adverse events while hospitalized, and many people do not receive care that they should receive, while others receive care that does not benefit them. Growth of health care spending is at historic lows: Medicare spending per beneficiary increased by approximately 2% per year from 2010 to 2014 — a rate far below both historical averages and the growth rate of the gross domestic product. Survey data show that more than 7 in 10 people who signed up for insurance in the new health insurance marketplace last year say the quality of their coverage is excellent or good. However, it will take additional effort to sustain and augment the positive changes we have seen so far.

We are dedicated to using incentives for higher-value care, fostering greater integration and coordination of care and attention to population health, and providing access to information that can enable clinicians and patients to make better-informed choices. We believe that, by working in partnership across the public and private sectors, we can accelerate these improvements and integrate them into the fabric of the U.S. health system.

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Ms. Burwell is the U.S. Secretary of Health and Human Services.

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Making Hepatitis E a Vaccine-Preventable Disease

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In this issue of the Journal, Zhang and colleagues provide data obtained from more than 110,000 healthy participants 16 to 65 years of age confirming that hepatitis E can be prevented by vaccination (pages 914–922). Initial results from this cohort study revealed that the vaccine candidate is safe and efficacious (95% efficacy over the 12-month period after vaccination). The current report further shows that Hecolin (the hepatitis E vaccine licensed in China in 2011) remains immunogenic and efficacious at least 4.5 years after completion of the three-dose schedule administered at 0, 1, and 6 months.

Since Zhang et al. conducted their study in China, they found protection mainly against hepatitis E virus (HEV) genotype 4, the viral strain that is most common in that country (see map). Additional studies are needed, however, to establish the vaccine’s efficacy in areas where the other three HEV genotypes predominate. In South Asia and certain areas in Africa, HEV genotype 1 is a leading cause of acute hepatitis, infecting millions of people each year and causing an estimated 70,000 deaths annually. Although hepatitis E is often a mild disease, HEV infection can cause fulminant hepatitis and death. As many as 20% of pregnant women who develop hepatitis E during the third trimester may die from the disease or its complications. Large epidemics caused by HEV genotype 1 are common, particularly among people living in crowded, unsanitary conditions, such as camps for refugees, and internally displaced people. In such settings, where HEV infection is mainly transmitted by the fecal–oral route, improvements in sanitation and provision of safe drinking water cannot typically be provided at a level that halts transmission, so epidemics can be prolonged. Hepatitis E vaccination could be a useful adjunct in these settings.

Although hepatitis E is known to be a problem in these areas, the absence of precise data regarding the burden of hepatitis E disease and related deaths is a major barrier to defining the clinical and public health applications of a hepatitis E vaccine. For example, in Bangladesh, a study in which standardized interviews
were conducted with family members and caregivers to assess the cause of maternal deaths revealed that one in five was related to jaundice; although published data suggest that about half those deaths could be related to hepatitis E, limited capacity for research hampered efforts to identify HEV as the cause. Furthermore, epidemiologic information on infection and disease during childhood is lacking. Prospective studies based on accurate HEV testing are needed to reliably estimate the incidence of hepatitis E and related mortality among pregnant women, their newborns, and children.

The gaps in data extend to the United States, where the lack of highly sensitive and specific tests approved by the Food and Drug Administration and the absence of surveillance case definitions limit definitive diagnosis and reporting of hepatitis E. Despite these limitations, laboratory testing conducted by the Centers for Disease Control and Prevention (CDC) at the request of health authorities and clinicians identified cases of hepatitis E that occurred as a result of autochthonous transmission of HEV genotype 3 in the United States. HEV genotype 3 infection in humans is thought to be a foodborne zoonosis resulting from consumption of raw or undercooked meat and offal of HEV-infected pigs, boars, and deer, although data that would conclusively establish a cause are often lacking. Some cases of HEV genotype 3 have occurred in recipients of solid-organ transplants, a population at risk for chronic hepatitis E.

In 2014, the CDC awarded funds to two U.S. national laboratories for sharing deidentified data from hepatitis testing, including tests for HEV antibody or HEV RNA. Epidemiologic studies, guided by enhanced surveillance, are needed to identify the populations that have a burden of HEV infection and may therefore benefit from vaccination. In the meantime, U.S. clinicians should include hepatitis E in the differential diagnosis of hepatitis, particularly for patients with a history of travel to areas where hepatitis E is endemic or when other more common causes of hepatitis have been ruled out.

If the efficacy of this HEV vaccine is determined to be pan-genotypic, several public health questions must be answered, including who should be vaccinated, when to vaccinate, and the cost-effectiveness of vaccination as a prevention tool. Additional data regarding the safety, immunogenicity, and efficacy of the hepatitis E vaccine in pregnant women, persons with chronic liver disease, and other vulnerable populations are needed. Before hepatitis E vaccination can be considered as an addition to the childhood vaccination schedule, safety and efficacy data are needed for children less than 16 years of age, including data on how this vaccine interacts with other vaccines when given simul-
On Taking Notice — Learning Mindfulness from (Boston) Brahmins
Michael W. Kahn, M.D.

I was a harried, green resident busily readying an elderly patient — call her Margaret — for hospital discharge when her face unexpectedly began glowing with pleasure. Looking me intently in the eye, she exclaimed, “I do hope you know Dr. Edgecomb!” But before I could respond, she continued, “Do you know what he told me when I left his office last time? ‘Now you just be sure to notice the crocuses by the doorway on your way out, Margaret; they’re lovely this year.’ That’s just the kind of person he is . . . and he was so right about the crocuses.”

“Isn’t that nice!” I replied, discreetly rolling my eyes and continuing to write prescriptions. How quaint it seemed: the elderly doctor, possibly taught by Osler’s students, trying to do as little harm as possible with his hoary knowledge; his elderly patient, evidently delighted to receive crocus-based medicine. Though I didn’t know Dr. Edgecomb (also a pseudonym) personally, I

taneously. Finally, field trials are needed to establish an effective vaccination series. Although studies of the vaccine suggest that two doses may effectively prevent hepatitis E, a well-designed evaluation of the effectiveness of fewer doses and shorter dosing schedules is required.

The World Health Organization’s Strategic Advisory Group of Experts (SAGE) on immunization recently cited the need for additional data regarding the incidence of HEV infection and disease and the safety and efficacy of the vaccine before recommending routine hepatitis E vaccination in countries where hepatitis E is highly endemic (www.who.int/wer/2014/wer8950.pdf). Yet SAGE recognized that the current lack of data should not preclude the use of this vaccine in special situations, emphasizing that it should be considered for controlling hepatitis E outbreaks.

Data on the disease burden will help to build a case for hepatitis E vaccination in both high-income and low-income settings. Robust data from public health surveillance and surveys can inform these efforts, helping to stimulate industry interest in vaccine development and production. Other hepatitis E vaccines are in development. However, an earlier promising candidate did not progress to licensure and production, presumably because of the lack of a well-defined market and indications for vaccination. To date, only the vaccine studied by Zhang et al. has progressed beyond a phase 2 clinical trial.

A hepatitis E vaccine could become a powerful new tool in the prevention and control of HEV transmission and disease. Most immediately, it can have a role in curbing outbreaks of hepatitis E in humanitarian crises. The benefits of broad adoption of hepatitis E vaccine could be far-reaching, if studies reveal that vaccination protects against all HEV genotypes and is safe and effective when used in people at highest risk for hepatitis E-related illness and death, including pregnant women. Given the sustained protection afforded by hepatitis E vaccination reported by Zhang et al., now is the time to answer these remaining questions and establish the public health applications of a hepatitis E vaccine.

The views expressed in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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