**Foreword**

In the past, it was believed that hepatitis E was only a problem in developing countries due to contaminated water supplies. It was also believed that in industrialized countries the majority of HEV infections were among people who had visited countries where HEV infection was widespread.

However, over the last few years, studies and news reports have surfaced that are painting a different picture of HEV infections in industrialized countries such as the United States. In the U.S., there is little information about the prevalence of HEV mainly because of the lack of surveillance and testing even though there have been small studies that have hinted that the prevalence of HEV is more widespread than previously believed. Recently, a large study on the prevalence of HEV was published that will give us a better picture of the estimated number of people in the U.S. who have been infected with HEV. The study results are somewhat alarming and should, at the very least, promote more dialogue about the need for more strategies for testing and educating the public about the risk factors and ways to prevent the transmission of HEV.

The hepatitis E virus is a hepatotropic, single stranded RNA virus. The main transmission route of HEV is fecal-oral due to HEV contaminated water supplies, but other sources of infection have been identified. The largest outbreaks of HEV usually occur in developing countries, but outbreaks also occur in developed countries.

HEV has 4 genotypes numbered 1 through 4 and 24 subtypes. HEV has been found in humans, and animals—genotype 1 and 2 is found only in humans whereas genotypes 3 and 4 have been found in humans and animals (pigs, boar, and deer). Genotypes 1 and 2 are mainly found in the subtropical and tropical areas of Asia, Africa, and the Americas. Genotype 3 is found worldwide and genotype 4 is confined mostly to Asia.
Hepatitis E (HEV)

Genotype distribution is indicative of transmission modes. For instance, genotypes 1 and 2 are mainly from contaminated water, whereas genotypes 3 and 4 can be transmitted from pigs or other animals to humans.

Transmission
HEV is transmitted primarily by the fecal-oral route — by drinking or eating contaminated food or water especially in countries that do not have sanitized sewage and water systems. There is some evidence that HEV may also be transmitted by the consumption of uncooked or undercooked shellfish, pigs, wild game and rodents.

The incubation period is usually 40 days, but it can range from 15 to 60 days.

Prevention
HEV can be prevented with vaccination and by following safety measures:

- Always follow basic food safety guidelines for washing and cooking food.
- Avoid eating uncooked or undercooked animal parts or organs that could possibly transmit HEV.
- In areas where there is a high prevalence of HEV avoid the drinking water (unless bottled), uncooked shellfish, unpeeled fruit and vegetables (unless personally prepared).

Symptoms
The most common symptoms of HEV are the typical hepatitis symptoms — jaundice (yellowing of the skin and whites of the eyes), malaise (out of sorts), loss of appetite, fever, diarrhea, abdominal pain, and muscle and joint pain. However, most people who become infected with HEV do not develop symptoms.

Normally, infection with acute HEV will resolve and the infected individual will develop antibodies that are protective against future infection. However, one study found that eight organ transplanted patients (HEV genotype 3 with severely compromised immune systems) had elevated liver enzymes and HEV RNA (viral load) over time, which would mean that HEV could lead to chronic infection. But it is unclear if this is a true chronic infection or just due to a weakened immune system that isn’t able to resolve the infection. Deaths associated with HEV are uncommon except that pregnant women and their unborn babies are at risk of death especially during the third trimester of pregnancy — although this is mostly confined to developing nations. In industrialized nations deaths related to HEV are rare and mostly occur in people who have received organ transplants and who have severely suppressed immune systems. Having another hepatitis virus could also lead to a more severe form of disease.

It was announced in January 2012 that China had approved the first HEV vaccine, HEV 239 vaccine, being sold under the trade name Hecolin.

The approval of the HEV vaccine was based on data released from a Phase III trial that included 97,356 subjects aged 16 to 65 years in China’s Jiangsu province. There were no acute cases of HEV reported in the group that received the vaccine compared to 15 confirmed HEV in the subjects who did not receive the vaccine.

The HEV vaccine is given by injection in three doses.

U.S. Prevalence
In a current study,1 18,695 participants in the Third National Health and Nutrition Examination Survey (NHANES III) were tested for HEV antibodies. Participants were 6 years of age or older. The study period was 1988 through 1994. The overall prevalence of HEV antibodies in the non-institutionalized U.S. population was 21%. The breakdown of the prevalence of HEV by race, sex, race/ethnicity, country of birth, and geographic region is shown in Table 1.
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The authors concluded that their study suggests that HEV is somewhat common in the general U.S. population. Previous studies in the U.S. suggested that the prevalence of antibodies to HEV was mostly due to people who traveled or who were from developing countries with a high prevalence of HEV. But in this study the authors theorized that many of the infections may have originated in the U.S. and may have been spread by exposure to swine. In this study and in previous studies the association between eating liver or other organ meats has been found to be a highly plausible route of infection. It is also interesting to note that this would explain why acute infection of HEV is rarely reported because HEV from genotype 3,4 (from swine) is believed to be less severe and acute symptoms may not necessitate a trip to a medical provider for testing and treatment. Another reason it goes undetected in the U.S. is that there are no FDA approved hepatitis E antibody tests available for general use.

Another study published in the *Journal of Viral Hepatology* by Fujiwara et al. (J Viral Hepat. 2014; 21 78-89) titled Chronic Hepatitis E: A Review of the Literature found that immunocompromised patients (organ transplant, HIV, blood tumors) who became infected with hepatitis E, mainly genotype 3,
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were more likely to develop chronic hepatitis E if they were not treated with antiviral treatment. Antiviral treatment usually involved pegylated interferon plus ribavirin. Of those not treated approximately 15% would develop liver and non-liver related complications and would quickly progress to cirrhosis, end-stage liver disease and death.

**Source:**

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The key findings of the study (NHANES)¹:
- HEV infection was uncommon among children, but became more common as people aged.
- People in the Midwest had the highest regional estimates and interestingly the Midwestern region of the U.S. has the largest swine population (pigs, hogs, and boar).
- The highest incidence of HEV was found in the metropolitan areas.

Risk factors for HEV included:
- Having a well as a source of tap water.
- Having HAV antibodies was associated with significantly lower odds of having HEV antibodies.
- Having a pet in the household.
- Consuming liver or other organ meats more than once per month.
- Having HCV.

Visit our websites to learn more about viral hepatitis:

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