Management of Cirrhosis Related Complications

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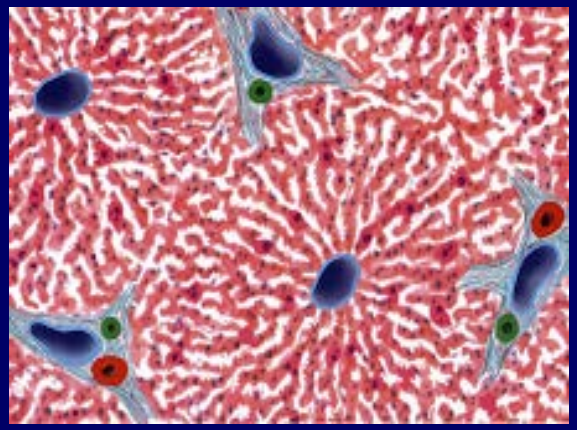
Disclosure

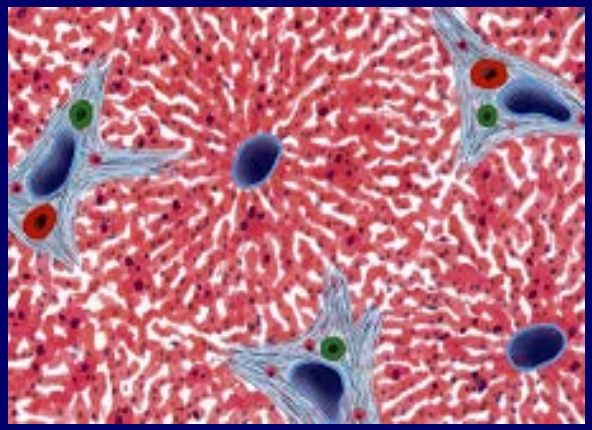
I have no disclosure related to this presentation

Liver Biopsy and Histologic Staging

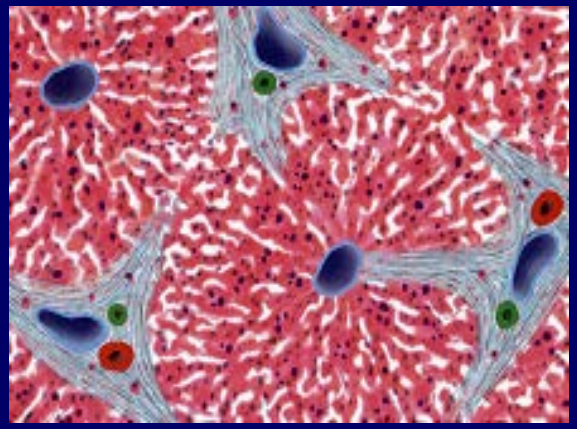
Stage 1



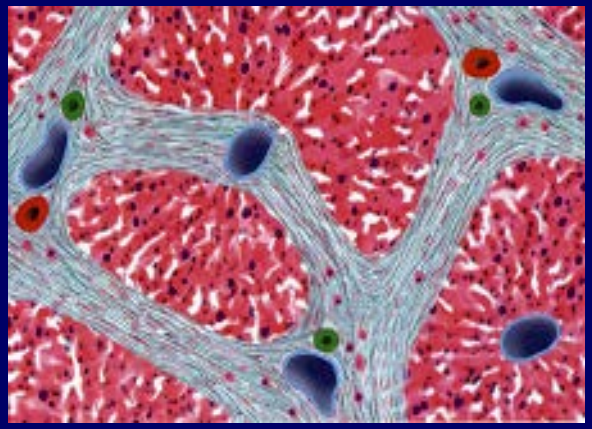
Stage 2



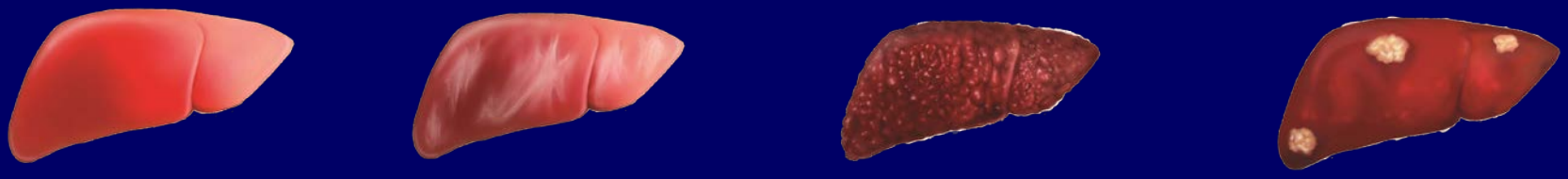
Stage 3



Stage 4



Chronic Liver Disease and Cirrhosis



Acute liver injury → Chronic liv dis → Cirrhosis → HCC / Decompensation

Hepatic Elastography: A Non-Invasive Way to Diagnose Cirrhosis

Complications of Cirrhosis

- **Primary complications include:**
  - Ascites and spontaneous bacterial peritonitis
  - Hepatic encephalopathy
  - Variceal hemorrhage
  - Cholestasis/Jaundice
  - Coagulopathy
- **Other complications that can occur include**:
  - Hepatic hydrothorax
  - Hepatorenal syndrome
  - Portopulmonary hypertension
  - Hepatocellular carcinoma
  - Portal vein thrombosis

Lefton HB et al. *Med Clin N Am* 2009;93:787-799

Ascites

- Most common complication of cirrhosis
- Only occurs when portal hypertension has developed
- ~60% of patients with compensated cirrhosis develop ascites within 10 years
- 50% mortality rate within 3 years
- Patients should generally be considered for liver transplantation referral

Arroyo V, Colmenero J. *J Hepatol*. 2003;38:S69-S89.
European Association for the Study of the Liver. *J Hepatol*. 2010;53:397-417.

Analysis of Ascitic Fluid: Serum-Ascites Albumin Gradient (SAAG)

- High SAAG ($\geq$ 1.1)
  - 97% accuracy in predicting PHTN
  - cirrhosis
  - AAH, HCC, cardiac ascites
- Low SAAG (< 1.1):
  - peritoneal carcinomatosis
  - TB peritonitis
  - peritonitis from connective tissue diseases

Approach: Ascites

- Treating underlying cause for cirrhosis
- Sodium restricted diet: 2 g NaCl/day
- No protein restriction
- Diet education of pt & care giver
- Oral diuretics: qAM dose is preferred
  - Spironolactone: 100-400 mg/d
  - Furosemide: 40-160 mg/d po
- Follow body weight & urine Na
- No NSAIDs or nephrotoxic meds

Ascites: Assessing Rx Response

- Follow body weight & urine Na/K daily
- Goal: urine Na>K
- When Ur Na>K, pt should be losing weight
- Avoid NSAIDs & nephrotoxic meds
- Avoid IV furosemide, it decreases RPF & causes azotemia in cirrhotic pts

Gastroenterology 1987;92:1859-63

Approach: Ascites

- Diet & dual diuretics: 90% Effective
- Refractory ascites: 10%
  - Liver transplant
  - Large-volume paracenteses q 2 wks
  - Transjugular intrahepatic portosystemic stent-shunt (TIPS)
  - Peritoneovenous shunt

TIPS for Refractory Ascites

- Side-to-side radiologic shunt
- Usually converts diuretic-resistant to diuretic-sensitive
- ~25% encephalopathy but treatable
- Much better control of ascites than taps
- Possible survival advantage

NEJM 2000;342:1701-7
Gastroenterology 2002;123:1839-47
Gastroenterology 2003;124:634-41

Spontaneous Bacterial Peritonitis (SBP)

- Previously ~20% prevalence on adm
- Now much less common: prevention
- PMN ≥250 cells/cu mm ± pos cult
- E. coli, pneumococcus, klebsiella, etc.
- Now Increasingly Resistant Flora
- Rx: cefotaxime IV 2g q8 hrs x 5d empiric, then tailor
- Follow Local antibiogram

UpToDate
Liver Internat 2010;30:1145-6
Hepatology 2012;56:2328-35

Principles of Evaluation & Treatment for SBP

- Tap all patients with new onset, on admission, & for deterioration
- Bedside inoculation of BCB
- Treat if PMN $\geq$250 and/or Sn or Sx of infection
- Avoid aminoglycosides
- Narrow antibiotic spectrum when possible
- Prevention with norfloxacin or Trim/Sulfa

Hepatology 2004;39:841-56

Empiric Antibiotic Choice

- Single-agent third-gen cephalosporin
- Cefotaxime: most data to support
- Ceftriaxone: suboptimal penetration
- Avoid nephrotoxic drugs
- 5 Days of Rx is usually enough

Hepatology 1985;5:457-62
Dig Dis Sci 1991;36:1782-6
AJG 2001;96:2206-10
Gastroenterology 1991;100:1737-42

Prevention of SBP – Prophylaxis

- Risk factors for development of SBP
  - Ascitic fluid protein concentration <1.0 g/dL
  - Variceal hemorrhage
  - Prior episode of SBP
- Prophylactic antibiotics

Drug Therapy	Dose /Duration
Norfloxacin	400 mg/day orally
Ceftriaxone	1g/day IV for 7 days
Double-strength sulfamethoxazole/trimethoprim	5 doses/week
Ciprofloxacin	750 mg as single oral dose/week

- Intermittent dosing of prophylactic antibiotics may select resistant flora; daily dosing preferred

Runyon BA. *Hepatology.* 2009; 49:2087-2107.

Albumin Plus ABx for SBP

- RCT of 126 pts with SBP: ABx vs ABx +Alb
- 1.5 g/kg in 6 Hrs & 1 g/kg on day 3
- 29% vs 10% mortality (p=0.01)
- Lowest mortality ever reported
- Survival advantage persisted at 3 months

NEJM 1999;341:403-9

Hepatic Encephalopathy (HE)

- 2nd Most common complication: 28% 10 yr
- Reversible metabolic confusion
- Drowsiness
- Dx: asterixis, trail test, not ammonia
- FHF: brain edema
  - Rx: Liver Transplant
- Cirrhosis: no brain edema
  - Rx: Lactulose, No Protein Restriction, Rifaximin

NEJM 1998;337:473-9
BMJ 1999;318:1391
NEJM 2010;362:1071-81

Hepatic Encephalopathy (HE)

- Most Commonly Intermittent
  - Precipitated By
    - ☒Dehydration
    - ☒Infection
    - ☒GI Bleeding
    - ☒Narcotics, Benzos
    - ☒Hypokalemia
- Chronic Severe

  Post-TIPS

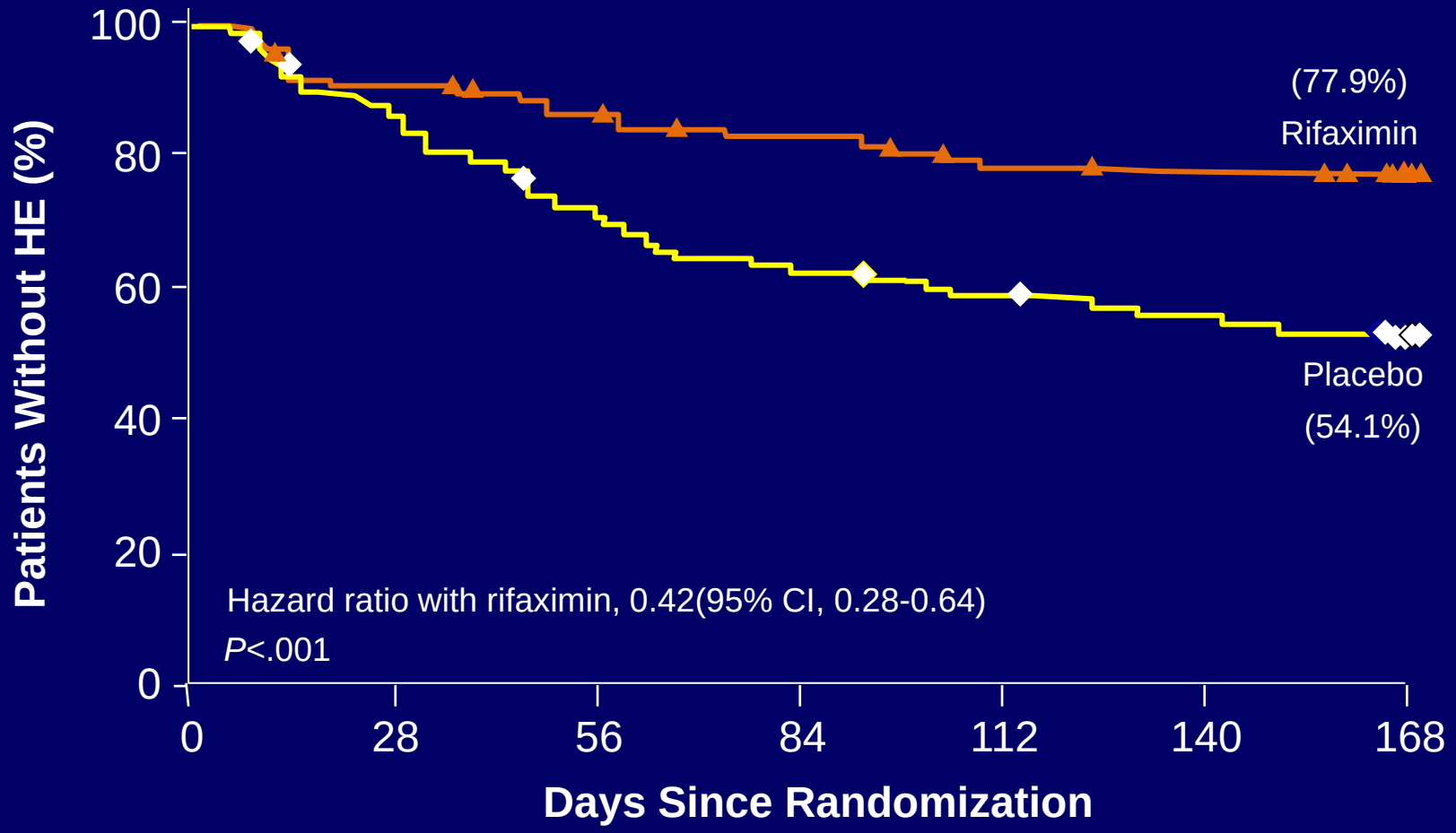
  Post Portosystemic Shunt

Current Therapy Options for HE

Drug Name	Drug Class	Indication
Lactulose	Poorly absorbed disaccharide	• Decrease blood ammonia concentration • Prevention and treatment of portal-systemic encephalopathy
Rifaximin	Non-aminoglycoside semi-synthetic, nonsystemic antibiotic	Reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients ≥ 18 years of age.
Neomycin	Aminoglycoside antibiotic	Not to be used, renal and ototoxic risk
Metronidazole	Synthetic antiprotozoal and antibacterial agent	Not approved for HE
Vancomycin	Aminoglycoside antibiotic	Not approved for HE

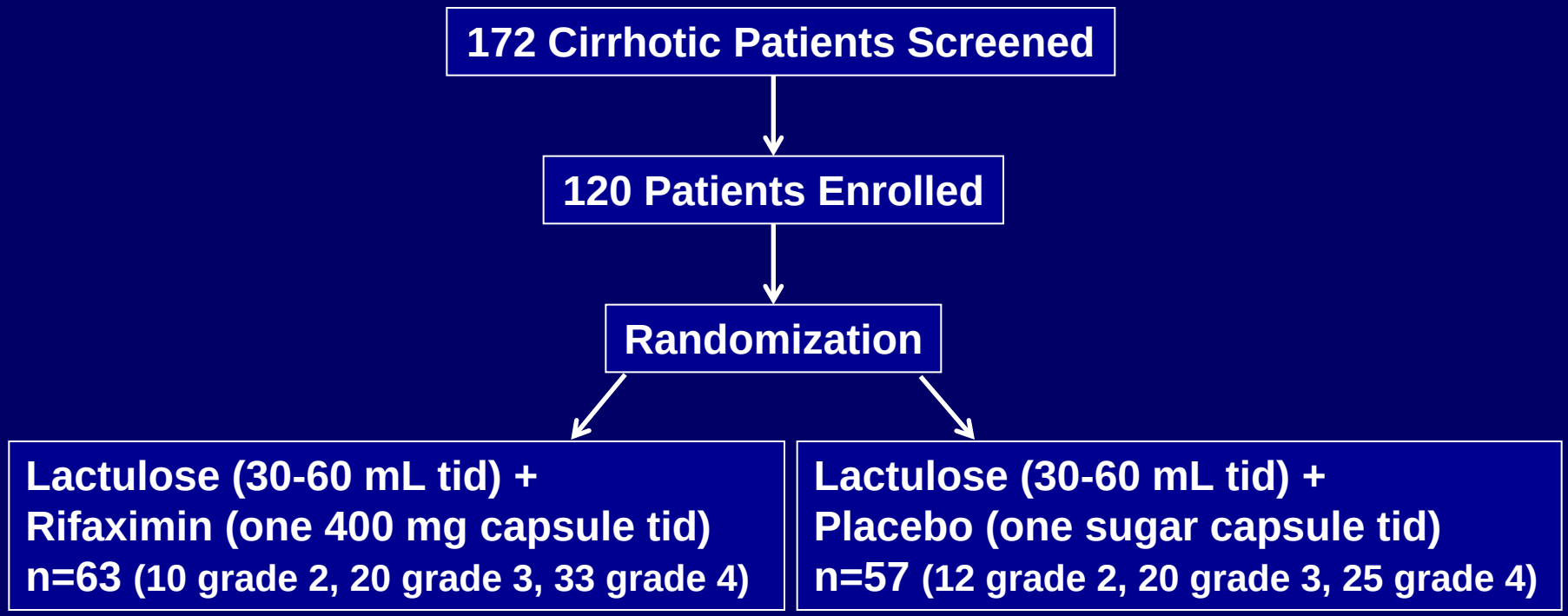
Adapted from http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/GastrointestinalDrugsAdvisoryCommittee/UCM203247.pdf, accessed 02/17/11 and http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022554lbl.pdf, accessed 02/17/11.

Rifaximin Treatment in HE: Time to First Breakthrough Episode (Primary End Point)



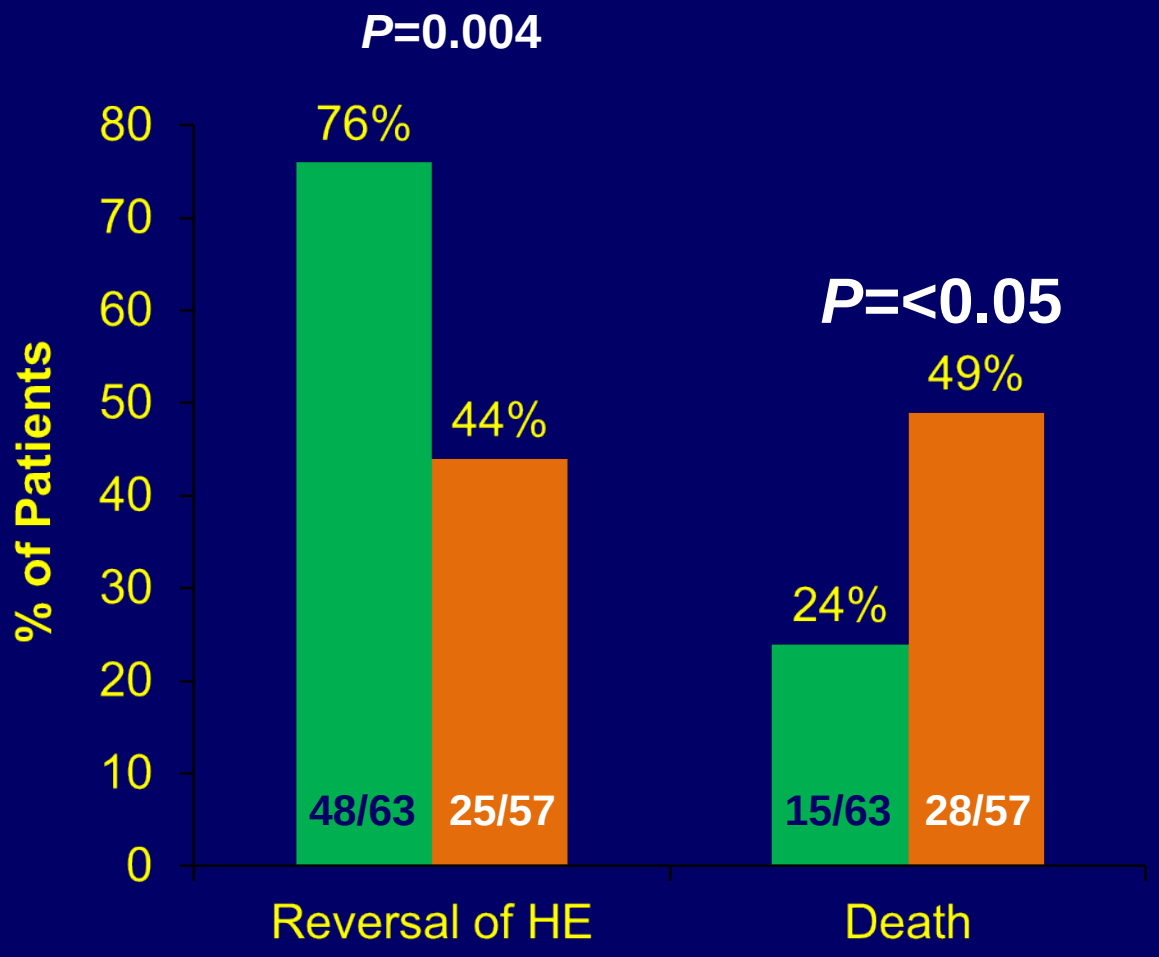
Bass NM et al. *N Engl J Med* 2010;362:1071-1081

Treatment Approach for Acute Overt Hepatic Encephalopathy: Lactulose + Rifaximin vs. Lactulose



Sharma BC et al. *Am J Gastroenterol* 2013;108:1458-1463.

Treatment Approach for Acute Overt HE: Lactulose + Rifaximin vs. Lactulose



- Treatment was given through nasogastric tube and continued until recovery of HE or a maximum of 10 days
- Hospital stay was shorter with Lactulose+ Rifaximin than with Lactulose + Placebo (5.8±3.4 vs. 8.2±4.6 days, *P*=0.001)

Sharma BC et al. *Am J Gastroenterol* 2013;108:1458-1463.

Gastroesophageal Varices

- Gastroesophageal varices present in ~50% of patients with cirrhosis
  - Presence correlates with severity of liver disease
  - 40% of Child A patients have varices
  - 85% of Child C patients have varices
- Cirrhotic patients without varices develop them at a rate of 8% per year
  - Patients with small varices develop large varices at a rate of 8% per year

Garcia-Tsao G et al. *Hepatology.* 2007;46:922-938.

Rx: Variceal Hemorrhage

- Octreotide IV in ICU (? Terlipressin)
- PRBC to keep Hb 7-9 g/dL
- FFP to keep INR <1.5 (Tradition)
- Ceftriaxone 1g IV, then norfloxacin 400 mg/day x 7 d
- Early endoscopy for banding, repeat
- Rarely, balloon tube needed
- Refractory: shunt surgery or TIPS

NEJM 2013;368:11-21

MELD Score and Timing for Tx Eval

What is MELD score

$$R = (0.957 \times \text{Log}_e(\text{creatinine mg/dl}) + 0.378 \times \text{Log}_e(\text{total bilirubin mg/dl}) + 1.120 \times \text{Log}_e(\text{INR}) + 0.643)) \times 10$$

Why MELD score

What MELD for considering referral for OLT evaluation and listing

MELD	90 Day Mortality
<10	2-8%
10-19	6-29%
20-29	50-76%
30-39	62-83%
>40	100%