conditions for the surgeon and be non-depressing to the baby and the uterine tone. The safest technique to date has probably been local analgesia, but there are few who would care to maintain that this is a pleasant experience. Some of these patients who had undergone previous sections have been most grateful for the intravenous induction and the subsequent freedom from unpleasant sequelae.

d-Tubocurarine has passed its experimental stage, and its early promise has been confirmed by further extensive experience. It is debatable whether any potent drug which is delivered into the blood stream can be called safe, but this one seems to be less dangerous than many others in daily use. On the other hand, among these patients were five who were seriously ill: two had eclampsia, having had several fits, two had had extensive haemorrhage from placenta praevia, and one had advanced pulmonary tuberculosis. They all had an uneventful convalescence and with the exception of the last mentioned were fit for discharge within three weeks.

Vomiting during the induction of anaesthesia with consequent aspiration pneumonia is acknowledged to be one of the hazards of this procedure. These patients have not had the usual sedative preparation. They are often admitted as emergencies "off the district," and are not infrequently stout and short-necked. All these factors tend to make the induction period a rather anxious time. The ill-advised insertion of an airway immediately after the initial injection did precipitate vomiting in one instance. A cuffed endotracheal tube was inserted, and the fact that suction was ready and to hand prevented any untoward result. Whatever the anaesthetic, these patients are very likely to vomit if they have had a recent meal. A rapid intravenous induction makes the emergency less likely, and the administration of *d*-tubocurarine undoubtedly facilitates the intubation which may be required as either a prophylactic or a therapeutic measure.

The freedom from curarization of the baby has not been surprising. Whitacre and Fisher (1945) have reported that "intocostarin" (Squibbs's biologically standardized extract of curare) has no effect on the infant—an observation which has been confirmed in the present series. Substitution of "kemithal" for thiopentone as an inducing agent and the small amount of anaesthetic which is required after *d*-tubocurarine are factors which have contributed to the wide-awake condition of these babies.

The good uterine tone that has been so marked a feature was not expected. This has been so striking that on two occasions it caused a temporary embarrassment to the surgeon, who found that his hand was being gripped by the contracting uterus as he extracted the child. This has so far not proved a serious handicap, and the otherwise good operating conditions have been ample compensation.

Finally, this technique, by avoiding long post-operative depression, which is especially menacing after this operation, undoubtedly contributes to a peaceful and trouble-free convalescence.

Summary

A technique for anaesthetizing patients undergoing caesarean operations using *d*-tubocurarine, "kemithal" and cyclopropane is reported. It has been used in 30 cases and the results are reviewed.

My grateful thanks are due to Mr. Percy Malpas and the other members of the obstetrical team at Whiston County Hospital for their help and confident co-operation.

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USE OF *d*-TUBOCURARINE CHLORIDE AND THIOPENTONE IN ELECTRO- CONVULSION THERAPY

BY

J. A. HOBSON, M.D., D.P.M., B.Sc.

Deputy Physician-in-Charge, Woodside Hospital; Honorary
Chief Assistant in the Department of Psychological Medicine,
St. Mary's Hospital, London

AND

FREDERICK PRESCOTT, M.Sc., Ph.D., M.R.C.P.

Clinical Research Director, Wellcome Research Institution,
London

Convulsion therapy for the treatment of psychiatric disorders was introduced in 1934 by Meduna, who injected convulsant drugs intravenously. The treatment, however, was so unpleasant that patients were unwilling to continue with it; the considerable rise in blood pressure that occurred rendered it unsuitable for cardiac and arteriosclerotic patients, and fractures and dislocations were very common. The introduction of electrical convulsion therapy (E.C.T.) (Cerletti and Bini, 1938) diminished the frequency of traumatic complications; but this form of therapy was still unpleasant for the patient, and the rise in blood pressure resulted in cardiovascular accidents which were sometimes fatal. Twenty deaths attributed to E.C.T. have been reported, and 16 of these were either definitely or probably due to cardiac failure (Feldman *et al.*, 1946). By the use of E.C.T. with hyperextension of the spine and mechanical restraint the incidence of compression fractures of the spine has been reduced to about 4% (Cook, 1944), although occasional fractures cannot be prevented. The use of spinal anaesthesia, which has recently been introduced to soften convulsions (Shorvon and Shorvon, 1943), is very limited, as it does not prevent fractures of the arms or jaw, it cannot be used in patients with high or low blood pressure, and it carries with it all the hazards of spinal puncture. Although Bennett (1940) was the first to report on the use of curare for softening convulsions in shock therapy, *d*-tubocurarine chloride, an alkaloid obtained from crude curare, was used at Woodside Hospital for a considerable time before the publication of this paper. Unfortunately the work was interrupted by the war and was not followed up (Palmer, 1939, 1946). Since 1940 many American workers have confirmed Bennett's observations without, however, modifying his technique.

Curare-like drugs minimize convulsions by paralysing voluntary muscle. They do this by blocking the nerve impulse at the myoneural junction, probably by preventing the effector substance in the muscle from reacting to acetylcholine. In the doses in which it is used clinically *d*-tubocurarine chloride acts almost exclusively on voluntary muscle and produces few side effects if oxygenation is adequate. A slight fall in blood pressure may occur immediately after its intravenous injection, followed by a slight rise. It has no significant effect on the human electrocardiogram (Gray and Halton, 1946; Prescott *et al.*, 1946). A slight overdose can, however, seriously depress respiration by paralysing the diaphragm, and both bronchospasm and laryngeal spasm have occurred following its use without an anaesthetic (B. G. B. Lucas, personal communication).

Preliminary Investigations

American workers report that combined curare and convulsion therapy is dreaded less by the patient than

convulsion therapy alone, but our experience is directly contrary to this. In our early experiments all patients complained bitterly of the terrifying feeling of suffocation and extreme weakness after an injection of *d*-tubocurarine chloride, and some refused further treatment. We first attempted to relieve the unpleasant symptoms by producing unconsciousness with a preliminary subconvulsive electric shock immediately after the injection of the *d*-tubocurarine chloride. It was found impossible, however, to gauge the dose to such a nicety that unconsciousness with a several-minute amnesia could be produced without the risk of muscular contractions of sufficient strength to cause trauma. It also seemed probable that a preliminary subconvulsive shock raised the electrical convulsion threshold, and it has been reported that subconvulsive shocks cause a serious fall in blood pressure (Silfverskiöld and Amark, 1943) and even cardiac arrest (Kalinowsky and Hoch, 1946). The use of subconvulsive shocks was therefore abandoned.

Preliminary anaesthetization with thiopentone ("pentothal") was found to be a much more satisfactory method of producing amnesia. No patient to whom we have administered thiopentone has remembered anything of either the curarization or the convulsion. Thiopentone has the additional advantages of aiding *d*-tubocurarine in combating the post-convulsive rise in blood pressure, in lessening post-convulsive excitement, and in minimizing the likelihood of bronchospasm which may occasionally follow the injection of curare-like drugs. Contrary to the observations of other workers who have used general anaesthesia with E.C.T. (Neustatter and Freeman, 1939; Fabing, 1942) we have not observed any tendency for thiopentone to increase the electrical convulsion threshold. If anything, the threshold appeared to be lowered, possibly because the thiopentone reduced the patient's excitement and apprehension, which is known to increase the electrical threshold (Kalinowsky and Hoch, 1946). In no case have we failed to induce a convulsion following administration of thiopentone.

Serious respiratory depression resulting from diaphragmatic paralysis is the chief danger of curare-controlled E.C.T., and unless facilities for controlled respiration are at hand a fatality can occur. There are four deaths reported in the literature from curare-controlled convulsion therapy, two of them most probably from respiratory paralysis (Charlton *et al.*, 1942; Cash and Hoekstra, 1943; Smith *et al.*, 1943; Bennett, 1943). Most of our patients were insufflated with oxygen under slight pressure, by means of an apparatus devised by Dr. Lucas, during the period between the administration of the *d*-tubocurarine chloride and the shock, and again following the convulsion if there was the slightest sign of cyanosis or respiratory depression. Unless a large overdose of drug is given the diaphragm recovers its function fairly quickly. In the present series of cases it did not become necessary to administer respiratory stimulants or "prostigmin," the pharmacological antagonist of *d*-tubocurarine chloride, ventilation with oxygen being quite adequate to combat any respiratory depression. To counteract the salivation produced by *d*-tubocurarine chloride all patients were given atropine sulphate intravenously in a dose of 1/100 to 1/50 gr. (0.65 to 1.3 mg.) at the same time as the latter.

Technique

The treatment was usually given in the morning. Patients had their ordinary sedative the previous night. They were allowed a cup of tea at breakfast-time, but no food in case of vomiting. Blood pressure, pulse rate, and temperature were taken before treatment. No methods of mechanical

restraint or attempts to hyperextend the spine were used. *d*-Tubocurarine chloride and atropine mixed in the same syringe were given intravenously, the syringe disconnected, and without removing the needle from the vein an injection of thiopentone administered immediately afterwards from another syringe. The dose of *d*-tubocurarine chloride required to give adequate relaxation was approximately 2 mg. per stone (0.3 mg. per kg.) of body weight, but this dose has to be varied according to the musculature, age, sex, and general condition of the patient. If the initial injection of *d*-tubocurarine chloride failed to soften the convulsion sufficiently it was increased in subsequent treatments. The lowest effective dose in the present series was 14 mg., and some very muscular male patients were given as much as 30 mg. without achieving full curarization. Generally speaking, males require more than females and the young more than the aged. The usual dose of thiopentone was 0.3 g., but this was increased if any tendency to bronchospasm or laryngospasm was noted at the first treatment. This complication was dealt with by anaesthetizing the patient more deeply with a second injection of intravenous thiopentone or with nitrous oxide and oxygen. After the injection of the *d*-tubocurarine chloride an interval of three to five minutes was allowed for curarization to reach its maximum before administering the electrical convulsion. A mouth gag was used only to prevent the possible biting of the lips immediately after the shock. The patient's limbs were not restrained.

Pulse rate and blood-pressure measurements were taken immediately before and after the convulsion, and at intervals of 15 and 30 minutes later. Temperature readings were taken at half-hourly intervals for two hours after the treatment. Many of the patients were insufflated with oxygen following the convulsion, and occasionally, if there was respiratory obstruction, an airway was inserted. Usually the patients passed into a quiet natural sleep after recovering from the convulsion. Out-patients were allowed to sleep for two hours before going home.

The treatment was usually given to patients twice weekly, and some who did not respond received short daily courses. One or two patients were given two convulsions in quick succession following a single injection of *d*-tubocurarine chloride and thiopentone. The average number of convulsions given was six, but several patients recovered from symptoms after only two or three. The greatest number of convulsions given to one patient was 20.

Clinical Material

d-Tubocurarine chloride and thiopentone were administered to 50 patients undergoing electrical shock therapy for psychiatric illness; approximately half were in-patients and half out-patients. In all 300 treatments were given. The large majority of the patients were suffering from depression, but a few schizophrenics and obsessional states were included. A careful clinical examination was made before the patient was subjected to convulsion therapy, and if any doubt existed as to the condition of the cardiovascular, respiratory, or skeletal systems, electrocardiographic or radiological investigations were first carried out. An attempt was made to collect as many patients as possible in whom unmodified E.C.T. would have been dangerous if not absolutely contraindicated. Included in the series were hypertensive, arteriosclerotic, and senile patients; patients who had previously sustained fractures in unmodified E.C.T. (one vertebral fracture, and one recently wired fracture of the condyloid process of the mandible); a patient who had previously had haematemesis from a peptic ulcer following unmodified E.C.T.; a patient with hernia; and a woman five months pregnant.

Observations

Within three to five minutes of giving the *d*-tubocurarine chloride and thiopentone the patient was relaxed and unconscious, respiration slightly depressed, and breathing mainly abdominal. Immediately after administering the shock the patient gave a slight jerk corresponding to the tonic convulsion, and after a latent period of a few seconds there was a very modified clonic convulsion (see Figs. 1 and 2). The arms, if they moved at all, were flexed slightly,

FIG. 1.—Patient undergoing unmodified convulsion therapy showing the stage of clonic convulsion and necessitating lumbar pads and physical restraint by three attendants.

FIG. 2.—Same patient undergoing electrical convulsion therapy after treatment with *d*-tubocurarine chloride and thiopentone. One attendant only is managing the patient, and in this case no mouth gag was used.

and the fingers were drawn up in the "accoucheur" position seen in tetany. Usually there was no gross movement of the legs. The cry and opisthotonos of the unmodified convulsion were absent. Although the muscles of the face are those most rapidly paralysed by curare drugs, these muscles contract most strongly in the curare-controlled convulsion. The muscles of the eyelids and face twitch repeatedly even when there is no movement of the limbs or trunk, so it is always possible to observe that a "convulsion" is taking place.

Sweating, which normally occurs during and after unmodified E.C.T., was usually absent. Slight depression of respiration with a short period of apnoea occurred in most patients, but apnoea lasting three minutes is also very common in unmodified E.C.T. (Woolley *et al.*, 1942). Slight cyanosis was observed in about a quarter of the treatments given, but this was not so frequent, so deep, or so prolonged as that commonly seen in unmodified E.C.T. Bronchospasm with deep cyanosis, which occurred in three very restless patients, was relieved by a second injection of thiopentone.

There is normally a considerable rise in blood pressure during and just after an induced unmodified convulsion. It may rise well above 200 mm. Hg (Silfverskiöld and Amark, 1943). There is normally an increase of 50 to 60 mm. in systolic pressure (Kalinowsky and Hoch, 1946; Jones and Pleasants, 1943). In this series with curare-controlled

convulsions the mean increase in systolic blood pressure was 6 mm. Hg (standard error ± 1.7 mm.). The diastolic pressure was much the same after the shock as before. It is possible that the rise of blood pressure in uncontrolled convulsions is partly due to the blood being squeezed from the muscles during their violent contractions and shunted into the general circulation, thus increasing the cardiac output and blood pressure. Stimulation of the medullary centres also undoubtedly occurs. It is conceivable that in convulsions modified by *d*-tubocurarine chloride the blood pressure does not rise appreciably because blood is retained in the vessels of the relaxed muscles.

There was often a fall in pulse rate immediately after the convulsion, followed later by a rise. Sometimes there was a fall in body temperature one-half to one hour after the convulsion. The maximum fall of temperature was 2° F. (1.1° C.), and the lowest temperature recorded was 96° F. (35.6° C.). This occasional fall was presumably due to the *d*-tubocurarine chloride, as there is usually a slight rise in temperature in the unmodified convulsion. A fall in temperature has also been noted in patients receiving *d*-tubocurarine chloride as an adjunct to anaesthesia (F. Evans, personal communication). It was observed that the effects of curarization passed off about twice as rapidly in a patient submitted to a curare-modified convulsion as in a subject receiving the same dose of drug without a convulsion. The most likely explanation is that electrical stimulation liberates increased amounts of acetylcholine at the neuromuscular junction and that this neutralizes the effect of the *d*-tubocurarine chloride.

Post-convulsive excitement, which is common after unmodified E.C.T., was rare in the present series, and when it did occur was checked by a second intravenous injection of thiopentone. Many of the patients on regaining consciousness expressed a wish to sit up. Sitting up usually relieves the feeling of suffocation which sometimes persists for twenty minutes or more after the injection of *d*-tubocurarine.

There were no complications such as fractures, dislocations, or muscle strains following any of the treatments, and the only unpleasant symptoms between treatments were headache and impairment of memory and concentration, which evidently resulted from the electrical convulsion. *d*-Tubocurarine chloride does not appear to influence the therapeutic effect of E.C.T. or to raise the electrical convulsion threshold. The percentage of patients recovered or markedly improved in the present series is roughly what might have been expected if unmodified E.C.T. had been given, but the number of patients is too small and their diagnoses too varied for any statistically significant conclusion to be drawn.

Discussion

The major drawbacks of E.C.T.—namely, fractures, dislocations, and cardiovascular accidents—are largely eliminated by the method described, and post-convulsive excitement is reduced. Preliminary curarization enables E.C.T. to be given to patients to whom unmodified E.C.T. would be dangerous. Mechanical precautions to prevent fractures and dislocations are rendered unnecessary. As no methods of restraint are needed one operator can carry out the treatment single-handed. If the patient should become restless on recovery he can be handled easily as, being lightly curarized, he is able to offer only feeble physical resistance.

The dose of both *d*-tubocurarine chloride and thiopentone needs careful assessment. Just enough barbiturate is required to produce about five minutes' narcosis, and sufficient *d*-tubocurarine to make fracture or dislocation impossible but not to depress respiration too deeply. No

patient should be given a curarizing drug unless efficient facilities for controlled respiration with oxygen are at hand and the administrator is competent to deal with the apnoeic patient. The injection of stimulants and analeptics cannot replace the provision of a clear airway and rhythmic insufflation of oxygen using a tightly fitting face-mask. Without the precautions described the treatment advocated might be disastrous, but we feel that with adequate precautions curare-controlled E.C.T. is so much safer than unmodified E.C.T. that we intend to adopt it as a routine procedure. We believe that if patients are curarized with due care the benefits of E.C.T. can be extended to those in whom it would be normally contraindicated. The therapeutic results of convulsion therapy do not depend on the production of a "convulsion," as originally suggested by Meduna (1935), because the end-results are just as good whether the curare-modified or the unmodified convulsion technique is used (Bennett, 1941).

Summary

The use of *d*-tubocurarine chloride and thiopentone for modifying electrical convulsions is described. In the dosage employed these drugs do not significantly affect the electrical convulsion threshold.

The advantages claimed for the method are: the traumatic complications of E.C.T. are avoided; there is no serious rise in blood pressure; it enables E.C.T. to be given to certain patients in whom otherwise convulsions would be contraindicated; post-convulsive excitement is minimized; the procedure can be carried out single-handed if desired; and the unpleasantness of E.C.T. for the patient is almost entirely eliminated.

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A registry of primary malignant tumours of bones has been set up with its headquarters at the Department of Pathology, the Royal College of Surgeons of England, with the intention of collecting records of cases of primary tumour or presumed primary tumour of bone (including joints and cartilages), especially those in which cure or prolonged alleviation has been attained by treatment. All cases claimed as five-year cures will be considered by the committee, but in future only those cases will be considered in which histological proof of the nature of the tumour can be obtained by biopsy or following amputation. In cases where histological diagnosis is in doubt the Consultant Panel in Morbid Histology, set up by the Pathological Society of Great Britain and Ireland in conjunction with the British Empire Cancer Campaign and the National Radium Commission, will be consulted. Those interested are invited to send records of relevant cases with amputation or biopsy specimens to Prof. R. A. Willis, M.D., F.R.C.P., Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2. Donors will be sent reports on the pathological investigation of specimens received, and in return will be asked for follow-up information regarding patients.

USE OF CURARE IN "POOR-RISK" PATIENTS

BY

GORDON OSTLER, M.B., B.Chir.

Senior Resident Anaesthetist, Hill End Hospital
(St. Bartholomew's)

This paper is based on 136 surgical cases in which curarization was performed at Hill End Hospital (St. Bartholomew's), and includes the observations of all the members of the anaesthetics department. All of these patients underwent operations of some severity, while most of them were in the "poor-risk" category. An analysis of the operations undertaken in this series is given in Table I.

TABLE I.—Operations Recorded

Partial gastrectomy	31	Hysterectomy	25
Cholecystectomy	7	Thoracoplasty	14
Resection of large gut	6	Lobectomy	8
For relief of intestinal obstruction ..	4	Pneumectomy	3
Other laparotomies	11	Ligation of patent ductus ..	2
Lumbar ganglionectomy	3	Pericardectomy	1
Urogenital operations	3	Other thoracotomies	14
Incisional hernia	2	Oesophagotomy	1
Resuture of burst abdomen	1		
		Total	136

Preparations and Dosage

I have used the general name "curare" to embrace all preparations not specifically designated. "Intocostarin" (Squibb), *d*-tubocurarine chloride crystals, "curarine" and "tubarine" ampoules (Burroughs Wellcome) have all been employed. The curarine chloride crystals were made up by us in a 1% solution in sterile distilled water or para-chlorcresol which was brought to the boil before bottling. It is impossible adequately to sterilize the crystalline powder in the autoclave. The potency of these preparations remained fairly constant as long as required, in some cases up to six months. An initial dose of 3 ml. of intocostarin or 15 mg. of curarine or tubarine was used for abdominal cases, with half the dose usually repeated later for closure of the peritoneum. All injections were made intravenously. The exact calculation of the dose by body weight has the theoretical objection that the number of the patient's myoneural junctions and his weight may not stand in direct relation. The dose was only slightly reduced for children, though very ill and feeble persons, with their slowed metabolism, need less curare and exhibit a prolonged effect. Individual reaction to the drug appears to be very variable, but there are too many factors modifying the patient's response to allow of accurate judgment.

All these preparations seemed generally to be reliable, although once intocostarin and once some curarine chloride made up by us failed to produce the effect expected. Neither of these failures can be attributed to the drugs, as subsequent injections from the same bottles produced the usual results. In the latter case the respiration remained adequate, and a considerable amount of ether was given before a lumbar sympathectomy could proceed with tranquillity.

Indications

Limitation of supplies demanded careful selection of cases, curare being used almost exclusively for abdominal and chest operations, particularly with "poor-risk" patients. There would seem to be little point in using curare for procedures where considerable muscular relaxation or very quiet respiration is not called for, as such operations can often be carried out under the narcosis induced as a preliminary to curarization.