**CORRESPONDENCE**

**NITROUS OXIDE AND MAMMARY CARCINOMA**

Sir,—In view of the favourable effect of nitrous oxide upon myeloid leukaemia (Eastwood et al., 1963) and lymphoma colony forming cells (Bruce, Lin and Bruce, 1970), we have examined the effect of nitrous oxide on mammary adenocarcinoma in mice.

After subcutaneous inoculation with tumour M8013 (mammary adenocarcinoma), one group of C3Bl10 mice was placed in one cage in a flow of nitrous oxide 80% and oxygen 20% which was passed for 11 of 13 consecutive days. A second identical group spent 11 of 13 consecutive days exposed to nitrous oxide 50% in oxygen, and a third identical group was kept in air (control group).

On the 13th day, the mice were weighed, the tumour diameters were measured and the leucocytes were counted (after bleeding to death). No effect of nitrous oxide 80% or 50% was observed on the growth of the tumours or on the leucocyte count in peripheral blood.

However, there was an obvious difference in loss of weight in the mice exposed to nitrous oxide, especially to the larger concentration (table I). Subsequently, we determined if nitrous oxide (mostly 80%) had any influence upon the effect of cytotoxic drugs. Mice with or without mammary adenocarcinoma M8013 were treated every 2nd day with one intraperitoneal injection of a cytotoxic drug—vincristine (Oncovin) 0.06 mg kg⁻¹ or cyclophosphamide (Endoxan) 50 mg kg⁻¹, actinomycin D (Lyovac cosmogen) 1.06 mg kg⁻¹, or cyclophosphamide (Endoxan) 50 mg kg⁻¹.

The mice were allocated to three groups, placed in a cage with nitrous oxide, one 2 h before, the second simultaneously with, and the third group 2 h after the injection of the cytotoxic drug. The animals remained approximately 20 h in nitrous oxide (overnight until the next morning). In most of these experiments, the combined therapy produced more weight loss and a higher mortality rate than nitrous oxide alone. The tumours of these mice were the same size as those in mice treated only with cytotoxic drugs, suggesting that nitrous oxide in combination with cytotoxic drugs did not influence M8013 mammary adenocarcinoma in C3Bl10 mice.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of animals</th>
<th>Tumour diam. (mm)</th>
<th>WBC count (10⁶/litre⁻¹)</th>
<th>Wt (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16</td>
<td>13.0</td>
<td>9.5</td>
<td>+1.4</td>
</tr>
<tr>
<td>N₂O 50%</td>
<td>16</td>
<td>14.5</td>
<td>12.1</td>
<td>−3.5</td>
</tr>
<tr>
<td>N₂O 80%</td>
<td>16</td>
<td>12.3</td>
<td>10.9</td>
<td>−7.7</td>
</tr>
<tr>
<td>O₂ 20%</td>
<td></td>
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</tbody>
</table>

If atropine 0.5 mg kg⁻¹ or atropine 0.5 mg kg⁻¹ with promethazine 1.6 mg kg⁻¹ or atropine 0.5 mg kg⁻¹ with propranolol 1.6 mg kg⁻¹ were administered i.v. just before placing the animals in nitrous oxide, there was less weight loss and a smaller mortality but no effect on the tumours, in comparison with mice treated with cytotoxic drug and nitrous oxide.

We conclude that the administration of nitrous oxide had no inhibitory effect on the growth of M8013 tumours in mice either alone or in combination with cytotoxic drugs.

L. DEEN

**REFERENCES**


**ETHICAL PROBLEMS IN INTENSIVE CARE**

Sir,—I would like to reply to Dr Searle's (1978) comments about my paper (Bishop, 1978).

By definition, any essay is sketchy and I would remind Dr Searle that the "anecdotal evidence" was based not only on my own experience, but also on that quoted in the references given.

I would also point out that his own evidence is anecdotal; this is understandable since politically delicate matters are rarely reported and what may be difficult for doctors to collect is impossible for nurses. Furthermore, the fact that evidence is anecdotal does not necessarily render it irrelevant.

While it would appear that an excellent interdisciplinary relationship between consultants in his hospital avoids the not infrequent dispute over treatment of the critically ill patient, Dr Searle must admit that such a relationship is not universal.

On the question of keeping terminal patients in an Intensive Care Unit, I do query the justification of blocking a highly specialized bed required by a patient with greater needs. I fully appreciate the psychological difficulties for both the relatives and the staff in this situation, which is why I personally advocate extension units to Intensive Care Units with beds unsupported by extensive monitoring equipment, and which require a lower ratio of staff.

It is reassuring to find that Dr Searle agrees that there is no place for pride or prejudice in making decisions on the subject under discussion. The fact that general acceptance of the indications for such decisions is difficult to achieve is no reason for not trying.

V. A. BISHOP

**REFERENCES**
