Immunizations and Medication Use in Cirrhosis: Which, How and When

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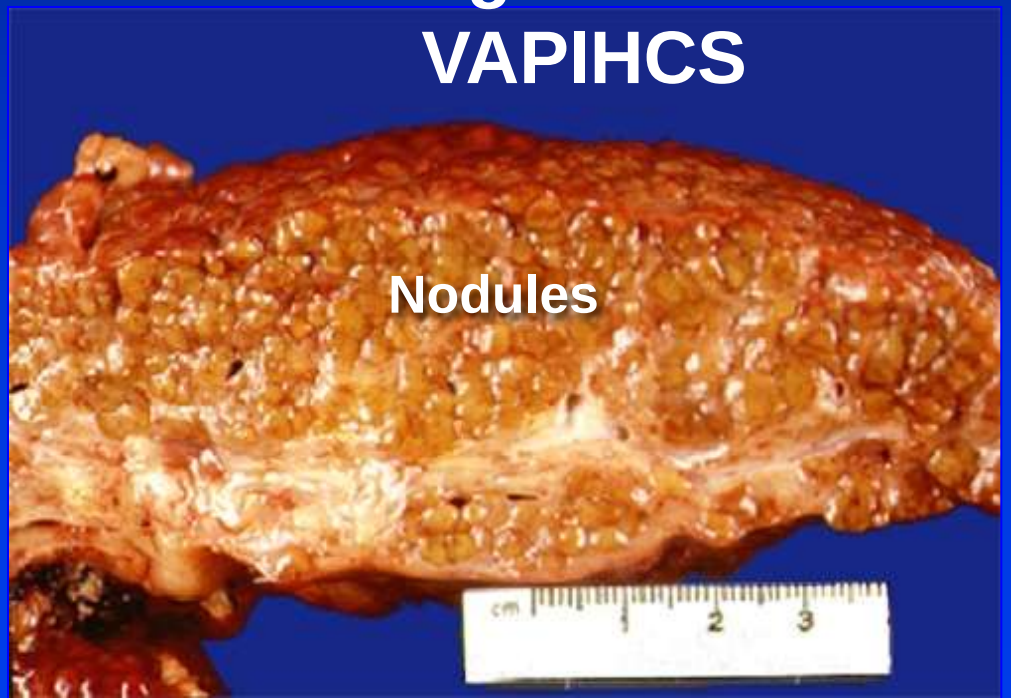
University of Hawaii School of Medicine
Chief, Center for Digestive and Liver Disease
VAPIHCS



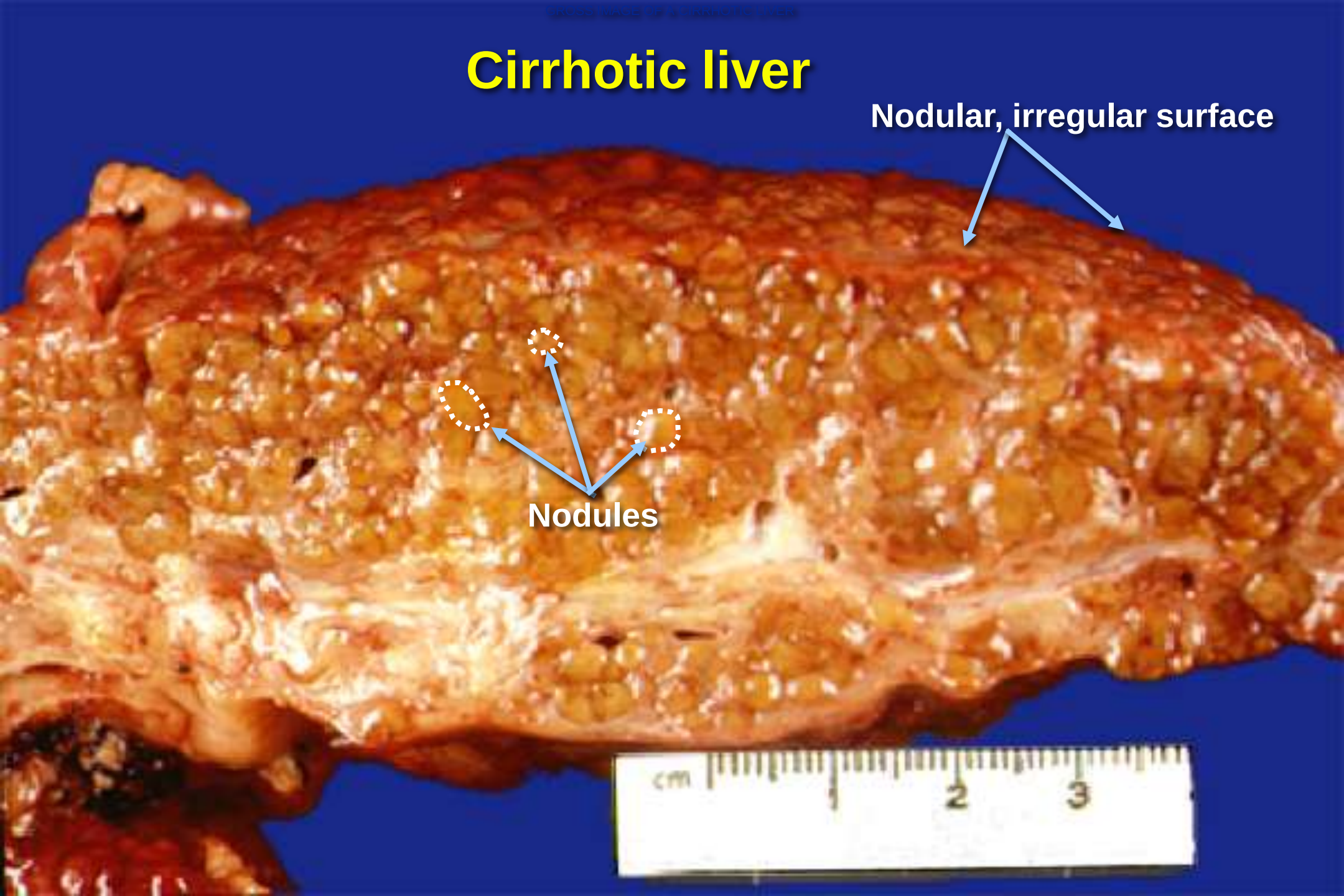
Objective

- Review cirrhosis and its natural history.
- Describe significance of immunizations in chronic liver disease.
- Understand the role of medications in chronic liver disease.

Cirrhosis

- End stage of any chronic liver disease
- Characterized histologically by regenerative nodules surrounded by fibrous tissue
- Clinically there are two types of cirrhosis:
  - Compensated
  - Decompensated

Cirrhotic liver



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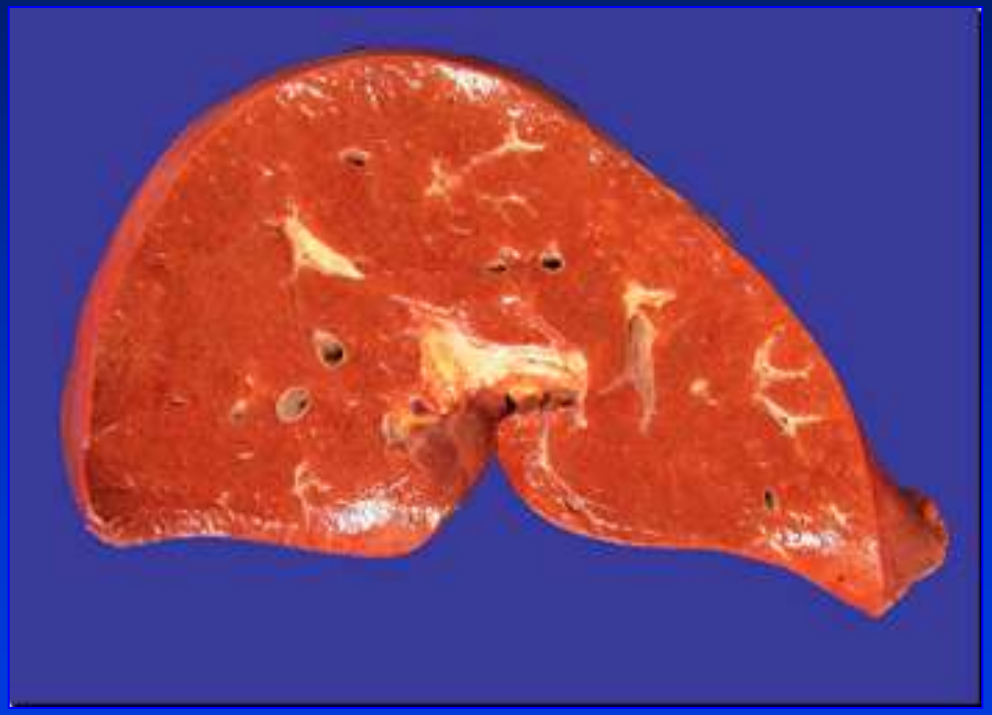
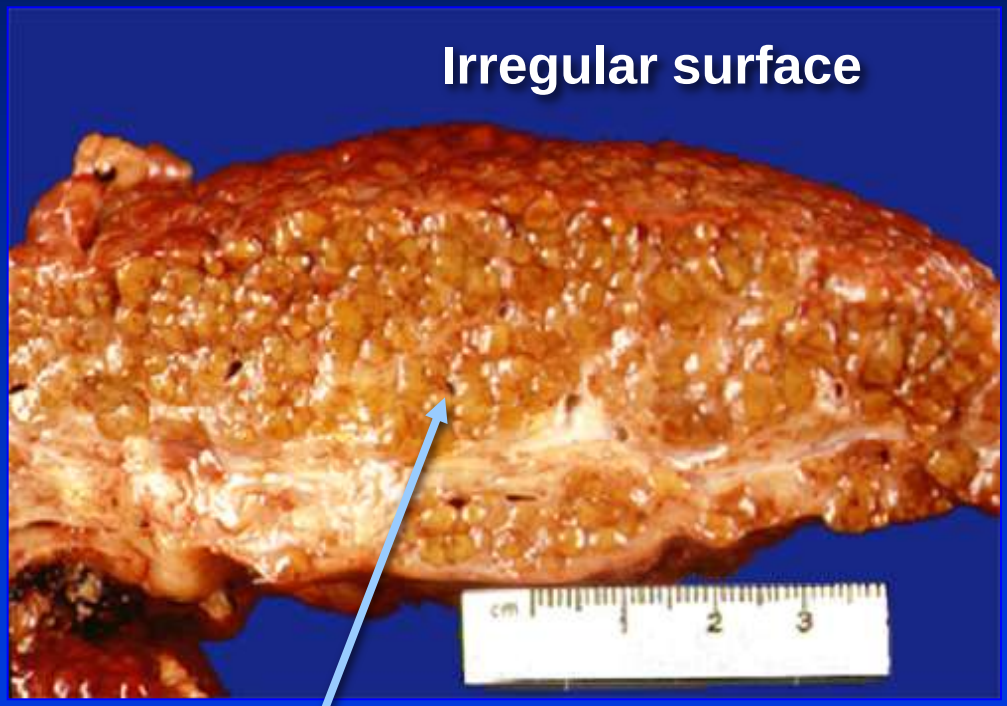


Cirrhosis



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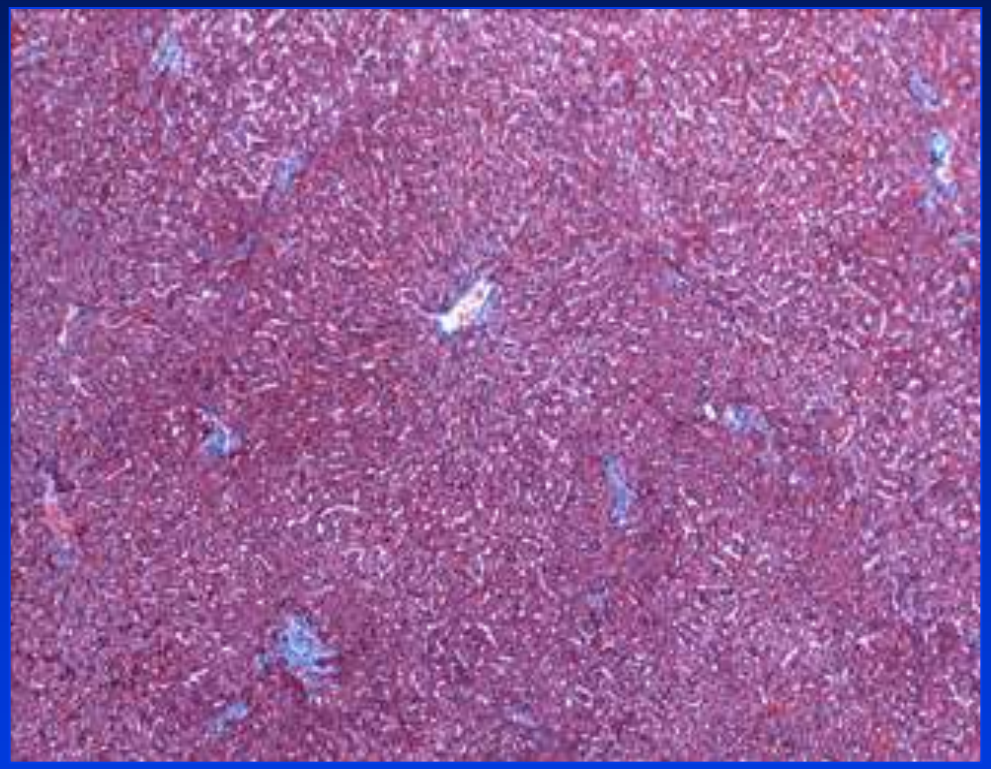
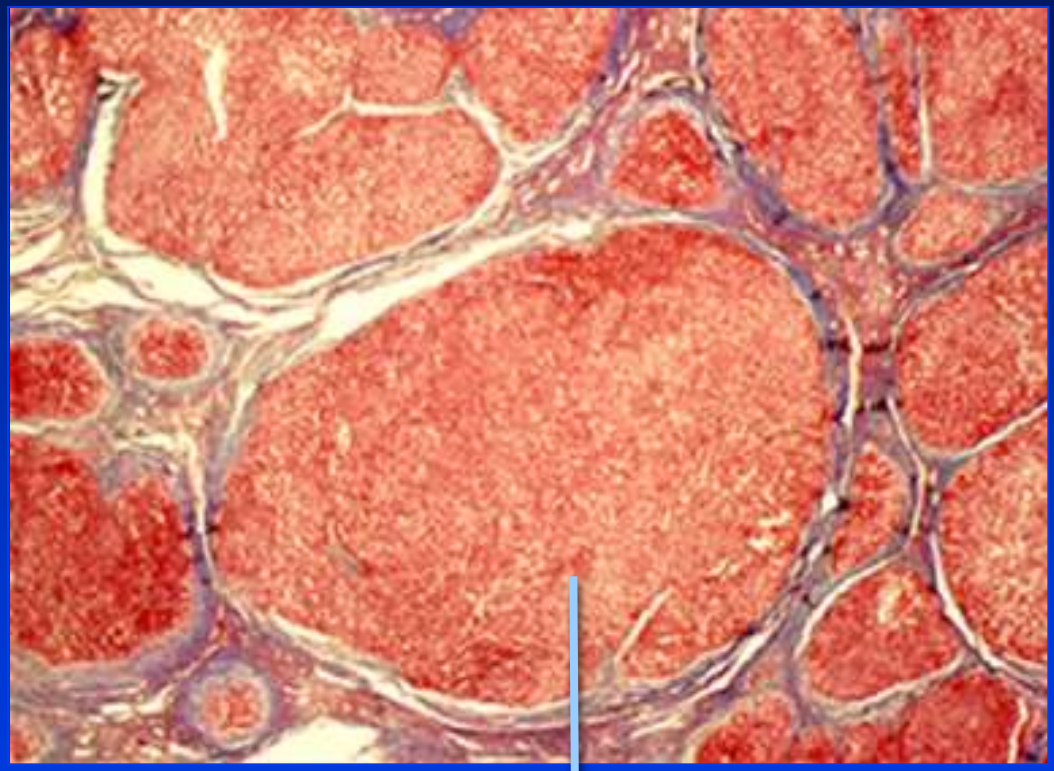


Cirrhosis



Nodules surrounded by fibrous tissue

Cirrhosis - Diagnosis

- Cirrhosis is a histological diagnosis
- However, in patients with chronic liver disease the presence of various clinical features suggests cirrhosis
- The presence of these clinical features can be followed by non-invasive testing, prior to liver biopsy

In Whom Should We Suspect Cirrhosis?

- Any patient with chronic liver disease
  - Chronic abnormal aminotransferases and/or alkaline phosphatase
- Physical exam findings
  - Stigmata of chronic liver disease (muscle wasting, vascular spiders, palmar erythema)
  - Palpable left lobe of the liver
  - Small liver span
  - Splenomegaly
  - Signs of decompensation (jaundice, ascites, asterixis)

In Whom Should We Suspect Cirrhosis?

Laboratory

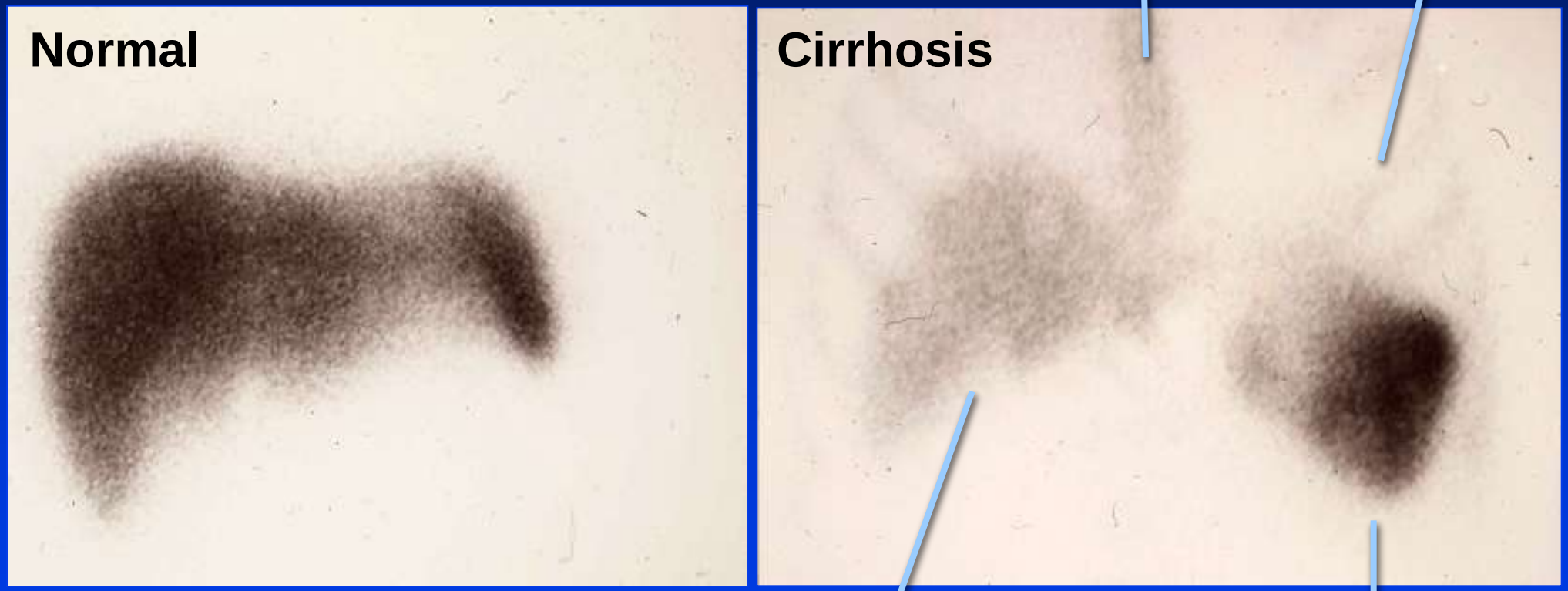
- Liver insufficiency
  - Low albumin (< 3.8 g/dL)
  - Prolonged prothrombin time (INR > 1.3)
  - High bilirubin (> 1.5 mg/dL)
- Portal hypertension
  - Low platelet count (< 175 x1000/μl)
- AST / ALT ratio > 1

In Whom Should We Suspect Cirrhosis?

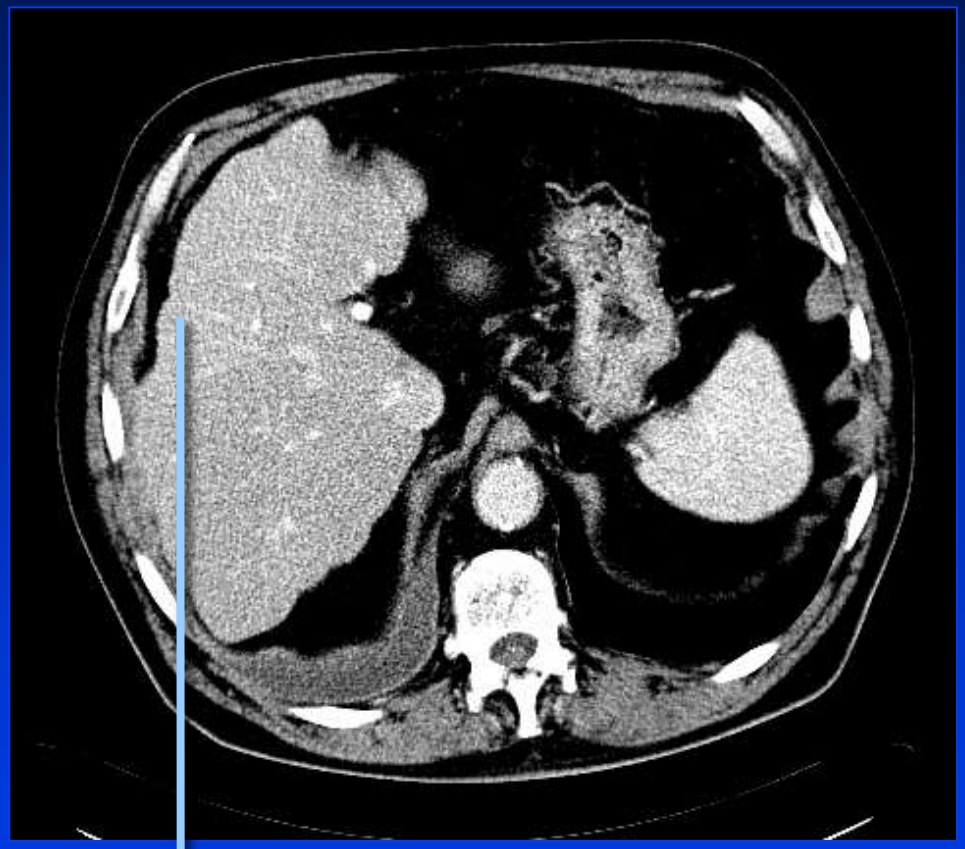
Imaging studies

- **Liver-spleen scan**
  - Small liver, irregular uptake
  - Splenomegaly
  - Colloid shift to bone marrow
- **CAT scan / Ultrasound**
  - Nodular liver
  - Splenomegaly
  - Venous collaterals

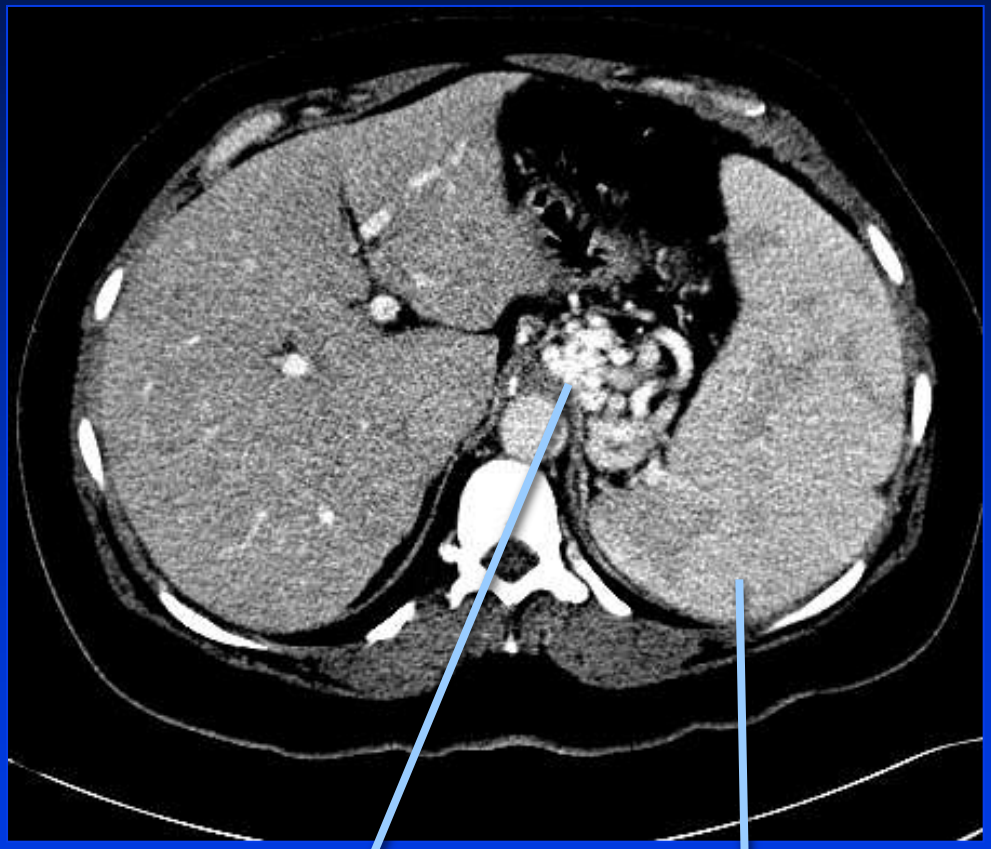
Liver-Spleen Scan



CAT Scan in Cirrhosis



Liver with an irregular surface



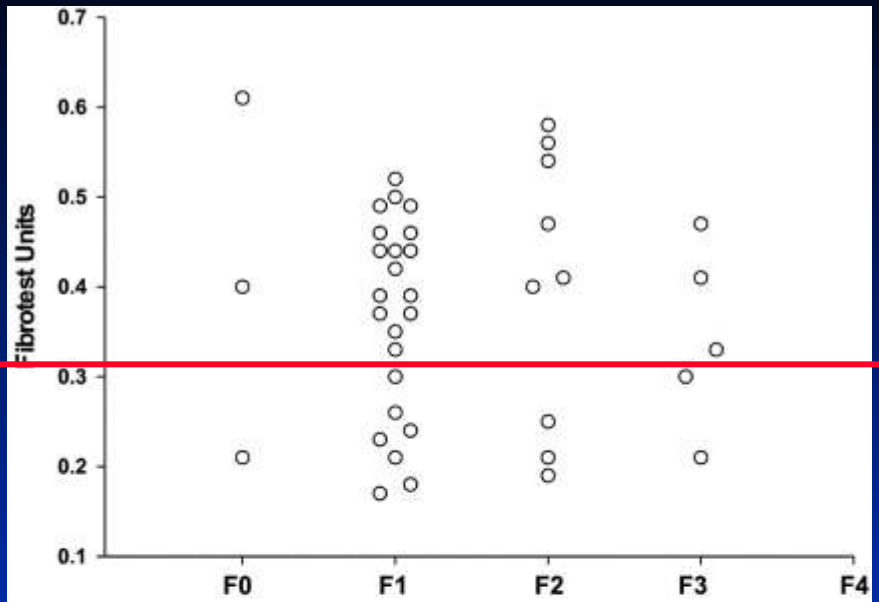
Collaterals

Splenomegaly

Confirmatory Liver Biopsy Is Not Always Necessary in Cirrhosis

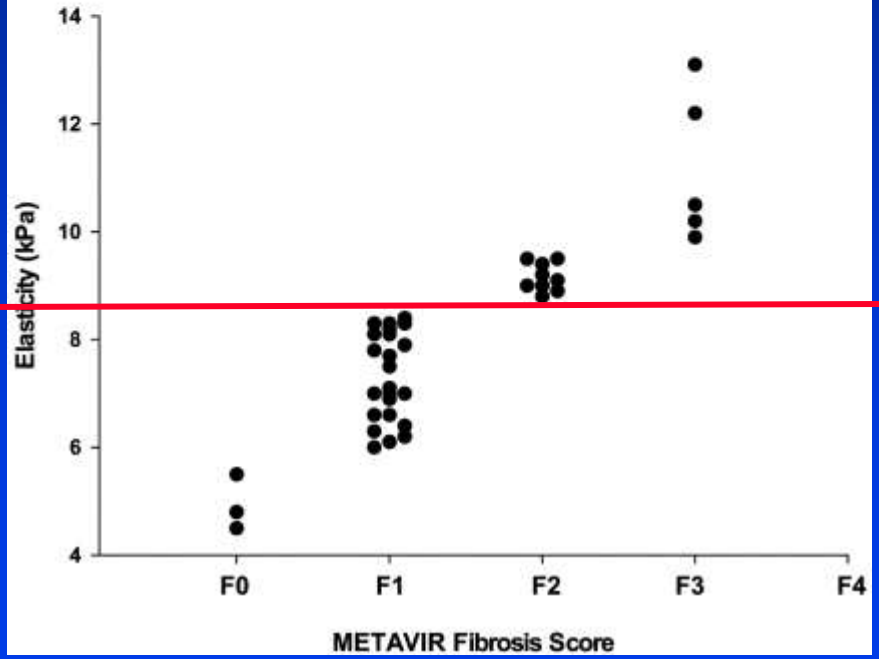
- Liver biopsy is **not** necessary in the presence of any of the following:
  - Decompensated cirrhosis (variceal hemorrhage, ascites, encephalopathy)
  - Liver-spleen and/or CAT scan diagnostic of cirrhosis
- Liver biopsy is **not** necessary for pre-transplant evaluation

Fibrotest



Optimal cutoff 0.31
Sensitivity 64%
Specificity 31%
Accuracy 43%
PPV 33%
NPV 62%

Fibroscan

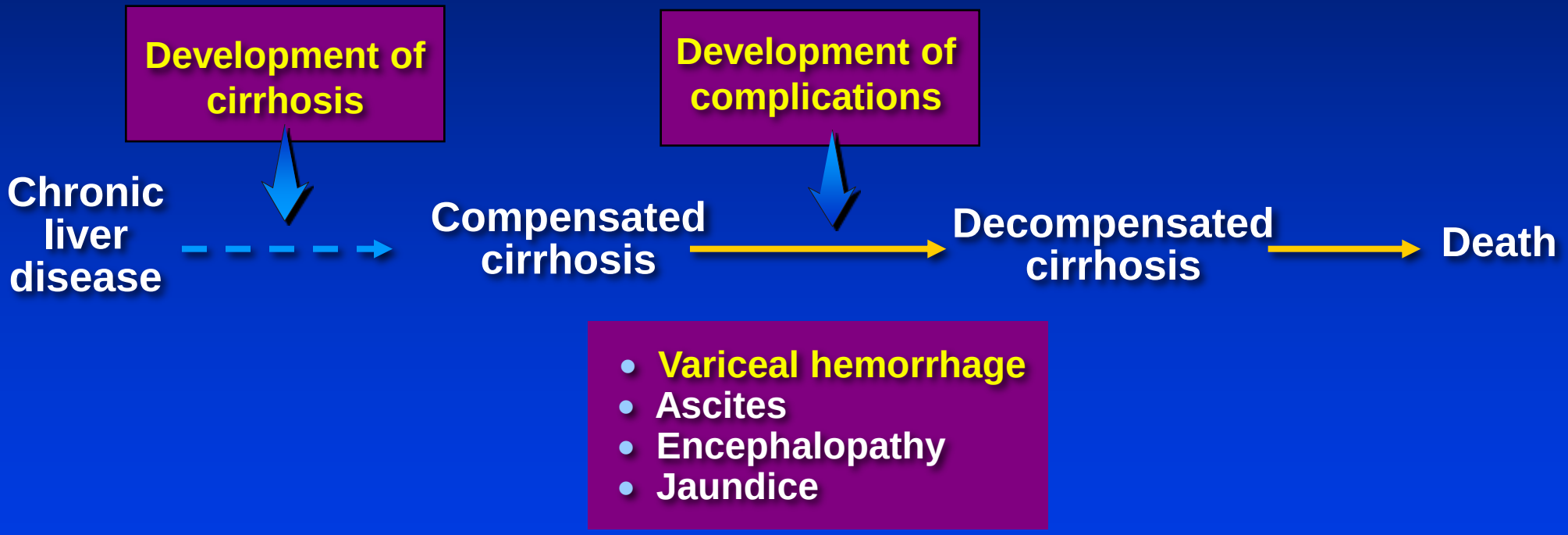


Optimal cutoff 8.74
Sensitivity 100%
Specificity 100%
Accuracy 100%
PPV 100%
NPV 100%

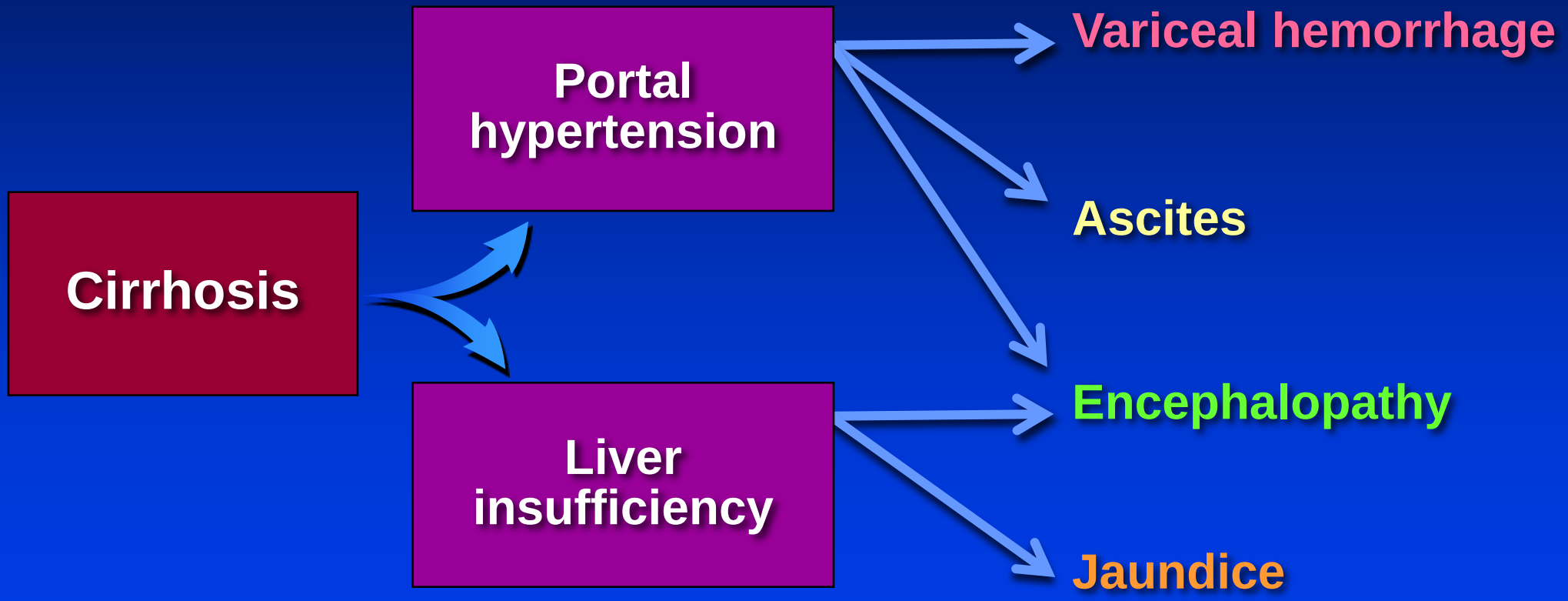
Colletta et al. Hepatology 2005;42:759

What is the Natural History of Cirrhosis?

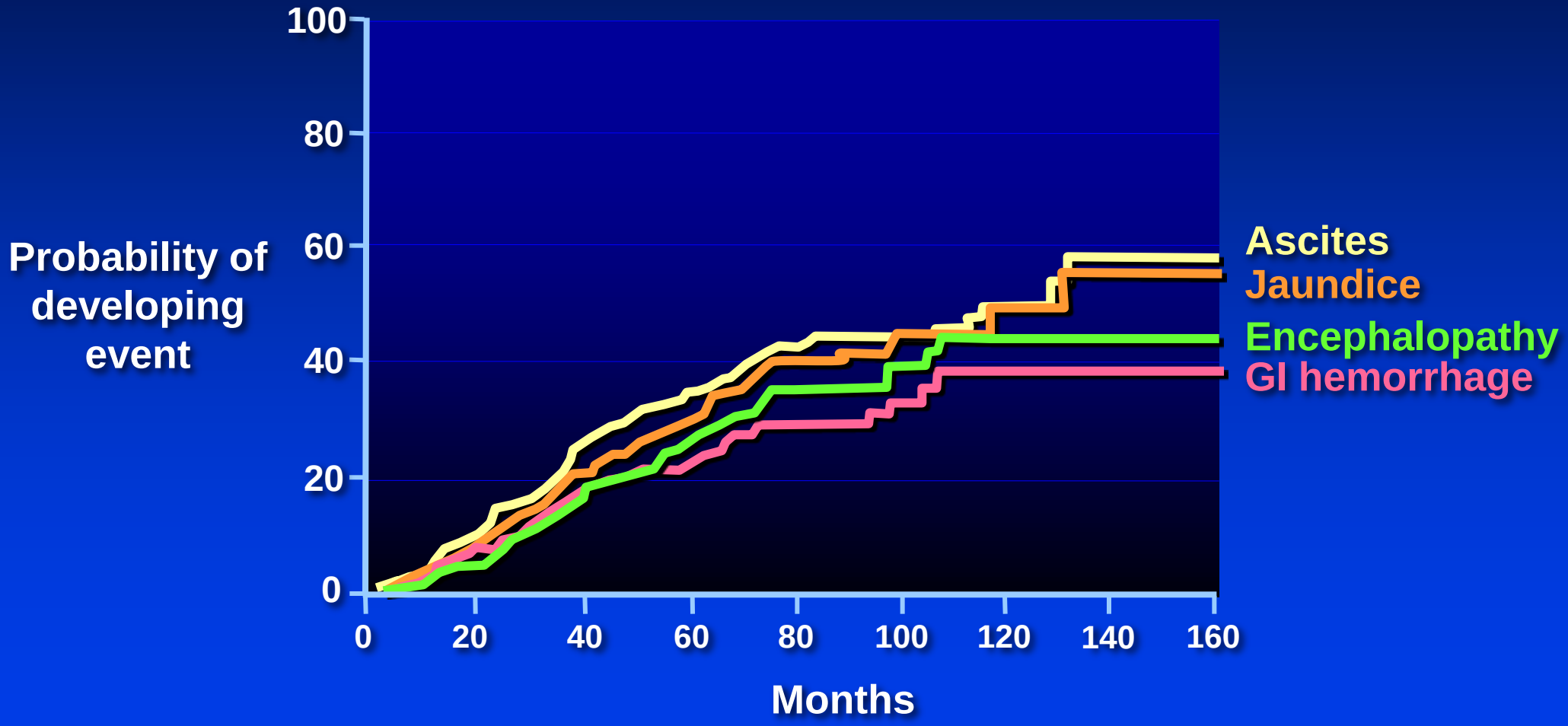
Natural History of Chronic Liver Disease



Complications of Cirrhosis Result from Portal Hypertension or Liver Insufficiency

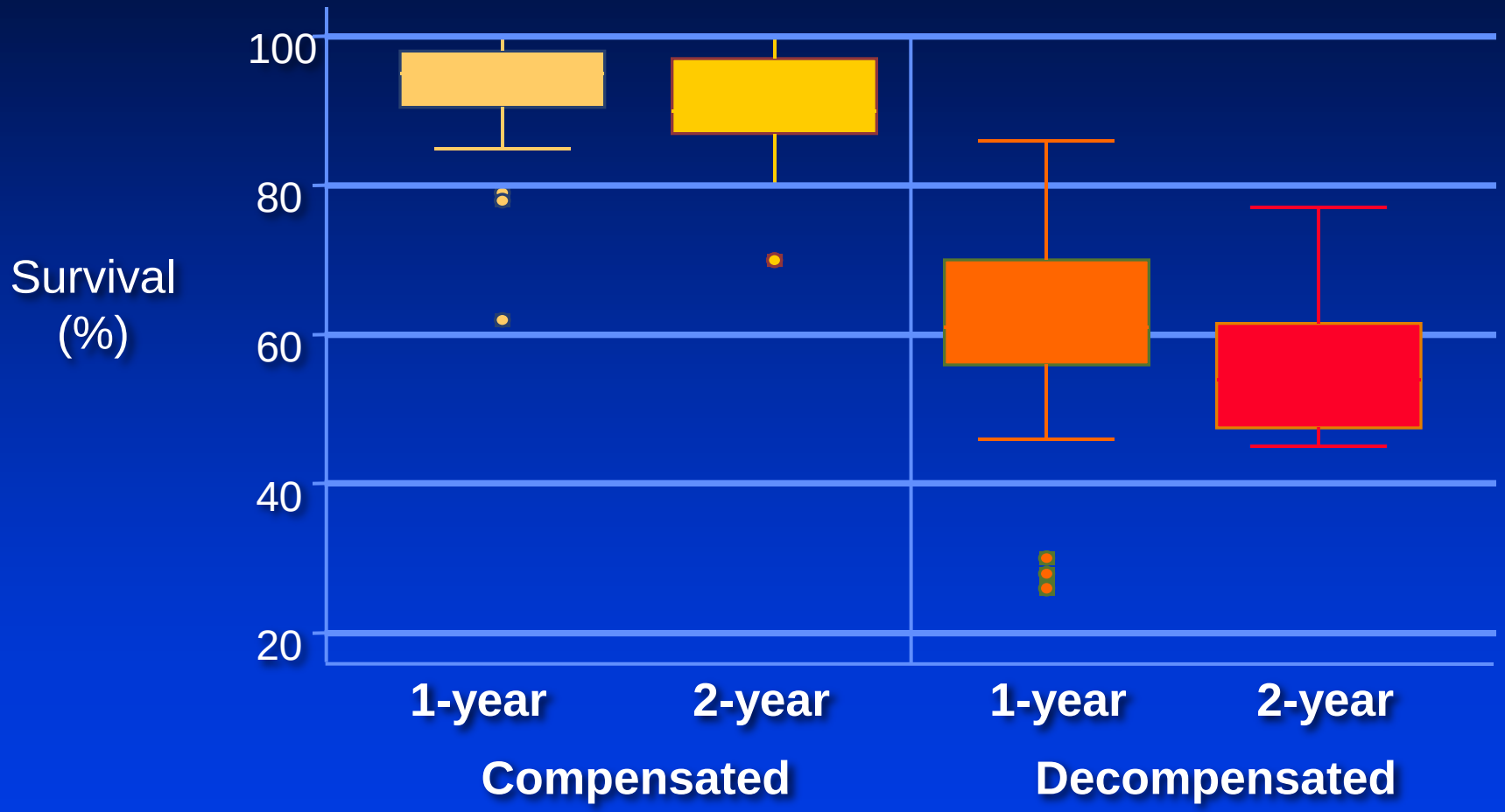


Development of Complications in Compensated Cirrhosis



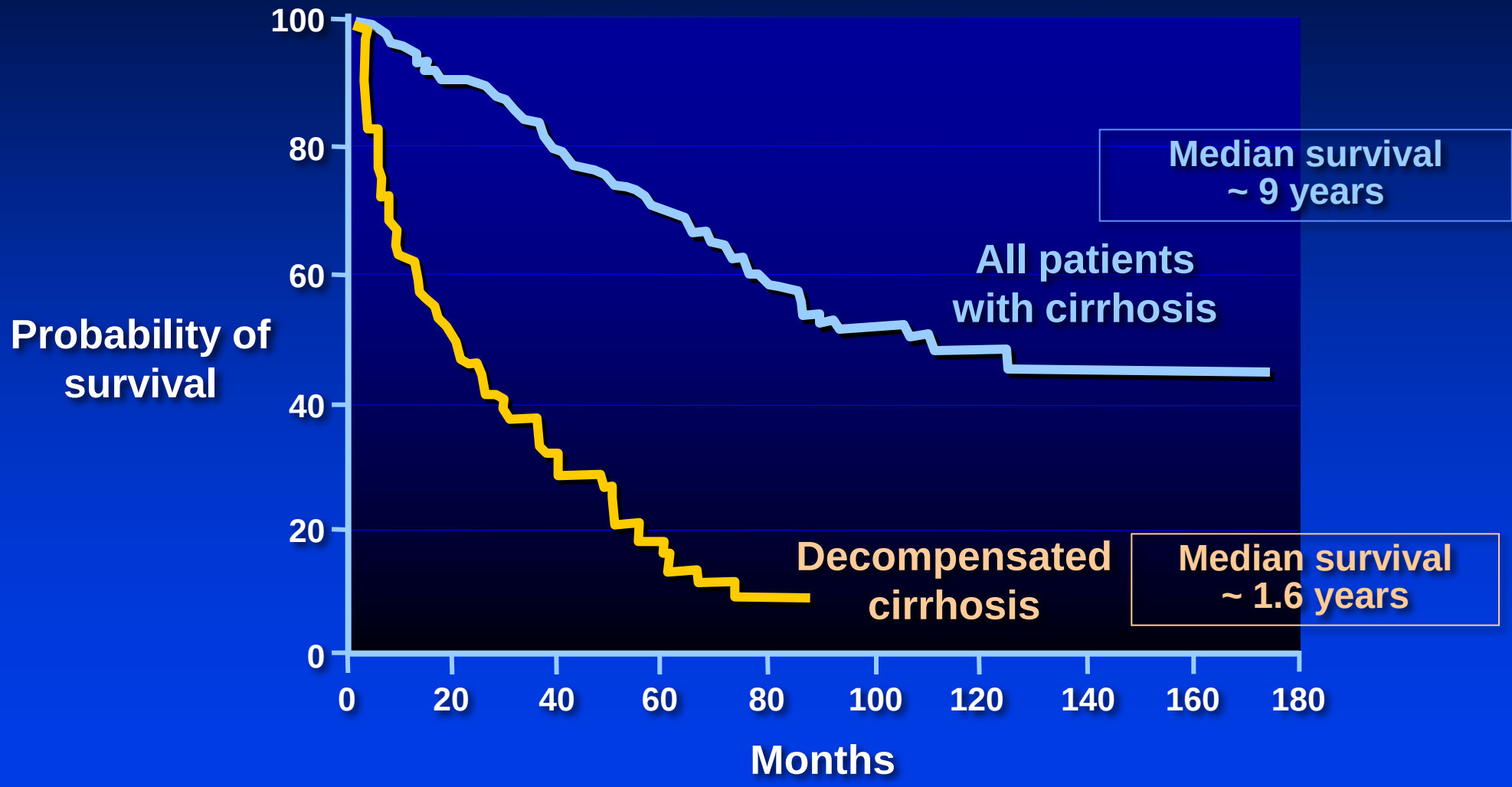
Gines et. al., Hepatology 1987; 7:122

Decompensation Shortens Survival



D'Amico, Garcia-Tsao, Pagliaro. J Hepatol 2006.

Decompensation Shortens Survival



Gines et. al., Hepatology 1987;7:122

Child-Turcotte Score

	Points		
	1	2	3
Encephalopathy	None	Minimal	Advanced
Ascites	None	Controlled	Refractory
Nutrition	Good	Fair	Poor
Bilirubin	<2	2-3	>3
Albumin	>3.5	3.0-3.5	<3.0

Child A: **5-6** pts Child B: **7-9** pts Child C: **10-15** pts

Child-Turcotte-Pugh (CTP) Score

	Points		
	1	2	3
Encephalopathy	None	Minimal	Advanced
Ascites	None	Controlled	Refractory
PT (sec prolonged) or INR	<4 <1.7	4-6 1.7-2.3	>6 >2.3
Bilirubin	<2	2-3	>3
Albumin	>3.5	3.0-3.5	<3.0

Child A: **5-6** pts Child B: **7-9** pts Child C: **10-15** pts

Vaccine Preventable Hepatitis (VPH) in Patients Chronic Liver Disease (CLD)

Vaccine-Preventable Hepatitis (VPH)*: Basic Facts

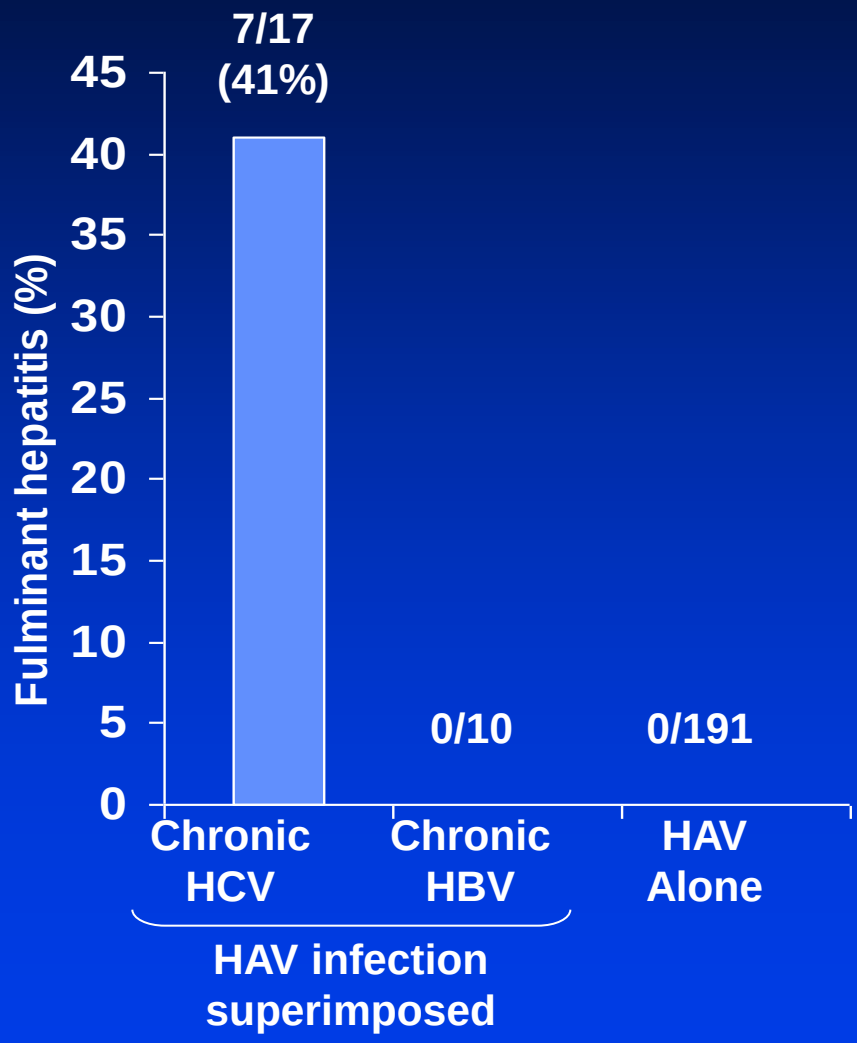
***VPH includes hepatitis A (HAV) and hepatitis B (HBV); Hepatitis C is not vaccine preventable[1]**

- Acute illness from either virus can cause significant morbidity; chronic HBV infection is associated with mortality[2]
- HAV is one of the most common vaccine-preventable diseases in international travelers[3]
- HBV is the cause of up to 80% of hepatocellular carcinomas[2]

1. Viral Hepatitis C Fact Sheet. http://www.cdc.gov/ncidod/diseases/hepatitis/c/fact.htm. Accessed January 29, 2009; 2. CDC. *Epidemiology and Prevention of Vaccine Preventable Diseases*. 10th ed, 2nd printing; 2008; 3. CDC. *Health Information for International Travel 2008*. Atlanta: US Department of Health and Human Services, Public Health Service, 2007.

Risk of Fulminant Hepatitis Following HAV Infection in Patients With CLD

- 595 Italian patients (mean age 29.1 years) with chronic HBV (n = 163) or HCV (n = 432) infection were prospectively monitored for 7 years
- At analysis, 27 patients had acquired HAV, 17 of whom had chronic HCV
  - 7 out of the 17 developed fulminant liver failure
- None of the HAV cases in HBV group progressed to liver failure



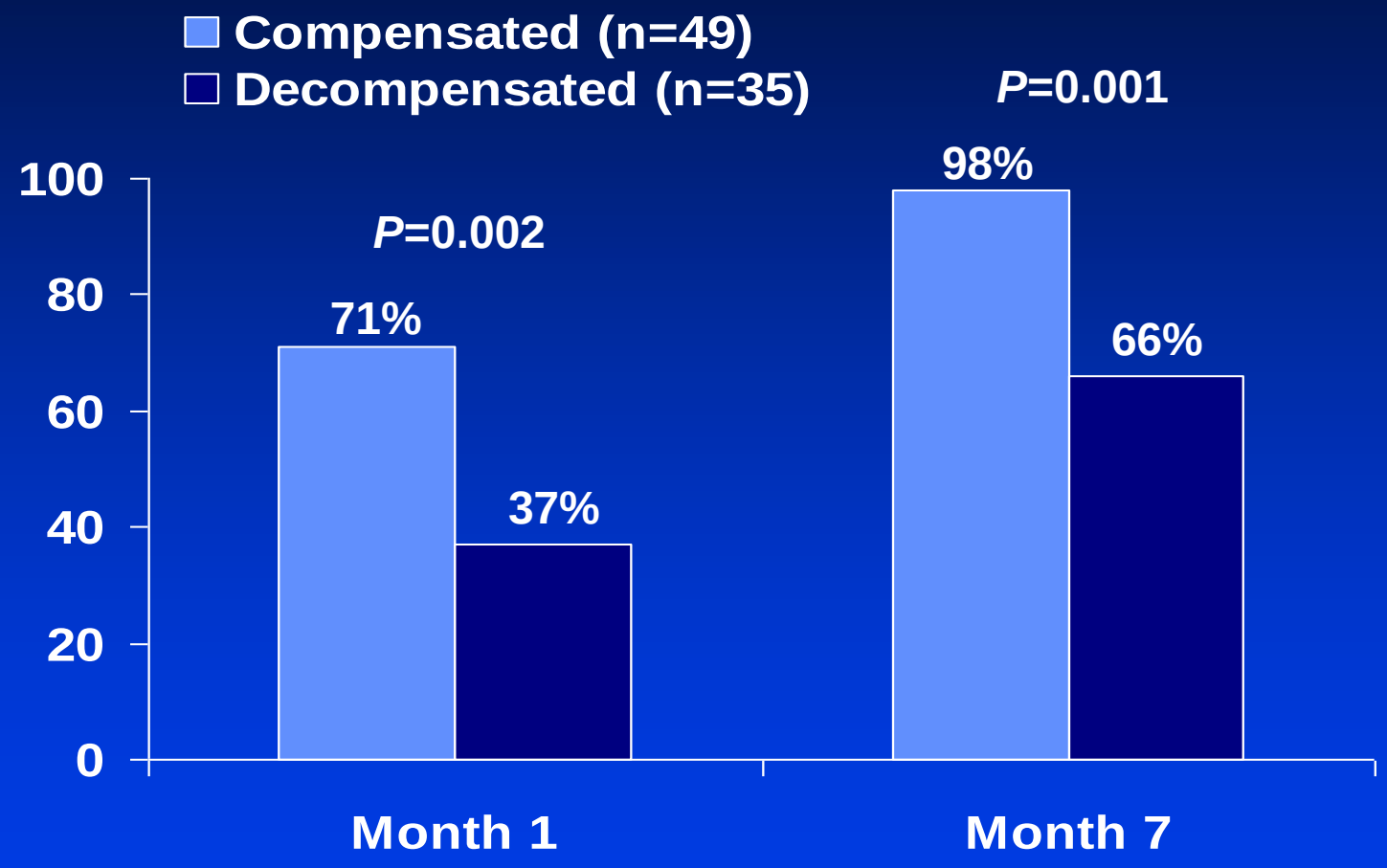
Vento et al. *N Engl J Med.* 1998;338:286-290.

More Severe Complications Can Occur When HCV Patients Are Coinfected With HBV

- 92 consecutive patients with HCV seen in Hadassah Medical Center Liver Unit (Jerusalem)
- HBV coinfection observed in 66%
- Coinfection associated with more complications
  - Bleeding esophageal varices
  - Hepatic encephalopathy
  - Spontaneous bacterial peritonitis
  - Hepatocellular carcinoma

Ilan et al. *Isr J Med Sci.* 1994;30:259-263.

Immunogenicity of HAV Vaccine in Decompensated CLD Patients



Arguedas et al. *Hepatology.* 2001;34:28-31.

HAV and HBV Vaccination Rates Are Low in Veterans with HCV

- MEDVAMC – serves >120,000 veterans
- HCV-infected patients were randomly sampled from VA data set between 2000 and 2005
  - Only 7.9% and 8.6% of the 3009 HCV-infected patients received hepatitis A and hepatitis B vaccinations, respectively
  - Only 6.5% and 8.2% of the subset of 275 HCV-infected patients with cirrhosis received hepatitis A and hepatitis B vaccinations, respectively

In this study there was significant underutilization of vaccination in patients with HCV

MEDVAMC=Michael E. DeBakey Veterans Administration Medical Center.

Hachem et al. *Aliment Pharmacol Ther*. 2008;28:1078-1087.

VPH Vaccination in Patients With CLD: Opinions in the Medical Literature

- Patients with CLD should be protected against VPH early in the natural history of their disease
  - Vaccine response in patients with mild-to-moderate CLD is similar to healthy subjects
  - The response to vaccination decreases in those with advanced disease or decompensated cirrhosis

Keeffe. *Am J Med*. 2005;118(suppl 10A):21S-27S.

VPH in Patients With CLD: Summary

- Although patients with CLD may not be at increased risk of acquiring HAV or HBV, they may be at increased risk of complications if infected
- Patients with CLD may benefit from vaccination early in their disease course

Medication Use in Cirrhosis

- Drug Induced Liver Injury (DILI)
- Role in GI Bleeding
- Effects on mental status
- Effects on renal and electrolyte balance
- Effects on hematologic status

Spectrum of Hepatotoxicity

- Subclinical: sulfonamides, salicylates, sulfonylureas
- Acute hepatic injury:

  Cytotoxic – acetaminophen

  Steatosis – amiodarone, AZT, ddi

  Cholestatic – bactrim, rifampin

  Extrahepatic – PCN, sulfa
- Chronic cholestasis: Intrahepatic (bactrim), biliary sclerosis (floxuridine)

Spectrum of hepatotoxicity (2)

- Granulomatous disease: amiodarone, sulfonamides, INH
- Chronic hepatic injury: chronic active hepatitis, steatosis (steroids, MTX, EtOH)
- Vascular disease: hepatic vein thrombosis (OCPs); SOS (herbs, OCPs, chemoTx); Peliosis hepatis (AZA, OCPs)
- Neoplasia: adenoma (OCPs); HCC (aflatoxin, alcohol)

Types of DILI

- Acute Injury – Hepatocellular & Cholestasis
- Chronic Injury – Steatohepatitis, Microvascular steatosis, Granulomatous hepatitis, Sinusoidal obstruction syndrome, Fibrosis, Peliois hepatis, Autoimmune hepatitis, Chronic hepatitis

Acute Hepatocellular DILI

- Acarbose, acetaminophen, allopurinol, aspirin, buproprion, diclofenac, ehtnaol, fluoxetine, halothane, isoniazid, ketoconazole,lisinopril, losartan, methyldopa,nefazodone, nevirapine, paroxetine, phenytoin, pyrazinamide, rifampin, risperidone, ritonavir, statins, sertraline, tetracycline, trazodone, valacyclovir, valproate.

Acute Cholestasis DILI

- ACE inhibitors, amoxacillin/clavulanate, anabolic steroids, azathioprine, chlorpromazine, clopidogrel

Chronic DILI

- Steatohepatitis- amiodarone, ethanol, tamoxifen, valproic acid
- Microvascular steatosis – ethanol, MTX, NRTI, tetracycline, valproic acid
- Granulomatous – allopurinol, carbamzepine, diltiazem, hydralazine, phenytoin, procainamide, quinidne, rosiglitazone, sufonamides.
- Sinusoidal obstruction syndrome – busulfan, cyclophosphamide, imuran

Chronic DILI

- Fibrosis – ethanol, MTX, methyldopa
- Peliosis hepatis – anabolic steroids, vinyl chloride
- Autoimmune – nitrofurantoin, minocyclin
- Chronic hepatitis – diclofenac, erythromycin, estrogens, ethanol, irbesartan, phenothiazine, sulindac, tricyclics.

Chronic DILI

- Mixed – amitryptilline, azathioprine, sulfonamides, phenytoin, nitrofurantoin
- Neoplasm – anabolic steroids, OCPs, vinyl chloride
- Ishemic necrosis - ergot

Classification of DILI

- Clinical/Laboratory – hepatocellular, cholestatic, mixed
- Mechanism – Direct, Idiosyncratic (immune-mediated, metabolic)
- Histologic findings – Cellular nectosis or apoptosis, cholestasis, fibrosis, granulomatous, sinusoidal obstructive syndrome VOD, phospholipoidosis

Herbal preparations with Hepatotoxic Potential

- Pyrrolizidine alkaloids: Crotolaria, Heliotropium, Mate’ (paraguay) tea; Senecio; Symphytum officinale (Comfrey); Ackee fruit; Atractylis gummifera; Azadirachza indica; Berberis vulgaris; Callillepsis laureola; Cassia angustifolia; Cocaine)Erythroxylon coca) Cycasin; Pennyroyal; Chapparal, creosote bush, greasewood; Sassafras; Skull ccp (Scutellaria); Germander (Teucrium Chamaedrys; Valerian; Mistletoe (Viscum Album)

Herbal preparations with Hepatotoxic Potential

Chinese herbal remedies and teas:

- **Lycopodium serratum (Jin Bu Huan)**
- **Ma-huang**
- **Syo-saiko-to (Xiao-chai-hu-tang)**

Star-Advertiser
Oct 9, 2013

STATE SEEKS HALT OF PRODUCT SALES

Health officials are asking stores to pull from their shelves a dietary supplement tied to liver damage

By Sarah Zoellick
szoellick@staradvertiser.com

Twenty-nine confirmed cases, 11 hospitalizations, two liver transplants and one death later, the state Department of Health on Tuesday finally confirmed the name of the dietary supplement linked to a surge in acute liver inflammation and liver failure in the isles, asking that sale of the product come to a halt.

Health Department staff traveled store to store Tuesday appealing to local retailers to voluntarily remove all formulas of the marketed "fat burner" OxyELITE Pro from their shelves while the agency continues to work with the Food and Drug Administration and Centers for

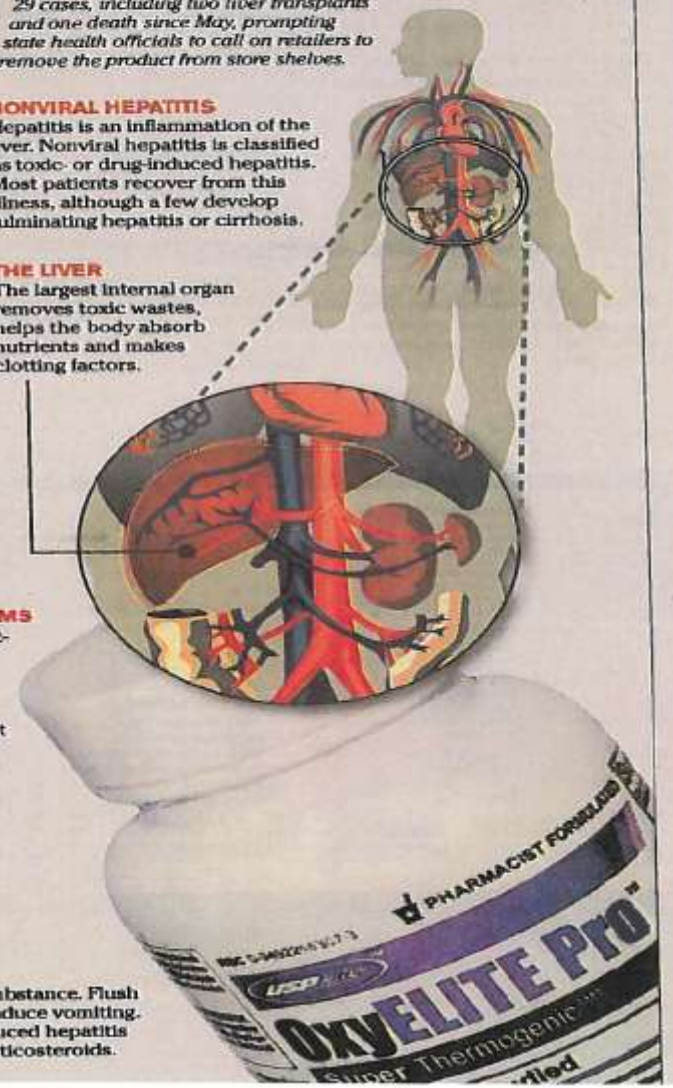
Please see **SUPPLEMENT**, *A8*

ALARMING LINK

The OxyELITE Pro supplement, which users take for weight loss or building muscles, is suspected in a rash of cases of acute hepatitis and liver failure in Hawaii. It has been linked to 29 cases, including two liver transplants and one death since May, prompting state health officials to call on retailers to remove the product from store shelves.

NONVIRAL HEPATITIS
Hepatitis is an inflammation of the liver. Nonviral hepatitis is classified as toxic- or drug-induced hepatitis. Most patients recover from this illness, although a few develop fulminating hepatitis or cirrhosis.

THE LIVER
The largest internal organ removes toxic wastes, helps the body absorb nutrients and makes clotting factors.



SIGNS AND SYMPTOMS
Clinical features of toxic- and drug-induced hepatitis vary with the severity of liver damage and the causative agent. In most patients, symptoms resemble those of viral hepatitis:

- Loss of appetite
- Nausea
- Vomiting
- Jaundice
- Dark urine
- Hepatomegaly
- Abdominal pain
- Clay-colored stools

TREATMENT
Remove the harmful substance. Flush from the stomach or induce vomiting. Patients with drug-induced hepatitis may be prescribed corticosteroids.

Number of supplement users with liver damage grows

Isle health officials are working with federal counterparts to track 30 cases

By Sarah Zoellick
szoellick@staradvertiser.com

The number people in Hawaii suffering liver damage linked to taking a dietary supplement for weight loss or muscle gain is now at 30, with the majority of cases on Oahu, state Department of Health officials said Wednesday.

There have been 21 cases reported on Oahu, seven on Hawaii Island, and one each on Kauai and Maui. The earliest of the cases goes back to May.

Eleven of the 30 patients have been hospitalized, two underwent liver transplants, and one died, DOH said.

The Maui patient, 48-year-old Sonnette Marras, died Oct. 4 after taking the dietary supplement OxyELITE Pro for several weeks to lose weight she had gained during her last pregnancy, her family has said. Marras had seven children, ranging in age from 1 to 26.

According to an obituary notice released Wednesday, Marras worked as a construction laborer for Local 368 of the Laborers' Union and also was a driver for Spedi Shuttle. She is survived by her companion, Michael Soriano; her mother, Gladys Marras; four daughters and three sons; and three brothers and three sisters.

The family declined to comment Wednesday, but before Marras died Soriano told Hawaii News Now that she was denied a liver transplant because doctors discovered a lump in her breast.

Speaking generally, Honolulu transplant surgeon Linda Wong said Wednesday that patients with active cancer do not receive organ transplants because anti-rejection medications can make cancer cells grow rapidly.

Wong said she has seen cases of liver damage and failure in the isles linked to dietary supplements before, maybe one or two a year, but that having so many in such a short time linked to a single product "seemed unusual" and was "not statistically normal."

Other supplements that have caused people health problems over the years include but are not limited to Hydroxycut, Chinese herbs and slimming teas, Wong said.

"I think that there's a lot of supplements that are being sold out there, and I think that people should tell physicians when they're taking these things and they should report symptoms immediately and not wait too long before more severe symptoms happen," she said.

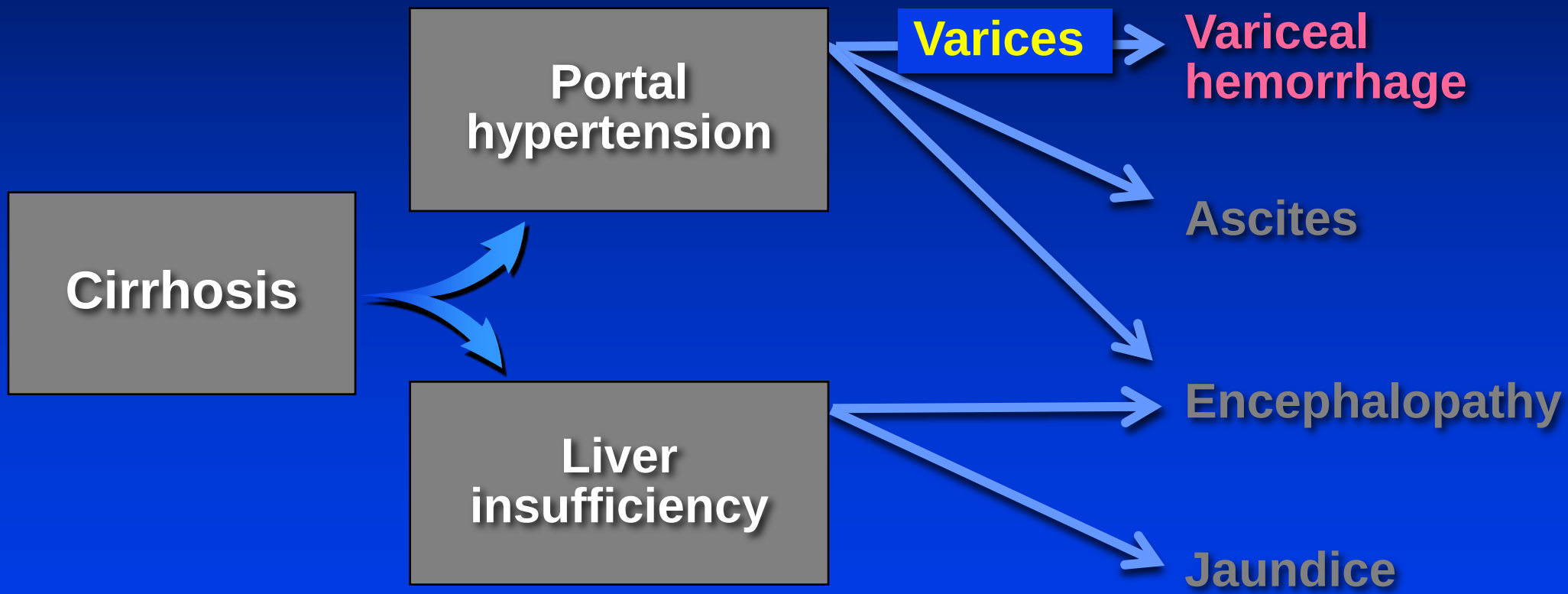
Although DOH, the Food and Drug Administration and Centers for Disease Control officially announced this week that OxyELITE Pro had been linked to 24 of the 30 cases of acute liver damage, the agencies still have not been able to pinpoint a precise cause for the epidemic. No cases have been reported in other states.

A spokesman for the FDA said Wednesday the agency is "working quickly to learn more" about which formulas of the weight loss and/or muscle gain supplement line were being taken by the affected patients and how a now-illegal formula of the product, which contains an ingredient known as DMAA (also known as 1,3-dimethylamylamine), was being purchased.

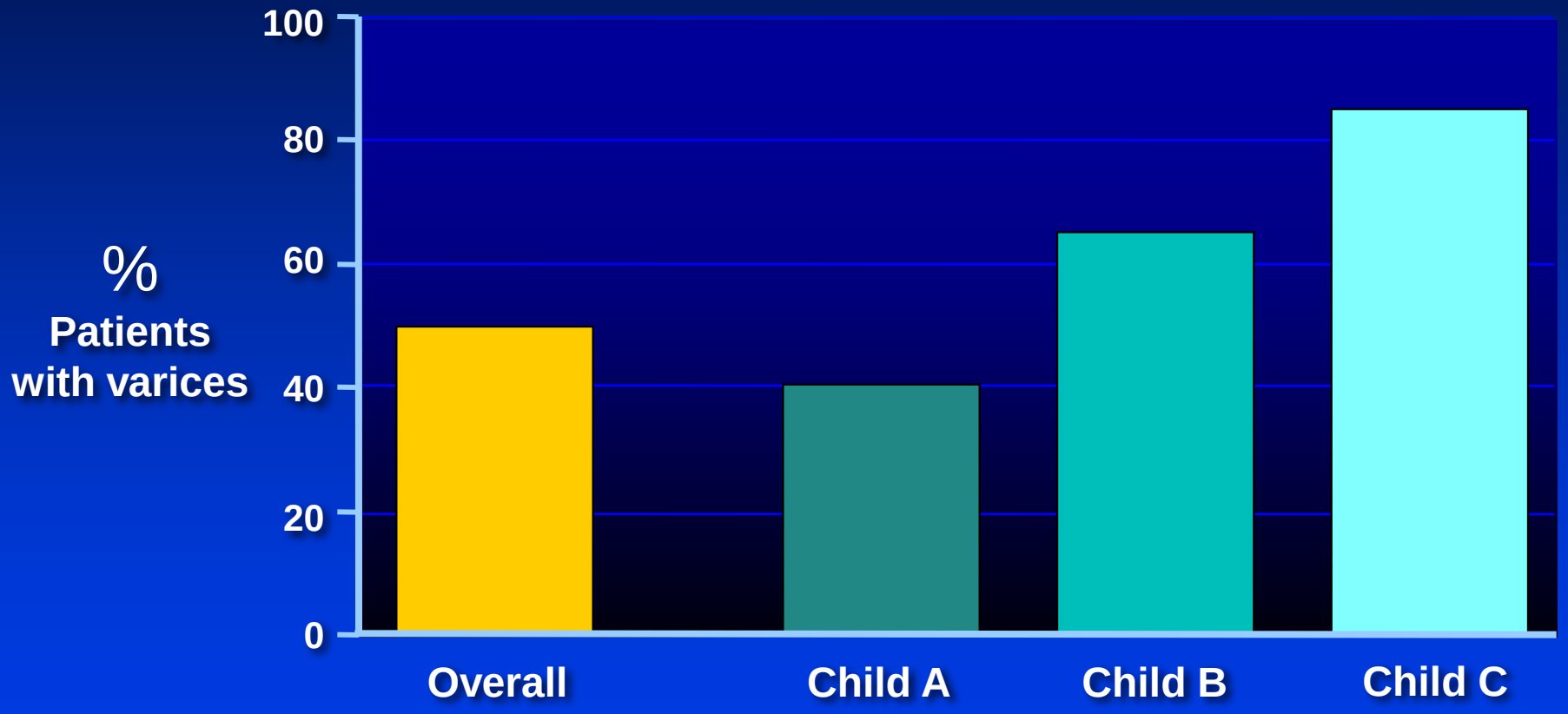
In the wake of the federal government shutdown that began Oct. 1, the FDA has been "doing what it can un-

Please see **PILLS**, *B3*

Complications of Cirrhosis Result from Portal Hypertension or Liver Insufficiency

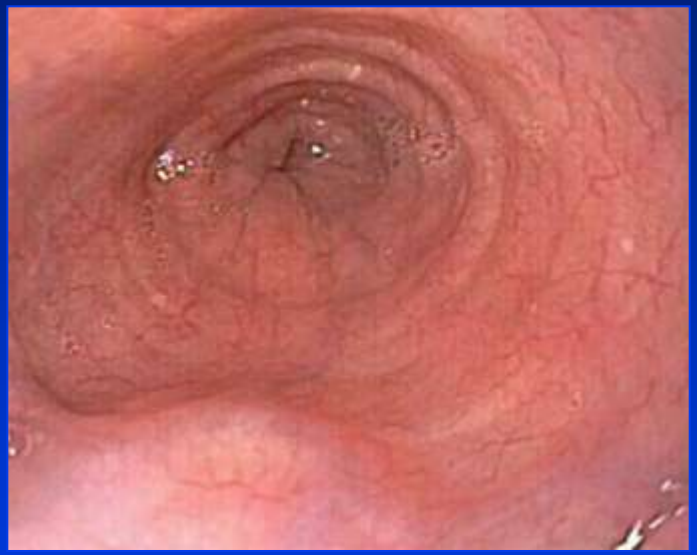


Varices are *present* in ~50% of patients with cirrhosis screened endoscopically at diagnosis

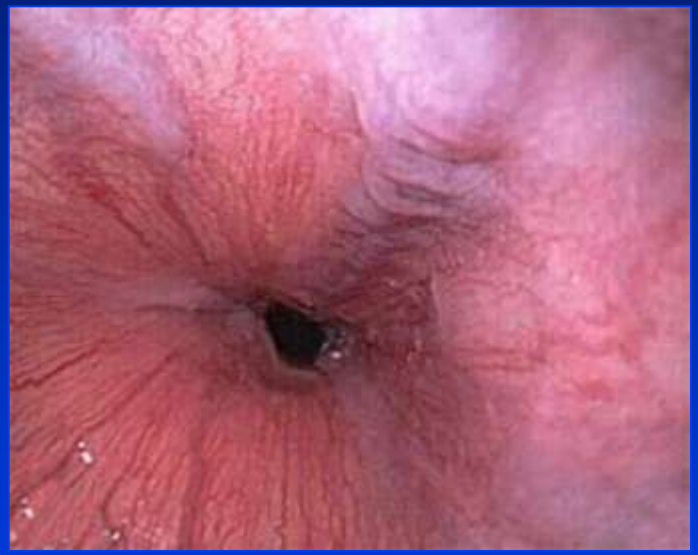


Pagliaro et al., Portal Hypertension: Pathophysiology and Management, 1994: 72

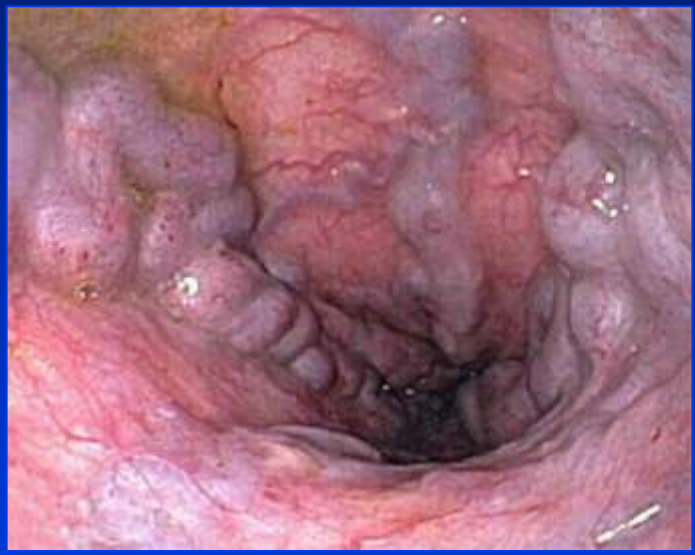
Varices Increase in Diameter Progressively



No varices

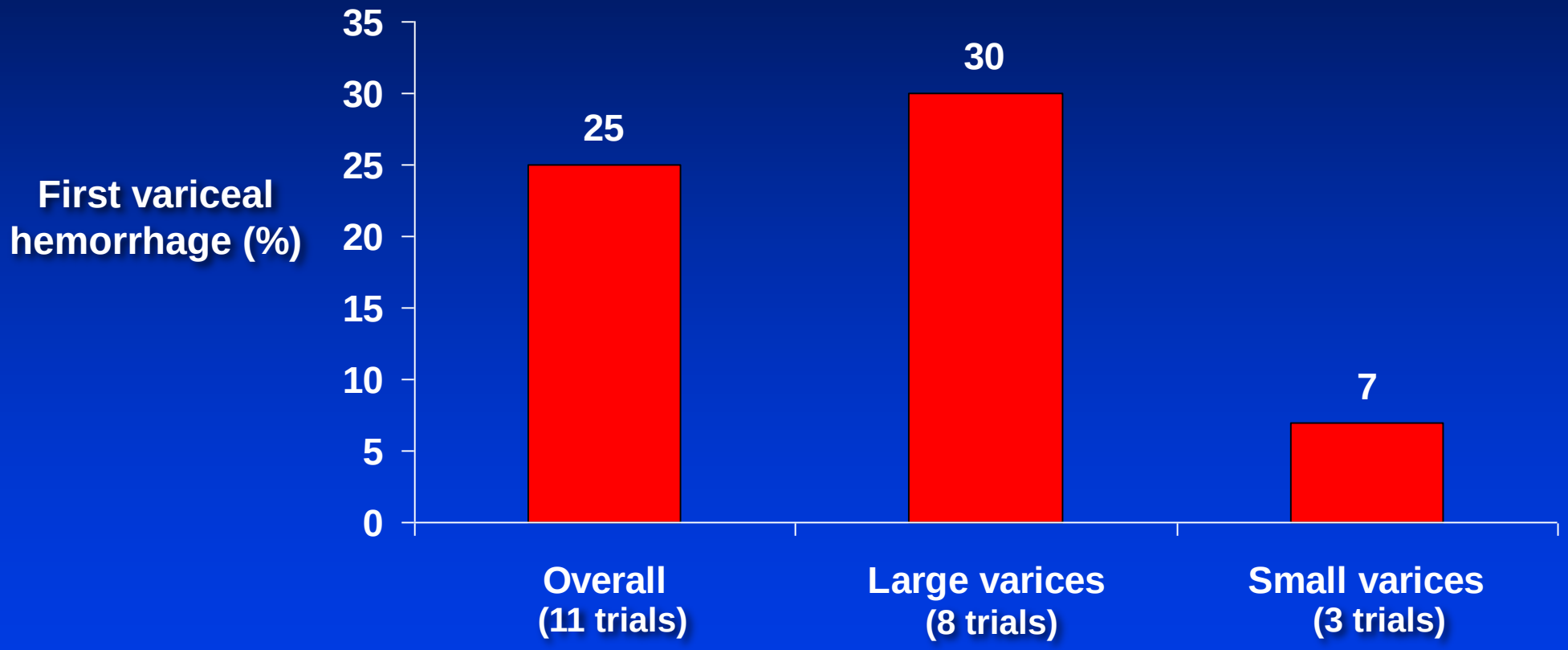


Small varices



Large varices

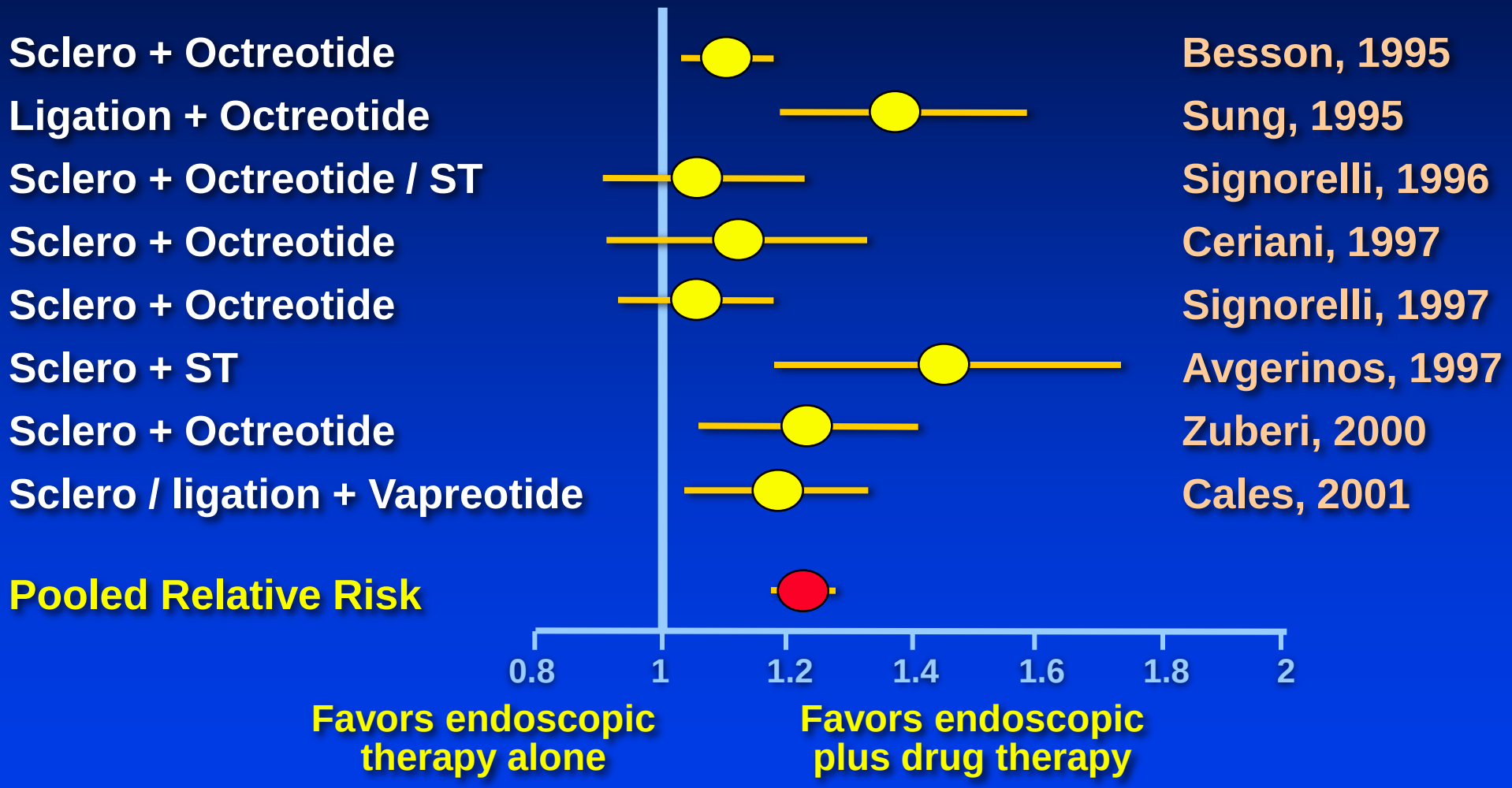
Large varices have a higher risk of first variceal hemorrhage than small varices



D'Amico et al., Sem Liv Dis 1999; 19:475

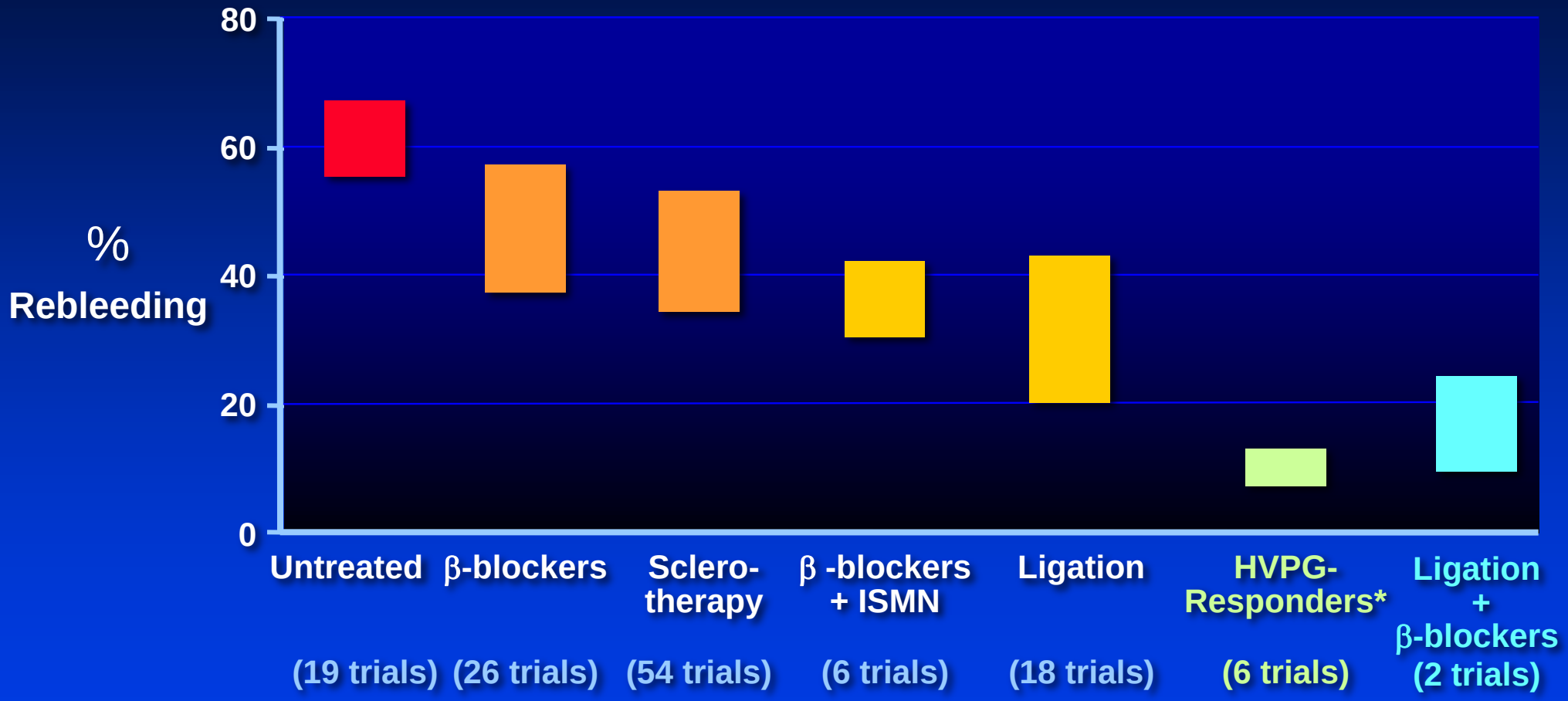
* Significantly lower

Combination Drug / Endoscopic Therapy is More Effective Than Endoscopic Therapy Alone



Bañares R et al., *Hepatology* 2002; 35:609

Lowest Rebleeding Rates are Obtained in HVPG Responders and With Ligation + β-Blockers



* ↓ HVPG <12 mmHg or >20% from baseline

Bosch and García-Pagán, Lancet 2003; 361:952

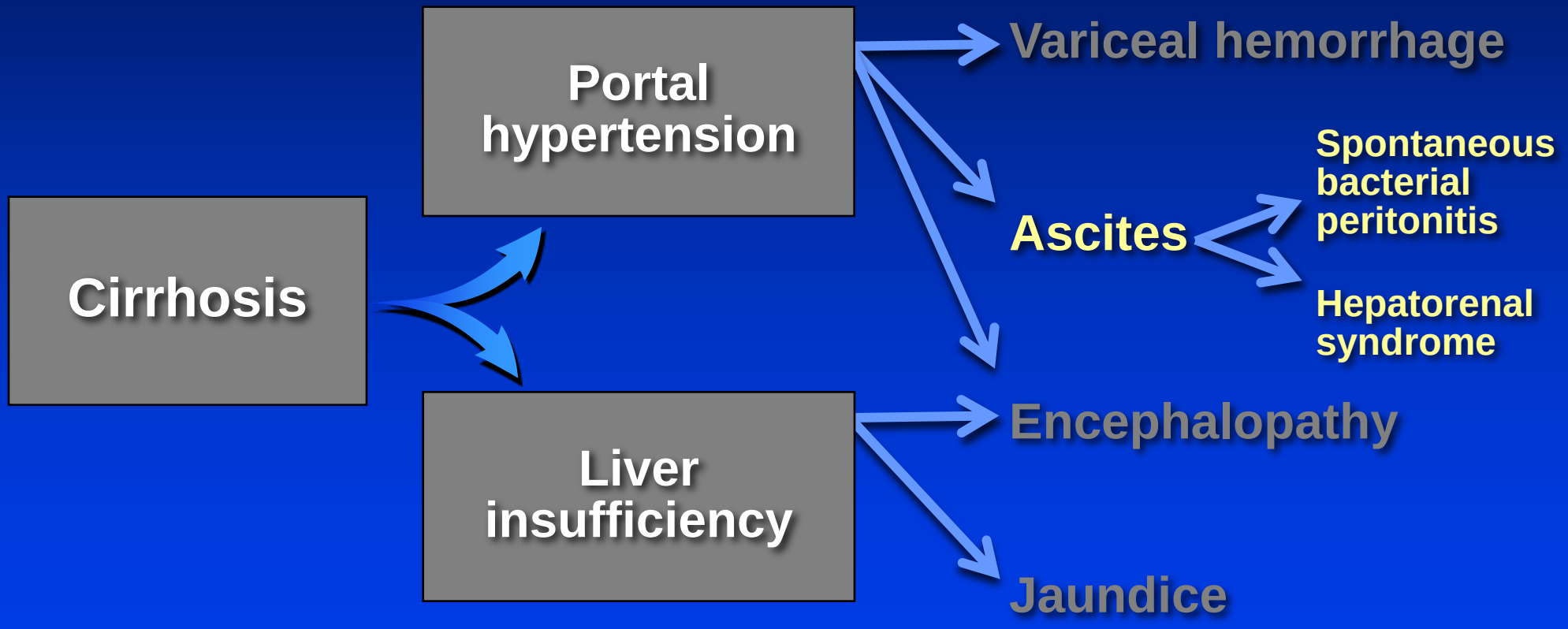
Varices: Medications to Avoid

- Drugs that can cause direct mucosal injury to esophagus or stomach – Salicylates, NSAIDs, Bisphosphonates, Ethanol
- Drugs that can cause ischemic necosis like ergot or can cause Sinusoidal Occlusive Syndrome or VOD – OCPs, herbs, chemotherapy eg, 5FU etc

Management of Compensated Cirrhosis

- Screen for varices as soon as diagnosis is made (upper endoscopy, Pillcam?)
- Patients with large varices require prophylactic therapy for variceal hemorrhage with non-selective beta-blockers or EVL
- Patients with small varices require repeat endoscopy in 1-2 years
- Patients without varices require repeat endoscopy in 2-3 years

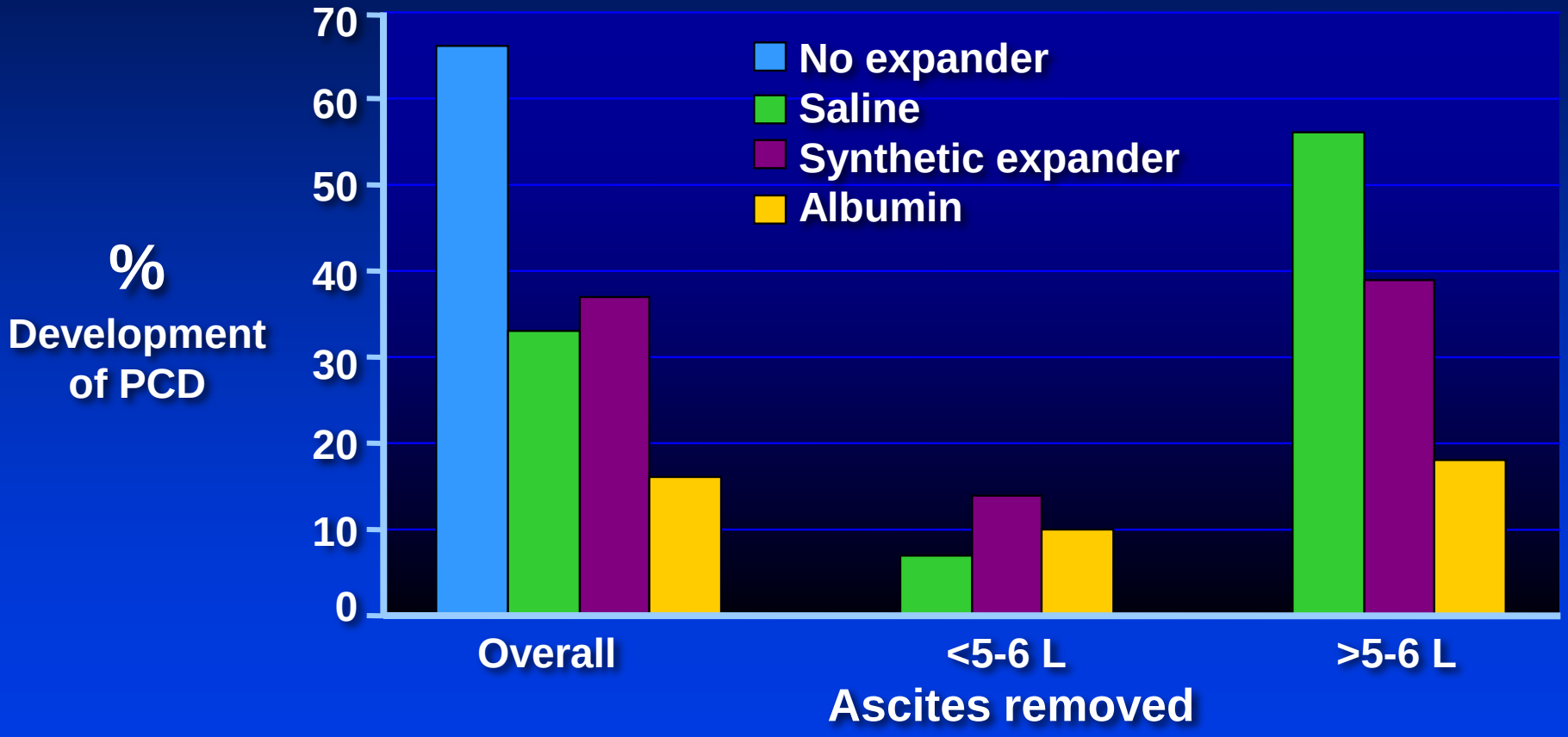
Complications of Cirrhosis Result from Portal Hypertension or Liver Insufficiency



Management of Decompensated Cirrhosis Ascites

- Salt restriction
- Diuretics
  - Spironolactone alone
  - Spironolactone + furosemide
- Avoid NSAIDs
- No water restriction unless serum Na <130
- Low threshold to perform a diagnostic paracentesis to investigate SBP
- No antibiotic prophylaxis if no history of SBP

Post-Paracentesis Circulatory Dysfunction (PCD) Depends on the Type of Plasma Volume Expander and the Amount of Ascites Removed



Gines et al., Gastroenterology 1988; 94:1493; Gines et al., Gastroenterology 1996; 111:1002; Sola-Vera et al., Hepatology 2003; 37:1147

Management of decompensated cirrhosis
Spontaneous bacterial peritonitis

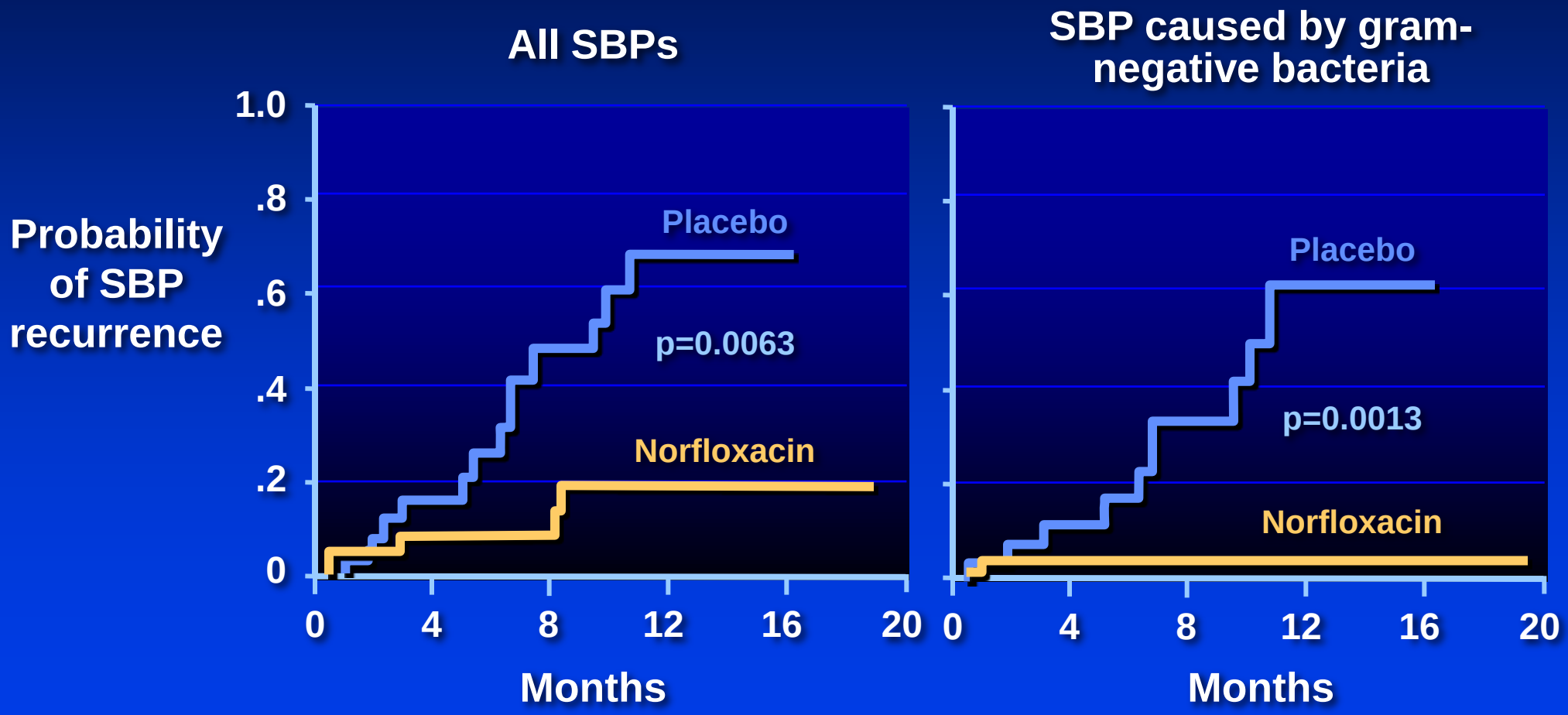
- **Diagnostic paracentesis:**
  - **At admission**
  - **Development of symptoms/signs of SBP, encephalopathy and/or renal dysfunction**
- **Diagnosis based on ascites PMN count > 250/mm^3**

Rimola et al. J Hepatol 2000.

Management of Decompensated Cirrhosis
Spontaneous bacterial peritonitis

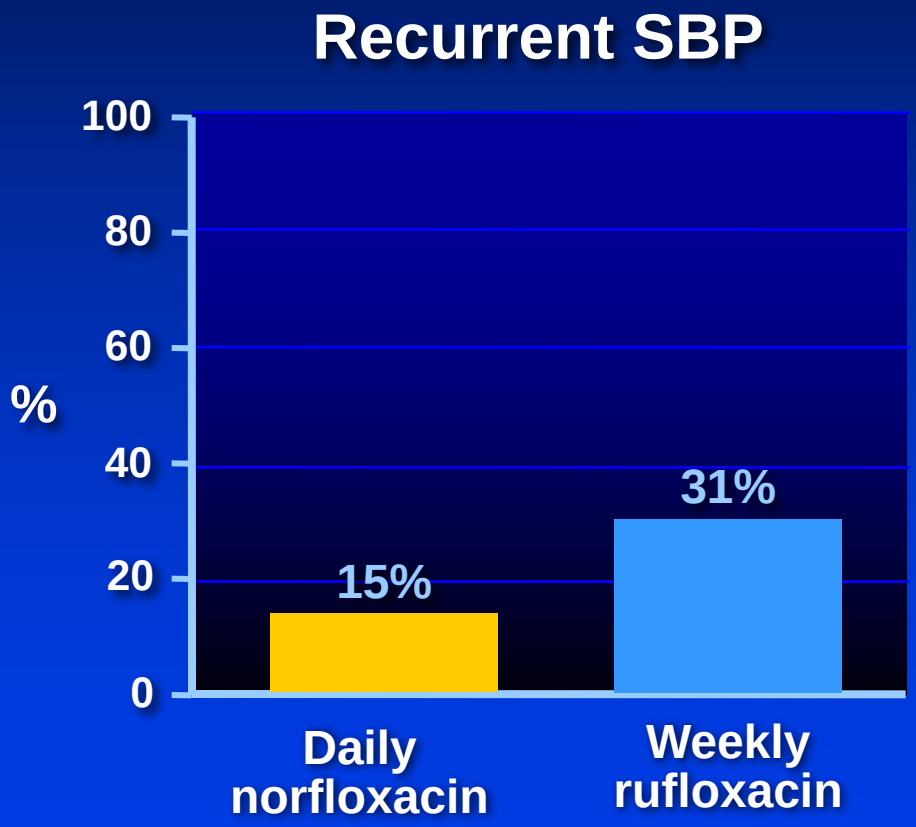
- Systemic antibiotics
  - Cefotaxime or ceftriaxone
  - Beta-lactam/beta-lactamase combination
  - Avoid aminoglycosides
- Albumin in patients with any renal dysfunction at diagnosis
- Start long-term antibiotic prophylaxis (norfloxacin) upon discharge from hospital

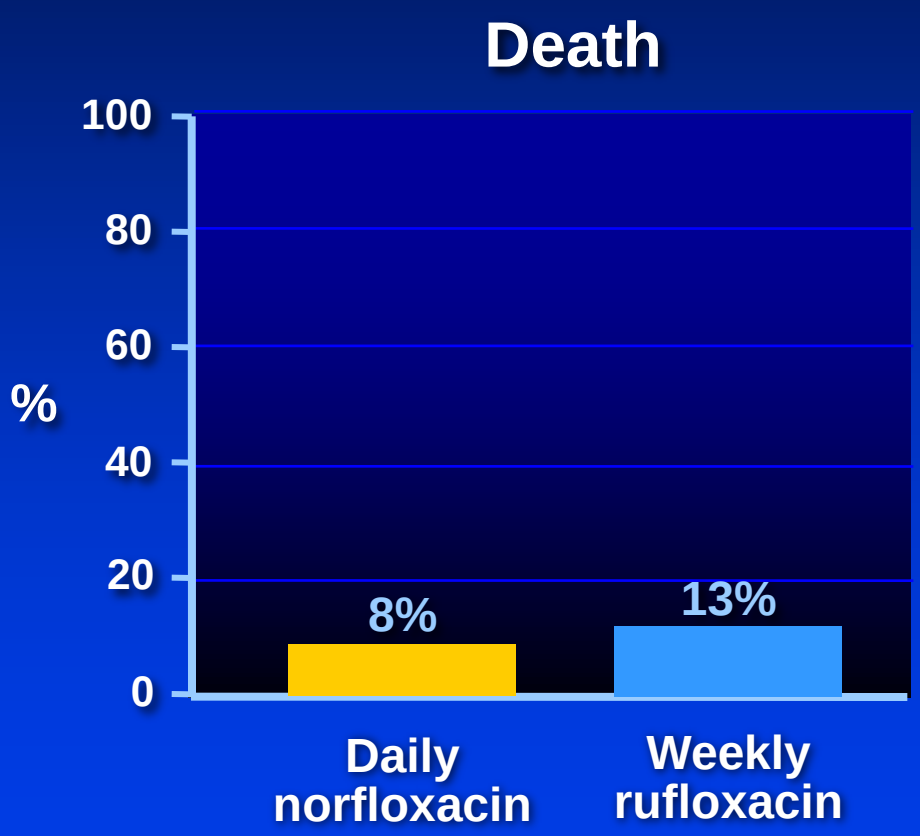
Norfloxacin Reduces Recurrence of Spontaneous Bacterial Peritonitis



Gines et al., Hepatology 1990; 12:716

Quinolones Administered Once a Week are not as Effective as Quinolones Administered Once a Day





Bauer et al., Dig Dis Sci 2002;47:1356

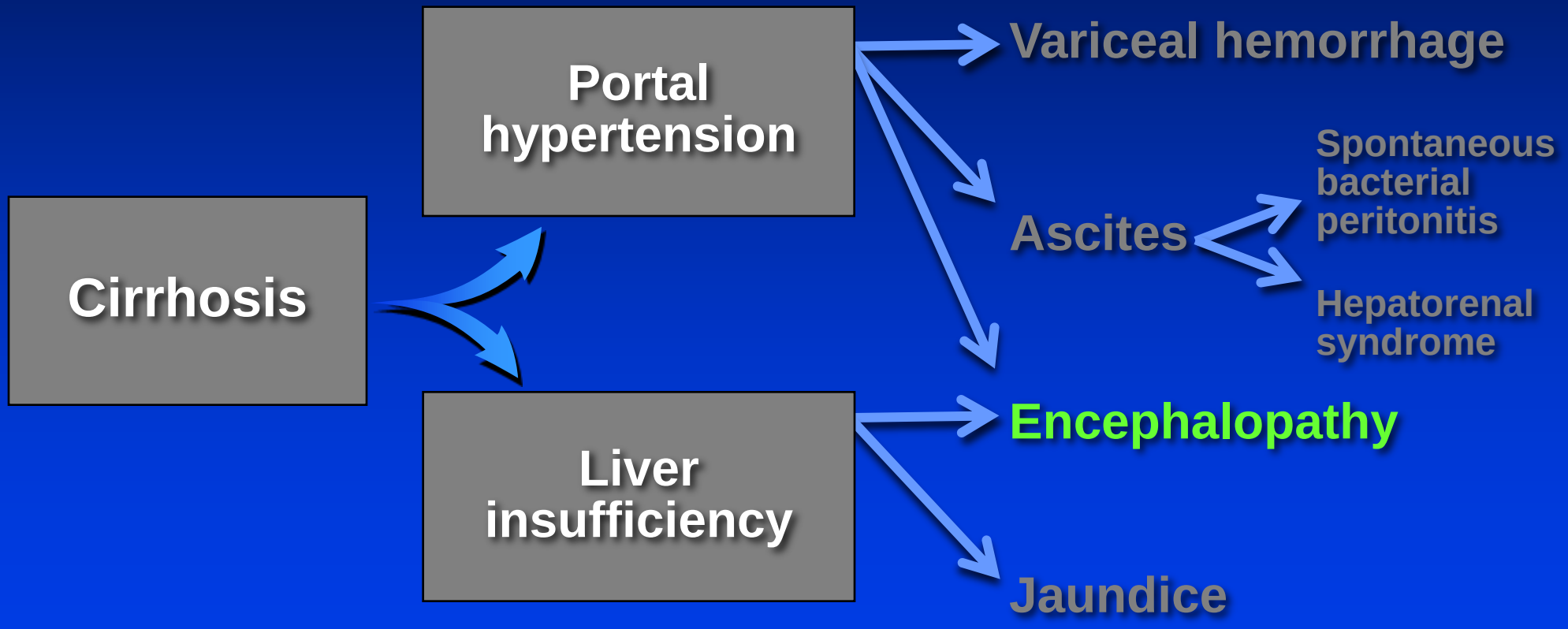
Management of decompensated cirrhosis
Hepatorenal syndrome

- Diagnosis of exclusion:
  - Sepsis
  - GI hemorrhage
  - Dehydration (prerrenal azotemia)
    - Overdiuresis
    - Diarrhea
  - Nitrates or other vasodilators
  - Nephrotoxic substances (aminoglycosides, dye)
  - NSAIDs
- Persistence of renal insufficiency despite ruling out all of the above, diuretic discontinuation + albumin expansion

Management of decompensated cirrhosis
Hepatorenal syndrome

- Treatment: liver transplantation
- Bridging therapy:
  - Vasoconstrictors (terlipressin, octreotide+midodrine, noradrenaline) + albumin
- Therapy requiring further investigation:
  - TIPS (in patients who have responded to octreotide + midodrine)
  - Extracorporeal albumin dialysis
- Ineffective therapy:
  - Dopamine
  - Hemodialysis

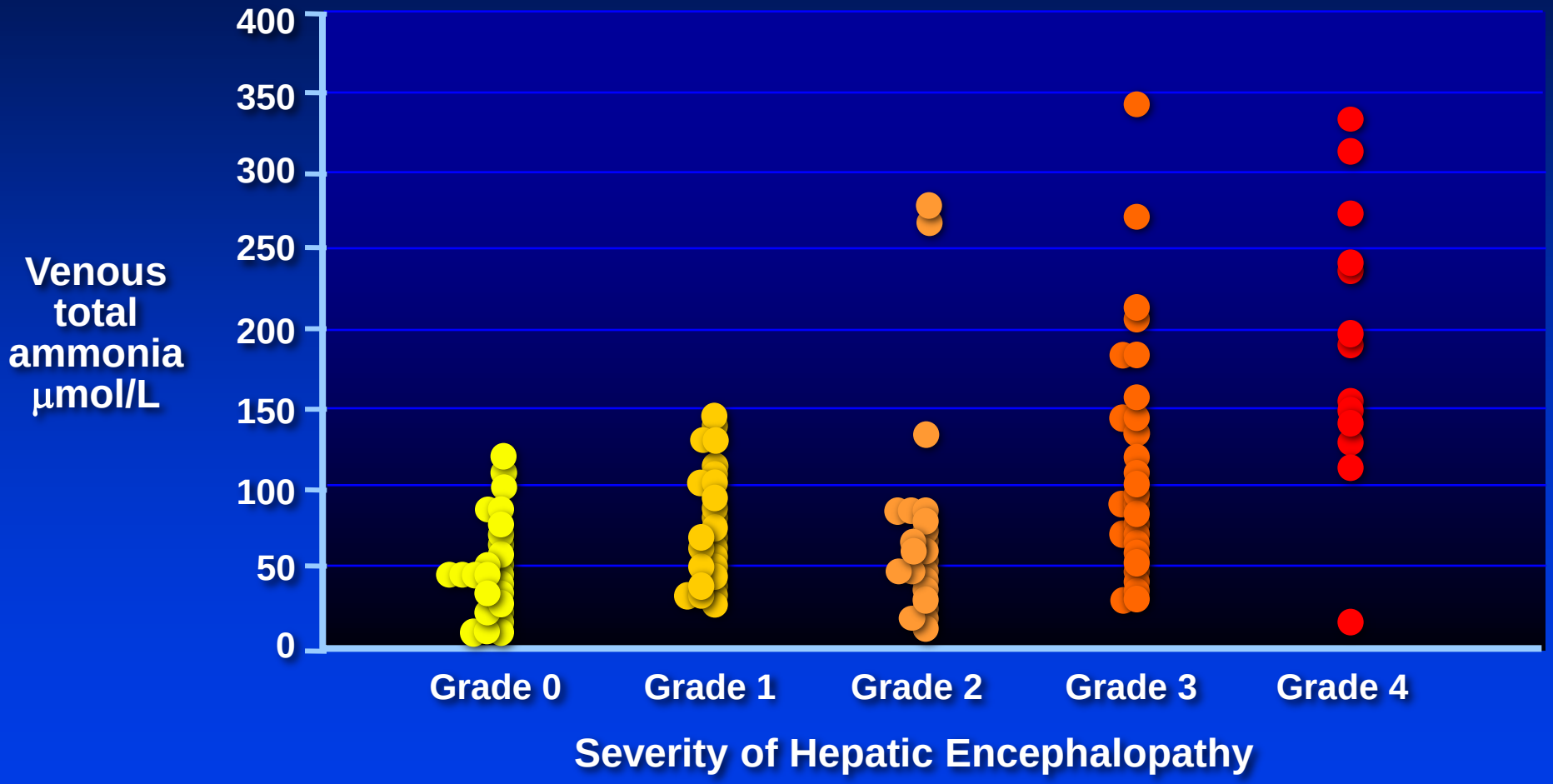
Complications of Cirrhosis Result from Portal Hypertension or Liver Insufficiency



Management of Decompensated Cirrhosis
Encephalopathy

- Identify and treat precipitating factor
  - Infection
  - GI hemorrhage
  - Prerrenal azotemia
  - Sedatives
  - Constipation
- Lactulose (adjust to 2-3 BM/day)
- Short-term protein restriction (if at all)

Poor Correlation of Ammonia Levels With Presence or Severity of Encephalopathy



Ong et al., Am J Med 2003; 114:188

Treatment Options for OHE

- Reduction of nitrogenous load from gut
  - Bowel cleansing
  - Non-absorbable disaccharides (lactulose)
  - Antibiotics (rifaximin, metronidazole)*
  - Agents that bind NH_3 in the gut
    - Na benzoate
    - Na phenylacetate
    - Na hydroxybutyrate
- Drugs that affect neurotransmission (flumazenil, bromocriptine)
- Manipulation of splanchnic circulation (occlusion of portal-systemic collaterals)
  - Occlude TIPS shunt if present

* Neomycin (historical interest).

Adapted from Blei AT et al. *Am J Gastroenterol*. 2001;96(7):1968-1976.

Antibiotics

- Activity against urea producing bacteria
- inhibit production of ammonia
- inhibit production of benzodiazepine-like ligands
- neomycin -- 6 gm daily (3 divided doses)
  - ototoxic, nephrotoxic
- Metronidazole -- 800 mg daily (1 week)
- Rifaximin -- 1200 mg daily
- treatment of H pylori

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 25, 2010 VOL. 362 NO. 12

Rifaximin Treatment in Hepatic Encephalopathy

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ABSTRACT

BACKGROUND

Hepatic encephalopathy is a chronically debilitating complication of hepatic cirrhosis. The efficacy of rifaximin, a minimally absorbed antibiotic, is well documented in the treatment of acute hepatic encephalopathy, but its efficacy for prevention of the disease has not been established.

METHODS

In this randomized, double-blind, placebo-controlled trial, we randomly assigned 299 patients who were in remission from recurrent hepatic encephalopathy resulting from chronic liver disease to receive either rifaximin, at a dose of 550 mg twice daily (140 patients), or placebo (159 patients) for 6 months. The primary efficacy end point was the time to the first breakthrough episode of hepatic encephalopathy. The key secondary end point was the time to the first hospitalization involving hepatic encephalopathy.

RESULTS

Rifaximin significantly reduced the risk of an episode of hepatic encephalopathy, as compared with placebo, over a 6-month period (hazard ratio with rifaximin, 0.42; 95% confidence interval [CI], 0.28 to 0.64; P<0.001). A breakthrough episode of hepatic encephalopathy occurred in 22.1% of patients in the rifaximin group, as compared with 45.9% of patients in the placebo group. A total of 13.6% of the patients in the rifaximin group had a hospitalization involving hepatic encephalopathy, as compared with 22.6% of patients in the placebo group, for a hazard ratio of 0.50 (95% CI, 0.29 to 0.87; P=0.01). More than 90% of patients received concomitant lactulose therapy. The incidence of adverse events reported during the study was similar in the two groups, as was the incidence of serious adverse events.

CONCLUSIONS

Over a 6-month period, treatment with rifaximin maintained remission from hepatic encephalopathy more effectively than did placebo. Rifaximin treatment also significantly reduced the risk of hospitalization involving hepatic encephalopathy. (ClinicalTrials.gov number, NCT00298038.)

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*Deceased.

N Engl J Med 2010;362:1071-81.

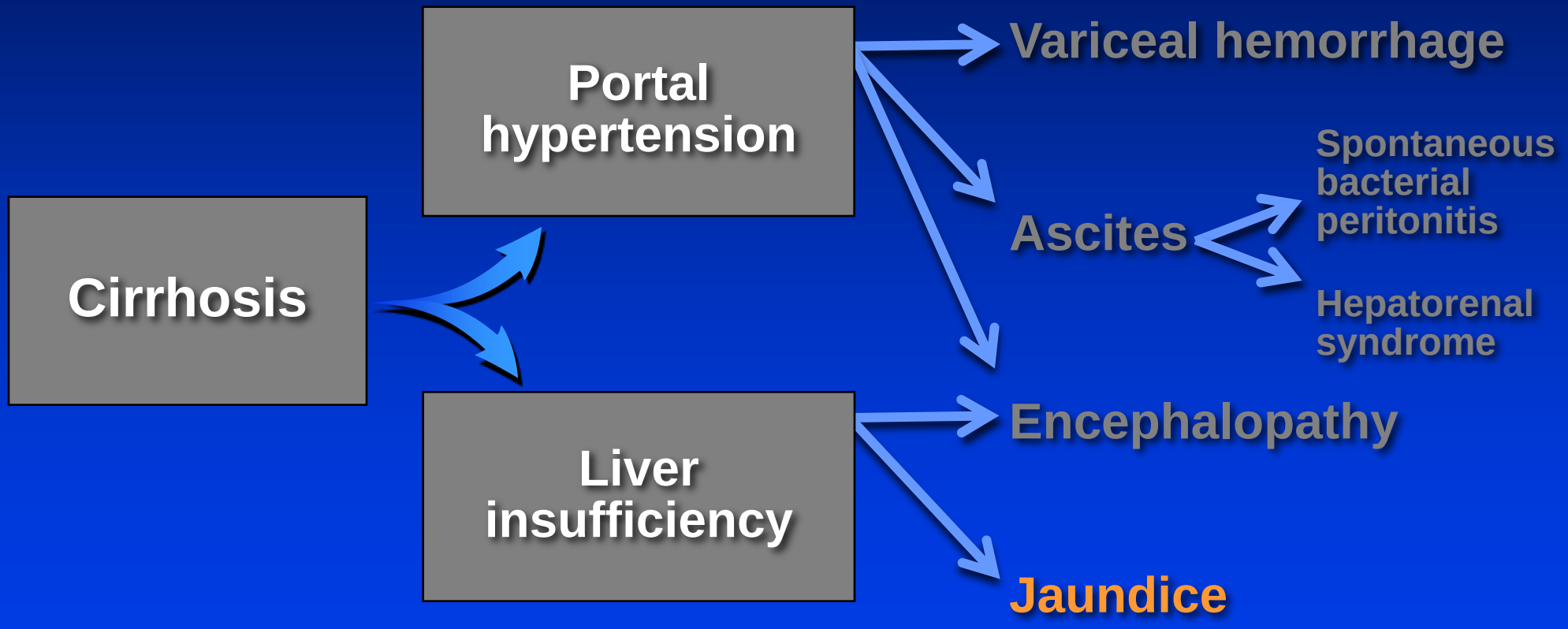
Rifaximin 550 Treatment in HE
Conclusions

- Rifaximin 550 mg b.i.d. for 6 months reduced the risk of a breakthrough HE episode by 58% (NNT=4)
  - Xifaxan 550 mg reduction in risk of HE breakthrough was maintained across all subgroups
- Rifaximin 550 mg b.i.d. for 6 months reduced the risk of HE-related hospitalization by 50% (NNT=9)
- Xifaxan 550 mg b.i.d. had a safety profile comparable to that of placebo in patients with history of HE treated for up to 6 months

b.i.d. = twice daily; HE = hepatic encephalopathy; NNT = number needed to treat.

Bass et al. *N Engl J Med*. 2010;362:1071-1081.

Complications of Cirrhosis Result from Portal Hypertension or Liver Insufficiency



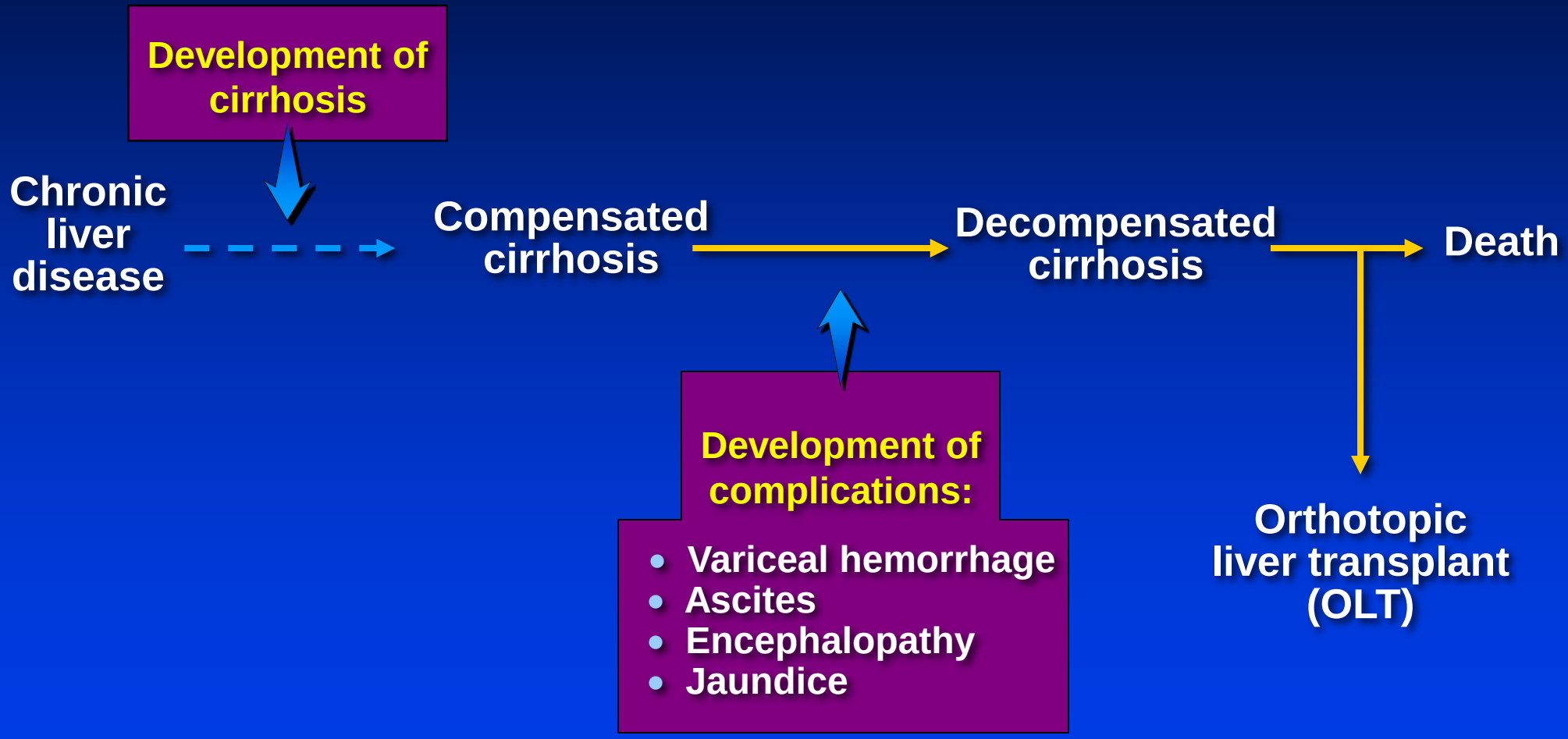
Management of decompensated cirrhosis
Jaundice

- No specific therapy
- Rule out the possibility of an “acute-on-chronic” disease
  - Alcoholic hepatitis
  - Drug hepatotoxicity
  - Biliary disease
- Accelerate transplant evaluation unless alcoholic hepatitis

Management of acute-on-chronic disease
Alcoholic Hepatitis

- Abstinence and nutritional support
- Of uncertain efficacy
  - corticosteroids: severe (DF>32 or HE)
  - pentoxifylline, infliximab
  - MARS
- Of no efficacy:
  - anabolic-androgenic steroids
  - propylthiouracil

Natural History of Chronic Liver Disease



Mahalo
A Hui Hou

Aloha!!!

Thank you
Till we meet again