Effects of Hypophysectomy on Lactate Metabolism in the Perfused Rat Liver*

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SUMMARY

Various aspects of lactate metabolism were compared in perfused livers from normal and hypophysectomized rats. Glucose production by livers from hypophysectomized animals exceeded that by normal rat livers largely due to enhanced rates of lactate gluconeogenesis. When perfusion was carried out with a nonrecirculating medium containing physiological levels of lactate, the rate of glucose synthesis from labeled lactate by livers from hypophysectomized rats was 3 to 4 times that of normal rat livers. Saturating levels of lactate were 6 to 8 mM lactate for livers from hypophysectomized rats and 14 mM lactate for normal rat livers. At these levels, the rates of gluconeogenesis in both groups were similar. Over a range of lactate concentrations from physiological to saturating levels, the rates of conversion of lactate to CO₂, glycogen, protein, and fatty acids were reduced below normal in livers from hypophysectomized rats. In livers perfused with 1 mM lactate, tissue levels of pyruvate, P-enolpyruvate, 2-P-glycerate, 3-P-glycerate, and glucose-6-P were increased above normal by hypophysectomy. At saturating lactate concentrations, levels of gluconeogenic intermediates in livers from normal and hypophysectomized rats were similar. These data, in addition to the similar rates of total lactate utilization, indicated that hypophysectomy affected a redistribution of substrate among competitive metabolic pathways. It was suggested that at physiological levels of lactate a reduction of substrate oxidation led to an increased availability of substrate for gluconeogenesis.

The hepatic level of cyclic adenosine 3′:5′-monophosphate was unchanged following hypophysectomy, suggesting that the increased rate of gluconeogenesis was not due to an elevation in the concentration of this nucleotide. Livers from hypophysectomized rats did not appear to respond to conditions which elevate the tissue level of this nucleotide since an overnight fast, or perfusion with glucagon, had no effect on the rate of conversion of lactate to glucose.

Many studies have emphasized the key role of pyruvate metabolism in the regulation of gluconeogenesis. The portion of the gluconeogenic pathway between pyruvate and P-enolpyruvate was shown to involve carboxylation of pyruvate to oxaloacetate followed by conversion of this intermediate to P-enolpyruvate (1-4). In rat liver, the enzyme catalyzing the first of these two reactions, pyruvate carboxylase (EC 6.4.1.1) was found to be present primarily in the mitochondria, whereas the enzyme catalyzing the second reaction, P-enolpyruvate carboxykinase (EC 4.1.1.32), was found mainly in the cytoplasm (1, 5, 6). Since mitochondria were found to be impermeable to oxaloacetate, it was proposed that this intermediate was converted to malate, aspartate, and fumarate which diffused into the cytoplasm where they were converted to P-enolpyruvate by way of oxaloacetate (7-9). The first step in the alternative pathway of pyruvate metabolism, oxidation to acetyl coenzyme A, is catalyzed by the mitochondrial enzyme, pyruvate dehydrogenase (EC 1.2.4.1). Competition between pyruvate carboxylase and pyruvate dehydrogenase for a limited concentration of pyruvate would indicate that the relative activities of these two enzymes would be important in the regulation of gluconeogenesis from pyruvate.

The present study was undertaken in an attempt to define the changes in pyruvate metabolism which contribute to the increased gluconeogenesis observed in livers from hypophysectomized rats. The preceding paper (10) presented evidence that the rate of gluconeogenesis from various substrates, including alanine, pyruvate, glutamate, and aspartate, was increased substantially above normal in perfused livers from hypophysectomized rats. On the basis of these studies it was suggested that a shift in pyruvate metabolism, from oxidation toward glucose synthesis, would account in part for the increased rate of gluconeogenesis from substrates entering the pathway at the level of this intermediate. In the present experiments, livers from normal and hypophysectomized rats were perfused with various levels of [14C]lactate and the incorporation of label into glucose, glycogen, CO₂, protein, and fatty acids was determined. Tissue levels of intermediary metabolites and the rates of substrate utilization were determined. Lactate was used since it was a more stable isotopic substrate than pyruvate and was equally effective as a gluconeogenic precursor.

EXPERIMENTAL PROCEDURES

Animals—Normal and hypophysectomized male rats of the Wistar strain (Carworth Farms) weighing 100 to 125 g were
used as liver donors. The animals were fed ad libitum on regular laboratory chow except for one series of experiments where they were fasted for 18 to 22 hours prior to perfusion. Hypophysectomized rats were used 12 to 14 days following surgery and any that gained demonstrable weight during the postoperative period were discarded. In order to maintain weight parity, normal rats were used when they were 1 week younger than the hypophysectomized animals. The results were not affected by this age difference.

Liver Perfusion—The technique of liver perfusion was similar to that described by Mortimore (11) and details for the preparation of the basic perfusion medium were presented in the preceding paper (10). Specific additions to the basic medium are presented in the legends to the figures and tables. The medium was equilibrated with humidified O₂-CO₂ (95:5%) at 37° and was either recirculated or passed through the liver at a single time (“flow-through” experiments) at a flow rate of 7.2 ml per min. The initial volume of recirculating medium was 50 ml. Prior to and at specific intervals during perfusion, samples of medium were collected into chilled tubes, centrifuged, and aliquots of the perfusate plasma stored frozen for subsequent analyses. At the end of perfusion, with the pump still running, livers were rapidly removed and frozen in Wollenberger clamps at the temperature of liquid nitrogen (12). Prior to analysis livers were pulverized in a percussion mortar precooled to the temperature of liquid nitrogen and the powdered liver tissue stored at -70°C.

Analyses—Methods for the determination of glucose, [¹⁴C]glucose, [¹⁴C]CO₂, liver glycogen, and the incorporation of radioactive substrate into glycogen were given in the preceding paper (10). Gluconeogenic intermediate levels in perchloric acid extracts of livers perfused with the basic medium minus glucose were measured spectrophotometrically by standard enzymatic techniques outlined in Bergmeyer (13).

Lactate uptake in recirculation experiments was calculated by determining the concentrations of lactate in perfusate plasma before and after perfusion (14). In perfusions performed with nonrecirculated medium, lactate uptake was estimated by summing the quantity of substrate converted to glucose, CO₂, glycogen, and fatty acids in the individual livers. Conversion to these products would have accounted for approximately 90% of the total lactate utilized (15).

The conversion of radioactive substrate to fatty acids was determined by methods similar to those outlined by Exton (16). Weighed samples of frozen, powdered livers were digested in 5 ml of concentrated perchloric acid, heated for 15 min in a boiling water bath and washed twice with the same solution. The precipitated protein was homogenized in 0.5 ml of concentrated formic acid and plated on weighed stainless steel planchets. After formic acid was evaporated, the planchets were reweighed and the radioactivity determined in a Nuclear Chicago gas flow counter. Appropriate corrections were made for protein self-absorption (18).

In all cases, radioactive determinations were corrected for counting efficiency and quenching. Data from recirculation experiments are presented in terms of disintegrations per min per unit weight of tissue, while those from “flow-through” experiments are reported in terms of micrograms of substrate converted to the particular end product per g of tissue per min. This calculation for conversion of radioactive substrate to [¹⁴C]glucose was given in the preceding paper (10).

Chemicals—The sodium salt of dl-[2-¹⁴C]lactic acid (specific activity 36.5 mCi per mmole) was obtained from Amersham-Searle. Sodium L(+)-lactic acid was obtained as a 40% solution from Schwarz-Mann Research Laboratories. Enzymes used to measure glycolytic intermediates were from either Boehringer Mannheim or Sigma Chemicals. All other laboratory chemicals were of standard reagent grade.

Statistics—Data are presented as the average of a specified number of observations ±1 S.E. Statistical differences between means were tested by the Student t test. p values are presented only when a statistically significant difference has been established.

RESULTS

In livers perfused with lactate as substrate, the effects of hypophysectomy on net glucose production were similar to those observed when amino acid substrates were used (10). As can be seen in Table I, livers from hypophysectomized rats produced more than twice as much glucose as livers from normal rats when perfused for 60 min with recirculating medium containing L-lactate at an initial concentration of 10 mM. To confirm that a significant portion of this glucose was formed from lactate, the conversion of [¹⁴C]lactate to [¹⁴C]glucose was measured during these perfusions. An increased rate of gluconeogenesis from lactate was indicated by the fact that [¹⁴C]glucose synthesis by livers from hypophysectomized rats was twice that by control livers.

Table I

Effect of hypophysectomy on glucose metabolism in livers perfused with lactate as substrate

Livers from normal and hypophysectomized rats were perfused for 60 min with a recirculated medium containing L(+)-lactic acid at an initial concentration of 10 mM and dl-[2-¹⁴C]lactic acid at a concentration of 0.02 μCi per ml. Mean values ± 1 S.E. are presented.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Condition of liver donor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>Net glucose production (μmoles/g/hr)</td>
<td>30.89 ± 2.22 (17)</td>
</tr>
<tr>
<td>[¹⁴C]Glucose production (μpmol/g/hr)</td>
<td>56,836 ± 2,678 (34)</td>
</tr>
<tr>
<td>Final glycogen content (μmoles of glucose/g)</td>
<td>253 ± 15 (17)</td>
</tr>
<tr>
<td>Lactate uptake (μmoles/g/hr)</td>
<td>69.4 ± 3.5 (11)</td>
</tr>
</tbody>
</table>

a Indicates the number of observations.

b Differs from normal by p < 0.001.
The contribution of glycogenolysis to the increased glucose production was determined by measuring tissue glycogen levels before and after perfusion. Following 60 min of perfusion the glycogen content of livers from normal rats was decreased by 59 μmoles of glucose per g (initial glycogen content was 312 ± 13 μmoles of glucose equivalents per g of liver), while levels in livers of hypophysectomized rats were decreased by 16 μmoles of glucose per g (initial glycogen content was 158 ± 30 μmoles of glucose equivalents per g of liver). These data excluded the possibility that glycogenolysis was a major contributor of the increased glucose production seen in perfused livers from hypophysectomized rats.

Although the increased rate of gluconeogenesis from amino acids following hypophysectomy was associated with an increased uptake of these compounds (10), the increased production of glucose from lactate seen in perfused livers from hypophysectomized rats did not appear to result from an increased uptake of this substrate (Table I). In these experiments, the uptake of lactate by livers from hypophysectomized rats tended to be greater but was not significantly different than that by livers from normal rats. This observation implied that total hepatic lactate utilization was unaffected, while its flux through the pathway of gluconeogenesis was quantitatively increased following hypophysectomy.

In experiments similar to those described in Table I, it was observed that raising the initial lactate concentration from 10 to 20 mM had little effect on the conversion of lactate to glucose by livers of hypophysectomized rats, but increased that by normal rat livers by 72%. This observation suggested that substrate availability for glucose production became limiting for normal rat livers during perfusion with a recirculated medium, while such a restraint was not apparent for livers of hypophysectomized rats. When livers were perfused with a recirculated medium, substrate was continually consumed and the perfusate composition was constantly changing. During 60 min of perfusion with recirculating medium the lactate concentration fell from an initial value of 10 mM to 2.8 ± 0.1 and 3.1 ± 0.2 mM in experiments with livers from normal and hypophysectomized rats, respectively. In order to maintain perfusate lactate concentrations at constant levels, the remaining experiments were performed with a nonrecirculated medium.

A nonrecirculated medium containing L(+)-lactic acid at varying concentrations was used to monitor the activities of various metabolic pathways utilizing this substrate. It can be seen in Fig. 1 that the rate of [14C]glucose synthesis from [14C]lactate increased as a function of the perfusate lactate concentration. Livers from hypophysectomized rats converted 3 to 4 times as much lactate to glucose as did normal rat livers when both were perfused with medium containing lactate concentrations within a physiological range of 1 to 4 mM. In livers from hypophysectomized rats the activity of the gluconeogenic pathway reached a maximum rate at 6 to 8 mM lactate, while for normal rat livers the apparent saturation level was attained at 14 mM lactate. The maximum rate of flux through the gluconeogenic pathway appeared to be similar in both groups, being 1.05 and 0.90 μmole of lactate converted to glucose per g per min in livers of normal and hypophysectomized rats, respectively. Half-saturation of the pathway in livers from hypophysectomized rats was reached at a lactate concentration of approximately 2 mM, while that in normal rat livers was reached at 7 mM. These data indicated that at physiological concentrations of lactate in the perfusate, flux through the gluconeogenic pathway in livers of hypophysectomized rats was greater than that in control livers, but the total capacity of the pathway in both groups was similar.

Fig. 2 shows the effects of hypophysectomy on lactate oxidation in the perfused rat liver. Similar to the data obtained with alanine and pyruvate (10), the rate of lactate oxidation by livers from hypophysectomized rats was significantly less than that by normal rat livers at all perfusate concentrations of lactate that were studied. As can be seen, conversion of labeled lactate to 14CO2 by the experimental livers was only 44 to 81% of the control rate, although the difference diminished with increasing perfusate lactate levels.

Shown in Table II are the effects of hypophysectomy on the conversion of lactate to fatty acids, protein, and glycogen under...
Effect of hypophysectomy on conversion of [14C]lactate to fatty acids, protein, and glycogen in perfused rat liver

Livers from normal and hypophysectomized rats were perfused as described in the legend to Fig. 1. Each value represents the mean of three to eight observations ± 1 S.E.

<table>
<thead>
<tr>
<th>Parameter measured and liver donor</th>
<th>Conversion of [14C]lactate to fatty acids, protein, and glycogen with perfusate lactate concentration at</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mm</td>
</tr>
<tr>
<td>Fatty acid</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>12.53 ± 1.47</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>1.40 ± 0.33a</td>
</tr>
<tr>
<td>Protein</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>26.00 ± 0.67</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>14.27 ± 0.53a</td>
</tr>
<tr>
<td>Glycogen</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>14.20 ± 1.03</td>
</tr>
<tr>
<td>Hypophysectomized</td>
<td>10.12 ± 0.06a</td>
</tr>
</tbody>
</table>

* a Differs from normal by p < 0.005.
* b Differs from normal by p < 0.05.
* c Differs from normal by p < 0.01.

Effect of hypophysectomy on levels of gluconeogenic and citric acid cycle intermediates in livers perfused with 1 mM lactate

Livers from normal and hypophysectomized rats were perfused as described in the legend to Fig. 1 except that glucose was omitted from the basic perfusion medium. Each value represents the mean of 5 to 10 observations ± 1 S.E. DHAP is an abbreviation for dihydroxyacetone phosphate.

<table>
<thead>
<tr>
<th>Parameter measured</th>
<th>Normal</th>
<th>Hypophysectomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td>1410 ± 60</td>
<td>1401 ± 120</td>
</tr>
<tr>
<td>Pyruvate</td>
<td>205 ± 10</td>
<td>234 ± 8a</td>
</tr>
<tr>
<td>P-enolpyruvate</td>
<td>119 ± 8</td>
<td>160 ± 6b</td>
</tr>
<tr>
<td>2-P-glycerate</td>
<td>71 ± 4</td>
<td>89 ± 4c</td>
</tr>
<tr>
<td>3-P-glycerate</td>
<td>58 ± 5</td>
<td>124 ± 15b</td>
</tr>
<tr>
<td>DHAP</td>
<td>107 ± 5</td>
<td>105 ± 8</td>
</tr>
<tr>
<td>Fructose-Ps</td>
<td>26 ± 2</td>
<td>25 ± 1</td>
</tr>
<tr>
<td>Glucose-6-P</td>
<td>33 ± 3</td>
<td>51 ± 4d</td>
</tr>
<tr>
<td>Acetyl-CoA</td>
<td>53 ± 2</td>
<td>24 ± 2e</td>
</tr>
<tr>
<td>Citrate</td>
<td>296 ± 36</td>
<td>127 ± 19f</td>
</tr>
</tbody>
</table>

* a Differs from corresponding normal value by p < 0.05.
* b Differs from corresponding normal value by p < 0.01.

These studies indicated that at physiological levels of lactate the amount of substrate available for gluconeogenesis was enhanced in livers of hypophysectomized rats as a result of diminished activity of alternative metabolic pathways. If this were the case, the increased gluconeogenic flux should be associated with increased levels of intermediates in the pathway. The steady state levels of gluconeogenic intermediates in livers perfused with a nonrecirculated medium containing 1 mM lactate are shown in Table IV. The finding that tissue levels of pyruvate, P-enolpyruvate, 2-P-glycerate, 3-P-glycerate, and glucose...
of gluconeogenesis in livers from hypophysectomized rats, while it more than doubled the rate in normal rat livers. In experiments with saturating concentrations of lactate in the perfusing medium, fasting of the normal but not the hypophysectomized animal induced an even faster rate of gluconeogenesis.3 In other studies, glucagon added in vivo had no effect on the rate of gluconeogenesis when livers from hypophysectomized rats were perfused with a recirculating medium containing 10 mM lactate ([14C]glucose production from labeled lactate was 116,103 ± 6,741 and 120,006 ± 5,262 dpm per g of liver per hr for hypophysectomized and hypophysectomized plus glucagon, respectively). Others have observed, that the rate of gluconeogenesis in livers of hypophysectomized rats did not respond to direct addition of cyclic AMP to the perfusing medium (26). Taken together, these data indicated that the rate of gluconeogenesis in livers from hypophysectomized rats did not respond to conditions which alter tissue levels of cyclic AMP.

**DISCUSSION**

The present results confirm the conclusions of the preceding paper (10) that livers from hypophysectomized rats exhibit a greatly stimulated rate of gluconeogenesis when they are perfused with medium containing limiting concentrations of substrate. Precursor availability for gluconeogenesis in the liver is dependent both on the amounts of substrate supplied to the liver and on the relative activities of the pathways utilizing the substrate. Increased formation of glucose, excluding glycogenolysis, could result from a direct stimulation of the gluconeogenic pathway per se or could be the more indirect consequence of redistribution of substrate away from competing pathways. The first alternative has been shown to be true in the perfused rat liver. Glucaen infusion rapidly stimulated the conversion of [14C]lactic acid to [14C]glucose and increased lactate uptake (27). Mallette et al. (28, 29) have observed similar effects of glucagon on amino acid gluconeogenesis. The conclusions of these studies were that glucagon directly stimulates the gluconeogenic pathway resulting in an increased total utilization of substrate. Many factors which directly stimulate the pathway of gluconeogenesis appear to affect the portion of the pathway between pyruvate and P-enolpyruvate. As measured in tissue homogenates, the activities of pyruvate carboxylase and phosphoenolpyruvate carboxykinase changed in direct relation to gluconeogenic activity. The enzyme activities were increased under conditions such as fasting and diabetes (30, 31). In the thyroxinectomized rat, when glucose formation was diminished, the activities of the enzymes were diminished (32). Pyruvate carboxylase activity has been found to be subject to allosteric activation by acetyl-CoA (2) and, thus, might be expected to be high at times when levels of acetyl-CoA within liver were rapidly replenished by β-oxidation of fatty acids. It has been proposed that the stimulation of gluconeogenesis by fatty acids is related to this mechanism (33). Based on analyses of glycolytic intermediate levels, Exton and Park (34, 35) have indicated that the site of stimulation by glucagon, catecholamines and cyclic AMP is located between pyruvate and P-enolpyruvate.

Enhanced glucose formation also could result from an increased availability of precursor consequent to diminished utilization through other pathways. The data presented here suggested that this mechanism primarily accounted for the increased rates of lactate gluconeogenesis observed in perfused livers from hypophysectomized rats. This conclusion was deduced from several observations. These include: (a) total lactate utiliza-

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1 The abbreviation used is: cyclic AMP, cyclic adenosine 3':5'-monophosphate.

2 The cyclic AMP assays were kindly performed by Dr. David R. Wade (College of Medicine, Pennsylvania State University).
tion was similar in livers from both normal and hypophysecto-
mized rats; (b) the conversion of lactate to products beyond
pyruvate which depended on the oxidation of substrate, e.g.
CO₂, acetoacetate, and fatty acids, was significantly impeded
in livers from hypophysectomized rats; (c) in perfusions with 1
mM lactate, acetyl-CoA concentrations were reduced in livers
from hypophysectomized rats; (d) incorporation of lactate into
protein was inhibited by hypophysectomy; (e) in perfusions
with 1 mM lactate, gluconeogenic intermediates at the beginning
of the pathway were increased following hypophysectomy; and
(f) in perfusions with saturating levels of lactate the equivalent
rates of gluconeogenesis and the similar levels of gluconeogenic
intermediates in livers from normal and hypophysectomized rats
indicated that the total capacity of the pathway was unaffected
by hypophysectomy.

This redistribution of substrate away from alternative path-
ways would be consistent with a decrease in the activity of the
pyruvate dehydrogenase reaction. The fact that pyruvate de-
hydrogenase activity is subject to both metabolic and hormonal
control, suggests that the enzyme could play a key role in the
regulation of intermediary metabolism. The activity of this
enzyme has been shown to be diminished in heart and kidney of
fasted and diabetic rats (36). In adipose tissue, pyruvate de-
hydrogenase activity was activated by insulin and inhibited by
epinephrine (37, 38). Garland and Randle (39) and Reed et al.
(40, 41) have demonstrated that pyruvate dehydrogenase is
inhibited by high levels of acetyl-CoA and NADH and is inac-
tivated by phosphorylation catalyzed by an ATP-specific protein
kinase. The apparent Kᵢ for acetyl-CoA in heart was found to
be 12.5 μM or 40% above the estimated heart acetyl-CoA levels
(39). Accurate measurements of the kinetic properties of pyru-
vate dehydrogenase in liver have not been reported.

If these same types of controlling mechanisms can be extrapo-
lated to liver pyruvate dehydrogenase, this enzyme can be as-
signed an important role in the regulation of gluconeogenesis.
Epinephrine has been shown to stimulate and insulin inhibit
the gluconeogenesis in liver (25, 27). Hepatic acetyl-CoA and
NADH levels were increased under conditions in which gluco-
neogenesis was stimulated (33, 42). Most studies on the regula-
tion of gluconeogenesis in liver have been done at saturating sub-
strate levels. Under more physiological conditions, i.e., at lim-
iting substrate availability, an inhibition of pyruvate dehydro-
genase would allow more pyruvate to be available to the gluco-
neogenic pathway leading to an increased production of glucose.
Other studies concerned with stimulated gluconeogenesis have
failed to rule out the possibility of decreased pyruvate oxidation
and increased availability of substrate as a contributory factor.
It is interesting to note that Exton and Park (35) have observed
that lactate gluconeogenesis in livers from fasted animals was
saturated at approximately 4 mM, whereas, in the present study
under similar conditions, 14 mM lactate was required to saturate
the pathway in livers from fed animals. This suggested a greater
capacity of alternative pathways to utilize lactate in livers
from fed animals. It is apparent that pyruvate dehydrogenase
activity could be an important determinant of the direction of
pyruvate metabolism. Under conditions of adequate carbo-
hydrate supply, such as glucose refeeding, high pyruvate de-
hydrogenase activity could result in an enhanced formation of
acetyl-CoA required by the stimulated rates of hepatic lipo-
genesis (43). When glucose supply is limited, as in fasting, a
reduction in the activity of this enzyme could result in the re-
distribution of available substrate to gluconeogenesis. No at-
tempt was made to directly study the activity of pyruvate de-
hydrogenase in the present experiments, although the possibility
of an inhibition in livers of hypophysectomized rats must be
investigated.

The situation of elevated rates of gluconeogenesis in livers of
hypophysectomized rats raises many questions about "traditional"
control mechanisms. Many of the usual stimuli for gluco-
geogenesis are missing in this animal. Adrenocortical atrophy followed hypophysectomy (44) and one would expect
circulating levels of the glucocorticoids to be diminished. These
hormones have a permissive effect on hepatic gluconeogenesis
and their presence was required for the effects of glucagon on
this process (45). Fatty acids have been shown to stimulate
gluconeogenesis in the perfused rat liver (23). This has been
attributed to an increased β oxidation of fatty acids leading to
enhanced supplies of acetyl-CoA and NADH. Both the ability
to mobilize depot fat and plasma fat levels were reduced by
hypophysectomy (24, 46). It is interesting to note that Has-
selblatt et al. (41) reported increased rates of amino acid gluco-
geogenesis in livers from rats treated with an antilipolytic agent.
They have demonstrated that the gluconeogenic capacity of
this tissue was unaffected and that the increase flux through the
pathway occurred in the absence of a stimulation of a specific step
between pyruvate and glucose.

Thus it appears that hypophysectomy represents an unique
situation in the understanding of the gluconeogenic process.
Many of the reported stimuli and permissive agents are missing
or deficient, but liver from fed hypophysectomized rats main-
tains the capacity for greater than normal rates of gluconeogene-
sis. This effect, observed when livers were perfused with physi-
ological levels of lactate, resulted from a redistribution of sub-
strate away from oxidative and protein-synthetic pathways
making more available for glucose formation.

REFERENCES

787-802
PC17-PC18
2603-2608
2259-2263
113-119
63, 1410-1415
Chem. 241, 2523-2532
787-802
2259-2263
Menschen Tier 270, 399-412
Academic Press, New York
Academic Press, New York
Chem. 247, 4966-5003
chem. J. 96, 289-290
439-441
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