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Short communication

Insufficient protection for healthy elderly adults by tetanus and TBE vaccines

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Abstract

Little information is available on post-vaccination antibody concentrations and the duration of protection in persons of more than 20 years of age. We, therefore, measured antibodies specific for tetanus (TT) or tick-borne encephalitis (TBE) virus in 734 adults (age 18–93 years, 382 females and 352 males) and evaluated these data in connection with the time point of the last vaccination against tetanus or TBE and age. This analysis revealed that the time of the last vaccination as well as age had highly significant effects on tetanus and TBE titers ($p < 0.001$). Our results show a strong decline in post-vaccination antibody concentrations with age, which sets in at the age of 40 in the case of tetanus, and is observed right throughout adult life in the case of TBE. Persons over 60 years of age frequently do not have protective antibody concentrations. We conclude that immunological responsiveness to vaccination decreases throughout adult life, and that conventional vaccination strategies designed for children and young adults cannot be uncritically applied in the elderly.

Keywords: Aging; Elderly; Vaccination; Antibody concentrations

1. Introduction

In the elderly, the incidence of severe infections, in particular, pneumonia and urinary-tract infections, is high [1,2] and the protective effect of vaccination is low [3], both due to the fact that the function of the immune system declines with age [4]. Many elderly people do not have immunity even against vaccine-preventable diseases like tetanus (45% without protective antibodies) or tick-borne encephalitis (TBE) (47% without protective antibodies) as previously shown [5,6]. Although tetanus infections diminished dramatically since the tetanus toxoid vaccine was first introduced, the disease has not disappeared. The incidence for tetanus in Austria is about five cases per year. Concerning TBE, the increasing vaccination coverage resulted in a more or less steady decline of the morbidity of TBE infections in Austria [7]. Maintenance of immunity is often not assured, and especially the elderly represent the main risk group to contract and die in terms of serious complications. These facts do, however, frequently escape public awareness. This is unfortunate given the demographic change to elderly populations taking place in many countries. As infectious diseases remain a major cause of morbidity and mortality in the elderly, which could be prevented by appropriate vaccination, information on post-vaccination antibody concentrations and the duration of protection from disease in persons of more than 20 years of age is urgently needed. We, therefore, measured antibodies specific for tetanus or TBE virus in healthy ambulatory adults and evaluated these data in connection with the time point of the last vaccination against tetanus or TBE, respectively.

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2. Methods

Seven hundred and thirty-four donors (age 18–93 years; 382 females, 352 males) had been vaccinated according to official recommendations by health authorities, i.e., vaccination against tetanus did not date back longer than 10 years and against TBE not longer than 3 years (Table 1). TBE vaccination is recommended for all persons likely to be exposed to tick attacks. The high frequency of vaccination against TBE is due to the fact that this disease is endemic in parts of Austria. All participants were recruited by local health authorities from five Austrian cities (Innsbruck 157; Linz 157; St. Pölten 159; Villach 132; and Vienna 127 participants), which they regularly visited for routine vaccinations and where their vaccination history was well recorded. The participants were randomly sampled. Primary immunization dated back many years in all participants and each participant had received two to five booster injections at regular intervals of 10 or 3 years, respectively. The study protocol was approved by the local ethical committee and all participants provided informed consent. A medical history was obtained. None of the individuals studied had a serious recent or chronic disease.

Antibody determinations against tetanus and TBE were performed by one-site enzyme-linked immunosorbent assay (ELISA) with solid phase-bound antigens [8]. TBE antibodies were not determined in persons with known exposure or vaccination against other diseases caused by flaviviruses. Sera were added at dilutions between 1:2000 and 1:64,000. According to the recommendation of WHO and NIBSC, full protection was assumed to be present at tetanus antibody concentrations of $\geq$0.1 IU/ml. As no independently published recommendation is available for TBE, antibody concentrations of $\geq$100 Vienna Units/ml were considered as fully protective following a recommendation of the vaccine manufacturer (Baxter Vaccines, Orth, Austria).

Statistic analyses were done by Spearman's rank correlation test to assess possible correlations between antibody concentrations and age, gender as well as time since the last vaccination. Fisher's exact test was used to statistically compare younger versus elderly adults below protective antibody levels. For the demonstration of the non-linear age dependency, a Lowess curve fitting was applied. To assess the independent effect of age, time since last vaccination and gender on titer levels, we performed a multiple regression analysis using log-transformed variables.

Table 1
Age distribution of samples

Age group	Frequency
<20	23
20–29	172
30–39	158
40–49	50
50–59	50
60–69	101
70–79	115
80–89	55
>90	10

3. Results and discussion

Our results show a strong decline in post-vaccination antibody concentrations with age. This relationship was evaluated by Spearman's rank correlation coefficient. In spite of variations (Figs. 1a and 2a) within each age group and at each post-vaccination time point, a clear-cut pattern was observed. For tetanus as well as TBE, a significant ($p < 0.01$) negative

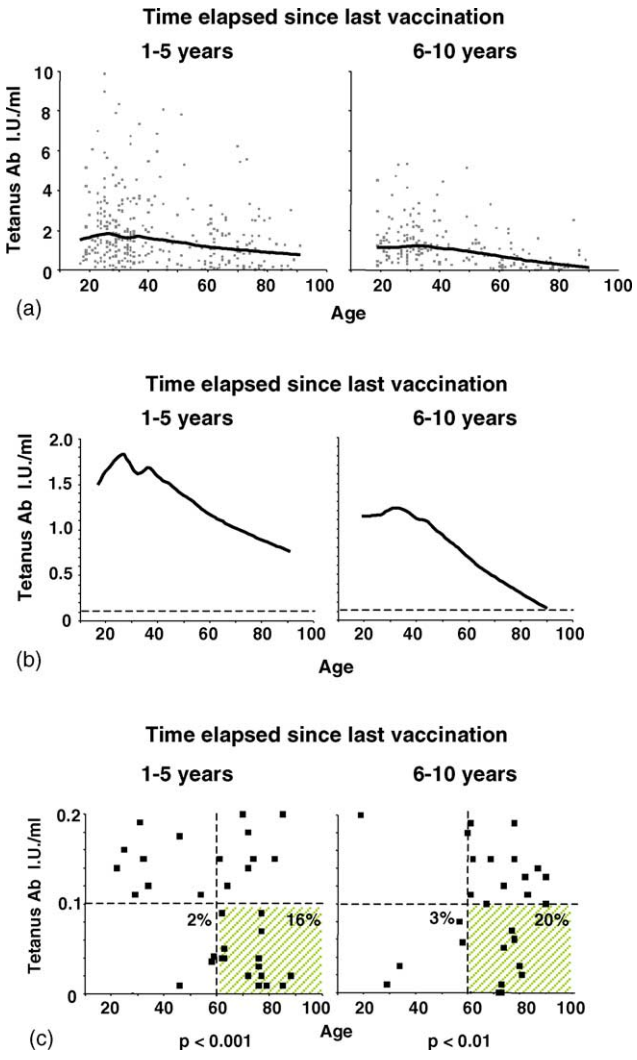

Fig. 1. Post-vaccination tetanus-specific antibody concentrations and protection from disease depend on age. Individual antibody concentrations and Lowess smoothing curves are depicted in panel (a). Fifty percent of the nearest data points were used for smoothing. Panel (b) shows details of the Lowess curves using a different scale to point out the dynamics of age-related changes in antibody concentrations. The dashed lines represent the antibody concentration generally considered as protective. Panel (c) shows antibody concentrations in individuals below the protective level (dashed lines) and statistically compares the percentage of persons without protective antibody levels in elderly (>60 years) and younger adults. Spearman's rank correlation test (a and b) and Fisher's exact test (c) were used for statistical analyses.

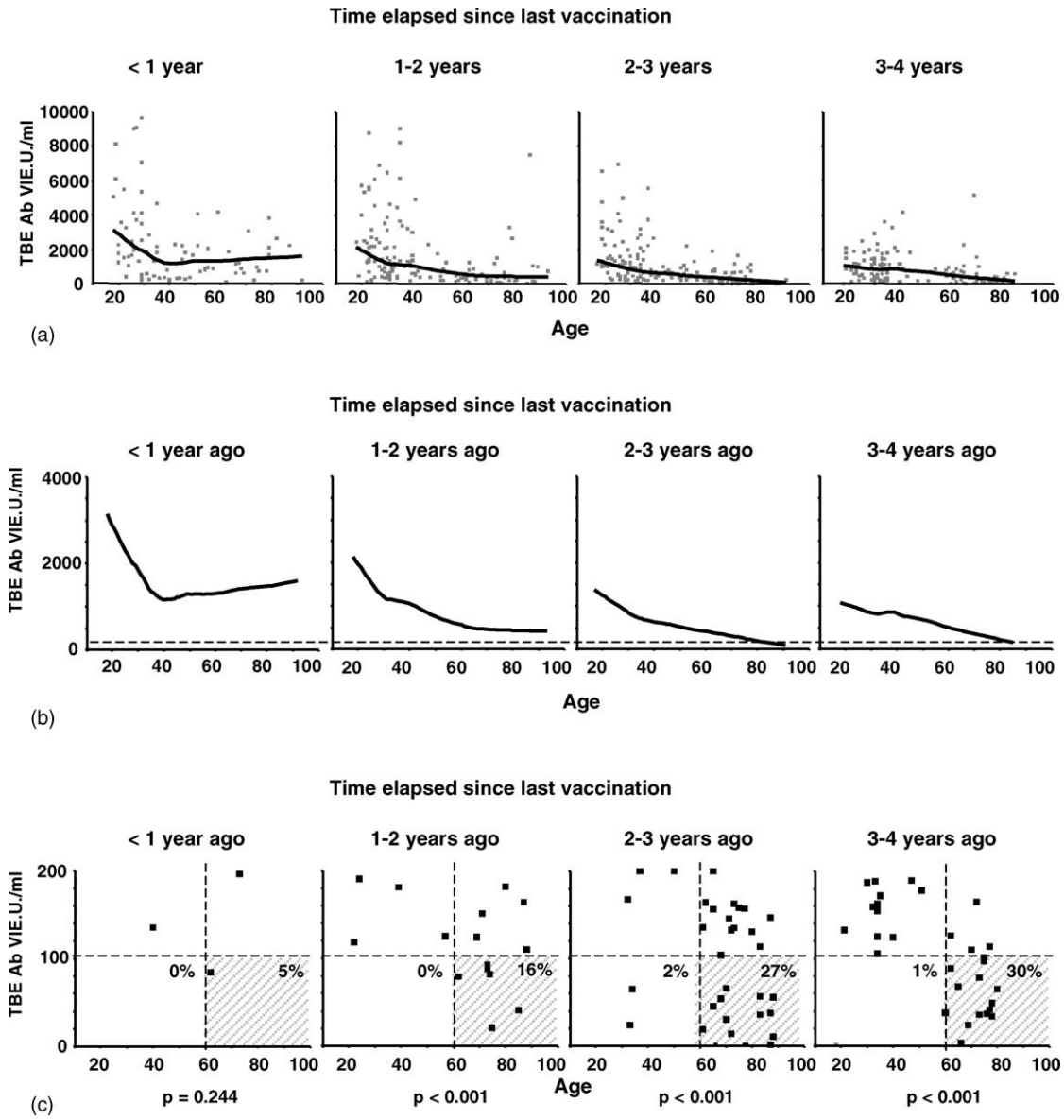

Fig. 2. Post-vaccination TBE-specific antibody concentrations and protection depend on age. Individual antibody concentrations and Lowess smoothing curves are depicted in panel (a). Fifty percent of the nearest data points were used for smoothing. Panel (b) shows details of the Lowess curves using a different scale to point out the dynamics of age-related changes in antibody concentrations. The dashed lines represent the antibody concentration generally considered as protective. Panel (c) shows antibody concentrations in individuals below the protective level (dashed lines) and compares the percentage of persons without protective antibody levels in elderly (>60 years) and younger adults. Spearman's rank correlation test (a and b) and Fisher's exact test (c) were used for statistical analyses.

correlation between antibody titer and age was found for all vaccination intervals.

In the case of tetanus, antibody concentrations were fairly stable up to the age of 40, but showed an almost linear decline afterwards (Fig. 1b). When vaccination dated back 1–5 years, the fitted Lowess curves were still above protective antibody concentrations, but declined to non-protective levels in old persons when vaccination dated back between 6 and 10 years. Antibody concentrations below the fully protective level occurred in 16% of persons of more than 60 years of age when vaccination dated back 1–5 years, and in 20% of the persons over 60 who had been vaccinated 6–10 years ago (Fig. 1c). Tetanus antibody concentrations below protective levels were very rare (≤3%) in persons under 60 years.

TBE post-vaccination antibody concentrations decreased in a more or less linear way throughout adult life (Fig. 2b). Only when vaccination dated back less than 1 year, there was a sharp bend in the curve around the age of 40 after which there was no further decline. Antibody concentrations below the protective level were rarely (≤2%) detected in persons under 60 years of age, but were observed in 5–30% of the persons over 60, depending on the time elapsed since the last vaccination (Fig. 2c).

Additionally, we performed a multiple linear regression analysis in order to assess the independent effect of age, time since last vaccination and gender on antibody concentrations. This analysis revealed that time of last vaccination had a significant effect on the tetanus titer ($t = -10.162$; $p < 0.001$) and on the TBE titer ($t = -6.224$; $p < 0.001$). Age was more important than time and showed a highly significant association with antibody concentrations in TT ($t = -12.108$; $p < 0.001$) and TBE ($t = 14.277$; $p < 0.001$). Gender influences were only significant with regard to the TT titer ($t = 2.311$; $p = 0.021$; higher antibody titers in male persons). Age and duration after last vaccination showed a significant relationship only in regard to the TT titer (age with duration TT, $r = 0.111$; $p = 0.006$) but not to the TBE titer (age with duration TBE, $r = 0.068$; $p = 0.104$). Although these results indicate that current immunization schedules may not provide sufficient protection in elderly persons, it has to be stated that the retrospective study design included the following limitations: although vaccination history was well recorded and a questionnaire was completed, some information might be inaccurate in terms of participants recall bias as well as of interpretive bias of the physicians obtaining the data.

Our results demonstrate that the level of humoral immunity induced by vaccination decreases throughout adult life. This leads to the loss of full protection in a considerable proportion of persons older than 60 years, in particular when the interval to the last booster injections becomes longer. This is a highly unsatisfactory situation. As in children, it should also be the goal of vaccination strategies for adults to guarantee full protection in the highest possible percentage of persons. A better awareness of the problems of adult vaccination would be of great importance to prevent infectious diseases in elderly persons.

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