“Upper Limits of Normal” Antistreptolysin O and Antideoxyribonuclease B Titers

GEORGE C. KLEIN, CAROLYN N. BAKER, AND WALLIS L. JONES
Center for Disease Control, Atlanta, Georgia 30333

Received for publication 17 March 1971

“Upper limits of normal” antistreptolysin O (ASO) and antideoxyribonuclease (ADN) B titers were determined on serum specimens from various age groups of pediatric patients with no history of a recent streptococcal infection and on healthy adult hospital employees. The upper limit of normal value is that level of antibody titer exceeded by no more than 15% of the total subjects in each age group. This value varies with the age of the subject, and the most pronounced differences are between the values of preschool age children, school age children, and adults. The upper limit of normal values for these groups were as follows: preschool age, ASO = 85(100); ADN B = 60(50); school age, ASO = 170(166); ADN B = 170(166); and adult, ASO = 85(100); ADN B = 85(100).

Serological tests such as the antistreptolysin O (ASO) and the antideoxyribonuclease B (ADN B) tests are used as laboratory aids in the detection of group A streptococcal infections and their sequelae, rheumatic fever and acute glomerulonephritis. A “positive” ASO test indicative of a recent streptococcal infection is generally considered to be one in which there is a two-dilution rise in titer between acute- and convalescent-stage serum specimens. Unfortunately, many times only a single specimen is submitted to the laboratory, or if two specimens are sent they may both have been collected during the convalescent stage of the infection. In the first instance, a demonstrable rise in titer is impossible and in the second instance it is much less likely to occur. An additional guideline is needed for specimens which fall into either of these categories. The purpose of the present investigation was to determine the “upper limit of normal” ASO and ADN B titers of various age groups of pediatric patients with no clinical history of a recent streptococcal infection. These upper limits of normal should prove useful as a guideline for suggesting a significant ASO or ADN B titer in the absence of a two-dilution step increase in titer.

MATERIALS AND METHODS

ASO and ADN B titers were determined on 425 and 433 sera, respectively, from patients in a children’s hospital. We did not attempt to select the patients, but we did exclude those with a clinical history of a recent streptococcal infection. The age of the patients ranged from newborn to 15 years. We also performed the tests on sera from apparently “healthy” adult hospital employees; we did not have access to sera from adult hospital patients. ASO titers were determined on 220 specimens and ADN B titers on 197 specimens from this adult group. To compensate for possible seasonal variation, the specimens were collected from November through March, which covers the peak season for streptococcal infections. Thus, the upper limits should be the maximum ones from the standpoint of seasonal variation. A microtitration technique employing serum dilutions of 1:60, 1:85, 1:120, 1:170, 1:240, 1:340, 1:480, 1:680, 1:960, 1:1,360, 1:1,920, and 1:2,720 was used for both the ASO and the ADN B tests. Details of the tests have been described previously (3, 4).

RESULTS

The distribution of ASO and ADN B titers by age group is presented in Tables 1 and 2. The first column under each age group contains numbers of subjects and the second column contains the cumulative percentages. The upper limit of normal ASO titer has previously been defined as that level of antibody titer exceeded by no more than 20% of the control population (7). The upper limit of normal ASO and ADN B titer used in the present study is that level of antibody titer exceeded by no more than 15% of the total subjects in each age group. If the latter definition is applied to the results in Tables 1 and 2, the upper limit of normal ASO titer and the cumulative percentages for the various age groups are as follows: <1 year = 85 (92%); 1–4 years = 60 (85%); 5–8 years = 170 (87%); 9–12 years = 120 (87%); 13–15 years = 170 (97%); and adult = 85 (85%). In the case of the ADN B titers, the upper limit of normal and the cumulative percentage are as follows: <1 year = 60 (89%); 1–4 years = <60 (88%);
DISCUSSION

Most of the reports in the literature dealing with "normal" ASO titers have been based on the study of healthy subjects. We chose pediatric patients with no clinical history of a recent streptococcal infection, rather than healthy subjects, for our study because we believe that their titers are more relevant as a base line for suggesting what constitutes a significant ASO of ADN B titer. The reason for this is that the majority of serum specimens submitted to a laboratory for ASO or ADN B tests will be from patients rather than from healthy subjects, even though the patients may not have a streptococcal infection. We had to use healthy subjects for the adult group in our study because we did not have access to hospital patients in this age group. Since we did not determine the upper limit of normal for both healthy subjects and patients in the same age groups, we do not know whether the upper limit of normal would differ in the two types of subjects. However, Mote and Jones (5) included patients with miscellaneous medical diseases as well as healthy subjects in their study and they found that the upper limit of normal ASO titer for the patient group was lower than for the healthy subjects. Therefore, our upper limit of normal titer for the adult group may be higher than it would have been if we had used patients for this group.

Ayoub and Wannamaker (1) determined the upper limit of ADN titers on a group consisting of 3 laboratory workers and 67 hospital patients with no clinical evidence of a recent streptococcal infection. The subjects ranged in age from 1 to 36 years; the mean age was 10.7 years. The upper limit of normal ADN B titer for this group was 250, whereas the upper limit of nor-
normal for our 9 to 15 year group was 170. A possible explanation for the difference may be geographical location (2); however, their upper limit of normal ASO titer for this same group of subjects was 166, which is in close agreement with our upper limit of normal ASO titer (Table 1). Our upper limit of normal ADN B titer is the same as our upper limit of normal ASO titer in the 13 to 15 year and adult groups, but the ADN B titer is lower than the ASO titer in both the preschool age and 5 to 8 year groups. Although the upper limit of normal ADN B titers differ from those of the ASO titers in some of the age groups, they nevertheless follow the same pattern of low preschool age titers, elevated school age titers, and low adult titers. The higher titers (ASO and ADN B) found in the school age group are thought to be due to more frequent exposure of this group to streptococci. The slightly higher titers of the less than 1-year group as compared with those of the 1 to 4 year group are thought to be due to placental transfer of antibody from the mother.

As we mentioned above, the titers may vary seasonally and perhaps geographically; however, the greatest variation is due to age of the subject. The most pronounced effect of age on both the ASO and ADN B titers occurs between three age groups, i.e., preschool (<5 years), school, and adults. Consequently, there is an upper limit of normal for each of these groups. The upper limit of normal ASO titer for the preschool and adult groups was 85 (100) and for the school age group it was 170 (166). Upper limit of normal ADN B titers were 60 (50) for the preschool group, 170 (166) for the school age group, and 85 (100) for the adult group. The figures in parentheses represent the upper limit of normal titer for the Rantz Randall dilution scheme (6).

LITERATURE CITED

1. Ayoub, E. M., and L. W. Wannamaker. 1962. Evaluation of the streptococcal deoxyribonuclease B and diphosphopyridine nucleotidase antibody tests in acute rheumatic fever and acute glomerulonephritis. Pediatrics 29:527-538.
2. Coburn, A. F., and R. H. Pauli. 1935. Limited observations on the antistreptolysin titer in relation to latitude. J. Immunol. 29:515-521.
3. Klein, G. C., C. N. Baker, B. V. Addison, and M. D. Moody. 1969. Micro test for streptococcal antideoxyribonuclease B. Appl. Microbiol. 18:204-206.
4. Klein, G. C., M. D. Moody, C. N. Baker, and B. V. Addison. 1968. Micro antistreptolysin O test. Appl. Microbiol. 16:184.
5. Mote, J. R., and T. D. Jones. 1941. Studies of hemolytic streptococcal antibodies in control groups, rheumatic fever, and rheumatoid arthritis. J. Immunol. 41:35-60.
6. Rantz, L. A., and E. Randall. 1945. A modification of the technique for determination of the antistreptolysin titer. Proc. Soc. Exp. Biol. Med. 59:22-25.
7. Wannamaker, L. W., and E. M. Ayoub. 1960. Antibody titers in acute rheumatic fever. Circulation 21:598-614.