occurs heterogenetically in guinea pig kidney and it could also be isolated from the Forrsman antigen although without increase in activity.

3. Horse serum is a poorer source for isolation of the so-called serum sickness antigen. The latter could be isolated from the serum, after removal of the albumin bodies by coagulation with heat, with an activity of 1:1,500.

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Dimethyl Ether of *d*-Tubocurarine Iodide as an Adjunct to Anesthesia.

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The capacity of curare to block efferent nervous impulses at the myoneural junction has long been known. Bennett[1] administered curare clinically to minimize the trauma to patients undergoing convulsive shock therapy. Subsequently, Griffith and Johnson,[2] and Cullen[3] reported the use of curare as an adjuvant for relaxing the abdominal muscles during inhalation anesthesia.

The dosage of *d*-tubocurarine chloride administered to patients during anesthesia rarely produces toxic cerebral or cardiovascular manifestations. The drug frequently produces moderate or severe respiratory depression. For this reason, other natural and synthetic compounds have been investigated. One of the more promising preparations is dimethyl ether of *d*-tubocurarine iodide.[4,5] This compound has a chemical formula $C_{40}H_{48}O_6N_2I_2 \cdot 3H_2O$. It will be referred to as M-curare. In animal experiments, Chen and Swanson[6] demonstrated that M-curare effectively decreases muscle tone without producing respiratory depression.

Experimental. We have administered M-curare to anesthetized patients of both sexes, ranging in age from 10 to 84 years of age. The degree of relaxation reported was based on the evaluation of the surgeon.

TABLE I.

Anesthesia	No. of patients	Range of initial dosage in mg		
		Min.	Max.	Avg
Cyclopropane	16	1	4	2
Ether	49	1	5	2.5
Nitrous oxide	35	1	6.5	3

The drug was dissolved in a distilled water and the curare adjusted to .5 mg per cc.* A preservative was added. The pH varied from 4.0 to 5.0. The solutions were stored at room temperature and used over a period of several weeks. Different lots of the drug were administered by the intravenous route. The initial dose consisted of 1 mg or more of the drug.

Data presentede in the table show the amount of M-curare required to produce adequate relaxation. The dosage recorded was given in one or more injections within a period of 10 minutes. Adequate relaxation was not noted in any patients who received less than 1 mg of M-curare.

It will be noted that an average of 2 mg of M-curare produced satisfactory relaxation in 16 patients receiving cyclopropane anesthesia. An average of 2.25 mg was required to produce adequate relaxation with ether

1 Bennett, A. E., *Am. J. Med. Science*, 1941, **202**, 101.

2 Griffith, H. R., and Johnson, G. E., *Anesthesiology*, 1942, **3**, 418.

3 Cullen, S. C., *Surgery*, 1943, **14**, 261.

4 King, H., *J. Chem. Soc.*, London, 1935, (pt. 2), 1381-1389.

5 Collier, H. O., and Paris, S. K., *Nature*, 1948, **161**, 817.

6 Chen, K. K., and Swanson, E. E., personal communication of unpublished data.

* Supplied by Eli Lilly Research Laboratories, Indianapolis, Ind.

anesthesia. With nitrous oxide anesthesia, the comparable dosage was 3 mg.

Relaxation produced by the initial dose of M-curare sufficed for surgical procedures, lasting 60 to 90 minutes. After this period, supplemental injections of .5 to 1 mg were infrequently required. The anesthesia level was maintained in lower plane I or upper plane II in all the patients. Reflexes were absent in 8 patients at the termination of surgery. Intubation was performed in 44 patients where the type of surgery made the technic mandatory.

No cardiovascular changes were noted in any of the patients. In no case could a fall in blood pressure be attributed to the drug.

Mild respiratory depression was observed in 9 patients in a series of 100 cases. In 7 of these, respiratory depression existed before surgery as the result of excessive premedication. One of the remaining cases received 7.5 mg of M-curare during a 15-minute period. Five minutes after the final injection, the rate of respiration decreased from a normal of 22 per minute to 14. Ten minutes later it had returned to the normal rate. Subsequently, the patient received injections of .5 mg and 1 mg without the development of respiratory embarrassment. Mild respiratory depression occurred in the other patient 3 minutes after the injection of 1.5 mg of M-curare. The rate of respiration decreased from a normal of 24 per minute to 16. This depression persisted for 5 minutes and the rate of respiration returned to a normal of 24. Subsequent injections of .5 mg and 1 mg of M-curare caused no untoward respiratory changes. Each of these patients maintained an adequate tidal exchange during the period of respiratory depression.

Discussion. The relaxation obtained with M-curare in this study was comparable to that obtained by other workers using *d*-tubocurarine chloride. The drug appears to have a selective action on skeletal muscle similar to that of *d*-tubocurarine chloride, but seldom affects the muscles of respiration.

No gross or microscopic changes were observed by Chen and Swanson[6] in any of the organs of the experimental animals which received lethal doses of M-curare. The median lethal dose (LD_{50}) of M-curare in rabbits by intravenous injection, plus and minus standard error, was found to be 0.031 ± 0.002 mg per kg of body weight. The average dose sufficient to produce head drop in rabbits was approximately 0.0167 mg per kg of body weight (usually referred to as a rabbit unit). A group of 8 rabbits tolerated one rabbit unit per day for 10 days. At the end of this period, 6 out of 8 rabbits succumbed to an LD_{50} injected intravenously. This gave evidence that neither tolerance nor cumulation had developed.

Summary. The administration of the dimethyl ether of *d*-tubocurarine iodide (M-curare) to 100 patients produced relaxation comparable to that of *d*-tubocurarine chloride. Respiratory depression was seldom observed and was of minor degree when present. Less M-curare than *d*-tubocurarine chloride is needed on a mg-for-mg basis.

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Effect of Two New Analgetic Agents on the Oxygen Consumption of Brain *In vitro*.

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Quastel and others[1,2,3] have conducted investigations on the actions of hypnotics and anesthetic agents on brain metabolism in which they have indicated parallels to exist between *in vivo* and *in vitro* activity. Similar studies by Elliott, Warrens, and James[4] suggest that, except for their findings on succinate oxidation, there is no evidence that morphine,