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**Effect of Ether and Iso-Amylethyl Barbiturate (Amytal) Anesthesia on the Glycogen Content of Skeletal Muscle.**

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The question of the glycogenolytic action of various anesthetic agents has received considerable attention in recent years, and although it is generally admitted that ether is a glycogen depleting agent, opinion on the influence of iso-amylethyl barbiturate (amytal) anesthesia remains divided. As a preliminary step in the investigation of the effect of various substances and procedures on the glycogen stores of the body, a series of experiments on the changes in the glycogen content of skeletal muscle under ether and amytal anesthesia was performed. Obviously, if specimens are to be removed under the influence of general anesthesia for the estimation of their glycogen content, the effect of the anesthetic agent on glycogen must be determined.

Brow and Long<sup>1</sup> showed that the glycogen content of heart muscle in fasted cats was reduced markedly with the closed mask method of ether administration, whereas there was only a slight reduction with the open method. Long,<sup>2</sup> employing the same species, showed that ether caused a distinct depression of the glycogen level of muscle. The results obtained by the majority of investigators concur with this work, although Hinsey and Davenport<sup>3</sup> have been unable to demonstrate any marked changes in the glycogen stores in skeletal muscle under the influence of ether anesthesia.

Amytal has become a popular anesthetic agent in recent years with investigators working on carbohydrate metabolism, because of the belief that it exercises a minimal effect on such metabolic processes. Page<sup>4</sup> showed that the blood sugar is not elevated beyond physiologic limits in dogs and rabbits under amytal anesthesia. Hines, Boyd and Leese<sup>5</sup> found that the substance did not alter the level of blood sugar in dogs, but that the ability to utilize glucose is impaired when this substance is injected by the continuous intra-

<sup>1</sup> Brow, G. R., and Long, C. N. H., *Current Res. Anesth. and Anal.*, 1930, **9**, 193.

<sup>2</sup> Long, C. N. H., *J. Biol. Chem.*, 1928, **77**, 563.

<sup>3</sup> Hinsey, J. C., and Davenport, H. A., *Am. J. Physiol.*, 1929, **88**, 286.

<sup>4</sup> Page, I. H., *J. Lab. and Clin. Med.*, 1923, **9**, 194.

<sup>5</sup> Hines, H. M., Boyd, J. D., and Leese, C. E., *Am. J. Physiol.*, 1926, **76**, 293.

venous method. Hines, Leese and Barer<sup>6</sup> found the levels of muscle glycogen to be practically the same in dogs under the influence of amytal anesthesia and in control animals. Cori<sup>7, 8</sup> considered amytal to have so little influence on carbohydrate metabolism that it might be employed in tolerance experiments for injected glucose in rats. Although amytal in itself has such a slight effect, Cori thinks that it greatly intensifies the depressive action of epinephrine on utilization of glucose.

Opposed to the foregoing view are Best, Hoet and Marks,<sup>9</sup> Long, and Hinsey and Davenport, all of whom found that amytal lowers muscle glycogen in the cat.

*Methods.* The experiments here reported were all performed on dogs. The ether was administered by the intratracheal method, and the amytal by the intravenous route. Specimens of muscle which acted as controls were secured in a few cases from corresponding muscles of the opposite side of the body, and in other cases specimens were removed from the same muscle, care being taken not to injure the blood supply of the part in question. The glycogen determinations were done by Pflüger's method. The usual precautions in this procedure were taken.

Four experiments were performed to determine the effect of ether anesthesia on muscle glycogen. In all experiments there was a decrease in glycogen although the amount that disappeared was variable. A representative protocol is given.

Experiment 1. The dog weighed 23 kg. Ether anesthesia was started at 8:30 a. m. and was continued during the course of the experiment. The data are as follows:

Muscle	Time A. M.	Glycogen %
Right sartorius	9:13	0.942
" "	10:55	0.416
Left sartorius	11:13	0.384
Right gracilis	9:18	0.832
" "	11:18	0.207
Left gracilis	11:20	0.200
Right quadriceps	9:15	0.870
" "	11:15	0.437
Left quadriceps	11:16	0.439
Right adductor	9:20	0.870
" "	11:20	0.758
Left adductor	11:24	0.747

<sup>6</sup> Hines, H. M., Leese, C. E., and Barer, A. P., *PROC. SOC. EXP. BIOL. AND MED.*, 1928, **25**, 736.

<sup>7</sup> Cori, C. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1925, **23**, 127.

<sup>8</sup> Cori, G. T., *Am. J. Physiol.*, 1930, **95**, 285.

<sup>9</sup> Best, C. H., Hoet, J. P., and Marks, H. P., *Proc. Roy. Soc. London*, 1926, **100**, 32.

Three experiments were performed to determine the effect of amytal anesthesia on muscle glycogen. A significant decrease in glycogen did not occur in any instance.

Experiment 2. The dog weighed 25 kg. During the procedure 58 mg. of amytal was administered intravenously. The glycogen values are as follows :

Muscle	Time A. M.	Glycogen %
Right sartorius	9:50	0.483
" "	11:55	0.551
Right gracilis	9:54	0.417
" "	12:01	0.591
Right quadriceps	9:52	0.344
" "	12:02	0.484
Right adductor	9:57	0.666
" "	12:05	0.680

We have shown repeatedly, as have numerous other investigators, that corresponding muscles of opposite sides of the body contain practically the same amount of glycogen. In the first protocol it is seen that the last 2 specimens of each group were taken almost simultaneously from opposite sides of the body, and in all cases there is fairly close correspondence in glycogen content. Furthermore, taking more than one specimen from a given muscle does not diminish its glycogen content provided there is no interference with the blood supply. In such a case the distal part of the muscle was used to obtain the first specimen, whereas the second specimen was removed from the proximal segment of the muscle.

Our results show that when ether is administered by the intratracheal method there is a coincident diminution of the glycogen content of skeletal muscle. On the other hand, muscle glycogen did not decrease significantly under anesthesia with amytal. On the basis of these experiments it would appear that amytal anesthesia is the anesthetic of choice in performing experiments involving muscle glycogen.

*Summary.* Corresponding muscles of opposite sides of the body contain similar amounts of glycogen. Prolonged ether anesthesia causes a marked decrease in the glycogen content of skeletal muscle. Amytal anesthesia causes little, if any, decrease in muscle glycogen content.