

Short Communication

Diphtheria Immunity of Different Age Groups in Turkey

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SUMMARY: In Turkey, the immunization policy against diphtheria involves childhood vaccination, and no routine booster dose is administered after 12 years of age. Information about the immune status of the population is important to predict the potential for epidemics, several of which have occurred recently in neighboring countries. The aim of this study was to assess the immune status of different age groups in Turkey against diphtheria. A total of 497 blood samples were collected, and diphtheria antitoxin levels were measured by the Enzyme Linked Immunosorbent Assay method. Titers below 0.1 IU/ml were considered to show insufficient immunity. Overall, 35.8% of the population studied showed insufficient immunity against diphtheria. Immunity rates varied significantly among different age groups ($P < 0.01$). Protective immunity rates were highest in the 3- to 6-year age group (81.3%) and the over 60 age group (81.2%). In subjects between the ages of 10 and 59 the percentage of people with insufficient immunity was above 30%. The lowest immunity rate was observed in the 20- to 29-year age group. No significant difference was seen between males and females in terms of protective effect of vaccination. This study indicates that people between the ages of 10 and 59 are susceptible to diphtheria in our country. Therefore, revaccination of adults with tetanus-diphtheria toxoids at every opportunity (military service, pregnancy, admittance to emergency room) should be considered as an immunization policy.

Diphtheria was once virulent disease responsible for high morbidity and a high mortality rate in children. Widespread immunization programs after the 1940s resulted in a sharp decline in the incidence and mortality of the disease in many developed countries (1-4).

In the early 1990s, diphtheria reemerged in Turkey's northeast neighbors, the New Independent States of the former Soviet Union (5,6). The causes of this outbreak were multifactorial, and one of the most important factors was insufficient population immunity. This epidemic gave rise to anxiety about the immune status of Turkey's population against diphtheria.

It is well documented that there is a continuous decline in antibody titer after vaccination against diphtheria (7-9). Absence of routine revaccination in adults might result in an increasing number of susceptible people in Turkey. The outbreak in neighboring countries highlighted the importance of follow-up studies of the immune status of our population. The aim of this study was to determine the antibody levels for diphtheria in different age groups in Ankara, Turkey.

A total of 497 blood samples were collected randomly from members of the population who were admitted to Gazi University Hospital from January to August 1997. Samples were obtained from the cord blood of 73 healthy mothers who had delivered in obstetric clinics; 64 children (33 males and 31 females) between 3 and 6 years of age who were followed in well-child clinics and had their routine vaccinations there; and 360 healthy persons (167 males, 193 females) between 10 and 80 years of age, stratified by age with approximately 50 subjects in each decade. The children in the 3- to 6-year age group had vaccination records in our well child clinics, which records confirmed that they had received their last doses

of diphtheria vaccine in their 18th month. For subjects in older age groups, a questionnaire was completed to provide information about the immunization status and history of diphtheria.

Quantitation of diphtheria specific antibodies was done using a commercially available IgG-specific Enzyme Linked Immunosorbent Assay (ELISA) kit (ELISA Diphtheria/ Diphtheria IgG, Virotech, order no: EN 129.00, Ch-B/lot: 70115-02, Genzyme Virotech GmbH, Rüsselsheim, Germany) that accurately discriminates diphtheria antibody levels equal to or higher than 0.1 IU/ml, while it has limited ability to differentiate values below 0.1 IU/ml (3). It has been suggested that values of <0.1 IU/ml be considered to indicate susceptibility, whereas sufficient immune protection can be expected when it is equal to or above 0.1 IU/ml (3,8).

Statistical analysis was performed using SPSS Win 8.0. Testing for statistical significance of immunity rates in different age and sex groups was performed by using the chi-square test. A P value of < 0.05 was considered statistically significant.

Among the 497 blood samples obtained, 73 were cord blood samples, in 53 (72.6%) of which diphtheria antibody levels were below 0.1 IU/ml. Among the remaining 424 blood samples, 152 (35.8%) had antibody titer <0.1 IU/ml, signifying insufficient immunity against diphtheria. Distribution of immunity rates among different age groups is shown in Table 1. Immunity rates among different age groups varied significantly ($P < 0.01$). The highest percentages of protective levels of diphtheria antibodies were in the 3- to 6-year and above 60-year age groups; 20- to 29-year age group had the lowest percentage of protective level of antibodies. Protection rates did not differ significantly among age groups of subjects between 10 and 39 ($P > 0.05$).

Protective levels of antibody titer (>0.1 IU/ml) against diphtheria were found in 138 (69.0%) of the males and 134 (59.8%) of the females. Protection rates in males and females were similar ($P > 0.05$). In addition, no significant

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Table 1. Immunity rates in different age groups

	Insufficient immunity (< 0.1 IU/ml) n (%)	Protective immunity (= 0.1 IU/ml) n (%)	Total n (%)
3-6 years	12 (18.7)	52 (81.3)	64 (100)
10-19 years	29 (43.2)	38 (56.7)	67 (100)
20-29 years	34 (57.6)	25 (42.4)	59 (100)
30-39 years	32 (46.4)	37 (53.6)	69 (100)
40-49 years	20 (32.2)	42 (67.8)	62 (100)
50-59 years	16 (29.1)	39 (70.9)	55 (100)
>60 years	9 (18.8)	39 (81.2)	48 (100)
Total	152 (35.8)	272 (64.2)	424 (100)

$P < 0.01$

difference was found between females and males in terms of protection in different age groups.

In Turkey, the immunization of children is performed by the Ministry of Health all over the country (10). Vaccination for diphtheria has been administered since 1937. Children receive the last booster dose of tetanus-diphtheria vaccine at 12 years of age, and no subsequent routine booster dose is recommended for adults. Routine immunization policies for DTP vaccines must be based on knowledge about a population's immunity, and serological studies are a useful tool in this respect. Although our study population does not represent the whole Turkish population, it does provide data on diphtheria immunity, particularly given that immunization policy in Turkey is standard over various regions (10).

In this study, we found that 35.8% of our study population had insufficient antibody levels against diphtheria (<0.1 IU/ml). It is generally accepted that when the antibody level is below the critical value, the subjects are unprotected against diphtheria, and when more than 30% of a population is unprotected there is the risk of epidemic (7). The most susceptible age group in this study was that of subjects between 20 and 29 years, 57.6% of which had insufficient antibody levels against diphtheria. In subjects between the ages of 10 and 49, overall insufficient antibody rate was above 30%. These findings are in agreement with the set of other studies, in which the prevalence of insufficient protection against diphtheria among adults was shown to range from 22.9% to 40% (4, 7, 11-13). The high percentage of insufficient protection against diphtheria found in our study was attributed to lack of routine adult immunization. Similar findings in previous studies may be due to the infrequency of adult revaccination in those industrialized countries despite its recommendation. A recent study from Turkey revealed that 79.1% of the study population had protective levels of antibodies against diphtheria, but the protection rate showed an age-related decrease reaching a minimum in the 30- to 44-year age group (14). The studies performed in developed countries have demonstrated that immunity levels against diphtheria continuously decrease with increase in age (4,12,15,16). In our study, immunity rates of people above 60 for diphtheria was significantly higher than those in 10- to 39-year-old adults. A similar age distribution of immunity was reported from Poland (2), and it was explained by the fact that younger generations had a reduced opportunity for acquiring or reinforcing natural immunity through subclinical infection because the disease had been so nearly eradicated. Our subjects around 60 were, historically, the first group to be vaccinated in Turkey, and their immunity was strengthened by natural booster doses

because diphtheria was yet prevalent. The subjects between 10 and 39 lacked both revaccination and natural boosters because diphtheria had been nearly eliminated in Turkey; therefore, this constitutes the most susceptible group.

Some studies have reported that insufficient immunity rates against diphtheria are more common among women than among men (6,17). This difference was attributed to higher revaccination rates in males resulting from military service or tetanus-diphtheria vaccination in emergency departments at the time of injury. Other studies reported no difference between the sexes (4,11,18). In our study, the protective antibody levels in males were higher than those in females, but the difference was not statistically significant. We did not expect to find a difference between the sexes because in Turkey there is no revaccination for diphtheria during military service, and in emergency departments only tetanus toxoid, as necessary, is given to people.

In our study, antibody levels against diphtheria in cord blood samples were also low. Ages of mothers from whom cord blood samples were obtained ranged between 16-43 (median age: 27). Pasetti et al. demonstrated a close correlation between maternal and newborn antibody titers, and the mean antibody titer determined in cord blood was significantly higher than the maternal titer (19). We did not study diphtheria antibody levels in the mothers in our study, but the low protective antibody levels in cord blood samples were thought to be a reflection of low antibody levels among these young adults, given that the lowest antibody levels observed in our study belonged to subjects in the 20- to 29-year age group. Low antibody titer in cord blood means that antibody titer in the newborn period will also be low, and any delay in primary immunization of infants may cause a serious risk for them. This finding may be important for countries in which the vaccine coverage rate in early childhood is low. Susceptible pregnant females represent an important group, which needs to be reimmunized to provide protection for newborns in the early months of life.

In conclusion, this study indicates that the preschool age group in our population is protected against diphtheria as a result of recent immunizations, and that a high proportion of elderly people still have sufficient antibody levels. However, given the gradual replacement of natural immunity by less durable vaccine-induced immunity, antibody levels may decrease in the elderly age group. Subjects between ages of 10 and 59 seem to be susceptible. Such a large pool of susceptible persons creates epidemic potential. Therefore, tetanus-diphtheria revaccination of adults should be considered as an immunization policy in our country. Opportunities for revaccination of adults such as military service, pregnancy, and admittance to emergency rooms should be utilized.

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