unmodified. Several complained of transient memory loss and impairment of concentration, and one became hypomanic; but these are complications of E.C.T., whether modified or not.

The nursing staff's opinion is quite clearly in favour of gallamine triethiodide and least favourable to D-tubocurarine chloride.

Discussion and Conclusions

E.C.T. is a highly successful form of treatment for many depressive illnesses. In its unmodified form it has certain risks, and, moreover, it cannot be administered to many patients who require it, because they happen to be suffering from physical disorders. A minority of patients also find it exceedingly unpleasant. The use of D-tubocurarine chloride, coupled with thiopentone, overcomes these drawbacks to a very considerable extent, but modification with this drug entails several risks, which many experienced people feel should restrict its use to those suffering from serious physical disorders. The introduction of C10 as a muscle relaxant has proved in some hands to be an agent so free from hazards that in some clinics it is thought that the faint risks of not using it in an uncomplicated case now outweigh the slight risk of using it in every case.

As a result of considerable experience with gallamine triethiodide in the past few months we are of the opinion that this relaxant has certain distinct advantages over C10, and that the time has now arrived for using it in combination with thiopentone and atropine in every case, unless there is some contraindication. Now that gallamine triethiodide is available, we hold the view that the use of D-tubocurarine chloride for modifying the convulsion of E.C.T. should be abandoned. None of these drugs should on any account be employed unless a means of ventilating the patient through an adequate airway with oxygen is at hand.

So far few adverse accounts of gallamine triethiodide have been reported, and no trouble whatever has been encountered in using it in our series of patients. It should not be employed in myasthenia, it should be used with caution in cases of impaired renal function, and it is probably wiser on theoretical grounds to use C10 in asthmatics.

The conclusions of this comparison are roughly expressed in summary form in Table II.

TABLE II.—Comparison of the Virtues of Three Relaxants in Modifying E.C.T.

Advantage	D-Tubocurarine (112 Treatments)	C10 (155 Treatments)	Gallamine Triethiodide (168 Treatments)
Miscible with thiopentone	0	+	+
Rapidity of effect	0	0	+
Relative absence of respiratory depression	0	+	+
Rapidity of recovery	0	+	or ++
Absence of side-effects	0	+	++
Antidote satisfactory	+	0	++
Cheapness	0	+	+

We wish to thank Dr. Henry Wilson for his interest, and Dr. D. V. Martin and Dr. W. J. B. Rogers, who administered half the treatments with which this paper is concerned.

ADDENDUM.—Since this paper was completed we have carried out 256 treatments on 39 patients, using gallamine triethiodide, thiopentone, and atropine. This further experience has not led us to alter our views.

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GALLAMINE TRIETHIODIDE AS AN ADJUNCT TO ELECTROPLEXY

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It is now accepted that curarization of a patient undergoing electroplexy for the treatment of mental disorder is a useful adjunct in avoiding traumatic complications, as it reduces the muscular force of electrically induced convulsions (Hobson and Prescott, 1949; Shepherd and Watt, 1949; Davis and Lewis, 1949). It has been established that tri-(diethylaminoethoxy)-benzene triethyliodide (gallamine triethiodide—"flaxedil") exerts a true muscle relaxant action, inhibiting the transmission of nervous impulses by acetylcholine and blocking transmission across the myoneural junction of voluntary muscle (Bovet *et al.*, 1947; Huguenard, 1948; Mushin *et al.*, 1949). The relaxant action is easily reversed by neostigmine or physostigmine (Wien, 1948). Wilson and Gordon (1949), while using gallamine triethiodide as a curarizing agent in anaesthesia for a series of 80 patients (20 adults and 60 children) undergoing surgical operations in the abdomen and in the chest, concluded that this drug produced adequate muscular relaxation and that it seemed to be devoid of undesirable side-actions. Other workers have had similar good results whilst using gallamine triethiodide in general anaesthesia (Ruddell, 1950; Doughty, 1950; Harrison, 1950).

It seemed to us that gallamine triethiodide might be of use in patients who required electroplexy with modification because of certain physical abnormalities. Twelve patients (two men, ten women) were selected who were thought to be suitable for convulsant

therapy and for whom there were physical contraindications to its use. Three patients were suffering from severe rheumatoid arthritis, one had recent tendon sutures across the wrists following a suicidal attempt, and the remainder were suffering from hypertension and arteriosclerosis. Their ages ranged from 40 to 73 years.

Method

In the morning, with the patients fasting, 1/100 gr. (0.65 mg.) of atropine sulphate was given to each of them 45 minutes before starting treatment. In every individual the first injection of gallamine triethiodide was given alone. It was our intention at the outset to give ten patients gallamine triethiodide alone for all treatments prior to the E.C.T. and then later to give ten other patients gallamine triethiodide plus thiopentone sodium and endeavour to make comparisons. But they so disliked the sensation of a feeling of suffocation with gallamine triethiodide alone that we decided after the first few injections to give all subsequent injections in combination with thiopentone sodium. For the first injection, or in some cases the first few injections, gallamine triethiodide was given as follows: 50 mg. was injected quickly, and an additional amount to a total of 60 to 100 mg. was given slowly during the next few minutes. We observed the relaxant effect of the drug by asking the patient to grip the hand, flex the feet, lift the leg off the bed, and raise the head from the pillow. When we had judged that sufficient relaxation was obtained we ceased injecting and noted the amount given. Subsequently this dosage was then given quickly at the next treatment. The dosage required varies from case to case, and must be calculated individually. We observed that once a satisfactory dosage was found this same amount produced sufficient relaxation at each subsequent injection.

Observations were made of the following: (1) the power to flex the fingers, by asking the patient to grip the observer's hand; (2) the power to raise the legs from the bed against the resistance of the observer's hand; (3) the power to raise the head from the pillow—the observer placed his hand on the patient's forehead and pressed downwards; (4) the plantar reflex, tested to demonstrate reflex activity; (5) blood pressure; (6) pulse rate; and (7) respiration rate.

Results

In doses of 60–100 mg. intravenously, with the subject conscious, complete paralysis of the flexor muscles of the forearm and the flexor muscles of the foot and leg developed within three to five minutes. The facial, orbital, ocular, and laryngeal muscles were affected

early, in two to three minutes, as evidenced by flickering of the eyelids, development of ptosis, difficulty in articulation, and slurring of speech. One patient said that she had gone blind, but on retracting her eyelids she could see, though vision was double.

The neck muscles were affected early and the patients were unable to raise the head. The muscles of the jaw were relaxed and the chin needed support. The small muscles of the hand, tested by grip, remained fairly strong until just before the paralysis of the intercostal muscles, when they weakened.

Complete relaxation of the abdominal muscles occurred in about three minutes. When all the muscles were in a state of relaxation, stroking the sole of the foot did not elicit the plantar reflex.

In two patients the paralysis induced by gallamine triethiodide was very soon neutralized by the injection of 1 mg. of neostigmine in each case. Full muscular power was regained in 10–15 minutes in these two patients.

We noted that when gallamine triethiodide was having its maximum effect the respiration increased in rate, often more than doubling its initial resting rate. Respiration became very shallow. The patient became distressed owing to the dyspnoea, and a rise in blood pressure occurred. The patient also became slightly cyanosed, but the administration of oxygen during this period did not produce any change in the blood pressure, nor did it add materially to the patient's comfort. When gallamine triethiodide was given alone it was found that a rise of at least 10 mm. Hg in systolic and diastolic blood pressure occurred (see Table). Often the rise was noted to be as much as 40 to 50 mm. Hg. We found, however, that when 0.25 g. of thiopentone sodium in 5 ml. of sterile water was given before the gallamine triethiodide was administered no vasopressor or depressor effects were caused by the subsequent injection of the drug (see Table). This suggests that the rise in blood pressure noted after gallamine triethiodide alone was due to the apprehension and distress caused by the giving of the injection and later by the paralysing effect of the drug, which made breathing difficult.

In most of the cases the blood pressure immediately after the convulsion was found to be lower when thiopentone sodium and gallamine triethiodide had been administered than when the latter alone had been given. Within 10–20 minutes after the fit the blood pressure and pulse rate had returned to resting normal in three cases in which the drug was given alone and in three cases in which it was given with thiopentone sodium. In all cases, after each injection of gallamine

Blood-pressure Recordings Before and After Intravenous Injections of Gallamine Triethiodide Alone and in Combination with Thiopentone Sodium

	Case 1 (66 yr.)	Case 2 (53 yr.)	Case 3 (66 yr.)	Case 4 (51 yr.)	Case 5 (57 yr.)	Case 6 (49 yr.)	Case 7 (58 yr.)	Case 8 (71 yr.)	Case 9 (63 yr.)	Case 10 (48 yr.)
Gallamine triethiodide	70 mg.	80 mg.	70 mg.	70 mg.	80 mg.	80 mg.	100 mg.	70 mg.	75 mg.	60 mg.
B.P. before G.T.	140/80	145/90	200/100	130/80	220/110	150/90	190/110	190/110	160/100	170/90
B.P. 1 min. after G.T.	150/90	150/100	240/130	140/90	240/120	160/100	240/120	190/120	200/120	180/100
B.P. 1 min. after E.C.T.	180/100	190/105	230/110	150/100	260/140	180/110	180/100	200/150	215/120	200/110
B.P. 20 min. after E.C.T.	140/80	140/90	190/90	130/80	230/110	150/90	190/110	190/110	190/120	170/80
Thiopentone sodium	0.25 g.	0.25 g.	0.25 g.	0.25 g.	0.25 g.	0.25 g.	0.25 g.	0.25 g.	0.25 g.	0.25 g.
B.P. before T.S.	130/80	150/90	200/100	130/80	225/110	150/90	190/110	190/100	160/100	170/90
B.P. 1 min. after T.S.	140/90	160/100	170/90	140/80	145/80	110/80	120/80	110/95	130/90	150/80
Gallamine triethiodide	70 mg.	80 mg.	70 mg.	70 mg.	80 mg.	80 mg.	100 mg.	70 mg.	75 mg.	60 mg.
B.P. 1 min. after G.T.	130/80	140/90	170/90	130/80	140/80	110/75	120/80	110/95	130/90	150/80
B.P. 1 min. after E.C.T.	150/90	140/80	180/100	140/90	160/100	150/90	150/90	150/100	150/90	160/90
B.P. 20 min. after E.C.T.	148/80	140/90	190/100	130/80	200/100	110/90	150/90	190/110	180/110	170/90

triethiodide the paralysing effects of the drug had completely disappeared at the end of 20 minutes. No difference in the disappearance of paralysing effects was noted between those cases given the drug alone and those who received it in combination with thiopentone sodium.

Description of Fit

When we had judged that sufficient relaxation and paralysis had occurred—usually within three to four minutes—a shock was given.

A fit was judged to be good by the flickering of orbicular and labial musculature; the arms and legs could be freely moved during the time the patient was in the "tonic" stage of the convulsion. In a somewhat less satisfactory fit the flexion of arms and legs could be easily overcome. On a few occasions apnoea was a little prolonged and the patient became cyanosed; oxygen and slight manual assistance to breathing soon overcame this, and natural respiration quickly returned.

Toxic Effects

No bronchospasm occurred after over 90 injections of this drug. There was no marked sweating, and on only one occasion did we see pallor. Slight areas of erythema with weal formation were noticed around the site of injection on several occasions, and twice a fleeting erythema occurred over face and chest. It is of interest to note that one patient who had been receiving E.C.T. with D-tubocurarine before gallamine triethiodide was introduced presented an extensive rash on face and chest and a large urticarial weal with an area of erythema 4 in. (10 cm.) in diameter around the site of injection on each occasion, but on changing to gallamine triethiodide only a very small weal with an area of erythema $\frac{1}{2}$ in. (1.25 cm.) in diameter occurred at the site of injection, and there was no generalized rash. This difference in reaction may be explained by the greater tendency of the natural product to cause histamine release. The use of gallamine triethiodide had no adverse effects on kidney function or blood picture in those cases tested.

Conclusions and Summary

Gallamine triethiodide ("flaxedil") was given to two men and ten women suffering from various physical conditions (hypertension, severe rheumatoid arthritis) and about to undergo electric convulsion treatment.

Dosage was determined in each case by studying the loss of power of various muscle groups: the neck muscles failed first, the hand grip relaxed just before the onset of intercostal paralysis.

After the induced fits, which were in no way impaired, recovery was rapid and complete within 20–30 minutes of the full dose.

The drug produced no fall in blood pressure, and there seemed to be fewer side-effects than with D-tubocurarine. A mild cyanosis from temporary apnoea occurred in several cases.

In two patients paralysis from gallamine triethiodide was completely abolished in 10–15 minutes by the injection of 1 mg. neostigmine.

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STERNAL MARROW CULTURES IN TYPHOID FEVER

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The only absolute proof that a patient is suffering from typhoid fever is the isolation of the organism. The widespread use of prophylactic injections of typhoid vaccine has to some extent lessened the value of *Salm. typhi* H and O agglutination. For this reason any method which will increase the number of cases yielding positive cultures should be explored.

The use of sternal marrow puncture for the detection of the organism has been stressed by several workers (Gerbasi, 1939; Ling *et al.*, 1940; Piaggio Blanco *et al.*, 1942). Gerbasi claims credit for the first systematic study of typhoid infection in children by examination of the bone marrow. He later used the method successfully in adults. He states that sternal marrow cultures often remain positive throughout the course of the illness even when other tests are negative. The bacillus may or may not appear in the blood during the initial febrile period, but it is a constant finding in the bone marrow, disappearing during the advanced stage of the disease or during recovery. He believes that the organism becomes fixed in the bone marrow and appears in the blood only in recurrent and temporary "spurts."

During a recent outbreak of typhoid fever at Evaton, Transvaal, 40 Bantu patients were admitted to Baragwanath Hospital under our care. We had, therefore, an excellent opportunity of testing these observations.

Methods

In order that there should be no doubt about the diagnosis in these cases, no case has been included which did not conform to one or more of the following criteria: (1) a positive blood culture; (2) a positive sternal marrow culture; (3) a urine or stool specimen containing typhoid bacilli; (4) a post-mortem examination