



Hepatitis E: urgent action needed

See Online for appendix of signatories

As discussed in a recent Editorial,¹ hepatitis E is increasingly recognised as an important emerging infection in developed countries; however, its heaviest burden rests in Asia and Africa, where disease is endemic and outbreaks are frequent. Surveillance in these areas is largely absent; commonly, the outbreaks go undetected and the real disease incidence is unknown, but we do know that pregnant women are disproportionately affected, with case-fatality ratios in the third trimester estimated as high as 10–25% with a high rate of stillbirths. In Bangladesh, one in five maternal deaths was associated with jaundice in verbal autopsy studies,² many of which were probably due to hepatitis E. Furthermore, large-scale protracted outbreaks of hepatitis E have occurred in areas of conflict and during humanitarian emergencies, with tens of thousands of cases and hundreds of deaths reported within each epidemic, often spanning over several years.³

The absence of effective tools to control hepatitis E leaves clinicians and public health practitioners powerless when confronted with the disease. Ribavirin has been successfully used to treat chronic cases, but is unlikely to be helpful in acute liver failure with hepatitis E, since the hallmark of severe disease is rapidly progressive hepatic encephalopathy often leading to death within days of symptom onset.⁴ Hepatitis E in endemic areas is a waterborne disease and should be prevented and controlled by ensuring access to safe drinking water and improved sanitation and hygiene. In practice, however, such access has been difficult to achieve, especially in displaced populations where those measures often seem to have little impact on epidemics.²

A safe and highly efficacious vaccine for hepatitis E was licensed in China in 2011. WHO recommends this

vaccine to be considered for use during outbreaks of hepatitis E.⁵ Several challenges associated with this vaccine, such as a lack of data about its efficacy in individuals outside the healthy, non-pregnant adult population in China, non-adapted vaccine presentation (bulky individual dose packaging without auto-disabling syringes and cold chain requirements) with a three-dose schedule, and an absence of WHO prequalification, prevent its wider public health use.

In October, 2016, we—a group of hepatitis E experts and stakeholders—organised a meeting at Médecins Sans Frontières in Geneva, Switzerland, to discuss ways to increase awareness of hepatitis E and to propose a roadmap for filling key knowledge and policy gaps to improve current control strategies, with a primary focus on outbreak control for vulnerable populations. We call for urgent action on hepatitis E. A better understanding of the disease, its burden, natural history, and routes of transmission is needed to improve our ability to prevent and control hepatitis E, and we appeal for an effort to make the one efficacious tool that we have—the vaccine—available to those who need it the most. To make it available will require the manufacturer to adapt the presentation of the vaccine for use in resource-limited settings and combine efforts with WHO and regulators to accelerate the process of WHO prequalification. In the meantime, the global health community must create awareness about this life-saving vaccine and assist countries to access it. Researchers need to engage in gathering data on the use of the vaccine in individuals younger than 16 years, in pregnant women, and as an outbreak response tool, including reduced-dose schedules to optimise its use in populations most at risk. Finally, we advocate for the inclusion of hepatitis E control strategies into the global hepatitis research and development agenda if the WHO goal of ending viral hepatitis by 2030 is to be achieved.

I declare no competing interests.

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- 1 The Lancet Gastroenterology & Hepatology. Hepatitis E: a neglected virus. *Lancet Gastroenterol Hepatol* 2016; **1**: 261.
- 2 Gurley ES, Halder AK, Streatfield PK, et al. Estimating the burden of maternal and neonatal deaths associated with jaundice in Bangladesh: possible role of hepatitis E infection. *Am J Public Health* 2012; **102**: 2248–54.
- 3 Teshale EH, Howard CM, Grytdal SP, et al. Hepatitis E epidemic, Uganda. *Emerg Infect Dis* 2010; **16**: 126–29.
- 4 Boccia D, Guthmann JP, Klovstad H, et al. High mortality associated with an outbreak of hepatitis E among displaced persons in Darfur, Sudan. *Clin Inf Dis* 2006; **42**: 1679–84.
- 5 WHO. Hepatitis E vaccine: WHO position paper, May 2015. *Wkly Epidemiol Rec* 2015; **90**: 185–200.

Direct-acting antiviral therapy for hepatitis E virus?

As highlighted by an Editorial in the December, 2016, issue of *The Lancet Gastroenterology & Hepatology*,¹ many gaps still exist in our knowledge of hepatitis E virus (HEV). Genotypes 3 and 4 infections can cause chronic hepatitis, cirrhosis that develops quite rapidly after infection, and extra-hepatic manifestations such as neurological symptoms and kidney injuries. Ribavirin monotherapy is effective for treating chronic HEV and HEV-associated glomerular disease, with sustained virological responses (SVRs) of 85–90%. For patients who relapse, retreatment with ribavirin for a longer period—eg, 6 months instead of 3 months—achieves viral clearance in some. However, for a few patients, ribavirin treatment fails. Mutations in HEV RNA polymerase have been noted before or during therapy in patients who relapse. However, the clinical relevance of such mutations in treatment failure is uncertain since findings from in-vitro

For action on hepatitis E see
<http://www.msf.ch/news/articles/detail/the-end-of-viral-hepatitis-by-2030-is-impossible-without-tackling-hepatitis-e/>