7135

Effect of Barbiturates in the Domestic Fowl.

THEODORE KOPPANYI AND WILLIAM S. MURPHY.

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

Of 12 full grown fowls, 2 received 350 mg., 7 received 225 mg., and 3 were given 150 mg. sodium barbital per kg. by vein. Fowls receiving the minimum anesthetic dose, 225 mg. of sodium salt per kg. or over, never recovered to the extent that they were able to stand or walk. Within a period of one week they all died in barbital coma showing involvement of the respiratory system. The examination of the urine showed that they never excreted more than 33% of the dose injected and as a rule the elimination varied between 15% and 25%. The concentration in the urine was 1 mg. of barbital per cc. or less, and only in the fowl receiving 350 mg. of the sodium salt per kg. did it reach 2.5 mg. per cc. Dogs under similar circumstances have excreted 6 mg. per cc. of urine or more.

Fowls receiving 225 mg. per kg. of sodium barbital or more show a retention of the drug in the blood varying from 0.15 mg. to 0.05 mg. per cc. even 5 days following the administration of the drug. Similarly, one can detect the presence of barbital in the organs one week after the administration.

Two fowls were given 225 mg. of sodium barbital per kg. and one hour later 20 cc. of a 3% solution of uric acid was injected over a period of one hour. They showed the unprecedented diuresis of over 250 cc. of urine during a period of 18 hours. Yet they never recovered from the drug and excreted during a period of 7 days 21.1% and 24.5% respectively of barbital in the urine, showing a retention of the drug in the body.

Three chickens received 150 mg. of sodium barbital per kg.; no anesthesia was produced, but ataxia was present. Two of the fowls excreted 45% and 37.7% respectively of the drug during a period of 17 days, showed a slow recovery from ataxia, and even 24 hours after injection 0.15 mg. per cc. of barbital was present in the blood. Thus chickens excrete barbital for over a far longer period than mammals.

Seven chickens received intravenously 60 mg. of dial and neonal respectively; 100 mg. of phenobarbital, 25 mg. of nembutal, and 20 mg. of pernoston per kg. of body weight. They all recovered within 24 hours from the anesthesia, showing traces of these drugs in the

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.