THE UTILIZATION OF ACETONE BODIES

III. THE INFLUENCE OF ADRENALECTOMY

By NORTON NELSON,* ISABELLE GRAYMAN,† and I. ARTHUR MIRSKY

(From the May Institute for Medical Research of the Jewish Hospital, Cincinnati)

(Received for publication, November 24, 1939)

That the adrenal gland plays a specific rôle in fat metabolism has been suggested for many years (1). More recently this hypothesis received further support when Long and Lukens (2) reported that adrenalectomy produces a marked reduction in the acetone body excretion of the depancreatized cat. This observation soon received ample confirmation by other investigators who found that adrenalectomy likewise reduced the excretion of acetone bodies, which follows phlorhizin intoxication (3), pregnancy (4), fasting (5), and the administration of extracts of the anterior pituitary gland (5, 6). The general conclusion derived from these observations implied that adrenalectomy inhibits the formation of acetone bodies and hence that the adrenal plays an essential rôle in fat catabolism.

The observation by MacKay and Barnes (5) that the adrenalectomized rat may develop a ketonemia after the administration of an extract of the anterior pituitary gland suggested to us that the adrenal glands may not be essential to ketogenesis. Consequently we studied simultaneously the blood and urine acetone body content of normal and adrenalectomized rats treated with an extract of the anterior pituitary gland. We found that whereas the acetone body excretion consequent to the administration of the extract was markedly decreased in the adrenalectomized rats, the blood acetone body level did not vary significantly from that of the pituitary-treated normal rats (7). From this it was con-

* Eli Lilly Research Fellow.
† Henry Wald Bettmann Fellow.
eluded that adrenalectomy impairs the function of the kidneys in such a manner as to increase the threshold for the excretion of acetone bodies. The subsequent reports by Shipley and Long (8), Neufeld and Collip (9), and MacKay and Wick (10) support this conclusion and indicate that acetonuria per se cannot be accepted as a criterion of acetone body formation (ketogenesis) or acetone body utilization (ketolysis).

Although the studies mentioned above (8-10) indicate that the adrenals are not essential for ketogenesis, they do not eliminate the possibility that the adrenals may play some rôle in either or both ketogenesis and ketolysis. Therefore it became of interest to investigate this question further by some precise procedure.

In the present study we have concerned ourselves with the influence of adrenalectomy on acetone body utilization. In order to eliminate the possible influence of spontaneous ketogenesis, it was necessary to study conditions under which acetone body formation was at a minimum. This can be achieved by studying animals which have received an injection of glucose, for under such conditions endogenous ketogenesis is negligible (11, 12).

In order to obviate the effects of absorption, diffusion, and variable rates of excretion, we studied the disappearance of intravenously administered acetone bodies (β-hydroxybutyrate) from the whole bodies of fed, glucose-treated rats. The amount utilized by an animal was computed by determining the difference between the amount of acetone bodies injected and that found in the animal after a definite interval of time.

**EXPERIMENTAL**

This study was carried out with female rats from our stock colony which were kept on a stock diet until a few minutes before the beginning of the experiment and which then received an intraperitoneal injection of glucose (100 mg. per 100 gm. of body weight). The animals were divided into two groups, in one of which the rats were operated upon 2 days previously under ether anesthesia and the adrenals removed and, in the other, only perirenal fat was removed. All animals after operation were given saline ad libitum.

1 Purina Fox Chow.
Within 40 minutes after the administration of glucose, the rats were given an intravenous injection of synthetic sodium β-hydroxybutyrate and were immediately placed in individual 1 liter beakers. The dosage of the β-hydroxybutyrate was kept between 8 and 9 mM per kilo of body weight and was injected by means of a tuberculin syringe.

In order to correct for the initial content of acetone bodies analyses were made on groups of glucose-treated adrenalectomized rats and rats with the mock operation, receiving no β-hydroxybutyrate.

**Table I**

*Effect of Adrenalectomy on Utilization of β-Hydroxybutyric Acid in Fed Female Rats*

Corrected for initial content: adrenalectomized rats = 0.07 mM per kilo, rats with mock operation = 0.02 mM per kilo.

<table>
<thead>
<tr>
<th>Experimental group (10 animals in each)</th>
<th>β-Hydroxybutyrate injected</th>
<th>Acetone bodies found 40 min. after injection</th>
<th>Acetone body utilization in experimental period</th>
<th>Reliability of difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mock operation</td>
<td>9.05 mm per kg.</td>
<td>2.67 mm per kg.</td>
<td>6.38 (±0.08)†</td>
<td>8.7</td>
</tr>
<tr>
<td>Adrenalectomy</td>
<td>8.33 mm per kg.</td>
<td>3.35 mm per kg.</td>
<td>4.98 (±0.137)</td>
<td></td>
</tr>
</tbody>
</table>

* Reliability of difference = (difference of means)/(standard error of difference). Standard error of difference = \(\sqrt{(S.E.M._1)^2 + (S.E.M._2)^2}\).

† Standard error of the mean, S.E.M. = \(\sqrt{(\Sigma d^2/n)/n}\).

At the completion of the experimental period of 40 minutes, the animals were killed by a blow on the back of the neck and the carcass was then ground up thoroughly in an ordinary meat grinder, the excreta in the beaker being thoroughly mixed with the ground tissue. Extracts of the ground rats plus excreta were prepared and their total acetone body content determined by the procedures outlined in previous reports (11, 12).

The pertinent data obtained by the above procedures are summarized in Table I. As in our previous studies (11, 12), only negligible amounts of acetone bodies were found in the glucose-treated rats, which indicates that spontaneous ketogenesis is at a minimum even in the adrenalectomized animals.

The utilization of acetone bodies is markedly depressed in the
Utilization of Acetone Bodies. III

adrenalectomized animals, as compared with the rats with the mock operation. Thus the rate of utilization of the adrenalectomized rats for the 40 minute interval is 1.40 mM per kilo of body weight slower than that of the group with the mock operation. This difference is statistically reliable, as indicated by the reliability of difference of 8.7.

DISCUSSION

In view of the preceding we can now state that following the administration of a ketogenic stimulus, the adrenalectomized rat, as compared to the normal, will show (a) a normal ketonemic response (7, 8, 10), (b) a diminished ketonuria (7–10), and (c) a diminished rate of acetone body utilization (Table I). The blood level of acetone bodies is dependent upon the difference between their rate of formation and their rate of excretion and destruction. Since the latter two are definitely diminished in the adrenalectomized animal, while the blood level is relatively unaffected, it becomes obvious that a similar decrease in the rate of acetone body formation must also occur. In other words, ketogenesis must definitely be diminished by adrenalectomy.

Of all the factors which have been studied with reference to their influence on acetone body utilization by the muscles, only one has been shown to be effective; viz., the metabolic rate. Thus it has been demonstrated that the administration of thyroxine and the consequent increase in metabolic rate are associated with a definite increase in the rate of acetone body utilization (13), whereas neither insulin nor glucose is similarly effective. Hence the converse is not improbable and any mechanism which will reduce the metabolic rate will be associated with a reduction in the rate of acetone body utilization. If that be the case, it is probable that the removal of the adrenals results in a decreased acetone body utilization in virtue of the general decrease in metabolic activity that ensues (14). Likewise it is probable that the reduced metabolism associated with adrenalectomy may produce a decrease in the rate of ketogenesis in spite of the fact that the adrenals per se are not essential for acetone body formation.

SUMMARY

Adrenalectomy produces a marked reduction in the rate of acetone body utilization.
It is probable that a similar reduction in the rate of acetone body formation occurs.

It is suggested that these changes are due to a general decrease in metabolic activity consequent to adrenalectomy.

BIBLIOGRAPHY

THE UTILIZATION OF ACETONE BODIES: III. THE INFLUENCE OF ADRENALECTOMY

Norton Nelson, Isabelle Grayman and I. Arthur Mirsky


Access the most updated version of this article at http://www.jbc.org/content/132/2/711.citation

Alerts:
• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 0 references, 0 of which can be accessed free at http://www.jbc.org/content/132/2/711.citation.full.html#ref-list-1