HEPATITIS DELTA VIRUS IN AUSTRALIA

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Background: Hepatitis delta virus (HDV) is a small, incomplete single stranded RNA virus that requires the surface antigen (HBsAg) of hepatitis B virus (HBV) for assembly and transmission. It is acquired by either a superinfection or co-infection with HBV. Infection with both HBV and HDV usually results in more severe disease than HBV mono-infection with more rapid progression to cirrhosis, increased hepatic decompensation and death. HDV infection occurs globally but there are some endemic areas such as the Amazon Basin, Eastern and Mediterranean Europe, the Middle East, parts of Asia and Africa and some Pacific Islands such as Kiribati where seroprevalence rates of 11-69% have been reported. There are 8 HDV genotypes with genotype 1 being the most common and most widely distributed. In Australia the seroprevalence of HDV is thought to be around 5% but it is under-diagnosed and under-reported. The aims of this study were to analyse the number of samples tested for HDV over a 5 year period and determine the best assays to make a diagnosis.

Methods: Serum samples that were sent to VIDRL for HDV antibody (anti-HDV), HDV antigen (HDAg) and PCR testing over a 5 year period between 2010 and 2014 were included in the study. There were 3161 requests for serology of which 3152 samples had sufficient volume for testing; and 834 requests for PCR. PCR was occasionally requested ad hoc, ie with or without a serology result. Positive HDV RNA samples were then tested in a quantitative assay. Sequencing and genotyping was also performed on 100 RNA positive isolates.

Results: Of the 3163 requests, 172 samples (5.4%) from 131 patients had detectable anti-HDV. An additional 22 samples yielded equivocal results and 11 had insufficient volumes for testing.
Only 4 samples tested positive for HDAg. PCR was not always requested even after positive serology was obtained and vice versa. Of the 834 requests for PCR, 253 (30%), from 131 patients had detectable HDV RNA. The 131 patients with detectable HDV RNA were not necessarily the same as those that were anti-HDV positive. If serology was performed on a PCR positive sample, anti-HDV was always detected. Nearly 70% of the HDV positive isolates were from males and over 50% were in the 20-40 year old age group. Of the 100 isolates that were sequenced and genotyped, 83 were genotype 1, 1 was genotype 2 and 16 were genotype 5 (an African genotype).

Conclusion: Whilst HDV is not extremely common in Australia, co-infection and super-infection with HBV does occur. HDV is not susceptible to the nucleos(t)ide analogues currently used to treat HBV and so HDV RNA can be detected in the absence of HBV DNA. As all HDV PCR positive isolates that had serology performed were anti-HDV positive, antibody testing should be the first line test to help diagnose

HDV infection. This will determine exposure to HDV. A positive anti-HDV should then be followed by a request for HDV RNA to determine current infection. Quantification of the HDV RNA can be helpful, particularly if therapy with interferon is being considered.