COMMENT AND RESPONSE

Zoster Vaccination for Persons Aged 50 to 59 Years

TO THE EDITOR: Le and Rothberg's recent analysis (1) supports the Centers for Disease Control and Prevention recommendation for herpes zoster (HZ) vaccine for immunocompetent people aged 60 years or older, despite U.S. Food and Drug Administration approval since 2011 for use in adults aged 50 years or older. We would like to counter these arguments and explain why physicians should recommend this vaccine to eligible persons aged 50 years or older.

The authors based their analysis on the assumption that the incidence of HZ would plateau after either 2010 or 2015. However, evidence suggests that HZ incidence continues to increase and is modeled to increase for 50 years (2). Earlier vaccination is more efficient against increasing HZ incidence.

Another assumption was that vaccine efficacy wanes at the same rate regardless of age. A recent study shows that reduction in vaccine efficacy is closely associated with age at vaccination in patients aged 60 or older (that is, protection of HZ vaccination lasts longer in younger patients) (3). According to the sensitivity analysis presented in the article, if vaccination efficacy decreases at half the rate in people aged 50 to 59 years, then the vaccine is cost-effective (incremental cost-effectiveness ratio, $48 457 per quality-adjusted life-year).

Finally, the productivity loss associated with HZ was estimated from a retrospective, telephone survey with a low response rate. A prospective study found that productivity losses were greater in younger patients (aged 50 to 59 years) than in older patients (aged ≥60 years) (4). A sensitivity analysis that considers increased loss of productivity would support vaccination in this younger age group.

Other studies have found that vaccination at age 50 years is cost-effective (5). We believe that further study is required to determine the true incremental cost-effectiveness ratio of HZ vaccination in patients aged 50 years or older. In the meantime, because the greatest number of HZ cases occur in people in their 50s when the vaccine is most effective in preventing disease, nonpain complications do not increase with age, vaccine duration of efficacy is likely to be longer, and loss of productivity is greater in this age group, we strongly recommend that immunocompetent persons in their 50s receive the HZ vaccine (6).

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IN RESPONSE: Mr. Kumar and colleagues take issue with several assumptions in our model. Their assertion that HZ incidence will continue to increase for 50 years is based on mathematical models from the 1990s. However, 2 large clinical trials of HZ vaccines conducted 10 years apart and with careful monitoring and adjudication of HZ cases reported almost identical incidence of HZ in the placebo groups (1, 2), which was similar to our modeled incidence.

We agree that initial vaccine efficacy is closely related to age at vaccination, as demonstrated in the Shingles Prevention Study. However, the model by Li and coworkers (3), which Mr. Kumar and colleagues cite, does not support the assertion that vaccine efficacy wanes more slowly in younger patients. Curiously, although that study was conducted by Merck, it ignores data from the Long Term Protection Substudy (LTPS) (4) and projects vaccine duration of 30 years or more. This estimate is not compatible with the observed efficacy in the LTPS. In our model, we assumed vaccine efficacy would decline at the rate seen in the LTPS. Because initial efficacy is higher in younger patients, vaccine protection takes longer to decline to zero in this group—about 14 years in our model versus 8 years for patients aged 60 years or older in the LTPS (4).

Regarding productivity losses, the small study by Drolet and colleagues (5) was based on convenience sampling and was conducted in Canada, which has different sick leave benefits than the United States. Moreover, they reported *less* productivity loss. Using their estimated productivity loss in our model actually increases the incremental cost-effectiveness ratio to $350 000 per QALY.

Finally, Preaud and colleagues' study (6) estimated the duration of vaccine protection based on Li and coworkers' study (3), resulting in an unrealistic cost-effectiveness estimate for younger patients.

Unless new long-term data on vaccine efficacy become available, we see no reason to reconsider the Advisory Committee on Immunization Practice's recommendation to begin vaccination at age 60 years.

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OBSERVATION

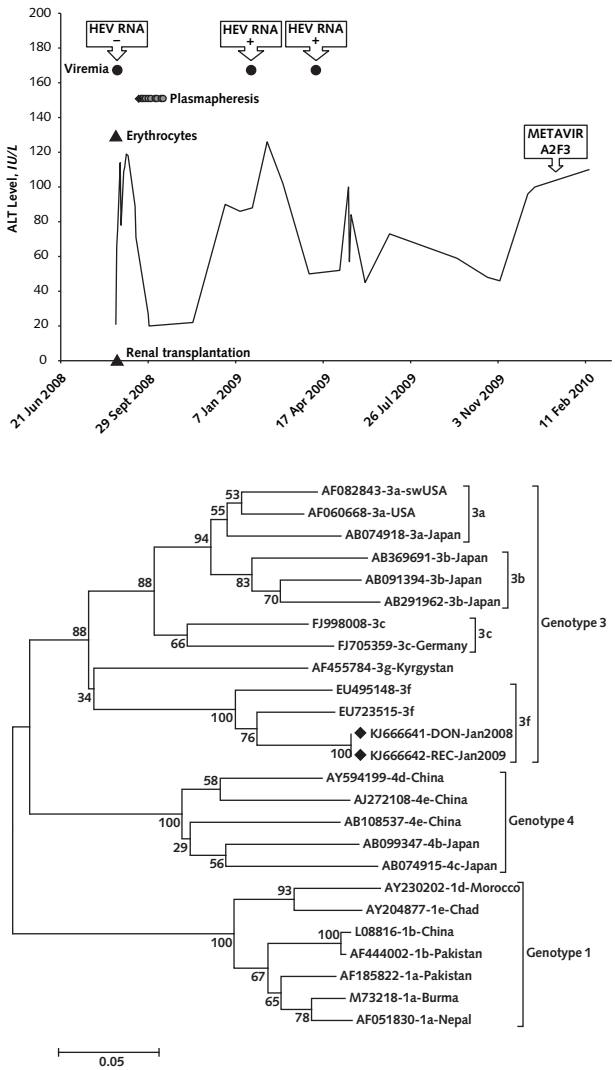
Transmission of Hepatitis E Virus by Plasma Exchange: A Case Report

Background: Hepatitis E virus (HEV) is most often transmitted through the fecal–oral route in contaminated drinking water or food, but it can also be transmitted by blood and blood products (1). The virus usually causes an acute, self-limited illness with symptoms typical of other hepatitis viruses; however, fulminant disease is possible and chronic infection can occur in immunosuppressed persons.

Objective: To report transmission of HEV to a kidney transplant recipient through plasma exchange.

Case Report: Our patient was a 48-year-old North African woman with vascular nephropathy. After 3 years of hemodialysis, she received her first kidney transplant from a deceased donor on 23 August 2008. The patient's initial immunosuppressive regimen included a 5-day course of antithymocyte globulin; methylprednisolone, 1000 mg/d, rapidly tapered to prednisone, 10 mg/d; tacrolimus with a target trough concentration of 10 to 15 ng/mL; and mycophenolic acid, 1440 mg/d. Her long-term regimen included continuation of prednisone, tacrolimus, and mycophenolic acid. Acute humoral rejection was diagnosed 28 days after transplantation and was treated with a 3-day course of methylprednisolone, 500 mg/d; 6 rounds of plasma exchange; and 4 courses of intravenous immunoglobulins (2). Aminotransferase levels remained above the upper limit of normal for more than 15 months

Figure. ALT levels after renal transplantation (*top*) and phylogenetic analysis (*bottom*).



The phylogenetic analysis was conducted on the Molecular Evolutionary Genetics Analysis (MEGA) software version 6 (www.megasoftware.net) using the Neighbor–Joining method from a Kimura 2-parameter distance matrix based on partial nucleotide sequences of open reading frame 1. Sequences are indicated by their GenBank accession number. The black diamonds indicate the sequences described in the case report. ALT = alanine aminotransferase; HEV = hepatitis E virus.

(**Figure**, *top*). Genome amplifications were negative for hepatitis B and C viruses, cytomegalovirus, herpes simplex virus, and Epstein–Barr virus. Test results for autoimmune and genetic liver diseases were negative, and liver ultrasound results were normal. Liver biopsy (25-mm specimen) showed extensive septal fibrosis (METAVIR fibrosis score F3). Nineteen months after transplantation, we detected HEV RNA genotype 3f (GenBank accession number KJ666642) in the patient's blood based on sequencing using open reading frame 1 (3), and she tested positive for anti-HEV IgG and negative for anti-HEV IgM. We confirmed that she had been infected for more than 1 year by finding HEV RNA in a frozen plasma sample drawn 5 months after transplantation. The kidney donor had

tested negative for HEV RNA, and our patient's stored blood samples tested negative for HEV markers before transplantation. The patient reported never having consumed pork or shellfish, foods that have been implicated in HEV transmission, and she had lived in France, where fecal–oral transmission of HEV is rare, since transplantation. The method of transmission remained undetermined until we tested for HEV RNA in stored samples of all 18 blood products used during the peritransplantation period. From a single sample of fresh-frozen plasma, whose donor had tested negative on multiple occasions for hepatitis C virus, HIV-1 and -2, and hepatitis B virus before the plasma was used, we recovered a strain of HEV identical to the one infecting the patient (**Figure**, *bottom*), with a viral load of 7.5 $_{log}$IU/mL. This plasma had been used during a plasma exchange for treating acute humoral rejection. We prescribed ribavirin monotherapy (10 mg/kg for 68 weeks) without changing the immunosuppressive regimen, and the patient had a sustained virologic response.

Discussion: The prevalence of HEV RNA in blood donors in France is 0.045% (4). Plasma exchange typically involves the removal of 2 to 5 L of plasma several times a week, which often is replaced with donor plasma. If replacement involves the typical 2.5 L (10 bags) of donor plasma, then the risk for HEV is 10 times greater than the risk involving a single bag. In some circumstances, replacement procedures use plasma that has been pooled from many donors (up to 100 in France and up to several thousand in some other countries) and then treated with solvents and detergents to inactivate infectious agents (5). However, this treatment is ineffective against HEV and pooling multiplies the risk for infection. On the basis of our findings, we believe that all kidney transplant recipients with abnormal liver function test results, especially those treated with plasma exchange, should be tested for HEV RNA.

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CORRECTION

Correction: The Consult Guys–A Real Headache: Anticoagulation and a Subdural Hematoma

In a recent video from The Consult Guys (1), the computed tomography image of the head originally included in the video at 1:56 showed a shift of midline structures in association with a hematoma. This has been replaced with a correct image, demonstrating a hematoma with no shift of midline structures.

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