Immigrant children who enter the United States without immunization records may be required to receive vaccines for diseases to which they are already immune or for which they have previously received immunization. We tested 669 newly arrived refugees (age range, 0–20 years) for antibody to measles, rubella, and varicella, to determine the seroprevalence of antibodies to these diseases in this group of immigrants. Five hundred forty-nine (82%) of 669 patients had antibody to measles, 545 (82%) of 668 had antibody to rubella, and 430 (64%) of 668 had antibody to varicella. Antibody to all 3 diseases increased with increasing age. No clinically significant differences in presence of antibody were noted by region of origin.

Children who immigrate to the United States may enter the country without immunization records, or they may enter with records that are not considered up-to-date by current US immunization standards [1]. Refugee children are especially likely to immigrate to the United States without immunization records because of the difficulty of maintaining records in situations of forced or unplanned migration and because of disruption of public health services and infrastructure in their countries.

Immigrant children may have been immunized against measles, rubella, or varicella, or they may have had these diseases in the past. Refugee children who do not have immunization records require proof of immunization to enter school; they may therefore receive “excess” vaccines (i.e., those that duplicate vaccines already received) or “unnecessary” vaccines (i.e., those for diseases that the children have already had) to comply with US immunization recommendations [2]. Immunization with excess or unnecessary vaccines may result in increased cost [3], increased potential for adverse events [4], and considerable inconvenience for families who are trying to resettle in the United States.

Testing patients for antibodies to vaccine-preventable diseases before immunization identifies children who may not need certain vaccines. Because serotesting involves drawing of blood, additional cost, and the possible need for additional medical visits, this strategy would be practical only if the seroprevalence of antibody in a population was high enough and the cost of serotesting was low enough, compared with that of the vaccine, to make testing cost-effective. Once information about age-specific seroprevalence is available, different models of serotesting and universal immunization can be explored. We studied the prevalence of antibody to measles, rubella, and varicella in refugee children from 6 regions of the world to assess (1) whether there is justification for developing policy that incorporates testing for antibody to selected diseases before universal immunization, and (2) whether the data support development of rapid, on-site methods of testing for antibody to vaccine-preventable diseases.
PATIENTS AND METHODS

Study population. The study population consisted of 669 refugees (age range, 0–20 years) who were screened by the Refugee Health Assessment Program at Boston Medical Center from March 1996 through January 2000. Refugees were classified into 1 of 6 groups on the basis of their geographic location of origin. Refugees from Kosovo were not classified as belonging to the same group as refugees from the former Yugoslavia because they arrived in large numbers during a limited period and because they were demographically and culturally different from other refugees from the Balkans.

Data and specimen collection. With the approval of the institutional review board of the Boston Medical Center, we obtained discarded serum samples and stored them at –70°C. For each subject, we recorded demographic information that included date of birth, birthplace, sex, and, when possible, history of immunization against measles, rubella, and varicella.

ELISAs. Serum samples were tested by ELISA (Diamedix) for the presence of IgG antibody to measles, rubella, and varicella. The rubella assay was designed to yield dichotomous, semiquantitative results, which were considered negative if the antibody concentration was <20 ELISA units (EU)/mL or positive if the antibody concentration was ≥20 EU/mL; the manufacturer’s reported sensitivity and specificity of the test were 99.6% and 75%, respectively. The measles and varicella assays yielded trichotomous, semiquantitative results, which were considered negative if the antibody concentration was <15 EU/mL, equivocal if the concentration was 15–20 EU/mL, and positive if the concentration was >20 EU/mL. The manufacturer’s reported sensitivity and specificity of the measles assay were 95.6% and 100%, respectively, and the reported sensitivity and specificity of the varicella assay were 98.4% and 98.2%, respectively.

Statistical methods. We calculated the age-specific prevalence of antibody to measles, rubella, and varicella as the number of tests for which results were positive divided by the total number of tests performed, with exact 95% CIs for proportions.

We created a variable post hoc that indicated 1 of 6 possible regions of origin on the basis of similar demographic and cultural factors. After stratification of the sample by region and disease, we divided the sample into 5 age groups (<1 year, 1 year, 2–4 years, 5–12 years, and 13–20 years). These age groups were chosen because (1) maternal antibody may affect antibody concentration in children <1 year of age, (2) vaccines against measles, rubella, and varicella are not given in the United States until children are ≥1 year of age, (3) there was a statistically significant difference between the concentration of antibody to varicella in children who were 1–4 years of age and that in individuals who were 5–20 years of age, and (4) individuals ≥13 years of age require 2 doses of varicella vaccine. We determined antibody prevalence by disease, age group, and region of origin. All analyses were performed using SAS software, version 8.2 (SAS Institute).

RESULTS

Patient population. The age range of the 669 refugees was 0–20 years. The refugees came from 6 regions of the world: the former Yugoslavia (290 refugees [43%]), East Africa (160 refugees [24%]), Kosovo (101 refugees [15%]), Vietnam (42 refugees [6%]), Iraq/Kurdistan (40 refugees [6%]), and the Caribbean (36 refugees [5%]). Of the 669 refugees, 31 (5%) were <1 year old, 27 (4%) were 1 year old, 92 (14%) were 2–4 years old, 301 (45%) were 5–12 years old, and 218 (33%) were 13–20 years old. Fifty percent of the refugees were male.

Five (0.7%) of the 669 patients received varicella vaccine before their clinic visit; 1 of these patients received vaccine 1 week before the clinic visit. A total of 264 patients (39%) received vaccine that contained measles (235 patients received measles-mumps-rubella [MMR] vaccine and 29 received measles vaccine) before the visit. No patient received single-antigen rubella vaccine.

Prevalence of antibody to measles, by age and region of origin. A total of 669 refugees were tested for antibody to measles; 549 (82%) had positive results, 26 (4%) had equivocal results, and 94 (14%) had negative results. Figure 1 (top) illustrates the prevalence of antibody to measles by age. Fifteen (48%) of 31 patients <1 year of age and 534 (84%) of 638 patients ≥1 year of age were positive for antibody to measles (table 1). Figure 2 (top) illustrates the seroprevalence of measles antibody, according to age and region of origin. There were no clinically significant differences in antibody concentration by region of origin.

Prevalence of antibody to rubella, by age and region of origin. A total of 668 patients were tested for antibody to rubella. 545 (82%) had positive results and 123 (18%) had negative results. Figure 1 (middle) illustrates the prevalence of antibody to rubella by age. Eighteen (58%) of 31 infants <1 year of age were positive for rubella, as were 527 (83%) of 637 patients ≥1 year of age (table 1). Figure 2 (middle) shows the seroprevalence of rubella antibody by age and region of origin. There were no clinically significant differences in antibody concentration by region of origin.

Prevalence of antibody to varicella, by age and region of origin. A total of 668 patients were tested for antibody to varicella; 430 (64%) had positive results, 13 (2%) had equivocal results, and 225 (34%) had negative results. Figure 1 (bottom) illustrates the prevalence of antibody to varicella by age group. Positive test results were noted for 13 (42%) of 31 children <1 year of age, 242 (58%) of 420 patients 1–12 years of age, and 175 (81%) of 217 patients 13–20 years of age (table 1). Figure 2 (bottom) illustrates the seroprevalence of varicella antibody...
Figure 1. Top, Prevalence of antibody to measles among 669 refugees aged 0–20 years, by age group (with exact 95% CIs). Prevalence of antibody to rubella (middle) or to varicella (bottom) among 668 refugees aged 0–20 years, by age group (with exact 95% CIs).
Table 1. Prevalence of measles, rubella, and varicella antibodies among 669 refugees aged 0–20 years, by age group.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>&lt;1 year</th>
<th>1–20 years</th>
<th>1–12 years</th>
<th>13–20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>15/31 (48)</td>
<td>534/638 (84)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rubella</td>
<td>18/31 (58)</td>
<td>527/637 (83)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Varicella</td>
<td>13/31 (42)</td>
<td>242/420 (58)</td>
<td>175/217 (81)</td>
<td>—</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. of children positive for antibody/no. of children who were tested (%).

by age and region of origin. There were no clinically significant differences in antibody concentration by region of origin.

**DISCUSSION**

Antibody to measles and antibody to rubella were present from an early age in refugee children, and varicella antibody was present in almost 60% of children at the time that they entered school. Antibody to measles or rubella could have been acquired through natural disease or by immunization; however, antibody to varicella was acquired primarily through natural disease, because few children were immunized against varicella.

In the youngest children (those <1 year of age), antibody may have been acquired transplacentally.

Antibody to measles was present in most refugee children ≥2 years of age. It is not unexpected that measles antibody would be prevalent at an early age; in 1996, for children who were 1 year of age, global vaccine coverage with a single dose of measles vaccine reached a peak of 81% [5]; however, it decreased to 72% in 1998 [6].

Rubella antibody was present in most refugees 2–20 years of age. The proportion of antibody acquired by disease was likely to be substantial, because fewer than one-half of developing countries include rubella immunization in their national immunization programs [7]. Data from African countries show that rubella is likely to be contracted early in life and that >80% of children in many parts of the continent are immune by 10 years of age [8]. A recent study of unimmunized individuals in Turkey reported that 71% of individuals acquired rubella infection before 10 years of age, and that rubella antibodies were present in 38% of children 1–4 years of age [9].

Despite a high prevalence of antibody to measles and rubella, sero-testing with ELISAs before immunization with MMR vaccine is not cost-effective because of the high cost of testing for antibody to 3 antigens and because of the low cost of the MMR vaccine, as assessed using a model described by Plans Rubio [10].

In our sample of children, antibody to varicella was acquired later in life than was antibody to measles or to rubella. In the United States and other countries with temperate climates, varicella tends to be a disease of preschool-aged and young school-aged children, with most children acquiring antibody by early adolescence [11]. Age-specific incidence of disease is therefore low in older school-aged children and in adolescents and adults [12, 13]. In contrast, varicella infection tends to occur later in life in the tropics [14]. Hypotheses proposed to explain these differences include virus inactivation at high temperature; epidemiologic interference from other viruses; residence in urban, compared with rural, locations; population density; and socioeconomic status [15]. In refugee populations, however, such distinctions may become blurred because of migration across areas of different climatic conditions and because of residence in crowded or densely populated areas, such as refugee camps. Outbreaks of varicella have, in fact, occurred in refugee camps in which Somali refugees were living (M. Cetron, personal communication). Disruption of typical patterns of transmission may explain why the seroprevalence of varicella in refugee children from East Africa resembled that of refugees from temperate regions. Seroprevalence of varicella in refugee children from the Caribbean and Vietnam, where there was less disruption of typical patterns of living before immigration, resembled that of stable tropical populations.

In the United States, varicella vaccine is available only as a single-antigen preparation that is given either as a single dose to children 1–12 years of age or as 2 doses to individuals ≥13 years of age. In an analysis based on seroprevalence data for this refugee population, Figueira et al. [16] demonstrated that it is cost-effective to test children for varicella antibody rather than to immunize if antibody prevalence exceeds 34%. In our patient population, it would therefore be cost-effective to test patients ≥5 years of age before immunization with varicella vaccine [16].

Testing for antibody to vaccine-preventable diseases is believed to be more cumbersome than immediate immunization and is used rarely. In the United States, parents have been found to prefer testing for varicella antibody over universal immunization; it is not clear whether immigrant families would have similar preferences [17]. Disadvantages of testing for antibody include having to draw blood samples, having to wait for results, the risk of susceptible children contracting the disease while awaiting test results, and the need for scheduling additional visits to administer needed immunizations. A total of 96% of children returned to our clinic for the follow-up visit; it is unclear whether such a high rate of return visits could be attained everywhere.

Because many immigrant families want to enroll their children in school without delay, clinical practitioners may immunize children to create the documentation required by school officials, rather than wait for the results of serologic tests before providing immunization. In our practice, although testing for varicella antibody is done routinely for all patients ≥7 years of age, some health professionals are reluctant to delay immunization while waiting for test results because of the po-
Figure 2.  Top, Prevalence of antibody to measles among 669 refugees aged 0–20 years, by age group and region of origin. Prevalence of antibody to rubella (middle) or to varicella (bottom) among 668 refugees aged 0–20 years, by age group and region of origin.
tential problem of delayed school entry. After we began universal testing for varicella antibody in our clinic, we reviewed whether the results of serologic tests were used to make decisions about varicella immunization. In the first year after serologic testing was implemented, 80 patients ≥7 years of age lacked a history of varicella. For 51 of these (64%) 80 patients, testing identified varicella antibody, yet 25 of these patients (50% of those who tested positive for varicella antibody) were given vaccine at the first clinic visit, despite the availability of results within 1 week and a 96% rate of compliance for second visits at our clinic.

Technology is becoming available to perform rapid testing for antibody to vaccine-preventable diseases (H. Paxton, personal communication). Ideally, these tests would be done on site in the clinic setting and would be used to determine the need for vaccines at the time of the clinic visit, thus eliminating the use of some unnecessary vaccines. New immigrants to the United States who arrive without immunization records are an ideal population for which this technology should be developed. This technology also has broad application to other populations of both children and adults, such as those who have lost immunization records but require documentation of immunity or vaccination (e.g., military recruits, health care workers, individuals entering school or university, travelers, and immigrants seeking to change their immigration status).

CONCLUSION

Antibody to measles and antibody to rubella were present at an early age in most refugees aged 0–20 years, and varicella antibody was present in more than one-half of refugee children by the time that they entered school. There were no clinically significant differences in antibody concentration according to region of origin. Given the current costs of serotesting, MMR vaccine, and varicella vaccine, it is cost-effective to perform testing for varicella antibody before immunization only among children ≥5 years of age. High levels of antibody to all 3 diseases, especially among school-aged children and adolescents, support pursuit of the development of rapid, on-site, inexpensive methods of testing for antibody to vaccine-preventable diseases that could be used in many settings.

References