urine and none in the blood after that period, and, of course, they all survived.

Normal chickens, then, behave essentially as nephropathic mammals. They show a decreased elimination of barbital and retention of barbital in blood and organs and ultimate fatality caused by the drug if given in anesthetic doses. They all recover from the sleep produced by barbiturates other than barbital.

We performed several experiments to determine the cause of this remarkable phenomenon. We found that normal chickens all excreted, in one hour, over 65% of a total dose of 6.0 mg. of phenolsulphonphthalein in one cc. injected intravenously, behaving in this respect exactly as mammals do. Chickens with 150 mg. of sodium barbital per kg. by vein excreted 50% of phenol red, whereas following 225 mg. they excreted 30% of the dye, or less. Therefore, in the fowl it would appear that barbital appreciably decreases kidney function as measured by the phenol red test.

It is also obvious from our data that fowls cannot concentrate barbital in the urine to the same extent as mammals.

A few preliminary experiments have been performed with turtles. The results show that these animals behave essentially like fowls. The remarkable behavior to barbiturates seems to be the same in all sauropsida.

7136

Effect of Barbiturates in Experimental Nephrosis.

WILLIAM S. MURPHY AND THEODORE KOPPANYI.

From the Department of Pharmacology and Materia Medica, Georgetown University, School of Medicine.

We have shown[1] that bilateral nephrectomy greatly modifies the action of barbiturates in dogs; they do not recover from barbital, but do so from other barbiturates such as nembutal, pernoston, etc. As a further extension of this study, we used nephropathogenic agents to produce tubular lesions in mammals and investigated the action of barbiturates in animals with nephrosis. Dogs and rabbits were used for these experiments.

A. Tartaric Acid. Two dogs received 600 mg. of tartaric acid (neutralized with sodium carbonate) per kg. subcutaneously and

[1] Koppanyi, Murphy and Krop, *Arch. Int. de Pharm. et de Ther.*, 1933, **46**, 76.

subsequently given 225 mg. of sodium barbital per kg. by vein. The recovery from anesthesia was delayed, but the total excretion was but slightly subnormal (71-76%). After complete recovery and stoppage of excretion, the same animals, now showing evidence of grave tubular lesions, were again given 225 mg. of sodium barbital per kg. intravenously. They did not recover from the anesthesia and excreted less than 2% of the drug. Histological studies showed almost complete tubular disintegration, the glomeruli remaining fairly intact. Animals receiving 600 mg. of tartaric acid but no barbital do not become anesthetized and outlive the barbitalized animals. (See also Underhill, Wells and Goldschmidt.[2])

B. Uranium Acetate. Three dogs and 2 rabbits were given 2 mg. uranium acetate in a 0.1% solution intravenously in divided doses over a period of 2 days. These animals did not recover from the depression produced by 225 mg. of sodium barbital per kg. by vein and excreted 41%, 38%, 8.7%, 2.3% and 1% of the drug respectively. The concentration of barbital in the urine was 1.0 mg. per cc., or less. Two dogs and one rabbit received in addition to uranium and sodium barbital, from 35 cc. to 50 cc. of a 10% glucose solution per kg. intravenously, excreting 56%, 38%, and 18% of the drug in the urine. Even though there appears to be an increase in the percentage of elimination in the diuretic animals, they never recovered from the barbital narcosis. The concentration of barbital in the urine was lower than in the non-diuretic animals. None of these animals, whether they were given glucose or not, ever recovered from barbital anesthesia and died within 114 hours following the administration of barbital. Three dogs similarly treated with uranium acetate, recovered within the usual periods from nembutal, pernoston, and neonal anesthesia.

C. Potassium Chromate. Four rabbits and one dog received 20 mg. of potassium chromate intramuscularly in divided doses over a period of 2 days and then were given intravenous injections of 225 mg. sodium barbital per kg. The 4 rabbits excreted only slightly subnormal amounts of the drug (from 50% to 75%); the dog, however, in which the chromate proved to be more destructive, excreted only slightly over 2%. The rabbits all recovered, but the dog died of barbital depression.

Four rabbits and one dog received, in addition to the doses of the former drugs, 50 cc. of a 10% glucose solution per kg. by vein. The rabbits recovered, excreting from 50% to 70% of barbital, the dog excreted only traces and died in barbital coma.

[2] Underhill, Wells and Goldschmidt, *J. Exp. Med.*, 1913, **18**, 317.

In all nephrotic animals receiving tartaric acid, uranium or potassium chromate and dying in barbital coma there was a retention of barbital in the blood until death, amounting to from 0.15 mg. to 0.05 mg. per cc. of blood.

In all animals the damage to the kidney function was checked by phenolsulphonphthalein elimination and subsequent histological examination.

Conclusions. In severe experimental nephrosis, dogs and rabbits behave with reference to barbiturates as bilaterally nephrectomized animals. They *never recover from barbital depression, remaining anesthetized until death,* show *retention* of barbital *in the blood,* and also *eliminate* a relatively *small percentage* of the drug in the *urine.* However, they do recover from the sleep produced by barbiturates other than those largely eliminated by the kidney. In less severe cases there is a retarded recovery and decreased elimination of barbital in the urine with no retention of the drug in the blood above normal.

7137 P

Influence of a Certain Fraction of Pancreas Lipids on Carbohydrate Metabolism of Depancreatized Dogs.*

A. G. EATON AND J. R. MURLIN.

From the Department of Vital Economics, University of Rochester.

Ever since the demonstration of the internal secretion of the pancreas there have been reports of substances antagonistic to insulin which increase the severity of diabetes. A blood sugar raising fraction of the pancreas reported by Gibbs, Root and Murlin[1] under the name of *glucagon* was precipitated by reagents which would precipitate the phospholipids and the cerebroside fractions of the pancreas fats. Further attention has been given recently to the separation of this fraction into its components. A fraction insoluble in acetone and ether, containing therefore the cerebrosides and some sphingomyelin has given some striking effects on the D:N ratios and the R.Q.'s of depancreatized dogs, but no consistent effect

* This paper was presented at the joint meeting of the Western New York branch and Section N of the A.A.A.S. at Syracuse, June 18, 1932.

1 Gibbs, C. B. F., Root, E. W., and Murlin, J. R., *Quart. J. Exp. Physiol.* Suppl. vol., 1923, 128.