Global polio campaign doomed to fail, experts warn

Five children in a secluded Amish village in the US contracted vaccine-derived polio, scientists announced in October, baffling epidemiologists about the infection's origin. But some experts say the episode is a clear warning that the global polio eradication campaign is unrealistic.

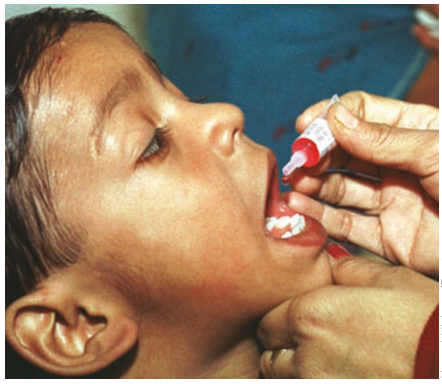
As the World Health Organization (WHO) and others focus on preventing wild polio, they say, virus shed by vaccinated individuals could continue to circulate in the population.

An eight-month-old baby in the village in central Minnesota, initially hospitalized with diarrhea and known to be immunocompromised, first contracted and transmitted the virus. But the virus itself appears to be from an oral polio vaccine administered two years ago, more than a year before the infected child was born, says Olen Kew, a virologist at the US Centers for Disease Control and Prevention.

That suggests that the virus came from someone else, perhaps in a developing country without adequate therapies to treat an immune disorder. "Someone else is exposed; it seems unlikely that that virus would have been circulating that long in the Amish community," says Kew.

Most people who contract polio can rid themselves of infection within eight weeks, but immunocompromised individuals can retain and spread the infection, in some cases for years. Nearly 30 chronic carriers have been reported since 1962, but the Minnesota child is the first known to put a virus into circulation. She transmitted the virus to the other children because they were not vaccinated, in accord with Amish belief.

Critics say the event points to a much deeper problem in the WHO's eradication scheme.



Kamal Kishore/Reuters

Drop shot: The oral polio vaccine leaves the door open for future outbreaks.

"Now we have here, in a country where almost everyone is immunized, these viruses are circulating. And they're circulating much more extensively than anyone realizes, I would guess," says Vincent Racaniello, a Columbia University microbiologist.

Since the Americas were declared polio free in 1994, surveillance has slipped, making it difficult to assess how much poliovirus is circulating in the population. The US stopped vaccinating children with the oral polio vaccine in 2000, switching to an inactivated vaccine that confers immunity in the bloodstream, but not in the intestines or throat. Those immunized with this vaccine could potentially pick up the live, weakened strains excreted by children who receive the oral vaccine and function as carriers of the virus.

In those vaccinated with the oral vaccine—particularly in immunocompromised individuals—the virus can also mutate and recover its ability to cause paralysis. Infected feces could then trigger an outbreak in areas with low vaccination coverage. Since 2001, there have been 12 such outbreaks, costing the WHO nearly $100 million.

The WHO's plan to eradicate polio relies heavily on the oral vaccine, in part because it is cheap and easy to administer in resource-poor countries. The plan calls for all countries to simultaneously stop using the oral vaccine three years after wild polio transmission has been interrupted worldwide. But that goal has proven elusive: the deadline has been moved back three times since 2000.

Even if the WHO reaches its goal, a small number of undetected but immunocompromised individuals could silently incubate and spread polio, leaving the door open to subsequent outbreaks, experts note.

"If you have an immunodeficient person today and we stop vaccination tomorrow, then 15 years from now, everybody younger than 15 years old would be unvaccinated, and they would be unprotected," concedes Harry Hull, Minnesota's state epidemiologist, who helped design the WHO's blueprint for eradication.

Experts say that before the WHO reaches its goal, it will need to stockpile and safeguard vaccine and seed stocks of the virus, strengthen surveillance, protect against the accidental or intentional release of polio into the environment, identify chronic carriers and develop antiviral drugs that could rid their bodies of infection.

"We do know that an unplanned strategy would be catastrophic," says Kew says. "We've got some hard, hard work ahead."

Bruce Diamond, New York

Europe's restrictive rules strangling clinical research

The number of large clinical trials across Europe is drastically down a year after new rules on clinical research went into effect, according to a study presented in early November. The rules, meant to promote Europe-wide research, might instead force scientists to limit their trials to a single country, experts caution.

National regulations on clinical research vary widely across Europe. The European Union Clinical Trials Directive, launched in May 2004, was intended to simplify the rules and establish a Europe-wide model for both academic and industry-sponsored trials (*Nat. Med.* 9, 1336; 2003). But since its launch, scientists have warned that the onerous new requirements and added paperwork and costs would hamper trials by academic scientists.

The number of Europe-wide trials submitted for research grants or ethical review has dropped 30–50% since the directive's launch, according to data from research institutes and funding agencies. The proportion of noncommercial trials has also declined from 40% to 14%. "Overall, Europe is witnessing a very negative consequence of the European directive," says Jaap Verweij, an oncologist at Erasmus University in Rotterdam.

The researchers chose eight countries, including the UK, France and Italy, based on their capacity to fund academic research, particularly in cancer, and the size of their population. The researchers assessed how each nation revised its laws to comply with the rules.

Although the directive harmonized some matters such as the time frame for authorizing new trials, it created significant differences in the ethical review of trials, sponsorship and liability issues, says lead investigator Markus Hartmann. Only four countries thus far have added express provisions for noncommercial trials into their legislation and of those, only Italy and Belgium are fully complying with the directive's requirements for academic research. Hartmann presented the data at the European Cancer Conference in Paris in November.

Ultimately, experts say, the requirements might put an end to Europe-wide multicenter trials and promote more national research projects. "The detail of the directive is being interpreted by each country in a slightly different way, which is especially frustrating for the lone academic investigator wishing to launch a multicenter trial," says Norman Williams, a clinical trials coordinator at University College London.

Xavier Bosch, Barcelona