POLIO VACCINE POLICIES -- To change or not to change

Donald A. Henderson, M.D., M.P.H.N
National Medical Association Annual Meeting
Chicago, Illinois
30 July 1996

The ACIP decided in June to recommend changes in the nation's polio vaccination schedule. The new policy calls for the inactivated Salk vaccine to be given by inoculation at 2 months and 4 months and for the oral Sabin vaccine to be given at 12-18 months with a second dose at school entry. This represents a significant change from the vaccination policy which was adopted more than 30 years ago when OPV was first licensed and which has since changed little. Clearly, that policy served this and most other countries well, culminating in 1991 in the eradication of poliomyeltis from the Western Hemisphere. What precipitated the change in policy? Does the rationale make sense?

PERSONAL CONCERNS

First, what are my credentials and my reasons for taking a special interest in this problem and coming here to address you. It is not because of a commercial interest. I have received no research grants, no salary support, no honoraria from any manufacturer.

Quite simply, I have been involved with polio vaccine policy and and vaccine delivery issues my entire professional life. Tremendous progress has been made toward the goal of polio eradication. I would not like to see the possibilities of reaching that goal compromised in any way by ill-considered policies.

I joined CDC in 1955 and spent my first years endeavoring to restore a nation's confidence in the Salk vaccine after a manufacturing error led to more than 100 vaccine caused cases. I worked on polio control programs, participated in research on the Sabin oral vaccine and was head of the CDC surveillance program when we discovered and described the small but definite risk of paralytic cases caused by OPV. In 1963, I proposed the creation of ACIP and served for three years as its first secretary.

Since 1985, I have chaired the PAHO Technical Advisory Group as we plotted strategy and tactics to eradicate polio from the Western Hemisphere and I have chaired WHO's global consultations on polio eradication.

The concerns which I have with the new policy I have shared with CDC and ACIP

but both the concerns and questions have simply been igneored.

THE ACIP

First -- a brief comment about the ACIP, its history and its method of operation. It was created in 1963 and has functioned over the past three decades to advise the public health community on the best, most appropriate use of vaccines for the U.S. population as a whole. For pediatric vaccines, it complements the work of the so-called RED Book Committee of the American Academy of Pediatrics which provides advice on vaccinating individual children in pediatric practice. ACIP's members and liaison representatives come from many different constituencies. Its recommendations are customarily developed after careful scientific evaluation and consensus building among the professional community so that the recommendations, when formalized, are seldom questioned. The new recommendations regarding polio vaccine policy represent an unprecedented departure from tradition having been promulgated despite many questions and objections by a number of reputable professional groups. I will endeavor today to summarize for you the stated background and rationale for the changes.

RATIONALE FOR CHANGE

The sole rationale for the change proposed by ACIP is to avert cases of VAPP (vaccine-associated paralytic polio). The hope is that by administering first, IPV, followed later by OPV, that some of these rare but important adverse reactions to OPV might be prevented. OPV, like other therapeutic and preventive products, can cause unwanted reactions. In the case of OPV, it is an illness similar to polio caused by naturally occurring "wild" viruses. This problem has been known since 1963 and, through research, efforts have been made to eliminate or at least reduce the risk but without success.

The risk of occurrence of VAPP is less than one case per 2,500,000 doses. SLIDE 1 This is based on the assumption that an average of 8-10 cases occur annually as was indeed the case throughout the 1980's. However, data for the most recent 5 years, 1990-1994, show an average of 5.8 cases. This is a substantial difference but without explanation. It is unlikely to reflect less complete reporting. To the contrary, reporting over recent years should be more complete than during earlier years because of added incentives to report cases -- specifically, the now ready availability of compensation through the federal vaccine injury compensation program and heightened surveillance because of the absence of domestic polio and the need to be alert for

importations.

Of the cases of VAPP, half are in vaccinees and half are in contacts. The CDC believes that the new sequential schedule might prevent cases occurring in vaccinees or, in other words, about half the number of VAPP cases -- specifically, either 3 cases or 4 to 5 cases depending on which data you wish to use. Even so, a cautionary note is needed because it is entirely speculative as to what, if any, proportion of the cases would actually be prevented given the fact that there is no experience with a schedule such as this in any other country. Of the very few, small countries which now use an IPV-OPV sequence, none follows a schedule which at all resembles the one recommended. Be this as it may, the recommended change in the schedule has other and adverse implications which counterbalance whatever small benefits may be offered. These I shall comment on further.

ADVANTAGES OF OPV

When, in the early 1960's, OPV was originally recommended to replace IPV, the risks and benefits had to be carefully weighed. Three particular benefits of OPV were felt to outweigh the small but definite risk of vaccine-associated cases.. First and most important is the fact that OPV induces immunity in the child's intestinal tract so that even if a child so protected is exposed to wild poliovirus, that virus will grow poorly or not at all and he is much less likely to transmit infection to others. SLIDE 2 A number of studies have been performed in which a type I vaccine virus has been fed to children with and without natural or vaccine-induced immunity. As is apparent in these studies, children who are naturally immune and those protected by OPV show similar levels of resistance to growth of the challenge virus. In contrast, IPV provides little protection -- in fact, there is little to differentiate children so protected from wholly susceptible controls. Because of this attribute of OPV, public health authorities have thus strongly favored its use as providing the best possible protection for the community as a whole. Note that these studies do not address the question of protection of the individual child. In fact, both vaccines and various combinations of the vaccines provide excellent individual protection. The important advantage of OPV, however, is its provision of intestinal immunity.

A second advantage of OPV is that the virus can be transmitted to other susceptible persons in the household, especially in lower socio economic areas. SLIDE 3 Thus, others are protected who may not have been vaccinated or whose vaccination

might not have been successful

The third advantage of OPV is that it is given by mouth and so is far easier to administer than IPV which requires inoculation--an important consideration because of the number of inoculations called for under present vaccination schedules.

INSTITUTE OF MEDICINE REVIEW -- 1988

In 1988, the Public Health Service asked the IOM to review polio vaccination policy, to review the benefits and risks of each of the vaccines and to recommend as to whether changes in the vaccine policy should be considered. An expert committee was convened and concluded:

1. "No change in the present policy is recommended at this time.

SLIDE 4 2. "The mixed IPV-OPV program is not recommended if DTP and eIPV must be given separately because of cumbersome administration and greater cost. Simplicity in vaccination schedules is important because of continuing problems with inadequate immunization rates in preschool children.

SLIDE 5 3.After a combined DTP-eIPV is licensed, consideration should be given to a regimen of two or more doses of eIPV followed by OPV.

CHANGE IN RISK OF IMPORTATIONS

Since the 1988 IOM review what has changed? As noted, the risk of VAPP appears to have diminished and 3 new antigens (8 additional inoculations) have been added to a now formidable vaccination schedule. However, the one change which ACIP identifies as being the deciding one in electing to change the vaccination policy is the diminished risk of wild poliovirus being introduced into the U.S. This country, as I'm sure you are aware, has been free of endemic polio since 1979. The ACIP draft report states that "in the U.S. the risk of poliomyelitis caused by wild poliovirus is exceedingly remote". It notes that no person infected with wild poliovirus is known to have entered the U.S. since 1986 and that a global eradication program is in progress which is targeted to eradicate polio by the year 2000.

I believe that it is generally agree that there is less of a risk of an importation now than in 1988 but is the risk so "exceedingly remote" that we can abandon our defense

against the community spread of wild poliovirus which is provided by OPV? It should be noted first that a decline in polio incidence in many parts of the world is to some extent counter balanced by markedly increased air travel and more travelers are young children, the ones most apt to be infected with wild poliovirus.

The ACIP draft report notes optimistically that the only case of polio in the U.S. since 1986 was a Nigerian child brought here for treatment. SLIDE 6 For reasons unknown, no mention is made of the fact that wild poliovirus was introduced into Canada in 1993 and again in 1996, the latter being a 15 month old Canadian child who had received 3 IPV inoculationsand returned from a visit to India with a Type I wild poliovirus strain in his intestine. Neither of these importations resulted in cases of paralytic disease. However, it seems to me that if the wild virus can and is being introduced into Canada, it can quite as easily, perhaps more easily, be introduced into the U.S. Given the fact that for every symptomatic case there are customarily several hundred who are infected but have no symptoms, it would seem a virtual certainty that the U.S., like Canada, is experiencing a number of importations annually but because of the high levels of intestinal immunity, the virus is not now spreading widely enough to be detected. In this respect, I would note that in June 1995, Sutter and his colleagues from CDC, in a report at an IOM meeting, stated that they estimated that there were between 40 and 200 undetected importations of wild poliovirus into the U.S. every year.

The fact that there is a goal of global polio eradication by the year 2000 has encouraged some to believe that we need not be concerned about levels of polio immunity for more than four years. Reality suggests otherwise. The year 2000 date, established in 1988, is a goal not an expectation. Although the Western hemisphere and some industrialized countries are clearly polio-free, the disease is still widely endemic throughout the whole of tropical Africa as well as populous areas of South Asia, among others. It is, in fact, endemic over an area roughly comparable to that when the smallpox eradication campaign began. These are the poorest countries, the most crowded and the ones with the least resources. Programs of some sort are being started or have begun in most such countries. However, none have yet to develop any sort of functional reporting-surveillance system. Thus, there is much yet to learn and many years of hard work ahead before eradication can be achieved. In brief, while the achievements to date are to be commended, the really difficult challenges lie ahead.

A NEW SCHEDULE AND HEIGHTENED SUSCEPTIBILITY TO DISEASE

Special problems are presented by the new schedule for polio vaccine calling for 2 inoculations of IPV at 2 and 4 months and administration of OPV at 6-12 months and 4-6 years. This change in the schedule will predictably have two serious consequences. First, it will create a rapidly growing pool of children susceptible of acquiring and transmitting wild poliovirus. Second, the additional inoculations, imposed on an already overburdened vaccine inoculation schedule, will require added clinic visits and, predictably, lower levels of compliance with vaccination recommendations.

OPV, through inducing intestinal immunity, now plays an important role in preventing spread of wild poliovirus but under the new schedule, the levels of intestinal immunity before school entry will be very low. SLIDE 7 Depicted here are the results of feeding OPV to children who have been protected by three different schedules -- OPV alone, IPV alone and 2 doses of IPV followed by one of OPV (the recommended new schedule). Of those children who have received 3 doses of OPV and subsequently are fed live vaccine, very few excrete the virus and those who do, for only a short time and in low titer. Such a response is believed to be similar to a child's response when challenged with wild poliovirus. Note the large proportion of children protected by 3 doses of IPV who excrete virus. Note that the new schedule calls for only one dose of OPV at 12-18 months. One dose of OPV provides significant protection against reinfection with type II poliovirus because this is the vaccine strain which grows best in the intestine. However, it offers little protection against poliovaccine types I and III, the two types which account for more than 95% of all paralytic cases. A second dose of OPV at 4-6 years will provide better intestinal immunity but, meanwhile, there will be a growing pool of preschool children fully susceptible to the two major types of poliovirus.

The additional inoculations present yet another problem. When, in 1988, the IOM recommended against an IPV-OPV schedule on the grounds that it would unnecessarily complicate and compromise the vaccination schedule, only 5 inoculations were then being recommended for children under 18 months -- 4 DTP and one dose of measles-mumps-rubella vaccine. Since 1988, ACIP has also recommended 4-5 inoculations of Hemophilus influenzae vaccine, three of Hepatitis B vaccine plus one of varicella vaccine -- bringing the total to 13 in all. SLIDE 8

Whereas in 1988, all vaccines could readily be provided during 4 well-child visits, a similar schedule today requires either that 3 or 4 vaccines be inoculated at each

visit or that additional visits be scheduled. Manufacturers are now working to combine a number of the vaccines into a single inoculation and there is every reason to believe they will succeed but it will take time. Health staff, meanwhile, are obliged to deal with the problem of too many inoculations for the usual number of well-child visits. Many parents and health personnel object to giving more than 2 inoculations at a single visit and thus added visits have to be scheduled. As has been shown repeatedly, immunization rates fall with each added visit, an effect particularly observed in lower socioeconomic areas. What vaccinations will be given first and which last? The recommendations of ACIP offer effectively no guidance as to how best to address the problem. Are we to expect a growing pool of children susceptible to measles or pertussis or Hemophilus or all of these, in addition to being more susceptible to wild poliovirus.

SUMMARY

Let me briefly summarize by noting that the ACIP recommendation for a new polio vaccination policy is predicated on the belief that many fewer cases of vaccine-associated paralytic poliomyelitis will occur; that the risk of imported polio is so remote that a substantial decrease in community-wide protection against polio is acceptable; and that a now overburdened vaccination schedule can readily accommodate additional inoculations in some unspecified manner without diminishing overall compliance with recommended vaccination schedules. As I hope is now all too apparent, each of these assumptions is seriously flawed.

So, what should we do? What would I do if I were the Secretary? Would I accept this recommendation which carries a price tag estimated to range from $20 to $75 million -- to perhaps prevent as many as 3 cases of VAPP at the expense of leaving a growing population of preschoolers susceptible to infection to wild poliovirus and compromising overall vaccination coverage, especially among inner-city, minority children? As is only too apparent, this recommendation has little to do with solving the real problems. Quite clearly, what we need are new vaccine preparations which combine a number of antigens in a single innoculation. We already have two of these: diphtheria-pertussis-tetanus and measles-mumps-rubella vaccines. Vaccine manufacturers are working on other combinations but progress has been slow. Thus, I would be inclined to create a Task Force comprised of manufacturers, scientists, public health staff and government vaccine experts to decide on a strategy, timetable and

VAPP CASES -- BY YEAR

Pre-Eradication	No. of cases	
1980	6	
1981	10	
1982	11	Average 9.6
1983	13	
1984	8	
Eradication in Progress		
1986	7	
1987	8	
1988	9	Average 8.0
1989	9	
1990	6	
Hemisphere free of polio		
1991	9	
1992	6	
1993	3	Average 5.8
1994	5	

INTESTINAL IMMUNITY

Children excreting virus after OPV I feeding (%)

	Naturally immune	OPV protected	IPV protected	Contacts
Ghendon (1961)	34	36	74	80
Henry (1966)		32	86	83
Onorato (1991)		25	63	

SPREAD OF OPV IN FAMILIES

	Upper economic		Lower economic	
Virus	No. contacts	Infected	No. contacts	Infected
1	29	2	22	9
2	9	0	36	14
3	25	3	31	22
	63	5 (8%)	89	45 (51%)

Source: Gelfand, et al 1959

POLIO IMPORTATIONS INTO NORTH AMERICA

Year	Age	Origin	Country	Vaccine Hx
1980	67	Mexico	U.S.	0
1980	4 mos	Mexico	U.S.	0
1984	25	Zaire	U.S.	5 IPV; 2 OPV
1985*	2	Haiti	U.S.	1 OPV
1986	29	Nepal/Burma	U.S.	3 IPV; 1 OPV
1993*	2	Nigeria	U.S.	0
1993	?	Netherlands	Canada	?
1996	15 mos	India	Canada	3 IPV

*Patient brought to U.S. for treatment after onset of disease abroad

INTESTINAL IMMUNITY
Children excreting virus after OPV administration (%)

Protected by:	Type I	Type II	Type III
3 OPV	4	3	10
2 IPV/ 1 OPV	27	11	54
3 IPV	18	54	78

Source: Modlin (1991)