CURARINE CHLORIDE AS AN ADJUNCT TO GENERAL ANÆSTHESIA

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Crude curare first became known to science when it was mentioned by Hakluyt in 1594, but it was not until 1935 that Mr. Harold King, D.Sc., F.R.S., of the National Institute for Medical Research, described the isolation of d-tubocurarine chloride. Messrs. Burroughs Wellcome and Co., working to King's specification, produced the first commercial supply of pure crystalline d-tubocurarine chloride and marketed it under the name of curarine chloride. It was a dry crystalline powder in a wax-sealed glass phial. The same firm now supply it in a sterile liquid form containing 10 mgm. of curarine chloride per ml. and register it under the name "Tubarine."

Prior to the introduction of Tubarine, this crystalline powder had to be sterilized and dissolved in a solvent before use. It was felt that although the powder could be autoclaved, provided all moisture was excluded, and then dissolved in sterile saline or distilled water the risk of future contamination of whatever remained of the solution was not negligible and therefore a self-sterilizing solvent would be more advantageous.

Glycero-Alcohol¹ (Glycerin 333, Aq. Dist. 146, 95 per cent Alcohol, 580 parts by volume) was chosen because it had been used as a solvent for various drugs for a number of years at the Bristol Royal Infirmary and no adverse phenomena had been noted.

The solution was made up to contain 10 mgm. of curarine chloride per ml. One particular sample was subjected to all the variations of temperature which could be expected under normal working conditions, and when assayed after being in
solution for 29 weeks it was found to have "Practically no loss in potency." Culture of several samples were all sterile.

All patients in this series were premedicated with Omnopon gr. 1/3 and Scopolamine 1/150, reduction being made for the aged and frail patients. The anaesthetic agents were used as follows: Pentothal and Cyclopropane; Pentothal and Nitrous Oxide; Cyclopropane; Nitrous Oxide, Oxygen and Ether or Trilene; and Ethyl Chloride and Ether from an Oxford Vaporizer.

For all abdominal cases 10–15 mgm. of curarine chloride were given intravenously about two or three minutes before the peritoneum was opened, and if the abdominal relaxation was not perfect further 5–10 mgm. were added until the necessary abdominal relaxation was obtained. Additional doses of curarine chloride of 10–15 mgm. were added during the operation whenever further relaxation was required, and a final dose, if necessary, of 5–15 mgm. was given for the closing of the peritoneum.

Ideal conditions for intubation were produced by slowly injecting intravenously a mixture of 15 mgm. of curarine chloride and 0.5 gr. of Pentothal. With Intocostrin (brand of curarine chloride supplied by E. R. Squibbs and Son of New York), Tubarine or curarine chloride dissolved in sterile Aq. Dist. or saline, a precipitate forms on adding it to Pentothal; this precipitate will redissolve on shaking the mixture, although sometimes not very readily. With Glyco-Alcohol as the solvent for the curarine chloride no precipitate was noted on mixing.

Anaesthesia was maintained in Plane 1 or upper Plane 2 (Guedel) throughout the operation. During the series of cases induced with Pentothal and maintained with Nitrous Oxide and Oxygen an effort was made to ascertain the duration of action of curarine chloride. These agents were selected in preference to more powerful ones which with a slight deepening of the plane of anaesthesia cause increased muscular relaxation. With Nitrous Oxide and Oxygen at a constant percentage the plane of anaesthesia would, if anything, tend to lighten, provided, of course, that the patient’s condition was not deteriorating. The
house surgeon would at regular intervals feel the tone of the rectus abdominis muscle and note was made of the time when tone returned. Average duration of activity of 1 mgm. of curarine chloride was found to be 1.2 minutes or conversely in one minute the body destroys or excretes 0.83 mgm. of curarine chloride.

It has been stated that the dose of curarine chloride should be reduced by 1/3 when Ether is the anaesthetic and this was confirmed.

The power of muscle fibres to contract on direct stimulation even when curarized is well demonstrated in myomectomies. The uterine muscle will be seen to contract markedly when the myoma is being “shelled out,” and due to this contraction bleeding from the cut surface of the uterine muscle has been noted to be very much less than in anaesthesias where no curarine chloride was used.

No complications were noted in this series which could be attributed to the curarine chloride. There was some increased oozing from the cut surface of the skin, but this was probably due to the fact that the blood-pressure remained constant throughout the operation, whereas it is more customary to expect some fall in blood-pressure during the long intra-abdominal operations with the deep plane of anaesthesia required. A slight increase of 5–10 mm. Hg. in the systolic pressure was noted in a few cases after the curarine chloride had been given and was attributed to the decreased tidal volume and hence an increased carbon dioxide level in the blood. This blood-pressure increase soon returned to normal after a manual compression of the breathing bag for a few minutes.

The general condition of the patients was superior to that normally seen after long anaesthesias, and post-operative nursing care was greatly reduced due to the rapid regaining of consciousness and co-operation, this in itself tending to decrease the chances of post-operative complications.

Vomiting was decreased in both incidence and severity.

The order of paralysis of muscles when increasing doses of curarine chloride are given is as follows: muscles innervated by
Curarine Chloride

Cranial nerves, muscles of the limbs, abdominal muscles and muscles of the thoracic cage and lastly the diaphragm. The dosage should, therefore, be carefully judged to paralyse only those muscles which if not relaxed would impair the operative field.

OPERATIONS

Upper abdominals:

<table>
<thead>
<tr>
<th>Type</th>
<th>Elective</th>
<th>Emergency</th>
<th>Procedure</th>
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<tbody>
<tr>
<td>Elective</td>
<td>32</td>
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<td>Partial gastrectomy</td>
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<tr>
<td>Emergency</td>
<td>19</td>
<td></td>
<td>Laparotomy</td>
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<td></td>
<td></td>
<td></td>
<td>Gastro-enterostomy</td>
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<td></td>
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<td>Upper ventral hernia</td>
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<td></td>
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<td>Nephro-lithotomy</td>
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<td>Perforations: gastric,</td>
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<td></td>
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<td>duodenal or jejunal</td>
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<td></td>
<td></td>
<td>Acute obstructions</td>
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Lower abdominals:

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<td>Hysterectomy</td>
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<td>9</td>
<td>Myomectomy</td>
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<td>9</td>
<td>6</td>
<td>Acute obstructions</td>
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<tr>
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<td>6</td>
<td>3</td>
<td>Ruptured ectopic</td>
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<td></td>
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<td>Hemi-colectomy</td>
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</table>

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Miscellaneous:

D and C, Haemorrhoidectomy 6
Intubation: Tonsillectomy, etc. 6
*Prior to abdominals where further curarine chloride was used 28

* These have not been included in the total as they already appear in the list of abdominals.
Types of Anaesthesia:

- Cyclopropane 42
- Pentothal and Cyclopropane 20
- Pentothal, Nitrous Oxide and Oxygen 49
- Nitrous Oxide, Oxygen and Ether or Trilene 4
- Ethyl Chloride and Ether (Oxford Vaporizer) 11

Respiratory complications:

<table>
<thead>
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<th>Type</th>
<th>Count</th>
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</thead>
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<td>Major</td>
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</tr>
<tr>
<td>Minor</td>
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Age limits in years: 13 to 78
Average: 43

Maximum duration of any anaesthetic: 3½ hours.
Maximum amount of curarine chloride given throughout any operation: 50 mgm.
Average amount of curarine chloride used per operation: 24.5 mgm.

Summary

A new solvent for curarine chloride is described for which the following properties are claimed:

1. Stability of curarine chloride in the solution.
2. Self-sterilizing.
3. No irritant action on veins.
4. No precipitate appears on mixing with Pentothal.

Perfect abdominal relaxation was obtained in this series of 114 unselected cases, and in the 12 extra-abdominal cases ideal conditions were created for the selected operation.

The use of ether in combination with curarine chloride is to be deprecated, as ether has already a curarizing action and an equally good operative field can be created with drugs less toxic than ether. If curarine chloride is used the dosage must be reduced by one-third.
Curarine Chloride

The power of muscle fibres to contract, even when paralysed by curare, on direct stimulation is well demonstrated in shelling out myomata and has a practical value in decreasing blood loss.

Prostigmine in doses of 1–1½ mgm. intravenously was found to counteract the action of curarine chloride.

Due to the minimal disturbance of the cardio-vascular system the poor risk patient seems to have a better chance of survival.

The paralysing effect of curarine chloride on muscles, and hence its effect on the muscles of respiration, makes it a drug which should not be employed light-heartedly by those not well versed in its use.

References