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## Effect of Nephrectomy on Duration of Action of Barbitals.

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Fitch and Tatum<sup>1</sup> have divided the barbitals into 2 groups based upon the duration of their action and upon the manner in which they cause death. They found that the longer acting barbitals (especially phenobarbital and barbital, ethyl-n-butyl barbital (neonal), iso-amyl barbital (amytal), ethyl iso-propyl barbital (barbituric acid of ipral), and also iso-propyl bromallyl barbital (noctal) cause death from pulmonary oedema, while the other barbitals, which they group as the short acting barbitals, when injected intraperitoneally in toxic doses cause death from depression.

Our finding that there is a marked difference in action of magnesium sulphate when administered to normal and to nephrectomized rabbits and to nephritic patients<sup>1, 2, 3</sup> led us to try this method of testing barbital action. Nephrectomy in etherized rabbits was done through a lumbar incision and was greatly accelerated by the use of a specially devised kidney fork. This was made from an ordinary table fork the first and third tynes of which were sawed off completely, the second and fourth being sharpened and bent around to form a semicircle of 3 cm. diameter. This was inserted through the lumbar incision so as to grasp the kidney, the renal pedicle passing through the space left by removal of the third tyne of the fork. A plate of spring phosphor bronze 7 cm. long and 2 cm. wide, sliding on a collar surrounding the handle of the fork was then pressed down so as to grasp the kidney completely, the kidney was drawn up through the incision and the renal pedical ligated. The incision

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\* This research was rendered possible by a grant of funds by the Hoffmann-LaRoche, Inc. (Basel, Switzerland, and Nutley, N. J.). The drugs used were kindly furnished by the following firms: Allylisopropylbarbituric acid, Hoffmann-LaRoche, Inc.; Pernocton, Riedel-de Haen, Inc.; Pentobarbital, Barbitalsodium and Neonal, Abbot Laboratories; Amytal, Eli Lilly & Co.; Phandorn and Phenobarbital, Winthrop Chemical Co.; Dial, Ciba Co., and Ipral, E. R. Squibb & Son.

<sup>1</sup> Fitch, R. H., and Tatum, A. L., *J. Pharmacol. and Exp. Therap.*, 1932, **44**, 325.

<sup>2</sup> Hirschfelder, A. D., and Serles, E. R., *J. Clin. Invest.*, 1932, **11**, 841; *J. Pharmacol. and Exp. Therap.*, 1932, **45**, 264.

<sup>3</sup> Hirschfelder, A. D. (with the technical assistance of V. G. Haury), *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 996.

was then sutured. The operation requires 15 to 20 minutes. The animals were allowed to recover completely from the ether anesthetic and the barbital was injected subcutaneously on the following day.

The duration of the anesthesia in nephrectomized animals, as compared with the controls receiving the same dose, gave a much sharper division than Fitch and Tatum's into 2 groups: 1. Barbital and phenobarbital whose narcotic action in nephrectomized rabbits is much longer than in the controls. 2. All the other barbital tested whose action was scarcely or not at all prolonged in nephrectomized animals as compared with the controls. Barbital gave nar-

TABLE I.

	Nephrectomized animals	Control animals
Allylisopropyl (barbital of allonal)	6	6
iso-amyl ethyl (amytal)	7	9
n-butyl ethyl (neonal)	8	9
calcium ethyl isopropyl (ipral)	8	9
di-allyl (dial)	10	10
cyclohexenyl ethyl (phanodorn)	9	9
2-butyl brom ethyl (pernocton)	9	8
ethyl 1-methyl butyl (pentobarbital)	8	8

cosis averaging 11.5 hours in 7 controls and 79.6 hours in 6 nephrectomized rabbits; phenobarbital, 13 hours in 8 controls and 36.5 hours in 9 nephrectomized. Barbital and phenobarbital narcosis usually lasted till the death of the nephrectomized rabbits.

It is, therefore probable that barbital and phenobarbital are excreted practically unchanged in the urine (as has been shown for barbital by Bachem,<sup>4</sup> Eddy,<sup>5</sup> Reinert<sup>6</sup> and Klingenfuss<sup>7</sup>) and that the other barbital are broken up in the intermediary metabolism, most probably in the liver.

<sup>4</sup> Bachem, *Arch. f. Exp. Pathol. u. Pharmacol.*, 1910, **63**, 228.

<sup>5</sup> Eddy, N. B., *J. Pharmacol. and Exp. Therap.*, 1928, **33**, 43.

<sup>6</sup> Reinert, M., *Arch. f. exp. Path. u. Pharmacol.*, 1928, **130**, 49.

<sup>7</sup> Klingenfuss, M., and Reinert, M., *Arch. f. exp. Path. u. Pharmacol.*, 1932, **165**, 416.