LETTERS TO THE EDITOR

ECG and echocardiographic diagnosis of pulmonary thromboembolism associated with central venous lines

Error.—Pollard et al retrospectively studied 21 children with central venous lines for parenteral nutrition by electrocardiography and eight by echocardiography.1 They state that ventilation/perfusion (V/Q) scan had a low sensitivity for detection of major pulmonary emboli based on the PIOPED investigators’ study of 933 adult patients.2 The echocardiogram (ECG) criteria used by Pollard et al were based on a study of 49 adult patients of whom half were diagnosed by V/Q scan alone.3 Pollard et al describe their ECG findings as diagnostic of embolism and dismiss use of the V/Q scan. Their ECG based method cannot be regarded as more accurate than the technique used to validate it.

The study of Pollard et al presents ECG criteria for right ventricular strain as diagnostic of venous embolism without any validation. Corroboration of the diagnosis is available in only two children who had emboli at necropsy. In addition ECG criteria based on adult normal values were applied to paediatric patients, for example the frontal QRS axis at 5–7 years is +11 to +143 allowing a normal child to achieve a positive criterion.4 The V/Q scan has however been validated in paediatric patients and also suggests that the pulmonary angiogram is of limited usefulness in chronic microemboli, while most authorities regard it as the gold standard.6

Pollard et al assert that the echocardiogram is very sensitive in establishing the diagnosis of pulmonary embolism, whereas the originator of the echocardiographic criteria suggests that it is an initial investigative tool.7 Pollard et al’s reference to our own study8 is inaccurate in stating that 12 of 34 children had thrombosis visualised on echocardiography. In fact of the 12 children who had thromboemboli four were diagnosed only by V/Q scan with unremarkable echocardiograms, while eight had echocardiograms showing right atrial thrombus or pulmonary hypertension; in five of the eight V/Q scans showed clots. In two patients with indirect echocardiographic evidence of pulmonary hypertension as the sole abnormality pulmonary embolism was diagnosed at necropsy.

Pulmonary embolism secondary to long term parenteral nutrition has been ignored for too long. An increased awareness of this complication will improve patient care but only if a clear diagnostic and management strategy is available. Pollard et al’s study concerns the use of V/Q scan and has given inappropriate prominence to ECG and echocardiographic diagnosis. These are valuable initial investigations which should lead on to V/Q scanning and if necessary to pulmonary angiography.

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Drs Pollard, Sreeram, Wright, Beath, Booth, and Kelly comment:
We are pleased that Dollery et al found our paper so stimulating but are disappointed that they seem to have missed the point and are left confused by the use of the ECG and echocardiogram. Dollery et al draw attention to an important study comparing the sensitivity of ventilation perfusion scanning (V/Q), ECG and ECHO.9 Further scrutiny of this paper revealed that while the V/Q scan correctly identified only 29 out of 49 patients with pulmonary embolism, ECG may pick up more cases than a V/Q scan we used echocardiographic information to draw attention to the fact that pulmonary thromboembolism is common in children with long term indwelling central venous lines and to advocate evaluation of preventative strategies. This view is supported by work previously published by Dollery et al,2 although we found a greater incidence of pulmonary embolism. We are grateful for the clarification of their study.

We have not dismissed the use of V/Q scanning or pulmonary angiography as they suggest and it is our practice to use these techniques as appropriate. We use ECG and echocardiography in appropriate clinical situations to establish a diagnosis of pulmonary thromboembolism. We think that the ECG and echocardiogram is helpful and possibly more sensitive than current ‘gold standards’ but there have been no prospective studies comparing these techniques with V/Q scanning and pulmonary angiography in children to confirm this. Without ECG and echocardiography in appropriate clinical situations it is impossible to draw firm conclusions. We suggest that Dollery et al should also await results of prospective comparative studies before pronouncing judgement on our observations.

We agree that ECG and echocardiographic diagnosis of pulmonary thromboembolism requires further validation in children and Dollery et al will find this clearly stated in our paper. We did use age appropriate paediatric reference values for the analysis of ECGs and echocardiograms and again, this is stated in the methods. Use of adult normal values would have been inappropriate. Until prospective data are available, we believe that clinicians may well find information from these readily available, non-invasive investigations helpful.

We had hoped to stimulate interest in the prevention of pulmonary embolism in parenteral nutrition dependent children with a goal we share with Clare Dollery and her colleagues.9


Persistent nocturnal cough in childhood: a population based study

The study by Ninan et al accepts that ‘it is now well established that in some cases isolated persistent cough may be the sole presenting manifestation of asthma’. However, at the same time Ninan et al try to discount isolated persistent nocturnal cough as a marker of asthma.3 This is a fact proved in two studies that the article refers to.2,3 However, the 12% of children with persistent nocturnal cough had been defined as those who had been recorded at least three months and not four weeks.

The second problem is relying on the parents’ history of persistent nocturnal cough. This is simply unreliable in our experience and has been proved in the small study by Falconer et al.4 This means that the reported persistent nocturnal cough is underestimated and inevitably has biased the results.

As it has been suggested the diagnosis of asthma is easier when cough is associated with wheeze, shortness of breath and tightness in the chest, although, in fact, none of these symptoms individually or collectively is specific for asthma. For example, exercise, cyanosis, bronchiectasis, tuberculosis, and other rare conditions may present in a similar way. Detailed history including type of cough may help in the differential diagnosis. For example, dry cough is more suggestive of asthma. Other studies have relied on diagnostic tests to confirm or refute the diagnosis of asthma rather than relying on history alone.2,3

Unfortunately in this study no diagnostic tests were applied to the children reported as persistent nocturnal cough. We also would have liked to know if the symptoms of the 12% of the 27 children with it had been controlled by the antihistamines and bronchodilators that they were taking. We therefore think it is rather misleading to discount persistent nocturnal cough as a marker of childhood asthma.

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Dr Ninan and Russell comment:
We thank Drs Madlon and Bugg for their comments. We would like to point out that the publication here is only a small part of a
much larger epidemiological study looking at changes in prevalence of respiratory symptoms and atopic diagosis in childhood over a 25 year period.\textsuperscript{1}

Ellicoting information on the duration of persistent nocturnal cough is a particularly thorny issue. Falconer et al.\textsuperscript{2} confirm the observations of Archer and Simpson\textsuperscript{3} that parental recording of nocturnal cough is inaccurate. They found significant under-reporting over a three month period and, by historical coincidence, we chose subjects who had at least three episodes of persistent nocturnal cough and each of these episodes lasted for at least one month. Recall for recent events in general is more accurate than distant events. We feel this may have minimised the bias towards under-reporting.

Over the last four decades, epidemiological studies have consistently used whoeze, compared with those who clinically presented with nocturnal cough, and tightness of chest as marker symptoms of asthma. Though uncommon medical conditions such as cystic fibrosis and bronchiectasis may present with similar symptoms, we believe that the numbers are small. All the children in the study were examined by a paediatrician (TKN) and none of these children had overt evidence of either cystic fibrosis or bronchiectasis.

Secondly, we based our study on a diagnostic test.\textsuperscript{2,3,4} Hospital based whereas this was a cross sectional community based study and we had constraints on the type of investigations that could be carried out. Long term prospective studies are needed for assessing effectiveness of control. This was designed as a prevalence study. We therefore have no information on effectiveness of control of persistent nocturnal cough.

Finally, we would like to reiterate that persistent nocturnal cough in epidemiological studies is not a good marker for asthma. This is a different population of children when compared with those attending hospital, where there is a greater tendency to diagnose asthma in this biased hospital population for very good reasons.


Sodium/glucose cotransporter activity in cystic fibrosis

Errors.—Enhanced intestinal sodium dependent glucose transport has been suggested to contribute to glucose intolerance in cystic fibrosis.\textsuperscript{1} Moreover, this increased absorption exacerbates the luminal dehydration that contributes to cystic fibrosis pathol- ogy. In the airways of those with cystic fibrosis, sodium absorption is also increased, and recent reports suggest that this arises from the failure of a direct inhibitory effect of the cystic fibrosis transmembrane conductance regulator (CFTR) on apical membrane sodium channels.\textsuperscript{2,3} Increased sodium/glucose absorption in cystic fibrosis intestine may therefore occur in a similar way, or could alternatively involve an intracellular mechanism. To distinguish between these possibilities glucose uptake by the human small intestine in children with and without cystic fibrosis has been measured using brush border membrane vesicles (BBMVs); this allows the study of membrane transport in isolation from intracellular components. BBMVs were prepared from endoscopic or Crosby capsule biopsies (duodenal or jejunal) taken from children presenting with non-specific gastrointestinal symptoms or failure to thrive. Each specimen was obtained from an individual child with control tissues divided on the basis of history into those showing no significant abnormality (n=46) or partial or total villus atrophy (n=3). Cystic fibrosis tissues (n=9) were obtained from pancreatic insufficient patients (six AF508/ ΔF508, two ΔF508/other, one unknown genotype) and they had normal mucosal morphology. BBMVs were incubated for 10 seconds at 20°C in 100 mM sodium thiosucinate and 100 µM 3H-2-deoxyglucose, and active sodium dependent glucose transport was calculated from the uptake differences in the presence or absence of phlorizin (250 µM). Results were analysed by non-parametric one way analysis of variance. Active uptake was observed in control vesicles from biopsies with no significant abnormality, but not in BBMVs prepared from biopsy specimens showing villus atrophy (p < 0.05 v no significant abnormality; fig 1), demonstrating that this preparation is sensitive to changes in epithelial function. However, active glucose transport in BBMVs from those with cystic fibrosis was not significantly different from controls with no significant abnormality (p > 0.05). This contrasts with studies of intact cystic fibrosis biopsy specimens\textsuperscript{1} where the rate of active sodium/glucose transport was approximately dou-

The fact that active glucose uptake is not enhanced in cystic fibrosis intestinal BBMVs where the intracellular machinery is absent, indicates that the membrane activity of the sodium/glucose cotransporter is not directly altered in this disease. If wild type CFTR does regulate intestinal sodium linked nutri-

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