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THE STATE OF POLIO VACCINATION IN THE WORLD: THE CASE FOR CONTINUING ROUTINE VACCINATION

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This article reviews the literature concerning polio vaccination and uses that information to evaluate the World Health Organization's announced plans to end polio vaccination early in the 21st century. The safe elimination of polio vaccination would require the elimination of all polio cases, including paralytic cases, mild, nonparalytic cases, and vaccine-associated cases; proof that polio does not have any nonhuman alternative host; proof that no one alive can still shed the poliovirus; proof that no poliovirus persists in the environment; and proof that no live poliovirus, either the wild type or the vaccine strain, exists in medical or terrorist hands. Because it does not seem possible to ensure that ending vaccination against polio would be safe, and given the fact the polio is a terrible and untreatable disease, it would seem prudent to continue polio vaccination for the foreseeable future.

Keywords eradication, IPV, OPV, WHO

One of the greatest achievements of the World Health Organization (WHO) was the eradication of smallpox, the disease that is generally recognized as being the greatest scourge of humankind. The development of the smallpox vaccine by Dr. Edward Jenner in 1796 allowed medicine to begin its assault on this deeply feared infectious disease.[1] In 1958 when WHO began a campaign to eliminate smallpox from the world, 250,000 cases were still being reported annually. WHO's diligent work around the world resulted in the total elimination of smallpox by 1980.[2] Because smallpox had no hosts other than humans, eliminating smallpox vaccination was possible. Its elimination was a further benefit to humanity because of the economic benefits of not having to produce and administer the vaccine and because of the absence of the rare complications resulting from the smallpox vaccine. The Centers for Disease

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Control (CDC) made a compilation of the adverse effects of this vaccine in 1968 and found that the frequencies of adverse effects per million primary vaccinated persons were as follows: vaccinia gangrenosa, 0.9; eczema vaccinatum, 10.4; generalized vaccinia, 23.4; vaccinal lesions resulting from accidental implantation of virus, 25.4; postvaccinal encephalitis, 2.9; other complication, 11.8; death, 1.0.[3] In recent years, WHO has been attempting to duplicate its remarkable accomplishment with smallpox by announcing its goal to eliminate polio worldwide by early in the 21st century.[4,5]

Therefore, we have reviewed the available literature concerning polio vaccination and evaluated its implications on WHO's goal of eliminating the need for polio vaccination in the near future. We are writing this paper in an attempt to examine areas of potential concern raised by WHO's plan. We hope to stimulate input from a wide variety of sources within the medical and scientific communities that will allow all available expertise to be brought to bear on these crucial and complex issues.

The development in 1949 of the technique of supporting polio virus growth by using rhesus monkey kidney cell tissue cultures made the development of polio vaccines possible and resulted in the awarding of the Nobel Prize in 1954 to J. F. Enders, F. C. Robbins, and T. H. Weller.[6] Before the introduction of the inactivated polio vaccine (IPV) by Salk in 1953,[7,8] the oral polio vaccine (OPV) by Koprowski and colleagues in 1952,[9] and the subsequent development of the Sabin vaccine in 1956,[10] polio was a much-feared disease. It is estimated that before the development of effective vaccines against it, polio which was recognized by the ancient Egyptians, Greeks, and Romans, had killed or crippled millions of people.

PROBLEMS WITH POLIO VACCINATION

The introduction of the polio vaccines changed all of this but not without a price. The history of the use of polio vaccines is marked by several unfortunate incidents, including the Cutter Laboratory catastrophe in 1955, in which the polio virus was inadequately inactivated in seven lots of vaccine and was then found to have caused paralytic disease in 204 people. Of these, 79 were vaccinated children, 105 were family members who had contact with vaccinated children, and 20 were community members who had contact with vaccinated children.[11] The licensing of monovalent OPV in 1960 and trivalent OPV in 1963, and the subsequent 1964 recommendation by the Committee on Infectious Diseases of the American Academy of Pediatrics that OPV replace IPV was followed by even more unintended adverse outcomes. These included the development of polio in unvaccinated people coming into contact with

those recently vaccinated, the exposure of a number of people to unintended viral contaminants, and the development of paralytic polio in some vaccine recipients.

It is well known that the recipients of OPV shed large amounts of the virus in their feces. In fact, it was hoped that fecal spread of vaccine-strain viruses would be a beneficial effect of OPV vaccination in that it was anticipated that the fecal spread of the attenuated vaccine strain would expose and thus protect unvaccinated individuals in the population. However, reports soon began to appear in the literature noting that some of those in contact with OPV recipients, especially older family members; developed cases of paralytic polio. This unfortunate side effect of the OPV has come to be called "contact polio."[12] Unvaccinated individuals develop contact polio after exposure to individuals vaccinated with OPV who shed virus that begins to mutate back into the virulent form. The mechanism of attenuation of the neurovirulence and that of the tendency toward reversion to neurovirulence has been described in a review by Racaniello.[13]

Additionally, live polio vaccine has been inadvertently contaminated by other viruses. The most notorious of these was Simian Virus 40, which is known to cause malignant transformation in human tissue culture cells.[14,15] Live polio vaccine has also been contaminated by various monkey viruses, bacteriophages, and endotoxins.[16–19]

In addition, OPV on occasion causes paralytic polio in vaccine recipients, especially in immunologically compromised children.[4] Children are commonly given the live vaccine at such an early age that it has not yet been recognized that they are immunocompromised. It has been estimated that each year in the United States alone there are 5 to 10 cases of vaccine-associated polio.[4] The United States government recognizes this inadvertent complication of OPV and provides compensation for such individuals through the Vaccine Compensation Act (VCA), which is administered through the United States Claims Court. As of January 31, 1998, the VCA had received a total of 5221 petitions for compensation to individuals thought to have been injured by childhood vaccines. These petitions resulted in 4349 claims' being adjudicated; of those, 2605 awards totaling 860.1 million dollars were made by the court. Of the total number of claims filed, OPV and IPV have been implicated in 10% of them.[20]

Despite all of the problems with polio vaccination, there can be no doubt that over all, polio vaccination has done far more good than harm. It has been estimated that between 1965 and 1984, the use of polio vaccine has prevented 5 million cases of paralytic polio.[21] The American Academy of Pediatrics has recognized that most of the current problems involving polio vaccination are associated with the use of

the live vaccine; therefore, they have begun to recommend a return to the use of enhanced-potency IPV, which produces a humeral antibody response which has been shown to be superior to that of OPV.[22,23]

WORK TO BE DONE BEFORE SAFELY ENDING POLIO VACCINATION

WHO has worked diligently in its attempt to eliminate polio worldwide. According to WHO statistics, the last case of wild-type polio in North America occurred in 1979.[4] WHO hopes to eliminate the last case of wild-type polio in the world by the early years of this century. It will then certify the world polio-free and subsequently eliminate polio vaccination.[4]

The elimination of polio vaccination in the United States alone would save an estimated $230 million per year and would also prevent the 5 to 10 cases of vaccine-associated polio that occur each year.[4] However, there are numerous reasons to be extremely cautious concerning WHO's plan.

First, the elimination of the wild type of polio worldwide by early in the 21st century is a goal that seems unlikely to be achieved. Despite the efforts of WHO, there are places where the polio virus still persists. A recent study done in Nigeria found the wild-type polio virus in 7 of 22 sewage samples collected from 11 locations. The authors concluded that the polio immunization campaign has not been successful in Nigeria.[24] This research illustrates the difficulties WHO has encountered and will continue to encounter in its attempts to eradicate the polio virus in places plagued by civil strife.

Second, despite WHO's claims that there have been no cases of wild-type polio in North America since 1979, there have been a number of reports that polio still exists in unvaccinated, susceptible individuals. For example, molecular detection has demonstrated the importation of the type 3 wild polio virus into Canada from the Netherlands in1993.[25,26] This discovery reveals that even in the more stable regions of the world, segments of the population may refuse all vaccines because of religious objections. These isolated groups and individuals have the potential to harbor the virus even now.

Third, unlike smallpox, polio is not easy to recognize; 95% of cases of poliomyelitis are unapparent or "minor" infections that are not easily diagnosed,[27] so there may be many unrecognized cases of polio worldwide.

Fourth, it cannot be denied that many cases of paralytic polio caused by the vaccine strain have been documented in the United States and the victims have been compensated by the VCA. There is good reason to believe that there are more such cases worldwide, most of them unreported. It is estimated that the rate of development of polio after receiving the

live polio vaccine is 0.16 per million for type 1, 0.02 per million for type 2, and 0.4 per million for type 3.[27] The CDC reports 133 confirmed cases of paralytic polio in the United States between 1980 and 1994. Of these, 125 cases were associated with OPV administration, 6 cases were classified as imported, and 2 cases were classified as indeterminate. Of the 125 cases that were associated with OPV administration, 49 occurred in immunologically normal recipients, 23 occurred in immunologically compromised recipients, 46 occurred in immunologically normal people who had contact with vaccine recipients, and 7 occurred in immunologically compromised people who had contact with vaccine recipients.[28] It is clear from the CDC data that the overall estimated risk for developing paralytic polio has remained relatively constant over the past 15 years.

Fifth, it is well documented in the medical literature that vaccine recipients shed large amounts of polio virus in their feces. Much of this virus has virulent potential. If WHO stops vaccinating, many children who have been recently vaccinated with OPV will be shedding large amounts of potentially paralytic polio viruses against which those born after the termination of the vaccination program will have no immunity. This brings up another issue: for how long after being vaccinated with a live polio vaccine does a person continue to shed polio virus in feces. The literature reports that immunologically normal persons can spread virulent polio virus in their feces for as long as 8 years after being vaccinated.[29] Another study, published in the New England Journal of Medicine, reports on a person who has been shedding neurovirulent revertant virus for 16 years.[30] Viral replication lasting as long as 7 years has been demonstrated by molecular studies of a patient with an immunodeficiency syndrome who developed vaccine-associated paralytic poliomyelitis.[31] Also, the issue is not how long after being vaccinated the average person may shed live polio virus in the feces. Rather, the question is, out of the 6 billion people on this planet, many of whom have had polio or have been vaccinated with OPV, how long will *one* of them continue to shed virulent polio virus. It also must be kept in mind that it is not clear whether either OPV or IPV confers lifelong immunity.[32] Therefore, the aged population maybe at potential risk should a large-scale epidemic breakout.

Sixth, it is not clear whether polio has an alternative, nonhuman host. It should be remembered that the polio vaccine is grown in monkey cells. It has been shown that primate species are capable of contracting the disease, as evidenced by the original studies conducted by Sabin to test the efficacy of his live polio vaccine.[10] Additionally, the polio virus grows in the intestines of humans. Therefore, it is entirely possible that polio is capable of growing in or interacting with bacteria

or other microorganisms found in the gut. This possibility is supported by the study of Bottiger and Herrstrom, who reported high titers of poliovirus in the sewers of Sweden, based on studies conducted at regular intervals between 1967 and 1990, despite the fact that indigenous polio ceased in Sweden in 1962, after 5 years of using killed polio vaccine. The virus isolates obtained were characterized by the use of monoclonal antibodies differentiating between vaccine and naturally occurring strains. Polioviruses of both kinds were isolated throughout the period.[33] Additionally, poliovirus has been shown to be capable of being spread by milk and to be carried by various species of biting insects, by some species of flies, including the common housefly, and by cockroaches.[34] In fact, the poliovirus has been shown to survive in the guts of feces-eating flies for about 2 weeks, and there is evidence that the virus may undergo multiplication in the guts of these flies.[34] Of course, if polio does indeed have alternative nonhuman hosts, the elimination of routine polio vaccination would be unwise.

Seventh, another potential problem to consider if polio vaccination is halted is that there is a possible threat that poliovirus could be used as an agent in biological warfare. This would be true even if polio were completely eliminated from the entire world. This will always be a possibility because the poliovirus genome is small (7.5 kb), its RNA sequence is known, and its complimentary DNA is infectious. Therefore, it would be possible for a terrorist to synthesize a new stock.[35] Additionally, based upon the fact that OPV vaccine recipients shed revertant neurovirulent strains of polio after vaccination, any clinic, doctor, or terrorist who has a vial of OPV vaccine could start a large-scale epidemic in a postvaccinational world—intentionally or inadvertently—by simply administering the vaccine to an unvaccinated person. It would be impossible for WHO to account for every single vial of OPV vaccine in the world.

CONCLUSIONS

It seems clear that WHO's plans are at best premature. The safe institution of such a recommendation would require: (1) the elimination of all wild-type cases in the world, including mild, nonparalytic cases; (2) the worldwide elimination of all vaccine-related cases of polio; (3) verification that polio does not have any alternative nonhuman hosts; (4) demonstration that not one of the people on this planet is currently shedding or is capable of shedding the poliovirus; (5) proof that no poliovirus persists in sewage or in other environmental sources; and (6) assurance that all vials of OPV sequestered anywhere on this planet have been collected and destroyed.

It would be very difficult to prove that not a single person who has had polio in the past or who has been vaccinated against polio with the

live vaccine is capable of shedding the poliovirus. Therefore, it would seem prudent to continue to routinely vaccinate all individuals with killed polio vaccine until all the people who have had the disease or who have been vaccinated with live polio vaccine have died. Considering humans' rapidly increasing life spans, this interim waiting period, during which coverage with killed polio vaccine should be provided, might be 150 years or more. It should be kept in mind, too, that because the poliovirus is spread via the fecal route, a very small number of people who are shedding the virus are potentially capable of causing a rapid and widespread epidemic of the disease. The current state of medical knowledge does not include any treatment that can prevent the crippling paralysis the disease can cause. If precautionary criteria are met, it would also seem prudent to institute a well-developed protocol to be used if there were to be an outbreak of polio anywhere in the world. Such a protocol would undoubtably include the stockpiling of large amounts of polio vaccine to contain the epidemic.

In conclusion, it would seem wise that WHO table its plans to discontinue routine polio vaccination on a worldwide basis until and unless the appropriate scientific studies have been completed. Additionally, we recommend communication among members of the scientific and medical communities to discuss the potential implications of the dramatic steps WHO is contemplating. In the case of a disease that is as catastrophic as polio, it is far better to be safe than sorry.

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