Immunization status of internationally adopted children in Rome, Italy

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Abstract

Aims: International adoption medicine is a relatively new specialty in pediatrics that has emerged to address the specific health care needs of internationally adopted children in high-income countries. This study ascertains the seroprotection rate for vaccine-preventable diseases, especially against pneumococcal diseases.

Patients and Methods: We evaluated 67 internationally adopted children that reached the International Adoption Unit of Bambino Gesù Children's Hospital, Rome-Italy. We collected demographic information, data from preadoption immunization records, results of laboratory testing for immunity to vaccine-preventable diseases (tetanus, pneumococcus, hepatitis B, hemophilus influenzae type b (Hib), measles), as well as results of screening for HIV, hepatitis C, quantiferon, immunological and nutritional status.

Results: For children that had received ≥3 vaccine doses of tetanus, overall protection was 94% of 31 vaccinated children; with 1–2 vaccine doses for hepatitis B and Hib respectively, protection was 45% of 29 vaccinated children and 63% of 8 vaccinated children, respectively. For children with one or more doses of measles vaccine, protection was 63% of 32 vaccinated children. Regarding pneumococcus vaccine (documented for eight children), 88% of children with one or more doses of vaccine had developed protective immunity.

Conclusions: International adoptees without a valid vaccine record need to undergo a complete schedule in accordance with their age and should receive all the vaccines in the adoptive country's schedule.

Key words: And pneumococcal immunization, immigrant children, internationally adopted children, vaccination status

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Introduction

According to data from the Italian Department of Social Services, during the last decade the number of internationally adopted children has been continuously increasing. In 2012, 3,106 children from 55 countries were internationally adopted by families in Italy and 31,529 children were adopted in the period from 2000 to 2012.[1]

International adoption medicine, a relatively new specialty in pediatrics has emerged to address the specific health care needs of adopted children after their arrival in high-income countries. One of the primary goals of international adoption medicine is the evaluation of adoptees for protective immunity, as routinely done for immigrant children.[2] International adoptees often have incomplete or no written immunization records.[3] Written documentation of immunization can be accepted as evidence of adequacy if the vaccines, dates of administration, number of doses, intervals between doses, and age of the child at the time of immunization are consistent internally and comparable to current World Health Organization (WHO) schedules and Italian schedules.[4]

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In Italy, immunization against diphtheria/tetanus (DT), polio (injectable poliovirus vaccine) and viral hepatitis B virus (HBV) vaccines is mandatory and their cost is sustained by the national health system. The cost of mandatory vaccines (pertussis, measles, mumps and rubella (MMA), pneumococcus [pneumococcal conjugate vaccine] and hemophilus influenzae type b [Hib]) is borne by the regional health authorities, which administer them free of charge. The national recommendations include administration of DT, oral polio vaccine, HBV, Hib, pertussis and pneumococcus at 3, 5, and 11 months of age and MMR at the 15th month and no later than the 24th month of life.[5]

Since serum antibody testing is widely accepted as a means of verifying immunity in healthy children,[6,7] we have routinely used serologic testing to determine the immunization status of internationally adopted children and to guide recommendation for immunization. The aim of the present study was to assess the immunization status of internationally adopted children; to determine if proof of immunization was associated with protective antibody levels; and to evaluate if nutritional status affects protective antibody levels.

Patients and Methods

Cross-sectional data were obtained from the International Adoption Unit of Bambino Gesù Children's Hospital, Rome-Italy between September 2012 and September 2013. We evaluated 67 internationally adopted children, 39 males and 28 females. The majority of them came from Eastern Europe (38): Russia (27), Czech Republic (4), Ukraine (4), Hungary (2), Armenia (1); 19 from Africa: Congo (5), Ethiopia (5), Burkina Faso (3), Nigeria (2), Senegal (2), Burundi (1), Kenya (1) while the remaining ten came from China (4); Vietnam (2); Italy (2); India (1) and Guatemala (1). At first clinic visit, demographic data were collected for all children, including area of origin, date of birth and age at adoption. Data from preadoption immunization records were also collected, including: Type and number of vaccine doses received and any other data available from records.

Routine evaluation included a complete medical history and physical examination. Laboratory testing for all children followed the usually recommended guidelines,[4,8] including tests for HIV, HBV, hepatitis C virus (HCV) and quantifier on. Immunological status was evaluated by means of serum immunoglobulins levels, flow cytometric counts of $CD3^+$, $CD8^+$ and $CD4^+$ lymphocyte subsets. Standard methods were employed.[9]

All samples were tested for vaccine-preventable diseases: For tetanus, immunoglobulin G (IgG) enzyme-linked immunosorbent assays (ELISA) were performed. The definition of protective antibody for tetanus was >0.10 IU/mL;[10] for pneumococcus an IgG ELISA to polysaccharide capsular antigen was used, and the definition of protection was >35 mg/L.[4,11,12] An ELISA for HBV (hepatitis B surface antibody/anti-HBs) was used, and the definition of protection was ≥10 mIU/mL. For Hib, an IgG ELISA to polyribosylribitol phosphate was used, and the definition of protection was >0.03 mg/L.[4] For measles, immunofluorescent antibody assays were used for 97 % of children with cut-off values of ≥1:8 for measles.[10]

Nutritional status was evaluated using baseline anthropometrics at the time of presentation and assessing the collected data on standard WHO growth charts.

Statistical analysis

Our primary outcome of interest was defining level of protective antibody for each vaccine antigen which served as a surrogate for immunity/protection.[13] Protective antibody level was examined by the number of documented vaccine doses administered in the country of origin; 95% confidence intervals were computed.

Results

A total of 67 international adoptees attended the clinic between September 2012 and September 2013. Seven of them had undergone vaccination immediately after arrival in Italy prior to first clinic visit and were excluded from the study. The origin and main characteristics of the children included in the study are shown in Table 1. Median age at adoption was 53.88 months (range: 28.24–92.03 months). The most frequent region of origin was Eastern Europe (n = 38, 57%), followed by Africa (n = 19, 28%) and other countries (n = 10, 15%). All the children had been in orphanages before adoption.

At first clinical examination, 18 (27%) and 13 (22%) children were below the 3rd percentile for body weight and height, respectively.

Forty-four children (73%), had a valid vaccination card, in accordance with the Advisory Committee on Immunization Practices requirements,[13] whereas 16 (27%) had no immunization documents [Table 1].

Table 1: Prevalence of valid documented immunization according to the regions of origin

Region	*n* (%)		Age at initial visit (months)		Documented immunization *n* (%)
	Total	Female	Median	Range	
Other countries	10 (15)	6 (75)	31.25	24.46-02.23	8 (100)
Africa	19 (28)	5 (29)	55.97	34.30-83.93	12 (71)
Eastern Europe	38 (57)	15 (43)	55.41	32.72-93.15	24 (69)

Table 2: Prevalence of immunization according to immunization records

Vaccine antigen	0 dose		1 dose		2 dose		Total	
	n (%)	95% CI	*n* (%)	95% CI	*n* (%)	95% CI	*n* (%)	95% CI
Tetanus*	6 (50)	12-88	5 (100)	48-100	31 (94)	79-99	42 (88)	74-96
HBV	7 (29)	4-71	8 (63)	24-91	29 (45)	26-64	44 (45)	30-61
Hib	9 (67)	30-93	34 (76)	59-89			43 (74)	59-86
Measles	11 (55)	23-83	32 (63)	44-79			43 (60)	44-75
Pneumococcus	35 (46)	29-63	8 (88)	47-100			43 (53)	38-69
BCG	16		27				43	

*Tetanus <3 doses; tetanus ≥3 doses. CI=Confidence interval; BCG=Bacillus calmette–guérin; Hib=Haemophilus influenzae type b; HBV=Hepatitis B virus

All children were negative for HIV, HBV, HCV and quantiferon test for tuberculosis infection. Regarding immunological response, immunoglobulin levels were normal, and only two children had CD4 values slightly lower (20–25%) than normal.

According to vaccination records [Table 2], the number of children that had received at least one dose of vaccine was 36 (60%) for tetanus, 34 (57%) for Hib, 37 (62%) for HBV, 32 (53%) for measles, 8 (13%) for pneumococcus and 27 (45%) for Bacillus Calmette–Guérin.

Table 3 shows the results of protective immunity to each administered vaccine antigen, stratified by the number of doses received. Thirty-one children received three or more doses of tetanus vaccine, and 94% of them developed immunity against tetanus antigen, five received <3 doses, and 100% of them were immune. Twenty-nine children received two or more doses of HBV, and 45% of them had evidence of protective immunity. For those receiving one or more doses of Hib vaccine (n = 8), 63% had evidence of protective immunity. Concerning measles vaccination, 32 children were vaccinated and 63% of them became immune. According to the vaccination records, 88% of the children who had received pneumococcal vaccination (n = 8) developed protective immunity.

Among the children tested coming from Eastern Europe (n = 35), 63% was immune to tetanus, 43% to Hib, 37% to HBV, 40% to measles and 14% to pneumococcus; for those coming from Africa: (n = 17) 35% was immune to tetanus, 29% to Hib, 12% to HBV, 18% to measles and 12% to pneumococcus. Table 4 shows the results of protective immunity to each vaccine-preventable antigen of children without a vaccination record: For tetanus (n = 18) 81% was immune; for Hib (n = 17) 15% was immune; for HBV (n = 16) 71% was immune; for measles (n = 17) 53% was immune and for pneumococcus (n = 17) 76% was immune.

Regarding the children below the 3rd percentile for body weight, of the 16 tested for tetanus and the 13 tested for Hib and measles, only one appeared not to be immune after receiving the vaccination. Of the 14 tested for HBV, two did not develop immunity after vaccination. Among the 15 tested for pneumococcus, only three of the fifteen vaccinated children were immune, and seven of nonvaccinated children were not immune.

Concerning children below the 3rd percentile for body height 13 (22%), only one was not immune for tetanus after vaccination. Regarding other vaccinations, one for Hib, two for measles, three for HBV and seven for pneumococcus were not immune, as they were never vaccinated.

Table 3: Results of protective immunity to each vaccine antigen stratified by the number of doses received

Vaccine	Other countries		Africa		Eastern europe	
	n (%)	95% CI	*n* (%)	95% CI	*n* (%)	95% CI
Tetanus						
<3	2 (100)	16-100	4 (25)	1-81	5 (100)	48-100
≥3	6 (100)	54-100	7 (86)	42-100	18 (94)	73-100
HBV						
<2	3 (67)	9-99	5 (20)	1-72	7 (57)	18-90
≥2	5 (40)	5-85	7 (29)	4-71	17 (53)	28-77
Hib						
≥1	6 (100)	54-100	7 (71)	29-96	21 (71)	48-89
Measles						
≥1	6 (50)	12-88	5 (60)	15-95	21 (67)	43-85
Pneumococcus						
≥1	2 (100)	16-100	2 (100)	16-100	6 (83)	36-100
BCG						
≥1	4 (100)	40-100	7 (100)	59-100	16 (100)	79-100

CI=Confidence interval; Hib=Haemophilus influenzae type b; HBV=Hepatitis B virus; BCG=Bacillus calmette–guérin

Table 4: Protective immunity to each vaccine antigen of children without a vaccination record

Vaccine antigen	No clinical record	
	n (%)	95% CI
Tetanus	18 (100)	81-100
HBV	16 (38)	15-65
Hib	17 (94)	71-100
Measles	17 (53)	28-77
Pneumococcus	17 (76)	50-93
BCG	16 (100)	79-100

CI=Confidence interval; Hib=Hemophilus influenzae type b; HBV=Hepatitis B virus; BCG=Bacillus calmette–guérin

Discussion

The continuous increase of international adoptions is a new challenge for pediatricians. Guidelines for immunization of internationally adopted children are lacking. Our study reports the correlation between protective antibody levels and performed vaccinations, to determine whether internationally adopted children had serologic evidence of protection against vaccine-preventable diseases and to determine if documentation of immunization was associated with protective antibody levels. In order to compare our results with previously published data in adopted children,[12-15] we report data for children who received ≥3 doses of vaccine for tetanus, ≥2 doses of HBV and ≥1 dose of measles, Hib and pneumococcal vaccines.

For tetanus, the Verla-Tebit study[15] found a lower proportion protected (87%) compared to our study (94%), which may be due to the different definitions of protection that were used (>0.50 IU/mL compared to >0.10 IU/mL in our cases).

The results of HBV testing are difficult to compare to other studies since many did not provide dose-specific data. For children with ≥2 doses of vaccine, we found that the proportion protected in our study was lower (45%) compared to the Verla-Tebit study, where 94% of children with ≥2 doses of vaccine were protected.[15]

There have been very few studies published about Hib and pneumococcal vaccine protection levels of children adopted from abroad.[16] To the best of our knowledge, our study is one of the first providing data on specific antibodies toward Hib and pneumococcal antigens in internationally adopted children. Only 62% of evaluated children had documentation of Hib vaccination, and 13% had records for pneumococcal vaccination. Only 76% of children with ≥1 documented dose of Hib vaccine had protection while 94% children without valid documentation had protection. Such high protection in this group of children may also be related to a past pneumococcal infection.

Regarding pneumococcal protection, 88% of children with ≥1 documented dose (eight children) had protection, whereas 76% of children without valid documentation were found to be immune.

In our study, 60% of children had documentation of measles immunization, and in contrast to other studies, we found that the majority of children with at least one dose of vaccine were protected.[13] In addition, measles protection increased with age regardless of vaccine history, suggesting that many children had prior infection with wild-type measles or had undocumented vaccination.

Since screening tests are recommended for all internationally adopted children, serologic testing for vaccine antibodies can be performed at the initial visit to guide immunization decisions for those without a complete immunization record. Given the high proportion of protective antibody levels observed in children with documentation of immunizations, a reasonable approach would be to consider birth country vaccine doses to be valid, similarly to the recommendations for other immigrants,[4] and to complete the series as appropriate for the child's age. If serologic testing is done and protective antibody levels are found for tetanus, Hib, pneumococcal or HBV, children should still complete the immunization series for that vaccine according to their age, if additional doses of vaccine are recommended by the national schedule. Furthermore, where it is not possible to perform pneumococcal serology testing, it is always recommended to supply an additional dose of pneumococcal vaccine.

To better interpret these results, some limitations should be considered. First, the small number of sample size (children and regions of origin); furthermore, the lack of medical records not allowing to collect clinical complete medical history before adoption (pharyngeal pneumococcal carriage or previous pneumococcal infection). Another potential bias is that in some children the presence of antibodies to measles could reflect a past infection by wild virus more than the vaccine induced immunity.

In any case, our recommendation is to vaccinate with a dose of MMR vaccine all children older than 15 months of age.

Additional studies to examine the cost-effectiveness of different strategies for immunization in internationally adopted children should be considered while taking into account the medical, financial and psychological effects of administering unnecessary immunizations.

Conclusion

Even if in some children we observed a divergence between the vaccination records from the original countries and the results of serological screenings, whenever it is not possible to perform serologic testing to verify immunity, children without a vaccine record need to undergo a complete schedule in accordance to their age. Moreover, particularly in the Italian context, the general recommendations on immunization include pneumococcal and meningococcal vaccines. Furthermore, for children coming from Eastern Europe with a valid vaccine card, the vaccination schedule should be continued according to their age; children without a valid vaccination card should receive the full schedule according to national recommendations. All those ≥15 months of age should receive one dose of MMR vaccine. Serologic testing for hepatitis B should be

performed, and susceptible children should receive a complete series (three doses) of HBV.

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