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Effect of Diet on Ketonuria in the Rat.

H. J. DEUEL, JR., J. S. BUTTS, AND L. HALLMAN.

From the Department of Biochemistry, University of Southern California School of Medicine, Los Angeles.

It was noted¹ that the fasting ketonuria in the rat rarely exceeded 2 mg. per day over periods of several days. More recently, instances of higher values in the excretion of acetone bodies in fasting rats fed sodium chloride solution have become increasingly frequent, so that at least 80% give higher results.

Thus, the average values of acetone bodies for fasting male rats were 7.7 mg. (0.0-45.3) for 34 rats on the first fast day and 12.3 mg. (0.6-27.2) for 11 animals on the second one. The corresponding averages on 19 female animals fasted for 3 consecutive days were respectively 2.8 mg. (0.0-18.8), 10.4 mg. (0.0-33.0), and 9.6 mg. (0.2-35.9). Moreover, it was found that although the same sex difference in the excretion of ketone bodies followed the administration of diacetic acid as was previously observed, the levels in our recent experiments during 5 days of fasting were consistently higher than those previously obtained. The only variation in experimental regime from that earlier employed to which these alterations could be ascribed, was a change in the stock diet. Because of the outbreak of pellagra in our colony, our previous high carbohydrate diet (II) had been fortified in Vitamin G several months earlier by the inclusion of 5% of desiccated liver therein (Diet III). It was found that the fasting ketonuria observed over periods of several days in rats previously on Diet III was gradually reduced to a low level when the animals were returned to Diet II (liver-free) for 60 days. The original level of fasting ketonuria of 4.9 (0.0-17.7) for 9 rats on the first fast day, 17.6 mg. (2.7-29.2) for 8 animals on the second day, and 15.1 mg. (3.5-30.3) for 5 rats on the third one was reduced after 60 days on Diet II to a mean of 0.9 mg. (0.6-1.2) for 9 rats on the first and 1.7 mg. (0.5-3.1) for the same animals on the second fast day.

On the other hand, when rats previously on Diet III were fed on a diet containing 45% of desiccated liver, the level of fasting ketonuria was slightly raised after 31 days. After 50 days the ketonuria reached abnormally high values in 7 of 8 animals used. The average

¹ Butts, J. S., and Deuel, H. J., Jr., *J. Biol. Chem.*, 1933, **100**, 415.

results for 4 males were 26.3 mg. (4.3-50.2) for the first fast day and 60.7 mg. (16.5-89.5) for the second one. The similar high levels which obtained in the 4 females were 10.5 mg. (0.6-22.4) and 46.1 mg. (3.8-113.4) for the 2 fasting days respectively. On one case an excretion of 113 mg. was found, which is the highest level of fasting ketonuria we have ever observed in the rat.

So far we have been unable to prevent the onset of the ketonuria by the administration of choline hydrochloride in doses of 60 mg. per day. The effect of the liver diet is probably to be ascribed to the mobilization of the fat in the liver as indicated by the experiments of Blatherwick *et al.*² Comparative studies on the relationship between the level of liver fat and the extent of fasting ketosis after employing diets high in various fats is in progress.

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Sexual Variation in Carbohydrate Metabolism. VII. Effect of Alkalosis on Fasting Ketonuria in the Rat.

J. S. BUTTS, H. J. DEUEL, JR., AND L. HALLMAN.

From the Department of Biochemistry, University of Southern California School of Medicine, Los Angeles.

Booher and Killian¹ first reported that abnormally large amounts of acetone bodies were associated in human subjects with conditions of uncompensated alkalosis which arose either from an excessive alkali administration or from the loss of HCl by excessive vomiting. Butts and Deuel² previously showed that no sex differences occurred in the slight ketonuria which occurs in fasting rats previously fed on a high carbohydrate liver-free diet although a definite sex variability was demonstrated in rats to which diacetic acid was administered. In the present tests sodium bicarbonate was fed to fasting rats in a dose of 2.17 mg. per sq. cm. of body surface by stomach tube in 3 divided doses daily. This corresponds with the alkali intake in tests in which sodium acetoacetate was administered in an amount of 1.5 mg. per sq. cm. per day (calculated as acetone). The acetone body excretion with the male rats over a 4-day experimental period

² Blatherwick, N. R., Medlar, E. M., Bradshaw, P. J., Post, A. L., and Sawyer, S. D., *J. Biol. Chem.*, 1933, **103**, 93.

¹ Booher, L. E., and Killian, J. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1923, **21**, 528.

² Butts, J. S., and Deuel, H. J., Jr., *J. Biol. Chem.*, 1933, **100**, 415.