the administration of synthetic oestrogen in the form of the contraceptive hormone ethynyl-oestradiol slightly increased the folic acid transported by mechanisms other than solvent drag. Pregnancy, a condition associated with elevated oestrogen concentrations (Shaikh, 1971), did not have a similar effect. Ovariectomy, which in common with the menopause is accompanied by low oestrogen concentrations (Labbsetwar, 1972; Saez et al., 1972), resulted in the greatest decrease in folic acid transfer, it being significant compared with that in male rats. This decrease was valid both when considering maximal transfer and also when solvent drag of folic acid was accounted for. Furthermore, the decrease in folic acid transfer was corrected towards normal when the replacement-therapy-hormone oestradiol was administered to ovariectomized rats. It is apparent from the present study that oestrogen does not affect folic acid transfer to any great extent. However, endocrine systems are complex, and both ovarian hormones and contraceptive steroids may have various subtle indirect effects on both the structure and function of the intestine. In this respect, the minor decreases in folic acid transfer observed in this strictly physiological study could over a prolonged period of time contribute to the development of folate deficiency.

We thank Professor J. A. Blair and Dr. C. J. Bailey for their interest in this study.


Loranne Agius and Dermot H. Williamson

Metabolic Research Laboratory, Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, U.K.

The rate of lipogenesis in non-shivering thermogenesis during cold exposure is well established (Foster & Frydman, 1979). During prolonged cold treatment, the rate of lipogenesis in vivo measured with "H2O increased severalfold in the rat (Trayhurn, 1979) and mouse (Rath et al., 1979). This increased rate was dependent not on the food intake but on the relative temperature change to which the mice were exposed (Rath et al., 1979). The importance of lipogenesis in thermogenesis has not been established, though it was suggested that the newly synthesized fatty acids may be subsequently oxidized.

Brown adipose tissue may be an important site of dietary-induced thermogenesis (Rothwell & Stock, 1979). This has been defined as the increased heat production induced by overeating for long periods (Himms-Hagen, 1979). However, although implicated in the "burning off" of excess food, the effects of a meal on brown-fat metabolism have not been documented. McCormack & Denton (1977) found that glucose administration to cold-adapted rats increased brown-fat lipogenesis, and this was prevented by anti-insulin serum. In the present study we have measured the rate of lipogenesis in vivo by using "H2O in the liver, white and brown adipose tissue (inter-scapular) in rats fed ad libitum and 60 min after giving an intragastric glucose load (2 mmol/100 g body wt.) to virgin and lactating rats. We chose the lactating rat for comparison because it becomes hyperphagic to meet the substrate requirements of the mammary gland. Thus, if brown fat is involved in the burning-off of excess food, it might respond differently to a glucose load during lactation.

In rats fed ad libitum, brown-adipose-tissue lipogenesis was 57% lower (on a fat-free-weight basis) in the lactating rat than in the virgin rat, but it increased 6-fold when the pups were removed (for 24 h) and the tissue weight increased by 35% (135%) in the lactating rat than in the virgin rat. After the load of glucose, hepatic lipogenesis was significantly (P < 0.025) increased in both the virgin (135%) and the lactating rat (62%). Brown-adipose-tissue lipogenesis was increased 8-fold (P < 0.0005) in the virgin rat, but showed no significant change in the lactating and weaned rats (Fig. 1). In the virgin rat after glucose treatment, brown-adipose-tissue lipogenesis was 10-fold higher than in liver and white adipose tissue, but in the lactating rat it was 41% lower.

The rate of lipogenesis in vivo was measured with "H2O as described by Robinson et al. (1978) in virgin, lactating and weaned (24 h) rats. fed ad libitum (CL), at 60 min after an intragastric glucose load (GB), and at 60 min after a subcutaneous injection of 2 units of insulin (II). The results are mean values with bars to indicate S.E.M. (n = five or six rats).

Fig. 1. Effects of a glucose load and insulin on brown-adipose-tissue lipogenesis in virgin, lactating and weaned rats

Brown adipose tissue to an oral glucose load in virgin and lactating rats

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Response of brown adipose tissue to an oral glucose load in virgin and lactating rats

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White adipose-tissue lipogenesis showed a similar response to that of brown fat after glucose and insulin treatment in the three conditions, though the rates were severalfold lower in white adipose tissue.

The differences in the basal lipogenesis in brown fat in the virgin, lactating and weaned states may be related to the plasma insulin concentration. Plasma insulin decreases during lactation (Robinson et al., 1978), but increases on weaning (Agius et al., 1979), and brown-adipose-tissue lipogenesis shows a similar pattern. The failure of glucose to elicit the same increase in lipogenesis during lactation as insulin suggests either that the insulin response to a glucose load may be decreased during lactation and weaning or that brown fat has a decreased sensitivity to insulin.

The fate of the newly synthesized fatty acids in brown adipose tissue after a glucose load is not known. However, if the newly synthesized lipids are catabolized within the tissue, the decreased rate of lipogenesis during lactation may be important in the direction of substrates to the mammary gland by preventing the ultimate oxidation of lipogenic precursors in brown fat.

This work was supported by the Medical Research Council and by the U.S. Public Health Service (grant no. AM-11748). L. A. is a Commonwealth Scholar and D. H. W. is a member of the External Staff of the Medical Research Council (U.K.).

A second site of vasopressin action on [1-14C]oleate metabolism in isolated rat hepatocytes: Increased formation of 14CO2

MARY C. SUGDEN, ALISON J. BALL and DERMOT H. WILLIAMSON

Metabolic Research Laboratory, Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, U.K.

Vasopressin increases conversion of oleate into esterified products in hepatocytes from fed rats and decreases ketogenesis (Williamson et al., 1980). The present communication indicates that, in addition to this cytoplasmic action of vasopressin, the hormone may act on intramitochondrial side(s), namely increased 14CO2 production from [1-14C]oleate. The increased 14CO2 production is dependent on the presence of Ca2+ ions in the incubation medium. Hepatocytes were prepared from fed female rats as described by Williamson et al. (1980). The incubation procedure and measurements of 14CO2 production from labelled substrates were as described by Whitelaw & Williamson (1977). Rates were calculated from plots of the values at 20, 40 and 60 min.

In the presence of extracellular Ca2+ (2.4 mM), addition of vasopressin to hepatocytes from fed rats increased oxidation of [1-14C]oleate to 14CO2 by 54% (Table 1). Vasopressin also increased 14CO2 production from [U-14C]proline (Table 1). Increased 14CO2 production from [U-14C]proline was observed in both the presence and the absence of unlabelled oleate (1 mM), but the stimulation was greater in the former case (47% versus 21%; see Table 1). The increased 14CO2 production from either [1-14C]oleate or [U-14C]proline was markedly decreased when Ca2+ was omitted from the incubation medium (Table 1).

Vasopressin causes a transient stimulation of the O2 uptake of perfused livers from fed rats (Hems et al., 1978). The data presented here suggest that this may be a consequence of increased oxidation of tricarboxylic acid-cycle intermediates to CO2 in the presence of vasopressin. Thus the oxidation to CO2 of both oleate (which is metabolized to acetyl-CoA) and proline (which is metabolized via glutamate to 2-oxoglutarate) was increased by vasopressin. Increased oxidation of oleate to CO2 may also contribute to the observed inhibition by vasopressin of ketone-body production from oleate (Williamson et al., 1980).

The mechanism by which vasopressin increases 14CO2 production from [1-14C]oleate and [U-14C]proline is not known. Such increases might result from increased tricarboxylic acid-cycle turnover. If tricarboxylic acid-cycle turnover is inhibited by β-oxidation of long-chain fatty-acyl-CoA to acetyl-CoA (possibly by competition for electron acceptors), then the effects of vasopressin on 14CO2 production might be explained by relief of this inhibition. This might arise as a consequence of stimulation of respiratory chain activity. Such a mechanism might explain why the effects of vasopressin on [U-14C]proline oxidation are less marked in the absence of Ca2+.

Table 1. Effects of vasopressin on [1-14C]oleate and [U-14C]proline conversion into 14CO2 in hepatocytes from fed rats in the presence and absence of Ca2+

The [1-14C]oleate concentration was 1 mM and the [U-14C]proline concentration was 5 mM. The results are mean values ± S.E.M. with the numbers of experiments in parentheses. Oleate oxidation is expressed as µmol of oleate oxidized/min per g wet wt. of cells. Proline oxidation is expressed as µg-atoms of proline C oxidized/min per g wet wt. of cells. Values that are significantly different from those obtained in the absence of vasopressin are indicated by: *P<0.025; **P<0.0005.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Oleate (1mM)</th>
<th>Proline (5mM) + oleate (1mM)</th>
<th>Proline (5mM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>-CaCl2</td>
<td>0.036 ± 0.003</td>
<td>-CaCl2</td>
</tr>
<tr>
<td></td>
<td>+CaCl2</td>
<td>0.037 ± 0.004</td>
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<td></td>
<td>(4)</td>
<td>(14)</td>
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<td>Vaso. (10mM)</td>
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<td>0.057 ± 0.005**</td>
<td>1.03 ± 0.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(14)</td>
<td>(14)</td>
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