EDITORIAL

nature medicine

The persistence of polio

Despite intense efforts to rid the world of poliovirus, it continues to persevere. Given the serious limitations of the existing vaccines, the feasibility of eradication must be reassessed.

On 12 January, the World Health Organization (WHO) announced that India, where polio is endemic, has not had a new case for one year. If two more years pass without new cases, according to WHO policy India can be officially declared free of polio. But the virus has still never been eliminated from Pakistan, Afghanistan or Nigeria, and outbreaks continue to reemerge in countries where viral transmission had previously been disrupted, suggesting that global eradication may prove elusive.

Current polio eradication efforts are modeled on the earlier success with smallpox, which was wiped out worldwide in 1977. That effort cost $300 million and took approximately ten years, and it proved to world health agencies that eradication of infectious disease is possible. In 1988, the WHO, Rotary International, the US Centers for Disease Control and Prevention, and the United Nations Children's Fund formed the Global Polio Eradication Initiative (GPEI), which aimed to rid the world of polio by the year 2000. Although this campaign has been successful in reducing the number of polio cases worldwide by 99%, the virus has not yet been wiped out, despite an expenditure thus far of $9.5 billion.

The countries that still struggle with polio are, not surprisingly, those with political and social climates that make it difficult for eradication efforts to operate effectively. But there is a more fundamental issue with the current strategy for poliovirus eradication. GPEI's working hypothesis in 1988 was that after new polio cases were halted, the virus would be unlikely to reemerge, and vaccination efforts—and their associated costs—could cease. But, more recently, scientists have come to appreciate that the strategy of halting vaccination may be unrealistic given current poliovirus vaccine technologies (*Science* **312**, 852–854, 2006).

Inactivated polio vaccine (IPV) is used in developed countries, but it is expensive to produce and requires cold storage and intramuscular administration. Because these requirements are impractical in the developing world, a live attenuated oral polio vaccine (OPV) is used instead. OPV is cheaper to make than IPV, does not require cold storage and can be delivered orally by workers who do not require specialized training. Although the smallpox vaccine required only one dose to achieve full protection, as many as seven doses are needed for OPV; incomplete vaccine coverage of the population has been responsible for some of the polio outbreaks in countries that had previously been polio free.

Alarmingly, OPV-derived viruses may, in rare cases, mutate or recombine with other enteroviruses in immunized individuals and reemerge in a virulent form to cause disease outbreaks in those who have not been immunized against poliovirus. This first happened in 2000 in Hispaniola, where there were 22 cases of acute flaccid paralysis linked to OPV-derived viral strains, and in other parts of the world in subsequent years. Given the threat of such OPV-derived outbreaks, it seems unlikely that immunization can ever be safely abandoned. A switch to IPV would eliminate the risk of vaccine-derived outbreaks, but its use is thus far not practical, and its efficacy at blocking disease spread is untested in the tropical climates that characterize much of the developing world.

The WHO is therefore investigating ways to make the IPV vaccine cheaper and easier for developing countries to use, such as using much lower vaccine doses than in the developed world, studying different adjuvants to augment immune responses, and examining alternative methods of administration. In addition, the WHO is examining whether the OPV seed strain could be used to manufacture IPV, which would allow it to be produced safely within developing countries. Nevertheless, until these efforts bear fruit, vaccination using OPV will continue to be necessary.

But will funders continue to support current vaccination strategies? The projected GPEI budget for 2012–2013 is $2.23 billion, which would fund personnel, environmental- and patient-surveillance efforts, and the cost of the OPV vaccine. However, with a current funding gap of $1 billion, some crucial components of the eradication effort may slip through the cracks unless additional funders can be found.

GPEI funding comes from governments, foundations and nongovernmental organizations. The countries that contribute the largest percentage of the current GPEI budget are India and the US, whereas governments in China, the Middle East, Southeast Asia and Central and South America so far have not provided funds. China, which shares a border with Pakistan, reported ten new polio cases just last year. The viral strain found in the Chinese cases was highly related to one circulating in Pakistan. Therefore, China in particular should take more initiative to ensure that eradication efforts will succeed.

Margaret Chan, director-general of the WHO, has stated that worldwide polio eradication is a "top operational priority" for her organization. But without global recognition of the need for a long-term commitment to immunization strategies, death and suffering from polio are likely to persist.

© 2012 Nature America, Inc. All rights reserved.
npg