Cirrhosis

• Final stage of chronic liver diseases.

• Histopathology: remodeling of the vascular architecture with septal formation and nodular groups of regenerating hepatocytes.

• Decompensated cirrhosis $\rightarrow$ portal hypertension and liver failure.
Macronodular cirrhosis. The liver is greatly enlarged. Its surface is coarsely nodular.
This type of cirrhosis is common in population with a high incidence of hepatitis B infection.
The most common cause of intrahepatic presinusoidal portal hypertension in the world is:

- A. Alcohol
- B. Budd-Chiari syndrome
- C. Schistosomiasis
- D. Hemochromatosis
- E. Portal vein thrombosis (PVT)
Classification of portal hypertension.
PATHOPHYSIOLOGY OF PORTAL HYPERTENSION

Obstruction to portal flow (cirrhosis/PVT/etc.)

Increased portal venous pressure

Increased production vasoconstrictors

Increased hepatic vascular tone

Increased hepatic vascular resistance

Peripheral, ↓ BP

Activate neurohumoral

Na and H₂O retention

Increased C.O.

Increased collateral flow

Splanchnic hyperemia

Portal hypertension
Abdominal computed tomography (CT) in patients with portal hypertension.
Ascites

- Most common complication of portal hypertension arising from cirrhosis, occurring at an annual incidence of 1%

- Its development heralds a significant change in clinical condition, with a median survival of 50% over 2 years

Management of ascites due to cirrhosis includes all of the following EXCEPT:

- A. Transjugular intrahepatic portosystemic shunt (TIPS) placement in a patient with advanced liver disease
- B. Six-liters paracentesis followed by intravenous (IV) albumin placement
- C. Spironolactone
- D. Furosemide
- E. Sodium restriction
Dietary Sodium Restriction

- The estimated mean sodium consumption among nonhypertensive adults in the United States is 3600 mg/day.

- Those with ascites are commonly advised to restrict dietary salt intake to 1.5 to 2 g per day, the lower value of which is considered adequate for daily needs.

(Ajani et al, 2005).
Aldosterone Antagonists

• Spironolactone and amiloride can be used as either monotherapy or in combination with loop diuretics.

• Although aldosterone antagonists are weak natriuretics, they are effective in patients with cirrhosis.

• Spironolactone – start at 50 to 100 mg daily.
• Its dose can be doubled every 3 days to a maximum of 400 mg per day.

(Perez-Ayuso et al, 1983).
Loop Diuretics

• As monotherapy for ascites, loop diuretics are often unsuccessful.

• The combination of loop diuretics and aldosterone antagonists is the most commonly used combination for moderate to severe ascites.

• The most commonly used loop diuretic is furosemide, beginning at doses of 20 to 40 mg daily.
• Limited evidence supports a role for albumin administration as an adjunct to diuretic therapy in ascites that is difficult to control

• Intravenous albumin administration does have a secure role in the prevention of renal dysfunction, in patients who develop spontaneous bacterial peritonitis

• Vasoconstrictor agents used in the treatment of hepatorenal syndrome are more effective when coadministered with albumin

(Gentilini et al, 1999).
(Ortega et al, 2002).
Vasopressin Receptor Antagonists

• The nonosmotic release of ADH – compensatory mechanism for splanchnic vasodilatation.

• Satavaptan is a selective AVPR2 receptor antagonist that has been tested in clinical studies.

• Conclusion - improvement in ascites and hyponatremia

(Soupert et al, arch surg, 2006)
(Ginès et al, 2008).
Refractory Ascites

• Ascites that persists despite dietary sodium restriction and high-dose diuretics (spironolactone 400 mg/day and furosemide 160 mg/day) is referred to as refractory ascites

Treatment options:
• therapeutic paracentesis
• transjugular intrahepatic portosystemic shunting (TIPS)
• peritoneal shunting
• liver transplantation.

• High-volume paracentesis, also known as therapeutic paracentesis, was reintroduced in 1987 as safe and effective.

• Studies comparing albumin to other colloidal agents have shown it to be more effective in preventing circulatory dysfunction in paracentesis when the volume removed is greater than 5 L.

• Similar findings have also been described in studies that have compared albumin to saline after total paracentesis.

(Ginès et al, 1987).
(Ginès et al, 1996).
(Sola- Vera et al, 2003).
Transjugular intrahepatic portosystemic (TIPS) shunt was first introduced experimentally in 1971, to create a pathway to bypass sinusoidal hypertension and thereby relieve portal hypertension.
Creation of a transjugular intrahepatic portosystemic shunt (TIPS).
Which of the following is true regarding a TIPS?

- A. It is contraindicated in patients with poorly controlled ascites.
- B. It has a significant rate of causing encephalopathy.
- C. It is considered to be a selective shunt.
- D. It is best used for long-term portal decompression.
- E. It has a low 1-year rate of shunt occlusion.
Transjugular Intrahepatic Portosystemic Shunts (TIPS)

• To date, four randomized controlled trials have compared TIPS with repeated high-volume paracentesis in the management of ascites.

• Conclusion: TIPS was associated with a greater sustained relief of ascites compared with paracentesis

(Rosch et al, 1971)
Comparison of Outcomes for TIPS vs. LVP in Four Randomized Trials

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>NO. OF PATIENTS</th>
<th>ESTIMATED 1-YEAR SURVIVAL*</th>
<th>RELIEF OF ASCITES</th>
<th>INCIDENCE OF HEPATIC ENCEPHALOPATHY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TIPS</td>
<td>LVP</td>
<td>TIPS</td>
<td>LVP</td>
</tr>
<tr>
<td>Rössle (2000)</td>
<td>29</td>
<td>31</td>
<td>69%</td>
<td>52%</td>
</tr>
<tr>
<td>Salerno (2004)</td>
<td>33</td>
<td>33</td>
<td>77%†</td>
<td>52%‡</td>
</tr>
<tr>
<td>Ginés (2002)</td>
<td>35</td>
<td>35</td>
<td>41%</td>
<td>35%</td>
</tr>
<tr>
<td>Sanyal (2003)</td>
<td>52</td>
<td>57</td>
<td>65%</td>
<td>66%</td>
</tr>
</tbody>
</table>

TIPS, transjugular portosystemic shunt; LVP, large-volume paracentesis

*Survival is defined as 1-year survival without liver transplantation in the studies of Rössle, Salerno, and Ginés. The data for Sanyal are given as overall survival.

†The total number of severe episodes of encephalopathy was greater in the TIPS group compared with the paracentesis group.

‡Identifies comparison with statistically significant P values.
Contraindication:

- severe pulmonary hypertension
- biventricular heart failure.

- The procedure-related risk of death during TIPS ranges between 1.7% and 3%

- Measure of portal hypertension is the hepatic venous pressure gradient (HVPG). However, the HVPG necessary for control of refractory cirrhotic ascites is unknown.

*Boyer & Haskal, 2009.*
Scoring systems for short term mortality from TIPS:

• Serum bilirubin alone;
• Acute Physiology and Chronic Health Evaluation II (APACHE II);
• Child-Turcotte-Pugh (CTP) class;
• Model for End-Stage Liver Disease (MELD)

(Rajan et al, 2002)
(Rubin et al, 1995)
(Malinchoc et al, 2000)
The Model for End-stage Liver Disease (MELD) score:

- A. Includes an assessment of the severity of ascites
- B. Includes the presence of encephalopathy
- C. Was originally designed to determine operative mortality for portocaval shunting
- D. Is not as useful as the Child-Pugh classification
- E. Predict 3-month mortality in patients awaiting liver transplantation
MELD uses the patient's values for serum bilirubin, serum creatinine, and the international normalized ratio for prothrombin time (INR) to predict survival.

$$MELD = 3.78[\ln \text{serum bilirubin (mg/dL)}] + 11.2[\ln \text{INR}] + 9.57[\ln \text{serum creatinine (mg/dL)}] + 6.43$$

Decreased survival after TIPS has been reported with MELD scores of 15 and greater.

(Ferral et al, 2004; Pan et al, 2008).
All of the following are part of the Child-Pugh scoring system EXCEPT:

- A. Overall nutritional state
- B. Presence of ascites
- C. Presence of encephalopathy
- D. Serum bilirubin
- E. International normalized ratio
Child-Pugh score (sometimes the Child-Turcotte-Pugh score) is used to assess the prognosis of chronic liver disease, mainly cirrhosis.

<table>
<thead>
<tr>
<th>Clinical and Lab Criteria</th>
<th>Points*</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td></td>
</tr>
<tr>
<td>Seconds prolonged</td>
<td>&lt;4</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>&lt;1.7</td>
</tr>
</tbody>
</table>

*Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)
Class A = 5 to 6 points (least severe liver disease)
Class B = 7 to 9 points (moderately severe liver disease)
Class C = 10 to 15 points (most severe liver disease)
Management of acute variceal bleeding. TIPS = transjugular intrahepatic portosystemic shunt.
Acute variceal hemorrhage is associated with a 15% to 20% mortality rate at 6 weeks.

Evidence supports the use of colloids over crystalloid and packed red blood cells.

Recombinant Factor VIIa has not been shown to benefit patients with cirrhosis with gastrointestinal (GI) hemorrhage over standard therapy.

(Abraldes et al, 2008; Villanueva et al, 2006)
(Shoemaker, 1987)
(Bosch et al, 2008).
Antibiotic prophylaxis

• Has been shown to decrease variceal rebleeding, and mortality rates in the setting of GI bleeding

• Norfloxacin use for 7 days (400 mg bid) in patients with two or more of the following: malnutrition, ascites, encephalopathy, or serum bilirubin level greater than 3 mg/dL.

• Ceftriaxone had better outcomes than norfloxacin when given intravenously in areas with known quinolone resistance

(Soares-Weiser et al, 2002).
(Fernandez et al, 2006).
Pharmacologic Agents

Drugs That Decrease Portal Blood Flow
- Nonselective β-adrenergic blocking agents
  - Somatostatin and its analogs
  - Vasopressin

Drugs That Decrease Intrahepatic Resistance
- α1-Adrenergic blocking agents (e.g., prazosin)
  - Angiotensin receptor blocking agents
  - Nitrates
Endoscopic Therapy

The two main endoscopic therapeutic choices are:

• endoscopic variceal ligation (EVL)
• sclerotherapy.

• Failure rates of EVL were estimated at 10% compared with 24% of sclerotherapy patients.

• Failure to control acute bleeding is also significantly more frequent in the sclerotherapy group

(Villanueva et al, 2006).
Variceal bleeding ligation techniques.

Endoscopic variceal sclerotherapy
- Needle passed through standard endoscope into varix. Injected sclerosing solution causes thrombosis of varix.

Endoscopic variceal ligation (banding)
- Suction pulls varix into inner sleeve
- Outer hood
- Ligating band
- Inner sleeve
- Band
- Inner sleeve withdrawn into outer hood, ejecting elastic ligating band around base of varix
Endoscopic views of gastric varices and esophageal variceal ligation-related ulcers.
Balloon Tamponade

The Sengstaken-Blakemore tube is primarily used:

- active bleeding despite attempted control by emergency endoscopic therapy
- during the transfer of patients to a tertiary care center
- to control a subsequent major bleed while awaiting emergency endoscopy
Sengstaken-Blakemore tube

Gastric and Esophageal Suction

Sengstaken-Blakemore Tube

Clamp

To Gastric Balloon

To Esophageal Balloon

Gastric Balloon
Esophageal variceal bleeding: secondary prophylaxis. TIPS = transjugular intrahepatic portosystemic shunt.
References:

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• Portal hypertension and its complications. - Sanyal AJ - Gastroenterology - 01-MAY-2008
"You may not need a liver transplant after all."

"I'll drink to that!"