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Subnormal Immunity to Inactivated Poliovirus Vaccine (IPV) in Previously Vaccinated Human Immunodeficiency Virus (HIV) - Infected Children

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ABSTRACT

Introduction: *Minimal data exists regarding prevalence of immunity to inactivated poliovirus vaccine (IPV) in previously vaccinated HIV-infected children.*

Methods: *Antibody titers to IPV against serotypes (ST) 1, 2 and 3 following 3-doses (primary series) and 4th and 5th doses (booster) were examined in 59 children who were born to HIV-infected mothers. Eight of those children tested negative for HIV by DNA PCR and served as the controls for the 3rd and 4th dose recipients. Anti-polio 1, 2, 3 antibody titers (1/dil) was measured by neutralization assay at Specialty Laboratory in New Jersey. Correlate of protective immunity (PI) was defined as antibody titer ≥1:8 for all serotypes. ST specific PI was correlated with the T cell counts and clinical disease categories within the HIV-infected children. PI status was compared between the HIV- infected and HIV- uninfected children and between the numbers of vaccine dose recipients within the HIV-infected children.*

Results: *Mean age of children at the time of vaccination was 6.6, 18.6 and 66.5 months in the 3rd, 4th and 5th dose recipients, respectively. The mean age of the HIV-infected and HIV- uninfected children was comparable in the 3-dose group. Among the 3rd and 4th dose recipients, prevalence of PI to all 3 ST was significantly (p= 0.002/ST1, 0.002/ST2 and 0.01/ST3) lower in the HIV-infected, compared to their uninfected counterparts; Within the HIV-infected children, prevalence of PI to ST 1 and 2 was around 7-10 percent for all dose recipients; and 28 percent to ST3 for the 5th dose vaccine recipients. The CD4 count was found to be significantly (p=0.009) lower (362/mm^3) in the 5th dose compared to the 3rd dose vaccine recipients (1072 /mm^3).*

Conclusion: *A significantly high proportion of HIV- infected children may remain unprotected against all ST of IPV even after their booster doses and thus may remain at risk for infection with all 3 ST of poliovirus when exposed to recipients of the live oral polio vaccine worldwide. Global implementation of IPV over OPV may be considered to prevent resurgence of poliovirus disease in the growing population of immunocompromised patients. Extra vigilance in the maintenance of protective immunity to poliovirus serotypes and surveillance of disease in the immunocompromised host may be deemed necessary for prevention of disease occurrence and timely diagnosis and treatment.*

Keywords
Vaccine, Polio, Antibody, and Protective titer

Introduction
Poliovirus disease elimination in the United States is a great success via global polio eradication initiative through mass vaccination and improved sanitation strategies. The last outbreak of poliomyelitis due to indigenously acquired wild poliovirus that occurred in the United States in 1979 was in unvaccinated individuals and United States was certified free of wild poliovirus in September 1994, with similar achievements in the Western Pacific Region in October 2000 and the European Region in June 2002 [1-3]. Elsewhere, in parts of Africa and Asia, war continues to serve as a major obstacle to the eradication initiative [3]. Thus, concerns remain regarding reemergence of poliovirus infection with the wild poliovirus not only in Asia and Africa, but also in the United States due to threat of imported cases from across the globe and increasing population of immunocompromised hosts including the human immunodeficiency virus -infected individuals. And alterations in the social, environmental, biological, and demographic conditions.

The threat of reemergence of the poliovirus disease in the United States had always been there due to the increasing number of unvaccinated individuals, immunocompromised hosts and increasing number of the imported immigrants and refugees from rest of the world where oral polio vaccine is still being used for routine vaccination purpose. A good example is the recent case of poliovirus disease in an unvaccinated person in Rockland County in New York City [4].

The Salk-type or inactivated poliovirus vaccine (IPV) was introduced in the United States in 1955 and Sabin-type live (attenuated) oral poliovirus vaccine (OPV) was introduced in the early 1960s. This broke the chain of wild poliovirus transmission. Cases of vaccine-associated paralytic poliomyelitis (VAPP) continued to occur between 1961-1989; from 1990 through 1999, 61 cases of VAPP were reported [5]. The vaccination policy changed from OPV to sequential schedule of IPV followed by OPV in 1997 and an exclusive IPV schedule was established in 2000. The global polio eradication initiative (GPEI) strategic plan for 2013-2018 envisioned global withdrawal of OPV vaccine by serotype, starting with serotype 2 OPV [6] by mid-2016 (last natural case occurred in India in 1999). With the onset of HIV epidemic in the 1990s, exclusive IPV was recommended for infants born to HIV-infected mothers. One of the most frequent sources of immunosuppression in infants from birth to 2 years of age is exposure to vertical transmission of HIV from infected mothers [7]. HIV-exposed but uninfected infants, as well as HIV-exposed and infected infants may be expected to experience lower immune responses due to indirect immunological consequences of antenatal HIV exposure. Nevertheless, HIV-exposed infants, both infected and uninfected, remain at increased risk of under-immunization and developing vaccine-preventable diseases including poliomyelitis [8,9].

Poliomyelitis is an acute viral disease produced by three antigenically distinct types of poliovirus (types 1– 3). The primary mode of transmission of poliovirus is through close association with an infected person. Two main routes of person-to-person transmission recognized are fecal-oral and droplet spread from the pharynx. While fecal-oral route is considered more common means of transmission [10], respiratory droplets is a critical and predominant mode of transmission in high income countries with a high proportion of immunocompromised population including human immunodeficiency virus infected individuals. Thus, maintenance of protective immunity to all three serotypes of poliovirus is critical to prevent resurgence of this disease in the immunocompromised population in the United States. The fact that poliovirus infection is overwhelmingly subclinical and case fatality rate is as high as 5-10 percent [11] may also pose a threat to transmission, morbidity and mortality of this infection in the vulnerable immunocompromised population. Therefore, a good level of protective immunity to all three poliovirus serotypes is deemed necessary to prevent poliovirus infection in HIV-exposed infected or uninfected children. A recent case of poliovirus disease with type 3 vaccine derived poliovirus (VDPV) was detected in stool specimens from an infant with primary immunodeficiency disorder (PID) in China. Surveillance for poliovirus in PID patients in China has shown an increased detection of immunodeficiency -related (iVDPV) cases [12].

Immune responses to all childhood immunizations are reportedly subnormal in HIV-exposed infected or uninfected children compared to those in their immune competent counterparts [13-19]. Only limited data in the literature is available regarding immunogenicity of the three serotypes of IPV in HIV-exposed infected or uninfected children. A recent South African study by Madhi et al. has demonstrated immunogenicity to all three serotypes of poliovirus one month after IPV vaccination. Following the three-dose primary series, the serotypes were lower in infected infants with vertically transmitted HIV when compared with the HIV-exposed uninfected infants [19].

Methods
The study was performed as a routine standard of care and data collection during an epidemic of vertically transmitted HIV infection in an academic institution in New York city. The study was conducted between January 1993 and March 1995. None of the children in the study or control group had received intravenous immunoglobulin at any time during the study.

Study Population
Fifty-nine HIV-exposed children born to HIV-infected mothers attending Pediatric Infectious Disease clinic were enrolled into the study. All infants were tested for HIV infection within one week of birth by HIV deoxyribonucleic acid (DNA) testing (qualitative) by polymerase chain reaction (PCR). Infants were followed up to a mean of 6 months of age when repeat blood samples were obtained and retested for HIV DNA by PCR. Of these children, fifty-one were found infected with HIV and only eight were uninfected.

HIV-Infected Children

Related information regarding HIV testing results, antiretroviral therapy, T cell count and viral load were obtained from the medical records of the patients. HIV-infected children were classified clinically as asymptomatic (class N), mildly symptomatic (class A), moderately symptomatic (class B) and severely symptomatic (class C) according to the centers for disease control (CDC) classification system [20]; acquired immunodeficiency syndrome (AIDS) category was designated if there was a clinical history of opportunistic infections or CD4 count less than 15 percent for the age.

HIV-Exposed Uninfected Children

Eight infants were HIV-exposed but uninfected who were born to HIV-infected mothers and seroconverted to uninfected status by 6- month of age. These children served as the control group for the 3-dose primary series and 4-dose vaccine recipients.

Polio vaccination

All HIV-exposed children (Infected and Uninfected) had received inactivated polio vaccine (IPV). Eighteen (10= infected; 8= uninfected) children had completed 3-dose primary series of the IPV. Twenty-nine (27=infected and 2=uninfected) of them had received the 1st booster dose (4 doses) and fourteen HIV-infected children had received the 2nd booster dose (5 doses) of IPV.

Determination of antibody titers

Anti-polio 1, 2, 3 antibody titers (1/dil) were measured by neutralization assay at Specialty laboratories,
New Jersey (NJ). Correlates of immunities to serotypes 1,2 and 3 were defined as antibody titers ≥8 1/dil.
Antibody titers were missed to be drawn in two HIV-uninfected children after their 3rd dose in the 4-dose group.

Immunologic and Virologic Studies

T and B cell analyses in the HIV group were performed by flow cytometry; HIV viral loads and HIV qualitative DNA tests in the infants were performed at birth, 2-4 and 6 months of age by PCR at Specialty laboratories in NJ.

Statistical Analysis

No statistical hypotheses were tested, and all evaluations were descriptive. Seroprevalence of protective immunities to poliovirus serotypes 1, 2 and 3 between the HIV and control groups and within the HIV-infected group were compared by two- tailed Fisher's exact test. Software Intercooled stata version 8.0 was used for statistical analysis. Effects of immunologic (CD4 and B cell count/ mm3) and virologic (viral load) parameters on immunity status within the HIV group were compared by two- tailed t-test.

Results

Fifty-nine HIV-exposed children born to HIV-infected mothers participated in the study. Of these children, fifty-one were infected with HIV and only eight were uninfected by HIV DNA PCR. All participants were born at term.

Immunogenicity

Primary vaccination series (3-dose): Mean (± SD) age of the ten HIV-infected and six HIV-exposed uninfected infants at vaccination (6.6 [± 0.84] vs.7.7 [± 3.01]) and at serology (12 [± 2.90] vs.13.75 [± 3.19]) were comparable. Prevalence of PI to all serotypes was not significantly different between the two groups.

Immunologic Parameters comparing HIV-Infected and Uninfected Children: Combined 3 and 4-Doses

Table 1: Comparing Immunologic Parameters; HIV-Exposed Infected and Uninfected Children:
Combined 3 and 4 -Dose Vaccine Recipients.

	HIV Infected n=37 (3-Dose=10 4-Dose=27)	**HIV Uninfected n=8 (3-Dose=6 4-Dose=2)**	P value
Age months at vaccination mean (± SD)	6.6 (± 0.84)	7.75 (± 3.01)	**0.001***
Age months at serology mean (± SD)	30.27 (± 15.19)	13.75 (± 3.19)	**0.004***
Interval vaccination-serology months mean (± SD)	15 (± 11.84)	6 (± 3.70)	**0.04***
Immune n (%) Serotype1	3/37 (08 %)	5/8 (62%)	**0.002**#
Serotype2	3/37 (08 %)	5/8 (62%)	**0.002**#
Serotype3	3/37 (08 %)	4/8 (50%)	**0.01**#

*two-tailed t-test #two-tailed Fisher's exact test.

Among the 3rd and 4th dose recipients combined (HIV-infected, n=37 and HIV-Uninfected, n= 8); prevalence of PI to all 3 ST was significantly (p=0.002/ST1, 0.002/ST2 and 0.01/ST3) lower in the HIV-infected, compared to their uninfected counterparts. The mean (± SD) time-interval between vaccination to serology was 15 (± 11.84) months for the HIV group and 6 (± 3.70) months for the HIV-uninfected control group (p=0.04).

Booster doses

Table 2: Characteristics of HIV-Infected Children.

	3 Doses n=10	**4 Doses n=27**	**5 Doses n=14**
Age months at vaccination mean (range)	6.6 (6-8)	18.4 (16-30)	66.5 (48-140)
Age months at serology mean (range)	12 (7-15)	37 (19-60)	99.85 (61-168)
Interval vac-serology months Mean (range)	5.4 (1-9)	18.4 (1-42)	33.2 (2-84)
Protective Immunity n (%) Serotype1	1/10 (10)	2/27 (07)	1/14 (07)
Serotype2	1/10 (10)	2/27 (07)	1/14 (07)
Serotype3	1/10 (10)	2/27 (07)	4/14 (28)
CD4/mm3 mean (range) p	1072 (10-2530) ns* (between 3 & 4 doses)	846 (4-2840) 0.04* (between 4 & 5 doses)	362 (0-790) 0.01* (between 3 & 5 doses)
CDC class B-C n (%)	5/10 (50)	10/27 (37)	6/14 (43)

*Two-tailed t-test.

Within the HIV-infected group, prevalence of PI to all three serotypes in the 4-dose recipients were seven percent and in the 5-dose recipients, it was seven percent to serotypes 1 and 2 but 28 percent to serotype 3.

Comparing CD4 count by number of doses in the HIV-infected Children

Table 3: Comparing Protective Immunity with Immunologic and Clinical Categories in All HIV-Infected Children (n=51).

	Protective immunity n (%) ST1	Protective immunity n (%) ST2	Protective immunity n (%) ST3
No evidence of suppression of CD4	2/17 (12)	1/17 (06)	3/17 (18)
Evidence of moderate to severe suppression of CD4	2/34 (06)	3/34 (09)	4/34 (12)
p	0.59*	1.00*	0.67*
CDC Class N-A n (%)	1/21 (05)	0/21 (0)	2/21 (10)
CDC Class B-C n (%)	3/30 (10)	4/30 (13)	5/30 (16)
p	0.63*	0.13*	0.68*

*two-tailed Fisher's exact test.

CD4 count/mm^3 was significantly (p=0.04) lower in the 5-dose (362/mm^3) compared to the 4-dose (846/mm^3) vaccine recipients and significantly (P=0.01) lower in the 3-dose (1072/mm^3) compared to the 5-dose recipients (362/mm^3).

Comparing immune responses between 4 and 5 dose recipients in the HIV-infected Children: **No**

Difference was noted for serotypes 1, 2 and 3.

Discussion

This study provides important immunogenicity data following the administration of IPV in HIV-exposed infected and HIV-exposed uninfected infants and children in the United States. There is paucity of data evaluating immunogenicity of IPV in this special group of immunocompromised patients. Although study was performed about two decades ago; the data is still relevant given the fact there is not enough data of polio immunogenicity in this group of immunocompromised people and this data can be extrapolated to other growing population of immunocompromised hosts in the United States. Although infants and children born to HIV-infected mothers currently are not getting infected due to implementation of highly active antiretroviral therapy in the pregnant women, concerns remain regarding circulating live polio virus from OPV recipients and susceptibility of the vulnerable populations globally. The recent case of VAPP in Rockland county in New York city underscores the importance of these data when extrapolated to the immunocompromised and unvaccinated population even in the United States.

All reported cases of paralytic poliomyelitis in the United States have been vaccine-associated VAPP [20-22]. The risk of VAPP is highest following the first dose of OPV and among immunodeficient persons. Since changing to an all-IPV immunization schedule in 2000, there have been only three cases of VAPP reported in the United States [23-24]. Of these reported cases, two had occurred in immunocompromised individuals.

Two phases of acute poliomyelitis have been distinguished: a nonspecific febrile illness (minor illness) and aseptic meningitis and/or paralytic disease (major illness) have been recognized in a small proportion of patients. The ratio of cases of inapparent infection to paralytic disease among susceptible individuals ranges from 100:1 to 1000:1 or more. Progression to maximum paralysis is rapid (2–4 days); between 2% and 10% of paralytic poliomyelitis cases are fatal. The vaccine polioviruses are able to replicate in the intestinal tract of inadequately immunized persons and may be transmitted to others with inadequate immunity. During these multiple infections, the viruses may regain some of the properties of wild polioviruses, such as transmissibility and neurovirulence. Clinical disease caused by these VDPVs is indistinguishable from that caused by wild polioviruses [25]. This raises concern regarding underdiagnosed subclinical cases of polio virus disease in the immunocompromised and unvaccinated population which may remain unrecognized. Thus, the actual number of poliovirus disease in the United States may be underestimated. Because inapparent infection with OPV or wild virus strains no longer contributes to the establishment or maintenance of poliovirus immunity in the United States, universal vaccination of infants and children is the only means of establishing and maintaining population immunity against poliovirus to prevent poliomyelitis cases and epidemics caused by importation of wild virus into the United States. Although seroprevalence studies have demonstrated high level of immunity in children [26], outbreaks of poliomyelitis continue to be reported among religious groups in the United States [27,28]. This finding reiterates the importance of developing further strategies to detect and prevent subclinical or clinical poliovirus disease in the immunocompromised population. Such strategies may include 1) surveillance and monitoring of protective immunities to poliovirus serotypes during febrile illnesses, or even as routine standard of care in this population. The poliomyelitis surveillance system is already in place to detect importation of wild poliovirus into the United States and detect the presence of vaccine-derived poliovirus in the United States. 2) Importance of rapid identification of suspected poliomyelitis cases is critical for identifying possible wild poliovirus transmission. Rapid detection of wild or virus-related cases permits the timely implementation of controls to limit the spread of imported wild poliovirus or cVDPVs and maintain the eradication of wild poliovirus in the United States. Moreover, rapid investigation of suspected cases will allow collection of specimens for poliovirus isolation, which is critical for confirming whether a case of paralytic poliomyelitis is the result of wild or vaccine-related virus infection. A rapid antigen-based test or polymerase chain reaction- based test may need to be developed. 3) Disease Reduction Goals: There have been only three cases of VAPP reported in the United States since 2000, when the use of OPV was discontinued. High coverage with poliovirus vaccine is required to maintain elimination of poliomyelitis in the United States until global eradication is achieved.

References

1. Centers for Disease Control (CDC) Follow-up on poliomyelitis-United States, Canada, Netherlands. Morbidity and Mortality Weekly Report. 1997; 46:1195-1196.
2. de Quadros CA, Hersh BS, Olive JM, et al. Eradication of wild poliovirus from the Americas: Acute flaccid paralysis surveillance, 1988–1995 Journal of Infectious Disease. 1997; 175: S37-S42.
3. Tangerman RH, Hull HF, Jafari H, et al. Eradication of poliomyelitis in countries affected by conflict. Bulletin of the World Health Organization. 2000; 78: 330-338.
4. Blythe Ryerson A, Lang D, Alazawi MA, et al. Morbidity and Mortality Weekly Report. 2022; 71; 1418-1424.
5. Sutter RW, Prevots DR, Cochi SL. Poliovirus vaccines. Progress toward global poliomyelitis eradication and changing routine immunization recommendations in the United States. Pediatr Clin North Am. 2000; 47: 287-308.
6. Grassly NC. Immunogenicity and Effectiveness of Routine Immunization With 1 or 2 Doses of Inactivated Poliovirus Vaccine: Systematic Review and Meta-analysis. The Journal of Infectious Diseases. 2014; 210: S439-S446.
7. Jones CE, Naidoo S, De Beer C, et al. Maternal HIV infection and antibody responses against vaccine-preventable diseases in uninfected infants. J Am Med Assoc. 2011; 305: 576-584.
8. Succi RC, Krauss MR, Harris DR, et al. Under-vaccination of perinatally HIV-infected and HIV-exposed uninfected children in Latin America and the Caribbean. Pediatr Infect Dis J. 2013; 32: 845-850.
9. Ndirangu J, Barnighausen T, Tanser F, et al. Levels of childhood vaccination coverage and the impact of maternal HIV status on child vaccination status in rural KwaZulu-Natal, South Africa. Trop Med Int Health. 2009; 14: 1383-1393.
10. Christie AB. Infectious diseases: Epidemiology and clinical practice. 4th Vol. 2. Churchill Livingstone; Edinburgh. 1987.
11. Krugman, Ward, Katz. 1977; Christie 1987; Mandell, Bennett, and Dolin, 2000.
12. Yao N, Liu Y, Xu J-W, et al. Detection of a Highly Divergent Type 3 Vaccine-Derived Poliovirus in a Child with a Severe Primary Immunodeficiency Disorder- Chongqing, China, 2022. Morbidity and Mortality Weekly Report. 2022; 71; 1148-1150.
13. Choudhury SA, Mishreki N. Subnormal immunity to H influenzae type B in previously vaccinated HIV-Infected children > =59 months of age and response to booster doses of the conjugate vaccine. Clinical Pediatrics. 2004; 43: 831-835.
14. Choudhury SA, Mishreki N. Subnormal immunity to H influenzae type B in previously vaccinated HIV-Infected children > =59 months of age and response to booster doses of the conjugate vaccine. Clinical Pediatrics. 2004; 43: 831-835.
15. Choudhury SA, Matin F. Subnormal and Waning Immunity to Tetanus Toxoid in Previously Vaccinated Human Immunodeficiency Virus - Infected Children and Response to Booster Doses of the Vaccine. IJID. 2013; 17: e1249-e1251.
16. Choudhury SA, Matin F. Seroprevalence of Antibodies to Measles, Mumps and Rubella (MMR) Vaccines in Previously Vaccinated Human Immunodeficiency Virus-Infected Children and their Control Counterparts. Journal Vaccines Vaccin Open Access. 2015; 5: 255.
17. Madhi SA, Izu A, Violari A, et al. Immunogenicity following the first and second doses of 7-valent pneumococcal conjugate vaccine in HIV-infected and -uninfected infants. Vaccine. 2013; 31: 777-783.
18. Simani OE, Izu A, Violari A, et al. Effect of HIV-1 exposure and antiretroviral treatment strategies in HIV-infected children on immunogenicity of vaccines during infancy. AIDS. 2014; 28: 531-541.
19. Koen A, Madhi S, Lyabis O, et al. Immunogenicity and safety of a hexavalent pediatric vaccine in HIV-exposed infected and uninfected infants in Republic of South Africa. Hum Vaccin Immunother. 2021; 17: 1770-1778.
20. CDC. Paralytic poliomyelitis - United States, 1980–1994. Morbidity and Mortality Weekly Report. 1997; 46: 79-83.
21. Prevots DR, Sutter RW, Strebel PM, et al. Completeness of reporting for paralytic polio, United States, 1980–1991. Arch Pediatr Adolesc Med. 1994; 148: 479-485.
22. Centers for Disease Control and Prevention. Imported vaccine-associated paralytic poliomyelitis – United States, 2005. Morbidity and Mortality Weekly Report. 2006; 55: 97-99.
23. DeVries AS, Harper J, Murray A. et al. Vaccine-derived poliomyelitis 12 years after infection in Minnesota. N Engl J Med. 2011; 364: 2316-2323.
24. Trimble R, Atkins J, Quigg TC, et al. Vaccine-associated paralytic poliomyelitis and BCG-osis in an immigrant child with severe combined immunodeficiency syndrome – Texas, 2013. Morbidity and Mortality Weekly Report. 2014; 63: 721-724.
25. Routh JA, Oberste MS, Patel M. Manual for the Surveillance of Vaccine-Preventable Diseases. Chapter 12: Poliomyelitis.
26. Chen RT, Hausinger S, Dajani A, et al. Seroprevalence of antibody against poliovirus in inner-city preschool children: implications for vaccination policy in the United States. JAMA. 1996: 275: 1639-1645.
27. Foote FM, Kraus G, Andrews MD, et al. Polio outbreak in a private school. Conn Med. 1973: 37: 643-644.
28. Strebel PM, Sutter RW, Cochi SL, et al. Epidemiology of poliomyelitis in the United States one decade after the last reported case of indigenous wild virus-associated disease. Clin Infect Dis. 1992; 14: 568-579.