

CHAPTER 5**Conclusions**

The general characteristics and public health risks associated with hepatitis E virus (HEV) have been described in the literature review. Waterborne outbreaks of hepatitis E have been reported in the neighbouring countries Namibia and Botswana, while the clinical cases reported in South Africa were mainly associated with a travelling history to countries where the disease is endemic (Grabow *et al.*, 1994; Grabow, 1997; South African Virus Laboratories Surveillance Bulletin, 2003). Indirect evidence suggested that some strains of HEV might be zoonotic, with swine playing a major role in the transmission of the virus to humans. This suggestion was validated by the reports of foodborne transmission of HEV (Matsuda *et al.*, 2003; Tei *et al.*, 2003; ProMed, 2004). Waterborne and foodborne transmission of HEV have not been recorded in South Africa, and the detection and characterisation of the virus in water resources and animals have not been described in this country. Final conclusions and future research have been summarised in this chapter.

Seroprevalence studies previously conducted in various communities in South Africa have indicated that HEV may be endemic in the human population of certain low socio-economic communities throughout South Africa (Grabow *et al.*, 1994; Tucker *et al.*, 1996). It is believed that water may play a role in the transmission of HEV strains among humans, or from swine to humans, in these communities, due to conditions of low hygiene and sanitation (Grabow, 2002).

The seroprevalence in swine reported in this study is the first documentation of the presence of anti-HEV IgG in animals in South Africa. It was found that the seroprevalence of HEV in swine in South Africa (15%) compared well with the seroprevalence reported in non-endemic countries (15% to 25%), which was significantly lower than that reported in endemic countries (27% to 74%) (Clayson *et al.*, 1995; Meng

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et al., 1999; Pina *et al.*, 2000; Arankalle *et al.*, 2001; Engle *et al.*, 2002; Choi *et al.*, 2003). Anti-HEV IgG was detected in provinces throughout South Africa, suggesting that swine might be a candidate reservoir for at least some strains of HEV. The differences in the seroprevalence of HEV among the provinces may be due to certain factors, such as different geographical conditions, densities of pig farms in each province and different HEV strains occurring in the provinces.

The prevalence of HEV in the domestic sewage samples and swine faecal specimens, as determined by reverse transcription-polymerase chain reaction (RT-PCR), may have been an over-estimate, as indicated by the confirmation of these results by sequencing analysis. Thus, in order to reflect the true prevalence of HEV in environmental and clinical samples, using this method, sequencing analysis must be done to confirm the results. Sequencing analysis of the RT-PCR amplicons revealed two human-related HEV strains (RSA-1 and RSA-2) detected in the sewage samples and two swine-related HEV strains (swRSA-1 and swRSA-2) detected in the swine faecal specimens. The strains detected in the sewage clustered together within genotype I (human-related Asian strains), while the swine associated strains were more diverse, with swRSA-1 and swRSA-2 related to genotypes III (human- and swine-related US strains) and IV (human- and swine-related Japanese strains) respectively. This is an indication that a number of diverse strains are circulating simultaneously in the human and swine populations in South Africa. Detecting swine-related HEV sequences, similar to that of human HEV sequences, in South Africa raises concern, as these strains may undergo genetic reversion to strains that might possibly cause disease in the human population. The seroprevalence of HEV detected in the human population in South Africa may have been due to swine-related strains being transmitted via water sources causing sub-clinical or low-grade infections in the human population.

It has been suggested that there might be more local cases of clinical hepatitis E in South Africa than previously thought (Grabow *et al.*, 1994; Grabow, 1997). It would, therefore, appear that cases of locally acquired hepatitis E may be occurring undiagnosed in South Africa. Routine testing for HEV infection should be considered in cases of non-A, non-B

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acute hepatitis, even in the absence of a travelling history, in particular in asymptomatic patients with unexplained elevated aminotransferase levels and in pregnant women (Clemente-Casares *et al.*, 2003; Widdowson *et al.*, 2003).

Currently several RT-PCR assays have been developed for the rapid detection of HEV in either clinical or environmental samples. The disadvantage of these assays are, however, that they amplify either a subset of HEV strains using a small number of primer sets or the majority of the HEV strains using a large number of degenerate primers (Grimm and Fout, 2002). This is due to the genetic diversity, which exists between the HEV strains, in particular between strains from different geographical regions. Therefore, a single molecular assay (multiplex PCR) must be developed that will simultaneously identify as many HEV strains as possible.

The results reported in this study extends the knowledge of the global distribution of HEV and it is evident that the disease is more widespread than traditionally thought. The seroprevalence of HEV and the prevalence of HEV-related sequences in human populations, as well as swine and other animal species throughout South Africa, will cast more light on the epidemiology of HEV in this country. The identification of additional human- and swine-related HEV isolates and the determination of their full-length genomic sequences will provide fundamental information in order to better understand the genetic divergence of the HEV strains circulating in South Africa.

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