Infectious Disease and Vaccination

Duration of Humoral Immunity to Common Viral and Vaccine Antigens

PURPOSE OF THE STUDY. To better define the duration of humoral immunity and the role played by memory B cells.

STUDY POPULATION. There were 45 human subjects followed for up to 26 years. These participants were recruited from the Oregon National Primate Research Center. The only inclusion criteria was that subjects had at least 3 serum samples banked for at least 3 years before the study began. The average age at the start and end of the study was 37 and 52 years, respectively.

METHODS. Blood samples were drawn at least annually, and serum was banked. Antibody titers were measured to vaccinia, measles, mumps, rubella, varicella-zoster, Epstein-Barr, tetanus, and diphtheria. Each subject gave an average of 14 serum samples over an average of 15.2 years. Also, the investigators measured antigen-specific memory B cells by means of limiting-dilution analysis and compared memory B-cell frequencies to their corresponding serum antibody levels. The majority of subjects had vaccination to smallpox in childhood and had recovered from the other viral diseases such as measles and rubella.

RESULTS. The antibody responses to viral antigens were very stable, with estimated half-lives ranging from 50 years for varicella-zoster to >200 years for measles and mumps. Against tetanus and diphtheria, the antibody responses waned more rapidly with half-lives of 11 and 19 years, respectively. The investigators also found that B-cell memory was long-lived, but there was no significant correlation between peripheral memory B-cell numbers and antibody levels for 5 of the 8 antigens.

CONCLUSIONS. Serologic memory for multiple antigens is maintained for remarkably sustained periods of time. Also, memory B-cell numbers did not correlate with antibody titers, which suggests that peripheral memory B-cells and antibody-secreting plasma cells may represent independently regulated cell populations and may play different roles in the maintenance of immunity.

REVIEWER COMMENTS. At the end of the study, the average age of the participants was 52 years. Most had received vaccination to smallpox, but most had also contracted natural measles, mumps, or rubella during childhood. This study population, therefore, does not represent our current population of children with complex schedules of vaccinations. Furthermore, we cannot conclude from this study that vaccination-induced immunity is necessarily as long-lived as natural infection-induced immunity. Nonetheless, this report does give fascinating insight into the “adult” side of immunity to many of the childhood diseases against which we vaccinate. This study also sheds light on possible mechanisms for sustained humoral immunity, which it seems may not entirely depend on regulation by memory B cells.

The Neglected Role of Antibody in Protection Against Bacteremia Caused by Nontyphoidal Strains of Salmonella in African Children

PURPOSE OF THE STUDY. To investigate whether specific antibody protects against nontyphoidal Salmonella (NTS) bacteremia.

POPULATION STUDIED AND METHODS. Admissions for NTS bacteremia during 1 year were reviewed (N = 352). Sera from 65 healthy Malawian children (median age, 24 months; range, 3–107 months) was used for in vitro NTS-killing assays. Purified immunoglobulin G (IgG) from patient sera was used to delineate the role of antibody versus complement. Immunoglobulin and complement deposition on bacteria was also assessed by flow cytometry. Complement dependency was tested by heat inactivation and by using C9-deficient serum.

RESULTS. Overall, 82% of the children with NTS bacteremia were <36 months old, but there was a nonuniform distribution with fewer-than-expected cases in children <4 months old (actual: 9.7% vs 16.7%), suggesting a role for passive humoral immunity. From healthy donors, 9 of 25 children <16 months of age had serum with normal in vitro killing, whereas 40 of 40 children >16 months of age did so. NTS killing in vitro was complement and membrane attack complex dependent. Effective killing corresponded to a specific IgG or IgM Salmonella titer of 1.5 U and was associated with the deposition of complement (C3 and C9) measured by flow cytometry. Resistance to killing by alternative complement activation was mediated by long-chain lipopolysaccharide and the rck gene product.

CONCLUSIONS. Salmonella-specific antibody that overcomes the complement resistance of NTS develops by 2 years of life in Malawian children and is mediated by specific IgG or IgM antibody.
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Brian A. Smart  
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