Hepatitis C: only a step away from elimination?

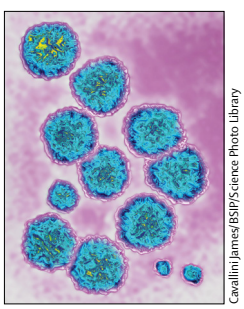
Globally, an estimated 185 million people are infected with hepatitis C virus (HCV). Acute HCV infections are usually asymptomatic. However, about 75% of patients develop chronic infection, which can lead to liver cirrhosis and hepatocellular carcinoma. 700 000 deaths worldwide could be attributed to HCV in 2013. While most people affected live in low-income and middle-income countries in Asia, Africa, and the Middle East, in the UK an estimated 200 000 individuals are infected with HCV, and annual deaths from HCV have quadrupled since 1996. These figures are appalling, surely. But the extraordinary recent developments in treatment for hepatitis C offer substantial grounds for optimism. A series of new drugs—more effective in viral clearance with fewer side-effects—are changing the landscape for hepatitis C.

Today's *Lancet* gives a sense of the remarkable past few years it has been for hepatitis C. As described in Daniel Webster and colleagues' comprehensive Seminar, until recently interferon in combination with ribavirin was the main treatment for hepatitis C, but eligibility, safety, tolerability, and effectiveness were limited. The development of direct-acting antiviral drugs towards NS3/4A protease, NS5B polymerase, and NS5A replication complex has progressed tremendously and now allows for interferon-free therapies. Four clinical trials with new regimens are published in today's issue. The C-WORTHY trial assessed a single-tablet once-daily regimen of grazoprevir (protease inhibitor) and elbasivir (NS5A inhibitor) with or without ribavirin for patients with HCV genotype 1. Eric Lawitz and colleagues report a sustained virological response (SVR) at 12 weeks, irrespective of ribavirin and duration of treatment. Similarly, Mark Sulkowski and colleagues report very encouraging results (SVR at 12 weeks: 87–97%) in patients co-infected with HIV. With about 25% of individuals infected with HIV being co-infected with HCV, inclusion of this group of patients in trials is also of utmost importance. In the PHOTON-2 trial, Jean-Michel Molina and colleagues specifically assessed the recently approved regimen sofosbuvir (NS5B inhibitor) plus ribavirin in patients infected with HCV genotypes 1–4 co-infected with HIV. They confirm the pan-genotypic potential of sofosbuvir (SVR 12 weeks: 84–89%), offering HIV co-infected patients a useful interferon-free option. The fourth trial published in today's issue goes a step further and assesses whether the addition of a third direct-acting antiviral drug to an interferon-free, ribavirin-free combination (sofosbuvir and ledipasvir) would allow shorter treatment duration—an important factor for a patient population in which treatment compliance and adherence can be an issue.

These trials are important because they offer new effective treatment options for HCV infection. "An opportunity now exists to almost eliminate this infection from the UK", wrote Roger Williams and colleagues in *The Lancet* Commission on Addressing liver disease in the UK. Highly effective new antiviral drugs not only can cure those treated but also can reduce transmission of HCV and therefore its prevalence. The Commission estimated that with these new antiviral drugs we could contemplate the "eradication of infections from chronic hepatitis C virus in the UK by 2030". Indeed, modelling studies for England showed that increasing diagnostic and number of people treated by 2·7 times would result in a 95% reduction in the prevalence of HCV infection, an 80% reduction in hepatocellular carcinoma, and avert 5200 deaths by 2030.

While new drugs offer new opportunities, new challenges also arise. Scaling-up treatment—in any country—will face important cost issues. But the high costs of these new medicines, which should be robustly scrutinised and, where appropriate, challenged, must not inhibit a careful and comprehensive analysis of the broader benefits they might bring. For example, as Melanie Calvert and colleagues argue this week, patient-reported outcomes offer the opportunity to have the patient's voice more forcefully heard in health policy decision making. The self-reported benefits to patients from these new anti-HCV regimens might prove to be substantial. And the financial returns from reduced health-care costs and higher economic activity might easily outweigh the expense of the medicines themselves. This kind of broader cost-effectiveness work needs to be urgently completed.

Next month, *The Lancet Infectious Diseases* is hosting its inaugural Viral Hepatitis Summit in Shanghai (April 10–12). We look forward to this meeting addressing the increasingly urgent need for a global plan to eliminate hepatitis C. With no vaccine in sight, if we are truly to contemplate elimination of hepatitis C by 2030, ensuring that treatments reach marginalised groups and are accessible to all those living with HCV will be crucial. ■ *The Lancet*



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This online publication has been corrected. The corrected version first appeared at thelancet.com on March 23, 2015

For ***The Lancet* Commission on Addressing liver disease in the UK** see http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)61838-9/fulltext