Protection against Tetanus and Diphtheria in Europe: The impact of age, gender and country of origin based on data from the MARK-AGE Study

Birgit Weinbergera,⁎, Michael Kellerb, Christina Putzera, Daniel Breitenbergerb, Bernhard Kollerb, Simone Fieglc, María Moreno-Villanuevad, Jürgen Bernharde, Claudio Franceschif, Konstantinos Voutetakisg, Efstathios S. Gonosg, Mikko Huremb, Ewa Sikorai, Olivier Toussaintj,1, Florence Debacq-Chainiauxj, Tilman Gruneb,2, Nicole Breusingb, Alexander Bürkled, Beatrix Grubeck-Loebensteinain

a Institute for Biomedical Aging Research, Universität Innsbruck, 6020 Innsbruck, Austria
b Landeskrankenhaus Hall, 6060 Hall in Tirol, Austria
c UMIT Private Universität für Gesundheitswissenschaften, Medizinische Informatik und Technik GmbH, 6060 Hall in Tirol, Austria
d Molecular Toxicology Group, Department of Biology, University of Konstanz, 78457 Konstanz, Germany
e BioTeSys GmbH, 73728 Esslingen, Germany
f Department of Experimental Pathology, University of Bologna, 40126 Bologna, Italy
g Institute of Biological Research and Biotechnology, National Hellenic Research Foundation, Athens 11635, Greece
h Department of Microbiology and Immunology, University of Tampere, 33014 Tampere, Finland
i The Nencki Institute of Experimental Biology, 02-093 Warsaw, Poland
j Research Unit on Cellular Biology, University of Namur, 5000 Namur, Belgium
k University Hohenheim, 70599 Stuttgart, Germany

ARTICLE INFO

Keywords:
Antibody concentrations
Tetanus
Diphtheria
Europe
Vaccination

ABSTRACT

Due to the successful implementation of vaccination strategies early-life morbidity and mortality due to infectious disease has been reduced dramatically. Vaccines against tetanus and diphtheria are among the most frequently used vaccines worldwide, but various studies in different European countries have shown that protection against tetanus and particularly against diphtheria is unsatisfactory in adults and older persons.

In this study we analyzed tetanus- and diphtheria-specific antibody concentrations in 2100 adults of different age from 6 selected European countries (Austria, Belgium, Germany, Greece, Italy, Poland) in order to investigate differences in the level of protection against tetanus and diphtheria across Europe. Our data reveal that tetanus- and diphtheria-specific antibody concentrations vary greatly between countries, which is also reflected in the percentage of persons with antibody concentrations below the protective level (0.1 IU/ml), which ranged from 2 to 31% percent for tetanus and 28–63% for diphtheria. In most countries, tetanus- and diphtheria-specific antibody concentrations decrease with age. This phenomenon is more pronounced in countries with generally low antibody levels, such as Italy, Poland and Greece. Interestingly, tetanus-specific antibody concentrations are generally higher in males than in females, which is probably due to vaccination during their military service or more frequent booster vaccinations after injuries, whereas no gender-related differences were found for diphtheria-specific antibodies.

In conclusion, our study demonstrates that the European population is not fully protected against tetanus and diphtheria. Measures to improve protection should include a life-long perspective on vaccination, more education to increase awareness of and compliance with vaccination guidelines, and a harmonization of recommendations and incentives across Europe.

http://dx.doi.org/10.1016/j.exger.2017.08.037
Received 11 July 2017; Received in revised form 23 August 2017; Accepted 24 August 2017
0531-5565/ © 2017 Elsevier Inc. All rights reserved.

Please cite this article as: Weinberger, B., Experimental Gerontology (2017), http://dx.doi.org/10.1016/j.exger.2017.08.037
1. Introduction

Due to the successful implementation of vaccination strategies early-life morbidity and mortality due to infectious disease could be reduced dramatically. Vaccines against tetanus and diphtheria are among the most frequently used vaccines worldwide.

Despite low incidences of tetanus and diphtheria in Europe with 161 cases of tetanus and 36 cases of diphtheria per year (mean from the time period 2009–2014) (http://apps.who.int/immunization_monitoring/globalsummary), vaccination against these diseases is still of importance. *Clostridium tetani* is found ubiquitously in soil and infection occurs mainly through contaminated wounds. Due to this mode of transmission, vaccination does not decrease the prevalence of the bacteria and there is no herd immunity effect, which means that each individual needs to be vaccinated in order to be protected. In contrast, *Corynebacterium diphtheriae* is transmitted from person to person via droplets. In the early 1990s a large outbreak with > 140,000 cases and > 4000 deaths occurred in the states of the former Soviet Union demonstrating that the pathogen is still present and can spread efficiently in a partially unprotected population (Vitek and Wharton, 1998).

We have previously shown that protection against tetanus and particularly against diphtheria is unsatisfactory in Austrian adults and older persons. Specific antibody concentrations of 0.01 IU/ml is sometimes considered to provide partial protection, but generally, concentrations above 0.1 IU/ml are defined as protective (Roper et al., 2013; Tiwari and Wharton, 2013). In a cross-sectional study we could demonstrate that tetanus-specific antibody concentrations decline with increasing time since the last vaccination and that antibody concentrations were lower in older adults compared to young adults (Hainz et al., 2005; Hainz et al., 2002). These results are in concordance with data from Israel (Matzkin et al., 1985). In a longitudinal observation, the half-life of tetanus antibodies has been estimated to be 11 years (Amanna et al., 2007), and similar results have also been reported for diphtheria-specific antibodies (von Hunolstein et al., 2000; Mathet al., 1997). In a local cohort of older adults (> 60 years) we had recruited in 2005 in Austria 12% and 65% of the participants were not protected against tetanus or diphtheria, respectively (Kaml et al., 2006; Weinberger et al., 2013). Interestingly, 53% of a young cohort (20–40 years) recruited 5 years later were also not protected against diphtheria, whereas all participants were protected against tetanus (Weinberger et al., 2013). Long-term follow-up of these cohorts revealed that antibody concentrations decline substantially already within 5 years after a booster vaccination (Grasse et al., 2016). Similar data have been reported in cohorts from Spain (Bayas et al., 2001), Belgium and Australia (Van Damme and Burgess, 2004), Italy (Filia et al., 2014) and France (Launay et al., 2009).

In this study we analyzed tetanus- and diphtheria-specific antibody concentrations in adults of different age from six European countries (Austria, Belgium, Germany, Greece, Italy, Poland) in order to investigate differences in the level of protection against tetanus and diphtheria across Europe, gender differences and the impact of age. General childhood vaccination against tetanus and diphtheria has already been implemented in most European countries between 1940 and 1960. Regular booster vaccinations for adults were recommended much later, i.e. in the 1980s to 1990s. Current vaccination recommendations in the six countries included in this study comprise two or three doses within the first 2 years of life, and two additional doses at ages 2–8 years and 9–18 years. Poland recommends one booster shot during adulthood, whereas all other countries recommend regular vaccinations every 10 year for adults, and booster intervals are shortened to 5 years for persons over the age of 60 in Austria (http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx).

2. Material and Methods

2.1. Study cohort and specimen collection

The samples used in this study were collected in the context of the collaborative project MARK-AGE, which aimed at identifying biomarkers of ageing (Burkle et al., 2015). In total 2100 samples were included in the analysis (Austria: n = 381; Belgium: n = 256, Germany: n = 345; Greece: n = 369; Italy: n = 380; Poland: n = 369). The study was designed to include similar number of subjects for all age groups (35–44 y: n = 472; 45–54 y: n = 537; 55–64 y: n = 557; 64–74 y: n = 534) and a balanced gender distribution within countries and age groups (females: n = 1068; 50.9%). Briefly, blood was drawn from the cubital vein after overnight fasting, and serum was prepared by centrifugation within 2 h after collection and stored at –80 °C. Information on vaccination status against tetanus was obtained using a self-administered questionnaire. No information was available regarding the vaccination status against diphtheria. The collection of human blood samples was approved by competent local authorities. Written informed consent was obtained from all participants.

2.2. ELISA

Tetanus- and diphtheria-specific IgG antibodies were measured centrally as described previously (Hainz et al., 2002) coating the plates with 100 ng per well tetanus or diphtheria toxoid (Statens Serum Institute). After blocking with 0.01 M glycine in PBS, tetanus or diphtheria standard (NIBSC) and diluted serum samples were added. Bound antibodies were detected via a HRP-conjugated secondary antibody (Chemicon) at a 1:60,000 dilution and TMB one component Substrate Solution (Diarect). The detection limit of the assays used was 0.01 IU/ml, and values below this concentration were set to 0.005 IU/ml for calculation of geometric mean concentrations (GMC). Ab concentrations above 0.1 IU/ml were considered protective (Roper et al., 2013; Tiwari and Wharton, 2013).

2.3. Statistical analysis

Differences in antibody concentrations between countries were analyzed using the Kruskal-Wallis Test, followed by Mann-Whitney U test and Bonferroni post hoc analysis. Differences between age groups and gender were calculated using the Mann-Whitney U test. Differences in the distribution of vaccinated and non-vaccinated individuals were calculated using the Chi Square test for independence assuming equal distribution for all groups.

3. Results

3.1. Self-reported vaccination history

Self-reported vaccination history for tetanus was available for 2032 participants and varied greatly between countries: Whereas 83% of the participants in Germany, 74% in Belgium, and 65% in Austria had been vaccinated in the past 10 years, the coverage was much lower in Italy with 38%, in Poland 23% and in Greece 10% (χ²(6) = 611.688, p < 0.0001). No information was available on childhood vaccination and the number of booster immunizations since then. No differences were observed between male and female participants and vaccination history was similar for all age groups in all countries except Greece where the percentage of recently vaccinated participants declined with increasing age (χ²(3) = 7.925, p = 0.048; 35–44 y:15%; 45–54 y: 13%; 55–64 y: 7%; 65–74 y: 5%) despite the fact that regular vaccination is recommended throughout adulthood.
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات