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BRIEF RESEARCH REPORT

Tetanus antibody protection among HIV-infected US-born patients and immigrants

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Abstract
Introduction Public health initiatives to immunize children and adults have effectively reduced the number of tetanus cases in the USA. However, in the Third National Health and Nutrition Examination Survey (NHANES III), immigrants from Mexico had a 67% nonprotective anti-tetanus antibody (ATA) level. Less work has been conducted among other vulnerable populations such as human immunodeficiency virus (HIV)-infected patients. The objective of this study was to measure ATA levels among the HIV immigrant population compared with US-born HIV-infected patients.
Methods A convenience sample of 158 HIV-infected individuals was recruited to determine the levels of ATA. A nonprotective level of ATA was defined as below 0.15 IU/ml.
Results Among the HIV-infected patients, 72% (114/158) were born in the USA. A total of 17% (27/158) lacked protective levels of ATA. A total of 6.1% (7/114) of those born in the USA lacked protection, compared to 45% (20/44) born outside the USA ($p<0.0001$).
Conclusion The results illustrate that the country of birth is an important predictor of ATA protection, even among HIV-infected patients.

Keywords Tetanus immunization · HIV-infected patients · Tetanus antibody protection

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Introduction

Tetanus is characterized by generalized rigidity and spasm of skeletal muscles that often progresses to respiratory failure and death. The clinical manifestations of tetanus are caused by the exotoxins made by *Clostridium tetani*, a gram-positive, anaerobic rod, which is found in soil, animal intestines and faeces [1]. The causative agent enters the human body through a wound where the toxins are produced and spreads via blood and lymphatics in order to wreak havoc on neurotransmitter release in the central nervous system.

Newly reported cases of tetanus-related deaths have dropped steadily since the introduction of tetanus toxoid into routine childhood immunization in the late 1940s [1, 2]. The Advisory Committee on Immunization Practices (ACIP) recommends that the first four doses of diphtheria-tetanus-acellular pertussis vaccine in childhood be administered at ages 2, 4, 6 and 15–18 months. The fifth dose is given at age 4–6 years with a subsequent tetanus and diphtheria toxoid (Td) booster given at age 11–12 years and then every 10 years thereafter [1, 3]. Since 2005, an adult tetanus, diphtheria and pertussis vaccine has been available for adult patients under the age of 65 [4].

During the period of 1998–2000, an average of 43 tetanus cases was reported annually in the USA [2]. It has been well documented that the elderly are less likely to have adequate

Table 1 Lack of tetanus protection by place of birth and age

Age (years)	All ages *n* (%)	22–29 *n* (%)	30–39 *n* (%)	40–49 *n* (%)	50–59 *n* (%)	60 & up *n* (%)	*p* value
US born	7/114 (6.1)	1/5 (20.0)	0/11 (0)	2/49 (4.1)	1/43 (2.3)	3/6 (50.0)	0.001
Foreign born	20/44 (45.5)	2/4 (50.0)	1/8 (12.5)	5/16 (31.3)	9/12 (75.0)	3/4 (75.0)	0.033

tetanus titres [2, 5–7]. Other patient populations, such as immigrants to the USA (foreign born), are also less likely to have protection against tetanus. In one study, 84% of adult immigrants over the age of 50 years did not have protective titres to tetanus compared to 21% of US-born individuals in the same age group [8]. In another study, 18% of immigrants lacked seroprotection despite a history of adequate immunization [9].

Another population that may be vulnerable to tetanus are individuals infected with the human immunodeficiency virus (HIV) [10, 11]. Previous serosurveys have suggested that HIV-infected patients are less likely to have adequate anti-tetanus antibodies (ATA). The progressive decline of CD4 levels in HIV-infected individuals could potentially lead to lost immunity to tetanus [10–12]. We speculate that immigrant status within the HIV patient population may confer an additional negative impact on tetanus immunity.

To determine whether the loss of immunity among HIV patients residing in the USA is a function of country of birth, this study quantifies ATA levels among HIV-infected persons born in the USA compared to those born in foreign countries and immigrated to the USA.

Methods

A convenience sample of HIV adult patients was recruited from an HIV outpatient centre based at a university teaching hospital from October 2006 through October 2007. To be eligible, individuals needed to be infected with HIV, be 18 years of age or older and agree to participate. A structured interview was conducted requesting age, gender, country of birth, military service, history of intravenous drug use, HIV infection and previous tetanus immunization. Serum samples were obtained and stored at −30°C for batch testing. Levels of ATA were measured using an antigen-specific IgG enzyme-linked immunosorbent assay (ELISA) kit (Bindazyme, The Binding Site, Inc., San Diego, CA, USA). A nonprotective level of ATA was defined as below 0.15 IU/ml, as per the manufacturer's recommendations. Data were analysed using descriptive statistics, Student's *t*-test and chi-squared analysis, and a p value <0.05 was considered statistically significant. The study was approved by the Human Subjects Review Committee at the North Shore-Long Island Jewish Health System and written informed consent was obtained from each patient.

Results

There were 158 HIV-infected subjects enrolled in the study. The mean age was 46 years (SD: 10.2, range: 22–71), 64% (101/158) were male and 72% (114/158) were born in the USA. A total of 17% (27/158) lacked protective levels of ATA. In a univariate analysis, neither age nor gender predicted ATA protection. However, the country of birth was associated with ATA protective levels. A total of 6.1% (7/114) of those born in the USA lacked protection, compared to 45% (20/44) born outside the USA ($p<0.0001$).

Since lower tetanus immunity has been reported with age greater than 50 years [2, 5–7, 13] we evaluated whether age differences in relation to country of birth accounted for the observed differences in protection. The mean age of those born in the USA was similar to those born outside the USA (47.5 years vs 45.1 years, $p=0.154$). Further, the number of individuals over 50 years born in the USA (40/114, 35%) was similar to the number over 50 years and born outside the USA (15/44, 34%, $p=0.906$).

Table 1 shows a detailed breakdown of age by decade, country of birth and immunity to tetanus. Overall, the frequency of ATA protection appeared lower in those born outside of the USA for the age groups shown when compared to those born in the USA. Of note, regardless of where the individual was born, there was a general trend for levels of protection to be lower in the youngest and the oldest groups. Within the US-born group the differences by age were sta-

Table 2 Immune status by region of birth

Place of birth	*n* (%)	Non-immune to tetanus, *n* (%)
Central America, South America, Mexico	9/158 (5.7)	3/9 (33.3)
Caribbean	24/158 (15.2)	10/24 (41.7)
Africa, Asia	9/158 (5.7)	7/9 (77.8)
Europe, Middle East	2/158 (1.3)	0/2 (0)
USA/Puerto Rico	114/158 (72.2)	7/114 (6.1)

tistically significant (p=0.001); within those born outside the USA the difference trends were also significant (p=0.033).

The frequency of protection of individuals born outside the USA somewhat varied when the general place of birth was evaluated (see Table 2). With regards to military service 2/44 (4.5%) of the foreign born served in the military of their country and of the US born 10/114 (8.8%) served in the US military. Only two of these persons, both of whom served in the US military, had non-immune titres. Regarding intravenous drug use 26/114 (23%) of US-born subjects admitted to past or current usage, while only one of those born outside the USA indicated IV drug usage (IVDU). All of the IVDU patients had immune titres. Data regarding past immunizations were not analysed as most patients (59%) were unsure of their history.

Discussion

Upon arrival to the USA, immigrants are required to show proof of tetanus immunization or receive the appropriate vaccinations to confer immunity. Despite this mandate, this study shows that the foreign-born individuals infected with HIV often do not have protective titres to tetanus compared to US/Puerto Rican-born HIV-infected individuals. The results illustrate that the country of birth is an important predictor of ATA protection, even among HIV-infected patients. These results are consistent with seroprevalence studies of immigrant groups in the general USA population, where 67% of Mexican Americans born outside the USA lack protection [14], and 86% of Korean Americans born outside the USA lack protection [9].

Much has been written in the literature regarding declining tetanus immunity in older patients with one study using an age cut-off of 50 years [2, 5–8, 13]. The ACIP guidelines have recommended that all patients 50 years and older be evaluated for completeness to tetanus and other immunization recommendations [15]. In our study, there were no differences in age between the USA and non-US-born subjects, so age did not explain these patterns of immunity. We speculate that either inadequate immunization practices in the countries of origin or poor individual compliance with decennial tetanus boosters may contribute to these differences. If so, vaccination history for immigrants at the time of US entry would require more rigorous scrutiny.

Among our study limitations are the over-sampling of men and testing a population from one region in New York, USA. While 66% of HIV-infected individuals enrolled in the study were men, it reflects the current epidemiology of the HIV/acquired immunodeficiency syndrome (AIDS) epidemic where the majority of cases occur among males [16]. Other limitations include patients not being asked about their primary medical care, when they immigrated to the USA or the amount of years spent living in this country.

In summary, for US-born individuals followed at an HIV clinic, having HIV does not appear to influence tetanus immune status. In our population of HIV-infected adults, 97% of US-born individuals had protective antibodies to tetanus (mean age 45), which is broadly similar to a 90% seroprevalence found in the general USA population (mean age 37) [7]. It is still unclear from this study whether a low level of ATA among foreign-born patients infected with HIV is due to being non-immunized, inadequately immunized or having lost immunity and further study is needed to address this. It is possible that those born in the USA may receive better primary and secondary immunization, better care for their HIV or both. Pending further study, clinicians who care for HIV patients born outside the USA should be aware they are less likely to have tetanus protection. For the outpatient provider this means taking a careful history for previous primary or secondary immunization, or checking ATA titres. For the emergency physician this means ensuring adequate immunization when treating routine wounds or considering providing tetanus immunoglobulin (TIG) for high-risk populations with substantial wounds.

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