

Improved general health of international adoptees, but immunization status still insufficient

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Received: 10 September 2008 / Accepted: 1 December 2008 / Published online: 6 January 2009
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Abstract We studied the demographic and clinical data from 495 adopted children seen between January 2002 and January 2007 to evaluate the medical condition and immunization status of international adoptees. The data of children from Chinese origin (53.5%) were compared to children arriving from other countries. Medical problems requiring treatment were present in 42.8% of the children. Parasitic gastrointestinal infection (22.0%) and skin abnormalities (22.4%) were diagnosed most often. Hepatitis B (1.2%) and tuberculosis (1%) were documented in some children; HIV, hepatitis C, and syphilis were not seen in any of the children. Antibody levels against diphtheria and tetanus were insufficient in about half of all children, particularly in those from China. In conclusion, most adoptive children had a good general health, with only a few having major medical problems. Many adoptive children had an inadequate immunization status.

Keywords China · Infectious diseases · Medical screening · Immunization

Abbreviations

ESR	erythrocyte sedimentation rate
CRP	C-reactive protein
PPD	purified protein derivate
BCG	Bacillus Calmette–Guérin
LTBI	latent tuberculosis infection

ToBI	toxin-binding inhibition
Anti-HBs	hepatitis B surface antibody
OR	odds ratio
CI	confidence interval
SD	standard deviation
WHO	World Health Organization
HbsAg	hepatitis B surface antigen
CCAA	China Center of Adoption Affairs
GAVI	Global Alliance for Vaccines and Immunization

Introduction

The number of international adoptees in the Netherlands has increased in recent years. In 2005, 1,420 children were adopted, representing an annual increase of almost 10% since 1995 [5]. However, fewer children are being presented for adoption because of local policies to find domestic adoptive parents [5]. As a result, more adoptive parents are willing to accept children with a special need, such as a congenital disorder or hepatitis B, as these children are less likely to find adoptive parents in their own country. While in the past, most adopted children came from Colombia and Brazil, nowadays up to 57% of all children arriving in the Netherlands come from China [5]. Since 1979 all children entering the Netherlands for adoption are screened medically, because many come from areas with limited health-care resources [15]. In spite of the extensive medical screening upon arrival in the Netherlands, there is little recent information on the health status of international adoptees. For this reason, we evaluated the medical condition and immunization status of international adoptees seen in our hospital during the past 5 years.

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Materials and methods

Demographic and clinical data from recently arrived, international adoptees seen at the Wilhelmina University Children's Hospital Utrecht in the period between January 2002 and January 2007 were retrieved from hospital records. The following data were collected: pre- and post-adoptive medical history, physical examination findings, and the results of a standard diagnostic screening program were collected. This program consisted of an extensive hematology and biochemistry analysis (full blood count including a white cell differentiation and red cell indices, eosinophil count, reticulocyte count), erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP), and levels of serum calcium, phosphate, albumin, creatinine, alkaline phosphatase, aminotransferases, and γ -glutamyl transpeptidase. Hemoglobin electrophoresis was performed if hemoglobinopathy was suspected.

Urinalysis was performed. A urinary tract infection was defined by bacteriuria, pyuria (>20 WBC/high power field) or a positive nitrite test in repeated urine analysis. Stools were examined for *Salmonella*, *Shigella*, *Campylobacter*, and *Yersinia* species, and for parasites (using the triple feces test [21]). As required by the Dutch immigration law, a chest X-ray was taken. A purified protein derivative (PPD) was performed on children without a Bacillus Calmette–Guérin (BCG) scar. Latent tuberculosis infection (LTBI) was defined by a positive PPD (>5 mm) without symptoms or radiographic findings; active (pulmonary) tuberculosis was diagnosed when clinical signs or symptoms were present with or without radiographic findings and was confirmed by a positive culture of gastric aspirate. Also serology for HIV, hepatitis B and syphilis was done; hepatitis C serology was added in 2003. The immunization status was determined against diphtheria, tetanus, poliomyelitis, and hepatitis B. Concentrations of antibodies to diphtheria and tetanus were measured using toxin-binding inhibition (ToBI) [9].

The levels of neutralizing antibodies against poliovirus types 1, 2 and 3 were determined by microneutralization assay, and converted to IU/ml by comparison of an in-house reference serum of known potency. To detect immunization against hepatitis B, hepatitis B surface antibody (anti-HBs) levels were measured using enzyme immuno assay.

Children younger than 6 months underwent the standard Dutch screening for inborn errors of metabolism (congenital hypothyroidism, phenylketonuria, congenital adrenal hyperplasia) until January 2006, after which 14 other diseases were added [2].

Statistics

Data were analyzed using SPSS. A χ^2 -test was used to determine whether the health condition of the largest group of adoptees, the Chinese children, differed from that

of the children originating from other countries. Relative risk, in the form of odds ratios (OR) and 95% confidence intervals (CI), was calculated.

Results

Demographic and clinical characteristics

A total of 495 children were evaluated. Although the children originated from 25 countries, the majority came from Asia, and most were Chinese girls (Table 1). The median age upon arrival in the Netherlands was 17.8 months (range 0–131 months), but the Chinese children were slightly younger than the children from other countries (median age in months: 17.1 versus 20.6).

Most children were screened within 2 months of arrival (mean 37.4 days, range 2–303 days), and in many cases medical records from the children's birth countries were not available. If present, these records were often incomplete or written in the native language only. The majority of adoptees were in a good physical condition. Malnutrition, defined as a weight-for-height less than two standard deviations (SD) of the World Health Organization (WHO) child growth standard [7], was seen in 13 of 461 children (2.8%).

Fifty-three children (10.7%), had congenital disorders, and these disorders were more common among Chinese children (14.7% versus 6.1%, OR 2.66, 95% CI 1.41–5.04). A cleft lip or palate was the most frequent congenital malformation, being present in 18 children (15 of which were Chinese). Complete correction had been performed in the country of origin in six children (33%) and partial correction in six other (33%). Fourteen children (2.8%) had congenital heart disease, and again, Chinese adoptees were significantly more often affected (4.5% versus 0.9%, OR 5.41, 95% CI 1.20–24.42). The condition had been corrected in all children. The Dutch parents of children with either a cleft lip or palate or a congenital heart disease had all been informed of the condition prior to adoption, and had chosen to adopt a "special need" child.

Twenty-one children had mild dysmorphic features, such as polydactyly (five children) or a clubfoot (four children). There was no significant difference in incidence between the Chinese children and the other children ($p=0.7$). Nearly one third of the children had skin disorders, most of which were mild. A skin abnormality was diagnosed in 111 children (22.4%), including: very dry skin or eczema in 69 children (13.9%), scabies in 17 children (3.4%), diaper dermatitis in 12 children (2.4%), fungal dermatitis in 10 children (2.0%), hemangioma in two children (0.4%) and bacterial skin infection in one child (0.2%).

Table 1 Country of origin and sex of adoptees screened between 2002 and 2007

Continent and Country	Total (%)	Male	Female
Asia			
China	265 (53.5)	29	236
Taiwan	23 (4.6)	13	10
India	19 (3.8)	3	16
Thailand	8 (1.6)	7	1
Philippines	6 (1.2)	4	2
Other	8 (1.6)	3	5
South and Middle Americas			
Colombia	56 (11.3)	38	18
Haiti	33 (6.7)	21	12
Brazil	16 (3.2)	9	7
Other	8 (1.6)	5	3
Africa			
Ethiopia	16 (3.2)	11	5
South Africa	16 (3.2)	7	9
Nigeria	9 (1.8)	4	5
Other	3 (0.6)	3	0
Europe			
Poland	5 (1.0)	2	3
Other	4 (0.8)	2	2
Total (%)	495 (100.0)	161 (32.5)	334 (67.5)

Blood, urine, and stool analyses

Hematological and biochemical screening was performed in 493 children. Anemia (hemoglobin <12 g/dl) was diagnosed in 38 children (7.7%). Hemoglobin electrophoresis was performed in 13 children with anemia and/or aberrant red cell indices. Of these, seven children (four of Chinese origin) had α -thalassemia trait, five had sickle cell trait (three originating from Haiti), and one had both (also originating from Haiti). Eosinophilia (>400 cells/mm³) was detected in 77 children (15.6%). Of these children, 20 had atopic skin disease, 13 had gastrointestinal parasites, and eight had both. Transient elevation of aminotransferases, without further clinical consequences, was observed in 43 children (8.7%). None of the children had serious biochemical abnormalities.

The urine of 468 children was analyzed, six (1.2%) of whom had a urinary tract infection. Ultrasonography revealed urinary tract abnormalities in one child. Parasites were detected in the stools of 108 of 492 (22.0%) children tested. Eleven children had multiple parasites. *Giardia lamblia* was the main parasite and was detected in 72 children (14.6%). Chinese children had a *G. lamblia* infection significantly less often than the other children (11.4% versus 18.4%, OR 0.57, 95% CI 0.34–0.94). Other parasites identified were *Dientamoeba fragilis* (13 children), *Hymenolepis nana* (13 children), *Trichuris trichiuria* (nine children), *Ascaris lumbricoides* (eight children), *Isospora belli* (four children), *Strongyloides stercoralis*

(two children), *Necator americanus* (one child) and *Chilomastix mesnili* (one child). A bacterial infection was diagnosed in six children (*Salmonella enterica* in three children and *Campylobacter jejuni* in three children).

Hepatitis B serology was performed in 494 children. Of these, 16 had positive hepatitis B core antibodies. Six children (1.2%), all born in Asia, were positive for HBsAg, indicating a chronic hepatitis B infection. In all cases, the adoptive parents had been informed about this condition prior to adoption. Ten children (2.0%) children were negative for HBsAg, indicating hepatitis B clearance. None of the 258 children screened tested positive for hepatitis C, and none of the 495 children tested positive for HIV or syphilis.

A chest X-ray was performed in all 495 children. A BCG scar was observed in 294 (59.4%) children; in the other 201 children, PPD testing was performed. A positive PPD was found in five children. Latent tuberculosis infection (LTBI) was diagnosed in three children and active (pulmonary) tuberculosis in two children. Mild abnormalities on the chest X-ray without further clinical consequences were observed in 35 children (7.1%).

Immunization status

According to available medical records, most children had received a complete course of immunization against diphtheria, tetanus, and poliovirus types 1–3. Antibody levels against diphtheria and poliomyelitis were determined in 379 children and against tetanus in 381 children. In total, 182 children (48%) had adequate protection against diphtheria (>0.1 IU/ml) and 106 (28%) had marginal protection (0.01–0.1 IU/ml). Chinese children were significantly less often fully protected than children from other countries (38.2% versus 67.2%, OR 0.302, 95% CI 0.19–0.47). While antibody levels against tetanus (>0.1 IU/ml) were adequate in 214 (56.5%) children, there was again a difference between Chinese children and children from other countries (levels were adequate in 40.9% versus 87.4% of children, respectively; OR 0.10, 95% CI 0.06–0.18). Marginal protection (0.01 IU/ml–0.1 IU/ml) was found in 86 children (22.6%). The antibody levels against diphtheria and tetanus were congruent in 73.9% of all children (similar for Chinese children and children from other countries; Table 2).

While there was adequate protection against all three polioviruses (>0.5 IU/ml for polio types I and III, >1.0 IU/ml for polio type II) in 269 children (71%), Chinese children were significantly less often fully protected than other children (66.5% versus 80.0%, OR 0.497, 95% CI 0.30–0.83) (Fig. 1).

The percentage of Chinese children with sufficient immunity against tetanus and diphtheria increased over the

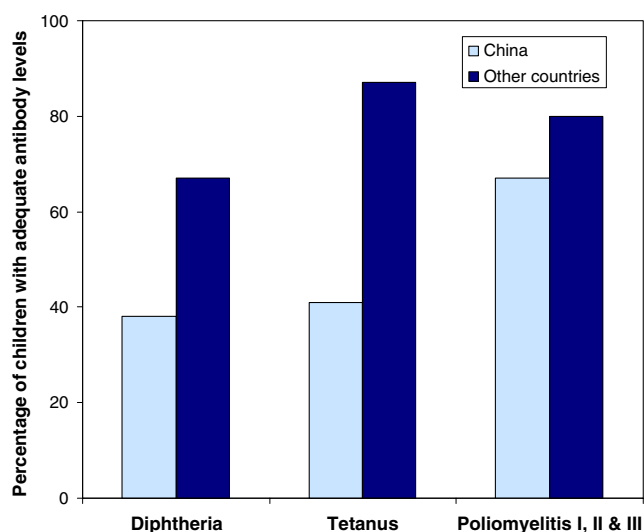
Table 2 Antibody levels against diphtheria, tetanus, poliomyelitis, and hepatitis B in international adoptees 2002–2006

Vaccination	All children total (%)	Chinese children total (%)	Children other countries total (%)
Diphtheria	182/379 (48.0)	96/251 (38.2)	86/128 (67.2)
Tetanus	214/381 (56.2)	103/252 (40.9)	111/127 (87.4)
Polio I, II & III	77/134 (57.5)	65/119 (54.6)	12/15 (80.0)
Hepatitis B	176/230 (76.5)	96/126 (76.2)	80/104 (76.2)

years, and this increase was significant when years 2002 and 2003 were compared with years 2005 and 2006 (for tetanus 26.0% versus 72.3%, OR 7.45, 95% CI 3.82–14.55; for diphtheria 26.2% versus 56.9%, OR 3.73, 95% CI 1.99–6.99). The percentage of children with sufficient immunity arriving from other countries was stable during these years. Protection against poliomyelitis was similar in children from China and other countries and did not change over the years.

Age of the adoptee upon arrival in the Netherlands (younger than 12 months, 12–24 months or older than 24 months) was not of significance for adequate protection against tetanus, diphtheria, or poliomyelitis.

Hepatitis B surface antibodies (anti-HBs) were positive in 363 of 494 children (73.5%); there was no significant difference between Chinese children and children from other countries. The percentage of children with adequate immunity against hepatitis B remained stable over the years 2002–2006.

**Fig. 1** Percentage of international adoptees with adequate antibody levels against tetanus, diphtheria, and poliovirus types 1–3

Discussion

While in 1995 the majority of adoptees arriving in the Netherlands originated from Southern American countries (mainly Columbia (21.2%) and Brazil (12.8%)), these days, China has become the major country of origin of adoptees arriving in the Netherlands (56.7% in 2005 [5]). In several other European countries such as Denmark, Norway, Spain, Sweden, and the United Kingdom and also in Australia, Canada, and the USA, Chinese children also form a major part of the adoptees [1, 20]. In contrast, for example, in Germany and Italy, relatively few adoptive children come from China, whereas many come from the Russian Federation and Ukraine, and, in Italy, also from Columbia, Ethiopia, and Brazil. In France, the number of children from China markedly decreased in 2007, whereas numbers from the other main countries for adoption (Columbia, Ethiopia, Haiti and the Russian Federation) remained stable [1].

Adoption from China became possible in 1991. Since 1996, the China Center of Adoption Affairs (CCAA) has been responsible for the adoption process. Unlike many other countries a steady and organized procedure for adoption was created. This might have been of influence for parents to adopt a Chinese child. Also, the Chinese one-child policy and the preference of many Chinese parents to have a boy [10] are of possible influence on the rise of Chinese adoptees in recent years. This rise may come to an end as new criteria for adoption of Chinese children were implemented in May 2007 [24].

All adoptees arriving in the Netherlands were screened according to a Dutch protocol, which is comparable to other international guidelines [6]. Most international adoptees seen in our hospital were in a good clinical condition with a normal nutritional status, although 42.8% of the children had one or more conditions requiring medical attention. While this percentage is comparable to that of earlier studies [18], the nature of the conditions appears to have changed. In the past, adoptees were often diagnosed with multiple conditions, with gastrointestinal and dermatological infections being frequently seen in combination with serious psychomotor retardation, malnutrition, or osteomalacia [14, 18, 19], but the adoptees in this study often had only a single condition requiring medical attention. However, dermatological conditions and gastrointestinal parasitic infections were still frequently diagnosed, and the proportion of children with a skin infection or *G. lamblia* infection was comparable to that in 1994. Strikingly, a bacterial gastrointestinal infection was seen in only 1.2% as compared to 12% in the past [18].

The decreased frequency of children with malnutrition and/or bacterial gastrointestinal infection may indicate that the quality and hygiene of orphanages and foster families

where adoptees stay before leaving their country have improved. Only a few children had serious illnesses, such as hepatitis B and tuberculosis, and none had HIV infection, hepatitis C, or syphilis. With the exception of syphilis (diagnosed in 1.7% of the children screened in 1994), these data are comparable to earlier data [12, 14, 18, 19] and suggest that screening procedures for these diseases in the countries of origin are generally adequate. None of the children had serious hematological or biochemical disorders. As expected, some children had hematological disorders, such as α -thalassemia or sickle cell trait. Because screening for these traits was not routine and was performed only if these disorders were suspected on the basis of hematological variables, it is likely that the number of adoptees carrying these traits was underestimated.

The children presented in this study had a better health status compared to adoptees arriving in other counties [11, 14, 19]. A possible explanation is that children arriving from Russia and Eastern Europe are known to have an increased risk for infections, mainly (latent) tuberculosis, *G. lamblia* infection and hepatitis B [11, 14, 19]. We can only speculate why the Chinese children presented in this study had less medical conditions requiring treatment than those in a similar study in the past [12], but it may be explained by improved conditions in Chinese orphanages in recent years.

Information on exposure to environmental pollutants among adoptees was not available for this group of children. Determination of the lead level is currently not part of the standard Dutch protocol. Recent studies indicated that Chinese children might have elevated blood lead levels, especially when they come from certain industrialized or urban areas. It was noted that blood levels increase with age and peaked at 6 years [12, 22]

A significant number of children, especially Chinese children, with congenital disorders were noted. The proportion of adoptees with a congenital disorder has increased from 5% in 1994 [18] to 10.7% in the present study. It appears that Dutch parents are more willing to adopt a child with a special need (S. Geelen, personal communication). All children with congenital disorders were in good general health, comparable to the children without a special need, and often complete or partial correction of the congenital disorder had taken place before arrival in the Netherlands. In comparison, 1.7% of the adoptees in the past had multiple congenital disorders with limited therapeutic possibilities [18].

Many children, especially Chinese children, showed insufficient antibody levels against diphtheria, tetanus, and poliomyelitis. During the years 2002–2004, the proportion of children with adequate antibody levels was even lower than that reported by Schulpen et al. in 1999 [16]; the figures of the years 2005/2006 were comparable to earlier

findings. As also found by others, immunization records of the country of origin were often unavailable or incomplete [17]. An exact time-interval between individual vaccinations and the measurement of antibody levels could not be determined. Single antibody level determinations should be interpreted with caution when the previous vaccination schedule is unknown. It is known that diphtheria antibodies decline with time after vaccination, but a course of three tetanus injections usually gives a durable response, which lasts for at least 5 years [3, 8]

Official Chinese reports for the World Health Organization mention a drop in immunization coverage in China in 2002/2003, with an improvement after 2004 [23]. The recent improvement might have resulted from the Chinese vaccination policy introduced in 2005, by which nationally recommended vaccinations were to be provided free of charge. Antibody levels against poliomyelitis types 1–3 were comparable to those in the past and coverage against hepatitis B was high in all adoptees, also in Chinese children. Seventy-six percent of the Chinese children had been vaccinated, which is in accordance with estimations given by the Chinese Ministry of Health in 2004 [13]. In 2002, the Chinese Ministry of Health and the GAVI (Global Alliance for Vaccines and Immunization) started a project to ensure availability of free vaccination against hepatitis B [4].

In summary, our study shows that the general clinical condition of adoptive children arriving in the Netherlands nowadays is better than in the past. A substantial proportion of the children had a congenital disorder, known to the adoptive parents prior to adoption. This suggests that parents are more willing to accept a child with a special need. Serious infectious diseases were rare and serious hematological or biochemical disturbances were not detected in any of the children. In many children, booster vaccinations were still indicated to improve their immunization status.

Conflict of interest The authors declare that they have no conflict of interest.

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