It has been shown, both in a previous communica-
tion (Dundee, 1956) and from the findings of
other workers, that thiopentone produces no
appreciable change in the blood sugar levels in
man. Slight hyperglycaemia resulted when
thiopentone—nitrous oxide—oxygen anaesthesia,
followed morphia and atropine as premedication
for operations on varicose veins. The rise in blood
sugar during operation differed significantly from
that produced by thiopentone alone, and it was
suggested that this may have been secondary to
respiratory depression produced by the morphia-
thiopentone combination.

It was also shown, in the same publication,
that thiopentone impairs the ability of the body to
deal with an extra load of glucose. Goldsmith
and Holmes (1957) have also found that a slightly
greater degree of hyperglycaemia resulted from
intravenous injections of dextrose given to patients
under thiopentone anaesthesia than from the
same dose given to the same subjects in the
conscious state.

This paper is concerned with the significance
of these effects of thiopentone—nitrous oxide—
oxygen anaesthesia, as applied to routine anaes-
thetic practice. The effects of pre-operative
medication and adjuvants given during thiopen-
tone—nitrous oxide—oxygen anaesthesia are
reported.

METHODS
All observations were made on fit adult patients,
who had no disease other than the pathology
necessitating the operation. All the anaesthetics
were given personally by one of us (J.W.D.) and
all the administrations were smooth throughout,
with no obvious ventilatory inadequacy, hyper-
carbia or hypotension. Where controlled respiration
was employed, the Aintree respirator was
used. With the semi-open circuit, the use of gas
flows of 6 litres nitrous oxide and 2 litres oxygen
per minute was the standard technique. These
flows were also used at the beginning of closed
circuit anaesthesia, but after 10 minutes they were
reduced to 2 litres of nitrous oxide and 1 litre
of oxygen per minute.

Blood sugar determinations were all carried out
by using the Folin-Wu technique as described by
Hawk et al. (1947). Duplicate or triplicate analyses
of seventeen random samples revealed an average
deviation of 2.5 ± 0.40 mg/100 ml (range 0–5)
from this mean reading. This amounts to an
average error of ±2.4 per cent with the tech-
niques used.

RESULTS
Pre-operative medication.
Table I shows the effects of morphia (10 mg)—
atropine (0.6 mg) and promethazine (25 mg)—
atropine (0.6 mg) premedication on blood sugar
in patients undergoing surface operations under
thiopentone—nitrous oxide—oxygen anaesthesia
with a semi-open circuit. These are compared
with the effects of thiopentone alone. It is appar-
ent that the use of either of these premedications,
the use of nitrous oxide—oxygen or simply the
performance of a surgical operation caused a
slight rise in blood sugar in combination with
thiopentone. Only in subjects who received
morphia—atropine did the rise in blood sugar
differ to a statistically significant degree. The
hyperglycaemia only lasted in any case for the
first hour of the anaesthesia.

The patients who were premedicated with
promethazine—atropine received appreciably
smaller doses of thiopentone than the morphia—
### Table I

*Average blood sugar changes during thiopentone-nitrous oxide-oxygen anaesthesia in subjects having no operation and in two groups of patients each with different pre-operative medication in whom body surface operations were performed. The average dose of thiopentone is also included.*

<table>
<thead>
<tr>
<th>Pre-operative medication</th>
<th>Operation</th>
<th>Nil</th>
<th>Morphia 10 mg; atropine 0.6 mg</th>
<th>Promethazine 25 mg; atropine 0.6 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time after induction (minutes)</td>
<td>Number of cases</td>
<td>Mean deviation in blood sugar (mg/100 ml)</td>
<td>Mean dose of thiopentone (mg/kg)</td>
</tr>
<tr>
<td></td>
<td>20- 40</td>
<td>8</td>
<td>+0.8±0.4</td>
<td>10.7</td>
</tr>
<tr>
<td></td>
<td>50- 70</td>
<td>8</td>
<td>0</td>
<td>16.1</td>
</tr>
<tr>
<td></td>
<td>80-100</td>
<td>6</td>
<td>+1.7±1.8</td>
<td>19.5</td>
</tr>
<tr>
<td></td>
<td>110-130</td>
<td>6</td>
<td>−1.7±1.4</td>
<td>23.8</td>
</tr>
<tr>
<td></td>
<td>140-160</td>
<td>5</td>
<td>0</td>
<td>26.7</td>
</tr>
</tbody>
</table>

### Table II

*Mean deviation in blood sugar in patients who received thiopentone-nitrous oxide-oxygen anaesthesia, with and without d-tubocurarine chloride and/or pethidine hydrochloride.*

<table>
<thead>
<tr>
<th>Adjuvant</th>
<th>Mean control blood sugar mg/100 ml</th>
<th>Time in minutes from induction</th>
<th>Number of observations</th>
<th>Mean deviation in blood sugar mg/100 ml</th>
<th>Thiopentone</th>
<th>d-Tubocurarine chloride</th>
<th>Pethidine</th>
<th>Mean dosage (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>98</td>
<td>0</td>
<td>14</td>
<td>+4.0±1.6</td>
<td>7.9</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20- 40</td>
<td>14</td>
<td>+4.0±1.6</td>
<td>10.3</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50- 70</td>
<td>14</td>
<td>+6.1±0.6</td>
<td>12.3</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80-100</td>
<td>11</td>
<td>+6.0±1.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>d-Tubocurarine chloride</td>
<td>83</td>
<td>0</td>
<td>15</td>
<td>+3.0±1.1</td>
<td>5.3</td>
<td>0.38</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20- 40</td>
<td>15</td>
<td>+3.0±1.1</td>
<td>6.7</td>
<td>0.43</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50- 70</td>
<td>12</td>
<td>+7.5±1.8</td>
<td>7.4</td>
<td>0.44</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80-100</td>
<td>10</td>
<td>+9.5±1.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Pethidine</td>
<td>96</td>
<td>0</td>
<td>12</td>
<td>−4.0±2.2</td>
<td>7.5</td>
<td>—</td>
<td>0.57</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20- 40</td>
<td>12</td>
<td>−4.0±2.2</td>
<td>10.0</td>
<td>—</td>
<td>0.84</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50- 70</td>
<td>12</td>
<td>−3.0±2.3</td>
<td>11.1</td>
<td>—</td>
<td>0.99</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80-100</td>
<td>12</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>d-Tubocurarine chloride</td>
<td>90</td>
<td>0</td>
<td>10</td>
<td>+1.8±1.4</td>
<td>7.4</td>
<td>0.34</td>
<td>0.43</td>
<td>—</td>
</tr>
<tr>
<td>and pethidine</td>
<td></td>
<td>20- 40</td>
<td>10</td>
<td>+2.8±1.8</td>
<td>8.7</td>
<td>0.35</td>
<td>0.58</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50- 70</td>
<td>10</td>
<td>+2.8±1.8</td>
<td>8.7</td>
<td>0.35</td>
<td>0.58</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80-100</td>
<td>8</td>
<td>+5.4±1.8</td>
<td>9.1</td>
<td>0.37</td>
<td>0.67</td>
<td>—</td>
</tr>
</tbody>
</table>
atropine cases. This was not due to any particular synergism between promethazine and thiopentone, but to the fact that these were the more recent cases, and it is now appreciated that satisfactory operating conditions can be obtained with smaller doses of thiobarbiturates (Dundee, Price and Dripps, 1956). However, the doses used in the morphia-atropine series were similar to those used in the controls, where no hyperglycaemia was found, and factors other than dosage of thiobarbiturate must have been responsible for the differences observed with the two types of preoperative medication.

Adjuvants.
In this study all the patients received 25 mg of promethazine and 0.6 mg of atropine, approximately one hour before induction of anaesthesia. Table II shows the changes in blood sugar when d-tubocurarine chloride (dtc) and/or pethidine were used as adjuvants to thiopentone—nitrous oxide-oxygen anaesthesia. These are compared with data from cases who received the thiopentone—nitrous oxide-oxygen anaesthesia. These are compared with data from cases who received the thiopentone—nitrous oxide-oxygen mixture alone. Respiration was mechanically controlled in patients who received the relaxant and a closed circuit technique was used. In the other cases spontaneous respiration with a semi-open circuit was used. Although the nature of the operations to be performed differed in cases receiving dtc from those who were not given a relaxant, as far as this study is concerned, they can be considered to be body surface procedures. In all cases anaesthesia was induced well in advance of the onset of surgery and no estimations were made after opening the peritoneum.

Thiopentone—nitrous oxide—oxygen—dtc caused a small, but statistically significant, rise in the blood sugar which increased with the duration of anaesthesia. However, allowing for the error in determination of blood sugar, this was no greater than in the patients who received no relaxant. In none of the patients who received pethidine, was there any significant change in the blood sugar.

Glucose tolerance.
These determinations differed from those in the previous study (Dundee, 1956) in that they were carried out under clinical conditions in subjects undergoing or about to undergo a wide variety of operations. The rate of infusion of glucose was constant throughout—100 ml of 5 per cent solution per half hour. The infusion was started within a few minutes of induction of anaesthesia. Blood samples were taken as near as possible to every half hour. An obvious precaution was to ensure that venous blood was never sampled from the arm used for the infusion.

Control readings, without anaesthesia, were made on patients who were premedicated and prepared for operation exactly as in the anaesthetized cases.

The findings with thiopentone—nitrous oxide—oxygen with and without dtc do not differ significantly from those in conscious subjects (table III). For the sake of clarity this is shown graphically in figure 1. Although there was a slightly greater degree of hyperglycaemia in the anaesthetized patients, this was never statistically greater than in the controls.

In the curarized patients, the final blood sugar reading was actually less than that obtained 30 minutes previously, even though the dextrose infusion was continued. In these seven patients, intra-abdominal procedures were in progress when the last blood sample was drawn and stimulation of the vagus, with consequent outpouring of acetylcholine (Wright, 1952) may be the cause of this apparently anomalous finding.

DISCUSSION
This study illustrates the fallacy of applying purely experimental findings to routine clinical practice. Although it has been shown that thiopentone interferes with the handling of an excess load of glucose, this evidence was obtained with doses of glucose greatly in excess of those employed during a routine infusion. With clinical doses of glucose, even though there may be some impairment of the glycogenolytic-glycogenic activity of the liver by thiopentone, the effect is so small as to be of no clinical significance in fit subjects. It may, however, be of some importance in diabetics who are not stabilized, but even in them clinical experience seems to indicate that the thiopentone—nitrous oxide—oxygen sequence, with or without dtc and/or pethidine, is as safe as any other technique of general anaesthesia.
<table>
<thead>
<tr>
<th>Anaesthesia</th>
<th>Mean control blood sugar mg/100 ml</th>
<th>Time in minutes from induction</th>
<th>Number of observations</th>
<th>Mean deviation in blood sugar mg/100 ml</th>
<th>Mean dose of thiopentone mg</th>
<th>Mean dose of d-tubocurarine chloride mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>96</td>
<td>0</td>
<td>14</td>
<td>+28 ± 3.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>25-35</td>
<td>14</td>
<td>+42 ± 5.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>55-65</td>
<td>12</td>
<td>+54 ± 3.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>85-195</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiopeptone-N2O-O2</td>
<td>97</td>
<td>0</td>
<td>14</td>
<td>+38 ± 6.0</td>
<td>600</td>
<td>9.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25-35</td>
<td>14</td>
<td>+49 ± 7.3</td>
<td>740</td>
<td>12.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55-65</td>
<td>12</td>
<td>+52 ± 4.6</td>
<td>860</td>
<td>12.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>85-95</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiopeptone-N2O-O2-d-Tubocurarine chloride</td>
<td>98</td>
<td>0</td>
<td>18</td>
<td>+34 ± 2.6</td>
<td>420</td>
<td>7.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25-35</td>
<td>18</td>
<td>+47 ± 6.0</td>
<td>567</td>
<td>9.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>55-65</td>
<td>15</td>
<td>+62 ± 5.8</td>
<td>521</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>85-95</td>
<td>10</td>
<td></td>
<td>553</td>
<td>8.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>115-125</td>
<td>7</td>
<td>+61 ± 7.5</td>
<td>553</td>
<td>8.5</td>
</tr>
</tbody>
</table>

**TABLE III**

*Blood sugar changes during infusion of 5 per cent dextrose at a constant rate, in conscious and anaesthetized subjects.*
available today, provided hypoxia and hypercarbia do not occur. The importance of these latter two factors in causing hyperglycaemia is shown when the effects of morphia and promethazine are compared (table I) as premedicant drugs. Although it has never been proven conclusively, many authors refer to the fact that promethazine is much less potent a respiratory depressant than the opiates (Hopkin et al., 1957).

McIntyre (1947) listed sixteen references to the hyperglycaemic action of curare. All this work was done with crude curare preparations using various animals. Four of these authors suggested asphyxia as the cause of the rise in blood sugar, two stated that it was not due to asphyxia, while the remainder made no mention of the effects of the drug on respiration. Histamine release, causing liberation of adrenaline is a possible cause of hyperglycaemia following dtc, but Macintosh and Paton (1949) have shown that 0.6 mg/kg of dtc was the smallest dose required to produce this effect. It is suggested from the results of the present study that the hyperglycaemic action of dtc is so small as to be of no clinical significance.

Ward and Dance (1957) have shown that suxamethonium, like dtc, has minimal effects on blood sugar. One must add to these statements the important provisos listed by Foster and Francis:

"... provided that (a) severe falls in blood pressure are avoided, especially during induction with thiopentone, (b) anoxia and carbon dioxide retention are at all times avoided, and (c) adequate depth of anaesthesia is maintained to prevent sympathetic stimulation (sweating, pallor, etc.)."

SUMMARY AND CONCLUSIONS

Thiopentone-nitrous oxide-oxygen anaesthesia with various forms of pre-operative medication and with various adjuvants, has been studied with reference to its effects on blood sugar and glucose tolerance. It was found that:

(1) Except where morphia and atropine was used for pre-operative medication, the thiopentone-nitrous oxide-oxygen sequence did not produce any appreciable degree of hyperglycaemia. The changes observed with morphia premedication are probably due to the respiratory depression which it produces when given prior to thiopentone.

(2) Neither d-tubocurarine chloride nor pethidine aggravates the effects of the thiopentone combination on blood sugar, provided adequate respiratory exchange and carbon dioxide elimination are maintained.

(3) Under clinical conditions the effects of thiopentone-nitrous oxide-oxygen, with or without d-tubocurarine chloride and/or pethidine, on glucose tolerance are so slight as not to increase appreciably the hyperglycaemia produced by a slow infusion of 5 per cent dextrose.

The fallacies of applying the findings of laboratory investigations to routine anaesthesia practice are discussed.

ACKNOWLEDGMENTS

Part of this data was published by permission of the editor of the British Journal of Pharmacology and Chemotherapy.

REFERENCES


BOOK REVIEW


Ear, nose and throat surgeons have always taken the closest interest in anaesthesia. Their anatomical field of work overlaps that of the anaesthetist, and neither worker can do his best if the other is inexpert. More than one anaesthetist can remember a kindly E.N.T. surgeon getting him out of difficulty by passing an endotracheal tube for him. Few anaesthetists of experience have not at some time or other murmured helpful words of advice to young E.N.T. surgeons whose enthusiasm has outstripped their experience.

Dr. Proctor, an E.N.T. surgeon of 15 years standing, was an anaesthetist at the John Hopkins Medical School for four years. He writes from the standpoint of the E.N.T. surgeon instructing in anaesthesia. There are no doubt surgical colleagues of Dr. Proctor in many parts of the world who cannot call upon the services of a specially trained anaesthetist. They will find his book an admirable and in the main reliable account of anaesthesia for their branch of surgery. They can cull sufficient from it to oversee the work of their nurse or orderly, or even to administer the anaesthetic themselves.

Anaesthetists too will read this book with profit. It does set out the opinions of an experienced surgeon and as such are worthy of respect. A particularly valuable section on the use of the local anaesthesia for ear, nose and throat procedures, shows the author at his best. This is a little offset by his spill-over, somewhat unwisely, into the field of thoracic anaesthesia and resuscitation of the newborn.

The book is a mixed bag. E.N.T. surgeons will find it of the greatest value, but should be cautious that their newfound knowledge does not bring them into conflict with their own highly trained anaesthetists. Anaesthetists will learn a great deal from such snippets of surgery as Proctor gives them, and should respect the sound common sense of the anaesthetic advice even though some of the techniques may be different from those in use in this country. The illustrations are few but helpful. Glossy paper would have made them clearer and more easy to study. Useful bibliographies are appended to the end of each chapter.

W. W. Mushin

CORRESPONDENCE

ERRATUM

Sir,—In spite of great care by all concerned a few minor errors crept into the final copy of my article on “Terminology and Symbols used in Respiratory Physiology” (Brit. J. Anaesth., 29, 534). None of them is serious, but perhaps those of your readers who wish to make use of the article may like to correct them.

p. 536 Table II (IV) : for v read T.

p. 538 Table IV (V) : for respiratory quotient read respiratory quotient.

Table IV (VII) : for \( \frac{P_{ACO}_2}{R} \) read \( \frac{P_{ACO}_2}{R} \)

for \( (I-R) \) read \( (I-R) \).

E. J. M. Campbell
Middlesex Hospital, London, W.1