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Perspective

Antibiotics for Both Moderate and Severe Cholera

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The 2010 Haitian cholera outbreak has pressed local and international experts into rapid action against a disease that is new to many health care providers in Haiti. The World Health Organization (WHO) has time-tested management protocols for emerging cholera outbreaks. These protocols have been used by the Haitian government to fight an epidemic that is merely one of several recent tragedies in Haiti. The use of these protocols has allowed for a high standard of care in this complex and evolving medical landscape. But whereas the current WHO cholera-treatment protocol (www.who.int/mediacentre/factsheets/fs107/en/index.html) recommends antibiotics for only severe cases, the approach of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), recommends antibiotics for both severe and moderate cases.

Several antibiotics are effective in the treatment of cholera, including doxycycline, ciprofloxacin, and azithromycin, assuming that the cholera strain is sensitive. Currently, the epidemic strain in Haiti is susceptible to tetracycline (a proxy for doxycycline) and azithromycin but is resistant to nalidixic acid, sulfisoxazole, and trimethoprim–sulfamethoxazole. The WHO advocates giving antibiotics to patients with cholera only when their illness is judged to be "severe." This recommendation is interpreted to mean that only patients who present with "severe dehydration" (≥10% dehydration) should be given antibiotics. By contrast, the ICDDR,B recommends antibiotics for patients with cholera who have severe dehydration as well as for those with "some dehydration" (5 to 10%) who continue to pass large volumes of diarrheal stool during their treatment. These recommendations apply only to patients who have symptoms typical of cholera — that is, less than 24 hours of acute watery diarrhea with dehydration and usually vomiting. It is crucial in triage to rapidly assess dehydration, rule out alternative causes of diarrhea that are common in areas with poor sanitation and coexisting infections, and rehydrate aggressively according to the WHO protocols.

With effective antibiotic therapy, the purging rate is lessened by about 50%, the illness is shortened by about 50%, and the duration of excretion of *Vibrio cholerae* in the stool is shortened to 1 or 2 days. Without effective antibiotic therapy, patients continue to

excrete *V. cholerae* for 5 or more days and shed for a longer period at home.[1-3] If antibiotics are used, patients recover more quickly and require less rehydration fluid. Nursing care is lessened, and patients are able to leave the treatment center earlier, as demonstrated in a study that showed dramatic resolution of diarrhea at 24 hours with azithromycin.[1] This approach maximizes the effectiveness of limited resources while optimizing patient care.

Regarding transmission, rice-water stools contain 10^{11} to 10^{12} *V. cholerae* organisms per liter. An infectious dose is 10^5 to 10^8 organisms. These numbers might explain why 50% of household contacts of a patient who is the index case in Bangladesh develop diarrhea about 2 days after the index case occurs.[4] Although some of these household contacts may have been infected from the same source as the index patient, many others are likely to be true secondary cases. Direct data are not available to determine whether household contacts are protected when the index case is treated with antibiotics. However, given the liter volumes of diarrhea, antibiotics will decrease contamination in the household.

We do not, however, recommend antibiotic prophylaxis for household contacts because of the programmatic difficulty in restricting the use of such prophylaxis only to those persons in the immediate family who are at highest risk[5] and because doing so would almost certainly drive antibiotic resistance. Since families of patients with cholera are at high risk for cholera themselves, they need targeted education about safe water and sanitation, appropriate home use of oral rehydration solution, and information about the availability of treatment facilities in case illness does occur.

Some may argue that emphasizing the importance of antibiotic therapy may lead to the misguided belief that this is the most important component in the overall management of patients with cholera. With careful training in instituting appropriate and aggressive rehydration followed by effective antibiotic therapy, this misunderstanding need not occur.

A practical reason for hesitancy regarding administering antibiotics to patients with cholera relates to the severe vomiting that usually accompanies infection. Vomiting generally stops within a few hours after patients are rehydrated; thus, the administration of the antibiotic should be delayed until the patient is able to take food and drink without vomiting. Doxycycline can be associated with nausea and should be taken with food and plenty of fluids.

In summary, the use of antibiotics is an urgent issue for all stakeholders, because effective antibiotic therapy shortens the duration of illness and reduces the shedding of thousands of infectious doses. Our goal is to promote more effective care for large numbers of patients with cholera while maximizing limited resources to keep patients who are discharged early from dying, reduce the number of repeat hospital admissions, and limit at-home shedding of *V. cholerae*. To achieve these aims, we believe that patients with moderate and severe cholera should be treated with antibiotics — especially in Haiti, and especially now.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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