Immediate Immunologic Reactions: Noncytolytic Mediator Release and Cytolytic Cell Destruction*

Edward J. Goetzl,† Shaun Ruddy,‡ Daniel J. Stechschulte,§ and K. Frank Austen

Department of Medicine, Harvard Medical School
and
Robert B. Brigham Hospital
Boston, Massachusetts

Two of the principal mechanisms by which immunologic reactions generate chemical mediators of the inflammatory response differ both in their mode of interaction with target cell membranes and in their ultimate effect on these membranes. In the cytolytic reaction [Fig. 1(A)] antibodies of certain immunoglobulin classes (IgM or IgG) bind to the target cell via combining sites specific for antigens which are either intrinsic to the cell membrane or have become passively bound to it. A resultant configurational change in the Fc portion of the antibody (Ashman and Metzger, 1971) is associated with the initiation of a sequence of reactions among certain serum proteins, the components of complement,* contained in the surrounding milieu. The

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†Investigator, Howard Hughes Medical Institute
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*By international agreement (Austen et al., 1968) the components of complement are symbolized by a letter “C” and an arabic number. They react with an erythrocyte (E) coated with antibody (A) in the sequence C1, C4, C2, C3, C5, C6, C7, C8, and C9. Fragments of components produced during the reaction are suffixed with letters (e.g., C3a, C3b) and the activated form of a component is symbolized by a bar over the number (e.g., C1).
physicochemical characteristics and mechanism of interaction of the nine components have recently been reviewed (Muller-Eberhard, 1968; Ruddy, et al., 1972). Chemical mediators of inflammation are generated during the complement reaction sequence per se, by the limited proteolysis of the components. These mediators represent both major (e.g., C3b, an enhancer of opsonization) and minor (e.g., C3a, an anaphylatoxin) fragments of component cleavage as well as complexes (e.g., C567, a chemotactic principle) formed by the interaction of products from different components. If completion of the reaction sequence occurs on a cell membrane, cytolytic destruction of the cell results which in some instances, may eventuate in mediator release. In the cytotoxic reaction (Becker and Austen, 1966), antibody molecules of certain immunoglobulin classes (IgE or IgG) bind via their Fc portions to unique receptors on the membrane of the target cell. The release of mediators from the cell is initiated by the union of antigen with its specific combining site on the antibody, leading to a form of immunologically-induced secretion. It is apparent, then, that although the antigen specificity of different classes of immunoglobulins may be the same, the consequences of their encounter with that antigen may be entirely different because of their different biologic specificity.

**COMPLEMENT-INDUCED CYTOLYSIS: THE ONE-HIT MODEL**

In immune hemolysis, the system from which most of the information about kinetics of complement-induced membrane damage has been de-