

The move to make testing more routinely available, or even to require that physicians offer it to patients, has encountered little opposition. But there is resistance to the elimination of pretest counseling and specific written consent, as well as to the adoption of an opt-out standard. Although Frieden rejects mandatory HIV testing, many fear that without a requirement for written consent, testing would in effect become compulsory. “This is not informed consent, and it is not even consent,” said one activist. It is rather an attempt “to ram HIV testing down people’s throats without their permission.”

According to advocates of change, the transformation of HIV disease into a complex chronic condition requiring long-term, ongoing clinical management means that the limits imposed when medicine had little to offer have

outlived their justification. Proponents argue that prevailing requirements impede wide-scale testing because they are burdensome and time-consuming. Furthermore, they relieve physicians of an obligation to offer testing. Less often acknowledged is the fact that an opt-out approach shifts the burden from those who would choose to undergo the test to those who would refuse.

Making it more difficult to say no may be justified by public health considerations, particularly by concern about preventable opportunistic infections in persons who are unaware of their HIV infection and about transmission to their sexual or needle-sharing partners. As state and local health policymakers consider the new CDC recommendations, it will be crucial that the assumptions — both spoken and unspoken — informing the new testing paradigm

be the subject of open, ethically informed, and evidence-based discussion.

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Getting Serious about Cholera

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Deaths from cholera are again making news, this time in Angola. According to the World Health Organization (WHO), Angola had reported 46,758 cases of cholera, including 1893 deaths, as of June 19, 2006.¹ The outbreak has affected 14 of 18 provinces, but nearly half the cases were reported in the coastal capital, Luanda, and another 17 percent in Benguela provinces. The overall case fatality rate is about 4 percent, although in some provinces, it has reached 30 percent. This outbreak represents another in a series of cholera epidemics in this country,² which is among the poorest in the world and is still recovering from years of armed conflict. Several other African

countries have also had recent outbreaks (see map), in the seventh pandemic of cholera caused by *Vibrio cholerae* O1 El Tor, which reached Africa in 1970.

In addition to the reported cases, many are either not reported or are labeled as “acute watery diarrhea.” Although 94 percent of the 101,383 cholera cases and 99 percent of the 2345 related deaths registered with the WHO in 2004 occurred in sub-Saharan Africa, these numbers present a misleading picture of the global cholera burden. *V. cholerae* infects persons in many developing countries, with the highest rates in Asia, but many Asian countries do not report their cases because of the effects on trade and travel, however

unwarranted. The true burden is probably several million cases in Asia and Africa, with fewer cases in Latin America. Assuming a case fatality rate of 4 percent (on the basis of treated cases), annual mortality of at least 40,000 to 100,000 is probable, and even this may be an underestimation: since many patients die before reaching a health care facility, the true number of deaths may be much higher.

In the 21st century, we know a great deal about cholera — its ecology, transmission patterns through contaminated water, and pathophysiology.³ Simple, inexpensive rehydration treatment is nearly 100 percent successful, and safe oral vaccines can prevent most



African Countries Reporting Outbreaks of Cholera or Acute Watery Diarrhea to the World Health Organization between 2003 and 2006.

cases. Yet cholera epidemics and deaths still occur. Strangely, the panic that frequently ensues does not seem to have prompted a sense of urgency among policymakers or funding agencies. How does one explain this disconnect?

First, cholera epidemics affect the poorest people in the poorest countries — those with no political voice. Second, therapy with intravenous and oral rehydration solution (ORS) plus antibiotics (e.g., doxycycline for sensitive strains) is inexpensive and highly effective, so there is little need for additional research funds to find a cure. Since cholera affects both adults and children, it generally escapes the attention of advocates for child survival. And many countries do not report their cases, nor do national authorities admit to having a problem or raise it as a priority. Finally, many policymakers have decided that improving

water and sanitation is the intervention of choice, but such improvements have not reached the groups at highest risk and will not reach them anytime soon, especially in countries such as Angola, where civil strife has prevented infrastructure development.

So, is there hope for controlling cholera? Our experience in Bangladesh, where infection is common (the annual case rate exceeds 2 per 1000 population) but deaths from cholera are unusual, provides considerable reason for optimism.

Cholera is easily treatable with aggressive rehydration therapy to restore circulating blood volume and antibiotics to shorten the course of illness and reduce the volume of fluid loss from the stool. At the hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh, we annually treat more than 110,000

patients who have diarrhea. In 2005, among the 2216 patients in our sample surveillance system, 682 (31 percent) were infected with *V. cholerae* O1 or O139, but none of them died; we estimated that there were 34,100 patients with cholera that year. Sometimes, during the epidemic season, the treatment ward must be extended into the parking lot, with tents to accommodate more than 500 patients per day. Patients, many of whom are in shock, with no detectable blood pressure or pulse on arrival, are immediately rehydrated and later given antibiotics. Within one or two days, they leave the hospital recovered and return to full productivity. The average cost for this lifesaving treatment is less than \$15 per patient.

In addition to the intravenous fluids used to rehydrate severely dehydrated patients, hydration is maintained with rice-based ORS to offset ongoing stool losses. Less severely dehydrated patients are rehydrated and treated with the same ORS, which was found to reduce purging by about 30 percent, as compared with glucose solutions. About 15 to 20 percent of our patients had severe, life-threatening dehydration and were likely to die from hypovolemic shock without treatment. Treatment for severe dehydration must be one of the most cost-effective health interventions available. Thanks to the training and deployment of government and non-governmental providers, case management for diarrhea is available throughout most of Bangladesh.

Effective management of cholera outbreaks requires anticipation of the natural seasonality of cholera and the resulting epidemic curve, which are largely determined by ecologic and climatic factors. Tracking cholera's seasonality with sentinel surveillance allows the



The Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh, during the Recent Diarrhea Season in Dhaka, 2006.

The hospital ward was extended into the parking lot with a temporary tarpaulin and bamboo structure to provide care for the large number of patients seeking treatment.

health care system to prepare for future epidemics by training staff and providing supplies for the next season. Cholera surveillance no longer requires an expert microbiology laboratory, since a rapid dipstick test is available.⁴

A sample of positive fecal samples should be sent to a reference laboratory for antibiotic-sensitivity testing, since the detection of antibiotic-resistant cholera is critical. Resistant strains are very common, and treatment protocols should be adjusted accordingly. At present, *V. cholerae* strains in Bangladesh are nearly all resistant to tetracycline, trimethoprim-sulfamethoxazole, and erythromycin; though the strains are still sensitive to ciprofloxacin, the minimal inhibitory concentration is increasing, and we are using azithromycin or multiple doses of ciprofloxacin. Patients with cholera recover even without an antibiotic if hydration is maintained, but antibiotics should be used for severely and moderately dehydrated patients to reduce purging and minimize the supply and logistical requirements for caring for a large patient population. During an epidemic in a resource-poor country, anti-

otics save lives. They should not be used prophylactically, however, since such use encourages the spread of resistant strains.

Cholera outbreaks should stimulate improvements in water quality and sanitation — moves that were critical for reducing cholera rates in Latin American cities where a sanitary infrastructure already existed. For less-developed countries, such improvements represent a long-term goal but not an immediate solution. Pilot studies have shown the effectiveness of point-of-use water purification and even of filtering water through a simple cloth filter to remove the plankton or other particles to which the bacteria attach, but these methods have not yet been scaled up into national programs.

The use of oral cholera vaccines (currently, only a killed whole-cell vaccine is available) is gaining recognition as a control strategy, and their effectiveness in the field is assisted greatly by indirect (herd) protection.⁵ Vaccine strategies work synergistically with safe water and sanitation to reduce risk: vaccinated persons are less likely to become infected and contaminate the environment, and safer water

improves vaccine effectiveness by reducing the bacterial inoculum consumed. As vaccine formulations become less expensive and more convenient to distribute, they will assume a greater role in reducing the risk of cholera in areas where it is endemic and among vulnerable refugee populations.

V. cholerae is part of the natural flora of the marine environment worldwide, but only 2 serogroups (O1 and O139) of the more than 200 that have been identified are responsible for cholera epidemics. Eliminating them from the environment is probably not an option, but by improving water supplies, we can interrupt their spread. Through surveillance, we can anticipate and prepare for outbreaks; with vaccines, we can immunize vulnerable populations; and with inexpensive treatments, we can save lives. These strategies are all within our abilities, if we make preparations and take cholera seriously.

Dr. David Sack reports holding a patent, with Cera Products, for an oral rehydration solution.

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