S.C.T.Z.—A NEW INTRAVENOUS ANAESTHETIC?

BY

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As a result of an investigation into the shock produced by the intravenous injection of thiamine chlorhydrate (vitamin B\textsubscript{1}), Charonnat, Lechat and Chareton (1953a, b, c) identified two distinct structures in the thiamine nucleus (fig. 1). Experiments showed that only the pyrimidine part was responsible for producing shock and that its stimulating action was opposed by the strongly depressant thiazole fraction. A number of derivatives of the thiazole fraction were then prepared and the hypnotic and sedative properties of one of these products (S.C.T.Z.) were confirmed clinically by Charonnat, Lechat and Chareton (1957). These workers also carried out chronic toxicity tests with S.C.T.Z. and demonstrated its anticonvulsant action in animals. The drug was shown to have no deleterious effects on the respiration or cardiovascular system of the rabbit, to be devoid of antihistamine activity and to have no curarizing action.

A clinical study of the use of S.C.T.Z. in anaesthesia was carried out by Laborit and his colleagues, who reported the results obtained in 80 cases in 1957. Their main finding was that the drug could rapidly produce sleep, yet the patient would continue to react to stimuli, no matter how deeply anaesthetized. No potentiating action with the volatile, gaseous or intravenous anaesthetics was observed. Neuromuscular transmission was unaffected by S.C.T.Z., and reflex activity was either unchanged or slightly enhanced with a slight increase in muscle tone. A variable degree of tachycardia and hypotension followed the intravenous injection of a dose sufficient to produce sleep, and severe tachycardia occurred after endotracheal intubation or other stimulation. Oxygen consumption was unaltered by S.C.T.Z. No disturbances in electrolytes were noted and nausea and vomiting after operation did not occur. There were no adverse local effects following injection.

The nearest approach to good surgical anaesthesia achieved by these French workers was with an induction by S.C.T.Z. followed by promethazine and pethidine and a continuous infusion of a
dilute solution of S.C.T.Z. In some cases chlorpromazine and hydergine were also used. Because of the multiplicity of drugs employed, it was very difficult to draw any definite conclusions from this publication as to the value of S.C.T.Z. in anaesthesia.

Attention has also been drawn to this preparation in an annotation in the British Medical Journal in 1957. This suggested that S.C.T.Z. may prove “a useful tool for the doctor”.

This paper reports a clinical trial of the drug in 40 cases. Where possible its action was compared with that of thiopentone which is the drug most frequently used in intravenous anaesthesia.

PHYSICAL PROPERTIES
The thiazole part of thiamine in a pure form is a colourless liquid; its hydrochloric ester is also a liquid, but the salts form white solids with a characteristic smell and taste. They are nearly all unstable in air.

The chemical composition of S.C.T.Z. is shown in figure 2. (It is not possible to say how the letters S.C.T.Z. were derived from the formula shown.) S.C.T.Z. is a colourless powder or crystals with a characteristic odour and melting point of 124°C. It is soluble in water, ethanol and methanol and insoluble in ether and benzene. The injectable preparation used was identical with that of the French workers and the 2 per cent solution was prepared as follows:

S.C.T.Z. 2 g
Glucose 2 g
NaOH 2 ml
Distilled water to 100 ml

SELECTION OF CASES
S.C.T.Z was used only in fit adult patients undergoing a variety of general or neurosurgical procedures. Availability of time for the induction of anaesthesia and of help in recording data were the only factors in deciding whether a fit patient received S.C.T.Z. or thiopentone for the induction of anaesthesia. Within the limitations stated, and except for a brief period where a 1 per cent solution of thiopentone was used for comparison, S.C.T.Z. was employed almost routinely by the author for approximately three months.

ANAESTHETIC TECHNIQUES
Initially it was planned first to use S.C.T.Z. as sole narcotic for minor procedures such as incision of abscesses, dressing of burns and examinations under anaesthesia. This was attempted in five patients, but for reasons which will be obvious later this technique was unsatisfactory and all five patients also required an intravenous barbiturate to produce surgical anaesthesia. No data is included from this group of cases.

Following this unsatisfactory start, it was decided to employ S.C.T.Z. for more major surgery in a manner similar to thiopentone and to prefer instances where a long-acting muscle relaxant would not be required. The distribution of the use of various techniques is shown in table I. There were two additional cases in which, by virtue of the quality of the anaesthesia, the use of S.C.T.Z. had to be abandoned during the induction and thiopentone used. These patients were in groups 1 and 2 and are not included in the final analysis of the data.

Techniques were standardized as far as possible and all anaesthetics were given personally by the author. Gas flows in nonrelaxant cases consisted of 6 litres of nitrous oxide and 2 litres of oxygen per minute. Only one analgesic was used throughout, consisting of a mixture of pethidine and levallorphan in concentration ratio of 100 to 1.25.

![Chemical structure of S.C.T.Z.](image-url)
TABLE I

Distribution of various anaesthetic techniques in this study.

<table>
<thead>
<tr>
<th>Group</th>
<th>Technique</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>S.C.T.Z. as a basal narcotic, followed by N₂O—O₂ and a volatile agent—no relaxant</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>S.C.T.Z.—N₂O—O₂ attempted</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>As above with long-acting muscle relaxant</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>S.C.T.Z.—N₂O—O₂—analgesic</td>
<td>11</td>
</tr>
<tr>
<td>5</td>
<td>As above with long-acting muscle relaxant</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>33</strong></td>
</tr>
</tbody>
</table>

This will be referred to by the proprietary name of Pethilorfan, and in the tables the dosage of pethidine only will be given. This combination was chosen because of reports by Swerdlow (1957) on its minimal depressant action on respiration, thus enabling the effect of the S.C.T.Z. to be observed. In groups 3 and 5 d-tubocurarine chloride was used exclusively as the muscle relaxant, with reversal of its action by atropine and neostigmine at the end of the anaesthesia. When endotracheal intubation was used in the other groups this was carried out with the help of suxamethonium (40–50 mg) and the larynx and trachea sprayed with a 4 per cent solution of lignocaine.

No apology is made for reporting such a small number of cases with a variety of techniques. Subsequent data will show that, in fact, it would not have been justified to extend this investigation unless all patients required a long-acting muscle relaxant. It was felt that data from such cases would be of little value as far as information on the action of the narcotic itself was concerned.

METHOD OF ASSESSING RESULTS

There was a great individual variation among the patients, both in regard to their requirements of the drug and in the quality of the anaesthesia produced by narcotic doses. The latter varied from a smooth induction and maintenance to conditions which made surgery extremely difficult. To simplify the analysis of data, all administrations have been reviewed and the results classified as follows:

Grade 1. Smooth induction and maintenance—similar to expectations from an intravenous thiobarbiturate.

Grade 2. Troublesome coughing, hiccup, uneven anaesthesia, movement by patient, etc. Operating conditions fair.

Grade 3. Very troublesome with extremely poor operating conditions.

In tables II–IV the induction period has been classified as above from the viewpoint of the anaesthetist, and the maintenance of anaesthesia from the viewpoint of the surgeon. It should be mentioned that the above classification only deals with the actual conditions produced by the drug for the circumstances stated and does not make allowances for its effect on the cardiovascular and respiratory systems. While data on these latter actions is available, this will not be described in the same detail. It is felt that the prime requirement of an intravenous narcotic is to produce sleep and good operating conditions with the same ease as is experienced with the recognized drugs. Only when these criteria are fulfilled is it necessary to analyze critically the side effects and compare these with those of other drugs.

The exact time taken from the end of the operation to recovery of protective reflexes and return to consciousness (as judged by ability to answer questions) was not recorded in every case. Where this exact data is not available the times are recorded as rapid, slow and very slow. These are simply a comparison of the recovery time with what would be expected from the use of thiopentone under similar conditions.

CLINICAL DATA

As mentioned previously, only the cases in which a long-acting relaxant was not used are described in detail. Details of cases in these groups are given in tables II and IV.

Induction of anaesthesia.

One of the obvious drawbacks of S.C.T.Z is that it is necessary to use a 2 per cent solution. The drug does not approach thiopentone in potency and thus large volumes of solution have to be used. After 20 ml the average patient felt sleepy within 30–40 seconds and the rapid injection of a second similar dose would usually cause the patient to yawn and the corneal reflex may
### Table II

Data of 6 cases in which S.C.T.Z. was used as a basal narcotic.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>Operation</th>
<th>Duration (min)</th>
<th>Pre-op. med.</th>
<th>S.C.T.Z.</th>
<th>Induction</th>
<th>Anaesthetic grade</th>
<th>Time (min)</th>
<th>Supplementary agents</th>
<th>Recovery</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>39</td>
<td>Laminectomy</td>
<td>135</td>
<td></td>
<td>A 0.8</td>
<td>0.8</td>
<td>80</td>
<td>1</td>
<td>+</td>
<td>Rapid</td>
<td>Rapid</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>46</td>
<td>Laminectomy</td>
<td>240</td>
<td></td>
<td>A 1.6</td>
<td>1.6</td>
<td>80</td>
<td>2</td>
<td>+</td>
<td>P 25</td>
<td>Slow</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>53</td>
<td>Vein stripping</td>
<td>60</td>
<td>P 1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>145</td>
<td>3</td>
<td>+</td>
<td>P 80</td>
<td>60 min 2-3 hr</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>32</td>
<td>Bougainage</td>
<td>17</td>
<td>P 0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>30</td>
<td>1</td>
<td>+</td>
<td>P 20</td>
<td>3½ hr Slow</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>68</td>
<td>Mastectomy</td>
<td>155</td>
<td>P 0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>25</td>
<td>1</td>
<td>+</td>
<td>P 50</td>
<td>15 min 3 hr</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>53</td>
<td>Mastectomy</td>
<td>145</td>
<td>P 0.8</td>
<td>0.8</td>
<td>0.8</td>
<td>60</td>
<td>3</td>
<td>+</td>
<td>P 50</td>
<td>Slow</td>
</tr>
</tbody>
</table>

All patients received atropine 0.6 mg in addition to pre-operative medication shown and all were maintained with N₂O—O₂. Intubation was carried out with the help of suxamethonium.

**Key:** For grades of induction and anaesthesia see text.

**Pre-operative medication:** A=Analgesic drug; P=Promethazine.

**Supplementary agents:** E=Ether; TCE=Trichlorethylene; P=Pethilorfan (mg).

**Comment:** *Could not carry on with N₂O—O₂—TCE because of tachypnoea: Pethidine (20 mg) given to slow rate.

† Coughing very troublesome during induction. Almost had to abandon use of S.C.T.Z.

### Table III

Details of 5 cases in which anaesthesia was attempted with S.C.T.Z.—N₂O—O₂ alone.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>Operation</th>
<th>Duration (min)</th>
<th>Pre-op. med.</th>
<th>S.C.T.Z.</th>
<th>Induction</th>
<th>Anaesthetic grade</th>
<th>Time (min)</th>
<th>Supplementary agents</th>
<th>Recovery</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>31</td>
<td>Cranietomy</td>
<td>180</td>
<td></td>
<td>1.05</td>
<td>0.95</td>
<td>100</td>
<td>1</td>
<td>1</td>
<td>Rapid</td>
<td>Slow</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>30</td>
<td>Haemorrhoidectomy</td>
<td>35</td>
<td>P 1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>150</td>
<td>3</td>
<td>2</td>
<td>Rapid</td>
<td>1 hr</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>36</td>
<td>Vein stripping</td>
<td>130</td>
<td>P 1.6</td>
<td>1.6</td>
<td>1.6</td>
<td>210</td>
<td>3</td>
<td>2</td>
<td>Rapid</td>
<td>Slow</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>53</td>
<td>Mastectomy</td>
<td>110</td>
<td>P 1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>130</td>
<td>3</td>
<td>15 min</td>
<td>1 hr</td>
<td>1 hr</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>62</td>
<td>Laminectomy</td>
<td>125</td>
<td>A 0.8</td>
<td>0.8</td>
<td>0.8</td>
<td>130</td>
<td>2</td>
<td>1 hr</td>
<td>4 hr</td>
<td>Never really settled</td>
</tr>
</tbody>
</table>

**Comment:** *Thiopentone had to be given in a hurry as control of anaesthesia was lost.

† See detailed cases.

**Abbreviations as in Table II.**
disappear. If a further dose is not given immediately this reflex will promptly return and the patient will object to the application of a face mask. Muscular movement in response to any, even minor, stimulus will be marked at this stage if a further needle prick is needed; it may then be necessary to restrain the patient.

One of the great difficulties experienced with S.C.T.Z. was to be certain of when the patient was asleep let alone judge the exact moment when a face mask should be applied or intubation attempted. There were on several occasions repeated attempts by patients made apnoeic with suxamethonium to resist intubation by moving the limbs, and even by trying to remove the tube. Despite this, when each patient was questioned closely at a later date as to their impressions of the onset of anaesthesia, none had any recollections either of the application of the mask or of intubation; all related that they had fallen asleep quietly, shortly after the needle prick. There is no evidence for delay in the onset of sleep as experienced with hydroxydione, and an impression was formed that the effects occurred as rapidly as with thiopentone.

On the basis of the classification already described, S.C.T.Z. was not as satisfactory a drug as thiopentone to precede maintenance of anaesthesia with a gaseous or volatile agent. In some cases induction was very prolonged and the uptake of the volatile agent was delayed by frequent movement, coughing and breath-holding. On one occasion (case 6, table II) a very prolonged and stormy induction occurred and was eventually terminated only by the use of a relaxant and intubation followed by 20 mg Pethilorfan and pulmonary inflation with nitrous oxide-trichloroethylene.

Where a volatile supplement to nitrous oxide was not used (table III) induction was even more prolonged and difficult. Two very troublesome situations arose: in one of these (case 2) the situation was only retrieved by the use of 100 mg thiopentone and in the other (case 4) by suxamethonium. The volume of solution needed to induce anaesthesia (40-80 ml) and the induction time (20-45 min) speak for themselves of the disadvantages of this mode of usage of S.C.T.Z.

It was felt that many of the drawbacks of S.C.T.Z. as an induction agent were due to its lack of analgesic potency. Excessive movement at the least stimulation substantiated this view. In table IV all the cases, with one exception (case 7) received a preliminary dose of Pethilorfan about 5 minutes before injection of the S.C.T.Z. This appreciably eased the difficulties of induction, and muscular movement was much less. However, there still remained the problem of deciding when the patient was asleep and the proper time to apply the face mask or perform intubation. Even including case 4, who was particularly resistant to the drug, the average dose of S.C.T.Z. was much less than that employed in the previous two series of cases.

It should be pointed out that the cases (tables II, III and IV) were not anaesthetized consecutively in the order in which they are presented. If this were so the better results in table IV could be attributed to increasing experience with the use of S.C.T.Z. In practice, the techniques were randomized and so it was found that the smoothness of induction did not appreciably alter with experience in using the drug.

Induction of anaesthesia in groups 3 and 5 (table I) where a long-acting relaxant was used were similar to those in the above groups. Again the induction was easier when a preliminary dose of Pethilorfan had been injected. It was always possible to terminate struggling with a large dose of d-tubocurarine and intubation was always easy. Nevertheless, there were a few patients who resisted this manoeuvre a little by movement of limbs and who attempted to remove the tube.

Tables II–IV make frequent mention of the presence of venous thrombosis at the injection site. In six out of the 33 cases this was preceded by pain during the initial injection (table V). This often delayed the induction as the patient would suddenly move the arm and the needle might become dislodged. No patient had any memory of this pain when questioned later.

Maintenance.

There is little that can be said of this aspect of anaesthesia from cases in table II, save that it was not always as smooth as one would have expected after a thiopentone induction. Coughing which started during the induction persisted periodically but to a lesser degree throughout the whole operation in two cases. Tachypnoea always
### Table IV

**Data on 11 cases anaesthetized with S.C.T.Z.—N₂O—O₂—Pethitorfan.**

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>Operation</th>
<th>S.C.T.Z.</th>
<th>Duration (min)</th>
<th>Pre-op. med.</th>
<th>Analgesic (mg)</th>
<th>Induction Grade</th>
<th>Time (min)</th>
<th>Anaesthesia grade</th>
<th>Recovery Reflexes</th>
<th>Final Reflexes</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>49</td>
<td>Vein stripping</td>
<td>P, P</td>
<td>50</td>
<td>0.8</td>
<td>0.8</td>
<td>60</td>
<td>50</td>
<td>75</td>
<td>1</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>17</td>
<td>Cystoscopy</td>
<td>A, P</td>
<td>15</td>
<td>1.0</td>
<td>0.8</td>
<td>80</td>
<td>50</td>
<td>20</td>
<td>1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>31</td>
<td>Laminectomy</td>
<td>A, P</td>
<td>150</td>
<td>0.8</td>
<td>0.8</td>
<td>80</td>
<td>25</td>
<td>25</td>
<td>2</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>36</td>
<td>Vein stripping</td>
<td>P, P</td>
<td>125</td>
<td>2.4</td>
<td>1.6</td>
<td>200</td>
<td>40</td>
<td>145</td>
<td>2</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>28</td>
<td>Cystoscopy</td>
<td>P, P</td>
<td>20</td>
<td>0.6</td>
<td>0.2</td>
<td>40</td>
<td>60</td>
<td>40</td>
<td>1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>20</td>
<td>Excision of cyst</td>
<td>P, P</td>
<td>20</td>
<td>0.8</td>
<td>0.8</td>
<td>80</td>
<td>50</td>
<td>70</td>
<td>2</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>39</td>
<td>Excision of ganglion</td>
<td>P, P</td>
<td>25</td>
<td>0.8</td>
<td>0.6</td>
<td>70</td>
<td>60</td>
<td>10</td>
<td>1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>28</td>
<td>Craniotomy</td>
<td>A, P</td>
<td>55</td>
<td>0.6</td>
<td>0.6</td>
<td>60</td>
<td>80</td>
<td>20</td>
<td>1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>17</td>
<td>Craniotomy</td>
<td>P, P</td>
<td>255</td>
<td>0.3</td>
<td>0.1</td>
<td>15</td>
<td>20</td>
<td>40</td>
<td>1</td>
<td>10</td>
<td>1</td>
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<tr>
<td>10</td>
<td>M</td>
<td>52</td>
<td>Excision of bursa</td>
<td>P, P</td>
<td>35</td>
<td>0.4</td>
<td>0.2</td>
<td>80</td>
<td>100</td>
<td>70</td>
<td>3</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>29</td>
<td>Craniotomy</td>
<td>P, P</td>
<td>195</td>
<td>0.8</td>
<td>0.2</td>
<td>50</td>
<td>20</td>
<td>70</td>
<td>1</td>
<td>15</td>
<td>1</td>
</tr>
</tbody>
</table>

**Comment:** Thrombosis

**Abbreviations as in Table II.**

### Table V

**Summary of some aspects of anaesthesia and sequelae.**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cases</th>
<th>Average rating</th>
<th>Average</th>
<th>Evidence of vein irritation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Induction</td>
<td>Maintenance</td>
<td>Duration (min.)</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
<td>1.8</td>
<td>1.5</td>
<td>124</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>2.2</td>
<td>2.1</td>
<td>116</td>
</tr>
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<td>3</td>
<td>6</td>
<td>1.6</td>
<td>2.1</td>
<td>160</td>
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<td>11</td>
<td>1.5</td>
<td>1.4</td>
<td>86</td>
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<td>5</td>
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<td></td>
<td>33</td>
<td>1.8</td>
<td>1.6</td>
<td>115</td>
</tr>
</tbody>
</table>
occurred when trichloroethylene was used, but in only one case (no. 2) was pethidine needed to slow the respiratory rate.

From table III, it is obvious that S.C.T.Z.-nitrous oxide-oxygen is not a satisfactory method for maintenance of anaesthesia. Patients moved frequently at the skin incision and also periodically during the operation. Extremely large doses of narcotic were needed to produce even a very indifferent quality of surgical anaesthesia. The notes, made following the most difficult case (case 3, table III), illustrate the difficulties encountered:

This was a 70 kg robust male to have unilateral excision of varicose veins. Induction was very slow; he complained of pain in the arm following the initial injection of the first 10 ml of solution, and had to be forcibly restrained for supplementary injections. Even after 60 ml (1.2 g), it was difficult to say whether he was asleep or not. A further 20 ml was given quickly and the face mask applied. There followed a long struggle and a high concentration of trichloroethylene was used for five minutes.

A further 40 ml (making a total of 2.5 g) of solution were injected just before the skin incision, but even after this the patient moved slightly. A further four skin incisions were made during this operation, and despite the injection of a further 90 ml S.C.T.Z. the patient moved violently at three of these. On one occasion it was absolutely necessary to use in addition 100 mg of thiopentone.

At the end of the operation the nitrous oxide was discontinued as the final skin suture was being tied and there was marked movement when the dressings were being applied. On return to the ward the patient was phonating and extremely restless. Half an hour later he was still restless and shivering intensely. Two hours after the end of the operation he still did not respond to questions or commands.

In table IV, the results obtained with S.C.T.Z.-nitrous oxide-oxygen-Pethilorfan were fairly satisfactory and it was felt that these were not much worse than would have been achieved if thiopentone had been used in place of the S.C.T.Z. It must be pointed out that extremely large doses of analgesic were used, and with such large doses, supplementary injections of the barbiturate would probably have been unnecessary. Of interest in the table is case 4, the patient described above undergoing a second operation. Anaesthesia was much smoother at the second operation although the requirements of S.C.T.Z. were still very high, and large doses of analgesic (185 mg Pethilorfan) were given.

The inability to continue anaesthesia smoothly with nitrous oxide-oxygen-Pethilorfan (with or without a relaxant) without the need of supplementary doses of the narcotic, makes one wonder if S.C.T.Z. is a pure narcotic without some excitatory action. In none of the cases where d-tubocurarine chloride was used was it possible to continue anaesthesia without supplementary doses of S.C.T.Z., despite hyperventilation and the use of large gas flows at the beginning to wash out alveolar nitrogen. Clinical experience with thiopentone shows that in similar circumstances anaesthesia could have been continued almost invariably with the gas mixture alone.

Recovery.

While it was common to have a return of the protective pharyngeal and laryngeal reflexes at the end of the operation, complete return of consciousness frequently took two to three hours, irrespective of the duration of the anaesthesia or the agents used to supplement S.C.T.Z. There did seem to be the danger of an apparently conscious patient lapsing back into deep sleep when stimulation was stopped. On the whole, the impression was formed that recovery from S.C.T.Z. was not as prompt as one would have expected from doses of thiopentone which produced the same degree of narcosis.

Postoperative restlessness occurred frequently after operation in patients who did not receive an analgesic drug. This was often accompanied by intense shivering. On only one occasion was this so serious as to cause concern, but the incidence was definitely greater than after thiopentone.

Irritant action on veins.

This has been mentioned in discussing the difficulties of induction of anaesthesia with S.C.T.Z. In all cases a careful search was made for the presence of thrombosis of veins on the day after operation and the 24 per cent incidence of the complication is much higher than figures reported by Hutton and Hall (1957) for thiopentone. There were no permanent ill effects from this complication.

Cardiovascular system.

As might be expected from the uneven anaesthesia which was obtained in most cases, the blood pressure and pulse records obtained are of little
value in determining the effects of S.C.T.Z. on the cardiovascular system.

In most cases where endotracheal intubation was carried out with S.C.T.Z. and a muscle relaxant, it was accompanied by a marked and sometimes fairly prolonged rise in blood pressure and tachycardia. There was no relation between this incidence and the nature of the relaxant used, and a typical chart is shown in figure 3. One could not say whether the topical application of lignocaine to the larynx and trachea reduced this reaction as the local anaesthetic was employed to enable patients to tolerate a tube during light anaesthesia, and not to facilitate intubation. It is unlikely that the lignocaine could have been effective by the time intubation was carried out. Skin incision frequently caused a similar but less marked rise in blood pressure.

While S.C.T.Z. did not seem to have a very marked hypotensive action when given intermittently, in three cases a continuous infusion was used to induce and maintain anaesthesia and in all of these some fall in blood pressure and tachycardia occurred. One such case is shown in figure 4. This effect was always transitory and no vasopressors were needed to restore the blood pressure to normal. Without having a 10 per cent solution of S.C.T.Z. available it is impossible to compare its cardiovascular effects with those of thiopentone.

\[\begin{array}{l}
\text{Blood pressure and pulse changes during induction with S.C.T.Z.} \\
\text{Male aged 51. Operation: Repair of hernia.} \\
\text{Pre-operative medication: Promethazine 25 mg, atropine 0.6 mg.} \\
\text{S.C.T.Z. in'g} \\
d.T.C. in mg \\
\text{TIME IN MINUTES} \\
\end{array}\]

\[\begin{array}{cccccccccccccc}
A & = & \text{Sleepy.} \\
B & = & \text{Corneal reflex present.} \\
C & = & \text{Corneal reflex absent.} \\
D & = & \text{Corneal reflex returned; moving legs.} \\
E & = & \text{Objected to injection; moved on stimulation.} \\
F & = & \text{Mumbling.} \\
G & = & \text{Objected to supra-orbital pressure.} \\
H & = & \text{Moving leg.} \\
J & = & \text{Good jaw tone; still mumbling and moving; winced on injection.} \\
K & = & \text{Hiccough.} \\
L & = & \text{Intubated; resisted mildly, moved arms. Inhaled with N}_2\text{O—O}_2. \\
M & = & \text{Coughed on tube; swallowing.} \\
N & = & \text{Red line noted along vein of injection.} \\
P & = & \text{Skin incision; movement of one arm.} \\
Q & = & \text{Moving arm slightly.} \\
dTC & = & \text{d-Tubocurarine chloride.}
\end{array}\]
S.C.T.Z.—A NEW INTRAVENOUS ANAESTHETIC?

Blood pressure and pulse changes during operation in a patient anaesthetized with S.C.T.Z.—

\[ d\text{-}tubocurarine chloride—N,O—O_2. \]


Pre-operative medication: Promethazine 25 mg, atropine 0.6 mg.

<table>
<thead>
<tr>
<th>A</th>
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**Respiration.**

Even less data is available on the respiratory effects of S.C.T.Z. than there are on its actions on the circulation. With induction doses employed in this study there seemed to be some increase in both the respiratory rate and tidal volume, but this could always be accounted for by the uneven inductions with frequent struggling. The 15 per cent incidence of coughing and 9 per cent incidence of hiccough following induction must be considered in the light of the fact that patients may have been too lightly anaesthetized at the time. Laryngospasm occurred in one case and later during the operation in the same case there was a decided suspicion of bronchospasm. On the whole, the incidence of untoward complications of respiration were unduly high with S.C.T.Z.

**Interaction with other drugs.**

S.C.T.Z. appeared to be less synergistic with the volatile narcotic and analgesics than thiopentone. This also applied to the muscle relaxants. No cases of prolonged apnoea or difficult reversal occurred in this series. The ability of d-tubocurarine chloride to “smooth out difficulties” in an abdominal case seemed to be distinctly less after S.C.T.Z.

**OVERALL SURVEY**

Some aspects of the quality of anaesthesia produced by S.C.T.Z. in the 33 cases in this study are shown in table V. There is no doubt that, with the dose and techniques used in this trial, the drug is definitely inferior to thiopentone.

Attention is drawn to the large volume of the 2 per cent solution used. These varied from 15
to 210 ml. At one time during the trial it was felt that the dilute solution (in relation to the potency of the drug) as compared with thiopentone might have been at least part of the cause of the trouble. To test this hypothesis eight unselected consecutive patients were anaesthetized by the author using a 1 per cent solution of thiopentone. Apart from the expected nuisance of having to handle several 20-ml syringes, no difficulties attributable to the drug occurred in any of these cases. It thus seems unlikely that the form of presentation is the cause of the uneven anaesthesia with S.C.T.Z.

DISCUSSION

An Annotation (1957) refers to S.C.T.Z. as “producing sleep without any degree of analgesia or anaesthesia”. This description is fully borne out by the experiences described above. It was unbelievably difficult to produce any resemblance to surgical anaesthesia in some of these patients who were undoubtedly “asleep”. This work shows that the terms “sleep” and “anaesthesia” are by no means synonymous, and excellent results reported with nitrous oxide-oxygen show that its action must be more widespread than the simple production of unconsciousness. The importance of some degree of analgesia may be inferred from this study. An alternative explanation of the unsatisfactory results achieved with S.C.T.Z. has already been suggested, namely some stimulant or convulsive action of the drug.

Whatever be the ultimate explanation, it is obvious that S.C.T.Z. has no place in present-day anaesthesia. It fulfils none of the criteria for a satisfactory intravenous agent (Dundee, 1956).

One is always interested in a new type of narcotic, and it is only by examining new drugs that one can expect to advance in the field of intravenous anaesthesia. The concept that narcosis can be produced by part of a vitamin molecule is a new one, and is surprising in light of findings which show the analgetic action of the vitamin B complex (Gould, 1953). Evidence is increasing to show that changing a single atom can completely reverse the action of a complex molecule. An example, well known to anaesthetists, is the conversion of some barbiturates to thiobarbiturates, changing a narcotic drug to a convulsant. It is hoped that further study will be carried out on the thiazole fraction of vitamin B₃, as a simple structural change may produce a more satisfactory anaesthetic agent.

SUMMARY AND CONCLUSIONS

Experimental work has shown that the thiazole fraction of thiamine chlorohydrate is a cerebral depressant as compared with the pyrimidine fraction. S.C.T.Z., a derivative of this thiazole fraction, has been used as an intravenous anaesthetic in 40 cases.

Results show that S.C.T.Z. is not a satisfactory agent for induction or maintenance of anaesthesia. It appears to be completely devoid of analgesic action and, despite its ability to produce sleep, it may have some stimulant action.

The experience obtained on this study has impressed the author with the importance of analgesia in the state of surgical anaesthesia.

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