The terminology of hepatic encephalopathy (HE) remained poorly defined for decades. One major problem was the lack of definition of what constituted acute versus chronic HE. Chronic HE caused more confusion because it was proposed to signify any bout of HE in patients with chronic liver disease, whereas others thought it denoted a protracted period of loss of consciousness. Numerous other versions were rampant. This mass confusion was solved by the report of the Hepatic Encephalopathy Consensus Group at the World Congress of Gastroenterology in 1998. This new multi-axial definition led to standardization of diagnosis and explosion in the field of research in HE.

The earliest hypothesis of the pathogenesis of HE implicated ammonia, although effects of appreciable concentrations of this neurotoxin did not resemble HE. Altered neurotransmission in the brain was suggested by similarities between increased GABA-mediated inhibitory neurotransmission and HE, specifically decreased consciousness and impaired motor function. Evidence of increased GABAergic tone in models of HE has accumulated; potential mechanisms include increased synaptic availability of GABA and accumulation of natural benzodiazepine receptor ligands with agonist properties. Pathophysiological concentrations of ammonia associated with HE, have the potential of enhancing GABAergic tone by mechanisms that involve its interactions with the GABAA receptor complex.

Hepatic encephalopathy (HE) represents the effects of liver dysfunction on the brain. When HE is clinically obvious (e.g., confusion, poor judgment, personality change), it is termed overt HE. The severity of HE is measured by different methods. Assessing the severity of HE is important for determining patient prognosis and effectiveness of therapy. This article discusses the different methods for grading HE, including clinical rating scales, neuropsychological tests, and neurophysiologic measures.
Assessment of Minimal Hepatic Encephalopathy (with Emphasis on Computerized Psychometric Tests)

Matthew R. Kappus and Jasmohan S. Bajaj

Minimal hepatic encephalopathy (MHE) is associated with a high risk of development of overt hepatic encephalopathy, impaired quality of life, and driving accidents. The detection of MHE requires specialized testing because it cannot, by definition, be diagnosed on standard clinical examination. Psychometric and neurophysiologic techniques are often used to test for MHE. Paper-pencil psychometric batteries and computerized tests have proved useful in diagnosing MHE and predicting its outcomes. Neurophysiologic tests also provide useful information. The diagnosis of MHE is an important issue for clinicians and patients alike. Testing strategies depend on the normative data available, patient comfort, and local expertise.

Brain Imaging and Hepatic Encephalopathy

Mark J.W. McPhail, Neeral R. Patel, and Simon D. Taylor-Robinson

Novel imaging techniques allow the investigation of structural and functional neuropathology of hepatic encephalopathy in greater detail, but limited techniques are applicable to the clinic. Computed tomography and magnetic resonance imaging (MRI) can rule out other diagnoses and, in MRI, give diagnostic features in widely available sequences. An internationally accepted diagnostic framework that includes an objective imaging test to replace or augment psychometry remains elusive. Quantitative MRI is likely to be the best candidate to become this test. The utility of MR and nuclear medical techniques to the clinic and results from recent research are described in this article.

Management of Overt Hepatic Encephalopathy

Vandana Khungar and Fred Poordad

Hepatic encephalopathy (HE) is a potentially reversible state of impaired cognitive function or altered consciousness in patients with liver disease or portosystemic shunting. Overt HE is a particularly pressing problem. Given the many targets of treatment and lack of a clear singular cause of overt HE, there is no consensus on a single best treatment. Over the past several years, high-quality studies have been conducted on the various pharmacologic therapies for HE and, as more data emerge, hopefully HE will become a much more easily treated complication of decompensated liver disease.

Management of Covert Hepatic Encephalopathy

Kevin D. Mullen and Ravi K. Prakash

Employability, driving capacity, and many domains of health-related quality of life are reduced in patients with minimal hepatic encephalopathy (HE). Moreover, once minimal HE is identified, more than 50% of patients develop overt HE within 30 months. Now that minimal HE has been shown to be associated with consequences, more studies are needed to assess
the cost effectiveness to treat it. This article discusses the issues regarding diagnosis and management of minimal HE, now called “Covert HE.”

Malnutrition in Cirrhosis: Contribution and Consequences of Sarcopenia on Metabolic and Clinical Responses 95
Pranav Periyalwar and Srinivasan Dasarathy
Malnutrition is the most common, reversible complication of cirrhosis that adversely affects survival, response to other complications, and quality of life. Sarcopenia, or loss of skeletal muscle mass, and loss of adipose tissue and altered substrate use as a source of energy are the 2 major components of malnutrition in cirrhosis. Current therapies include high protein supplementation especially as a late evening snack. Exercise protocols have the potential of aggravating hyperammonemia and portal hypertension. Recent advances in understanding the molecular regulation of muscle mass has helped identify potential novel therapeutic targets including myostatin antagonists, and mTOR resistance.

Hepatic Encephalopathy After Transjugular Intrahepatic Portosystemic Shunt 133
Oliviero Riggio, Silvia Nardelli, Federica Moscucci, Chiara Pasquale, Lorenzo Ridola, and Manuela Merli
Transjugular intrahepatic portosystemic shunt (TIPS) has been used for more than 20 years to treat some of the complications of portal hypertension. When TIPS was initially proposed, it was claimed that the optimal calibration of the shunt could allow an adequate reduction of portal hypertension, avoiding, at the same time, the occurrence of hepatic encephalopathy (HE), a neurologic syndrome. However, several clinical observations have shown that HE occurred rather frequently after TIPS, and HE has become an important issue to be taken into consideration in TIPS candidates and a problem to be faced after the procedure.

Extent of Reversibility of Hepatic Encephalopathy Following Liver Transplantation 147
R. Todd Frederick
Although hepatic encephalopathy (HE) is prevalent in the cirrhotic population, it has also been considered a potentially reversible condition. Liver transplantation represents the ultimate reversal of the decompensated cirrhotic state and should provide the best option for the reversibility of HE. However, the neurologic compromise associated with HE in the cirrhotic patient may not be completely reversible. Theories regarding fixed structural and reversible metabolic deficits as well as persistence of the hyperdynamic state with continued portosystemic shunting have been proposed to explain this lack of complete reversibility. Whether this remnant neurologic deficit is clinically significant remains unclear.

Hepatic Encephalopathy and Health-Related Quality of Life 159
Giampaolo Bianchi, Marco Giovagnoli, Anna Simona Sasdelli, and Giulio Marchesini
The impact of overt hepatic encephalopathy on health-related quality of life is well defined, but it remains to be demonstrated how much the presence
of minimal hepatic encephalopathy (MHE) might impair patients’ perceived health status. MHE reduces cognitive abilities, with specific impairment in manual abilities, which can lead to a depressed mood that impairs perceived health status. Therefore, all subjects with cirrhosis should be systematically screened for MHE by validated tools. Early detection and treatment is mandatory to improve the quality of life of patients with advanced cirrhosis, their social isolation, and their daily lives.