Response to Letters:

We write in response to the letters of Sonder and van den Hoek\(^1\) and Lachish and Schwartz (above) to answer the questions they have raised in relation to our study “The incidence of HBV and HCV infection in Australian travelers to Asia.”\(^2\) Our original study was not designed solely for the purpose of determining the seroprevalence of dengue in travelers, as suggested by Sonder and van den Hoek. The cohort has also been used to study the risk of acquiring influenza, Japanese encephalitis, as well as dengue fever.\(^3\)–\(^5\) However, it would have been ideal for us to collect additional serial blood samples and additional demographic and travel information from study participants after their return consultation, but this was not feasible owing to restrictions placed on us by our ethics committee, a limitation we acknowledged in our report.

Both letters have raised concerns regarding the time frame from travel to testing in relation to the incubation periods of hepatitis B virus (HBV) and hepatitis C virus (HCV). The letters of Sonder and van den Hoek and Lachish and Schwartz are both incorrect in their interpretation of incubation periods. They have stated that both infections have relatively long incubation periods, making acquisition during study unlikely or impossible, but this is incorrect as the incubation periods for both viral infections are highly variable and very short incubation periods have been described for both viruses.

With regard to HBV, the incubation period for acute hepatitis B infection can be as short as 2 to 6 weeks.\(^6,7\) Our traveler with acute HBV seroconversion traveled through China for 22 days and had post-travel blood samples taken 8 days after return to Australia, well within the incubation period for acute HBV. Regarding the question of sensitivity and specificity for the serological testing used in the study, we are very confident that our results reflect a true seroconversion. For HBV, we used the validated commercial system AxSYM Architect I2000SR analyzer and ARCHITECT anti-HBs, anti-HBc, and HBsAg (Abbott). The overall sensitivity of the Architect anti-HBc assay (ref 7C17 34-3095/R4) is 98.63% [95% confidence interval (CI): 96.83%–99.55%]. More importantly, the overall specificity of the Architect anti-HBc assay (ref 7C17 34-3095/R4) is as high as 99.42% (95% CI: 99.09%–99.65%). The pre-travel blood samples demonstrated a negative anti-HBs and anti-HBc antibody, whereas the post-travel blood samples demonstrated a positive anti-HBc and anti-HBs antibody titer of >1,000 mIU/mL. The traveler was HBV polymerase chain reaction (PCR) and HBsAg negative, a result consistent with either clearance of acute hepatitis B infection or occult infection.\(^6,8,9\)

It therefore remains most likely that the traveler with HBV acquired his infection in China, where the prevalence of HBV is estimated to be greater than 8%\(^7\) in contrast to Australia where the estimated prevalence of chronic HBV infection is between 0.68 and 0.85%.\(^10\)

Both letters also raised questions regarding the two travelers with HCV infection. The incubation period for HCV ranges from 6 to 112 days.\(^7,11\) HCV viremia is detectable within 2 to 14 days of exposure and HCV-specific antibodies can be detected as early as 20 days using third-generation assays such as the ones we used.\(^11,12\) The first traveler visited Vietnam for 14 days and had post-travel blood samples taken 23 days after return to Australia and the second traveler visited Thailand for 14 days and had post-travel blood samples taken 6 days after return to Australia. Both these time frames are within the incubation period of acute HCV. We are confident that our results reflect true seroconversions. The overall specificity of the Abbott Architect anti-HCV (ref 6G37 B6C370) assay is 99.60% (95% CI: 99.45%–99.71%). The sensitivity of the Architect anti-HCV is 99.10% (95% CI: 96.77%–99.89%).\(^13,14\)

Both travelers with HCV seroconversion were HCV PCR negative. HCV RNA was tested using a well-validated commercial qualitative RT-PCR assay (COBAS AMPLICOR Roche). The negative HCV PCR may reflect either clearance of virus or the intermittent nature of the viremia that may occur early in the course of HCV infection.\(^11\) Clearance of viremia is also not unusual because it is well recognized that between 15 and 50% of acute infections resolve spontaneously and will therefore be HCV PCR negative.\(^15\)

HCV prevalence estimates for Thailand and Vietnam are approximately 7.5 and 21%, respectively.\(^16\) In Australia the estimated prevalence of HCV is 1.4%.\(^17\) It is therefore most likely that the two travelers acquired HCV infection while traveling in Asia.

In their letter, Lachish and Schwartz have made reference to their recent publication in the Journal of Travel Medicine.\(^18\) The methodology used in this study was vastly different to ours as the analysis was based on testing returned travelers who presented to their clinics with hepatitis; however, the study has several limitations including: not testing paired pre- and post-blood sera on their study population; not stating whether travelers had visited single or multiple destinations, yet confidently stating where these infections were acquired; not performing virological testing for HBV PCR or viral load; and not stating whether travelers were acquired HCV infection while traveling in Asia.
the assays used. These limitations make it difficult to draw any meaningful conclusion from their study.

Accurately defining travel-associated infectious risks is difficult, particularly for infections that can also be acquired locally. We believe that the findings of our study, which used optimal methodology involving collection of both pre- and post-travel blood samples, are not only valid but will also have important implications for travelers and health practitioners by highlighting the importance of advising travelers regarding the possible risks of HBV and HCV infections and the need for HBV vaccination where appropriate.

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References