Preface

History of Hepatic Encephalopathy

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Editor

Hippocrates (460–371 BC) first recognized the relationship between the neuropsychological and physiologic changes observed in liver disease (Figs. 1 and 2). At that time, Hippocrates noted that there was a poor clinical outcome associated with delirium that was preceded by jaundice.1

Between 221 BC and 200 AD, the Qin-Han dynasties in Chinese medicine described the liver as having dynamic function connecting other organ systems via meridians.2 According to ancient Chinese medicine, the liver housed an individual’s spiritual consciousness that was responsible for emotion, communication, and expression.3 The clinical manifestation of liver disease was a result of an imbalance within one or more of the meridians, which resulted in mental disorders, skin changes, and bleeding.4

In 700 AD, the Aztec people described illness as an imbalance between the souls: the tonalli, the teyolia, and the ihiyotl.5 The ihiyotl soul resided in the liver, known to the Aztecs as eltapachtli. The ihiyotl was able to leave the body if it was summoned by a spiritual calling via the wind or an individual’s breath.6 The Aztecs observed that when individuals had an imbalance of the ihiyotl, they would become confused and agitated.7 After the Spanish conquest of the Aztec Empire, there was a spread of endemic diseases between the 1600s and the late 1700s.6 During this time, individuals would develop a yellow hue to their skin, fever, and confusion, and ultimately, die.8 Autopsies conducted on these individuals found that their livers were pale and firm.8

As the clinical manifestations of hepatic encephalopathy became more prevalent throughout the world, there was an emergence of herbal remedies throughout China, India, and what is now Mexico. Traditional Chinese medicine evaluated each individual’s manifestation of hepatic encephalopathy and determined an appropriate herbal treatment based on the afflicted organs, accumulation of toxins, and imbalanced yin-yang system.3,4 Traditional Indian medicine (Ayurveda) was first practiced
3000 years ago and normalized liver function through a multifaceted approach of ingesting herbal remedies, nutrition, physical activity, and purification treatments.\textsuperscript{9,10} The Aztec physicians, known as ticitl, used lippia dulcis, hojas de callito, and linaria to treat illnesses that were related to the liver.\textsuperscript{6}

Although the clinical presentation of hepatic encephalopathy was described during the seventeenth and eighteenth centuries, the pathophysiology remained unclear until the early to mid-1900s.\textsuperscript{11} During the 1940s and the 1950s, a number of advances were made in understanding the pathophysiology of hepatic encephalopathy. These developments came after a subgroup of individuals hospitalized in psychiatric facilities with delirium and mental status changes were found to have underlying liver disease.\textsuperscript{12} This condition was termed portal-systemic encephalopathy and encompassed a clinical spectrum that was largely dependent on the cause of the liver disease.\textsuperscript{11} It was noted that encephalopathy secondary to infectious hepatitis was rapid in onset with a worse
prognosis, whereas encephalopathy secondary to portal cirrhosis was usually gradual in onset and sometimes precipitated by an inciting factor, such as gastrointestinal bleeding, infections, or toxin ingestion, and had the potential to be reversed.13

From the late 1950s to the mid-1960s, the role of ammonia was studied as a causative force driving the clinical syndrome of hepatic encephalopathy. It was hypothesized that the liver was unable to excrete ammonia from systemic circulation, and the accumulation of ammonia led to the clinical manifestation of hepatic encephalopathy.14,15 The neurologic changes were thought in part to be due to excessive amounts of ammonia having direct access to the brain by way of large collateral portal vessels.16 However, many studies subsequently demonstrated that ammonia levels did not correlate with the degree of hepatic encephalopathy and that prompted further investigation into the role of ingested protein and bacterial activity in the gastrointestinal tract.14,16-19 Managing gastrointestinal bleeding and reducing dietary intake of protein were routinely implemented to reduce the clinical burden of hepatic encephalopathy.20 During the 1970s, it was found that the inability to manage toxic ammonia and ammine metabolites found in cirrhotic patients could be managed by antibiotics and enemas to decrease the bacteria and their production of ammonia from nitrogenous wastes within the gastrointestinal tract.21,22

Serial electroencephalographic (EEG) studies by the 1980s were able to detect delirium prior to clinical manifestations of hepatic encephalopathy.23-25 EEGs were also used to correlate clinical improvement in hepatic encephalopathy due to the effects of antibiotics, enemas, and reduction of dietary protein.23,26,27 In the last 3
decades, novel approaches to managing and evaluating patients with hepatic encepha-
olphathy have been studied. It is hoped that this issue on hepatic encephalopathy
will provide the clinician with a detailed review of the epidemiology, management, and
its impact on health care in a succinct and enjoyable manner.

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