Vasoconstrictors (VC) are Increased

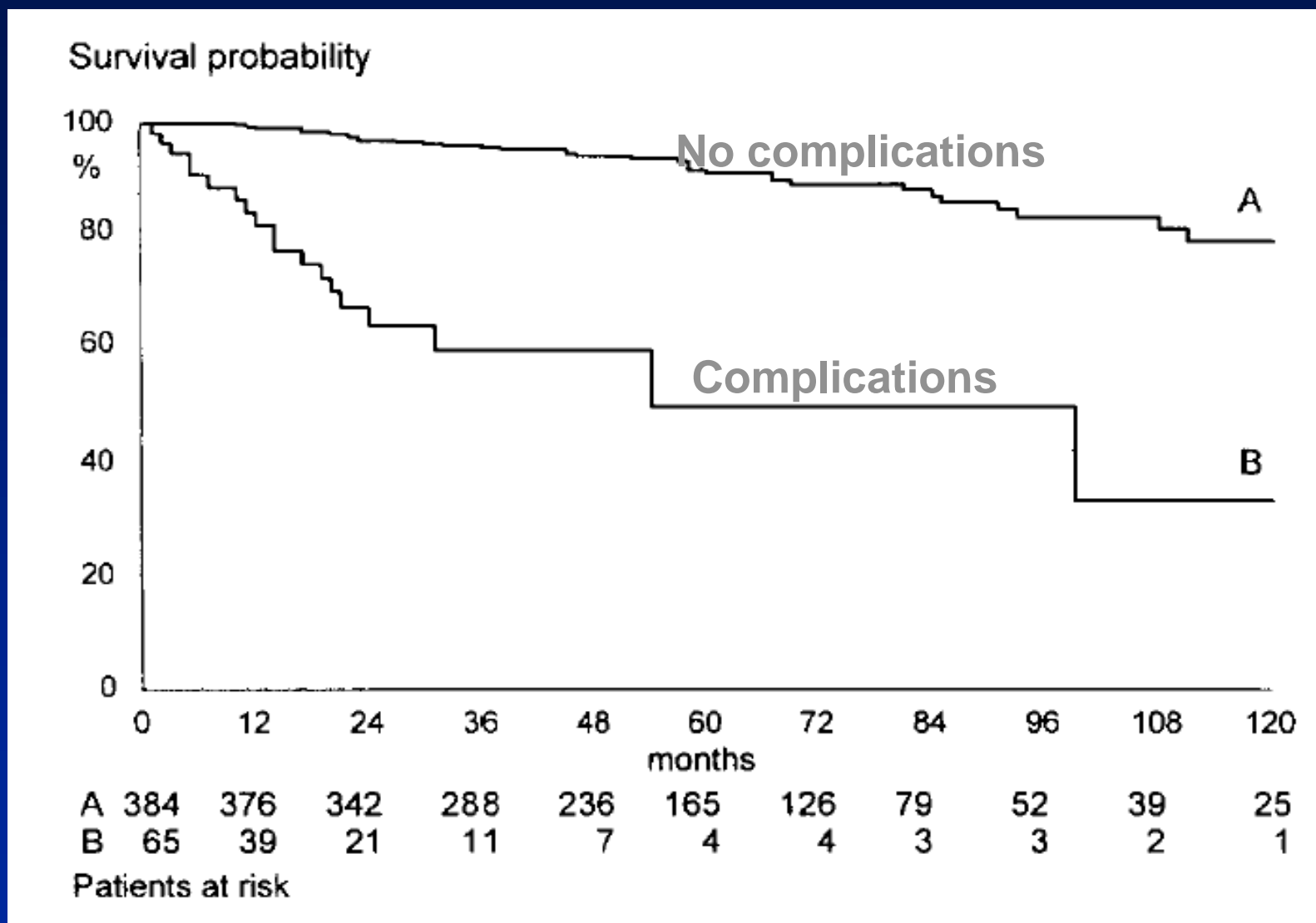


# Cirrhosis

Prognosis

# Stable cirrhosis in absence of complications

(Fattovich, Gastroenterology 1997)



Platelets <115,000 > predictor



# Stable Cirrhotic

- Routine Health Maintenance
- Surveillance for HCC
- Screening and prophylaxis of varices
- SBP prophylaxis

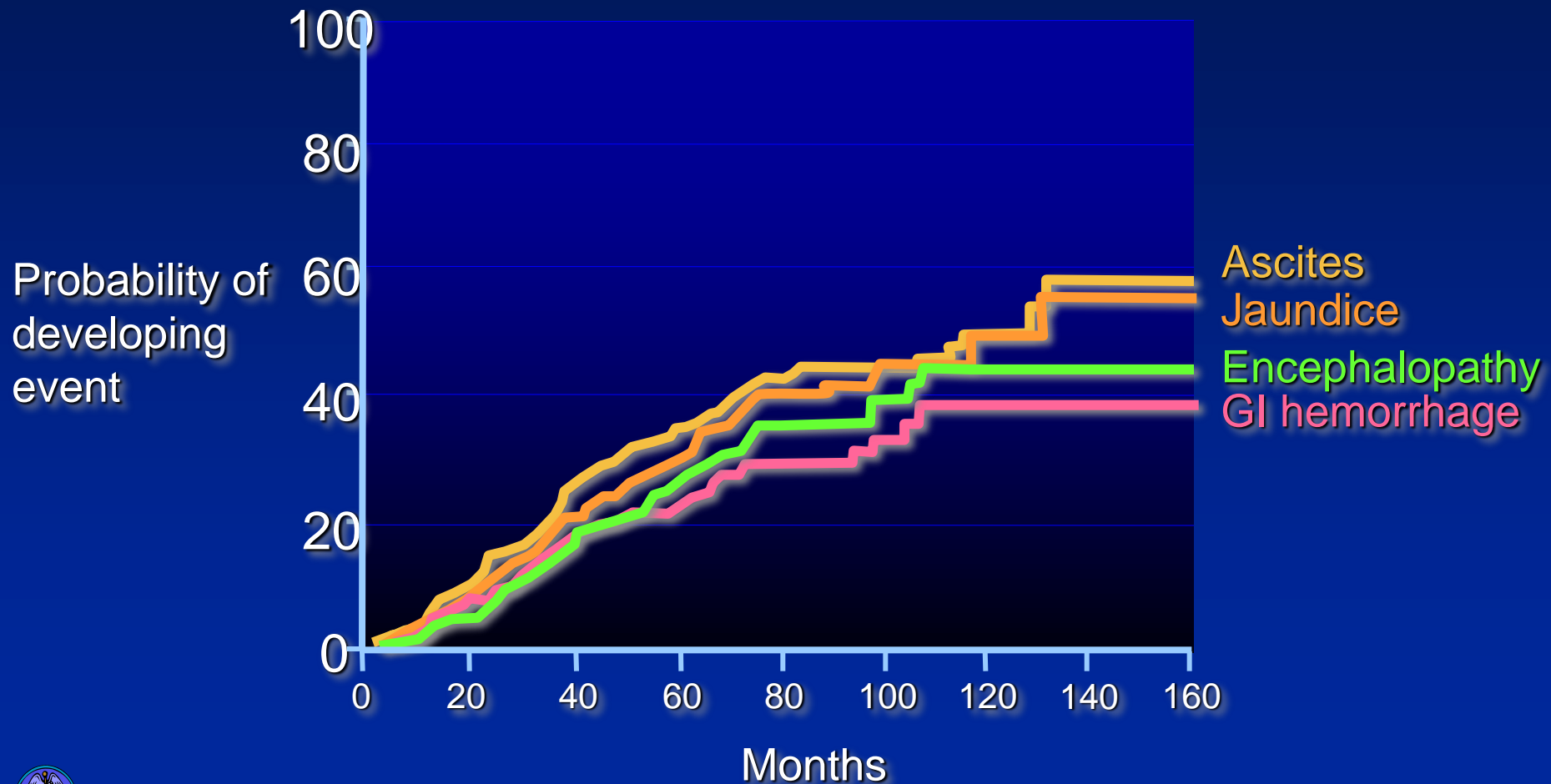
# Management of the stable cirrhotic: HCC surveillance

- Cirrhosis is high risk factor for HCC: 23 fold risk after 3.5 years (Chalasani, Amer J Gastr 1999)
- If presenting with symptoms, median survival is 4 months
- Surveillance:
  - AFP sensitivity 64%/specificity 91%
  - UTZ sensitivity 59-74%/specificity 94%
  - Optimal frequency unknown

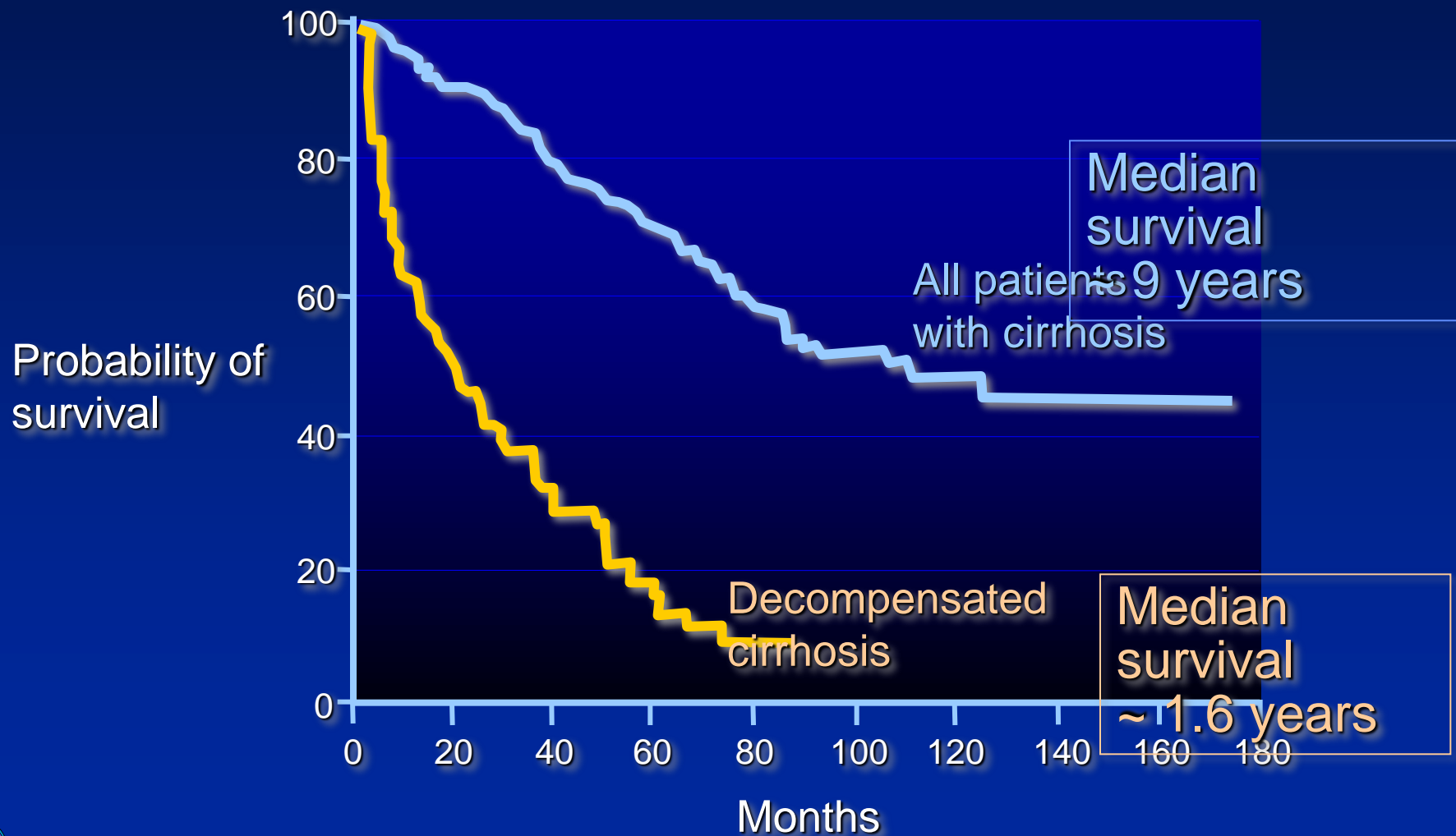
# Cirrhosis

Complications

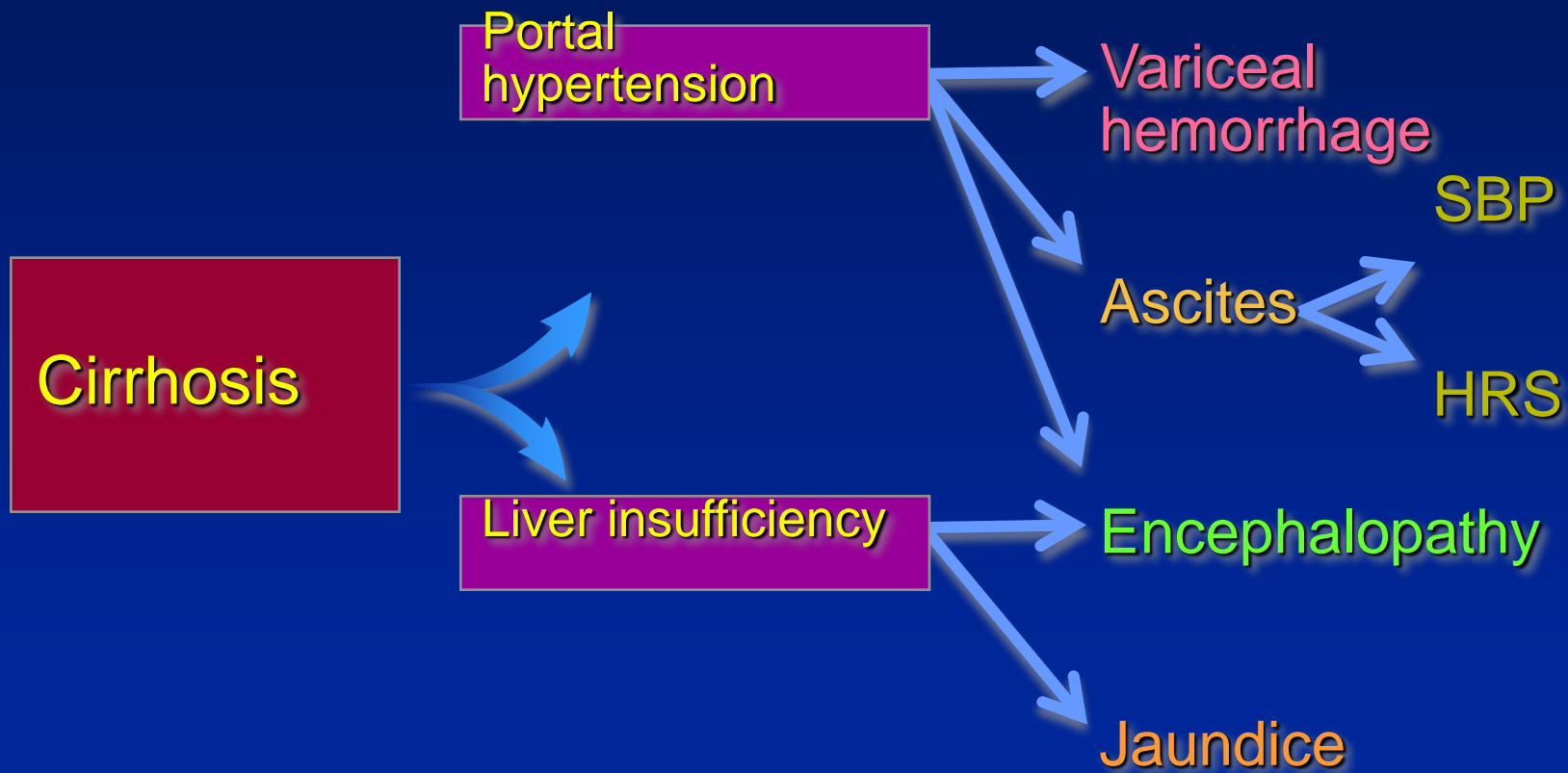
# Development of Complications in Compensated Cirrhosis



# Decompensation Shortens Survival



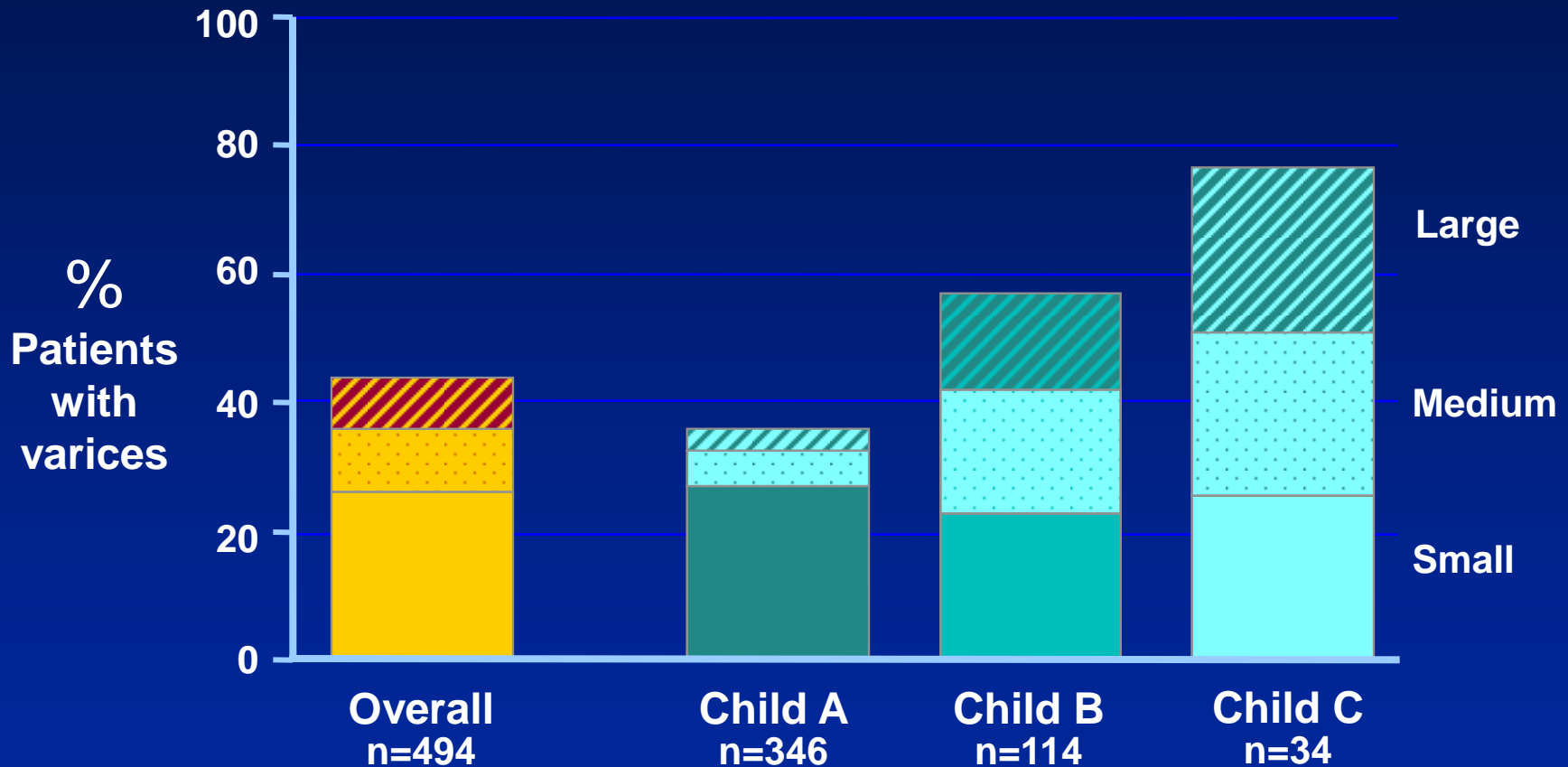
# Complications of Cirrhosis Result from Portal Hypertension or Liver Insufficiency



# Cirrhosis

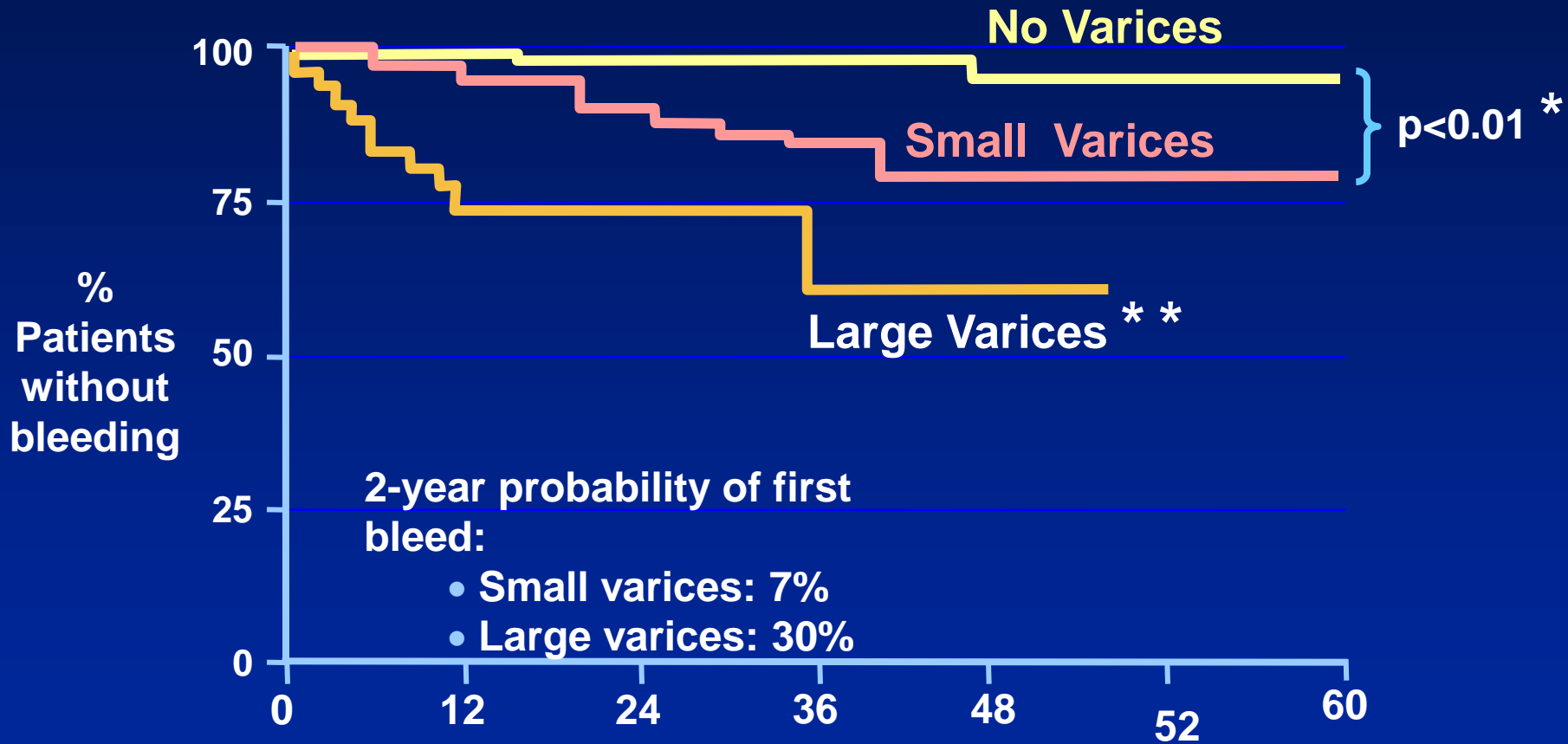
Varices

# Prevalence and Size of Esophageal Varices in Patients with Newly-Diagnosed Cirrhosis





# Large Varices are more Likely to Rupture



\*Merli et al., *Hepatology* 2003; 38:266, \*\*Conn et al., *Hepatology* 1991; 13:902

# Varices Increase in Diameter Progressively



No varices

Small varices

Large varices

7-8%/year

7-8%/year





Variceal hemorrhage



Varix with red signs

Predictors of hemorrhage:

- Variceal size
- Red signs
- Child B/C

# Treatment of Acute Variceal Hemorrhage

## General Management:

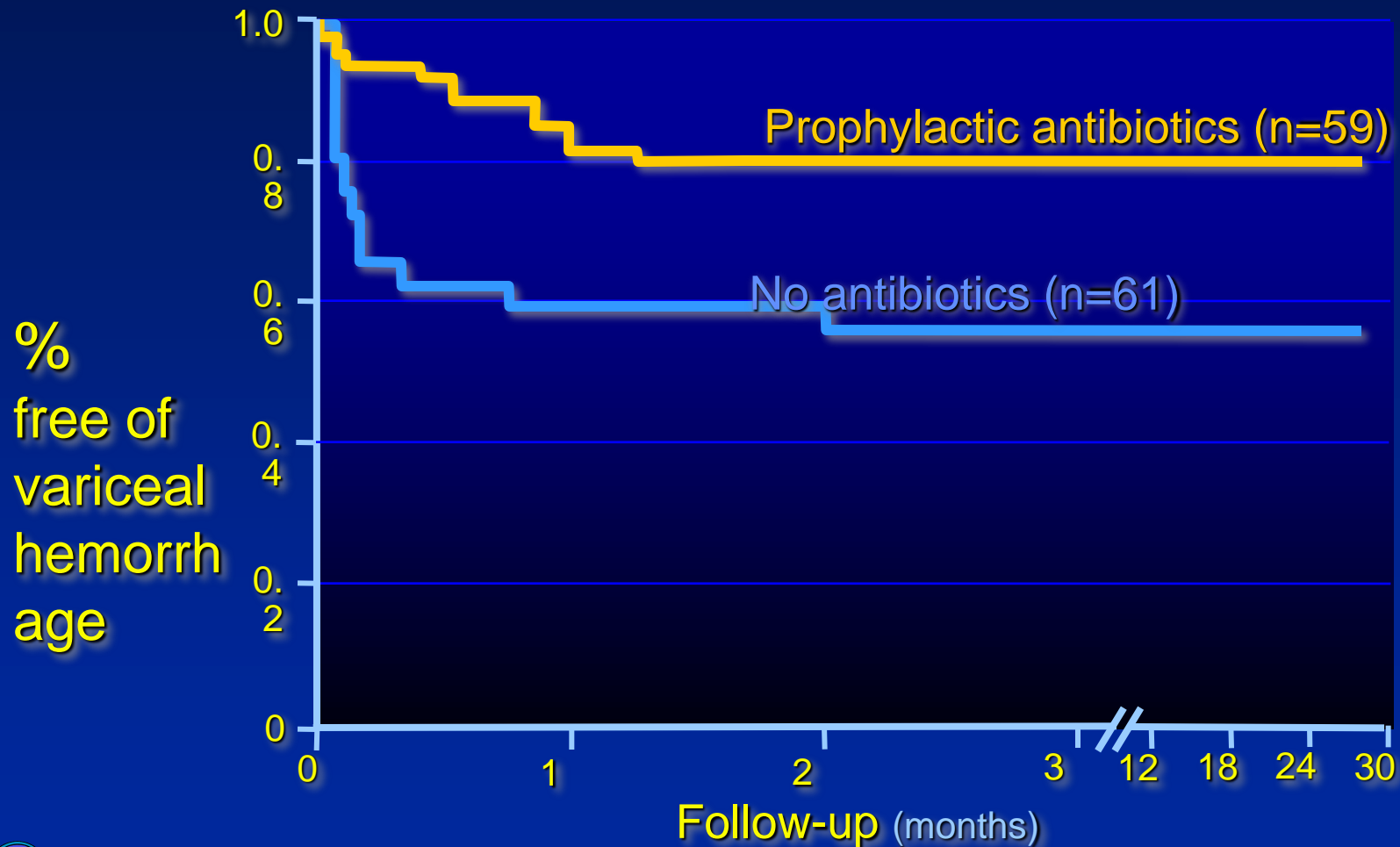
- IV access and fluid resuscitation
- Do not overtransfuse (hemoglobin ~ 8 g/dL)
- Antibiotic prophylaxis

## Specific therapy:

- Pharmacological therapy: terlipressin, somatostatin and analogues, vasopressin + nitroglycerin
- Endoscopic therapy: ligation, sclerotherapy
- Shunt therapy: TIPS, surgical shunt



# Probability of Remaining Free of Recurrent Variceal Hemorrhage



# Prophylaxis of Variceal Hemorrhage

## Diagnosis of Cirrhosis

### Endoscopy

No Varices

Small Varices

Medium/Large Varices

Follow-up EGD in 2-3 years\*

Follow-up EGD in 1-2 years\*

Beta-blocker therapy

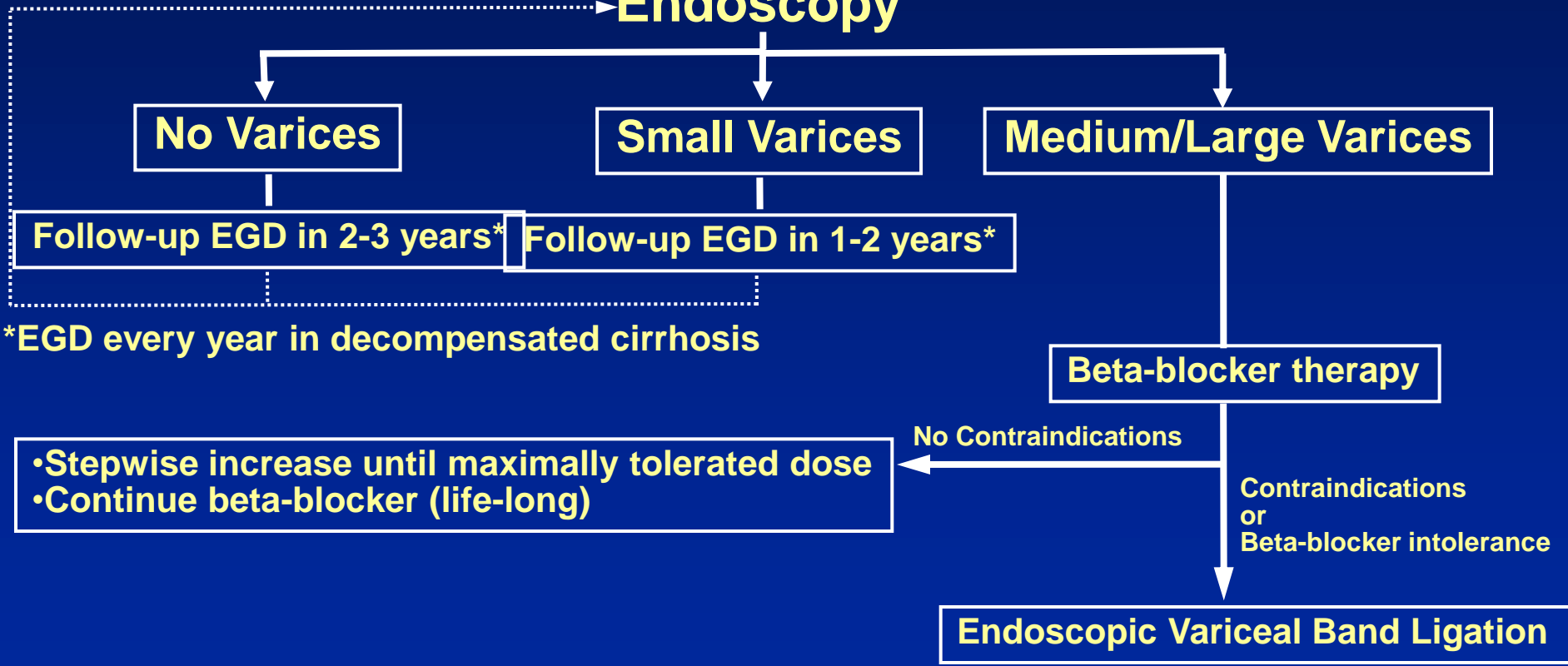
No Contraindications

Contraindications  
or  
Beta-blocker intolerance

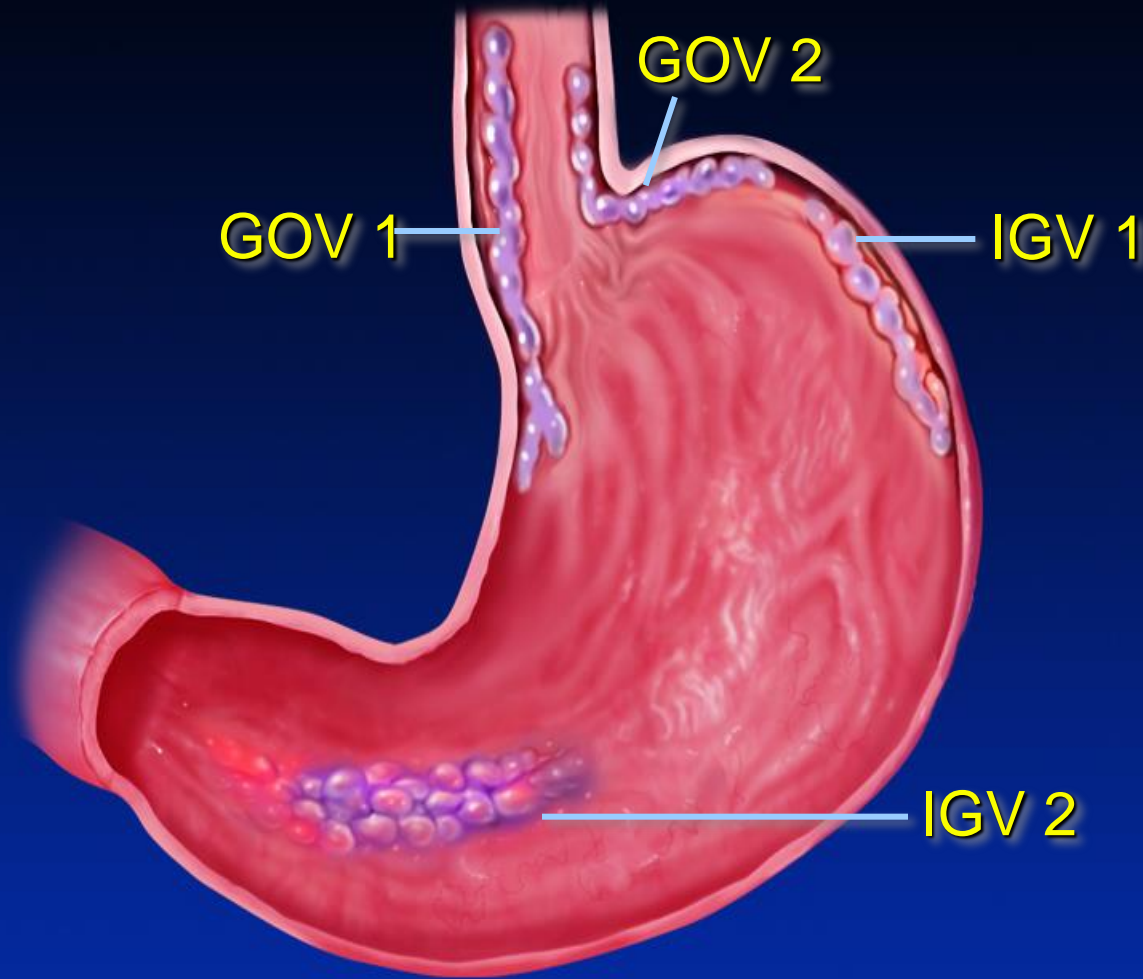
- Stepwise increase until maximally tolerated dose
- Continue beta-blocker (life-long)

Endoscopic Variceal Band Ligation

\*EGD every year in decompensated cirrhosis



# Classification of Gastric Varices



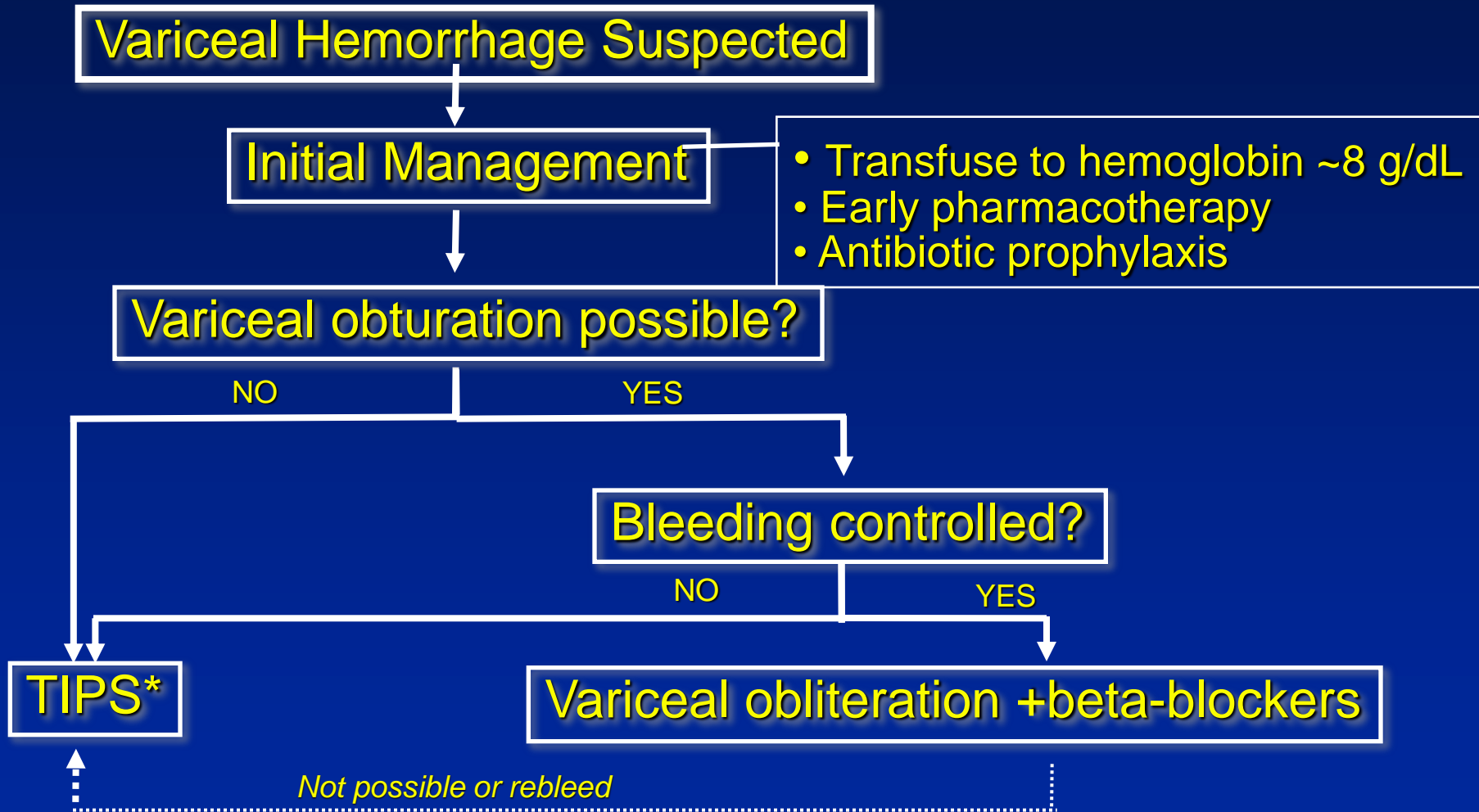
# Gastric Varices

- 10-15% of variceal bleeding episodes
- Limited data from controlled trials
- Optimal therapy not known
- Vasoactive drugs used.
- Endoscopic cyanoacrylate injection:  
90% control of bleeding
- Balloon tamponade with Linton-Nachlas tube
- TIPS: 90% control of bleeding





# Management of Bleeding Gastric Varices

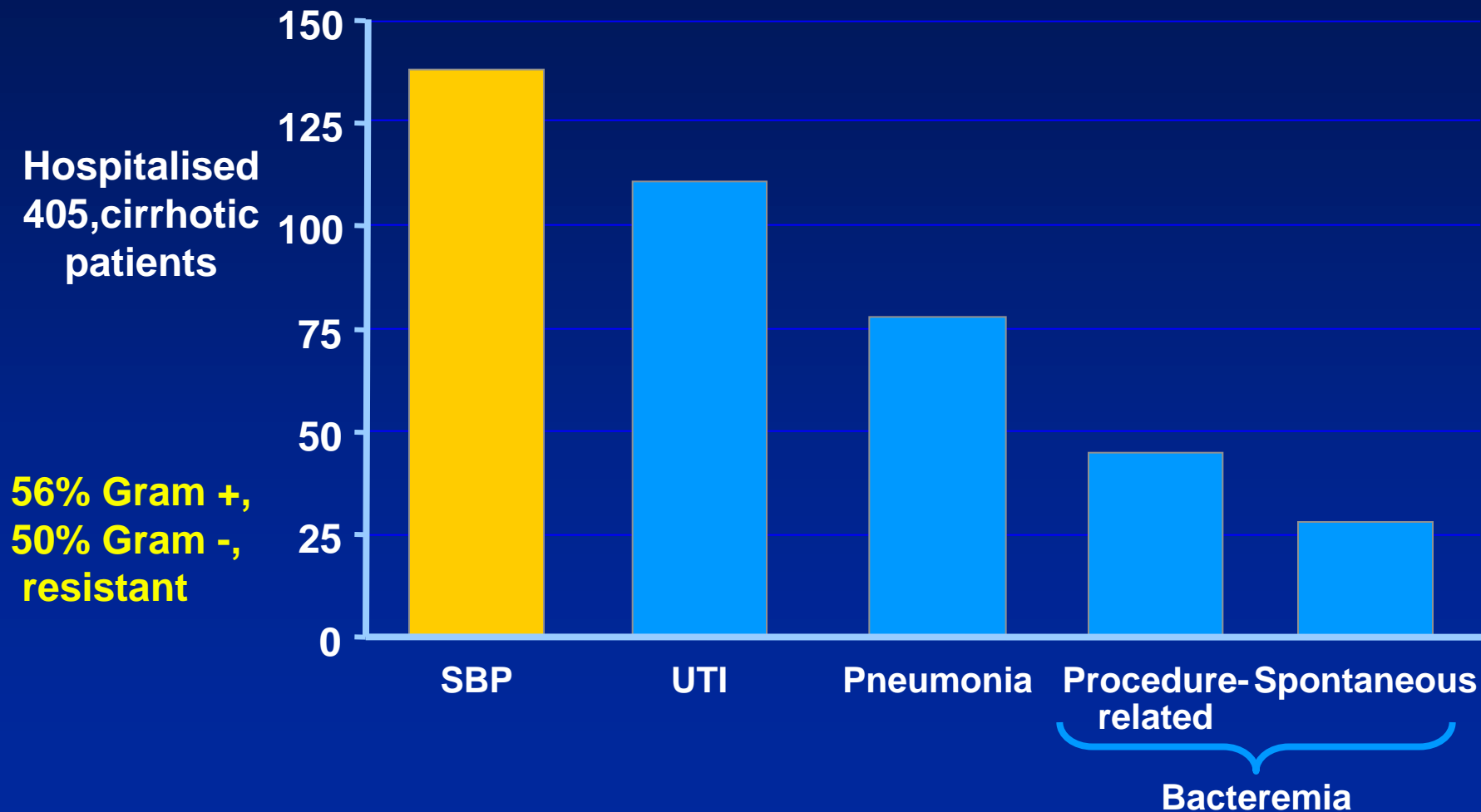


\*Surgical shunt may be considered for Child's Class A

# Cirrhosis

Spontaneous Bacterial Peritonitis

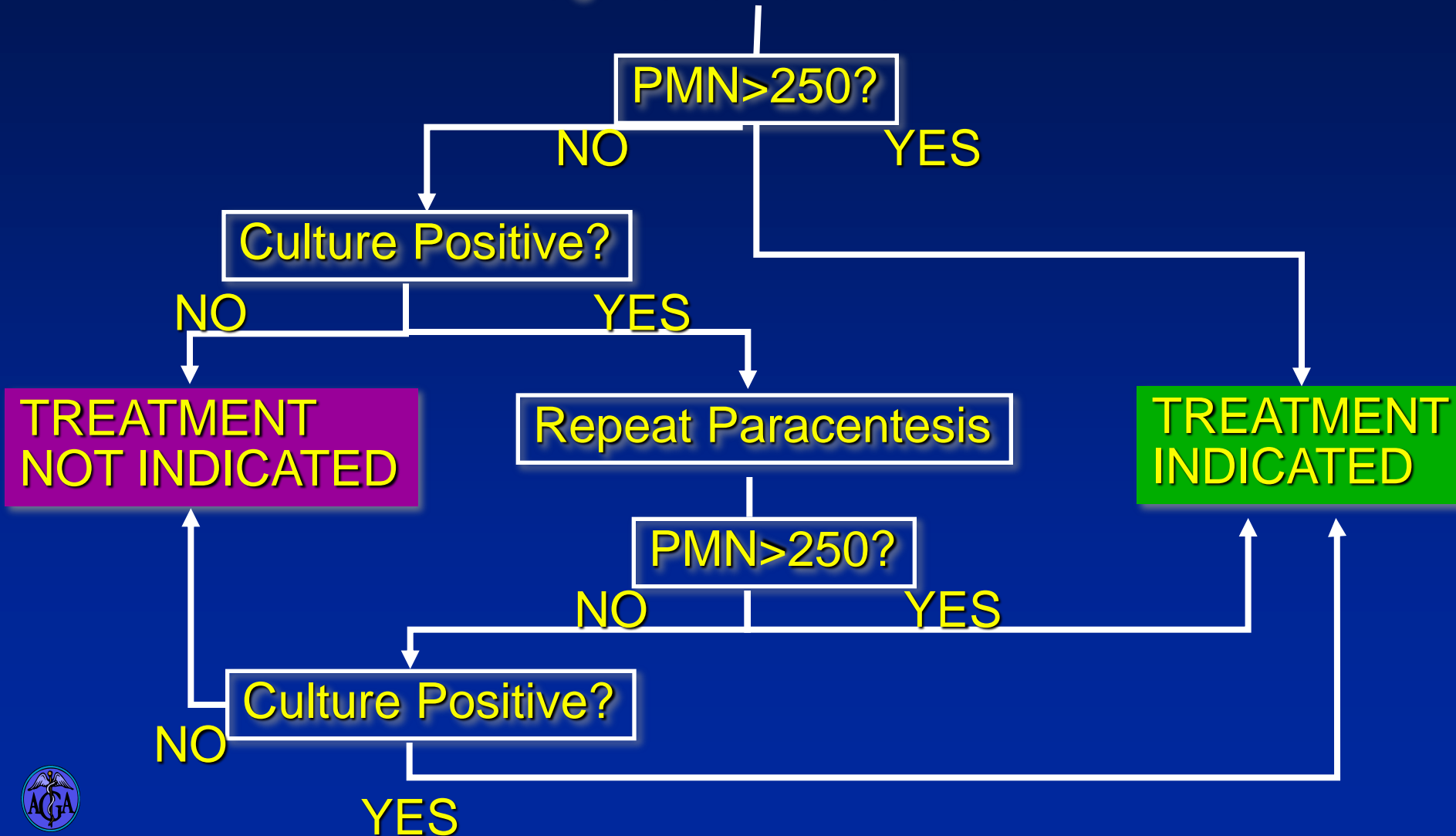
# Spontaneous Bacterial Peritonitis (SBP) is the Most Common Infection in Cirrhotic Patients



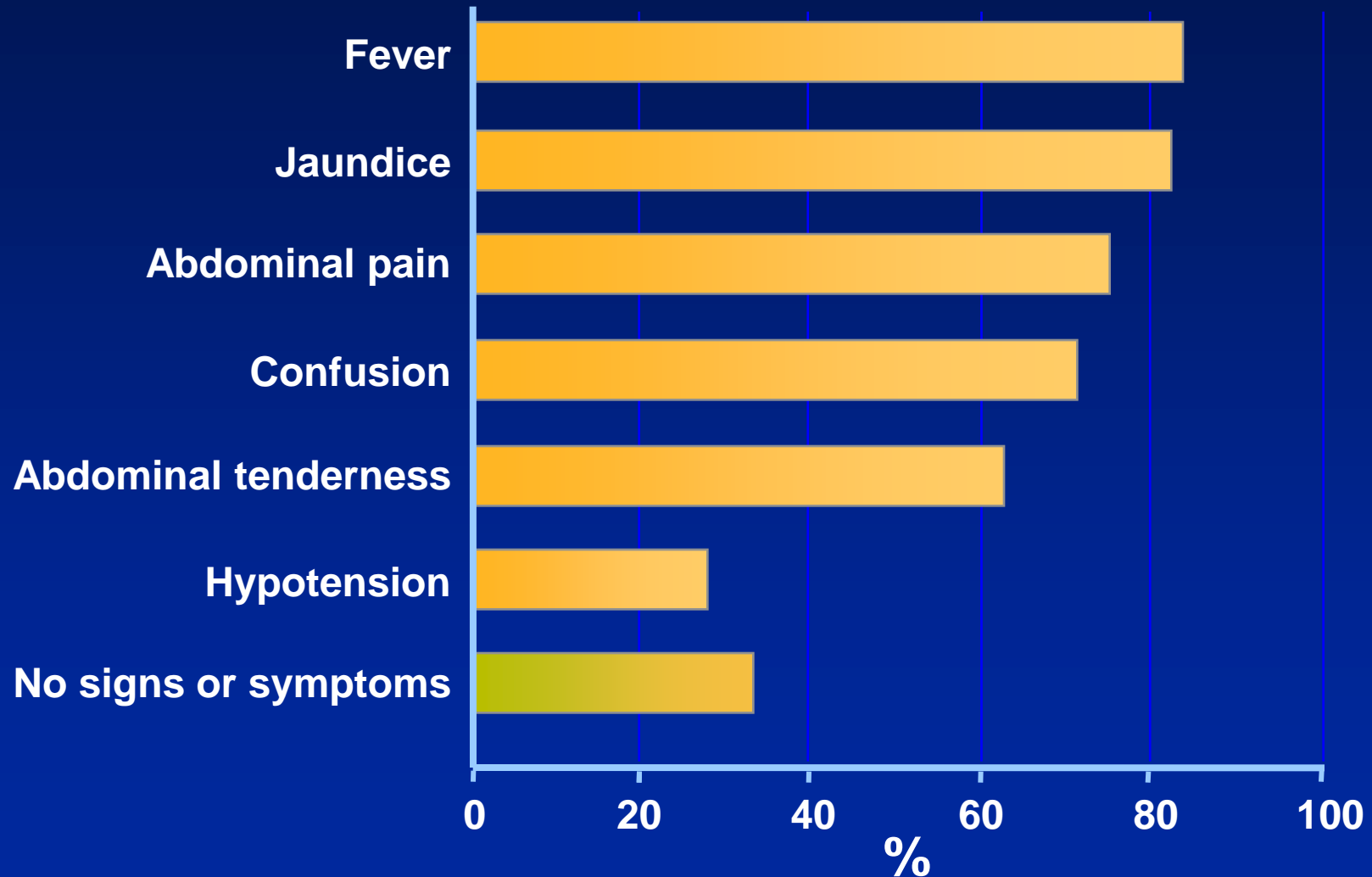
*Fernández et al., Hepatology 2002; 35:140*

# Diagnosis and Management of Spontaneous Bacterial Peritonitis

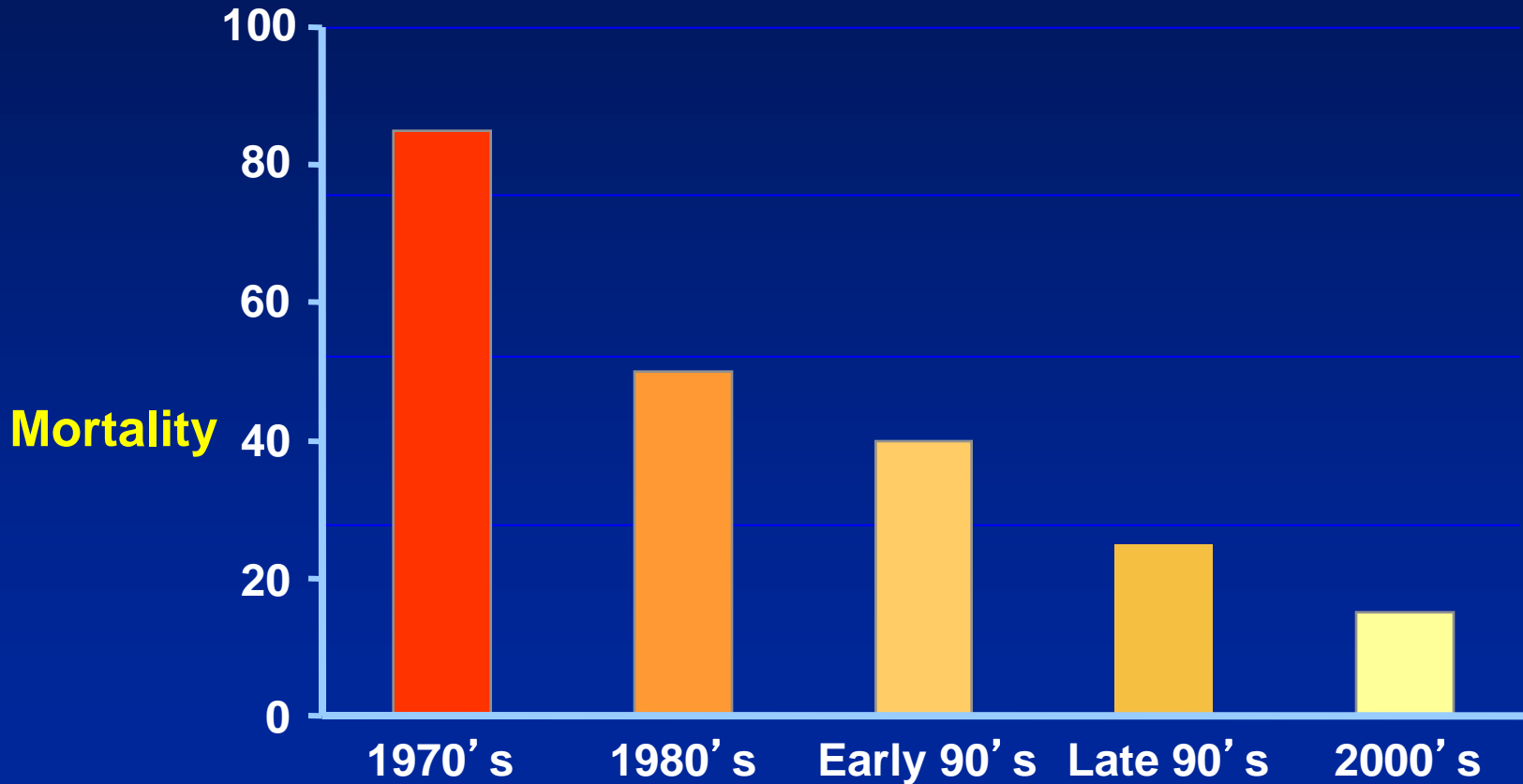
## Diagnostic Paracentesis



# Clinical Characteristics of Spontaneous Bacterial Peritonitis



# Mortality Associated with SBP has been Decreasing by Early Diagnosis and Treatment



# Spontaneous Bacterial Peritonitis Use of Intravenous Albumin

Albumin (plus antibiotics) is indicated if:

- BUN > 30 mg/dL
- creatinine > 1.0 mg/dL
- bilirubin > 4 mg/dL

Albumin is not indicated in patients with a predicted 100% cure and survival:

- community-acquired SBP
- no GI hemorrhage
- no encephalopathy
- normal renal function



# Indications for Prophylactic Antibiotics to Prevent Spontaneous Bacterial Peritonitis

- **Cirrhotic patients hospitalized with GI hemorrhage (short-term)**
  - **Norfloxacin 400 mg p.o. BID x 7 days**
- **Patients who have recovered from SBP (long-term)**
  - **Norfloxacin 400 mg p.o. daily, indefinitely**
- **Weekly quinolones not recommended (lower efficacy, development of quinolone-resistance)**
- **Patients with low albumin in ascitic fluid.**



# Cirrhosis

Hepatorenal Syndrome

# Two Types of Hepatorenal Syndrome

## Type 1

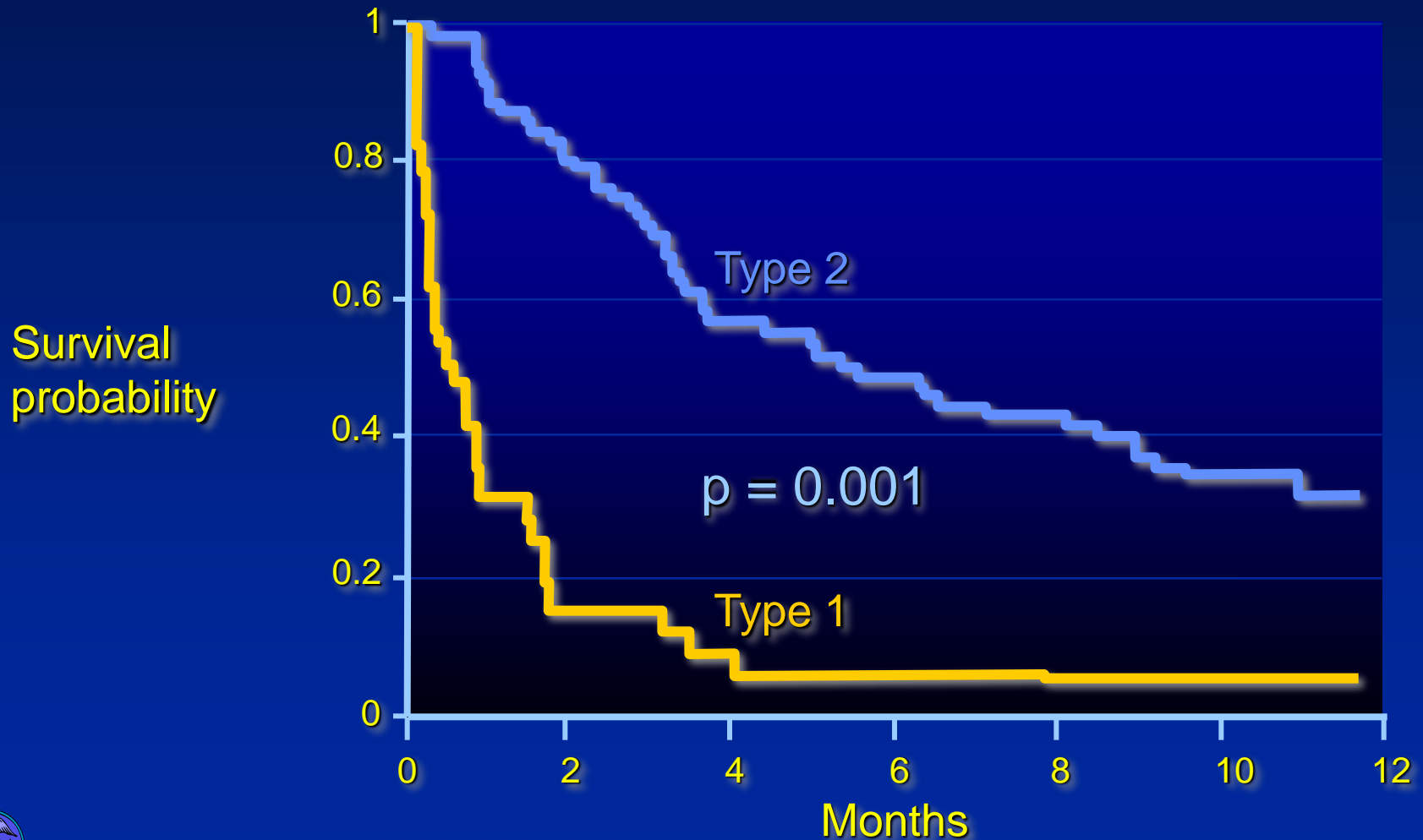
- Rapidly progressive renal failure (2 weeks)
- Doubling of creatinine to  $>2.5$  or halving of creatinine clearance (CrCl) to  $<20$  ml/min

## Type 2

- More slowly progressive
- Creatinine  $>1.5$  mg/dL or CrCl  $<40$  ml/min
- Associated with refractory ascites



# Survival in Different Types of Hepatorenal Syndrome (HRS)



# Cirrhosis

Liver Transplantation

# Patient Selection Criteria for LT

- Accepted indications for LT
  - Advanced chronic liver disease
  - Acute liver failure
  - Unresectable hepatic malignancy
  - Inherited metabolic liver disease
- No alternative form of therapy
- No absolute contraindication to LT
- Willingness to comply with follow-up care
- Ability to provide for costs of LT

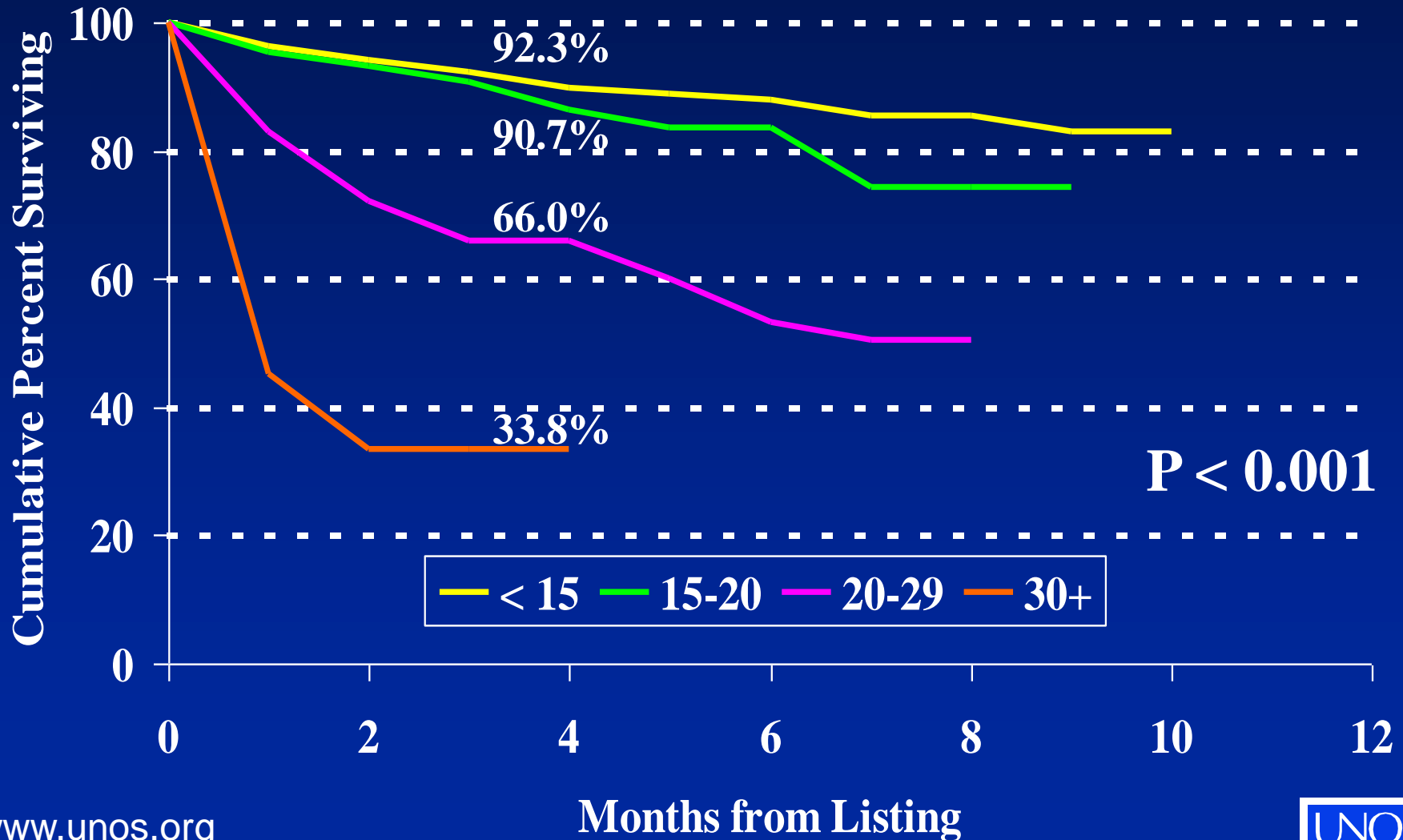
# Evaluation Process

- Assessment of Liver Disease Severity and Prognosis
- Presence of Complications
- Comorbidities
- Psychosocial Issues and Support

# Evaluation Process

- Routine Biochemical and Hematological Panels (CBC, Creat. INR, LFTs, ABO)
- Serological Screen ( Hepatitis Panel, HIV, EBV, CMV)
- Imaging of Abdomen
- Medical Consultations and Evaluations as clinically indicated ( e.g. ID, Cardiology)
- Age appropriate Cancer Screening

# MELD and Survival





# Liver Transplantation in the U.S.

## *Current Status*

- 1-year patient survival: 85–90% in most centers
- 3-year survival 75-80%; 8-year survival 60-70%
- ~6,000 LT/year last 3 years in ~110 centers
- >17,000 patients on LT waiting list
- ~1,800 deaths/year on waiting list last 3 years
- Mismatch between qualified candidates and available organs limits application of LT

# Reasons for Early Referral to Transplant Center

- Timely, stepwise evaluation of candidate
- Patient and family education about LT
- Intervention for confounding issues
  - Chemical dependence
  - Obesity and other medical issues
- Financial counseling
- Program selection by patient
  - Center-specific results, facilities, relationships with staff, etc.

# Ascites

- Presentation of a variety of diseases
- Initial workup includes paracentesis
- In cirrhosis onset of ascites predicts poor longterm prognosis

# Cirrhosis

- Anticipate complications
- Screen for varices, HCC
- Refer for liver transplant once index complication occurs

# Key Issues in Liver Transplant

- Indications
- Organ Allocation
- Care of the Cirrhotic Patient
- Recurrent Disease

# **Selection for Liver Transplantation**

# Contraindications to LT: Absolute

- Active alcohol or substance abuse
- Advanced cardiopulmonary disease
- Systemic sepsis, unresponsive to Rx
- Multiorgan failure; multiple pressors
- Extrahepatic malignancy
- Severe pulmonary hypertension
- Severe psychiatric disease likely to affect compliance

# Contraindications to LT: Relative

- General debility
- Advanced age
- Extensive portal/mesenteric thrombosis
- Social isolation and limited support
- HIV seropositivity
- Cholangiocarcinoma