NAFLD—the next global epidemic

The future is fatty. Dramatic changes in the lifestyle and diet of the global population are fuelling a worldwide epidemic of obesity and the increasing prevalence of NAFLD. Experts now predict that the next epidemic in chronic liver disease will be a direct result of this increased incidence of obesity and NAFLD. *Nature Reviews Gastroenterology & Hepatology* therefore commissioned a special focus issue on NAFLD to provide a comprehensive overview that covers the breadth of basic, translational and clinical research on this important condition.

Fatty deposits in the liver result in a disease spectrum—from simple steatosis with no symptoms, through to NASH, fibrosis and cirrhosis, which can result in liver cancer, liver failure and death. Importantly, NAFLD is set to replace viral hepatitis as the primary cause of end-stage liver disease and liver transplantation over the next decade or so, with the disease affecting both adults and children. The question now facing hepatologists worldwide is, what can be done to help reverse this trend?

Before clinicians can successfully manage NAFLD and help reverse its destructive effects on the liver, the underlying disease mechanisms need to be properly understood. Importantly, this knowledge could help in the development of novel therapies as well as accurately pinpointing individuals who are not only at risk of NAFLD in general, but also those who are at greatest risk of progression to the most serious forms of the disease. As such, [Ariel Feldstein and co-workers](#) provide new insights into the pathogenesis of NAFLD and NASH, in particular noting the mechanisms responsible for liver injury and fibrosis. The development of NAFLD is a result of the interplay between host genetics,

the environment (diet in particular) and, as discussed further by [Wajahat Mehal](#), the gut microbiota.

From this improved understanding in pathogenesis, it is clear that NAFLD is a complex disease, with considerable variation in severity amongst individuals. In their Review, [Quentin Anstee and Christopher Day](#) discuss the underlying genetics of NAFLD and argue that genetic variation might account for the heterogeneity in disease phenotype and progression. Tackling the issue of progression, [Anna Mae Diehl et al.](#) provide explanations as to how NAFLD-related cirrhosis can ultimately progress to hepatocellular carcinoma, discussing the evidence available from preclinical models and clinical studies in patients.

Accurate diagnosis and staging of NAFLD is of utmost importance, with histological examination the gold standard in diagnosis. However, novel noninvasive methods to diagnose liver disease are rapidly evolving and [Laurent Castera](#) provides practical insights into how these methods can be used in the context of NAFLD. Upon diagnosis of NAFLD or NASH, appropriate management must be started. Importantly, NAFLD can be managed successfully with diet and lifestyle changes, but pharmacological intervention is warranted when these methods fail. [Vlad Ratziu](#) explores the latest evidence from clinical trials on the pharmacological agents currently available to treat NASH and the new therapies that are emerging.

Many challenges lie ahead in the NAFLD field. In the final article of the Focus issue, [Rohit Loomba and Arun Sanyal](#) discuss how NAFLD is a global problem, with emphasis on the need for improved awareness of NAFLD at the society level and more consideration of NAFLD in health policies worldwide to secure a better future for coming generations.

The unpalatable truth is that NAFLD could almost be considered the human equivalent of foie gras (loosely translated from French as ‘fat liver’). As we overeat and ‘force-feed’ ourselves foods that can result in serious health implications, however, having such a buttery texture in human livers is not a delicacy to be enjoyed by hepatologists in clinical practice!

By highlighting key issues in NAFLD, we at *Nature Reviews Gastroenterology & Hepatology* hope that the lessons learned from the articles in this special issue will help set the future research agenda for NAFLD and provide ‘food for thought’ on how best to prevent and manage this condition. Before the dire predictions about NAFLD become reality, surely the time for intervention is now?

doi:10.1038/nrgastro.2013.197

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Competing interests
The author declares no competing interests.