

namivir, which is the focus of an ongoing phase 3 trial and available on compassionate-use basis, currently appears to be the antiviral of choice for treating hospitalized or immunocompromised patients with serious influenza caused by most oseltamivir-resistant variants, including H1N1-subtype viruses harboring the H275Y mutation. However, one U.S. government-sponsored randomized trial of intravenous peramivir in hospitalized patients was recently terminated by its data and safety monitoring board because of futility with regard to reaching its primary end point. Such findings highlight the impor-

tance of developing antiviral agents with new mechanisms of action, and ongoing work on new inhibitors directed against influenza polymerase, hemagglutinin, M gene, and other targets offers promise.

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## The Cure for Cholera — Improving Access to Safe Water and Sanitation

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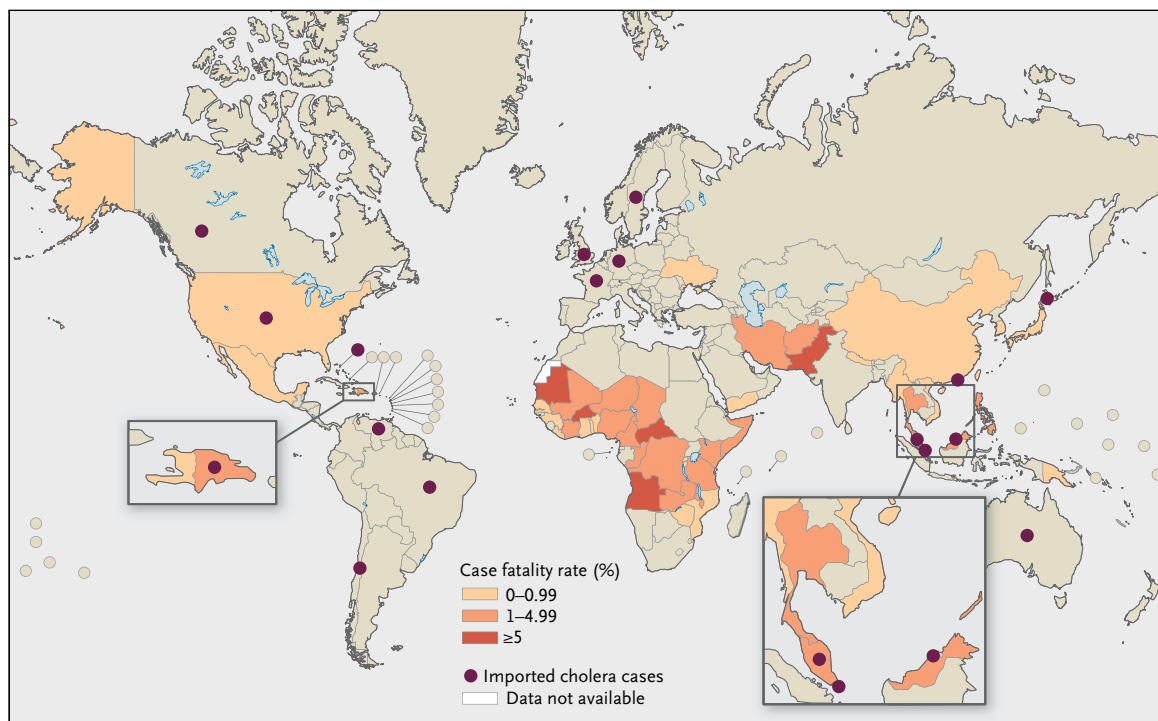
Whenever epidemics of cholera occur, the global public health community is energized. Experts meet, guidelines for control are reviewed and reissued, and new and modified interventions are proposed and promoted. In the past two decades, these things happened after cholera appeared in Latin America in 1991, in the wake of the Rwandan genocide and the ensuing refugee crisis in Zaire (now Democratic Republic of Congo) in 1994, in Zimbabwe in 2008, and in October 2010, at the onset of the ongoing epidemic in Haiti (see article by Barzilay et al.). But even when it is not covered in the news or noticed by the public, cholera occurs regularly in the developing world, and the annual number of cases reported to the World Health Organization

(WHO) has increased over the past few years to more than half a million cases and 7816 related deaths reported from all regions in 2011 (see map).<sup>1</sup> Moreover, these reported numbers grossly underestimate the actual global burden of cholera: the WHO estimates that 3 million to 5 million cases and 100,000 to 200,000 deaths due to cholera occur annually.

Among the latest developments in cholera control are the recommendations that antibiotic agents be given to patients with moderate dehydration, as well as to those with severe dehydration (always in conjunction with aggressive oral or parenteral rehydration), that all patients be treated with zinc, and that use of an improved two-dose oral cholera vaccine be expanded. The vaccine

has been administered successfully in pilot trials in a number of locations where cholera is endemic and, in 2012, during epidemics in Haiti and Guinea. The WHO recently agreed to establish a vaccine stockpile for emergency use to encourage greater production at lower cost. These developments are welcome additions to the anticholera armamentarium, but public health professionals know that they do not address the underlying problem.

The best intervention for long-term cholera control and, for that matter, for the control of the great majority of diarrheal diseases is the strategy that eliminated epidemic cholera from the United States and Northern Europe long before either marketed antibiotics or effective vaccines existed. The development and



#### Countries Reporting Cholera in 2011.

Data are from the Global Task Force on Cholera Control, World Health Organization.

maintenance of water and sewage treatment systems assured safe drinking water and safe disposal of sewage for all, keeping contaminated sewage out of water, foods, and the environment. The strategy not only eliminated cholera but also dramatically reduced mortality related to diarrheal diseases of all causes.

There has been some progress. At the global level, the proportion of people who lack sustainable access to safe drinking water has already been reduced by more than half since 1990; that was Millennium Development Goal (MDG) 7, which was achieved in advance of the target date of 2015. However, this success has been uneven and inequitable. Only 63% of people who live in the least-developed countries around the world have access to improved water supplies.

In Africa, where this MDG has not been met, the proportion is 61%. For sewage disposal (or sanitation), the picture is not even this bright: at the current rate of progress, the MDG will not be met globally until 2026, and 2.5 billion people still live without even modestly improved sanitation facilities, such as a well-constructed privy. In fact, stunningly, 15% of the world's population, more than 1 billion people, have no facilities at all and still defecate in open areas.<sup>2</sup>

Ensuring safe water and improved sanitation is a difficult proposition. The technological problems are manifold — rapid urbanization and growing megacities are outstripping the existing municipal waterworks, which cannot keep up with construction and maintenance demands. In rural areas, treating drinking water

with point-of-access and point-of-use solutions, including chemical and solar disinfection and safe water storage in the home, must be further expanded as an interim measure toward providing access to safe water sources.<sup>3</sup> The costs of improving and maintaining infrastructure in order to meet the MDGs can be daunting, depending on the technologies used; some estimates put these costs at well over \$50 billion per year.<sup>4</sup> To justify the expenditures that will be required, we need cost-utility analyses that are based on the best data possible, not just those that are readily available. These calculations should take into account the direct benefits of reducing diarrheal diseases and accompanying mortality and also other benefits, such as improved nutrition of children and lower rates of helminthic infection, hep-

atitis, and other diseases transmitted by the fecal–oral route.

Personal and community responsibilities are critical. Individual, household, and community approaches to sustained access and proper use of safer water sources and improved sanitation facilities will depend on effective behavior change and communications strategies. In some places, ingrained cultural practices and a lack of education may be impediments. The political will of international, regional, national, and local authorities will need to be developed, exercised, and maintained. There is no quick fix for improved water and sanitation; achieving equity will be a long, hard road, but the human, economic, and societal results surely justify the investment and the effort.

These challenges — technological limitations, costs, behavioral customs, and lack of education and of political will — should be seen not as absolute barriers to moving forward but rather as problems to be solved. Similar objections have been raised before when bold programs have been proposed — for example, in regard to expanding access to antiretroviral treatment to poor people in developing countries. That effort, though still not com-

pletely successful, offers a model for providing safe water and improved sanitation. The ethical imperative of treating sick and marginalized people with medicines that are currently available to some but not to all is not so different from the imperative to provide all people with safe drinking water, sewage disposal, and food that is not contaminated by human feces. For now, they are available only to some.

Nothing said here has not been said before, often at greater length and depth.<sup>5</sup> But the message bears repeating, frequently and insistently. Cholera, rightly feared for both the terrifying loss of life it can cause and for the panic it incites in affected populations, is as much a symptom as a disease. It is a symptom of insufficient investment by the global development community in assuring access to safe water and improved sanitation — of providing only a Band-Aid solution to a difficult problem. Because fecal–oral transmission is the predominant means by which people contract cholera, the frequency of cholera cases in the 21st century reflects the indisputable fact that the current state of development leaves more than a billion of the poorest and most marginalized people at risk of ingesting feces with their food

and water. As long as that is the case, it is difficult to be satisfied — notwithstanding the real successes that have been achieved — with the state of public health in developing countries.

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## Use of Health IT for Higher-Value Critical Care

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The patient had not yet coded but was spiraling downward, prompting a request for a bed in the intensive care unit (ICU). But the ICU had no available beds. Hours passed before the

decision was made that another patient could safely be “bumped” out of the unit to accommodate our patient. After the transfer, in the empty room strewn with unused bottles, procedure kits, and

hospital gowns, there was a moment of peaceful quiet but weariness. The team was exhausted from worrying that the patient would code before being transferred to the ICU, from running