Lactoferrin and Eosinophilic Cationic Protein in Nasal Secretions of Patients with Experimental Rhinovirus Colds, Natural Colds, and Presumed Acute Community-Acquired Bacterial Sinusitis

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To distinguish sinusitis from uncomplicated “colds,” we examined lactoferrin and eosinophilic cationic protein (ECP) in nasal secretions. Lactoferrin titers were $\geq 1:400$ in 4% of persons with uncomplicated colds and controls but in 79% of persons with sinusitis or purulent sputa. ECP levels were $> 200$ ng/ml in 61% of persons with colds and $> 3,000$ ng/ml in 62% of persons with sinusitis. Nasal lactoferrin helps distinguish sinusitis from colds.

Acute respiratory illnesses contribute significantly to acute morbidity, physician visits, and absenteeism from work and school (15). The common cold is a viral rhinosinusitis (VRS), with a computerized tomography (CT) scan showing sinus involvement in 87% of adults with colds (5). Acute community-acquired bacterial sinusitis (ACABS) complicates a small proportion of VRS, with reports ranging from 0.5 to 2% (1, 2). The “gold standard” for diagnosis of ACABS is sinus aspirate culture yielding an identifiable bacterial strain. However, sinus aspirate is not appropriate for routine clinical use, and a readily available, simple test for ACABS that may require antibiotic treatment is badly needed.

In addition, allergy and eosinophil involvement in some patients with chronic sinusitis is well recognized (7, 8, 12, 13). The neutrophil marker lactoferrin (LF) and the eosinophil marker eosinophilic cationic protein (ECP), respectively, are potentially useful markers of neutrophilic inflammation in fecal, cervicovaginal, and sputum samples (3, 11, 14, 16, 17) and of eosinophilia in nasal washings (9).

We therefore compared LF titers and ECP levels in nasal secretions or washes from healthy adults, volunteers with experimental rhinovirus colds, adults with natural colds, and adults with presumed ACABS.

We examined nasal secretion specimens (blown into a plastic wrap and weighed for dilution) from 9 healthy adults, 9 adults with natural colds with a history of $< 7$ days of symptoms, and 16 adults who presented to one of two primary-care outpatient clinics with a history of at least 7 days of stable or worsening respiratory symptoms (suggested as a clinical indicator of ACABS) (4). We also examined nasal washings from 32 previously healthy volunteers exposed to an experimental rhinovirus (Hank’s strain), a subset of whom went on to acquire virus (Hank’s strain), a subset of whom went on to acquire sinusitis from colds.

To distinguish sinusitis from uncomplicated “colds,” we examined lactoferrin and eosinophilic cationic protein in nasal secretions of patients with experimental rhinovirus colds, natural colds, and presumed acute community-acquired bacterial sinusitis.
FIG. 1. Reciprocal LF titers for controls and various respiratory infections. Reciprocal LF titers in nasal secretions or sputum specimens are most often ≥400 in subjects with presumed ACABS, bronchitis, or pneumonia (19 of 24; 79%), while they are most often <400 in healthy subjects and those with both natural and experimental rhinovirus colds (77 of 80; 96%) (P < 0.001 by Fisher’s exact test). Eleven control saliva and 8 purulent sputum specimens are included from reference 11 for comparison.

FIG. 2. ECP levels in nanograms per milliliter for all specimens available for study, obtained by using either urea (for nasal washes) or specimen weight (for nasal secretions) as noted in the text. Twenty-seven (79%) of 34 subjects with presumed ACABS or colds (natural or experimental) had ECP levels of >200 ng/ml, while none of the 12 baseline controls did (P < 0.001 by Fisher’s exact test). Furthermore, 10 (62%) of 16 specimens from subjects with presumed ACABS had strikingly elevated ECP levels (>3,000 ng/ml), while no specimens from 18 subjects with colds (natural or experimental) and none of the 12 baseline control specimens did (P < 0.001 by Fisher’s exact test).
with only 3 of 18 (17%) controls and subjects with natural colds ($P < 0.01$ by Fisher’s exact test).

ECP concentrations for all specimens available for study are shown in Fig. 2. Levels of ECP of $>200 \text{ ng/ml}$ were considered elevated. While none of the 12 subjects with experimental rhinovirus colds had a baseline nasal secretion ECP concentration of $>200 \text{ ng/ml}$ before infection, all 22 available nasal secretion specimens from subjects with presumed ACABS, and specimens from 5 (42%) of 12 subjects with experimental rhinovirus colds, had ECP levels of $>200 \text{ ng/ml}$. Altogether, 27 (79%) of 34 subjects with presumed ACABS or colds (natural or experimental) had ECP levels of $>200 \text{ ng/ml}$ (versus 0 of 12 baseline controls; $P < 0.001$). Furthermore, 10 (62%) of 16 specimens from subjects with presumed ACABS showed strikingly elevated ECP levels ($>3,000 \text{ ng/ml}$, including 3 specimens with LF titers of $<400$), while only 3 of 18 subjects with colds (natural or experimental) and none of the 12 baseline controls had ECP levels of $>3,000 \text{ ng/ml}$ ($P < 0.01$).

We conclude that LF measurement in patients with acute respiratory illness may prove to be useful in distinguishing uncomplicated colds from colds complicated by ACABS. Furthermore, the involvement of eosinophils, as indicated by ECP concentrations in nasal secretions, suggests that allergy may also be involved in a substantial portion of colds and sinusitis syndromes. These pilot studies should be extended to patients with sinus puncture and culture as well as antibiotic responses to define the ultimate place for nasal LF and ECP measurement in patient management decisions, such as when antibiotics may be indicated.

REFERENCES