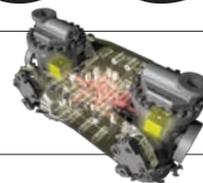


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About 200,000 people in Haiti have been sickened by cholera since the outbreak began in October.

PUBLIC HEALTH

Cholera vaccine plan splits experts

Opinion is divided over how to tackle the disease in Haiti.

BY DAVID CYRANOSKI, PORT-AU-PRINCE

Rarely heard in Haiti before October, 'cholera' is now an insult that children fling at one another in the teeming camps that still house more than a million people displaced by last January's devastating earthquake. Graffiti blames the disease on either the current administration — now in a contested election crisis — or the United Nations. The disease is as much a fixture in people's lives as the endless piles of rubble that remain uncleared a year after the quake.

Last week, as the country remembered the 230,000 people killed in the disaster, officials of international health agencies fine-tuned their

recommendations for moving forwards with a large-scale cholera-vaccination programme. It is a controversial idea that, just months ago, with little vaccine available and the epidemic spreading rapidly, was shunned as impractical and probably ineffectual (see *Nature* **468**, 483–484; 2010). Now, with emergency care centres in place, at least in the most heavily populated areas, health officials can finally look ahead and think about how a vaccination programme might combat a disease that has become entrenched in the country.

However, *Nature's* interviews with key partners in the proposed vaccination effort reveal significant disputes on how to proceed. Most experts in the international community

recommend a limited pilot project that would determine whether to scale up and how to use cholera vaccines in future outbreaks elsewhere. The Haitian government, caught in a febrile political environment and fearful that those denied vaccination might feel resentful, is demanding immediate, broad coverage.

With no recent exposure to cholera, Haiti's population lacks natural immunity and the disease has spread quickly. Roughly 3,800 have died, with another 189,000 falling ill, since 21 October, when cholera was first recognized as the culprit. At the end of October, a local medical aid agency, GHESKIO, supported by the UN Children's Fund (UNICEF), proposed vaccinating children under five living in two slums that have not yet reported large outbreaks. "There are 200,000 people without any toilets. They collect it and dump it in the sea," says Jean-Claude Mubalama, UNICEF's chief of health in Haiti for the past five years. "If cholera arrives there, it will be very bad."

The Haitian ministry of health (MSPP) and the World Health Organization (WHO) rejected the proposal, pointing out that not enough vaccine was available. They also feared that vaccination would foster a false sense of security, causing people to relax sanitary measures; and that it would take resources away from treating the sick, or from vaccine drives against measles and other diseases. "The voice of reason was to focus on saving lives," says Jon Andrus, deputy director of the Pan American Health Organization (PAHO), the WHO's regional office. "I had driven around Port-au-Prince and seen dead bodies in the street."

In December, however, an expert committee convened by the WHO decided that vaccination should be tried, partly because they had located extra sources of the only WHO-approved vaccine, Dukoral, an expensive two-dose vaccine made by Crucell, based in Leiden, the Netherlands. On 13 January, the expert committee, including representatives from the WHO, the US Centers for Disease Control and Prevention, the US National Institutes of Health (NIH), UNICEF, the US National Vaccine Program Office and others, held a teleconference to fine-tune a vaccination plan that could form the basis of a more detailed WHO-coordinated campaign strategy. The committee is recommending a pilot project using the currently available 250,000–300,000 doses of Dukoral, and the creation of a stockpile of the vaccine for the future. ▶

► The vaccination effort “can’t be done nationwide and it won’t have a major public-health impact”, says Andrus, but it could reveal just how effective the vaccine would be in a mass immunization of a population already widely affected by cholera. Dukoral has not been used on such a scale before, although studies of thousands of people have shown it to be about 80% effective. The committee has not worked out where the campaign would be focused. “You can find areas where cholera is endemic, and that may give you a targeted population where it may have a larger impact,” suggests Médecins Sans Frontières epidemiologist Kate Alberti.

“The bacterium won’t go away. It has established itself.”

The campaign could also help to reach the country’s remote rural populations, which have a higher mortality rate. Although vaccine drives in Africa and elsewhere have faced resistance, Haitian people are eager to be vaccinated, says François Lacapère, a vaccine expert for PAHO/WHO in Haiti. Yet many Haitians are also sceptical of aid agencies’ motives. Suggestions that foreigners accidentally introduced the disease (see ‘How did the outbreak begin?’) have given rise to unfounded rumours. Some people living in a camp that was once the Petionville golf course in Port-au-Prince, for example, make completely unsubstantiated claims that they have seen UN staff poisoning reservoirs in an attempt to further debilitate Haiti so that international powers can take over.

Even if the programme can win enough trust, using the world’s entire stockpile of doses would still leave most Haitians without vaccine — a controversial prospect for the beleaguered government. Jean Ronald Cadet, the MSPSP’s vaccination programme manager, says the country is “90%” ready to go ahead with a campaign — but not on the small scale the WHO-convened expert group envisages.

Asked about the small pilot project proposed by the group, Cadet says “No way,” shaking his head. He insists that Haiti would only consider starting to vaccinate with more than 1 million doses, with a goal of eventually reaching 6 million people. “It would depend on the pressure that the international community can put on manufacturers.” Who would pay for the doses? “The international community,” he says. “They brought us cholera, they have to take responsibility for taking care of it.”

But mass vaccination of millions of people would necessitate much more vaccine production. About 1 million doses exist of another vaccine, Shanchol, which might be approved for use by the WHO by March (it is already approved for use in India). If production of both vaccines went into overdrive, Lacapère estimates that about 5 million doses could be prepared annually. This availability would be dependent on an advance-purchase decision, and with a six-month lag time to delivery.

Epidemiologist Renaud Piarroux of the University of the Mediterranean in Marseilles, France, says that if vaccination is going to be tried, it should be done on a large scale. “I think it can be helpful, but it should be given to

millions of people in order to expect a notable effect,” he says. But he doesn’t see a large campaign as practical. “This will cost a lot and will require time to get a sufficient number of doses. I would prefer this money be used to improve water-supply networks and to reinforce sanitation activities,” he adds. In an unpublished paper, Piarroux presents data on a large cholera outbreak in Darfur, Sudan, that happened just two years after a mass-vaccination programme, suggesting that any coverage might be of limited duration.

Others hope for a more aggressive approach. Matthew Waldor, an infectious-disease expert at Harvard Medical School in Boston, Massachusetts, says public-health officials should consider trying Peru-15, a live attenuated vaccine being developed by a consortium including Harvard Medical School and the NIH. Peru-15 is not yet in phase III trials, but has been proved safe and effective in thousands of patients, Waldor says.

Whatever approach is tried, one thing is certain: cholera is there to stay. It is likely that the bacteria now have a stronghold in Haiti’s water, says Alberti. “Then you have a constant transmission between humans and the aquatic environment.” With poor sanitation, little access to clean water and difficulties in reaching people to treat them — not least due to gang warfare in the slums — the country

can expect repeated outbreaks, Alberti says.

Andrus agrees: “The bacterium won’t go away. It has established itself.” ■

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Haiti’s cholera
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CHOLERA SOURCE

How did the outbreak begin?



In October 2010, rumours quickly spread in the Haitian press that a Nepalese United Nations peacekeeping base was to blame for bringing cholera to the country. An Associated Press report of excrement from the base being dumped in the Artibonite river fuelled the controversy. On 1 November, the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, reported genetic analyses suggesting the strain was from southeast Asia, not the one more commonly seen in Latin America. On 7 December, epidemiologist Renaud Piarroux of the University of the Mediterranean in Marseilles, France, concluded in a report for the French foreign ministry that the cases originated from near the Nepalese peacekeeping base. “I am certain that it started only a few days after a battalion of soldiers came from Katmandu, a city which was subjected to a cholera outbreak at that time,” he says.

On 9 December, a more detailed genetic

analysis, led by Matthew Waldor of Harvard Medical School in Boston, Massachusetts, upheld the CDC’s conclusions (C. S. Chin *et al. N. Engl. J. Med.* **364**, 33–42; 2011). The analysis, based on samples from Haiti and strains from Latin America and Bangladesh, cannot definitively confirm a Nepalese source, says Waldor. The strain could have arrived with other south Asians, or from west

Africa. “But the Nepalese hypothesis is fairly convincing,” he says.

The UN initially questioned whether it was important to pin down the origin of the cholera. But on 6 January, it appointed a committee of four scientists to investigate the claims. Waldor says that a definitive answer could come from sequencing about 20 strains — from Haiti, Nepal and West Africa, as well as more recent strains from Latin America and other south Asian countries — and by checking blood samples from Nepalese troops in Haiti for antibodies. “The truth is important,” Waldor says, because it could help to understand the risk of cholera transmission from peacekeepers in the future.

Piarroux says that the international community’s responsibility for the epidemic should fuel efforts to eliminate the disease. “We are responsible for importing cholera — we have to fight against it with an iron will.” **D.C.**