Polio Immunization: Benefits and Risks

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There are epidemiological as well as legal risks to polio immunization. The physician should compare the risks of vaccination with the risks which attend nonvaccination. Another view of the incidence of paralysis following oral poliovaccine (OPV) shows that the risk is about 1.6 cases per 10^6 nonimmune children given OPV and that this rises to about ten cases per 10^6 nonimmune adults exposed to OPV. There is little evidence of reversion to virulence of the virus and it is proposed that susceptibility of vaccinees and contacts to OPV is genetic. The risk of contracting poliomyelitis from either vaccine or wild virus rises about tenfold from the age of about three years to about ten years and thereafter remains constant. The risk of vaccinating children must be balanced against a tenfold risk of vaccinating when older and against a very much higher risk of paralysis or death from a wild virus.

Present vaccination policies have virtually eliminated wild virus from the United States but have left many nonimmunes. The consequences of reintroduction of wild virus are examined, and the legal implications of genetic susceptibility are briefly discussed.

Since 1955, the use of the Salk injected poliovaccine (IPV) and Sabin oral poliovaccine (OPV) has reduced the number of cases of poliomyelitis from about 10 per 100,000 population to 0.01. The decision to use the poliovaccines for mass vaccination is irrevocable, in that failure to use them now would result eventually in epidemics. The use of the vaccines to immunize everyone does carry some risk of vaccine-induced disease; there are, however, several different ways of expressing this risk. If the vaccine is used in such a way that not all persons receive it, the risk of vaccine-associated cases is decreased but those not vaccinated are at increased risk from wild virus either imported or when met abroad. If a significant proportion of each age group is not vaccinated, the number without immunity in the population will continue to rise until, eventually, an epidemic will occur. Because some cases are attributed to the vaccine and because manufacturers have been sued, there are legal implications in the use of the poliovaccines.

In this paper, these aspects of poliovaccination are examined so that physicians and health care providers can be aware of the epidemiological risks and legal implications[1]: laws can be changed, responsibilities may be shirked, but the medical consequences of vaccine use may be inexorable.

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The risks accompanying vaccination are far less than the risks of immunizing only some of the population.

The Risks of Oral Poliovaccine (OPV)

The use of OPV involves two kinds of risk: some people may be peculiarly susceptible to vaccine strains and there is a risk of reversion from vaccine-type to wild-type strain. Reversion may occur during manufacture or in passage in vaccinees or contacts. The risk is usually calculated as the total of Vaccine Associated Cases (VAC) divided by the number of doses of vaccine distributed. Thus, Van Reken[1] quotes the current risk for vaccinees as 0.063 per 10^6 doses of trivalent OPV (TOPV) and for contacts as 0.193 per 10^6 administered doses. However, the figures for 1965 to 1972 of 0.08 vaccine cases per 10^6 doses would be more accurate, as vaccine was given only to children in this period.[2] The figure of $0.08/10^6$ is based on 205 million doses distributed, but in that eight-year period only about 28 million children were born and not all were given OPV. A more realistic view would express the rate as cases per 10^6 nonimmunes given the vaccine. Such a calculation excludes doses distributed but not given, doses inactivated before given, and doses given to those already immune, for whom, so far as we know, there was no risk. Many vaccinees acquire immunity as contacts before receiving OPV: almost all of the child contact cases occur in those under five years of age. For the period 1966 to 1973 in the United States about 70 percent of young children were given OPV with 16 vaccinee and 10 contact cases of poliomyelitis and probably seven cases in children with various immunologic deficiencies.[3] As most of the contacts were also vaccinees at another time, the risk was 1.6 cases per 10^6 vaccinated among children under five years of age, a risk 25 times greater than that quoted by Van Reken.[1]

For those over five years of age, most of the contact cases occurred in parents of vaccinee children; the risk for nonimmune adults can, therefore, be calculated. There are about two children in each family of two parents, but even if the parents are nonimmune, they will be exposed and gain immunity with the vaccination of the first child. The number of parents at risk will therefore be almost equal to the number of child vaccinees. A recent serosurvey in the United States[4] showed that about 90 percent of the 20 to 40-year age group was immune, so that the nonimmune parents totalled nearly 2×10^6 with 20 contact cases: a rate of 10.2 per 10^6. This is about eight times greater than for young children. The rate for adults may be an underestimate: not all parents may be infected, in some families there may be only one parent or only one parent may be at home when the child is excreting virus and there may be fewer nonimmunes than calculated.

That the rate for adults is higher than that for children, could be due to an increase in virulence of the vaccine virus during passage. There is, however, no epidemiologic evidence for increased virulence as there is, for instance, no clustering of contact cases. The degree of residual paralysis is similar to that in the Cutter Incident. Although it has been known that adults were more susceptible than children to paralysis by wild virus, until recently, an explanation has been lacking. The author has proposed that susceptibility to poliomyelitis is genetic and may be explained on the basis of a single locus with two populations of susceptibles, homozygotes and heterozygotes.[5] Homozygotes become susceptible by three years of age and constitute two percent of all children whereas heterozygotes become susceptible more slowly, reaching a maximum at ten years of age. Using the Hardy-Weinberg equation,* the heterozygotes should total 24 percent[5]; analysis of many epidemics shows about two percent of nonimmune children with paralysis and up to 26 (2 + 24) percent of nonimmune adults with paralysis.[6] About 13 times as many adults as children are susceptible to poliomyelitis unless protected by antibody. It is possible that children and adults who are susceptible to vaccine-associated poliomyelitis form a small subgroup of those genetically susceptible.

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*If p^+ is the gene for susceptibility to poliomyelitis and p^- is the gene for nonsusceptibility, the Hardy-Weinberg equation,

$$p^+p^+ + 2p^+p^- + p^-p^- = 100\%,$$

may be used if one of the populations is known, because $p^+ + p^- = 1$. If p^+ p^- is two percent then the heterozygotes (p^+p^-) must comprise 24 percent.

Paralysis Following Vaccination

Poliomyelitis-like paralysis may have many causes unconnected with poliovirus. For a clinical diagnosis of poliomyelitis, there must be residual paralysis; nonparalytic poliomyelitis caused by the vaccine is by definition not recorded or recognized. For the period 1966 to 1973, there were 18 recipient and 34 contact vaccine-associated cases (VAC) (excluding those with immune deficiencies) whose residual paralysis was recorded as minor, significant, or severe.[3] There was no statistically significant difference in the severity of paralysis when compared by age or vaccinee-contact status. Surprisingly, there is little difference when all the VACs are compared with the 272 cases of poliomyelitis caused by wild virus in the same period.[3] The percentages of residual minor, significant, and severe paralysis were 20 and 21 percent, 54 and 52 percent, and 26 and 17 percent, respectively, for VAC and wild virus cases; in addition, ten percent of the persons with wild virus infections died.

The Risk of Paralysis if One Is Not Vaccinated

The number of reported cases of paralytic poliomyelitis has fallen from 13,850 cases in 1955, before widespread use of the Salk vaccine,[2] to only three cases in the first nine months of 1975.[1] The original widespread use of the Sabin OPV led to a very large part of the United States population receiving OPV either as vaccinees or as contacts. There were two results: most persons became immune or received a boost to their previous immunity and, in some ways just as important, the spread of wild virus was dramatically reduced. The continued absence of poliomyelitis rests more with this absence of wild virulent virus than with the immune status of young children. Although wild virus is only rarely recovered from sewage, it is circulating, as occasional small outbreaks and isolated cases show.[7] Occasionally, wild virus may spread through a group of nonimmunes as in the Christian Science School in Connecticut in 1972.[8] Cases appeared in the football and rugby teams with nine cases among adolescents 12 to 17 years of age—a case rate of 24 percent, very close to the 26 percent predicted by the genetic theory.[5,6] Similar outbreaks and cases among those who do not accept immunization have occurred in Holland[6]* and also recently in Sweden.[9]

The unvaccinated therefore face a number of risks:

1. as a child contact, from OPV given to other children;
2. as a child exposed to wild virus;
3. as an adult contact when OPV is given to his own or other children;
4. as an adult when given OPV prior to travel to a country where poliomyelitis occurs;
5. as an adult receiving OPV as vaccinee or contact during a mass immunization program following cases of poliomyelitis;
6. as an adult exposed to wild virulent virus either in the United States or, if unvaccinated, when traveling abroad.

The probability of each of these risks is different. As shown above, the risk from OPV for a child is about $1.6/10$,[6] but as an adult it is about $10.2/10^6$; the risk from wild virus is about two percent at two years of age rising to 26 percent at age ten and above. Parents should consider the true risks; the risk of vaccination for the child or the later risk of exposure as an unvaccinated adult to either vaccine or wild virus.

Exposure to vaccine virus can be decreased. It might be possible for adult travelers to receive inactivated poliovaccine (Salk-type IPV). Adults who have neither children of their own nor nephews and nieces are at less risk as contacts. However, the risk of exposure to wild virus cannot be accurately forecast.

The Risk of Epidemics

Wild virus is circulating in many tropical countries and the reported cases of paralytic poliomyelitis represent a small fraction of those which actually occur. There were 329 cases of acute poliomyelitis reported from Nigeria for 1972,[10] but every year about 350 new cases of paralyzed children attend the orthopedic clinic of

*There is another outbreak in Holland at the moment! From April 15 to July 17, 1978, there have been 81 cases of poliomyelitis among the same religious group which does not accept vaccination. The outbreak is probably not yet over; 3 cases were confirmed on July 17. (Government announcement of July 17, 1978, printed by VRIJ NEDERLAND on July 18, 1978.

Table 1. Maximum Number of Those Susceptible to Wild Poliovirus in a US Town of 100,000 Persons

	Population by Age Groups (years)				
	0-2	3-9	10-39	40+	Total
Population[17]	5,000	12,000	47,000	36,000	100,000
With no immunity to Type 1 in 1971 survey[4]	25% 1,250	20% 2,400	8% 3,760	13% 4,680	12,090
Maximum number of cases if:					
1. 1 in 1,000 susceptible	1	2	4	5	12
2. genetically susceptible*	25	336	978	1,217	2,556
Maximum number of deaths**	3	20	147	406	576
* Genetically susceptible[5]	2%	14%	26%	26%	
** Case fatality rate[5]	10%	6%	15%	33%	

the University College Hospital, Ibadan.[11] Epidemics continue in Kenya despite the use of poliovaccines, and Metselaar has recently postulated that selection of virulent strains may be occurring in third world countries.[12] At least some cases of paralytic poliomyelitis in countries in which poliomyelitis has been almost eliminated occur when travellers bring with them poliovirus acquired abroad. In England and Wales in 1974, three of five polio victims acquired the disease in the Indian subcontinent.[13]

Wild virus is therefore constantly introduced into countries in which vaccination is incomplete, and there is a growing population of young children without immunity.[14] Eventually, a plane will arrive from abroad with several persons excreting wild poliovirus. The median incubation period for poliomyelitis is about 12 days and can be as long as 28 days: a considerable dispersal of poliovirus could occur before cases were diagnosed and tracing of contacts, and contacts of contacts, could be very difficult. Mass vaccination would prevent many further cases. However, if cases had occurred in several large cities, the number of doses required would be very large unless vaccine were given to only selected groups. Two recent court judgments for damages against drug companies manufacturing poliovirus vaccines (OPV)[15,16] have done nothing to increase the supply of vaccine or the confidence of those who have to administer it. Health authorities may think twice before ordering mass vaccination and there may not be enough vaccine available.

If the proportion of persons at each age with no immunity against Type 1 poliovirus—the most frequently met in past epidemics—is taken from the latest US serosurvey,[4] then the maximum number of cases can be calculated. The enormous differ-

ence in the number of cases predicted by the assumed case rate from the 1950s and that by the genetic model is apparent in Table 1—a 200-fold difference. The genetic model predicts a rate in the total population of 2.5 percent, including 0.5 percent death rate. Moreover, if the immunity gap is allowed to remain, then the present zero to nine-year age group will move into the ten-years and over age group with the maximum susceptibility rate of 26 percent, thus increasing considerably the possible cases. In 1971 the low proportion of persons aged 10 to 39 years without immunity was a reflection of their exposure to wild viruses before 1962 and the large numbers who were given Salk vaccine and Sabin OPV in the campaigns of 1956 to 1964.

Although the figure of 2,500 cases seems very large, this should be compared with over 2,000 cases of paralysis in two-year-old children in New York in 1916—a rate of 1.9 percent—and 55 cases out of 222 Eskimos over four years old at Chesterfield Inlet in 1948.[5,6] It should also be remembered that in 1962-1963 there were more than one hundred cases of poliomyelitis in Massachusetts during the mass poliovaccine campaigns there and many of these cases were adults.

It is, of course, unlikely that a wild poliovirus would spread through the entire population and especially through adults over 40 years of age, who would have little contact with small children. Nevertheless, the wild virus spread through New York in 1916 and must have infected almost every child under the age of five years. As there were almost no cases in those over seven years,[18] there must have been either total immunity in the older age groups or no spread of virus to them. Poliovirus spread through the entire Eskimo population in Chesterfield Inlet in the winter of 1948,[19] and through adult populations in Greenland.[6] In the United States, there have been outbreaks of poliomyelitis with high paralytic rates in schools, institutions, camps, and hospitals.[6] It is difficult to predict how far poliovirus would be transmitted through the populations of countries like the United States, as there is no previous knowledge of its dispersal in a population with between 10 and 20 percent not immune in every group, but with high standards of hygiene. Unfortunately, vaccination policies have almost certainly resulted in considerable groupings of persons with low incomes, poor housing, very low vaccination rates and little immunity. These groups are not only themselves very vulnerable but are likely to be the reservoirs for spreading virus to others.

What Are the Legal Implications?

There has not yet been an action by a contact vaccine-associated case against a manufacturer or the US government. Nor has there been an action by an unvaccinated person with paralysis from a wild virus, suing a physician for *not* explaining the real risk of refusing immunization!

A number of persons have successfully sued the manufacturers of vaccine on the grounds that the poliovaccine has left them with paralysis. In one case, damages were awarded despite the opinion of the expert witnesses that the paralysis was caused by the epidemic wild virus and not by the vaccine virus given for prophylaxis.[20] The assumption has been made by both legal and public health experts that paralysis in vaccine-associated cases (VAC) has resulted from a reversion of the vaccine virus to virulence. The tests for reversion can only be made if virus is recovered from the patient; recovery of virus from the cerebrospinal fluid is rare so that most tests will be made on virus from stools. This is not necessarily the same virus as that which reached the central nervous system; moreover, reversion of virus may just as easily occur in subculture in the laboratory. The tests for reversion are usually genetic marker tests on the virus in vitro: these tests correlate well with virulence tests on virus strains injected directly into the spinal cord of a monkey. Whether such tests show a causal correlation or a coincident correlation is a matter for debate.[21] Wild strains replicate at 40.0 C as determined by the reproductive capacity temperature test and are termed rct^+, whereas vaccine-like strains do not and are rct^-. It may be that the ability to replicate at 40.0 C is necessary for virus replication before and after entry into the central nervous system, but another and so far unidentified property may be necessary to allow entry to the central nervous system.[22]

It is, however, now accepted that one group of vaccinees is peculiarly susceptible to vaccine strains of poliovirus which have not reverted to virulence. These are children with immune deficiencies, mainly hypogammaglobulinemics who comprise about ten percent of all VAC and almost all the deaths from vaccine.[23] It is probable that

only those who are genetically susceptible are at risk.[5,6,23,24] These children are also susceptible to many diseases and thus appear to have no claim against the manufacturer of a vaccine.

If, as argued above, many, if not most, vaccine-associated cases are genetically susceptible to vaccine virus, the case for compensation is considerably weakened. The theory of genetic susceptibility predicts that the VACs would be the most susceptible to paralysis by wild virus. The manufacturers might claim that because severity of paralysis is age-dependent,[5,25] the person who was a vaccine-associated case had suffered less damage from the vaccine than he would be liable to if he later succumbed to a wild virus.

Conclusions

Only about 60 percent of children are currently receiving OPV although many of the remainder are vaccinated as contacts or at school. As these children reach adulthood, more of the nonimmunes will become genetically susceptible and consequently will be at risk as contacts of child vaccinees. The number of adult contact cases will therefore probably increase. However, if fewer women have children, as opposed to women having fewer children, and if one parent families increase, fewer adults will be exposed to child excretors.

The national policy on polio vaccination recommends that children be given OPV when 12 to 13 years old.[26] This would be excellent if it were intended as a booster for everyone immunized in early childhood. Unfortunately, it is intended as a primary immunization for those who have not received previous OPV. For the reasons given in this paper, the safest age for immunization with OPV is 1 year: the national policy is an attempt to rectify the embarrassing failure of the immunization program.[27]

The risk of contracting poliomyelitis from the vaccine is very low, less than 1 for every 400,000 nonimmune persons given OPV.[24] Moreover, the theory of genetic susceptibility to poliomyelitis predicts that those who contract poliomyelitis from OPV would be those who would suffer paralysis or death from a wild virus.[5] The theory of genetic susceptibility is not proved; only a major epidemic due to lack of immunity in adults, could produce more evidence for it. Let us ensure that this proof is never obtained by ensuring that all children are immunized.[28]

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