LETTERS TO THE EDITOR

RSV prevention

EDITOR,—I recently saw the UK guidance for the use of synagis (Palivizumab) brought out by the manufacturer and contributed to (rendorsed) by a number of UK experts. My interpretation of the IMpact-RSV (respiratory syncytial virus) study1 appears to be at variance to the conclusions drawn and the recommendations of the “guidance”.

To me, in the above mentioned study,1 compared to placebo, Palivizumab: (a) did not reduce deaths from RSV related hospitalisation by 55%—the primary outcome of interest. Based on (b), the “guidance” recommends Palivizumab for premature infants of <36 weeks’ gestation who are <6 months old at the start of RSV season as well as those with bronchopulmonary dysplasia <2 years old who have required medical treatment within six months of the RSV season beginning.

Looking at the data in another way, one would need to treat 16 suggested “at risk” babies (20 for babies with bronchopulmonary dysplasia) to prevent one RSV related hospitalisation. Is it worth it in clinical or economic costs?

Clinical—There was no evidence that RSV illness was less severe among hospitalised Palivizumab recipients than among hospitalised placebo recipients. (The paper provides figures for secondary efficacy end points as per 100 treated children. I suppose they are clinically more relevant than for per 100 hospitalised children.) Although statistically insignificant, both the RSV related deaths occurred in the Palivizumab recipients. Three per cent of placebo recipients (but 15 of 53 hospitalised placebo recipients) and 1.3% of Palivizumab recipients (but 13 of 48 hospitalised Palivizumab recipients) had RSV intensive care unit admissions. Only 0.2% (one of 500 treated or 53 hospitalised) placebo recipients and 0.7% (seven of 1002 treated or 48 hospitalised) Palivizumab recipients required mechanical ventilation. Similar conclusions can be drawn for total ventilator days. In other words, reduction in hospitalisation rates does not necessarily equate with reduction in severity of illness.

Economic—As 16 at risk infants need to be treated to prevent one hospitalisation, and as the infants would receive five monthly injections of the antibody costing between £424 (US$680) and £706 (US$1130) per infection (depending on their weight), the cost of preventing one hospitalisation from RSV related illness is at least £3 200 (US$51 000). I do not know the latest figures for a paediatric inpatient stay but analogies from neonatal “special care” category days would suggest that a six to eight day admission (calculated figures from the IMpact-RSV trial) should not cost more than £1800 to £2500 (US$2880–4000).

So I see very little clinical benefit to those “at risk” children who receive Palivizumab and get RSV illness nor do I see any economic advantage to prevention of RSV related hospitalisations. Indeed both the PREVENT1 and Impact-RSV1 studies show much lower rates of hospitalisation among the placebo infants than for historic data, which has been attributed among other things to “extensive education”. The valid conclusion then should be that education is the most important tool for prophylaxis against RSV hospitalisation.

The “guidance” suggests drawing conclusions from local RSV hospitalisation rates but these are affected by geographic and social factors as much as clinical ones. Moreover, would local figures have any meaningful value if a large multinational study fails conclusively to prove clinical or economical benefits of the treatment? I do not dispute that there will be an occasional baby with such severe lung disease that any help, however welcome, would be welcome. But a generalised preventive measure such as this will be difficult to justify.

Have I got it all wrong?

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R M NICHOLL on behalf of the Evidence Based Neonatal Medicine Appraisers: C Cane, E Costales, U Chovodath, S Goldberg, J Halbertsat, S Hughes, S Lindsay, S Saliga, S Shebah
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Table 1 RSV antibody: clinically useful measures of effect

<table>
<thead>
<tr>
<th>Event</th>
<th>CER</th>
<th>EER</th>
<th>RRR</th>
<th>ARR (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admission (all)</td>
<td>10.6%</td>
<td>4.8%</td>
<td>55%</td>
<td>5.8% (3 to 9)</td>
<td>17 (11 to 33)</td>
</tr>
<tr>
<td>(Premature (no BPD))</td>
<td>8.1%</td>
<td>1.8%</td>
<td>78%</td>
<td>6.3% (3 to 10)</td>
<td>16 (10 to 39)</td>
</tr>
<tr>
<td>Previous BPD</td>
<td>12.8%</td>
<td>7.9%</td>
<td>39%</td>
<td>5.1% (0.4 to 9.8)</td>
<td>20 (10 to 250)</td>
</tr>
</tbody>
</table>

CER, control event rate; EER, experimental event rate.

Expenditure per unit of antibody (95% CI)

<table>
<thead>
<tr>
<th>Event</th>
<th>(Q)</th>
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<tbody>
<tr>
<td>Hospital admission (all)</td>
<td>25 000 (16 000 to 49 500)</td>
</tr>
<tr>
<td>(Premature (no BPD))</td>
<td>24 000 (15 000 to 58 500)</td>
</tr>
<tr>
<td>Previous BPD</td>
<td>30 000 (5 000 to 37 500)</td>
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Interhospital transfer of sick children: proposal for a unified approach

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1 Rashid A, Bhuta T, Berry A. A regionalised transport service, the way ahead? Arch Dis Child 1999; 80:188–92.

Definitive diagnosis of nut allergy

Editor,—We are concerned that the general readership of Archives of Disease in Childhood may be misled by a paper based on results of non-standardised or obsolete tests used in the diagnosis of children with potentially severe allergies to peanut and tree nuts.

The implicit confidence of the paper’s title is not supported by the experimental approaches. Although we would like to express our concern about the following specific points.

1. It cannot be assumed a nut is “the only possible allergen” in a composite food. Any allergenic food can cross contaminate a “safe food.”

2. Intradermal testing is not considered standard practice and has no place in the modern management of food allergy.

3. Rubbing the forearm until erythema is induced makes distinction from dermographic impossible. Skin contacts that cause allergic reactions are usually minimal and non-traumatising. Percutaneous skin prick testing (SPT) with negative and positive controls—usually performed in this study—is easy to perform, causes minimal discomfort compared to blood sampling, and is considered safe. It also provides an immediately available result with wide application.

4. Our findings also suggest that non-standardised practice in the field of investigating anaphylaxis is playing with fire and does nothing to reassure parents.

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Urinary glycosaminoglycan excretion in urticaria

Editor,—Ackoy et al reported urinary glycosaminoglycan (GAG) excretion to be significantly diminished in children with idiopathic urticaria compared with controls, and proposed that urinary GAG may play an important role in the study reduction of calcitriol in children.1,2 Our findings do not fully support this hypothesis.3 We evaluated urinary GAG excretion in 22 children with calcium oxalate stones (eight with absorptive hypercalciuria, six with renal hypercalciuria, eight with normocalciuria) and in 20 age matched controls. There was no significant difference in total urinary GAG between the two groups. In terms of the various GAG fractions, patients with renal hyper-
renal calculi is a matter for debate requiring further investigation. The role of urinary GAGs in the formation of calcium oxalate crystallisation in vitro, the excretion of urinary GAGs are significant inhibitors of crystallisation. On the basis of these and other studies, the difference in the urinary GAG excretion of children with idiopathic urolithiasis and healthy controls. There was no difference in the urinary GAG excretion of healthy children and adults, whereas the Leeds children were included in the study of Raynor and colleagues, the Newcastle children were identified solely on the basis of slow postnatal growth. They suggest that our study included “many children who . . . proved to be small or to have low centile rankings.”

Varicella: to vaccinate or not to vaccinate?

EDITOR,—I am in complete agreement with Dr Aebi that strategies for delivering varicella vaccine effectively are critical to the success of immunisation programmes. In the USA great efforts are being made in this direction. Nevertheless, despite the licensure of varicella vaccine for routine use in the United States in March 1995, deaths from varicella continue in children and adults. (At my hospital, a 37 year old, previously healthy man died recently of varicella pneumonia.) The US Centers for Disease Control and Prevention has set goals for eventual vaccine coverage rates of over 90% within the next decade. Since morbidity and mortality continue to occur in the USA, it is very difficult for me to believe that there is little problem with varicella in Europe. It may be that studies so far have not been large enough or have not been truly representative sampling. Varicella is clearly a disease associated with many complications. It should also be remembered that varicella vaccine provides protection against herpes zoster as well as against chickenpox.

In the USA, the best approach to ensure vaccine delivery has been to require immunisation before school entry. This rationale may or may not be useful for all countries. As the efficacy of antimicrobials continues to decrease due to resistant organisms, it is likely that the world will become more dependent on vaccines to protect the populace from infections. Society must be prepared to develop effective means and strategies to protect its children from infectious diseases.

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A randomised controlled trial of specialist health visitor intervention for failure to thrive

EDITOR,—I was surprised to read in Raynor et al’s recent paper the statement that their study was “the largest randomised controlled trial on children with failure to thrive in this country.” Our study tried nearly three times as many children and was published four months before their paper was accepted.

Did they think that it was a true trial? It conforms to CONSORT guidelines, with random allocation to treatment, and all patients enrolled prospectively (not retrospectively as they suggest). Did they feel the children in their study did not “thrive” or require intervention? They suggest that our study included “many children who . . . proved to be small or to have low postnatal weight gain” and that “failure to weight gain” should be reserved for children where there are associated physiological or emotional issues. This is of course not just semantics. Wright’s own recently published work suggests that the intellectual and growth risks are low in children identified by weight screening alone.

The second difference regards the intervention itself. The Leeds children received intensive individualised help from a highly experienced health visitor with special training in assessment, counselling, and nutrition. In comparison, the Newcastle health visitors’ training consisted of only a few hours and the intervention was often only one or two visits. Where there is such a discrepancy in the results, given the relative difference in intensity of the interventions, it is not entirely clear.

We noted that our study numbers were small, although 83 children is a sizeable sample from any single clinic. It is unlikely that any one centre can enrol enough patients using the strict clinical diagnosis outlined above, and I fully support Wright’s contention that larger (almost definitely multicentre) studies are required to produce definitive results.

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