A 'one-health' approach to the study of hepatitis E virus

In association with

Researchers at University College Dublin are currently investigating the presence of hepatitis E virus in human sewage and Irish waterways. Here, Dr Nicola Fletcher presents an overview of a 'one-health' approach to the study of hepatitis E virus

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AN EMERGING ZOONOTIC VIRAL INFECTION

Hepatitis E virus (HEV) is the leading cause of acute hepatitis in humans worldwide.[1,2] In developing countries, infection is associated with large water-borne outbreaks. However, in recent years, HEV cases have increased in developed countries including Europe, the US and Japan, and these cases are locally acquired and sporadic. In Ireland, HEV has been a notifiable disease in humans since 2015, and the Irish Blood Transfusion Service (IBTS) has screened blood donations for HEV since 2016 (www.hpsc.ie). Currently, there are no vaccines and no specific treatments for HEV infection.[3]

Recent studies have revealed that HEV infections in Europe, including Ireland, are associated with genotype 3 HEV, and are acquired through zoonotic transmission, mainly through consuming pork products from infected animals and through close contact with infected pigs.[3] Many infections with HEV result in a self-limiting acute disease, and so HEV infections often are undiagnosed. Some people, including individuals with pre-existing liver disease and immune-compromised individuals, including solid-organ transplant patients, can develop more severe disease. Neurological disease and other non-hepatic manifestations also occur in a proportion of cases, although the reasons for these are not well understood.[4]

An on-farm survey investigating seroprevalence of HEV in Irish breeding pigs in 2015 highlighted that 27% of pigs were IgG positive, but animals on 81% of farms surveyed were seropositive.[4] This study indicated that a large number of Irish farms have evidence of HEV infection. A recent large-scale UK study investigating the prevalence of HEV at slaughter reported that 92.8% of pigs were IgG positive, with 20.5% HEV RNA positive at the point of slaughter.[5] In France and Germany, a correlation between HEV infection and consumption of raw pork liver sausage, has been established, and one study reported that 30% of these sausages were positive for HEV RNA, indicating that these pigs may have been actively replicating virus at the point of slaughter.[3] However, DNA sequencing studies have revealed that viruses circulating in pigs do not always match those found in infected humans.[5] This indicates that there must be further sources of HEV transmission to humans, which may be travel-associated or could be as a result of unidentified reservoir species with the potential to transmit infection to humans.

UNIDENTIFIED RESERVOIR SPECIES AND ENVIRONMENTAL CONTAMINATION

While consumption of contaminated pork meat or direct contact with infected pigs is a recognised route of HEV transmission to humans,[6] the ability of other farmed or wild species to transmit infection to humans is unclear.[7] Other routes of infection may also play a role, including contamination of watercourses and crops. Deer can also become infected with HEV and transmission to humans through consumption of venison has been confirmed in rare cases.[8] While waterborne transmission is mainly associated with HEV genotype 1 and 2 infections in developing countries, in developed countries water can also be contaminated by human or animal waste, including sewage and agricultural effluent, containing HEV genotypes 3 and 4. Shellfish, including oysters, which are filter feeders, can become indirectly infected with HEV, and there are several reports of detection of HEV in shellfish in Spain, Slovenia, the Netherlands, the UK and Japan.[3]

At UCD, our current research is investigating the presence of HEV in human sewage and Irish waterways, to measure levels of virus in the environment and the likely source of this contamination.

STUDY OF HEPATITIS E IN HUMANS AND PIGS

HEV is extremely difficult to culture in the laboratory, and this has hampered studies to understand the biology of the virus which creates major challenges in the development of treatment strategies for HEV. The liver is a highly specialised, 3D organ, and our current research efforts are aimed at developing model systems that mimic the features of this unique organ in the laboratory. We are currently developing liver organoids, which are 3D spherical 'mini livers', and are using these to understand how HEV infects pig

and human liver cells. We are using these model systems to understand the virus lifecycle and to evaluate novel antivirals to identify candidate molecules for potential treatment of HEV infection. We are using a newly developed soft x-ray microscope, based at UCD and developed by Irish company SiriusXT Ltd, to visualise infected cells in exquisite detail, which will give us a unique insight into the mechanisms that HEV uses to infect cells. This work is being carried out in collaboration with the University of Birmingham, who have a wealth of experience in understanding the biology of the liver, The National Virus Reference Laboratory at UCD and SiriusXT Ltd. This research is funded by the Wellcome Trust Institutional Strategic Support Fund and by Horizon 2020, the EU's research and innovation programme.

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