

Case histories

Liver cirrhosis

In a footnote to his erotically charged botanical poem *The Loves of the Plants* (1791), Erasmus Darwin, Enlightenment freethinker and Charles Darwin's grandfather, offered his own eccentric take on the myth of Prometheus as a metaphor for the effect of hard drink on the liver: "The swallowing of drams cannot be better represented in hieroglyphic language than by taking fire into one's bosom; and certain it is, that the general effect of drinking spirituous liquors is an inflamed, schirrous, or paralytic liver". Two major themes in the history of medicine have shaped our understanding of cirrhosis (from a Greek conjunction meaning yellowish disease): a long story of cultural, political, and clinical attitudes towards alcohol consumption, and an almost equally fractious set of debates over the function of the liver.

In Hippocratic physiology the liver was, so to speak, the place where the outside (in the form of chyle, digested food) became the inside (in the form of hot and nourishing blood). For classical physicians it made sense, then, that this dense, mysterious organ would lie at the root of diseases linked to an excess of food or drink. In the second century, Aretaeus of Cappadocia discussed a group of patients with jaundice and "hard livers", who were "somewhat pale, green, swollen about the loins and feet". His contemporaries and their followers in Renaissance and early modern Europe advised a plain diet, with purging and bloodletting, though they acknowledged that the disease could prove intractable.

But if a small volume of blood circulated endlessly, as the English physician William Harvey demonstrated in *De Motu Cordis* (1628), the classical view of liver physiology could not possibly be true. Pathologists like Matthew Baillie continued to observe the "tuberculated" livers often found at the autopsies of heavy drinkers, while the radical French anatomist Xavier Bichat—one of the leaders of the anatomical Paris medicine at the end of the 18th century—argued that an organ as large and as densely vascularised as the liver must do more than just secrete bile.

Over the next century the secrets of this curious organ were revealed, as western medicine began to engage with the laboratory as a site of research and diagnosis, with the new perspectives emerging from cell theory and biochemistry, and with the exacting and often mystifying discipline of microscopy. The French physiologist Claude Bernard gave the liver a central role in his concept of the *milieu intérieur*, responsible for regulating levels of glucose and fat in the bloodstream. Microscopic studies, meanwhile, revealed the intricate structure of the parenchyma and the way in which its cells could atrophy if they were compressed by fat or fibrous scar tissue. In a short paper published in 1911, Frank Burr Mallory,

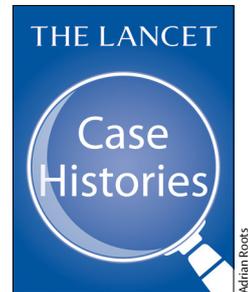
Professor of Pathology at Harvard Medical School, drew on new clinical and pathological work to redefine cirrhosis as a syndrome: "a chronic, progressive, destructive lesion of the liver combined with reparative activity and contraction on the part of the connective tissue".

By the early 20th century, clinicians knew that several conditions—schistosomiasis, cancer of the bile duct, hepatitis, malaria—could cause cirrhosis. But Mallory was writing less than a decade before Prohibition in the USA, in a nation riddled with anxieties over drunkenness, and the framing of cirrhosis in the 20th and 21st centuries reflected the enduring association between the disease and chronic alcoholism. Experiments on animals in the 1950s showed that alcohol toxicity, rather than the nutritional deficiencies associated with alcoholism, was responsible for cirrhosis, though the pharmaceutical revolution in the second half of the 20th century threw up no effective drug treatments.

Liver transplant, developed in the 1960s and 1970s, has brought hope to those with end-stage liver disease, though it remains a costly and complex procedure with substantial side-effects. Many governments have sought to reduce the demand for transplant through legislation and social programmes that seek to tackle alcohol consumption and addiction—strategies with their own seemingly intractable difficulties. Recent research has elucidated various forms and stages of the disease, and the mechanisms behind it—but the steady increase in mortality in high-income countries suggests that a truly effective response to cirrhosis has yet to be found.

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For more on **Case histories** see **Comment** *Lancet* 2016; **387**: 211 and **Perspectives** *Lancet* 2018; **391**: 2595

Further reading

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Nicholls J. The politics of alcohol: a history of the drink question in England. Manchester: Manchester University Press, 2009

Rotskoff L. Love on the rocks: men, women and alcohol in post-World War II America. Chapel Hill, NC: University of North Carolina Press, 2002

