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Excretion of Urea in the Rabbit at Different Age Periods.*

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Urea determinations have been made in many kinds of animals and under various conditions, but the literature apparently does not contain any reference to a relationship of urea excretion in normal rabbits to the age of the animal. This investigation was therefore undertaken to ascertain the daily amount of urea nitrogen excreted in the urine of rabbits from birth to adult condition. Fifty-one rabbits were used, including all ages from fully grown fetuses to adult animals.

Collection of urine. To collect the urine from the fetuses the mother was killed by decapitation, and the abdomen of the fetus after removal from the uterus was opened by an incision. The urine was removed by means of a fine hypodermic needle. The same method was used for collecting urine from the new born rabbits up to the age of 4 days. In these experiments practically no urine was found in the bladders of 8 fetuses and 12 new born rabbits, 2 to 5 minutes after parturition, except for a very small drop occasionally encountered, which was not sufficient to make urea determination by the procedure employed. Dr. Wallin† informs me that he has made similar observations on the absence of urine in the bladder of fetuses or new born rabbits. It is interesting to note that whenever the new born rabbits were permitted to feed, the bladder was seldom, if ever, found to be full. On the other hand, if they were taken away from the mother at birth and starved for from 10 hours to 3 days, the bladder on opening was almost always full of urine.

In one set of experiments animals over 10 days old were kept in metabolism cages, the urine being collected in a beaker placed underneath, and changed every 24 hours. No attempt was made to squeeze out the urine from the bladder. The animals were fed hay (dried alfalfa), fresh lettuce, celery, grass, rolled barley, and water *ad lib.* The younger animals were fed milk, with the additions of bread crumbs in some cases.

* An abstract of this paper was presented before the American Association of Anatomists at Rochester, March, 1929.

† Wallin, I. E., personal communication.

In one experiment an animal from the age of 26 days to that of 98 days was kept on a special diet consisting of measured amounts of milk, sucrose, and dried alfalfa.

In a second experiment 2 litter mates were maintained at a constant body weight while they were advancing in age. Since one of these animals, Rabbit R., died of starvation, the other was permitted to gain somewhat in weight to keep it alive. No record was kept of the amount of food consumed.

In the third experiment 3 litter mates were used, 2 of which received a special diet consisting of measured amounts of crushed barley, dried alfalfa and fresh lettuce, the third, control animal, receiving the same foods *ad lib.*, from the age of 43 days to that of 92 days.

The object was to maintain the weight of the 2 animals constant by giving just enough food to keep them alive. Actually the animals were allowed to gain about 100 gm. each in the course of the experiment, because previous experience had shown that otherwise the animals would die of starvation.

Determination of urea. Urea was determined according to the method of Folin and Youngburg[1] by direct Nesslerization.

From an analysis of the results it is evident that the amount of urea in the urine increases with the age as well as with the weight of the animal, from 1.5 mgm. at the age of 6 hours to about 1200 mgm. in the adult. The concentration of urea in the urine was variable.

Diet seems to have a definite influence on the amount of urea in the urine, the urea increasing on diets rich in proteins and certain amino acids. The decrease in urea nitrogen on changing to a diet poor in proteins was striking. In one instance it fell from 260 mgm. to 53 mgm. in one day and continued at a low level throughout the period of this low protein diet. The increase in urea nitrogen after changing the diet from the low protein to the ordinary diet was slow but definite.

The volume of urine decreased from 96 cc. to 6.6 cc. per 24 hours and continued at a low level on the diet poor in proteins. As soon, however, as the diet was changed back to the ordinary (rich in proteins and in some amino acids) the volume of the 24 hour urine increased at once from 38 cc. to 76 cc. and continued at a high level.

The amount of urea in the urine increased steadily with advancing age from 200 mgm. at the age of 42 days to 1100 mgm. at the age of 90 days, even when the weight of the animal was kept almost stationary by a diet qualitatively adequate but insufficient in quantity.

[1] Folin, O., and Youngburg, G. E., *J. Biol. Chem.*, 1919, **38**, 111.

Their urea excretion was approximately the same as in the control animals, although the control rabbits were over 500 gm. heavier than either one of the undernourished rabbits.

In the case of Rabbit L, the increase in the amount of excreted urea nitrogen was not nearly so pronounced as in the other rabbits, which may have been due to the fact that this animal did not receive an adequate amount of fresh vegetables.

The case of Rabbit R is interesting because the animal died of starvation. A few days before death, when the weight of this rabbit began to decline, the amount of urea nitrogen excreted in the urine increased considerably, from 58 mgm. to 510 mgm. This is fully discussed by Morgulis[2] under *"Premortal Rise in Nitrogen Elimination."*

The amount of daily urea nitrogen seems to agree fairly well with the findings of Christman and Lewis,[3] and Addis and Watanabe,[4] in adult rabbits. The work of Christman and Lewis also shows that the addition of certain amino acids causes a definite increase in the urea nitrogen of the urine of rabbits, which is in agreement with the results of my experiments.

The absence of urine in the bladder of fetal and of new born rabbits appears to indicate that urea excretion does not begin until after the birth of the animal. Some stimulus appears to be responsible for the inception of the kidney activity. The nature of this stimulus has not been discovered.

Conclusions. 1. It is definitely shown that the urea excretion in the rabbits' urine is very low at birth and gradually increases with advancing age of the animal. 2. The amount of urea in the urine increases with the age of the animal, even when its body weight is kept stationary by a qualitatively adequate diet when fed in insufficient amount. The effect of change in body weight on the urea excretion is of secondary importance. 3. The work of Christman and Lewis[3] as shown in their Tables 1 to 4 is confirmed by these experiments; that the urea in the rabbits' urine increases on diets rich in proteins and decreases on diets poor in proteins and in certain amino acids.

My thanks are due to Professor I. E. Wallin for his interest and suggestions.

[2] Morgulis, S., "Fasting and Undernutrition," E. P. Dutton & Co., N. Y., 1923, 135.

[3] Christman, A. A., and Lewis, H. B., *J. Biol. Chem.*, 1923, **57**, 379.

[4] Addis, T., and Watanabe, C. K., *J. Biol. Chem.*, 1917, **28**, 251.