Inhaled sodium cromoglycate

The systematic review and meta-analysis performed by Tasche and colleagues appears to have been carried out with commendable thoroughness. The results seem clear cut: sodium cromoglycate is ineffective as maintenance therapy in children with asthma. However, their conclusions are not objective but depend in the final analysis on their multi-variate regression model. Perhaps this is where the most important bias has crept into the analysis.

As in the case of many new drugs, clinical trials are first carried out in adults, later in schoolchildren, and finally (if ever) in infants and pre-schoolchildren. This appears to have been the case with sodium cromoglycate since, of the studies included in their review, 12 out of 14 conducted before 1981 involved schoolchildren while, of those published since 1981, nine out of 10 involved pre-schoolchildren. The authors point out that “age of the children . . . was strongly correlated with year of publication”.

They chose to interpret the positive effect size of older studies as an indication of publication bias. An equally reasonable interpretation might be that sodium cromoglycate is more effective in schoolchildren than in pre-schoolchildren.

I wonder if the authors could calculate the size of the treatment effect in their selected trials separately for those trials predominately involving schoolchildren and those involving predominantly pre-schoolchildren.

Systematic review and meta-analysis often lend spuriously objectivity to the assessment of efficacy. In the final event statistics provide guidance, and some form of subjective judgement is required as to the clinical relevance of the analysis.

For both schoolchildren and pre-schoolchildren and for both outcome measures (cough and wheeze) the test of homogeneity was negative: the study results were heterogeneous in both age groups. The pooled results, using the method of Desmoulin and Laird,1 are shown in table 1.

These results seem to confirm Silverman’s assumption that SCG is more effective in schoolchildren than in pre-schoolchildren, although even in schoolchildren the tolerance interval for wheeze still includes zero. However, we think the conclusion of an age specific effect is as yet unwarranted. All studies in schoolchildren were performed in the early years of SCG, at a time when the quality of design and reporting of trials was not much of an issue. All the studies were performed on small numbers of children, thus yielding estimators with low precision, and used a crossover design, a design which is apt to yield biased results in cases of incomplete follow up. Publication bias might also account for these findings, given the funnel plot results. To confirm these results, a trial of adequate size needs to be performed in schoolchildren.

BTS guidelines on TB

This excellent guideline,1 chaired by Dr Peter Ormerod, is very welcome. However, on page 888, under the heading Public Health Law, an important Act has been omitted—namely, Section 47 of the National Assistance Act 1948, as amended in 1951. This requires a doctor (usually a public health doctor) to consider, through a legal process, the compulsory removal to hospital of a person following certain strict criteria—for example, old age and infirmity, living in insanitary conditions, unable to look after oneself.

We have been approached in the past to invoke Section 47 on a patient with tuberculosis—although such a request and actual use is, I suspect, negligible in the UK as a whole. However, its use is still possible and will also not “be undertaken lightly” as was correctly stated for Sections 37 and 38 of the Public Health Act 1984. An attempt to use Section 47 on a patient with tuberculosis some years ago was frowned upon when a doctor pursued the

Table 1 Effect of sodium cromoglycate on cough and wheeze in pre-schoolchildren and schoolchildren

<table>
<thead>
<tr>
<th>Group</th>
<th>Cough Pooled effect (95% CI)</th>
<th>Cough Tolerance interval</th>
<th>Wheeze Pooled effect (95% CI)</th>
<th>Wheeze Tolerance interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-school children</td>
<td>0.12 (0.03 to 0.22)</td>
<td>-0.12 to 0.36</td>
<td>0.08 (0.00 to 0.16)</td>
<td>-0.11 to 0.27</td>
</tr>
<tr>
<td>Schoolchildren</td>
<td>0.26 (0.17 to 0.35)</td>
<td>-0.02 to 0.50</td>
<td>0.29 (0.16 to 0.43)</td>
<td>-0.07 to 0.66</td>
</tr>
</tbody>
</table>

Correspondence to: Dr M G Pearson.

was not significant in either group when (overall, aspirin, metamizole, paracetamol) consumption was found to be significantly higher in AIA patients with mild, asthma and the amount of analgesic consumption was evaluated by a Spearman’s non-parametric correlation test was applied to the data. It is already known that the clinical course of patients with AIA is more severe than for those with analgesic tolerant asthma, and the overall consumption of analgesics and paracetamol by AIA patients has been found to be higher. It should also be added that the increased consumption of paracetamol in these patients results from physicians’ analgesic preference and our re-analysis showed a weak relation. Certainly the clinical and epidemiological surveys should be evaluated separately, but our results seem to support the results of Shaheen et al. Since these retrospective surveys might include “recall bias”, prospective studies of asthma patients could help to elucidate the difference between the analgesic consumption of patients with AIA and those without analgesic intolerance. Spearman’s non-parametric correlation test was applied to the data. It is already known that the clinical course of patients with AIA is more severe than for those with analgesic tolerant asthma, and the overall consumption of analgesics and paracetamol by AIA patients has been found to be higher. It should also be added that the increased consumption of paracetamol in these patients results from physicians’ analgesic preference and our re-analysis showed a weak relation. Certainly the clinical and epidemiological surveys should be evaluated separately, but our results seem to support the results of Shaheen et al. Since these retrospective surveys might include “recall bias”, prospective studies of asthma patients could help to elucidate the difference between the analgesic consumption of patients with AIA and those without analgesic intolerance.

### Table 1

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Asthma (n=103)</th>
<th>AIA (n=191)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild (n=56)</td>
<td>Moderate (n=43)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>2.3 (5.3)</td>
<td>4.3 (11.3)</td>
</tr>
<tr>
<td>Metamizole</td>
<td>1.9 (4.4)</td>
<td>4.0 (7.9)</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>1.6 (2.1)</td>
<td>2.6 (5.0)</td>
</tr>
<tr>
<td>Total analgesic consumption**</td>
<td>7.0 (11.8)</td>
<td>12.4 (15.8)*</td>
</tr>
</tbody>
</table>

1 Reference group.
*p<0.05.
**Other analgesics not included.

Spearman’s non-parametric correlation test was applied to the data. It is already known that the clinical course of patients with AIA is more severe than for those with analgesic tolerant asthma, and the overall consumption of analgesics and paracetamol by AIA patients has been found to be higher. It should also be added that the increased consumption of paracetamol in these patients results from physicians’ analgesic preference and our re-analysis showed a weak relation. Certainly the clinical and epidemiological surveys should be evaluated separately, but our results seem to support the results of Shaheen et al. Since these retrospective surveys might include “recall bias”, prospective studies of asthma patients could help to elucidate the difference between the analgesic consumption of patients with AIA and those without analgesic intolerance. Spearman’s non-parametric correlation test was applied to the data. It is already known that the clinical course of patients with AIA is more severe than for those with analgesic tolerant asthma, and the overall consumption of analgesics and paracetamol by AIA patients has been found to be higher. It should also be added that the increased consumption of paracetamol in these patients results from physicians’ analgesic preference and our re-analysis showed a weak relation. Certainly the clinical and epidemiological surveys should be evaluated separately, but our results seem to support the results of Shaheen et al. Since these retrospective surveys might include “recall bias”, prospective studies of asthma patients could help to elucidate the difference between the analgesic consumption of patients with AIA and those without analgesic intolerance.

Paracetamol and asthma

We were interested to read the article by Shaheen et al on the relationship between paracetamol and asthma.1 We have been interested in patients with analgesic induced asthma (AIA) since 1991 and now have a reference be-

## Book Review


This is the third edition of the standard textbook on high altitude medicine. Although it is only five years since the second edition appeared, the book has been extensively revised to take into account the recent explosion of interest in high altitude medicine. As the authors mention in their preface to the third edition, there have been over 1500 publications since 1995 on altitude related topics. All the chapters in this edition have been updated to take into account these recent publications and additional sections on commercial activities at altitude have been added. I was interested to receive this new edition because, by chance, the first edition of this book was the first medical textbook I ever bought. At the time I was a student planning a trip to the Himalayas and wanted to learn more about the pathophysiology of the life threatening forms of acute mountain sickness, high altitude pulmonary oedema, and high altitude cerebral oedema. The book provided an excellent overview of the subject and introduced me to other interesting topics. Comparing the first and third editions, it is interesting to note that relatively little advance has been made in terms of understanding the pathophysiology of high altitude pulmonary and/or cerebral oedema, despite their increasing importance given the greater numbers of individuals travelling to high altitude now compared with 20 years ago. Those advances which have been made are well summarised in the relevant chapters of the third edition.

High Altitude Medicine and Physiology remains the standard textbook in its subject area. It is comprehensive and well referenced and yet remains eminently readable. This is not a handbook of emergency medicine for the use of doctors or mountaineers travelling to altitude, but a book which covers a much broader subject area. It should be on the bookshelves of all individuals interested in the effect of altitude on the human body. —IH

## Notice

**Respiratory Medicine**

A conference on Respiratory Medicine will be held at the Royal College of Physicians of Edinburgh on 26 October 2001. For further information contact Ms Eileen Strawn, Symposium Coordinator. Telephone 0131 225 7324. Fax 0131 220 4393. Email: e.strawn@rcpe.ac.uk. Website: www.rcpe.ac.uk.
Paracetamol and asthma

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Thorax 2001 56: 585
doi: 10.1136/thorax.56.7.585c

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