Phagocytosis of bacteria by eosinophils in infectious-related asthma


In the microscopic examination of sputum and nasal secretion samples from 100 patients with allergic and/or infectious involvement, 11 with intrinsic or infectious-related asthma demonstrated intracytoplasmic gram-positive cocci within vacuoles of eosinophils. Evidence for similar eosinophil phagocytic function could not be found in the cytologic study of secretions from those patients with respiratory tract involvement of primary extrinsic allergic etiology.

The association of eosinophilia with identifiable extrinsic allergic states of man is a familiar and well-recognized occurrence. However, the clinical findings of respiratory tract infection and an eosinophilic cytology of the secretions are also often prominent and characteristic features in some patients with hyperplastic sinusitis and intrinsic asthma of undetermined etiology. There has thus been reason to question whether the factors of infection and eosinophil granulocyte responses might both be related to possible immune reactivity involving sinonirhinobronchial tissue. This thought gave additional interest to our findings of morphologic evidence for phagocytosis of bacteria by eosinophils in the microscopic examinations of nasal secretion and sputum samples in patients with infectious-related asthma.

In evaluating the possible significance of this report, it may be pertinent to consider specific points in our knowledge of eosinophilia derived from studies of experimental situations and animal models.

1. Eosinotactic stimuli may be effected by antigen-antibody reaction and/or complex formation.

2. Incorporation of immune complexes, mast cell granules, and non-

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specific particles of delineated size within the cytoplasm of eosinophils has been demonstrated.

3. Phagocytosis of cell antigens by eosinophil leukocytes of immunized animals was favored by the presence of corresponding antibody.

CLINICAL REPORT

While routinely examining sputum samples, our attention was directed to a casual microscopic finding of unknown significance. Where both bacteria in

![Figure 1](image_url)

**Fig. 1**
Smears prepared from sputum (A, C, D) and nasal secretion (B) taken from patients with intrinsic (infectious-related) asthma. Intracytoplasmic inclusions of (phagocytized) bacterial cells by eosinophils are demonstrated. An unusual degree of avidity is seen in specimen C taken from a patient with associated hyperplastic sinusitis. (Gram stain [A, B]. Original magnification: A, x 970; B, x 570. Eosin-methylene blue stain [C, D]. Original magnification: C, x 570; D, x 970.)
large numbers and a profusion of eosinophils as predominating cells were present, phagocytosis was occasionally noted. We then set out to study carefully the respiratory tract secretions from 100 consecutive patients with nasal and/or bronchial involvement in which either primary or secondary infection formed a demonstrable part of the clinical picture. Nasal secretions and sputum samples were obtained for comparative study from patients with: (1) allergic rhinitis and/or asthma in which extrinsic allergens were etiologic factors and episodes of superimposed respiratory tract infection were only acute and transient; (2) intrinsic asthma; and (3) chronic bronchitis. Six specimens of nasal secretion and/or sputum from each patient were prepared by conventional Gram stain and eosin-methylene blue techniques.

Inclusions of bacterial cells within the cytoplasm of eosinophils were consistently identified in all smears prepared from the multiple specimens of secretions taken from 11 patients (Fig. 1). Criteria including the plane of microscopic focus and demonstration of bacterial cells within (phagocytic) vacuoles helped to rule out confusion with bacteria presenting at or on the eosinophil cell surface. Since phagocytosis of mast cell granules by eosinophils has been reported, the associated absence of basophilic granular cells and basophil leukocytes was ascertained, and the possibility of mistaken identity with "basophilic body" inclusions was avoided.

**Summary of the clinical features of 11 patients reported**

*Sex.* There were 3 men and 8 women.

*Ages.* There were ten adults ages 38 to 71 years and one child age 5.

*History.* All had long-standing infectious-related asthma. The 10 adults required management with small maintenance dosages of corticosteroids (prednisone 5 to 10 mg., daily) in addition to long-term or periodic antibiotic administration.

*Skin reactivity.* Eight patients were skin test negative. In the other 3 patients positive intracutaneous test reactions to house dust and other inhalant extracts were demonstrated. However, the superimposed element of chronic bronchial infection had long overshadowed earlier possible etiologic roles for underlying extrinsic inhalant allergens in these situations.

*Associated upper respiratory tract involvement.* Three patients with identical microscopic findings in the nasal secretions had associated histories of nasal polyps, aspirin sensitivity, and suppurative and hyperplastic maxillary-ethmoid sinusitis requiring earlier surgical intervention.

*Secretions.* (1) Immunodiffusion studies showed IgA and IgG were present in all samples. (2) Cytology was totally or predominantly eosinophilic. Polymorphonuclear neutrophil leukocytes were absent or relatively few in number. (3) Intracytoplasmic-identified bacteria were all of gram-positive coecal species, i.e., streptococci and pneumococci.

Bacterial cell inclusions within (phagocytic) vacuoles of eosinophil leukocytes were not found in the multiple specimens of secretions taken periodically from: (1) 3 patients presenting with a similar clinical picture of intrinsic asthma; (2) 63 patients with allergic rhinitis and/or extrinsic asthma, in whom typically
during a symptomatic phase of allergic reactivity few bacteria, presumably of
normal flora, were present in the predominating eosinophil cytology and in
whom, during the course of a superimposed upper or lower respiratory tract
infection, a profusion of bacteria along with large numbers of polymorpho-
nuclear neutrophilic leukocytes appeared among the eosinophil cell population;
or (3) 18 patients with chronic bronchitis in whose sputum relatively few
eosinophils were identified within a predominantly polymorphonuclear leukocyte
cytology. There was no relation of these microscopic findings to associated treat-
ment factors, i.e., corticosteroids, antibiotics, or symptom-relieving drugs, or to
previous injection treatments with allergenic extracts in the 3 skin test-positive
adults.

COMMENT

The first observation of eosinophil phagocytosis of bacteria in lower animals
was reported almost 75 years ago.\textsuperscript{11} That this phenomenon might also occur in
man was indicated a few years later in a description of phagocytosis by
eosinophils within purulent abscess material.\textsuperscript{12} However, this finding was
reported only infrequently thereafter.\textsuperscript{13} Subsequent study suggested that, in
contrast to polymorphonuclear neutrophils, eosinophils ordinarily show no
phagocytic activity but under experimental conditions may become phagocytic.\textsuperscript{13}

While smaller microorganisms, e.g., mycoplasmas, are as avidly phagocytized
by eosinophils as by polymorphonuclear neutrophils, such is not the case for
most bacteria.\textsuperscript{14} Since it is not known whether size or antigenic function of
particles presenting at the cell surface could be critical factors, it may be
pertinent to take note of the delineated conditions under which we noted
eosinophil phagocytosis of bacteria in this study. Large populations of both
eosinophils and bacteria might allow for their frequent in vivo contact by
chance. However, evidence of phagocytosis was not seen under similar quantita-
tive conditions when, during the course of superimposed acute respiratory tract
infections in patients with extrinsic allergic activity, increasing numbers of
bacteria appeared transiently in eosinophil-containing secretions.

It is of interest that in each instance of this microscopic finding the only
bacteria demonstrated were gram-positive cocci. Since \textit{Hemophilus influenzae}
is commonly identified in bronchial infection, we especially sought but could not
find intracytoplasmic inclusions of small gram-negative rods. On the basis of
available information, we can enter this only as an observation without inter-
pretation. Possible critical determinant factors for eosinophil phagocytosis (e.g.,
size, antigenicity, and pathogenicity of infecting microorganisms; character of
antibody responses; role of serum complement; and effects of the presence of
more avidly phagocytic polymorphonuclear neutrophilic leukocytes and their
products) are subjects of our extended investigation.

The pathophysiologic nature of intrinsic asthma is a relevant consideration.
Absence of an identifiable etiology in a disease with suspected hypersensitivity
manifestations has led to the thought that an antigen of bacterial source might
provide an immune reactant for an allergic mechanism.\textsuperscript{15} The concept of
bacterial sensitization, although still unproved, might explain the avidity of
Phagocytosis of bacteria by eosinophils for infecting bacteria similar to their pinocytotic functions for soluble antigen-antibody complexes. In any event, our experience in the diagnostic study and management of these patients differs from that of Lowell who reported the finding that when eosinophils were abundant in purulent sputum and nasal secretion, infection was often absent.

This communication is intended only as a preliminary report to suggest an investigational lead. It is hoped that continued study will help to define those in vivo circumstances responsible for the emergence of eosinophilia, phagocytic functions for eosinophils, and hypersensitivity mechanisms associated with bacterial infection. In turn, perhaps additional insight can be gained into the etiology and diagnosis of infections-related asthma.

REFERENCES