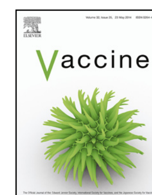
Vaccine 32 (2014) 5624–5631

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Humoral responses to independent vaccinations are correlated in healthy boosted adults

Lori Garman[a,b], Amanda J. Vineyard[a], Sherry R. Crowe[a,1], John B. Harley[c,d], Christina E. Spooner[e], Limone C. Collins[e], Michael R. Nelson[e], Renata J.M. Engler[e], Judith A. James[a,b,f,*]

[a] Oklahoma Medical Research Foundation, Department of Arthritis and Clinical Immunology, Oklahoma City, OK 73104, USA
[b] Oklahoma University Health Science Center, Department of Microbiology and Immunology, Oklahoma City, OK 73104, USA
[c] Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229, USA
[d] Cincinnati Veterans Affairs Medical Center, Cincinnati, OH 45220, USA
[e] Walter Reed National Military Medical Center, Bethesda, MD 20814, USA
[f] Oklahoma University Health Science Center, Departments of Medicine and Pathology, Oklahoma City, OK 73104, USA

ARTICLE INFO

Article history:
Received 6 December 2013
Received in revised form 11 July 2014
Accepted 6 August 2014
Available online 17 August 2014

Keywords:
Anthrax vaccine adsorbed
Measles
Mumps
Tetanus
Hepatitis B
Pertussis

ABSTRACT

Background: Roughly half of U.S. adults do not receive recommended booster vaccinations, but protective antibody levels are rarely measured in adults. Demographic factors, vaccination history, and responses to other vaccinations could help identify at-risk individuals. We sought to characterize rates of seroconversion and determine associations of humoral responses to multiple vaccinations in healthy adults.

Methods: Humoral responses toward measles, mumps, tetanus toxoid, pertussis, hepatitis B surface antigen, and anthrax protective antigen were measured by ELISA in post-immunization samples from 1465 healthy U.S. military members. We examined the effects of demographic and clinical factors on immunization responses, as well as assessed correlations between vaccination responses.

Results: Subsets of boosted adults did not have seroprotective levels of antibodies toward measles (10.4%), mumps (9.4%), pertussis (4.7%), hepatitis B (8.6%) or protective antigen (14.4%) detected. Half-lives of antibody responses were generally long (>30 years). Measles and mumps antibody levels were correlated ($r = 0.31$, $p < 0.001$), but not associated with select demographic features or vaccination history. Measles and mumps antibody levels also correlated with tetanus antibody response ($r = 0.11$, $p < 0.001$).

Conclusions: Vaccination responses are predominantly robust and vaccine specific. However, a small but significant portion of the vaccinated adult population may not have quantitative seroprotective antibody to common vaccine-preventable infections.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

Current United States (U.S.) vaccination practice calls for administration of standardized sets of vaccinations to populations defined by age and in some cases, sex, with the assumption that essentially everyone will respond by generating protective and long-lived antibody titers [1]. Most vaccinations are given during childhood, and follow-up antibody titers are rarely assessed. This vaccination approach generates herd immunity, affords general disease control, and protects most children from vaccine-preventable disease. However, this approach does not consider primary vaccine failure, in which an adult may not develop protective immunity even with booster vaccination; secondary vaccine failure, where antibody titers decline with time; nor the failure of many adults to

Abbreviations: MMR, measles, mumps, and rubella vaccine; Td/Tdap, tetanus vaccines; HBs, hepatitis B surface antigen; AVA, Anthrax vaccine adsorbed; PA, protective antigen; AA, African Americans; EA, European Americans; OD, optical density; SD, standard deviations.

* Corresponding author at: Department of Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, 825 NE 13th St., Oklahoma City, OK 73104, USA. Tel.:+1 405 271 4987; fax: +1 405 271 7063.
E-mail address: jamesj@omrf.org (J.A. James).
[1] Present address: PharmAthene, Inc, One Park Place Suite #450, Annapolis, MD 21401, USA.

http://dx.doi.org/10.1016/j.vaccine.2014.08.005
0264-410X/© 2014 Elsevier Ltd. All rights reserved.

receive recommended boosters. The recent resurgence of pertussis has demonstrated that waning vaccine-induced immunity allows endemic infections in adults, endangering potentially susceptible children [2,3].

In the U.S., most people are vaccinated against measles, mumps, tetanus, pertussis and, since 1991, hepatitis B as children (Supplementary Table 1). Current recommendations for adult boosters include doses of tetanus toxoid with diphtheria (Td or Tdap) every 10 years, and most recently, a single booster of acellular pertussis [4], but non-influenza vaccine coverage in civilian adults is only 40–60% [5]. In contrast, upon enlistment military personnel are generally given MMR if not already immune, Td/Tdap boosters, the standard hepatitis B vaccination series, and anthrax vaccine adsorbed (AVA) if deemed at risk [6].

Primary vaccine failure rates vary greatly. Primary MMR failure rates in children against both measles and mumps are 2–7% [7]. Hepatitis B vaccination in adolescents or adults has a primary failure rate of 2–10% for two or three doses [8,9]. Acellular pertussis vaccinations have fairly high primary failure rates of 11–29%; in addition, antibody is short-lived [2,10]. AVA and tetanus vaccinations both have very low primary failure rates (<3%) [11,12]; although, antibody titers generated in response to AVA wane rapidly [13,14]. Primary vaccine failure is thought to be vaccine-specific and may be primarily controlled by select variations in genes encoding HLA proteins, pattern recognition receptors, or cytokines [1,7,15–18]. However, other genetic associations with vaccination response, including polymorphisms in cytokines and cytokine receptors, sex, or environmental factors such as stress, obesity, and smoking, may influence the individual response to multiple vaccinations [19–25]. To our knowledge, only two studies to date have compared concurrent vaccination responses to multiple vaccine antigens within a given individual, and both used pediatric cohorts [7,26].

Expecting that vaccine responses would be similar for vaccines that induce antibody generation via comparable mechanisms, we hypothesized that adult vaccination response to protein vaccines containing aluminum adjuvant (tetanus toxoid vaccines, pertussis vaccines, hepatitis B, and AVA, see Supplementary Table 1) would be strongly correlated, and that responses to live attenuated viral preparations (measles, mumps) would be strongly correlated. We measured antibody titers against measles, mumps, tetanus toxoid, whole pertussis, protective antigen (PA, from AVA), and hepatitis B surface antigen (HBs) and determined protective seroprevalence, examined the impact of vaccination history or demographics on antibody levels, and evaluated the extent to which antibodies directed toward components of different vaccines were correlated.

2. Materials and methods

2.1. Human subjects

Military personnel ($n = 1465$) who had been immunized at least 3 times with AVA provided informed written consent and vaccination history, sex, age, and race information. Institutional Review Board approval was obtained from the Oklahoma Medical Research Foundation, Walter Reed Army (after August 2011, Walter Reed National Military) Medical Center Vaccine Healthcare Centers (VHC) Network/Allergy-Immunology and Womack Army Medical Center, Fort Bragg Regional VHC. Peripheral blood was collected; plasma was isolated, aliquoted, and stored at $\leq -20\,^{\circ}$C until testing. Descriptions of all potential measles, mumps, tetanus, pertussis, anthrax, and hepatitis B vaccinations an individual in this cohort may have received are found in Supplementary Table 1. Detailed vaccination history (Table 1) was available for AVA or hepatitis B vaccination for 100% of individuals tested for PA or HBs antibody, respectively. Of those tested for measles, mumps, tetanus, and pertussis antibody levels, 75.5% (1019/1350), 74.1% (1000/1350), 85.9% (1159/1350), and 0.4% (6/1350) had detailed vaccination histories for the respective vaccine. Acellular pertussis vaccines were introduced in the 1990s. Only 1.8% (24/1350) of this cohort was less than 1 year old in 1990, suggesting the vast majority received at least one dose of whole-cell pertussis vaccination.

2.2. Anthrax protective antigen and hepatitis B surface antigen ELISAs

Ninety-six-well microtiter plates (Corning, Lowell, MA) were coated with 1 μg/well of recombinant PA (List Biological Laboratories, Campbell, CA) or 0.02 μg/well recombinant HBs (Cell Sciences, Canton, MA). Diluted plasma was added, followed by anti-human IgG conjugate (Jackson ImmunoResearch, West Grove, PA) and *para*-nitrophenylphosphate substrate (Sigma-Aldrich, St. Louis, MO), with washing between steps. The optical density (OD) was detected using a Dynex MRX II microplate reader (Dynex Technologies, Chantilly, VA). Concentration of PA and HBs antibodies were calculated from standard curves of the reference sera AVR801 (BEI Resources, Manassas, VA) [27] and WHO international standard 07/164 (NIBSC, Potters Down, UK), respectively. Greater than 10 IU/L of anti-HBs is defined as positive or protected, and a good response is defined as 100 IU/L [8,28]. Non-human primate studies estimate the level of anti-PA IgG that predicts 80% survival in the year following a 3 dose priming series varies from 5.4 to 97.3 μg/mL depending on the time since last vaccination [29]. Therefore, individuals with anti-PA IgG <5.4 μg/mL, 5.4–97.3 μg/mL, and >97.3 μg/mL are considered negative, equivocal, and positive, respectively.

2.3. Measles, mumps, rubella, tetanus, and pertussis ELISAs

IgG commercial ELISAs were performed according to manufacturer protocols (measles, mumps, and rubella: Bio-Rad Laboratories, Redmond, WA; tetanus: MP Biomedicals, Philadelphia, PA; pertussis: Genway Biotech, San Diego, CA). Absorbance was read at 405 nm (measles, mumps, and rubella) or 450 nm (tetanus) against the reagent blank using a Dynex MRX II microplate reader (Dynex Technologies, Chantilly, VA), and index values or antibody concentrations were determined based on a standard curve. Per manufacturer directions, mumps and rubella index values of >1.1, 0.9–1.1, and <0.9 were considered positive, equivocal, and negative for protective levels of antibody. Greater than 0.2 IU/mL of anti-measles and greater than 0.1 IU/mL anti-tetanus were considered protected [30]. Concentration of measles and pertussis antibodies were calculated from standard curves of the WHO international standards 97/648 and 06/140 (NIBSC), respectively. Individuals with greater than 10 IU/mL anti-pertussis were considered positive [28,31]. Individuals with optical densities outside the range of the standard curve were tested again at a higher dilution. A subset of equivocal values was run again with repeatable results.

2.4. Statistical analysis

Analyses included correlation analyses (Spearman), comparison of the medians (Mann–Whitney U), and tests of proportion (Fisher's Exact test). Non-normal data were log transformed prior to analysis. For tests of proportion, equivocal values were included within the positive group. Analysis of predictors of vaccination response was performed for each vaccination independently and included sex, race, age at last vaccination, number of vaccinations, and time since last vaccination. Age at last vaccination is approximate and was calculated from age at sample draw. Where years post vaccination served as the predictor variable (Fig. 2), log-transformed data

Download English Version:

https://daneshyari.com/en/article/10964302

Download Persian Version:

https://daneshyari.com/article/10964302

Daneshyari.com