Follow-Up Study of ASO, ADN-B and ASK Levels in Children with Rheumatic Fever

NOBUO WATANABE, M.D., MUNEMITSU KOBAYASHI, M.D.
AKIRA ARIMURA, M.D., AND MASAHIRO OSHIMA, M.D.

In a total of 6 patients with rheumatic fever, antistreptolysin O (ASO), antistreptodeoxyribonuclease-B (ADNase-B) and antistreptokinase (ASK) titer was followed up for 3 months to 6 years. The mean periods of time of normalization of these serological tests were 4 months in ASO, 35 months in ADNase-B. In ASK, the period varied vastly in the range from 5 weeks to 4 years 1 month.

Clinically it is not so easy to differentiate rheumatic heart disease from mitral valve disease of unknown etiology. In the case of high ADNase-B level, the patients may be considered to have been attacked by rheumatic fever sometime during a preceding period of as long as about 35 months.

HEMOLYTIC streptococci are rich in enzymes, and in the presence of infection, antibodies to them are produced, the representative of which are antistreptolysin O (ASO), antistreptokinase (ASK), and antistreptohyaluronidase (ASH). Of these antibodies, the determination of ASO is widespread.

In 1979, we reported the determinations of the antibody to the antigen from hemolytic streptococci, DNAse-B (ADN-B), in acute glomerulonephritis, scarlet fever, vascular purpura, tonsillitis and rheumatic fever! In the present paper, we report comparative changes in AND-B, ASO and ASK titers as revealed by follow-up determinations.

MATERIALS AND METHODS
A total of 6 patients, including 5 patients with rheumatic fever and 1 with chorea, were followed up for 3 months to 6 years to check for changes in ADN-B, ASO and ASK titers. Of the 5 patients with rheumatic fever, 3 were complicated by carditis.

Of the serological reaction tests, Rantz-Randall's method was used for the determination of ASO titer, the kinase test for ASK titer, and the streptonase-B test, available from Wampole Laboratories, Cranbury, N.J., U.S.A., for ADN-B titer.

Regarding the upper limits for the normal ranges of ASO, ADN-B and ASK titer, 333, 480, and 1280, respectively, the periods of time to their normalization were studied.

RESULTS
Table I shows the ASO, ADN-B and ASK titers on admission and the periods of time needed for normalization of these serological reactions.

ASO titer on admission was 625 in 3, 833 in 1 and 1250 in 2 patients. It took from 3 weeks to 10 months, 4 months on an average, until
normalization.

ADN-B titer on admission was higher than 1360 in 3, and 1360 in the other 3 patients. It took from 1 year 6 months to 4 years 2 months until normalization in 5 of the patients. The other patient was followed up for only 3 months, during which period this parameter was not normalized. Normalization of this parameter took an average of 35 months.

ASK titer on admission was 81,920 in 3, 40,960 in 1, and 5,120 in another of the patients. In one other patient, this parameter was not determined on admission. The period for normalization of this parameter varied vastly from 5 weeks to 4 years 1 month.

Fig. 1 illustrates the data from 1 of the patients.

**DISCUSSION**

According to Stollerman, the rate of abnormally elevated ASO titers in rheumatic fever is 78%; that of ASO and ASH titers, 90%, and that of ASO, ASH and ASK titers, 95%. In other words, hemolytic antibody titers as determined by hemolytic streptococcus serological reactions
are increased in this disease. Shulman et al.3 described that ASO and ADN-B titers were normalized in 18 to 36 months in 17 patients with rheumatic fever associated with mitral insufficiency, while anti-group A carbohydrate still remained elevated after these periods of time; therefore, the latter proved a suitable retrospective test means.

In our present study, ASO titer was normalized in 4 months on an average; ADN-B titer, in 35 months, and ASK titer, in 28 months. However, because the materials included only a few patients and also because the tests were made only at 3- to 6-month intervals due to difficulty in frequent serological tests after discharge, it may be said that the periods for normalization of these parameters were not accurately obtained. Klein et al.4 reported that the normal range of ADN-B titer was 60 for children, 170 for school children and 85 for adults. The results of studies in Japan indicate higher titers, being 480 for children at ages of 6 to 15; therefore, it may be reasonable to consider that the normal range of this antibody titer is 340 to 640.5 In the present study, the upper limit for its normal range was defined as 480, and on this criterion, the periods to its normalization were studied.

In diseases not derived from bacterial allergy even among infections induced by hemolytic streptococci, unlike rheumatic fever, the serological reactions seem to be normalized rapidly. For the diagnosis of the presence or absence of infection by a serological reaction test, it is a fundamental rule to compare the determinations of paired serum samples. The test is made at 3- to 4-week intervals, and changes in titer are not less than 2 dilution steps. In rheumatic fever, however, it is necessary to judge the test results, bearing in mind the characteristic pattern that the titer is very rapidly elevated at onset and that it take several months for the elevated titer to be normalized.

It is not clinically easy to differentiate congenital deformity of the mitral valve, rheumatic cardiopathy and mitral valve disease of unknown etiology from each other. If ADN-B and other serological reactions are positive, however, a rheumatic disease may be suspected. If ASO titer is increased, the patient may be considered to have been attacked by rheumatic fever during the preceding 3 months, and if ADN-B titer is increased, he may have been attacked sometime during a preceding period of as long as 35 months.

REFERENCES