MODULATION OF NEUTROPHIL Fc AND C3b RECEPTORS
Relationship with the Phagocytic Process and Activation of the Respiratory Burst

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Abstract—The effect of the interaction between human neutrophils and aggregated IgG on the expression of the receptors for the Fc portion of IgG (FcR) and for the C3b (C3R) has been investigated. Incubation of neutrophils with the appropriate concentrations of aggregated IgG at 37°C caused the loss of both the FcR and the C3R. This loss (modulation) was energy dependent (i.e., did not take place in cells incubated in the cold) and irreversible in that neutrophils did not reexpress either of the two receptors even upon prolonged incubation in vitro. The mechanisms leading to the modulation of FcR and C3R were different. FcR modulation was independent of the activation of the respiratory burst, since it occurred also in neutrophils from chronic granulomatous disease patients and was not induced by treatment of normal neutrophils with drugs such as phorbol myristate acetate (PMA), known to activate the respiratory burst. The FcR modulation was rather related to the redistribution ("capping") and endocytosis of the FcR induced by the interaction with aggregated IgG. This possibility was supported by the finding that FcR modulation was blocked by inhibitors of phagocytosis and by the observation that aggregated IgG, tagged with a fluorescent dye, were "capped" and subsequently endocytosed by metabolically active cells. Modulation of C3R was dependent upon the activation of the respiratory burst induced by the interaction of aggregated IgG with the neutrophils. This hypothesis was also supported by the finding that the modulation of C3R was induced by treatment of the cells with PMA and did not occur in chronic granulomatous disease neutrophils treated with aggregated IgG or PMA. Furthermore the modulation of C3R was inhibited by the addition of catalase, suggesting that such modulation was consequent to the damaging effect of the oxygen active by-products on the receptor structures. In addition to the C3R modulation described above, another type of C3R loss was observed. This occurred in chronic granulomatous disease (CGD) neutrophils following interaction with the appropriate antigen-antibody-complement complexes. In these cells, phagocytosis of the complexes caused a concomitant modulation of the C3R that was possibly related to the redistribution and endocytosis of the C3R structures.

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INTRODUCTION

Human neutrophils, like those of other animal species, have surface receptors for the Fc portion of IgG (1, 2). These receptors (FcR) bind preferentially to the human IgG1 and IgG3 subclasses, and their avidity for the substrate is greatly enhanced when the IgG molecules are aggregated by the specific antigen or, in some experimental systems, by chemical or physical means (as reviewed in reference 3). The interaction between the neutrophil FcR and its ligand (presented in the appropriate molecular form) triggers a number of events such as the release of lysosomal enzymes, certain cytotoxic functions on nucleated cells and the attachment to and the ingestion of opsonized particulate antigens (4-7).

Neutrophils also possess surface receptors for the cleavage products of the third complement component (C3b and C3bi) (as reviewed in reference 8). These receptors seem to subserve mainly the role of facilitating the adherence of the cells to the opsonized targets rather than that of triggering directly some or all of the functions mentioned above (5, 9-11).

Previous in vitro studies on other cells equipped with FcR have demonstrated that the interaction between FcR and the appropriate ligands causes a temporary or sometimes irreversible loss of the FcR function. This phenomenon, generally referred to as "modulation," has been amply documented for human and murine monocytes or macrophages (12-15) and for some human lymphocyte subset populations (16, 17). The modulation of macrophage FcR (and in some instances of C3R) has been indicated as responsible for the defective clearance of circulating immune complexes (18) observed in some diseases such as, for example, systemic lupus erythematosus (19), nephritis (20), Sjögren syndrome (21), vasculitis (20), or biliary cirrhosis (22).

In the present study, we have investigated the fate of both FcR and C3b receptor (C3R) of neutrophils upon interaction with the specific ligands. It will be shown that, following this interaction, there is an irreversible modulation of both the receptor functions. Furthermore, the interaction between the FcR and aggregated IgG leads to the irreversible loss of the C3R receptor function. Such a loss takes place only in neutrophils capable of initiating a respiratory burst and is likely to be consequent to the damaging effect that oxygen-active by-products, released by the cells, may have on the C3R structures.

MATERIALS AND METHODS

Neutrophil Suspensions. Blood from healthy donors or chronic granulomatous disease (CGD) patients was used.