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Author's reply to the Letter "The emergence of zoonotic rat hepatitis E virus infection"

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We thank Dr. C. Adlhoch and Dr. SA Baylis for their comments on our study describing the impact of rat hepatitis E virus (*Orthohepevirus C* genotype 1 or HEV-C1) on human health in Hong Kong (1, 2). We concur with them that HEV-C1 infection is currently a blind spot in hepatitis E diagnostic testing. As they point out, routinely used molecular assays for HEV diagnostics or blood donor screening would not be able to detect HEV-C1 (3). Although we demonstrated that the Wantai HEV IgM and IgG kits (Wantai, Beijing, China) may cross-react with HEV-C1 patient sera (1), HEV-A/HEV-C1 discriminatory assays would be a valuable asset to HEV diagnostics.

For 40 of the HEV IgM positive/ RNA negative patients with sufficient sample volume, we also attempted conventional RT-PCR using universal consensus primers as described previously (3). These primers would theoretically be able to detect highly divergent species within the family *Hepeviridae*, but all samples tested negative. As noted in our study, our real-time RT-PCR primers and probes were specific for HEV-C genotype 1, which circulates in rats (1). However, HEV-C is very diverse with four putative genotypes circulating in a variety of rodents and ferrets (4). Our HEV-C1 real-time RT-PCR would not detect HEV-C genotypes 3 and 4, which circulate in field mice and voles (4). However, we judge that urban dwellers in Hong Kong are less likely to be exposed to these genotypes.

The route of transmission of HEV-C1 between rats and humans is elusive. None of our patients had a history of rat meat consumption and the practice is uncommon in Hong Kong. Indeed, almost all of them even denied rat infestation in their domestic premises. We considered adulteration of food products or natural HEV-C1 infection of pigs to be possibilities, therefore we tested for HEV-C1 in 212 pork products and samples, but no sample tested positive (1). We agree that extensive epidemiological investigations are required to identify the definitive source of HEV-C1 infection.

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