LETTERS TO THE EDITOR

Serum eosinophil cation protein measurements in monitoring pulmonary inflammation in asthma

Editor,—Based on their findings that serum eosinophil cation 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.

Following the same line of reasoning, the level of airways hyper-responsiveness was advanced as a putative marker of disease activity in asthma in 1984.1 In cross sectional epidemiological studies, however, it was shown later that although asthmatics averaged more hyper-responsiveness than do normal subjects, the amount of overlap of airway responsiveness levels between the groups was large.2 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.3 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 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 unslected, 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 atrophic inflammatory response in the airways.

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Dr Koller and Eicher 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.3 These data are of importance in the understanding of bronchial inflammation, but they reveal abnormalities of the bronchi only and cannot properly quantitate the inflammation. In 1995, 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.4 In addition, other investigators demonstrated that serum ECP was related to eosinophil activity in the bronchial system3 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. 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 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 is true for ECP. Therefore, 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). In addition, longitudinal investigations showed that ECP concentrations were decreased by the administration of inhaled corticosteroids associated with improvement of lung function.1 These data are encouraging and a longitudinal follow up study is now under way.


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

Dr 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 review of our panel’s methodology also shows that photographs were taken from many of our cases.2 Incomplete legal and clinical data, disregard for healing and timing of examination (70% seen 15 days after assault), and the use of colposcopepictures out of the context of full forensic examination were also common in the record. Our experience underscores the importance of an accurate forensic assumption panel. 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 associated with abuse.5 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 sexual assault is important. Dr Blumenthal’s comment on reflex anal dilatation reflects media preoccupation—which was only one of many signs 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 so strong as to rule out all other causes of sexual 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.6 Repeated penile-genital contact confirmed that 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 prepuberal child was regarded as the norm. Most examiners would disagree, the criterion of normality being based on well researched studies in non-abused girls.3,4 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. Although a medical expert 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 based on research reviewed in Thomas’ text 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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children. 'Backlash' has influenced American paediatricians' willingness to report abuse. More accurate recording of findings including photographs will help.


A new clinical sign in Williams syndrome

Editor,—Williams syndrome is a well recognised condition with typical facies, supravalvular aortic stenosis, mental retardation, and a characteristic personality.1 In a large series (n=235) 96% of patients demonstrated a deletion of the elastin gene from the long arm of chromosome 7.2 Strabismus is common in Williams syndrome3 and this may contribute to subnormal binocular vision and reduced stereopsis. In a recent study of 28 patients with typical features and deletion of the elastin gene an interesting sign was noted. On further inquiry it was found to have been present in 30% (n=9) of cases. The observation is that as children they have a great reluctance in changing the surface on which they are walking or playing. A typical example would be going from a tiled to a carpeted surface. The child would stop at the interface and refuse to proceed. They may then feel out the new surface with either a probing foot or in some cases descend to all fours to confirm the suitability of the next surface. The process of transfer may take several minutes. Patients describe this observation in both indoor and outdoor settings. It would seem that there is a problem in determining depth perception when there is either a new pattern or colour to the surface. A reluctance to proceed may reflect a fear of falling to the next surface. Similar difficulties are experienced in attempts to descend stairs. Another interesting observation in this group is that parents describe the childhood of the patient as undemanding, having a variable visual pattern, and conflicting visual inputs that contribute to the uncertainty of the surface. Several of the children experienced great distress when faced with this circumstance. As the children grow older the problem diminishes and most have no fears or concerns in changing surfaces by 8 years of age.

This clinical sign has not been described previously in this group and I am unaware of any other paediatric group who demonstrate a similar sign. I would be most pleased to hear from any other groups who may have made similar observations.

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Calculation of the need for paediatric intensive care beds

Editor,—While we support efforts to correct the country's deficiencies in paediatric intensive care and we applaud Milne and Whitby's academic approach to the issue, we feel compelled to comment on their paper.1

The use of a model that matches patterns of use of intensive care units in segmented or decentralised intensive care delivery systems cannot help determine the true bed requirement of a centralised system. Because the authors fail to acknowledge the improved efficiency of larger intensive care units in terms of duration of admission, their model overestimates the numbers of beds required by a given population under such circumstances.

Most importantly we should emphasise that measures of the efficiency of paediatric intensive care are not restricted to economics or length of stay. The evidence that centralised paediatric intensive care facilities decrease mortality is very convincing. In the UK we have collectively failed to adequately recognise and address these issues, despite the BPA report and its reviews (referredenced in the article). We therefore have to accept the risk of morbidity and mortal consequences.

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Drs Milne and Whitby comment:

The purpose of our paper was to draw attention to the striking similarity between estimates of paediatric intensive care bed need made by different authors working in different health care systems, with different population sizes, and one would assume, with different levels of efficiency. We would certainly not conclude from our data that we had identified the correct level of paediatric intensive care provision, but have rather sought to identify a currency with which debate can properly take place. The comments of Drs Pearson and Ralston on the efficiency of larger intensive care units reflect the views of Shann cited in the discussion of our paper. The importance of intensive care in reducing mortality and morbidity is one that we would not dispute, but again this was not the focus of our article.


22q11 deletion: a cause of asymmetric crying facies

Editor,—We agree with Hamish et al that permanent facial asymmetry in the newborn has many causes.2 Facial asymmetry present only on crying has been described as a separate entity and termed asymmetric crying facies (ACF).3 ACF is due to hypoplasia of the depressor anguli oris muscle and has been described in association with congenital heart disease as cardiofacial syndrome.4 This syndrome may include abnormalities of other systems and may be inherited in an autosomal dominant manner with variable expression.

We agree with Trainer et al that microdeletions of chromosome 22q11 detected on fluorescent in situ hybridisation (FISH) are responsible for a wide range of clinical presentations including cardiac abnormalities.5 Five patients with cardiofacial syndrome have been found to have a microdeletion of chromosome 22q11.6

We have recently seen an 8 year old girl who presented with ACF without cardiac abnormalities who had 22q11 deletion demonstrated on FISH. This is the first such case and we believe that this represents a further expansion of both the differential diagnosis of facial asymmetry and the phenotype of the newborn and the 22q11 phenotype.

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Expulsion of ventriculoperitoneal shunt tubing

Editor,—In reply to the letter by Dr Swann on the supposedly unique occurrence of expulsion of ventriculoperitoneal shunt tubing,1 I would like to describe another case, not of expulsion but extrusion of ventriculoperitoneal tubing per rectum.

A first twin born caesarean section on our delivery unit at 26 weeks' gestation had a stenotic neonatal course necessitating a ventriculoperitoneal shunt for haemorrhagic hydrocephalus. He subsequently needed a ventriculoperitoneal shunt. He was readmitted at the chronological age of 8 months with vomiting and swelling over the shunt site. He was suspected of having a shunt infection and was treated with intravenous cefotaxime and flucloxacillin. After 24 hours in hospital the nursing staff noticed, while changing the baby's nappy, extrusion of the shunt per rectum.

He was immediately transferred to the neighbouring neurosurgical unit who were somewhat puzzled that we had not noticed anything on the free end—it had disappeared back up into the abdominal cavity. He grew Echerichia coli from the cerebrospinal fluid and