

Dear Editor

Eosinophil and Neutrophil Activity in Wheezing Infants

Okamoto *et al.* published in the journal their interesting findings on eosinophil cationic protein (ECP) in hospitalized wheezing and non-wheezing infants aged <24 months.¹ There were no significant difference in plasma ECP concentration between 36 wheezing (mean 18.5, SD 16.1 ng/mL) and 33 non-wheezing (12.6, 8.8) patients.¹ Evidently, the study was underpowered to reveal the difference (in mean, 6.1 ng/mL) as statistically significant. The values 16.0-20.0 ng/mL (ug/L) have been suggested as upper normal limits of serum ECP.² Though the authors did not present any categorized data, elevated values were obviously more common in wheezing children. Instead, ECP concentrations in the nasal fluids were higher in 17 wheezing (mean 1733, SD 660 ng/mL) than in 13 non-wheezing (680, 450, $p = 0.018$) patients.¹ The problem concerning ECP measurement in respiratory samples is how to standardize the sample and to present the concentration. That's why no reference values are available. In most studies, ECP in respiratory samples have been expressed per mg of mucus or per mg of albumin in the mucus.^{3,4} Nasal washing samples studied by Okamoto *et al.*¹ may be more problematic.

In 1992-1993, ECP was studied in serum and nasopharyngeal aspirates (NPA) in 92 infants hospitalized for wheezing at age <24 months.^{4,5} At entry, 15% of the patients had serum ECP >16 ug/L (ng/mL),⁵ and they were at risk for post-bronchiolitis wheezing (86 vs. 43%, $p < 0.01$) during the 4-month follow-up period. At entry, the median NPA ECP was 397 ng/g mucus, and the upper quartile was 870 ng/g. The median concentration was 200 ng/g in the RSV cases vs. 550 ng/g in cases with no virus detected ($p < 0.01$).⁴ From later studies we know, that cases with no viruses detected were rhinovirus infections, and rhinoviral finding was a strong predictor of later asthma.⁶ Children with NPA ECP >870 ng/g tended to have more post-bronchiolitis wheezing, but the main result was that children with high NPA ECP benefitted more than other children from the early intervention with inhaled budesonide or cromolyn sodium.⁴ During the 12-year follow-up, the risk of chronic asthma (asthma at all visits at median ages 4, 7 and 12 years) was 2.9-fold if blood eosinophils were $>0.45 \times 10^9/L$, 1.6-fold if serum ECP was $>20.0 \text{ ug/L}$ and 6.7-fold if NPA ECP was $>815 \text{ ng/g}$ in infancy. The analyses were adjusted for atopy and viral etiol-

ogy of bronchiolitis.⁷ Instead, the more specific marker of neutrophil activation, myeloperoxidase measured from frozen samples obtained in infancy, had no association with later outcome.⁸ The results highlighted ECP in respiratory secretion as a predictor of chronic asthma at school age after early childhood wheezing.

Okamoto *et al.* concluded that ECP level in nasal fluid reflects the severity of airway inflammation in infants.¹ Children with high ECP in airways seem to benefit from early anti-inflammatory medication with inhaled budesonide and cromolyn sodium.³ Two important markers, rhinoviruses and ECP, can be studied in the same nasal or nasopharyngeal samples. However, better standardized sampling of respiratory specimens allowing the assessment of reference values for ECP is needed.

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