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Seroprevalence of antibodies against the three serotypes of poliovirus and IPV vaccine response in adult solid organ transplant candidates

Luciana Gomes Pedro Brandão [a,*], Guilherme Santoro-Lopes [b], Silas de Souza Oliveira [c], Edson Elias da Silva [c], Pedro Emmanuel Alvarenga Americano do Brasil [a]

[a] Laboratório de Pesquisa em Imunização e Vigilância em Saúde (LIVS), Evandro Chagas National Institute of Infectious Diseases (INI – Fiocruz), Rio de Janeiro, Brazil
[b] Department of Preventive Medicine, Federal University of Rio de Janeiro, Brazil
[c] Enterovirus Laboratory, Oswaldo Cruz Institute (IOC – Fiocruz), Rio de Janeiro, Brazil

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ABSTRACT

Objectives: To assess the prevalence of protective antibody titers to polioviruses in adults candidates for solid organ transplant (SOT), and to assess the immunogenic response to inactivated polio vaccine in this population.
Methods: The study included SOT candidates referred to Immunization Reference Centre of Evandro Chagas National Institute of Infectious Diseases from March 2013 to January 2016. It was conducted in 2 phases. The first one, a cross-sectional seroprevalence study, followed by an uncontrolled analysis of vaccine response among patients without protective antibody titers at baseline. Antibody titers to poliomyelitis were determined by microneutralization assay.
Results: Among 206 SOT candidates included, 156 (76%) had protective antibody titers to all poliovirus serotypes (95% CI: 70–81%). Proven history of oral vaccination in childhood was not associated with higher seroprevalence of protective antibody. In 97% of individuals without protective antibody titers at baseline, there was adequate vaccine response with one dose of inactivated polio vaccine.
Conclusions: A relevant proportion of adult candidates for SOT does not have protective titers of antibodies to one or more poliovirus serotype. One dose of inactivated vaccine elicited protective antibody titers in 97% of these subjects and should be routinely prescribed prior to SOT.

1. Introduction

At the beginning of the 20th century, poliomyelitis was an epidemic disease that caused paralysis in many thousands of children, especially in countries with temperate climate, resulting in a public health problem with enormous psychosocial impact. With the advent of specific vaccines, inactivated (1955) and attenuated (1961), the disease has been gradually eliminated in most of the countries [1].

In 1988, following the success of polio control in the Americas, the World Health Organization (WHO) launched the Poliomyelitis Eradication Initiative, recommending the oral attenuated vaccine in the children's basic immunization schedule and in annual campaigns (National Immunization Days – NIDs) [2]. The oral vaccine has favorable characteristics for large-scale use, such as ease of application, low cost and transmission of the vaccine virus to contacts (secondary vaccination) [3,4]. This strategy resulted in a marked fall in the number polio cases in the world (from 350.000 cases in 1988 to 22 in 2017) and in the elimination of poliovirus serotype 2 in 1999 [5,6].

Despite this great progress, the eradication of the disease has not yet been achieved. In the final step of polio eradication, it is essential to maintain adequate immunity in the population even in regions where the disease has already been eliminated. The persistence of endemic areas for wild poliovirus poses a risk of dissemination and reintroduction of the disease in all parts of the world. In 2013, wild poliovirus 1 was isolated from several environment samples in Israel, without the occurrence of polio cases [7–9]. In 2014, wild poliovirus 1 was isolated from sewage samples collected at Viracopos International Airport in Brazil (Campinas, São Paulo), with genetic sequencing close to a strain isolated from a case in Equatorial Guinea [10]. These events show the potential for reintroduction and silent dissemination of the virus.

* Corresponding author at: Laboratório de Pesquisa em Imunização e Vigilância em Saúde (LIVS), Evandro Chagas National Institute of Infectious Diseases (INI – Fiocruz), Av. Brasil 4365, Manguinhos, Rio de Janeiro, RJ 21040-360, Brazil.
E-mail address: luciana.pedro@ini.fiocruz.br (L.G.P. Brandão).

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In addition, the vaccine-derived poliovirus (VDPV) has the potential for neurovirulence and transmissibility similar to the wild-type virus [11]. The identification of an increasing number of immunodeficient patients with sustained shedding of VDPV for months to decades shows that the risks of using the attenuated vaccine may extend over a prolonged period of time, even after the overall discontinuation of oral vaccine [12]. Therefore, the attenuated vaccine, which was one of the pillars in disease control, should be replaced by inactivated vaccine to reduce the risk of VDPV chronic elimination by immunodeficient subjects, thus contributing to polio eradication [11].

In most cases of immunodeficiency-related vaccine-derived poliovirus (iVDPV), the immunodeficiency has been diagnosed only after the development of paralysis [12]. In addition, approximately 7% of iVDPV cases were infected by vaccinated contacts [13]. This reinforces the need to identify susceptible individuals, especially in groups of immunodeficient patients in regions where the oral vaccine is still used.

Solid organ transplant (SOT) recipients represent a growing population living under perennial immunosuppression. Recommendations for polio vaccination of adult SOT candidates and recipients are not uniform among guidelines from different countries and medical societies. Most of them recommend routine polio vaccination only for children and for adult transplant candidates/recipients belonging to high risk groups, such as travelling to a polio endemic area or with occupational risk of exposure [14–19]. However, data on seroprevalence of protective antibodies among SOT recipients are scarce. In fact, the only study which addressed this issue in adult SOT recipients, found that only 3% of renal transplant recipients had protective titers of antibodies against all three serotypes of polioviruses [20]. Such low levels of protective antibodies could render this growing group of patients vulnerable to reemergence of poliovirus infections and to chronic vaccine derived poliovirus infection. Moreover, hypogammaglobulinemia, which is the most significant risk factor for prolonged elimination of attenuated poliovirus in individuals with primary immunodeficiency [21], has been reported in 16–63% of SOT recipients. These data highlight the need of further studies assessing the seroprevalence of protective antibodies to poliovirus in SOT candidates and recipients in order to guide the preventive strategy in this population, as part of the international efforts to poliomyelitis eradication in the world.

The main objectives of this study were to assess the prevalence of protective antibodies titers to the three serotypes of poliovirus and to determine the IPV (inactivated polio vaccine) response in adult SOT candidates.

2. Methods

2.1. Study design

A cross-sectional study was conducted to determine the prevalence of protective antibodies against poliovirus in adult SOT candidates, followed by a one arm follow-up assessment of vaccine immunogenic response in candidates with low or undetectable initial antibody titers to at least one poliovirus serotype at baseline.

2.2. Population

This study consecutively included SOT candidates, aged 18 years or older, attended at the Reference Center for Special Immunobiologicals (CRIE) of the Evandro Chagas National Institute of Infectious Diseases (INI- Fiocruz) in Rio de Janeiro (Brazil), between March 2013 and January 2016. CRIE is a public reference center of the National Immunization Program that receives patients from public and private institutions for immunizations of special groups.

2.3. Procedures

At the first visit, after obtaining informed consent, a standardized questionnaire with information about clinical, vaccination and family history was filled in. Data collected included age, sex, living in rural area at infancy, OPV vaccination at childhood, number of siblings, contact with polio cases during life, number and age of children, OPV vaccination of children, living with children <5 years of age at the date of the first visit, underlying organ disease, comorbidities such as hepatitis C infection, HIV infection, diabetes mellitus, current use of immunosuppressive drug, hemotransfusion, smoking and, body mass index (BMI). For renal transplant candidates, information about type and duration of renal replacement therapy and use of erythropoietin was also collected. For hepatic transplant candidates, MELD score and Child-Pugh were calculated.

All volunteers, at the first visit, were submitted to blood collection for the following tests: serology for poliovirus, hemogram and albumin. Serologies for hepatitis C and HIV were included in individuals with unknown serological status. In liver transplant candidates, prothrombin time (INR) and serum levels of bilirubin and creatinine were additionally determined.

Patients without protective polio antibody titers received one to three dose of IPV with a minimum interval of 30 days between doses. Immunological response was checked 30 days after each dose of vaccine. The IPV vaccine used in this study was produced by Sanofi Pasteur (Lyon, France) and was distributed by Brazilian Ministry of Health's National Immunization Program for special groups.

2.4. Endpoints and laboratory method

The primary endpoint was seroprevalence of poliovirus protective titers. The secondary endpoint was vaccine response among candidates who at baseline did not have protective titers of antibodies to at least one poliovirus serotype. Both these outcomes were defined by detection of titers $\geq$1:8 of antibodies against all three poliovirus. Antibody titers against poliovirus 1, 2 and 3 were determined by microneutralization test, according to the protocol of the World Health Organization (12), at the Enterovirus Laboratory (WHO Regional Reference Laboratory), at Oswaldo Cruz Institute (Fiocruz, Rio de Janeiro, Brazil). Neutralization titers were expressed as the reciprocal of the highest serum dilution capable of reducing 50% of the cytopathic effect in cells. The sera were serially diluted from 1:8 to 1:512.

2.5. Statistical analysis

Categorical variables were described by their absolute counts and percentages. Numeric variables were described by their median and interquartile range. Prevalence of protective antibodies titers was estimated with its 95% confidence interval (95%CI). The central tendency of the antibody titers to each poliovirus serotype was described by their geometric mean and standard deviation.

The year of birth was categorized according to the historical milestones of polio control in Brazil: 1955, year when immunization with inactivated vaccine began; 1962, year of introduction of oral attenuated vaccine; 1973, year of implementation of the Brazilian National Immunization Program, and 1980, year of start of routine annual national vaccination campaigns.

Data analysis was conducted with R-project (R Foundation) version 3.3.1 (2016) [22].

2.6. Ethics approval

This study was approved by the Committee of Research Ethics of INI-Fiocruz (protocol number 12718913.0.0000.5262). A written informed consent was obtained from every participant.

3. Results

During the study period, 206 patients were included. Among these, there were 130 (63%) candidates for kidney transplantation; 69 (34%), for liver transplantation; 5 (2%) for heart transplantation, and 2 (1%) for combined kidney-liver transplantation. The general characteristics of the studied population are described in Table 1. Most patients (76%) were born before initiation of the National Immunization Program in Brazil in 1973 and only 11 individuals (5%) had proven polio vaccination at childhood. Five subjects reported cases of polio in household contacts.

The general characteristics of these two subgroups of SOT candidates are summarized in Tables 2 and 3. Among renal transplant candidates (Table 2), the main underlying disease was arterial hypertension (42%) and the majority (89%) of them were on renal replacement therapy, for a median time of 2 years. Among candidates to liver transplantation (Table 3), the main underlying disease was chronic hepatitis C (64%). A high proportion of them (n = 25; 36%) were listed to transplantation because of hepatocellular carcinoma. This fact probably explains the high frequency of liver transplant candidates with MELD score below 10 and Child Pugh A.

3.1. Seroprevalence

Of the 206 participants, 50 (24%; 95% CI: 19–30%) had no protective antibody titers to one or more poliovirus serotypes. Thus, 156 (76%; 95% CI: 70–81%) were protected to all three polio serotypes. There was no statistically significant difference in seroprevalence of protective antibody titers among serotypes, 31 (15%, 95% CI: 11–21%) had no protective titers for poliovirus 1; 28 (14%, 95% CI: 10–19%) for poliovirus 2 and 34 (16.5%; 95% CI: 12–22%) for poliovirus 3, 16 (8%; 95% CI 5–12%) had no antibody protective titers for the three serotypes (Table 4).

Table 2
Characteristics of the 103 kidney transplant candidates.

Variables	n (%)
Etiology of renal disease	
Hypertension	55 (42)
Glomerulopathies*	17 (13)
Polycystic kidney	15 (12)
Diabetes mellitus	13 (10)
Indeterminate cause	18 (14)
Others	12 (9)
Dialytic therapy	
No	14 (11)
Hemodialysis	102 (78)
Peritoneal dualysis	14 (11)
Dialysis time (years)	2 (0.68, 4.4)[a]
Use of erythropoietin	117 (90)
Hemoglobin (g/dL)	12 (10, 13)[a]
Total leukocytes (10^3 células/mm^3)	7 (5.5, 8.7)[a]
Platelets (10^3 células/mm^3)	216 (188, 251)[a]
Albumin (g/dL)	3.8 (3.6, 4)[a]

* Primary and secondary glomerulopathies.
[a] Median (interquartile range).

3.2. Vaccine seroconversion

Of the 50 susceptible candidates, 45 were vaccinated (1 died, 1 moved, 1 did not return, 2 transplanted before the opportunity of vaccination) and 41 returned for collection of the second serology sample (3 transplanted, 1 not returned). Thirty-nine (97%; 95% CI: 92–100%) had vaccine seroconversion after one dose of vaccine, and one individual responded only after the second dose of vaccine. This patient was born in Minas Gerais State, in 1956, and lived in rural area until the age of 14 years. He was a kidney transplant candidate, with chronic renal disease of indeterminate cause, on peritoneal dialysis since 2013 and had titers <1:8 for all three

Table 1
General characteristics of the solid organ transplant candidates.

	Renal (%)	Liver (%)	Heart (%)	Renal + Liver (%)	Total (%)
Number of patients	130 (63)	69 (34)	5 (2)	2 (1)	206 (100)
Age[a]	45.5 (34, 54)	59 (54, 63)	63 (57, 63)	62.5 (62, 63)	53 (42, 61)[a]
Year of birth					
1936–1955	24 (18)	42 (61)	3 (60)	2 (100)	71 (35)
1956–1961	17 (13)	16 (23)	2 (40)	0 (0)	35 (17)
1962–1973	42 (32)	10 (16)	0 (0)	0 (0)	52 (25)
1974–1980	17 (13)	1 (1)	0 (0)	0 (0)	18 (9)
1981–1996	30 (23)	0 (0)	0 (0)	0 (0)	30 (15)
Lived in rural area	30 (23)	23 (33)	2 (40)	2 (100)	57 (28)
Proved polio vaccine at childhood	11 (8)	0 (0)	0 (0)	0 (0)	11 (5)
Number of siblings	3 (2.0, 6.0)	4 (3.0, 7.0)	4 (3.0, 9.0)	17 (16.5, 17.5)	2 (1.0, 3.0)[a]
Children received polio vaccine					
Sabin	96 (74)	60 (87)	3 (60)	2 (100)	161 (78)
Ignored	34 (26)	9 (13)	2 (40)	0 (0)	45 (22)
Lives with children <5 years	20 (15)	19 (28)	1 (20)	1 (50)	41 (20)
Diabetes	15 (12)	21 (30)	3 (60)	0 (0)	39 (19)
Hepatitis C	3 (2)	44 (64)	0 (0)	1 (50)	48 (23)
HIV	3 (2)	2 (3)	0 (0)	0 (0)	5 (2)
Auto-immune diseases	7 (5)	3 (4)	0 (0)	0 (0)	10 (5)
Transfusion	67 (52)	30 (43)	3 (60)	2 (100)	102 (50)
Transfusion last 6 m	13 (10)	2 (3)	0 (0)	0 (0)	15 (7)
Tobacco use	4 (3)	9 (13)	0 (0)	0 (0)	13 (6)
BMI					
<18.5	9 (7)	3 (4)	0 (0)	0 (0)	12 (6)
18.5–24.9	70 (54)	28 (41)	2 (40)	2 (100)	102 (50)
25–29.9	34 (26)	22 (32)	3 (60)	0 (0)	59 (29)
>30	17 (13)	16 (23)	0 (0)	0 (0)	33 (16)

[a] Median (interquartile range).

Table 3
Characteristics of the 69 liver transplant candidates.

Variables	n (%)
Etiology of liver disease	
Hepatitis C	44 (64)
Alcohol	8 (12)
Biliary*	7 (10)
Others	10 (14)
Hepatic nodules	25 (36)
MELD	
≤10	22 (32)
11 a 18	40 (41)
19 a 25	7 (23)
Child Pugh	
A	19 (28)
B	32 (46)
C	18 (26)
Hemoglobin (g/dL)	12 (11, 14)[a]
Total leukocytes (10^3 células/mm^3)	4.8 (4, 6)[a]
Platelets (10^3 células/mm^3)	88 (60, 119)[a]
Albumin (g/dL)	3 (2.5, 3)[a]
Total bilirrubin (mg/dL)	1.5 (1, 3)[a]
Creatinine (mg/dL)	0.96 (0.8, 1)[a]
Prothrombin time (INR)	1.32 (1.2, 1.5)[a]

* Primary and secondary biliary diseases.
[a] Median (interquartile range).

poliovirus serotypes. In one individual, the second sample was collected only after the second dose of vaccine. There were no reports of vaccine-related adverse events. The geometric mean of antibody titers after application of the first dose of vaccine was high for all three serotypes, from 386 (±2.6) for poliovirus 1469 (±2.3) for poliovirus 2 and 501 (±1.7) for poliovirus 3.

4. Discussion

Serological surveys play a relevant role in identifying protection gaps in populations and in defining vaccination strategies. In the final step of polio eradication, polio seroprevalence studies have increased in importance and show significant differences between populations, which reinforce the necessity of national seroprevalence data [23–26]. Nevertheless, despite the growing number of individuals with some type of immunodeficiency, polio seroprevalence data in this population is scarce. At the best of our knowledge, a single study was conducted to estimate prevalence of polio protection in adult SOT recipients. In this study, lower protective antibody titers in SOT recipients (3%) and in the control group (12%) were detected compared with our study [20]. These results, however, may be influenced by different cutoff points used in our study (≥1:8) and in the study conducted by Huzly et al. (>1:8).

Our study was carried out among candidates to different types of SOT that were mostly born before the start of the Brazilian National Immunization Program in 1973, a fact that increases the probability of lack of previous vaccination. Although the observed seroprevalence of protective antibodies were higher than at first expected, our results show that a relevant proportion of adult SOT candidates did not have detectable levels of protective antibodies titers for at least one poliovirus. In addition, vaccination of these subjects with just one dose of IPV was associated with adequate immunogenic response.

The analysis of the general characteristics of the studied population showed that most of the individuals (95%) did not have a childhood vaccination record. Even among those born after National Immunization Programs, only 23% had proven childhood vaccination. This reflects the lack of vaccination culture among adults at Brazil and the lack of perception that the vaccination record is a document that must be kept for life. Of the eleven patients with proven childhood vaccination, three did not have protective levels of neutralizing antibodies. This finding suggests that one should not rely solely on childhood immunization record to decide whether to prescribe anti-poliomyelitis vaccination to SOT candidates.

It is important to ensure that SOT candidates have protective titers of polio antibodies prior to the start of immunosuppression, especially in areas with vaccine virus circulation. Polio antibody titers below 1:8 may indicate susceptibility or fall of antibody titers over the years, with persistent memory immunity. Nevertheless, although immune memory seems to prevent disease, it may not be capable of preventing infection and elimination of virus in feces [27]. In Brazil, the National Immunization Program has switched gradually the first three doses of OPV in childhood vaccination to IPV since 2012, however OPV is still used for the booster doses (15 months and 4 years) and in annual campaigns.

In our study, 97% of transplant candidates showed adequate immunogenic response after 1 dose of inactivated polio vaccine, with high antibody titers detected 30 days after vaccination, a finding that is similar to what has been described among healthy adults [28,29]. In the study by Huzly et al. (1997), the vaccine response of recipient organ transplant patients after 1 dose of inactivated vaccine was also good (86.6%, 86.2% and 92.4% for serotype 1, 2 and 3, respectively). It is worth noting, however, that this study was conducted in the 1990s, when the immunosuppressive regimens had a lower potency. Currently, standard immunosuppressive therapy includes the combination of at least three drugs and is associated with lower immunological response to various vaccines such as influenza, human papillomavirus, meningococcus [30–33]. Therefore, vaccination should be ideally done prior to transplantation and as early as possible in the course of the disease, as the immune response to many vaccines is suboptimal in the more advanced stages of organ dysfunction [34,35].

Some limitations of the study should be considered. There was no control group in the study that could allow a comparison of the results found in SOT candidates with those of a sample with similar demographic characteristics from the general population. Titration

Table 4
Seroprevalence rate and geometric mean antibody titers by polio serotype in solid organ transplant candidates.

	Renal (n = 130)		Liver (n = 69)		Heart (n = 5)		Renal + Liver (n = 2)		Total (n = 206)	
	Seroprevalence	GMT	Seroprevalence	GMT	Seroprevalence	GMT	Seroprevalence	GMT	Seroprevalance	GMT
All three serotypes	92/130 (71%)		58/69 (84%)		4/5 (80%)		2/2 (100%)		156/206 (76%)	
Poliovirus 1	108/130 (83%)	37.1 (3.2)	61/69 (88%)	82.1 (3.6)	4/5 (80%)	55.4 (3.9)	2/2 (100%)	256 (2.7)	175/206 (85%)	50.5 (3.5)
Poliovirus 2	112/130 (86%)	43.5 (3.1)	60/69 (87%)	112 (3.4)	4/5 (80%)	107.6 (1.9)	2/2 (100%)	128 (1)	178/206 (86%)	61.8 (3.4)
Poliovirus 3	105/130 (81%)	43.1 (3.8)	60/69 (87%)	93.2 (3.8)	5/5(100%)	60.4 (3)	2/2 (100%)	45.2 (1.6)	172/206 (84%)	56.9 (3.9)

GMT – geometric mean titers (standard deviation).

of polio antibodies after application of the first dose of vaccine was done only 30 days after application. A shorter interval, such as 7 days, would have allowed us to assess immunological memory [27] and analyze whether the vaccination boosted an immune memory response or acted as a totally new exposure to the immune system.

Future seroprevalence studies in SOT candidates and recipients in different epidemiologic context may further contribute to establish an evidence based recommendation for polio immunization in this population. Determination of antibody protective titers after initiation of immunosuppression in the post-transplant would be of great interest in assessing the persistence time of the protective antibodies. Surveillance for asymptomatic poliovirus excretion in feces in post-transplant subjects and correlation with serum gamma globulin level would be extremely relevant to identify the potential risk of prolonged elimination of poliovirus in this population.

5. Conclusions

A relevant percentage (24%) of adult candidates for organ transplantation did not have protective titers of polio antibodies. One dose of IPV against poliomyelitis was safe and resulted in protective antibody titers in 97% of transplant candidates. Our results suggest that immunization with IPV should be routinely considered for adult SOT candidates regardless of age and childhood vaccine history, especially in areas where attenuated vaccine is still used.

6. Conflict of interest

The authors declare no conflicts of interest.

All the authors have substantially contributed to the conception and design of the study, to the acquisition, analysis and interpretation of data, drafting the article or revising it critically for important intellectual content and approved its final version.

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References

[1] CDC. Poliomyelitis. Epidemiol. Vaccine Prev. Dis. 13th ed., Washington D.C.; 2015. p. 297–310.
[2] Kew OM, Sutter RW, de Gourville EM, Dowdle WR, Pallansch MA. Vaccine-derived polioviruses and the endgame strategy for global polio eradication. Annu Rev Microbiol 2005;59:587–635.
[3] Kalkowska DA, Tebbens RJD, Thompson KM. The probability of undetected wild poliovirus circulation after apparent global interruption of transmission. Am J Epidemiol 2012;175:936–49. https://doi.org/10.1093/aje/kwr399.
[4] Alexander LN, Seward JF, Santibanez TA, Pallansch MA, Kew OM, Prevots DR, et al. Vaccine policy changes and epidemiology of poliomyelitis in the United States. JAMA 2004;292:1696–701. https://doi.org/10.1001/jama.292.14.1696.
[5] WHO. Poliomyelitis 2017. <http://www.who.int/mediacentre/factsheets/fs114/en/> [accessed March 19, 2018].
[6] GPEI. Global eradication of wild poliovirus type 2 declared; n.d. <http://polioeradication.org/news-post/global-eradication-of-wild-poliovirus-type-2-declared/> [accessed December 21, 2017].
[7] Shulman LM, Martin J, Sofer D, Burns CC, Manor Y, Hindiyeh M, et al. Genetic analysis and characterization of wild poliovirus type 1 during sustained transmission in a population with >95% vaccine coverage, Israel 2013. Clin Infect Dis 2015;60:1057–64. https://doi.org/10.1093/cid/ciu1136.
[8] Anis E, Kopel E, Singer SR, Kaliner E, Moerman L, Moran-Gilad J, et al. Insidious reintroduction of wild poliovirus into Israel, 2013. Euro Surveill 2013;18:19.
[9] Kaliner E, Kopel E, Anis E, Mendelson E, Moran-Gilad J, Shulman LM, et al. The Israeli public health response to wild poliovirus importation. Lancet Infect Dis 2015;15:1236–42. https://doi.org/10.1016/S1473-3099(15)00064-X.
[10] WHO. Detection of poliovirus in sewage, Brazil; 2014.
[11] Garon JR, Cochi SL, Orenstein WA. The challenge of global poliomyelitis eradication. Infect Dis Clin North Am 2015;29:651–65. https://doi.org/10.1016/j.idc.2015.07.003.
[12] CDC. Update on vaccine-derived polioviruses — worldwide, January 2014–March 2015; 2015. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6423a4.htm> [accessed July 14, 2016].
[13] Guo J, Bolivar-Wagers S, Srinivas N, Holubar M, Maldonado Y. Immunodeficiency-related vaccine-derived poliovirus (iVDPV) cases: a systematic review and implications for polio eradication. Vaccine 2015;33:1235–42. https://doi.org/10.1016/j.vaccine.2015.01.018.
[14] Australian Government Department of Health. The Australian immunisation handbook. Groups with special vaccination requirements; 2013. <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part3~handbook10-3-3#3-3-3> [accessed March 2, 2016].
[15] Danziger-Isakov L, Kumar D, the AST Infectious Diseases Community of Practice. Vaccination in solid organ transplantation. Am J Transplant 2013;13:311–7. https://doi.org/10.1111/ajt.12122.
[16] Ministério da Saúde, Brasil. Manual dos Centros de Referência para Imunobiológicos Especiais; 2014. <http://www.saude.pr.gov.br/arquivos/File/-01VACINA/manual_crie_.pdf> [accessed March 29, 2016].
[17] Public Health Agency of Canada. Canadian immunization guide. Imminization of immunocompromised persons; 2014. <http://www.phac-aspc.gc.ca/publicat/cig-gci/p03-07-eng.php> [accessed March 2, 2016].
[18] Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58:e44–e100. https://doi.org/10.1093/cid/cit684.
[19] ABTO. Associação Brasileira de Transplantes. Vacinação pré e pós transplante de órgãos em adultos; n.d. <www.abto.org.br/download/recomendacoes-vacinacao.docx> [accessed March 29, 2016].
[20] Huzly D, Neifer S, Reinke P, Schröder K, Schönfeld C, Hofmann T, et al. Routine immunizations in adult renal transplant recipients. Transplantation 1997;63:839–45.
[21] Driss N, Ben-Mustapha I, Mellouli F, Ben Yahia A, Touzi H, Bejaoui M, et al. High susceptibility for enterovirus infection and virus excretion features in Tunisian patients with primary immunodeficiencies. Clin Vaccine Immunol CVI 2012;19:1684–9. https://doi.org/10.1128/CVI.00293-12.
[22] R Core Team. R: the R project for statistical computing; 2016. <https://www.r-project.org/> [accessed November 22, 2016].
[23] Kiffer CRV, Conceição OJ, Santos EB, Sabino E, Focaccia R. Estimated prevalence of immunity to poliomyelitis in the city of São Paulo, Brazil: a population-based survey. Braz J Infect Dis 2002;6:232–43. https://doi.org/10.1590/S1413-86702002000500004.
[24] Pírez MC, Olivera I, Diabarboure H, Montano A, Barañano R, Badía F, et al. Seroprevalence of anti-polio antibodies in a population 7 months to 39 years of age in Uruguay: implications for future polio vaccination strategies. Vaccine 2009;27:2689–94. https://doi.org/10.1016/j.vaccine.2009.02.042.
[25] Reinheimer C, Friedrichs I, Rabenau HF, Doerr HW. Deficiency of immunity to poliovirus type 3: a lurking danger? BMC Infect Dis 2012;12:24. https://doi.org/10.1186/1471-2334-12-24.
[26] Wallace GS, Curns AT, Weldon WC, Oberste MS. Seroprevalence of poliovirus antibodies in the United States population, 2009–2010. BMC Public Health 2016;16. http://doi.org/10.1186/s12889-016-3386-1.
[27] Abbink F, Buisman AM, Doornbos G, Woldman J, Kimman TG, Spaendonck MAEC. Poliovirus-specific memory immunity in seronegative elderly people does not protect against virus excretion. J Infect Dis 2005;191:990–9. https://doi.org/10.1086/427810.
[28] Resik S, Tejeda A, Diaz M, Okayasu H, Sein C, Molodecky NA, et al. Boosting immune responses following fractional-dose inactivated poliovirus vaccine: a randomized, controlled trial. J Infect Dis 2017;215:175–82. https://doi.org/10.1093/infdis/jiw492.
[29] Vidor E, Plotkin SA. Poliovirus vaccine—inactivated. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. Elsevier Saunders; 2013. p. 573–97.
[30] Kumar D, Blumberg EA, Danziger-Isakov L, Kotton CN, Halasa NB, Ison MG, et al. Influenza vaccination in the organ transplant recipient: review and summary recommendations. Am J Transplant 2011;11:2020–30. https://doi.org/10.1111/j.1600-6143.2011.03753.x.
[31] Kumar D, Unger ER, Panicker G, Medvedev P, Wilson L, Humar A. Immunogenicity of quadrivalent human papillomavirus vaccine in organ transplant recipients. Am J Transplant 2013;13:2411–7. https://doi.org/10.1111/ajt.12329.
[32] Cowan M, Chon WJ, Desai A, Andrews S, Bai Y, Veguilla V, et al. Impact of immunosuppression on recall immune responses to influenza vaccination in

stable renal transplant recipients. Transplantation 2014;97:846–53. https://doi.org/10.1097/01.TP.0000438024.10375.2d.
[33] Wyplosz B, Derradji O, Hong E, François H, Durrbach A, Duclos-Vallée J-C, et al. Low immunogenicity of quadrivalent meningococcal vaccines in solid organ transplant recipients. Transpl Infect Dis 2015;17:322–7. https://doi.org/10.1111/tid.12359.
[34] Miller MA, Rathore MH. Immunization in special populations. Adv Pediatr 2012;59:95–136. https://doi.org/10.1016/j.yapd.2012.04.017.
[35] Kim YJ, Kim SI. Vaccination strategies in patients with solid organ transplant: evidences and future perspectives. Clin Exp Vaccine Res 2016;5:125. https://doi.org/10.7774/cevr.2016.5.2.125.