However, several years ago, Haifer and Plit measured the temperature changes during two minutes of nebulization of histamine from a Wright nebulizer and found it to be exactly the same as in the present report.

They went on to investigate whether this temperature drop may have any clinical effect and compared the response to inhaled histamine (PC$_{20}$) between nebulizers operating at different but constant temperatures. The nebulizers were designed to prevent any temperature drop during nebulization. Two groups of asthmatic patients were studied: one group inhaled the aerosol at constant 30°C, whereas the other inhaled the aerosol at constant 23°C. In both groups the results were compared to those obtained during the usual test performed at room temperature (23°C) without keeping the temperature constant. The results (PC$_{20}$ in mg/ml) are presented in the table.

Thus, keeping the temperature constant increased PC$_{20}$ (reduced airway reactivity) compared with the standard method. The higher the temperature was kept, the greater PC$_{20}$ (reactivity was further reduced).

Deducing from Cockcroft's study (Figure 2 and Discussion), one would assume that, compared to the usual method, keeping the temperature constant would prevent the observed reduction in nebulizer output and hence PC$_{20}$ should be smaller. The results of Haifer and Plit's study (which showed an opposite effect) contradicted this assumption. Moreover, the fact that the effect was enhanced at higher (constant) temperatures indicate a significant role for temperature in the results. Indeed, we have recently demonstrated the importance of temperature in modifying airway response even in normal subjects.

In view of Haifer and Plit's results, the report of Cockfort et al is important not only in terms of standardization and methodology but also in clinical terms.

### Table

<table>
<thead>
<tr>
<th>Group</th>
<th>Usual, Room Temp</th>
<th>Constant 23°C</th>
<th>Constant 30°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>0.39</td>
<td>-</td>
<td>3.29</td>
</tr>
<tr>
<td>Group 2</td>
<td>1.75</td>
<td>2.35</td>
<td>-</td>
</tr>
</tbody>
</table>

To the Editor:

We would like to thank Dr. Amirav for bringing the data of Haifer and Plit to our attention. We apologize for having missed their abstract.

The results of constant temperature PC$_{20}$s are interesting and have important clinical relevance. We carefully avoided any clinical predictions based on the results in our paper. Since the reduced output at cooler temperatures represents chiefly a reduction in evaporation, we would have expected warm vs cool nebulization to have produced little difference. Since there may be a tendency for reduced solute output (not certain from our calculations), we might have expected a small change in the opposite direction to that described in the abstract by Haifer and Plit.

The surprise in the data of Haifer and Plit is not the direction but the magnitude of the change; warm nebulization (30°C) produced almost a ten-fold reduction in response to histamine compared to room temperature (23° to 16°C). The mechanism of this difference remains unclear to us. The authors' speculation that two minutes of tidal breathing of an aerosol between 23° and 16°C might enhance airway responsiveness to histamine based on additive or synergistic effect of cold air seems unlikely, since this represents a very small thermal burden on the airways. It is more likely that the reduced responsiveness with the warm nebulization represents an alteration in the physical characteristics of the aerosol. Alterations in solute output or particle size could possibly explain these changes. The Wright nebulizer generally produces a small particle size (1.0 to 1.5 microns mass median diameter). Previous reports of Wright nebulizers produced from a new manufacturer showed that with similar mass output run at room air temperature, a four-fold reduced response was observed. Further investigations (Hargrave, personal communication) suggested the most likely explanation for this reduced output was an unacceptably low mass median diameter particle size of the order of <0.8 microns. This represents a rather small deviation from the usual Wright nebulizer particle size, and although we are not certain what happens to particle size with temperature, a small reduction in mass median diameter induced by the warmer solution could explain the results documented in the abstract.

D. W. Cockcroft, M. D., F.R.C.P(C), and T. S. Hurst, M. Vet. Sc.,
Division of Respiratory Medicine,
University Hospital
Saskatoon, Saskatchewan, Canada

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### Methemoglobinemia After Lidocaine Administration

To the Editor:

In an otherwise complete summary of adverse affects associated with the use of lidocaine topical anesthesia for flexible bronchoscopy, Dr. Kirkpatrick failed to mention an unusual but potentially dangerous complication that can be most confusing if unrecognized. After topical administration to the nasal mucosa, lidocaine occasionally causes severe methemoglobinemia in patients who have the heterozygous form of NADH-Methaemoglobin reductase deficiency. Benzocaine (an ingredient in cetacaine topical anesthetic) can rarely cause methemoglobinemia when applied to the mucous membranes of normal individuals.

The sudden and otherwise unexplained development of severe respiratory distress and cyanosis during or after bronchoscopy should raise the possibility of methemoglobinemia. The diagnosis is confirmed by the characteristic brown color of the blood and by two laboratory findings: 1) arterial oxygen tension may be normal, but oximetry shows a low arterial oxygen saturation, and 2) the quantity of methemoglobin in the blood (measured directly by spectropho-