Preface
A Focus on Drug-Induced Liver Injury

Drug-induced liver injury (DILI) is a clinically relevant, costly, and potentially catastrophic condition that affects persons in diverse settings of care. As indications for pharmacotherapy expand with the development of new drugs, so also does the potential for DILI in a greater number of people. The expansion of access to health care, including prescription drug coverage, in the United States may put more persons at risk for DILI. Though not well studied, it appears that recognition of patterns of injury consistent with DILI may not be optimal in primary care and even a more specialized setting. This knowledge gap creates an educational opportunity on which this issue of Clinics in Liver Disease focuses.

The reader is well introduced to the epidemiology of this global condition in both the general population and specific subsets. Host and environmental susceptibility are extensively covered. An entire article is dedicated to our growing understanding of the genetic underpinnings of DILI as well as the limitations of our current knowledge in this area. Illustrations of current and potential applications of genetic testing in DILI are also provided.

A comprehensive overview of our established methods of DILI causality assessment, including the Roussel Uclaf Causality Assessment Method, the Maria and Victorino Scale, and the Naranjo Adverse Drug Reactions Probability Scale, highlights the assets and limitations offered and introduces the reader to the DILI Network Structured Expert Opinion methodology and how it may help further our ability to better establish causality while raising issues of scalability. Clinicians will be well served to review an article dedicated to common patterns of injury and their potential corresponding offending agents.

The DILI-sim Initiative, a public-private partnership using Quantitative Systems Toxicology to build a model that may predict liver safety liabilities during drug development, provides mechanistic insights, predicts susceptible populations, and is
highlighted as a novel development that may enable a more refined approach to all these challenging issues.

No comprehensive review of DILI is complete without a dedicated histology article. Patterns of injury and other critical information, including prognosis, which a liver biopsy provides, are reviewed. Highly clinically relevant illustrations of these patterns of injury are provided and summarized in a table that both the nonspecialist and the consultant will find very useful.

No manifestation of DILI is more severe or dramatic than acute liver failure (ALF), which carries a high-mortality toll in the absence of the option of liver transplantation. The management of acetaminophen-induced ALF is expanded on. Importantly, the psychosocial liabilities of graft failure associated with ALF are presented. Of course, clinicians also face a dilemma in prescribing drugs known to have potential hepatotoxicity to persons with chronic liver disease. Our current understanding of this issue, which translates to clinical practice, is summarized.

Statins are arguably the most commonly prescribed pharmacologic agents in the United States and possibly worldwide. Not surprisingly, the issue of possible DILI secondary to statins comes up very frequently in a busy hepatology consultant’s practice and affects a broad spectrum of prescribers and patients. This very relevant issue is explored with emphasis on not only the remarkable liver safety of these drugs in the general population but also their possible protective role in the setting of liver disease.

The last articles of this issue deliberately focus on agents that have come to occupy a disproportionate role in the cause of DILI in today’s society. The uses and misuses of analgesics, including narcotics, are well documented, and insights into the potential DILI liabilities of these drugs are offered. Agents used for analgesia purposes that are covered include tricyclic antidepressants and anticonvulsants and also ubiquitously used nonsteroidal anti-inflammatory drugs, acetaminophen, and opioids.

We hope that this special DILI issue of Clinics in Liver Disease will be of use to both the busy clinician and the consultant. Ample references are provided at the end of each article to those interested in a deeper dive into any specific topic that the scope of this publication was unable to accommodate. A future that may include a more extensive use of personalized medicine may refine our decision-making process when drugs are prescribed and positively impact the significant toll of DILI in the general population.

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