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**Preface: Portal Hypertension**
Jorge L. Herrera

**Pathophysiology of Portal Hypertension**
Yasuko Iwakiri

Portal hypertension is a major complication of liver disease that results from a variety of pathologic conditions that increase the resistance to the portal blood flow into the liver. As portal hypertension develops, the formation of collateral vessels and arterial vasodilation progresses, which results in increased blood flow to the portal circulation. Hyperdynamic circulatory syndrome develops, leading to esophageal varices or ascites. This article summarizes the factors that increase (1) intrahepatic vascular resistance and (2) the blood flow in the splanchnic and systemic circulations in liver cirrhosis. In addition, the future directions of basic/clinical research in portal hypertension are discussed.

**Invasive and Noninvasive Methods to Diagnose Portal Hypertension and Esophageal Varices**
Roberto de Franchis and Alessandra Dell’Era

Assessing the presence of clinically significant portal hypertension and esophageal varices is clinically important in cirrhosis. The reference standard techniques to assess the presence of portal hypertension and varices are the measurement of the hepatic vein pressure gradient and esophagogastroduodenoscopy, respectively. Some newer methods have shown a good performance, but none have been proven precise enough to replace hepatic vein pressure gradient measurement or esophagogastroduodenoscopy for the diagnosis of portal hypertension or the presence and grade of esophageal varices.

**Pharmacologic Management of Portal Hypertension**
Annalisa Berzigotti and Jaime Bosch

Progress in the knowledge of the pathophysiology of portal hypertension has disclosed new targets for therapy, resulting in a larger spectrum of drugs with a potential role for clinical practice. This review focuses on pharmacologic treatments already available for reducing portal pressure and summarizes drugs currently under investigation in this field.

**Role of Transjugular Intrahepatic Portosystemic Shunt in the Management of Portal Hypertension**
Richard Parker

A transjugular intrahepatic portosystemic shunt (TIPS) is an expandable metal stent inserted via the jugular vein that creates a shunt from the portal vein to the systemic circulation via an artificial communication through the
liver. It is used to treat complications of portal hypertension. In addition to rescue treatment in variceal bleeding, TIPS can play an important role in prevention of rebleeding. TIPS can improve symptoms if medical treatment of ascites or hepatic hydrothorax has failed, but may not improve survival. Selected cases of Budd-Chiari syndrome improve with TIPS. This article discusses the indications, evidence, and complications of TIPS.

Primary Prophylaxis of Variceal Bleeding

Douglas A. Simonetto, Vijay H. Shah, and Patrick S. Kamath

Primary prevention of variceal bleeding is an important and long-debated topic in the management of patients with cirrhosis and esophageal varices. Prophylaxis is recommended for high-risk patients with small esophageal varices (advanced liver disease and/or presence of red wale marks) and those with medium/large varices. Nonselective β-blockers and endoscopic band ligation have been shown to be equally effective in primary prevention of variceal bleeding and are the only currently recommended therapies. Controversy still exists, however, regarding which one of these strategies is preferred. This article reviews the established recommendations and recent advances in the prevention of first esophageal variceal bleeding.

Management of Acute Variceal Bleeding

Jorge L. Herrera

Endoscopic Band Ligation (EBL) of esophageal varices accompanies the article

Acute variceal bleeding (AVB) is the most common cause of upper gastrointestinal hemorrhage in patients with cirrhosis. Advances in the management of AVB have resulted in decreased mortality. To minimize mortality, a multidisciplinary approach addressing airway safety, prompt judicious volume resuscitation, vasoactive and antimicrobial pharmacotherapy, and early endoscopy to obliterate varices is necessary. Placement of a transjugular intrahepatic portosystemic shunt (TIPS) has been used as rescue therapy for patients failing initial attempts at hemostasis. Patients who have a high likelihood of failing initial attempts at hemostasis may benefit from a more aggressive approach using TIPS earlier in their management.

Secondary Prophylaxis for Esophageal Variceal Bleeding

Agustín Albillos and Marta Tejedor

Combination therapy with beta-blockers and endoscopic band ligation (EBL) is the standard prophylaxis of esophageal variceal rebleeding in cirrhosis. Beta-blockers are the backbone of combination therapy, since their benefits extend to other complications of portal hypertension. EBL carries the risk of post-banding ulcer bleeding, which explains why overall rebleeding is reduced when beta-blockers are added to EBL, and not when EBL is added to beta-blockers. TIPS is the rescue treatment, but it could be considered as first choice in patients that first bleed while on beta-blockers, those with contraindications to beta-blockers or with refractory ascites, and those with fundal varices.
Gastric and Ectopic Varices
Zachary Henry, Dushant Uppal, Wael Saad, and Stephen Caldwell

Although often considered together, gastric and ectopic varices represent complications of a heterogeneous group of underlying diseases. Commonly, these are known to arise in patients with cirrhosis secondary to portal hypertension; however, they also arise in patients with noncirrhotic portal hypertension, most often secondary to venous thrombosis of the portal venous system. One of the key initial assessments is to define the underlying condition leading to the formation of these portal-collateral pathways to guide management. In the authors’ experience, these patients can be grouped into distinct although sometimes overlapping conditions, which can provide a helpful conceptual basis of management.

Portal Hypertensive Gastropathy and Colopathy
Nathalie H. Urrunaga and Don C. Rockey

Portal hypertensive gastropathy (PHG) and colopathy (PHC) are considered complications of portal hypertension. Both entities are clinically relevant because they may cause insidious blood loss or even acute massive gastrointestinal hemorrhage. Endoscopic evaluation is necessary for the diagnosis of PHG and PHC. The existence of different endoscopic criteria for PHG and PHC makes consensus difficult and results in a broad range of reported prevalence. Therapy targeted at reduction of portal pressure and mucosal blood flow has been used to treat acute bleeding; nonselective β-blockers are the most frequently used agents. Further studies are needed to clarify the natural history, pathogenesis, and treatment of PHG and PHC.

Hepatopulmonary Syndrome
David G. Koch and Michael B. Fallon

The hepatopulmonary syndrome (HPS) is a pulmonary complication of cirrhosis and/or portal hypertension whereby patients develop hypoxemia as a result of alterations in pulmonary microvascular tone and architecture. HPS occurs in up to 30% of patients with cirrhosis. Although the degree of hypoxemia does not reliably correlate with the severity of liver disease, patients with HPS have a higher mortality than do patients with cirrhosis without the disorder. There has been progress into defining the mechanisms that lead to hypoxemia in HPS, but to date there are no therapeutic options for HPS aside from liver transplantation.

Portopulmonary Hypertension
Rodrigo Cartin-Ceba and Michael J. Krowka

Portopulmonary hypertension (POPH) is the presence of pulmonary arterial hypertension in patients with portal hypertension. Among liver transplant (LT) candidates, reported incidence rates of POPH range from 4.5% to 8.5%. In patients with LT, intraoperative death and immediate post-LT mortality are feared clinical events when transplantation is attempted in the setting of untreated, moderate to severe POPH; therefore, POPH precludes LT unless the mean pulmonary artery pressure can be reduced to a safe level and right ventricular function optimized. Specific
pulmonary artery vasodilator medications seem effective in reducing pulmonary artery pressures and improving right ventricular function and survival.

Hepatic Hydrothorax
John Paul Norvell and James R. Spivey

Hepatic hydrothorax (HH) is an uncommon complication in patients with end-stage liver disease. Only 5% to 10% of patients with end-stage liver disease develop HH, which may result in dyspnea, hypoxia, and infection, and portends a poor prognosis. The most likely explanation for development is passage of fluid from the peritoneal space to the pleural space due to small diaphragmatic defects. Initial management consists of diuretics with dietary sodium restriction and thoracentesis, and a transjugular intrahepatic portosystemic shunt may ultimately be required. Afflicted patients can develop morbid and fatal complications, pose management dilemmas, and should warrant evaluation for liver transplantation.

Non-cirrhotic Portal Hypertension
Shiv K. Sarin and Rajeev Khanna

Non-cirrhotic portal hypertension (NCPH) encompasses a wide range of disorders, primarily vascular in origin, presenting with portal hypertension (PHT), but with preserved liver synthetic functions and near normal hepatic venous pressure gradient (HVPG). Non-cirrhotic portal fibrosis/Idiopathic PHT (NCPF/IPH) and extrahepatic portal venous obstruction (EHPVO) are two prototype disorders in the category. Etiopathogenesis in both of them centers on infections and prothrombotic states. Presentation and management strategies focus on repeated well tolerated episodes of variceal bleed and moderate to massive splenomegaly and other features of PHT. While the long-term prognosis is generally good in NCPF, portal biliopathy and parenchymal extinction after prolonged PHT makes outcome somewhat less favorable in EHPVO. While hepatic schistosomiasis, congenital hepatic fibrosis and nodular regenerative hyperplasia have their distinctive features, they often present with NCPH.

Surgery in Patients with Portal Hypertension: A Preoperative Checklist and Strategies for Attenuating Risk
Gene Y. Im, Nir Lubezky, Marcelo E. Facciuto, and Thomas D. Schiano

Patients with liver disease and portal hypertension are at increased risk of complications from surgery. Recent advances have allowed better optimization of patients with cirrhosis before surgery and a reduction in postoperative complications. Despite this progress, the estimation of surgical risk in a patient with cirrhosis is challenging. The Model for End-Stage Liver Disease (MELD) score has shown promise in predicting postoperative mortality compared with the Child-Turcotte-Pugh score. This article addresses current concepts in the perioperative evaluation of patients with liver disease and portal tension, including a preoperative liver assessment (POLA) checklist that may be useful towards mitigating perioperative complications.