IMMUNE RESPONSE TO EXTRACELLULAR AND SOMATIC ANTIGENS IN STREPTOCOCCAL INFECTION AND SEQUELAE

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Abstract—The aim of the present study is to define the temporal relationships of the IgM and IgG responses to streptococcal group A carbohydrate (CHO) in rabbits and in man. Rabbits were immunized with group A streptococci and the development of anti-group A carbohydrate (ACHO) was studied. ACHO which appeared one week after the beginning of immunization belonged to the 19S class of immunoglobulins (IgM). A two- to four-fold rise in ACHO titers and immunoglobulins of the 7S class (IgG) were observed after two weeks. Three weeks after the beginning of immunization, the ACHO titer was at a maximum. In the following months no further rises in titer were seen, and the antibodies belonged mostly to the IgG class. IgM and IgG responses to streptococcal CHO and to extracellular antigens in patients with pharyngitis, acute rheumatic fever (ARF), and acute glomerulonephritis (AGN) were studied. Higher values of IgM were found in pharyngitis and AGN sera than in ARF sera, probably reflecting the interval between streptococcal infection and time of bleeding. ACHO antibodies persisted in patients' sera for long periods and belonged to IgG and IgM. This suggests a continuous, rather than a persistent, production of ACHO.

INTRODUCTION

The host immune response to streptococcal extracellular and somatic antigens is very important, not only for the study of streptococcal infections, but also for understanding the pathogenic mechanisms involved in the development of the nonsuppurative sequelae of group A streptococcal infections. Improvements in immunological techniques have diminished the difficulties in defining streptococcal infections. Antibody responses to the various extracellular antigens were studied extensively (1–10). Immunological techniques based on extracellular antigens are limited by the absence of group specificity of these antigens. Groups A, C, and G produce anti-
genically similar products, and other serologic groups occasionally syn-
thesize these enzymes (11, 12). Antibodies to the group-specific polysac-
charide (ACHO) are difficult to demonstrate by conventional methods.
Several authors, using complicated methods, have reported the presence of
antibodies to group A streptococcal polysaccharide in sera of patients with
acute infections and nonsuppurative sequelae. Rantz and Randall detected
ACHO antibodies by means of a capillary precipitin test (13), Halbert et al.
(14) and Zimmerman et al. (11) by double diffusion in agar, Karakawa et al.
and Slade et al. used several agglutination methods (15, 16), and Goldstein
et al. used a radioimmunoassay method (17). The interest in group A poly-
saccharide and in the immune response in patients sera increased when some
authors demonstrated the presence of antigens common to both group A
streptococci and heart tissues, as well as cross-reacting antibodies in the
sera of patients with rheumatic fever and rheumatic heart disease (18-20).
The ACHO were found to be of long duration in patients after rheumatic
fever and rheumatic heart disease (7, 21, 22). This prolonged persistence
could not be confirmed in Zimmerman’s study (11).

A simple method for measuring ACHO by microagglutination was
developed by Redys (23). Using this method, our laboratory conducted ex-
tensive studies on the sera of patients with rheumatic fever, glomerulone-
phritis, and pharyngitis (24). The microagglutination test seems suitable for
the detection of recent group A streptococcal infections in cases in which
streptococci cannot be isolated. The purpose of this study is to examine the
dynamics of the immune response to group A streptococcal polysaccharide
in rabbits, and to compare this with the host response in patients with
pharyngitis, rheumatic fever, and glomerulonephritis at different stages of
the disease.

MATERIALS AND METHODS

**Immunization of Rabbits.** Ten rabbits were immunized intravenously twice weekly with
heat-killed group A streptococci C203S (group I). Another ten rabbits were immunized in the
same way with cells digested with pepsin and trypsin (group II) (23). The low quantity of protein
contamination was verified by the very low absorbancy at 280 nm. All animals were bled prior
to immunization and then weekly during the entire period of the study.

**Patients’ Sera.** Sera from children with acute rheumatic fever (ARF) and acute glomeru-
lonephritis (AGN) were supplied by the Bikur Holim hospital. Eighteen sera of patients with
ARF and 28 sera of patients with AGN were examined. Sera from patients with acute pharyn-
gitis were obtained from microepidemics of severe pharyngitis.

Blood was taken at the acute phase of the disease and four weeks, two months, and four
months later.

**Antibody Determination.** ACHO were measured by the microagglutination test (23),
using Cooke Engineering Co. microtiter equipment and U-microtiter plates. The plates were