

Immunization status of internationally adopted children in Italy

Enza Viviano^{a,*}, Francesco Cataldo^b, Salvatore Accomando^b,
Alberto Firenze^a, Rosalia Maria Valenti^a, Nino Romano^a

^a Department of Hygiene and Microbiology, University of Palermo, Via Del Vespro 133, 90127 Palermo, Italy

^b Department of Pediatrics, University of Palermo, Italy

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Abstract

An increasing number of internationally adopted children is coming to Italy, and their immunization status is unknown. We evaluated the immunization status of such children in Palermo, Italy.

We searched for the presence of a BCG scar in 88 children, 49 boys and 39 girls (mean age 76 ± 32 months), most of whom (98%) came from Eastern Europe. Presence of BCG scar was observed in 59 (67.1%) of them, included five children without any pre-adoptive medical records. Twenty-three out of 29 children without any evidence of BCG scar were tested by Mantoux. Seven (30.4%) of 23 were tuberculin positive and diagnosed as having latent tuberculosis infection. We also examined immunization status against poliovirus 1–3, tetanus, diphtheria, pertussis, measles, mumps, rubella and hepatitis B of 70 internationally adopted children and we compared it with the pre-adoptive immunization records of their birth country. Protective titers ($>1:8$) against poliovirus 1–3, were found respectively in 67.1%, 91.4%, 42.8% of 70 immunized children, and only 38.5% of them had at the same time full protection against all three types of poliovirus. Protective titers against tetanus and diphtheria were found in 91.4% and 95.7% of 70 vaccinated children. Presence of antibodies against pertussis, measles, mumps and rubella was observed respectively in 16 (32.6%) of 49, 40 (62.5%) of 64, 28 (56%) of 50 and 24 (85.7%) of 28 children who had received the vaccine. As regards hepatitis B, only 20 of 29 vaccinated children had detectable hepatitis B surface antibodies, while four of 29 vaccinated and two of 41 not vaccinated children were positive for both hepatitis B surface antibodies and hepatitis B core antibodies. Finally three of 41 not vaccinated children were both hepatitis B surface antigen and hepatitis B core antibodies positive.

No relation was found between health status and immunization and between age and antibody positiveness of vaccinated children except for hepatitis B, therefore the youngest immunized children were more likely to be hepatitis B surface antibodies positive.

Our data suggest that internationally adopted children should be tested for their immunization status on arrival in the adopting country, because they are not protected in a sufficient way against vaccine-preventable diseases and their pre-adoptive immunization records sometimes are lacking and frequently are scarcely reliable.

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1. Introduction

During last decade international adoption of children has increased in Italy, in close connection with the reduction of births and the number of adoptable Italian children. The number of international adoptions have more than doubled from 1600 to 3398 between 1993 and 2004 [1]. In addition, the

distribution of birth countries of these children has changed markedly over time: before 1990 the main birth countries of the internationally adopted children were Brazil, Chile and India, the Eastern European countries are now the main source, accounting for more than 60% of children placed in 2000–2004 [1].

Internationally adopted children are a particularly vulnerable population [2–4], as they come from underdeveloped countries with inadequate health care resources, and have numerous health problems, including retarded growth, iron

* Corresponding author. Tel.: +39 91 6553659; fax: +39 91 6553647.
E-mail address: eviviano@igiene.unipa.it (E. Viviano).

deficiency anemia, rickets, infectious disease, and emotional and behavioral problems. One important health problem concerns their immunization status against vaccine-preventable diseases [5–10]. Indeed, although most of them leave their country of birth with a medical record and a written immunization certificate, there are serious doubts concerning the accuracy of the vaccination records and the effectiveness of vaccines received, because immunogenicity may have been impaired due to inappropriate storage and immune response may have been decreased due to malnutrition. In addition, immunization schedules in these countries of birth often differ from those in Italy.

To our knowledge, there are sparse data concerning the immunization status of children who came to Italy following an international adoption, as well as their risk of infectious vaccine-preventable diseases. A recent Italian study on 45 adopted children coming from developing countries reported that almost half of them were not protected against diphtheria, tetanus and poliovirus and only 31% resulted immunized against hepatitis B (10).

These reasons prompted us to examine the immunization status of internationally adopted children, and to compare it with the immunization certificates of their birth countries.

2. Materials and methods

From April 2002 to March 2005 the International Adoption Center at II Pediatric Clinic of Palermo University evaluated 88 internationally adopted children, 49 males and 39 females (mean age 76 ± 32 months, range 17–153 months). The majority of them came from Eastern Europe: Ukraine (64), Russia (11), Poland (4), Rumania (3), Bulgaria (2), Hungary (2); the remaining two came from India. All of them resided in orphanages before adoptions and were referred to our center by their adoption agencies, the Juvenile Law Court of Palermo or adoptive parents' groups. They represented 92.6% of the children who had been internationally adopted in the district of Palermo during the studied years. Most of them (81/88,) were seen in our center within 4–6 weeks of their arrival in Italy. Only 7/88 children came to our center after a longer time (six subjects after 8–10 months, and one after 2 years).

The majority of the internationally adopted children (83/88, 94.3%) had medical records from their birth countries that had been translated from the original into the Italian language by official bilingual translators of the Italian Embassy. The remaining five children lacked medical records from their birth countries. The medical records included the child's medical history and vaccinations received in the native country.

Informed consent to participate in the study was requested to adoptive parents and the study protocol was approved by Ethical Committee of Pediatric Department of Palermo University. The presence of the scar for Bacillus Calmette-Guerin (BCG) vaccine was searched in each child and compared with the pre-adoptive immunization records. When the BCG scar

was present, chest-X-ray and erythrocyte sedimentation rate (ESR) were performed. When the BCG scar was lacking, a tuberculin skin test (TST) was performed by the Mantoux technique with purified protein derivative (PPD, five tuberculin units). Chest radiograph and ESR were also performed when the TST was weakly or strongly positive (≥ 5 and 10 mm, respectively, after 48–72 h). Seventy-five/eighty-eight of the internationally adopted children (40 males, 35 females) provided a blood sample to determine antibody titers against tetanus, diphtheria, pertussis, poliovirus 1–3 and measles–mumps–rubella (MMR). Serologic markers for hepatitis B infection, surface antigen (HBsAg), surface antibody (HBsAb), core antibody (HBcAb), were also assayed.

Seven children could not be tested because their new Italian parents refused to give informed consent for serological assays, and six others had been vaccinated during the 8–10 months between their arrival in Italy and their evaluation at our centre.

The 75 children serologically tested (70 with and five without pre-adoption immunization records) were from Ukraine (55), Russia (10), Poland (4), Rumania (2), Bulgaria (2), Hungary (2) and India (1).

The results of serological assays of 70 adopted children were compared with the pre-adoption immunization records.

The assays for tetanus, pertussis and MMR antibody as well as for *hepatitis B virus* (HBV) markers were carried out by standard enzyme-linked immunosorbent assay (ELISA). Diphtheria and poliovirus 1–3 antibodies titers were carried out with neutralization tests. The micro-neutralization assay to measure immunity to poliovirus was performed according to the guidelines for WHO/EPI collaborative studies on poliomyelitis [11], the titration of samples starting at 1:5.

Statistical analysis were performed using χ^2 -test and a *P*-value of <0.05 was considered to indicate significance.

3. Results

A BCG scar was observed in 59/88 (67.1%) internationally adopted children (included the five children without pre-adoptive medical records), whereas it was absent in 29/88 (32.9%) of them, despite certification of a previous BCG vaccination in their pre-adoption immunization records (Table 1). All of the children with a BCG scar did not pre-

Table 1
Bacille Calmette-Guerin (BCG) immunization and tuberculin skin test (TST) screening of international adopted children

	Positive/tested [n (%)]
BCG scar positive	59 ^a /88 (67.1)
BCG scar negative ^b	29/88 (32.9)
TST positive > 10 mm	2/23 (8.7)
TST positive > 5 mm	5/23 (21.7)

^a Fifty-four with pre-adoptive records and five without pre-adoptive records.

^b Only 23 were submitted to TST.

form TST, only ESR and a chest radiography that gave normal results in each adopted child.

TST was carried out on only 23/29 children without a BCG scar, because the parents of the remaining six children refused it. Sixteen/twenty-three (69.6%) of them had a negative TST. Five (21.7%) had a moderately positive TST (TST \geq 5 mm) (Table 1), with a normal ESR, normal chest-X-ray, and no clinical signs of tuberculosis. They were diagnosed as having latent tuberculosis infection (LTBI), and received isoniazid prophylaxis, because we did not have documentation of their previous exposure history. Their native countries were Ukraine (four children) and Bulgaria (one child). The two remaining internationally adopted children without a BCG scar had a highly positive TST (TST \geq 10 mm) (Table 1). They did not have tuberculosis symptoms; their ESR and chest X-rays were normal and they were diagnosed as having LTBI and treated with isoniazid. Their native country was Ukraine.

All adopted children with pre-adoptive records have reported a complete immunization (\geq 3 vaccine doses) against poliovirus types 1–3, whereas, neutralizing antibody were detected in 82.8%, 98.6% and 62.8% of samples respectively (Table 2). The positive rates were lower if, according to WHO, only titers higher than 1:8 were considered protective (Table 2). In addition, if antibodies against all three types of poliovirus were considered together, only 27/70 (38.5%) of the adopted children were contemporaneously fully protected (titers > 1:8) against the three poliovirus types.

Two children were simultaneously sero-negative to all three types of poliovirus: one, who is 5 years old, coming from Ukraine, was residing in Italy for 1 month. This child, in despite of documentation of complete vaccination in her pre-adoption record, also lacked antibodies against tetanus, diphtheria and hepatitis B, all of which are compulsory vaccinations in Italy (Table 3). The second one (4 years old), from Bulgaria, was living in Italy for 2 years and lacked a pre-adoption immunization record from the native country. The other four children without certificate were fully protected against poliovirus 1–3.

For tetanus and diphtheria (Table 4), 91.4% and 95.7%, respectively, of the tested children with pre-adoptive records had antibody titers higher than the cut-offs (0.1 and 0.01 IU/ml, respectively), which are considered to be protective [12,13]. However some authors define full protection against diphtheria and tetanus only with values higher than

Table 2

Evaluation of antibodies titers for poliovirus 1–3 among 70 internationally adopted children with reported vaccination in their pre-adoptive immunization records

Antibodies against poliovirus	Titer \geq 1:5 positive/tested [n (%)]	Titer \geq 1:10 positive/tested [n (%)]
1	58/70 (82.8)	47/70 (67.1)
2	69/70 (98.5)	64/70 (91.4)
3	44/70 (62.8)	30/70 (42.8)

Table 3

Childhood immunization schedule Italy, 2005–2007^a

Vaccine	Schedule
Diphtheria–tetanus–pertussis	3, 5, 11–13 months, 5–6 years, 11–15 years
Inactivated polio	3, 5, 11–13 months, 5–6 years
Hepatitis B	birth (only if mother HBsAg+) – 3, 5, 11–13 months
<i>Haemophilus influenzae</i> type b	3,5, 11–13 months
Measles, mumps, rubella	13–15 months, 5–15 years
Pneumococcal	3–36 months
MenC	3–36 months
Varicella	13–24 months, 11–15 years

^a Gazzetta Ufficiale Repubblica Italiana No. 86 14/04/05 Suppl. Ord.

Table 4

Evaluation of antibodies titers for tetanus, diphtheria in the 70 adopted children with reported vaccination in their pre-adoptive immunization records

Antibody against	Positive ^a /tested [n (%)]
Tetanus	64/70 (91.4)
Diphtheria	67/70 (95.7)

^a Values higher than 0.1 IU/ml for tetanus and 0.01 IU/ml for diphtheria.

0.1 IU/ml [14,15] and 0.5 IU/ml, respectively [16]. By these criteria, only 72.8% of the children would be fully protected against tetanus and 85.7% against diphtheria, on the contrary, all of the children have reported in their pre-adoption immunization records a full immunization (\geq 3 vaccine doses).

Among the five children without certificate only one, who is 3 years old, was negative for diphtheria.

No relation was observed between immunity for polio–diphtheria–tetanus and age of the children. The previous immunization records of 70 internationally adopted children also diverged from the serological results obtained for not compulsory vaccination in Italy namely pertussis, measles, mumps and rubella. The antibodies against these infectious diseases in many of them were absent, even if their pre-adoptive records reported previous vaccinations, whereas presence of antibodies were observed among many of these children, though their pre-adoptive immunization records did not refer previous vaccinations (Table 5).

Vaccinated children were more likely to be antibodies positive than not immunized children only for rubella (Table 5). According to the immunization records, the vaccine doses

Table 5

Evaluation of antibodies positivity for pertussis and measles–mumps–rubella (MMR) in the 70 children with and without reported vaccinations in their pre-adoptive immunization records

Antibody against	Antibody positive/no. of children with reported vaccinations in their pre-adoption records [n (%)]	Antibody positive/no. of children without reported vaccinations in their pre-adoption records [n (%)]	χ^2 -test, <i>P</i>
Pertussis	16/49 (32.6)	12/21 (57.1)	0.055
Measles	40/64 (62.5)	3/6 (50)	0.550
Mumps	28/50 (56)	8/20 (40)	0.230
Rubella ^a	24/28 (85.7)	22/42 (52.3)	0.009

^a Values higher than 15 IU/ml.

Table 6
Evaluation of hepatitis B markers in the 70 children with pre-adoptive immunization records^a

Hepatitis B markers	HBsAb+ ^b , no. of children	HBsAb+ HBcAb+, no. of children	HBsAg+ HBcAb+, no. of children
29 Children with reported vaccinations	20	4	0
41 Children without reported vaccinations	3	2	3

^a 38/70 (54.2%) adopted children had no serological markers for HBV, although their pre-adoptive records reported previous hepatitis B vaccination for five of them.

^b Values > 10 U/ml.

administered in their countries corresponded to immunization schedule recommended by WHO. No significant association was found between antibody presence and age of the children.

As concerns hepatitis B (Table 6), that in Italy is a compulsory vaccination, among 29 children with reported vaccination in their pre-adoptive records, 20 (68.9%) were positive for hepatitis B surface antibody (19 received three vaccine doses, and one children only one dose). Moreover, also three of 41 children without reported vaccination in their records were positive for HBs antibody. Besides, four of 29 vaccinated against hepatitis B (two received three doses of vaccine and two only two) were positive for both anti-HBs and anti-HBc, as well as two of 41 who had not reported vaccination. Among 41 children without vaccination, three had HBsAg and HBcAb. The remaining 38 (54.2%) of 70 internationally adopted children had no serological markers of hepatitis B, although their pre-adoptive records reported previous HBV vaccinations for five of them (range: 6–12 years old). Immunized children were more likely to be HBsAb positive than not vaccinated children ($P < 0.0005$) and, among immunized children, significant association was found between youngest children (1–4 years) and presence of HBs antibody ($P = 0.0356$).

Among five children without immunization record, three were negative for all hepatitis B markers, one was positive for HBsAb and one for HBsAb and HBcAb also.

Many of adopted children had associated medical problems including malnourishment (51.2%) similarly to other population of internationally adopted, but no relation was found between immunity and health status.

4. Discussion

International adoptions have been increasing in our country during the last decade, pressing health workers to deal with new and troublesome problems. In particular, infectious diseases need appropriate screening [17–21], however the care of adopted children also poses challenges to the accept-

ability of vaccinations reported in pre-adoption certificates, because these may be not written, wrongly reported or not correspond to the recommended Italian vaccination schedule [5–10].

In this respect, we evaluated 88 internationally adopted children for tuberculosis, nearly all (86/88) coming from Eastern Europe, and we examined immunization status against poliovirus, tetanus, diphtheria, measles, mumps, rubella and hepatitis B of 75 of them, 70 reported a pre-adoption immunization records and five lacked medical record from their birth countries. Internationally adopted children are at risk for having active or latent tuberculosis, because this infection is highly prevalent in places from which many of them come, namely Eastern Europe and South Asia [19,20]. For this reason tuberculosis screening is recommended as soon as they arrive in the adopting country. In our casuistry, 83/88 of the internationally adopted children had a pre-adoption record that certificated a BCG vaccination. However, 29/88 lacked a BCG scar, of whom seven had a positive TST and were diagnosed as having LTBI. Our results are in accordance with previous studies, mainly on internationally adopted children coming from East Europe [3,18–21], and emphasize the importance of maintaining a high index of suspicion for the sake of these children and also to prevent the transmission of tuberculosis to other household members, as reported previously [22].

Our data also underline that many internationally adopted children, in despite of their satisfactory vaccination records, do not have adequate protection against poliomyelitis. Indeed, only 67.1%, 91.4% and 42.8% of our 70 studied children had antibody titers $\geq 1:10$ for poliovirus 1–3, respectively, and only 38.5% of them were fully protected against all three types of poliovirus. Of great concern, two of our studied children were sero-negative for all three types of poliovirus. Our findings are similar to previous studies on internationally adopted children [5,7,8] that showed complete poliovirus immunization of no more than 2/3 of them. These findings are high divergent when compared with those reported in the Italian population. A recent study [23] of Italian children (aged 0–15 years) showed that the rates of antibodies (titer > 1:8) against poliovirus 1–3 were respectively 97.3%, 96.6% and 92.2%. The reasons of these low rates in antibodies against poliovirus among internationally adopted children are uncertain and might be due to out-dated, poorly stored or biologically less powerful vaccines, and inaccurate immunization records from their birth countries. We also observed lower seroprevalence to types 3 and 1 than to type 2 poliovirus. The precise causes of this finding, already reported in some parts of developing world [7,24], are not clear. Available data suggest that type 2 poliovirus infection (or type 2 polio-vaccine virus) and infections of other enteric pathogens, very common in some developing countries, may interfere with the immune response to type 1 and 3 polio-vaccine virus [25]. Moreover, the intervals between oral doses of each type of vaccine might be important in view of the prolonged enteric excretion of vaccine virus and

its potential interference with response to subsequent doses [26]. However, further investigations of these and other factors, that might influence the serological response to OPV in children of developing countries, are needed. A very good immunological response was observed in all of the 70 adopted children who were reported to have received at least three doses of diphtheria and tetanus vaccines, with seropositivity of 95.7% and 91.4%, respectively, using cut-off values 0.01 IU/ml for diphtheria and 0.1 IU/ml for tetanus. Conflicting data concerning these vaccinations are reported in the literature, ranging from high to low antibody rates [5–10]. However, a full comparison of our data with those reported in literature would not be valid because these values may vary according to laboratory methods used and cut-off values chosen, which are not always reported [5–10]. The available data in Italy regards vaccines administered to the children between 12 and 24 months, that for diphtheria and tetanus indicates a percentage of 96.5% [27].

As regards the other vaccinations recommended by the Italian immunization schedule, the antibodies against *Bordetella pertussis*, measles virus, mumps virus and rubella virus were found in only a part of the children whose pre-adoptive records reported vaccinations and no relation between immunization and age was found. Conversely, antibodies were present in several adopted children whose pre-adoptive records did not report the vaccinations, perhaps as result of a past infection or not registered vaccination. Also these findings clearly indicate that the pre-adoptive immunization certificates of the internationally adopted children are scarcely reliable. Any way if we analyze the vaccines administered to Italian children between 12 and 24 months Ministry of Health data indicates for pertussis a percentage of vaccinated children of 95.6% and for MMR of 83% [27].

Hepatitis B is a world wide problem in all adopted children coming from developing countries, with the highest rates of infection in those from eastern Europe [3,8,20], especially from Romania [21]. Many of our studied children, 41 of 70 (58.5%), according to their vaccine certificates, were not immunized against hepatitis B. This finding is consistent with the fact that hepatitis B vaccination is not usually performed in most countries from which they come and where instead the virus is highly spread, suggesting the need for hepatitis B serological screening as soon they come to the adopting country. In Italy, children between 12 and 24 months vaccinated against hepatitis B exceed the 95%, since it is a compulsory vaccination [27].

On the other hand, nine adopted children, three of who were reported to have received hepatitis B vaccination in their country of origin, had serological evidence of a past hepatitis B infection, specifically anti-HBc and including three with HBsAg. These data suggest that serological screening on immunization status for hepatitis B should be performed in all newly internationally adopted children to identify and, when found, to treat patients with hepatitis B infection not diagnosed in their native country.

Finally, with our work we found that a high proportion of children in the international adoption group was not protected in a sufficient way against those diseases which are targeted with vaccinations in Italy. At this regard, in agreement with the Italian laws, at present we can refer only to a Circular by the Ministry of Health [28] that suggests re-vaccinating subjects who have unknown, incomplete or undocumented vaccination status.

However, we and other groups [5–10] have observed sometimes lack of immunization schedules and frequently that there are divergences between the registered records of the original countries and the results of serological screenings. Therefore, as guidelines following this study, we suggest that all the internationally adopted children, with and without any official immunization records, should be always tested for their immunization status as soon as they come to the adopting country, in order to perform vaccinations whether antibodies titer are inadequate. Future research efforts are necessary to implement the proposed guidelines regarding immunization status of internationally adopted children, because at present only limited data are available to determine the most cost-effective approach to ensure their complete immunization while avoiding a possible extra-immunization effects.

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