

Hepatitis E: we have seen the footprint in the sand, let us hunt the beast

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Commentary

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In an earlier issue of *Epidemiology and Infection*, Oeser *et al.* report on efforts to improve surveillance of acute hepatitis E in the UK [1]. Hepatitis E has been known for some decades as a cause of large water-borne outbreaks in Africa and Asia (genotypes 1 and 2) [2, 3]. Its role as a cause of sporadic acute hepatitis from zoonotic sources [4] in Europe (genotype 3) has been recognised more recently. Various sero-epidemiological surveys [5, 6] reported higher seroprevalence than expected. This has led to questioning the true magnitude of the burden of disease associated with indigenous hepatitis E virus (HEV) infections in Europe. Serological studies are used to generate age-specific curves of seroprevalence that allow estimating the force of infection. They can also generate hypotheses with respect to modes of transmission if the prevalence of antibodies is higher in one group than in another. However, they are limited in three ways. First, they estimate the prevalence of antibodies to HEV, for which the specificity is difficult to measure since there is no gold standard for never having been infected with HEV. Second, the exact duration of the persistence of IgG against HEV is unknown [3]. Third, antibodies to HEV are only a marker of serological evidence of past or present infection. These pieces of evidence are like footprints in the sand.

Symptomatic HEV infection, for the most part, leads to acute hepatitis. Chronic infections happen uncommonly in immune-suppressed individuals [7]. Good epidemiological practice suggests that acute diseases are studied with measures of incidence. Public health surveillance for acute disease, despite all its limitations, generates a description of the events by time (months, years), place (geographical area) and person (individuals, groups). To capture trends in acute hepatitis E incidence, WHO proposes to implement enhanced case reporting of acute hepatitis [8]. For clinically defined acute hepatitis, enhanced case reporting consists of (a) *in vitro* diagnosis for all markers of acute viral hepatitis and (b) collection of information on potential exposures during the incubation period [8]. Use of an adequate referent exposure period of an acute infection informs on modes of transmission in a more reliable way. Enhanced case reporting can be done nationwide when the public health system and *in vitro*-diagnosis capacity are strong. In countries where this is not possible, sentinel surveillance is the preferred method. In short, we need to hunt the beast itself.

Data from enhanced case reporting for acute hepatitis build on information from serological surveys and improve the description of the epidemiology of acute HEV infection [9]. Enhanced case reporting also documents trends in new infections with HAV, HBV and, to some extent, HCV. The working case definition of acute HCV infection as a non-A, non-B, non-E acute hepatitis that is positive for biomarkers of HCV infection, albeit imperfect, documents trends in new HCV infections [10]. In the USA, for example, the use of this case definition was instrumental in detecting the recent outbreak of HCV infection associated with injection drug use after years of decreases in reported rates. Overall, the enhanced case reporting measures morbidity, the severity of disease and case fatality [11]. It guides public health response with evidence and assists with documenting the elimination of viral hepatitis as a public health threat (reduction in mortality by 65% and incidence by 90%) as targeted with the Global Health Sector Strategy on viral hepatitis [12].

Therefore, to better describe acute hepatitis E in Europe, we recommend implementing enhanced case reporting on a larger scale, particularly when sero-prevalence data suggests indigenous HEV transmission. Acute infections with hepatitis viruses create a unique window of opportunity to understand how hepatitis viruses are transmitted. We need to make full use of that opportunity to prevent new avoidable infections with HEV and other hepatitis viruses.

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