ANTIGEN-INDUCED EOSINOPHIL CHEMOTACTIC FACTOR (ECF) RELEASE BY HUMAN LEUKOCYTES

BEATE M. CZARNETZKI, WOLFGANG KÖNIG, and LAWRENCE M. LICHTENSTEIN

The Johns Hopkins University School of Medicine at The Good Samaritan Hospital, Clinical Immunology Division, 5601 Loch Raven Boulevard, Baltimore, Maryland

Abstract—A complement-independent eosinophil chemotactic factor (ECF) is described which is released from peripheral leukocytes of allergic and normal human volunteers after antigen stimulation and after exposure to anti-IgE. Dose response and time-release curves for ECF and histamine run closely parallel in this system. Histamine by itself is shown to have no effect on chemotaxis at the concentrations present in antigen-induced release, but is inhibitory at very high concentrations. Evidence suggests that the ECF released from human leukocytes is derived from basophils and is similar, or identical, to the ECF released from mast cells.

INTRODUCTION

Eosinophils are known to participate prominently in many diverse inflammatory reactions, including parasitic infections and allergic reactions of the immediate and delayed type. Their origin, function, and fate are, however, poorly understood. Studies in the 1960s demonstrated their preferential accumulation in areas of repeated injections with foreign proteins (1) and their ability to phagocytize antigen–antibody complexes (2, 3), although less efficiently than neutrophilic polymorphonuclear leukocytes (4). Their granules contain a specific peroxidase, several enzymes, and four major proteins (5, 6, 7), but none of these components has so far been shown to specifically modify the reactions where eosinophils are found in prominent number.

1 This work was supported by Grants 07290 and 08270 from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.
2 Publication No. 197, O'Neill Research Laboratories.
3 Dr. Czarnetzki is recipient of the Stetler Research Fund for Women Physicians.
4 Requests for reprints should be sent to Dr. Beate M. Czarnetzki at the address above.
Research into the factors causing accumulation of eosinophils at tissue sites has met with more success, partly due to the development of convenient in vitro methods of chemotaxis (8). Early in vivo methods had shown eosinophil accumulations in tissues after antigen–antibody complex injection (9, 10) and with nonspecific stimuli such as injections of glycogen (11). In recent years, several lymphocyte-derived factors have been purified that attract eosinophils directly (12, 13) or indirectly after interaction with antigen–antibody complexes (14). Two major eosinophil chemotactic factors (ECFs) have been found to be associated with humoral-type immune reactions. Ward et al. (15, 16, 17) demonstrated that factors of the complement system (C5 and C5a) attract eosinophils as well as neutrophils. A noncomplement-associated ECF was first reported by Kay et al. (18) in studies of antigen-induced mediator release with guinea pig lung. The presence of this eosinophil chemotactic factor of anaphylaxis (ECF-A) was further demonstrated in human lung fragments (19), human nasal polyps (20), human lung tumor tissue (21), rat mast cells (22), and leukemic basophils (23). ECF-A has been shown to be a low-molecular-weight acidic protein (22), and its release from cells can be modulated by chemicals affecting the cyclic AMP system (24), as has been shown previously for histamine (25), another preformed mast-cell- and basophil-associated mediator.

Several years ago, Parish (26) reported the antigen-induced release of an ECF from peripheral leukocytes of atopic patients as well as from monkey leukocytes. The cell of origin and the physical and chemical characteristics of this factor were not further defined.

In the present study, peripheral leukocytes of healthy and atopic adults were studied for the release of an ECF from basophils that might be comparable to the ECF-A previously described in mast cells and leukemic basophils. In addition, factors governing the release of this factor from cells, some of its physical and molecular characteristics and its relationship to histamine release are described.

MATERIALS AND METHODS

The following equipment and reagents were used: Chemotaxis chambers (Ahlco Machine Co., Southington, Connecticut), sodium metrizoate (Triosil-75, Nyegaard and Co., AS, Oslo, Norway), cellulose nitrate filters (Sartorius, Membranfilter GMBH, Göttingen, West Germany), brass cassette for staining of filters (Schleicher and Schuell, Inc., Keene, New Hampshire), hematoxylin stain solution (Fisher Scientific Co., Fair Lawn, New Jersey), Chromotrop-2R (Chroma-Gesellschaft, Stuttgart-Untertürkheim, West Germany), m-Xylene (Eastman Kodak Co., Rochester, New York), Permount (Fisher Scientific Co., Fair Lawn, New Jersey), medium-size Hartley-strain guinea pigs (Camm Research Institute, Wayne, New Jersey), human albumin (Behringwerke, AG, Marburg/Lahn, West Germany), Angiocath IV catheters (Desert Pharmaceutical Co., Sandy, Utah), Dextran Blue