

Hepatitis E Virus Infection in Travelers

Eli Schwartz,¹ Nancy Piper Jenks,³ Pierre Van Damme,⁴
and Eithan Galun²

From the ¹Sheba Medical Center, Tel-Hashomer, and the Sackler School of Medicine, Tel Aviv University, Tel Aviv; ²Hadassah University Hospital, Jerusalem, Israel; the ³Peekskill Area Health Center, Peekskill, New York, USA; and the ⁴University of Antwerp, Antwerp, Belgium

Hepatitis E virus (HEV) is a major cause of clinical hepatitis in regions of endemicity, affecting primarily young adults and travelers to these areas. We present 5 cases of acute HEV infection in travelers and review 143 cases of HEV infection found by a literature search that were contracted in areas of endemicity. Fulminant hepatitis occurred in 2.7% of the reported cases; 2 of these were fatal. The destination of most of the travelers with acute HEV infection was the Indian subcontinent. The overall risk of contracting HEV infection for travelers appears to be lower than the risk for hepatitis A virus infection. Pregnant women and individuals with underlying liver disease may be a risk for severe infection.

Hepatitis E virus (HEV) is a major cause of epidemic hepatitis and acute, sporadic hepatitis in adults in many developing countries. The virus was suspected on epidemiological grounds for many years and was isolated, cloned and fully sequenced in the early 1990s [1]. With the exception of a few isolated cases, individuals from developed countries who have had acute HEV infection have been travelers to countries where HEV is endemic. In this report, we present the first documented cases of acute HEV infection in Israeli travelers, which occurred shortly after the travellers returned from Asia, and review the documented cases of acute HEV infection in travelers.

Patients and Methods

Patients who presented with acute hepatitis from 1992–1998 at the travel clinics of either the Sheba Medical Center or Misgav Ladach Hospital, Tel-Hashomer, Jerusalem, Israel or at the Liver Unit of Hadassah University Hospital, Jerusalem, were tested for hepatitis A, B, and C. Five patients were serologically negative for all 3 infections, and hepatitis E was suspected. Serum samples from these patients were examined by EIA for IgG and IgM antibodies to HEV (Abbott Laboratories, Abbott Park, IL). The serum samples were subsequently sent to the Centers for Disease Control and Prevention (Atlanta, GA) to confirm the results of IgG and IgM antibodies to HEV.

A further search for returning Israeli travelers with acute HEV infection was done by a telephone survey. All travel clinics in Israel were surveyed annually from 1992–1998. Clinic directors were

asked to report any acute cases of HEV infection in returning travelers.

A MEDLINE search of the literature from 1986–1997 was conducted to find published case reports of individuals with acute HEV infection associated with travel. The following key terms were used: hepatitis E; non-A, non-B hepatitis; traveler's hepatitis; and travel medicine. Abstracts from two international meetings on viral hepatitis and the 1991–1997 biennial meetings of the International Society of Travel Medicine also were reviewed.

Results

Five Israeli travelers presented with acute hepatitis and were found to be HEV-positive after returning to Israel. All 5 had traveled to the Indian subcontinent (table 1). Four were diagnosed by IgM antibodies to HEV within 2 weeks after their return; the fifth patient did not have his serum checked until 3 months after his return, when tests showed he had only IgG antibodies to HEV. No additional cases of travelers with acute HEV infection were identified from the telephone survey.

The literature review revealed 51 individual cases of acute HEV infection associated with travel (table 1). The mean age of 26 travelers was 30.1 years (range, 6–65 years). Thirteen (48%) of 27 travelers were male. Forty (80%) of 50 travelers had been to the Indian subcontinent (India, Nepal, Pakistan). The mean duration of travel for 20 travelers was 3.7 months (range, 1 day to 12 months). All travelers lived in developed countries; however, 8 (15.7%) of 51 travelers were originally from Asia.

In addition to individual cases of travelers with acute HEV infection, there were 3 case series of acute HEV infection in groups of travelers, including 42 French soldiers who contracted HEV infection when serving in Africa and Asia and 50 travelers with acute HEV infection who were from the United Kingdom (table 1).

Most travelers completely recovered after acute illness. How-

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Reprints or correspondence: Dr. Pierre Van Damme, Center for the Evaluation of Vaccination, WHO Collaborating Center for Prevention and Control of Viral Hepatitis, University of Antwerp, Universiteitsplein 1, B-2610 Antwerp, Belgium (pvdamme@uia.ua.ac.be).

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Table 1. Summary of data on cases of acute HEV infection in travelers after visiting countries of endemicity.

Origin	No. of cases	Destination	No. of cases, outcome	Reference(s)
Israel	5	Nepal, India	5, R	PR
North America	8	India, Pakistan, Nepal, Bangladesh, Mexico	8, R	[2–8]
Australia	1	Thailand, Nepal	1, R	[9]
United Kingdom	57	Pakistan, India, other areas of endemicity	54, R; 1, FH; 2, severe HEV infection	[10–14]
Netherlands	3	Bangladesh, Somalia, Middle East	3, R	[15]
Scandinavia	8	Nepal, India, Pakistan, other countries	7, R; 1, FH and death	[16, 17]
Nepal ^a	4	Nepal	4, R	[18]
Japan	1	China	1, R	[19]
Italy	16	India, Somalia, other areas of endemicity	15, R; 1, FH and death	[20, 21]
France	45	India, Somalia, Chad	44, R; 1, FH	[22–26]

NOTE. FH, fulminant hepatitis; HEV, hepatitis E virus; NR, not reported; PR, present report; R, recovered.

^a Expatriates.

ever, fulminant hepatitis occurred in 4 (2.7%) of the 148 travelers, 2 of whom had underlying liver disease (a 6-year-old girl with Wilson's disease and a 65-year-old man with chronic hepatitis C). Two of the 4 individuals with fulminant hepatitis died. The overall mortality rate was 1.4% (2/148). None of the soldiers were reported to have fulminant hepatitis [24–26]. Two pregnant women in their third trimesters had severe cases of HEV infection [13].

Discussion

HEV has been found to be a major cause of acute hepatitis in adults in several developing countries. Most travelers from developed countries are not immune to HEV and therefore may be at risk for acute HEV infection when traveling to areas of endemicity. There is no vaccine available, and immune serum globulin offers no protection against HEV infection [27].

From 1986–1997, we found 148 reported cases of acute HEV infection associated with travel, of which 98 were reported in detail. In Israel, the rate of HEV seropositivity among healthy blood donors is 2.8% [28]. We estimate that >100,000 Israelis travel annually to countries where HEV is endemic. However, during a 6-yr period, only 5 cases of acute HEV infection in travelers returning to Israel were documented. The occurrence of HEV infection in travelers appears to be quite low, in spite of the low level of natural immunity. This finding is in contrast to the risk of hepatitis A virus (HAV) infection for travelers, the incidence of which has been reported to be 3–20 cases per 1000 nonimmune persons who travelled to areas where HAV is endemic [29]. HEV is known to be less infectious than HAV, which is demonstrated by the fact that the rate of secondary spread of HEV is lower than that of HAV (2% vs. 15%) [30].

Possible reasons for the relatively low number of cases of acute HEV infection in travelers include gross underreporting, misdiagnosis, subclinical infections, and dual infection, leading to the diagnosis of other more common hepatitises. Since the incubation period for HEV infection is 40 days (range, 15–60 days), long-term travelers may be overseas when the disease occurs. However, the incidence of HEV infection may indeed

be low. Serological studies of travelers have demonstrated a low risk for HEV infection. A prospective study conducted in 1993 examined 104 short-term (<3 months) travelers from Louisiana who were going to countries where HEV is endemic; all participants were negative for antibodies to HEV before travel and remained negative when IgM and IgG antibodies were examined 7–12 weeks after their return to the United States [31]. A 1995 retrospective study of 328 North American missionaries serving in various locations in Africa, Asia, and Central and South America from 1967–1984 demonstrated no seroconversion [32]. Larger studies of seroconversion to HEV in travelers are needed to determine this risk.

In summary, the risk of acute HEV infection for travelers to regions of endemicity appears to be low, and acute HEV infection in these travelers is rarely fatal. Pregnant women and individuals with underlying liver disease may be at greater risk for severe infection. Most documented cases occurred in travelers who remained in areas of endemicity for ≥ 1 month (although one traveler spent only 1 day in such an area). With the lack of an available vaccine, strategies to prevent HEV infection in travelers are food and water precautions, such as those offered to prevent other enterically transmitted infections.

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