

Hepatitis E: A newcomer to the hepatitis alphabet – Case report and review of the literature

KARL WEISS MD, LOUISE POIRIER MD, SYLVAIN VARIN MD, CLAIRE BELIVEAU MD, MICHEL LAVERDIÈRE MD

K WEISS, L POIRIER, S VARIN, C BELIVEAU, M LAVERDIÈRE. Hepatitis E: A newcomer to the hepatitis alphabet – Case report and review of the literature. *Can J Infect Dis* 1995;6(1):34-37. The first Canadian case of hepatitis E is described in a patient who travelled to Asia for a six-month period and spent most of his time in India. Hepatitis E shares some similarities with hepatitis A, notably the mode of transmission and the absence of chronic course. However, a few important differences have been noted, including a higher mortality rate and a high fatality rate in pregnant women. Hepatitis E is very common in developing countries and should be suspected more often in individuals with gastrointestinal complaints returning from endemic areas.

Key Words: *Hepatitis E*

L'hépatite E : Un nouveau venu dans l'alphabet des hépatites

RÉSUMÉ : Nous décrivons dans cet article le premier cas confirmé d'hépatite E chez un patient revenant d'un voyage en Asie. L'hépatite E présente de nombreuses similarités avec l'hépatite A, notamment son mode de transmission et l'absence d'un état de porteur chronique. Néanmoins, il existe quelques différences, entre autre un taux de mortalité plus élevé de façon générale et une sévérité marquée de la maladie chez la femme enceinte. L'hépatite E est une pathologie très fréquente dans les pays en voie de développement et doit être recherchée chez les individus retournant de zones endémiques.

A 35-YEAR-OLD CAUCASIAN MALE PRESENTED TO THE travel clinic of the authors' hospital (Clinique des maladies tropicales, Hôpital Maisonneuve-Rosemont, Montréal) in June 1993, complaining of abdominal pain, diarrhea and jaundice. He was returning from a six-month vacation in Asia, having spent most of his time in India. The patient's symptoms started 10 days after his return. While in India, the pa-

tient was tattooed on his thighs, and he lived in suboptimal conditions. He drank nonbottled water, ate a variety of uncooked foods and was repeatedly subjected to potentially contaminated water (river water) in his daily hygiene. The patient was a nurse, had no particular medical history, was an occasional smoker and did not drink alcohol. When ques-

Département de Microbiologie-Infectiologie, Hôpital Maisonneuve-Rosemont, Montréal, Québec

Correspondence: Dr Louise Poirier or Dr Karl Weiss, Département de Microbiologie, Hôpital Maisonneuve-Rosemont, 5415 de l'Assomption, Montréal, Québec H1T 2M4. Telephone (514) 252-3817, Fax (514) 252-3898

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tioned, the patient was ambivalent regarding his sexual orientation and denied any drug use. Before leaving for Asia, the patient went to a different travel clinic where he received all the appropriate immunizations (human gamma globulins, typhoid vaccine, diphtheria-tetanus:d2T5). During his trip, the patient did not take any medication. He was previously immunized against hepatitis B due to his occupation and had no history of liver disease. Physical examination was normal except for jaundice and mild right upper quadrant tenderness. Blood tests revealed abnormal liver functions (Table 1), and a moderate amount of bilirubin was detected in the urinalysis. Abdominal ultrasound was normal except for a moderately thickened gallbladder. No hepatomegaly was seen. Serologies for hepatitis A (immunoglobulin [Ig]M antihepatitis A virus [HAV]), hepatitis B (hepatitis B surface antigen, IgM antihepatitis B core antigen), hepatitis C (HCV) (anti-HCV), antihuman immunodeficiency virus and IgM anticytomegalovirus were negative. Serum was collected in June 1993 for hepatitis E antibody detection. The test was performed at the Centers for Disease Control and Prevention in Atlanta, Georgia by a microplate ELISA method using a recombinant antigen made on the premises (personal communication). The test was positive. At a follow-up visit in July, the patient was no longer experiencing his original discomfort and liver function was back to normal. This is, to our knowledge, the first confirmed case of hepatitis E diagnosed in Canada.

REVIEW OF THE LITERATURE

Hepatitis E is a rarely encountered type of hepatitis in the western world. The first documented outbreak of hepatitis E (diagnosed retrospectively) occurred in India in 1955 (1); it was supposedly related to the ingestion of contaminated water and resulted in over 50,000 cases. Since then, more incidences were documented of what was previously called 'enterically acquired non-A non-B hepatitis'. The virus associated with hepatitis E was isolated in 1989 by Krawczynski and Bradley (2,3). It is a nonenveloped virus of 27 to 34 nm (3) consisting of a single-stranded, positive-sense RNA molecule (4). Morphologically, hepatitis E virus (HEV) has some similarities with caliciviruses (5), but molecular characterization shows significant differences; the final taxonomic classification of HEV is still unclear. During the past two decades, many outbreaks have been described in several countries, but India remains a region where this type of hepatitis seems to be highly prevalent (6-9), probably largely due to water contamination. Other countries where cases have been described include: Turkey (10), Ethiopia (11), Sudan (12), Egypt (13), Morocco (14), Algeria, Tunisia and Bangladesh (15), Burma, Pakistan and China (16), the former USSR (17), Mexico (18), Senegal (19) and Ivory Coast (19) (Figure 1). As more information on the disease incidence and distribution becomes available, it appears that hepatitis E is a major cause of hepatitis in developing countries, if not the most common cause in adults (5).

In the western world, the disease has always been related to travelling to endemic areas. In the United States, four cases were confirmed by serology between 1989 and 1992

TABLE 1
Laboratory values

	Results		Normal range of values
	June 8, 1993	July 27, 1993	
AST (U/L)	615	24	0-40
ALT (U/L)	1245	41	0-40
Total bilirubin (μmol/L)	126	32	0-21
Creatinine (μmol/L)	74		80-120
BUN (μmol/L)	4.3		2.5-7.1

ALT Alanine aminotransferase; AST Aspartate aminotransferase; BUN Blood urea nitrogen

(20): one patient acquired hepatitis in Mexico and the other three on the Indian subcontinent. Imported cases have also been reported in Europe, notably in the United Kingdom (21), the Netherlands (22) and Spain (23). The transmission of HEV is very similar to that of HAV. The incubation period ranges from two to nine weeks, with a mean of 45 days (20). A fecal-oral route has been implicated and proved by the virus being transmitted to a volunteer (24). HEV is not transmitted vertically (25), and there are no chronic carriers. Person to person transmission by casual contact is still controversial (7,26). Hepatitis E symptoms are similar to those of hepatitis A, but a few differences can be observed. First, the mortality rate seems to be higher – 1 to 2% overall – 10-fold greater than that for HAV. The attack rate is highest among young adults 15 to 40 years old, who for the most part are already anti-HAV-positive. Aside from a few outbreaks (7,27), it is a relatively uncommon condition in children. Another particular finding is that HEV causes severe disease in pregnant women, with a fatality rate reaching 25% in certain studies (11,16), the peak occurring in the third trimester. Why hepatitis E is responsible for such mortality during pregnancy remains unknown. Since viral hepatitis is the most common cause of jaundice in pregnant women in North America, it is important to remember that hepatitis E has a significantly different clinical course in pregnant patients (28).

Diagnostic tests have recently been developed but are still not easily available for routine testing in North America. Krawczynski and Bradley (2) were the first to use a fluorescent antibody blocking assay for HEV antibodies in serum. However, an important drawback of the test was inability to differentiate between past and present infection. An HEV ELISA has since been developed at Genelabs Technologies Inc (California) (27), using antigens derived from ORF2 and ORF3 of the Burma and Mexico strains. Acute phase sera were collected during outbreaks in India, Pakistan and Mexico and tested positive with the HEV ELISA. The test was used to document cases in the United Kingdom and in an epidemiological survey of hepatitis E in Hong Kong (29). Finally, a Western blot assay for hepatitis E antibodies served as a laboratory tool in a Sudanese outbreak (12). All these tests performed fairly well and were able in some instances to differentiate between IgM and IgG antibodies. While more data are accumulated on their sensitivities and specificities (27), these tests could

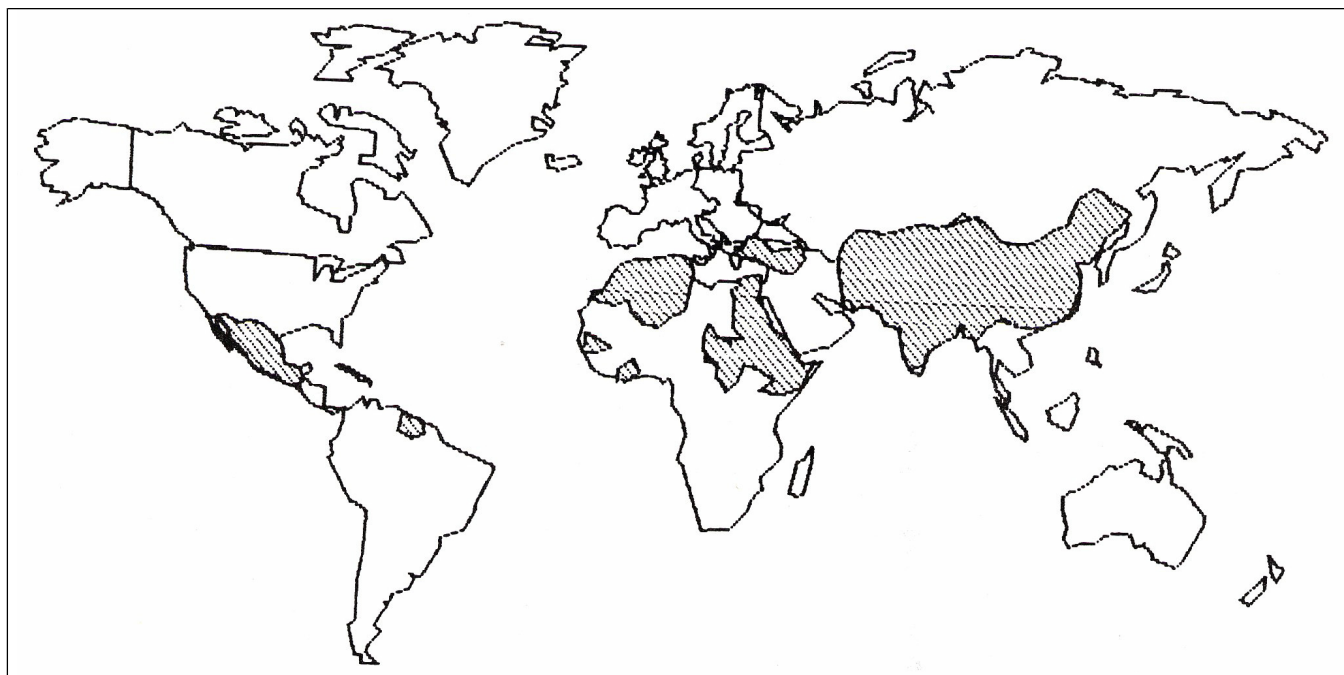


Figure 1) Regions where cases of hepatitis E have been confirmed (shaded areas)

be available in the near future for routine serology.

Treatment of hepatitis E is mainly supportive, and, as with other types of hepatitis, prolonged prothrombin time, hypoglycemia and altered mental status at admission are ominous signs. There is no vaccine available, and an Indian study failed to prove any protective effect of immune serum globulin from an Indian source as prophylaxis (26). Hepatitis E is rarely encountered in Canada; nevertheless, it should be suspected in any traveller returning from a developing country or in a recently landed immigrant from an endemic area presenting with symptoms of acute hepatitis. As Canadians are more

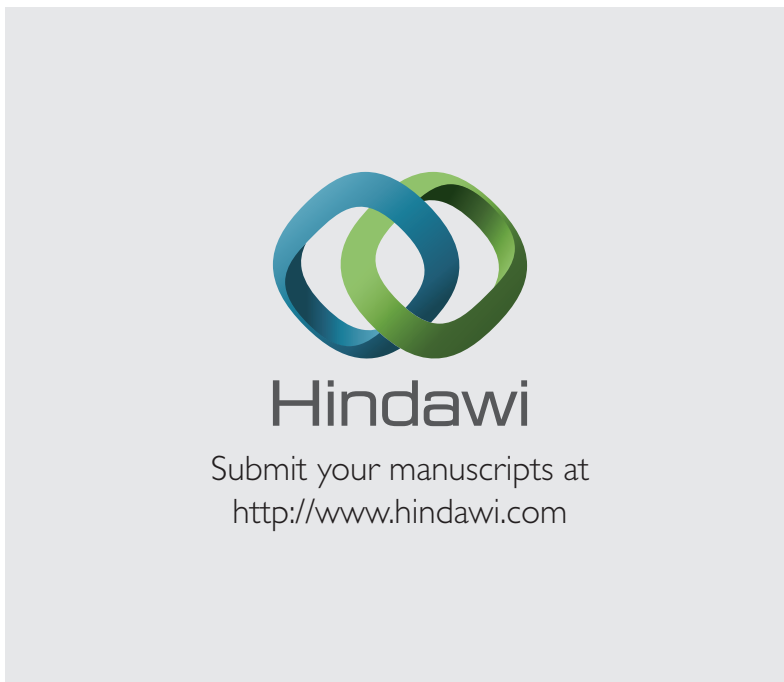
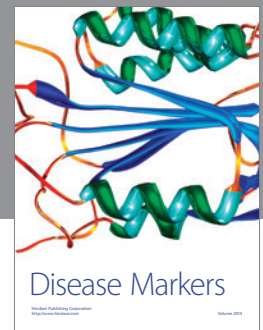
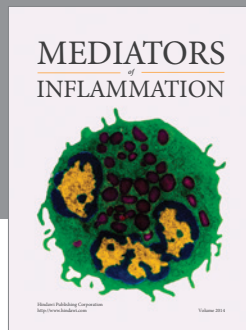
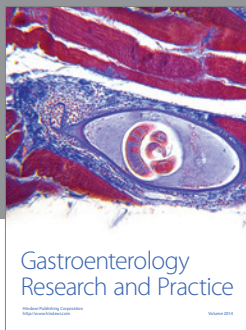
and more often travelling to exotic destinations, physicians in this country should be aware of the existence of hepatitis E, which is likely underreported. It is worth noting that, since March 1994, hepatitis E serology has been available for selected cases at the Laboratory Centre for Disease Control in Ottawa.

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