the light, more refractile capsule about the darker somatic body of the gonococcus. The capsule possessed structural rigidity and appeared to have a definite elastic outer membrane, as the India ink particles were seen to cause indentations when they hit up against it. The ink particles then rebounded, as though caused to do so by the contraction again of the membrane.

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## Effects of Increased Metabolism on Ketosis

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In animals in a state of ketosis exercise has been reported not to change significantly the rate of excretion of ketone bodies.[1, 2] Increased activity of isolated diabetic muscles causes marked increase in rate of disappearance of these substances.[3] Elsewhere we have suggested that these apparently contradictory findings can be reconciled if the liver increases its production of ketone bodies as a result of exercise.[4] To test this hypothesis, the ketone excretion of the human subject on a constant ketogenic diet was determined during several days. The urine was divided into day and night portions at 8 A.M. and 8 P.M. In several different experiments each lasting several days, the amount of muscular activity during the daytime period was increased on certain days by strenuous exercise (tennis) for at least 2 hours and on some days it was cut down to a minimum by rest in bed. The ordinary activity was light laboratory work. Regular hours for sleep were maintained during the night periods throughout. From Table I it is obvious that except for days of complete inactivity the nocturnal excretion of ketone bodies is definitely higher than the diurnal. There is also a tendency for the daytime output to be less, the greater the activity. At the same time the night periods which follow days of high activity tend to have more ketonuria than those which follow days

1 Barker, S. B., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 893; *J. Physiol.*, 1939-40, **97**, 394.

2 Drury, D. R., *California and Western Medicine*, 1936, **45**, 1.

3 Blixenkrone-Moller, N., *Hoppe-Seyler's Z. f. Physiol. Chemie.*, 1938, **253**, 423.

4 Barnes, R. H., Drury, D. R., Greeley, P. O., and Wick, A. N., *Am. J. Physiol.*, 1940. **130**, 144.

TABLE I.

Ketone Body Excretion in Urine, as Grams per Period of Human on Constant Ketogenic Diet.

| Day | Period | Exp. 1 | Exp. 2 | Exp. 3 | Exp. 4 |
|---|---|---|---|---|---|
| 1 | Day | E 1.68 | .83 | 1.26 | .69 |
| | Night | 8.25 | 2.26 | 2.24 | 1.11 |
| 2 | Day | .95 | .75 | E 1.08 | E 1.33 |
| | Night | 3.71 | 2.03 | 6.15 | 2.18 |
| 3 | Day | E .68 | E .67 | E 2.51 | R 2.96 |
| | Night | 5.42 | 4.30 | 5.88 | 1.73 |
| 4 | Day | 1.20 | 1.37 | R 5.50 | E .53 |
| | Night | 2.86 | 3.83 | 5.22 | 2.04 |
| 5 | Day | R 2.59 | E .85 | 2.91 | |
| | Night | 3.45 | 4.07 | 4.44 | |
| 6 | Day | | 1.44 | | |
| | Night | | 3.54 | | |

E—Indicates strenuous exercise (tennis 2 hours or more) at some time during the period.

R—Indicates rest in bed during the period.

The diet was constant during every experiment. There were slight differences in diet between the different experiments.

of low activity. These results would suggest that muscular activity decreases the concentration of ketone bodies in the body at the time of this activity but that in the subsequent rest period the rate of production of these substances by the liver is accelerated.

This question was investigated by a special experiment carried out on 2 successive days with the subject on the constant ketogenic diet. On the afternoon of the first day he engaged in heavy exercise (tennis) and kept at rest during the evening. On the following day he rested in the afternoon and engaged in ordinary activity during the evening. In another pair of days on the same constant diet, the subject engaged in ordinary activity on the first day, exercised in the afternoon of the second day and rested in the period after that. The results are given in Table II and again indicate that ketone excretion is not increased during exercise but may be augmented in a period of rest following the activity.

These results may be due to decreased function of the kidneys during exercise. It is known that the rate of urea excretion is diminished during strenuous exercise.[5] In our next experiments we followed the effect of exercise on the blood ketone body level, using the method of Barnes and Wick.[6] In preliminary experiments it

[5] Addis, T., and Drury, D. R., *J. Biol. Chem.*, 1923, **55**, 629.

[6] Barnes, R. N., and Wick, A. N., *J. Biol. Chem.*, 1939, **131**, 413.

TABLE II.
Urinary Excretion of Ketone Bodies in mg per Hour.

| Exp. 1 | | | Exp. 2 | | |
|---|---|---|---|---|---|
| Time | 1st day | 2nd day | Time | 1st day | 2nd day |
| 11 P.M.- 7 A.M. | 150 | 126 | 12 M. - 6 A.M. | 86 | 58 |
| 7 A.M.-10 " | 161 | 172 | 6 A.M.-12 N. | 17 | 38 |
| 10 " - 1 P.M. | 58 | 77 | 12 N. - 6 P.M. | 14 | E 26 |
| 1 P.M.- 4 " | E 18 | R 108 | 6 P.M.-12 M. | 24 | R 217 |
| 4 " - 7 " | 59 | 75 | | | |
| 7 " -11 " | R 109 | 82 | | | |

E—Indicates strenuous exercise during the period.
R—Indicates rest in bed during the period.

TABLE III.
Effect of Exercise on Blood Ketone Level. Values Expressed as mg Ketone Bodies per 100 cc Blood.

| | Exp. 1 | Exp. 2 | Exp. 3 | Exp. 4 |
|---|---|---|---|---|
| Immediately before exercise | 7.7 | 15.7 | 11.9 | 6.6 |
| Immediately after exercise | 3.7 | 9.6 | 8.9 | 4.3 |

Exercise was running at medium steady rate for 20 minutes.

was found that a fast of 20 hours was adequate to produce a definite ketonemia with the blood ketone level steadily rising as the fast was continued. The method of procedure adopted was as follows: After a fast of 20 hours a blood sample for ketone body determination was taken. The subject then exercised for about 20 minutes. The exercise was running at a steady medium pace—not enough to give an oxygen debt. Another blood sample was taken on completion of the exercise. The results are given in Table III. There is a significant drop in all cases as a result of the exercise. In 5 control experiments it was found that the average rate of rise of the blood ketone level after 20 hours of fasting was 2.2 mg % per hour. The actual drop caused by the exercise is then greater than appears from the differences found. We can conclude that a short brisk period of exercise will give a definite lowering of the blood ketone concentration and hence that changes in ketone excretions in the urine caused by exercise are not due simply to change in function of the kidneys during this time.

*Summary.* The human subject in a ketogenic state excretes less ketone bodies during exercise than ordinarily. There seems to be an increased excretion in a subsequent rest period. The blood concentration of the ketone bodies is also decreased during a short period of exercise.