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## Brief communication

# Seronegativity to polio viruses among previously immunized adult candidates to solid organ transplantation

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## ABSTRACT

In the current effort to eliminate polio from the world, it is important to recognize and vaccinate susceptible groups, especially immunocompromised patients living in countries where attenuated polio vaccine is still used. In this report, we describe the frequency of protective antibodies in a small sample of adult SOT candidates in whom previous vaccination could be ascertained. Patients included in this report were selected among the participants of an ongoing prospective study carried out at the Reference Center for Special Immunobiologicals of the Evandro Chagas National Institute of Infectious Diseases in Rio de Janeiro, Brazil. Among the first 100 patients enrolled in this study, only seven adult SOT candidates had proven polio vaccination at childhood. Three of these seven patients (43%) had no protective antibody titers to one or more poliovirus subtype before solid organ transplant. Proven childhood vaccination against polio does not reliably provide lifelong protective antibody titers for adult SOT candidates and should not be used as a criterion to analyze the need for vaccination in this population.

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In the early twentieth century, polio was an epidemic disease, which caused paralysis in thousands of children, resulting in a public health problem with enormous psychosocial impact.

After the advent of specific vaccines, inactivated (in 1955) and attenuated (in 1961), the disease has been eliminated in most countries.

Despite the current progress toward eradication of the disease, in 2014, the spread of wild poliovirus to polio-free countries was recognized as a Public Health Emergency of

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International Concern,<sup>1</sup> and there was a recent demonstration of silent circulation of wild poliovirus 1 in Israel.<sup>2</sup> These are alerts that reintroduction of wild poliovirus in areas where the disease had been eradicated may still be threatening, especially for groups of under immunized people. In addition, in countries such as Brazil, where oral live attenuated poliovirus vaccine (OPV) is still used, infection caused by vaccine derived polioviruses remains possible, especially in immunocompromised individuals.<sup>3</sup>

In the final step of polio eradication, seroprevalence studies have increased in importance and can point to immune gaps in specific populations.<sup>4-6</sup> Serum neutralizing antibody titers, the traditional measure of vaccine-induced immunity, have a reliable correlation with protection against paralytic poliomyelitis. However, it is a limited determinant of virus replication in the intestinal tract. Mucosal immunity is presumed to have a key role in protecting against enteric and pharyngeal infection with poliovirus, and hence it could be crucial in diminishing the efficiency of transmission.<sup>7</sup>

In recent decades, solid organ transplantation (SOT) has become a therapeutic alternative for many irreversible conditions such as chronic renal failure and liver cirrhosis. The success of SOT, however, depends on lifelong use of immunosuppressive drugs, which makes the individual susceptible to various infectious diseases. Vaccination pre- or post-transplantation is a recommended strategy to reduce vaccine-preventable diseases.<sup>8</sup> Although a previous study has demonstrated very low seroprevalence of protective antibodies to poliovirus in patients who received a kidney transplantation,<sup>9</sup> recommendations regarding polio vaccination for adult SOT candidates and recipients are not uniform and in some countries (including Brazil) vaccination is only indicated for adult patients who had not been previously immunized or for those planning to travel to risk areas.<sup>8,10-13</sup>

In this report, we describe the frequency of protective antibodies in a small sample of SOT candidates in whom previous vaccination could be ascertained. Patients included in this report were selected among participants of an ongoing prospective study carried out at the Reference Center for Special Immunobiologicals of the Evandro Chagas National Institute of Infectious Diseases (INI-Fiocruz) in Rio de Janeiro, Brazil. This study includes candidates for any type of SOT, aged 18 years or older who had no contraindication to vaccination with inactivated polio vaccine (IPV) and gave a written informed consent to participate in the study. This report includes only the subset of patients in whom previous vaccination could be confirmed by checking the vaccination card. Data collected from each patient in the first visit included age, sex, underlying organ disease, comorbidities such as hepatitis C infection, HIV infection, diabetes mellitus, current use of immunosuppressive drug, and previous OPV vaccination. A blood sample was collected in the first visit for determination of antibody titers against poliovirus 1, 2 and 3. This was performed by microneutralization test, according to World Health Organization protocol,<sup>14</sup> at the Enterovirus Laboratory (WHO Regional Reference Laboratory), of Oswaldo Cruz Institute (Fiocruz, Rio de Janeiro, Brazil). Titers  $\geq 1:8$  were considered protective. Patients with titers below 1:8 received one dose of IPV (Sanofi Pasteur). A second blood sample was collected after 30 days to evaluate the immunogenic response to

vaccination. This study was approved by the Ethics Research Committee of INI (12718913.0.0000.5262).

Among the first 100 patients enrolled in this study, only seven SOT candidates had proven polio vaccination at childhood, all were kidney transplant candidates. Three of these seven patients had no protective antibody titers to one or more poliovirus subtype. The first patient was a 30-year-old male patient, with chronic renal insufficiency caused by Alport Syndrome, in conservative treatment. He had received nine OPV doses. The last dose was in 1987. Sample collected in 2013 for poliovirus serology revealed titers  $<1:8$  for all three subtypes of poliovirus. The second case was a 37-year-old female, with chronic renal failure caused by arterial hypertension, on hemodialysis since July 2012. She had received three OPV doses, last dose in 1980. Sample collected in 2013 for poliovirus serology revealed titers  $<1:8$  for poliovirus 2 and 1:16 for poliovirus 1 and 3. The last patient was a 25-year-old female, with chronic renal insufficiency caused by arterial hypertension, on conservative treatment. She had received seven doses of OPV, last dose in 1993. Sample collected in 2014 for poliovirus serology revealed titers  $<1:8$  for poliovirus 1 and 3, 1:8 for poliovirus 2. None of these patients were on immunosuppressive therapy, and HCV and HIV serology were negative in all of them. The three patients developed protective titers of antibodies to all poliovirus after vaccination with one dose of IPV.

Brazil maintains high immunization coverage for poliomyelitis. It is estimated that  $>93\%$  of the child population receives polio vaccine. The current national immunization schedule for poliomyelitis consists of three doses of IPV in the first year of life (at 2, 4 and 6 months), followed by two boosters (at 15 months and between the 2nd and 4th year) using OPV. Additionally, there are annual massive national campaigns with two doses of oral vaccine, one month apart, for all children (two months to five years old). Until 2012, only OPV was used in the national vaccination program. Thereafter, IPV progressively replaced OPV in the first three vaccine doses, but OPV is still used as booster doses and in annual campaigns.

The transmission of OPV viruses from a recently vaccinated child to a non-immunized immunocompromised individual in the community is associated with two potential hazards. Immunocompromised hosts have higher probability to develop flaccid paralysis after being exposed to OPV.<sup>15</sup> In addition, prolonged viral replication in immune deficient hosts could increase the probability of OPV viruses regaining fitness and neurovirulence.<sup>3</sup> To reduce these risks, the Brazilian Society of Organ Transplantation recommends that adult SOT candidates and recipients who had not been previously immunized should be vaccinated with IPV. However, the Brazilian Ministry of Health in line with the national guidelines of other countries recommends that IPV should be used only by children and travelers to polio risk areas.<sup>8,10-13</sup>

The identification of three adult SOT candidates who did not have protective levels of neutralizing antibodies despite proven immunization at childhood suggests that childhood immunization is not a reliable predictor of protection against poliovirus infection for adult SOT candidates. Natural or vaccine-induced polio immunity may wane with aging<sup>16</sup> and in SOT candidates, with advanced stages of organ

dysfunction, the immune response to vaccines can be compromised.<sup>17</sup> Although, immune memory seems to prevent clinical disease, it may not be capable of preventing infection and viral shedding in feces.<sup>16</sup> This finding lends support to the approach recommended by the American Society of Transplantation which is to routinely vaccinate SOT candidates and recipients with IPV, although recognizing that this intervention is not based on high-quality evidence.<sup>8</sup>

In conclusion, in the current effort to eliminate polio from the world, it is important to recognize and vaccinate susceptible groups, including immunocompromised patients, especially in the large number of countries in which circulation of attenuated polio vaccine virus still occurs. Our findings suggest that proven childhood vaccination against polio does not reliably predict lifelong protection among adult SOT candidates even in a context of large scale attenuated virus circulation. Therefore, further studies are necessary to elucidate the best strategy to prevent poliovirus infection in this population.

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### Conflicts of interest

The authors declare no conflicts of interest.

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