

LETTERS TO THE EDITOR

Serum eosinophil cationic protein measurements in monitoring pulmonary inflammation in asthma

EDITOR,—Based on their findings that serum eosinophilic cationic protein (ECP) concentrations are increased in asthmatics compared with controls, and that ECP concentrations are related to disease activity, Koller and coworkers propose that ECP may be used for monitoring inflammatory activity in asthma.¹

Following the same line of reasoning, the level of airways hyper-responsiveness was advanced as a putative marker of disease activity in asthma in 1984.² In cross sectional epidemiological studies, however, it was shown later that although asthmatics on average showed more hyper-responsiveness than do normal subjects, the amount of overlap of airway responsiveness levels between the groups was large.³ In long term prospective studies of patients with asthma, the degree of airways responsiveness showed hardly any relationship to disease activity in the individual patient.⁴ Thus, a statistically significant relationship of a putative marker to disease activity in selected groups of patients does not imply that the variable under study is a useful marker of disease activity in the individual patient in clinical practice.

The same argument may apply to ECP concentrations as a marker of asthma activity. The interesting findings of Koller and coworkers, in my opinion, do not allow the conclusion that ECP is useful as a marker of disease activity in asthma. Before such a conclusion can be drawn more information is needed about (a) the distribution of ECP concentrations in unselected, larger groups of patients and healthy subjects, preferably in an epidemiological study, and (b) the relationship of serum ECP concentrations to other markers of disease activity (for example, symptoms, lung function, peak expiratory flow, airway hyper-responsiveness) in a large number of patients followed up prospectively for a prolonged period of time.

Obviously, it would be wonderful if serum ECP concentrations were a reflection of inflammatory activity in the airways in the individual patient. It is unlikely, however, that the concentration of a single mediator from a single effector cell, measured in peripheral blood, would accurately reflect the overall severity of the complex asthmatic inflammatory response in the airways.

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Drs Koller and Eichler comment:

We agree with Dr Brand that epidemiological studies for a prolonged time period are required to emphasise the importance of ECP measurements in monitoring asthma activity. Since 1985 bronchial biopsies have been undertaken in patients with asthma demonstrating the importance of eosinophils in asthma.⁵ These data are of importance in the understanding of bronchial inflamma-

tion, but they reveal abnormalities of the bronchi only and cannot properly quantitate the inflammation. Thus, studies have been performed to evaluate the use of mediators in bronchoalveolar fluid (BALF), which is assumed to reflect cell activity such as ECP for eosinophil activation, to assess inflammation in both large and small airways. These studies demonstrated that ECP in BALF was correlated with asthma severity.⁶ In addition, other investigators demonstrated that serum measurements of ECP were related to eosinophil activity in the bronchial system⁷ and thus to disease activity.

Of course the eosinophil is not the only (pro)inflammatory cell in the asthmatic lung but it plays a very important part in asthma by releasing highly cytotoxic proteins which are assumed to be causative for many histomorphological and functional changes in the asthmatic lung.⁷ These findings are having an effect on management and anti-inflammatory treatment has become first line treatment in asthma. But so far no variable is available in routine assessment to determine the efficacy of treatment in suppressing inflammation. The measurement of activity markers of other inflammatory cells in asthma, such as lymphocytes, neutrophils or mast cells, failed to correlate with disease activity as has been observed for ECP.⁶ Thus, assessment of ECP in serum especially in children provides the potential to assess inflammation in asthma based on its relation to asthma activity, which we are able to demonstrate in cross sectional studies in a large number of children (n=175).¹ In addition, longitudinal investigations showed that ECP concentrations were decreased by the administration of inhaled steroids associated with improvement of lung function.¹ These data are encouraging and a longitudinal follow up study is now under way.

- 1 Koller DY, Herouy Y, Götz M, Hagel E, Urbanek R, Eichler I. Clinical value of monitoring eosinophil activity in asthma. *Arch Dis Child* 1995; 73: 413-7.
- 2 Murray AB, Ferguson AC, Morrison B. Airway responsiveness to histamine as a test for overall severity of asthma in children. *J Allergy Clin Immunol* 1984; 68: 119-24.
- 3 Pattemore PK, Asher MI, Harrison A, Mitchell EA, Rea HH, Stewart AW. The interrelationship among bronchial hyperresponsiveness, the diagnosis of asthma, and asthma symptoms. *Am Rev Respir Dis* 1990; 142: 549-54.
- 4 Clough JB, Williams JD, Holgate ST. Profile of bronchial responsiveness in children with respiratory symptoms. *Arch Dis Child* 1992; 67: 574-9.
- 5 Beasley R, Roche WR, Roberts JA, Holgate ST. Cellular events in the bronchi of mild asthma and after bronchial provocation. *Am Rev Respir Dis* 1989; 139: 806-17.
- 6 Bousquet J, Chané P, Lacoste JY, et al. Indirect evidence of bronchial inflammation assessed by titration of inflammatory mediators in BAL fluid of patients with asthma. *J Allergy Clin Immunol* 1991; 88: 649-60.
- 7 Venge P, Hakanson L. The eosinophil and asthma. In: Kaliner M, Persson C, Barnes PJ, eds. *Asthma. Its pathology and treatment*. New York: Marcel Dekker, 1989: 477-502.

Child sexual abuse—have we learned the lessons of Cleveland?

EDITOR,—In 1987 a large number of children living in Cleveland, UK were diagnosed as sexually abused and were taken into care. There was a public outcry which culminated in a judicial inquiry. Much of the evidence hinged on the interpretation of a physical sign, reflex anal dilatation. Both then and now allegations of sexual abuse in the UK are rarely documented by photography that

could be independently scrutinised. The lack of independent scrutiny was a major factor in Cleveland.

In a recent report from Leeds 109 children were examined after referral for suspected child sexual abuse.¹ All but two had abnormal signs. In 59 cases the physical evidence was strong enough to confirm penetrative activity. This report is in stark contrast to a report from the USA where photographs and records of 236 children with perpetrator conviction were reviewed.² The majority reported penile-genital contact yet confirmatory signs were only found in 14%. The authors concluded 'it's normal to be normal'. In the Leeds study a transverse hymenal diameter of less than 4 mm in the prepuberatal child was regarded as the norm. Most examiners would disagree, the criterion of normality being based on well researched studies in non-abused girls.³⁻⁶ These indicate that hymenal diameter is age dependent and is frequently in excess of 4 mm. The vast difference between the British and American study must surely lie in interpretation.

In Britain a medical opinion for the defence is usually based on the forensic physician's statement. The terminology is often confusing and accuracy is hindered by the lack of photographic evidence. An opinion given without recourse to the visual evidence detracts from its validity and is potentially misleading. Unless photography becomes a routine part of the investigation of child sexual abuse we will have learned nothing from the Cleveland experience.

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Drs Hobbs, Wynne, and Thomas comment:

We agree with Dr Blumenthal that photographic recording of genital and anal findings is valuable in child sexual abuse evaluation. Contrary to Dr Blumenthal's information, photographs were taken of many Cleveland children including those independently reviewed by the second opinion panel. Photographs were taken for all cases in our study. A recent atlas illustrates colposcopic findings from many of our cases.⁷ Incomplete legal and clinical data, disregard for healing and timing of examination (70% seen 15 days after assault), and the use of colposcope pictures out of the context of history and examination record were some criticisms of Adams' methodology. There remain difficulties with normal studies of genitalia and over precise measurements of hymenal rim. Adams' assertion of an adequate posterior hymenal rim measuring 1-2 mm troubles us. Only 1% of children had abnormal anal findings, although 28% described penile-anal contact.

While some children can be 'normal' after contact abuse (oral abuse, masturbation of adult by child, healing taking place from incident to examination), abusive penetration of vagina and anus in our experience frequently causes injury and why not?

The Royal College report states that the most commonly held view is that a hymenal orifice diameter greater than 4 mm (labial separation) is strongly correlated with abuse.⁸ In all studies, there is change in diameter with age, examination position, degree of relaxation but enlargement is rarely the only sign, rather the summation of findings is important. Dr Blumenthal's comment on reflex anal dilatation reflects media preoccupation—this was only one of many signs in Cleveland