regime. The criticism which may be made of experiments with short chain aldehydes, ketones, ketoacids, etc., in dogs prepared by fasting and phlorhizin alone are not applicable to the results obtained with animals which have been subjected to cold until all glycogen has been exhausted; nor is it necessarily implied that alanine, aspartic acid, lactates, propionates, and many other bland substances which have been studied might not yield entirely satisfactory results even in the presence of a residue of glycogen.

99 (916)

On the difference in the response of animals of different ages to a constant quantity of uranium nitrate.[1]

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The following report is based upon the difference in the response of forty-eight animals of different ages to a constant quantity of uranium nitrate.

Dogs have been employed in all of the experiments. The animals have varied in age from puppies of four months old, to animals of extreme old age, one of the animals having reached the age of twenty years.

All of the animals have received uranium nitrate in the dose of 6.7 mgs. per kilogram on two successive days. The uranium was given subcutaneously.

The animals were fed on raw meat and bread.

In a recent publication[2] it has been shown that when a constant quantity of uranium nitrate is given to young and full grown animals, that the age of the animal influences the total output of urine and also the composition of the urine. The total output of urine in a twenty-four hour period was greater in the adult animals. The percentage of glucose in the urine (Benedict determination) was greater in the adult animals than in the puppies.

In the urine of the puppies acetone was either absent or present

[1] Aided by a grant from the fund for Scientific Research of the American Medical Association.

[2] MacNider, *Jour. of Pharm. and Exper. Ther.*, IV, 6, 1913.

in very small amount. The urine of the adult animals invariably contained acetone.

The present series of forty-eight animals shows the same differences in the total output of urine and in the composition of the urine as has been above referred to.

In addition, these animals of different ages show certain other characteristics which are apparently dependent upon the age of the animal.

1. Ten of the animals were puppies varying in age from four to eight and a half months. Only one of these animals developed a glycosuria within the first twenty-four hours following the initial injection of 6.7 mgs. of uranium. The percentage of glucose in the urine of this animal was 0.103 per cent.

2. In none of the puppies was acetone present in the urine following the first injection of uranium.

3. Following the second injection of uranium all of the puppies developed a glycosuria. The percentage of glucose varied from 0.35–1.1 per cent.

4. Following the second injection of uranium only two of the puppies showed the presence of acetone in the urine. The amount of acetone was exceedingly small.

The full-grown animals and old animals have shown the following differences in their response to the same quantity of uranium per kilogram that was received by the puppies.

1. With three exceptions, the remaining thirty-eight adult animals all developed a glycosuria within twenty-four hours following the first injection of 6.7 mgs. of uranium. The percentage of glucose varied from 0.18–1.61 per cent. The three highest percentages of glucose—1.61, 1.59 and 1.24 per cent were obtained in old animals.

2. Following the second injection of uranium all of the full grown animals became glycosuric. The percentage of glucose varied from a minimum of 1.47 per cent to a maximum of 2.86 per cent.

3. Acetone was present in the urine of all of the full grown animals following the first injection of uranium excepting the three animals that failed to develop a glycosuria following the first uranium injection.

That the above differences in the response of puppies and adult animals to a constant quantity of uranium are not dependent upon the relative weight of the different animals and therefore associated with the total amount of uranium received by the animal but are associated with the difference in the age of the animals is clearly shown by the following experiments:

Experiment 18.—Puppy, aged 7 months. Weight 9.35 kilos. The animal received 6.7 mg. of uranium nitrate per kilogram on two successive days. The urine following the first injection contained neither glucose nor acetone. Following the second injection of uranium the urine contained 0.35 per cent. glucose and a trace of acetone.

Experiment 38.—Full-grown animal, old, weight 7 kilos. Following the first injection of 6.7 mg. of uranium nitrate per kilogram the urine contained acetone and the animal developed a glycosuria. Glucose was present in 1.21 per cent. Following the second injection of uranium the amount of acetone was apparently greatly increased. Glucose in the urine had increased to 2.84 per cent.

The experiments were terminated by either shooting, or killing the animals with chloroform or ether.

In the account which is to follow of the fatty changes which are induced in the liver and kidney of the animals of different ages, none of the animals which were subjected to the effect of an anesthetic will be included. As has been previously shown the anesthetic very greatly increases these changes.[1]

Frozen sections were made at once and stained by Herxheimer's Scharloch R method for fat. The sections were counter stained by Mayer's Haemalum. It is important for both of these stains to be fresh.

The frozen sections have shown that the amount of fat in the liver and in the kidney of puppies which have been given uranium nitrate is very much less than in the adult animals. The fat in the liver is found as dust-like particles which serve to outline the bile capillaries while the epithelium of the interlobular bile ducts contains larger quantities of fat in the form of coarse granules. The cytoplasm of the liver cells contains numerous small fat droplets, but the principal localization of the fat is either within the

[1] MacNider, *Jour. Med. Research*, XXVIII, III, 1913.

bile capillaries or in that zone of the cell which immediately surrounds the capillaries.

In the kidneys of these animals the fat first appears in the loops of Henle. The fat is most pronounced in the ascending limb of Henle's loop.

In puppies and young dogs the fat is in small amount and appears in the form of minute granules in the epithelium lining these tubules. In adult animals and especially in old animals the fat is very greatly increased in amount and is seen in the form of large granules which may coalesce to form masses which serve to outline the course of the tubule.

There is apparently an association between the amount of fat found in the liver and kidney of animals of different ages with the amount of glucose present in the urine. The puppies and young animals which show a low percentage of glucose in the urine show a small amount of fat in the liver and kidney.

The full-grown animals and old animals which have shown an earlier appearance of glucose in the urine and a percentage of glucose which has been much higher than has been found in the puppies also show fatty changes in the liver and kidney of much greater severity.

100 (917)

Variations in resistance of red blood cells in sheep.

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In the course of complement fixation work we have noticed that the specimens of blood cells obtained from different sheep under exactly similar conditions occasionally show marked differences in their susceptibility to laking by specific lytic serum. When this was first noticed we were using two sheep as a source of blood, and as the sheep whose cells were more highly resistant was one which had been bled repeatedly and profusely it was natural to attribute the increased resistance of the cells to this.

We determined to investigate this question and also to find out whether the increased resistance was a specific resistance to