Trabajo realizado por el equipo de la Biblioteca Digital de CEU-Universidad San Pablo

Me comprometo a utilizar esta copia privada sin finalidad lucrativa, para fines de investigación y docencia, de acuerdo con el art. 37 de la M.T.R.L.P.I. (Modificación del Texto Refundido de la Ley de Propiedad Intelectual del 7 julio del 2006)
enzyme appeared practically inactive in the same conditions (Table 1). This different inhibitory effect of pyrazole in the two species was also observed with a concentration of 200 µM (Table 1), which produced a partial inhibition of the human enzyme and complete inhibition of the rat enzyme. These findings demonstrate that human, but not rat, liver contains a pyrazole-insensitive activity. The presence of pyrazole-insensitive alcohol dehydrogenase activity in human liver has been reported in another study (Li et al., 1977), and, since it exhibits a high K_m for ethanol, it may influence the ethanol-elimination rates in vivo when blood ethanol concentrations are very high. Present results indicate that this pyrazole-insensitive activity is absent from rat liver. At the same time, the lower enzyme activity and V_max values found for rat liver alcohol dehydrogenase indicate that in this species the enzyme system becomes saturated at lower ethanol concentrations than in humans, which would favour either its greater elimination in unoxidized form or its greater transformation through the alternate pathway, e.g., the microsomal ethanol oxidizing system (Orme-Johnson & Ziegler, 1965) and/or catalase (De Duve & Bauduin, 1966). This question is as yet unresolved, and the species-specific effects described should be considered when using the rat as an experimental model for alcohol effects in humans.

This study was performed with a grant from the Comisión Asesora de Investigación Científica y Técnica, Ministerio de Educación y Ciencia, Spain. We are grateful to J. J. P. Warburg for giving us the details for the alcohol dehydrogenase assays, to Milagros Morante for her excellent technical assistance and to Carlene S. Delgado for her editorial help.


Liver glycogen and glyceroide glycerol formation as compared with glucose synthesis in 24-h starved virgin and pregnant rats

ANTONIO ZORZANO and EMILIO HERRERA
Departmento de Investigación, Centro Ramón y Cajal, Ctra. Colmenar Km. 9, Madrid 34, Spain

Enhanced liver glucose production during starvation is initially sustained by augmented glycogenolysis, which causes a rapid decrease in glycogen stores (Herrera & Freinkel, 1968; Phan et al., 1974). An increase in liver gluconeogenesis also occurs soon after the onset of starvation (Schimmel & Knobil, 1970; Llobera & Herrera, 1980), not only contributing to the net glucose release by the liver but avoiding complete depletion of its glycogen content. In this way, liver glycogen synthesis in starvation represents a gluconegeneic process. A similar mechanism seems to occur in the synthesis of glyceroide glycerol from gluconeogenic substrates, which is also enhanced with starvation (Soley et al., 1983). To determine whether there is a constant relation between the synthesis of either liver glycogen or glyceroide glycerol and glucose production independent of the gluconeogenic substrate used, in the present work we administered intravenously 1 µCi of [U-14C]alanine, [3-14C]pyruvate or [U-14C]glycerol (from The Radiochemical Centre, Amersham, Bucks., U.K.) containing 0.2 mmol/200 g body wt. to 24-h starved virgin rats. As gluconeogenesis is known to be greatly increased during starvation at late gestation in the rat (Herrera et al., 1969), the same experiment was performed in 24-h starved 21-day pregnant rats, to determine also whether differences in the gluconegeneic activity alter such relations. Animals were decapitated 10 min after injection and blood [14C]glucose, liver [14C]glycogen and [14C]glyceride glycerol were purified and determined as described elsewhere (Herrera et al., 1969; Chaves & Herrera, 1980; Carmanii & Herrera, 1980). As shown in Table 1, the ratio of liver [14C]glycogen to blood [14C]glucose, corrected to 200 g body wt., was the same with all three substrates and in both pregnant and virgin animals. The ratio of liver [14C]glyceroide glycerol to blood [14C]glucose was always higher than that of [14C]glyceride glycerol to [14C]glucose and, although values did not differ among substrates, they were consistently higher for pregnant than for virgin animals.

The present results show that in the starved condition there is a constancy in the proportional amount of newly synthesized glucose which is converted into liver glycogen or released to

Table 1. Ratios of liver [14C]glycogen or [14C]glyceride glycerol to circulating [14C]glucose synthesized from gluconeogenic substrates in the 24-h starved virgin or 21-day-pregnant rat

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rats ...</td>
<td>Virgin</td>
<td>Pregnant</td>
</tr>
<tr>
<td>[U-14C]Alanine</td>
<td>0.44 ± 0.05</td>
<td>0.24 ± 0.05</td>
</tr>
<tr>
<td>[3-14C]Pyruvate</td>
<td>0.55 ± 0.07</td>
<td>0.62 ± 0.05</td>
</tr>
<tr>
<td>[U-14C]Glycerol</td>
<td>0.42 ± 0.07</td>
<td>0.54 ± 0.13</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>Virgin</td>
</tr>
<tr>
<td></td>
<td>2.23 ± 0.45</td>
<td>6.99 ± 0.59</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2.64 ± 0.25</td>
<td>5.60 ± 0.41</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>2.90 ± 0.31</td>
<td>7.57 ± 1.22</td>
</tr>
</tbody>
</table>

1983
circulation, and this process seems to be independent of the administered substrate. Since glycogen stores remain low in spite of parallel enhancement of liver glycogenolysis and glucogenesis with starvation, it may be proposed that in this condition a considerable proportion of glucogenic substrates is initially transformed to liver glycogen, which becomes a direct precursor of circulating glucose. Enzymic conditions for maintaining simultaneous enhancement of liver glycogenolysis and glycogenolysis have been identified in the starved rat liver (Roach & Larner, 1976; Hems & Whitton, 1980). This persistent futile cycle in the presence of increased glucogenesis may have two main functions: (i) to ensure maintenance of a permanent minimum glycogen content in liver, which is replenished as primer, and (ii) to allow rapid recovery of glycogen stores whenever food is available after starvation while glucogeneses is still augmented.

Formation of glyceride glycerol from glucogenic substrates may be facilitated in the starved condition by the cytosolic redox state of the liver (Lindall & Lazarow, 1964; Williamson et al., 1967; Berdanier et al., 1979) facilitating esterification of incoming fatty acids. This hypothesis is supported by the augmented proportional formation of 14C-glyceride glycerol from the administration of tracers in the starved, late-pregnant rat (Table 1), where it is known that lipolysis is greatly enhanced (Leat & Ford, 1966; Knopp et al., 1970), inducing the liver to increase its contribution of glucogenic substrates for the synthesis of glyceride glycerol. This explanation also coincides with the fact that liver is the main receptor site of unesterified fatty acids released from adipose tissue by lipolysis (Mampel et al., 1981), which is known to be enhanced in the starved condition (Schimmel & Knobil, 1970). Esterification of fatty acids in liver also changes proportionally according to fatty acids availability (Debeer et al., 1981); thus deviation of glucogenic intermediates to glyceride glycerol formation in the starved condition accounts for the temporary esterification of the incoming fatty acids in the liver.

This study was supported in part by a grant from the Fondo de Investigaciones Sanitarias de la Seguridad Social of Spain. We thank Caroline S. Delgado for her editorial help.


Transfer from mother to foetus of L-alanine and glycerol in fed and 48 h-starved pregnant rats

In the present study, L-1U-14C]alanine and [U-14C]glycerol were used as tracers, since they cross the placenta by different mechanisms: the first by active transport against a gradient (Hill & Young, 1973), and the second by diffusion in favour of the gradient (Gilbert, 1977). It is also known that circulating concentrations of these maternal metabolites are affected conversely by starvation: L-alanine decreases (Girard et al., 1977), glycerol increases (Girard et al., 1977). As shown in Table 1, 20 min after infusion of L-1U-14C]alanine through the left uterine artery, total radioactivity in plasma of foetuses from the left uterine horn was much greater than in their mothers, whereas radioactivity in plasma of foetuses from the right side was significantly lower than in the mother's plasma or in foetuses from the left side. These results confirm previous findings (Hill & Young, 1973) and indicate that, whereas plasma radioactivity in foetuses from the left side corresponds to the direct transfer of L-1U-14C]alanine infused through the left uterine artery, plasma radioactivity present in the foetuses from the right side results from dilution of the tracer in the maternal circulation. When the same experiment was conducted in pregnant rats after 48 h of starvation, the radioactivity present in plasma of foetuses from the left uterine horn did not differ from that in foetuses from the same side in fed mothers (Table 1). There was, however, a significant increase in total plasma radioactivity in foetuses from the right side in starved as compared with fed mothers. This difference parallels the increased plasma radioactivity in the 48 h-starved as compared with the fed mothers (Table 1); thus the ratio of plasma radioactivity in mothers and their foetuses remained unchanged in both fed and starved conditions. The present results indicate that maternal-foetal transfer of L-alanine is not affected by starvation, and any change in the availability of this amino acid

Vol. 11