Tetanus and Diphtheria Immune Status of Patients in a Family Practice

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Sera obtained randomly from 37 patients seen at a family practice center were evaluated for protective antibodies against tetanus and diphtheria using in vivo toxin neutralization methods. The patients' ages ranged from 1 to 99 years. Seventy-four percent and 83 percent of patients were found to have protective antitoxin titers against tetanus and diphtheria, respectively. No significant differences in immune status were detected among different sexes or races. Whereas the mean age of subjects susceptible to tetanus was significantly greater than for those with protective antibody levels, this was not the case with diphtheria. It is postulated that natural diphtheria infection may be responsible for the high degree of protection noted among older subjects surveyed. Practical as well as educational benefits that may be obtained from a study of this nature are discussed.

Despite their relative infrequency in this country, tetanus and diphtheria are associated with considerable morbidity.[1] It is regrettable that even though relatively safe and effective immunization agents are available, there has been no substantial decrease in the case-fatality ratio of these disorders during this century.[2]

Edsall[3] has aptly termed tetanus "the inexcusable disease." Diphtheria might be similarly considered in this light. It has been shown that tetanus toxoid is nearly 100 percent and diphtheria toxoid over 90 percent effective in inducing antibody response.[1] Maintenance of defenses against tetanus and diptheria is relatively easy and safe compared with the consequences of contracting the actual diseases.

Most studies of tetanus and diphtheria immunity have focused on the pediatric age group. Ferguson et al,[4] using the chart review method, have described deficiencies in tetanus and diphtheria immunization patterns among young patients in a family practice program. Additionally, several reports have emphasized that a substantial proportion of adults, especially the elderly population, is at risk for these diseases.[2,5-7] For example, Crossley et al,[2] in a study of adults in urban Minnesota, recently reported that a majority of middle-aged females and of older patients of both sexes was susceptible to tetanus and diphtheria because of inadequate serum antibody levels.

The present study was undertaken to help determine the tetanus and diphtheria immune status in outpatients of widely varying ages in a family practice setting.

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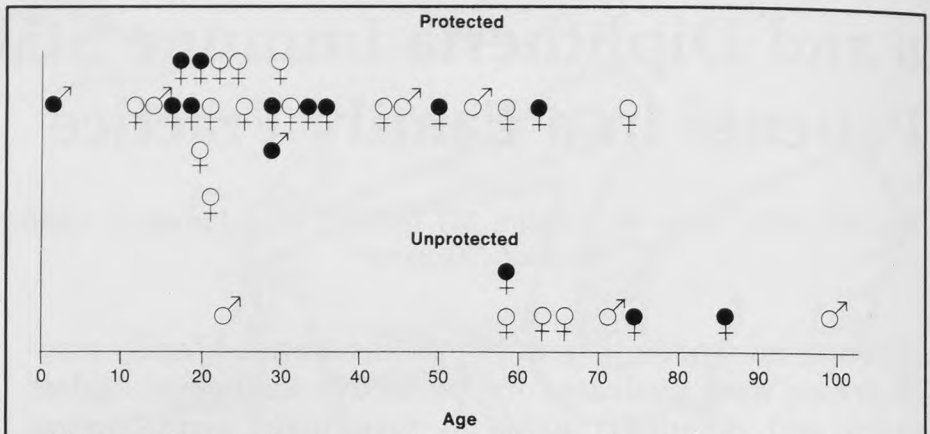

Figure 1. Tetanus immune status in 35 patients aged 1 to 99 years (mean age = 40 years). Opened areas on symbols for sex refer to white patients and closed areas to black patients. Protection defined as serum antitoxin titer ≥0.01 AU/ml. Statistical analyses for sex, $\chi^2 = 0.16$, $P = 0.69$; for race, $\chi^2 = 0.006$, $P = 0.94$; for age, $t = 4.96$, $P < 0.0001$

Methods

Aliquots of sera from patients undergoing routine laboratory testing at the Capstone Medical Center (Tuscaloosa, Alabama), a training site for family practice residents and medical students, were collected and forwarded to the Massachusetts Department of Public Health Biologic Laboratories for determination of tetanus and diphtheria antitoxin levels. The study was conducted in a double-blind manner. On the day of the study, sera were collected consecutively from patients having blood drawn for routine laboratory studies, and portions of the sera were saved for antibody analyses. A total of 34 sera were tested for both tetanus and diphtheria antibody titers. One additional serum was tested for tetanus antibody only, and two sera were tested only for diphtheria antibody levels. The mean age of subjects studied for both tetanus and diphtheria immunity was 40 years, with age ranges for both studies of from 1 to 99 years. As is representative of the patient population of the medical center where the study was conducted, the majority of the subjects were female and about 60 percent were white. Demographic features of the population studied, including age, race, and sex, are shown in Figures 1 and 2.

Tetanus antibody levels were determined by neutralization titrations in mice[8] and diphtheria antitoxin by neutralization titrations in the skin of rabbits.[9] Although in vitro methods for titrating antitoxin levels are less expensive and time consuming, they are also less precise and less reliable in estimating the immunity of specific persons compared to the in vivo methods used in this study.[7] Results are expressed in antitoxin units per milliliter of sera in comparison to the standard antitoxin provided by the Bureau of Biologics of the Food and Drug Administration. Patients with antitoxin levels less than 0.01 antitoxin units (AU) per ml serum were considered at risk for tetanus or diphtheria as previously described.[10,11] Family practice residents and attending physicians were notified of the immune status of their patients at completion of the study. Statistical analyses to determine possible influences of race and sex on immune status were performed using the chi-square test with Yates correction; Student's t test was also employed to determine the influence of age on immunity.

Results

Tetanus Antibody

Results of the tetanus antitoxin determinations in 35 patients are shown in Figure 1. Nine patients

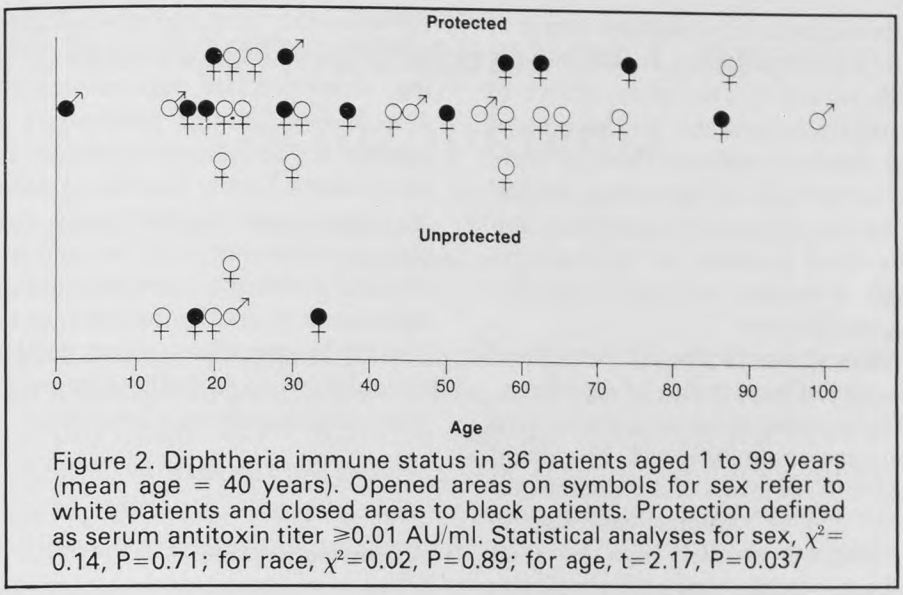

Figure 2. Diphtheria immune status in 36 patients aged 1 to 99 years (mean age = 40 years). Opened areas on symbols for sex refer to white patients and closed areas to black patients. Protection defined as serum antitoxin titer ≥0.01 AU/ml. Statistical analyses for sex, χ^2= 0.14, P=0.71; for race, χ^2=0.02, P=0.89; for age, t=2.17, P=0.037

(25.7 percent) ranging in age from 22 to 99 years were found to be at risk for developing tetanus. Twenty-six subjects (74.3 percent) ranging in age from 1 to 73 years were found to be protected against tetanus as determined by antibody titers equal to or greater than 0.01 AU/ml. In the relatively small patient sample, no significant influence of race or sex on immune status was noted. However, the mean age of subjects at risk of tetanus (66 years) was significantly greater ($t = 4.96$, $P < 0.0001$) than those with protective antibody levels (mean age 31 years).

Diphtheria Antibody

Diphtheria antitoxin levels found in 36 sera are shown in Figure 2. Whereas six (16.6 percent) of the subjects had antibody levels below the accepted protective level, the remaining 30 subjects had protective levels of diphtheria antibody. Again, no significant differences were noted between sexes or races. Of interest is the finding that, in contrast to tetanus immunity, the mean age of subjects at risk of diphtheria (21 years) was younger ($t = 2.17$, $P < .05$) than those with protective antibody levels (mean age 44 years). This finding, however, is of borderline statistical significance and may well have been influenced by the small number of subjects, especially in the very young age groups, in which a higher degree of immunity might be expected.

Discussion

Nearly 100 years ago, Louis Pasteur wrote, "When meditating over a disease, I never think of finding a remedy for it but, instead, a means of preventing it." This century has witnessed notable advances in immunization practices. Indeed, successful immunization programs have contributed to the increased longevity and the "graying of America." The recent elimination of smallpox offers a vivid documentation of the success that may be achieved with effective vaccination programs.

Although safe and effective immunizing agents for tetanus and diphtheria have been available for over 50 years, protection against these potentially fatal diseases is unfortunately not universal. Nearly 20 years ago, Levine and Wyman[12] conducted a nationwide survey to determine immunity to tetanus among military recruits. They found that 35 percent of the subjects were unprotected, with extremes of seven percent unprotected subjects in the state of Washington to 65 percent unprotected in Alabama.

A large proportion of tetanus cases are found among elderly persons,[1] a population whose immune status has been shown to be inadequate in several studies.[2,5-7] The present study revealed that in a limited sample of outpatients with ages ranging from 1 to 99 years, 74 percent had protective levels of antibody against tetanus. This compares favorably with other surveys and suggests

considerable improvement in the immune status of inhabitants of this area compared to Levine and Wyman's earlier survey.[12] The latter study, of course, is not strictly comparable to the present survey since the subjects, military recruits, were mainly confined to one sex and age group. As had been noted by other workers,[2,5,7] however, immunity to tetanus was found to be inversely related to age, with a majority of elderly subjects being at risk for this disease.

Recently, Crossley[2] noted that 77 percent of urban Minnesota adults were at risk of diphtheria. In the present study, using more accurate in vivo methods to determine antibody levels, 83 percent of subjects had protective levels of diphtheria antitoxin. Of interest and at variance with several other studies[2,5,7] was the relatively high degree of diphtheria immunity in older subjects studied in this survey (Figure 2). Unlike tetanus antibodies, which are not naturally acquired after neonatal life, diphtheria antibody can be acquired by natural infection. This might account for the higher diphtheria antibody titers noted among adult residents of this area, and is currently being investigated.

The recommended schedule for active immunization of normal infants and children consists of administration of diphtheria and tetanus toxoids combined with pertussis vaccine (DPT) at 2 months, 4 months, 6 months, and again at $1^1/_2$ and 4 to 6 years of age. Combined tetanus and diphtheria toxoids (adult Td) is recommended for those greater than six years of age, with booster immunizations at ten year intervals to sustain immunization.[4] Primary immunization for adults who have never received toxoid consists of three intramuscular injections of Td, with 4 to 6 weeks separating the first and second doses and 6 to 12 months between the second and third doses.[1] Ruben and colleagues[5] have recommended that two doses of Td toxoid separated by at least one month be given to elderly subjects who have not previously received two or more Td immunizations. Using such a regimen, these workers were able to demonstrate a 100 percent seroconversion to immune levels in older subjects.

Goodman[13] has stated that, "In addition to promoting . . . broad-reaching immunization programs in the public sector, we need to improve the performance of individual health care providers in practicing preventive medicine. For physicians, the optimum time and place to acquire this aptitude is in medical school and postgraduate training, when practice patterns are still formative." The findings of this preliminary survey will be used by the authors to emphasize further to medical students, family practice residents, and attending physicians the continuing need to practice proper preventive medicine and to consider tetanus and diphtheria immunization as an important component of routine health care in patients of all ages. A large-scale study to delineate further the variables involved in the immunity of this patient population is currently underway.

Acknowledgements

The authors are indebted to Leo Levine, Chief, Vaccine Section, Biologic Laboratories, State Laboratory Institute, Massachusetts Department of Public Health, Jamaica Plain, Massachusetts, for his encouragement, advice, and assistance in this project. The authors also gratefully appreciate the competent technical assistance provided by William C. Latham, Joseph Waggett, Bradford Rost, and Leeson Campbell.

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