TNBS derivatives. The base-exchange enzyme is apparently closely linked to a translocation mechanism phospholipids are in the cisternal leaflet of the bilayer (Fig. 1a). Consistent with this, the specific activities of the labelled PS and PE were more than 6-fold greater than those of the TNBS derivatives. The base-exchange enzyme is apparently closely linked to a translocation mechanism so that newly synthesized PS is rapidly transferred to the cisternal leaflet where it is decarboxylated to form PE, which is also retained in the cisternal leaflet.

Using phospholipase C as a probe (Higgins, 1979), we found that none of the PC formed via the serine base-exchange pathway was available for hydrolysis by phospholipase C. Under the same conditions, approximately half of the total phospholipids and 85% of the total PC were hydrolysed. The specific activity of the cisternal leaflet PC was more than 400 times that of the cytosolic leaflet PC. This is in contrast to our previous finding that PC formed by the CDP-choline pathway is retained in the cytosolic leaflet (Higgins, 1979). PC synthesized by different pathways therefore have different locations and the pools of PC on either side of the bilayer do not equilibrate.

Incorporation of $^3$H-serine into very low density lipoprotein secreted by isolated hepatocytes

When isolated hepatocytes were incubated with $^3$H-serine, the labelled base was incorporated into the cell PS, reaching a peak after 30 min. PE was labelled more slowly and very little label appeared in the cell PC after 90 min incubation. There was no significant secretion of phospholipid for the first 60 min of incubation and after this lag period only PC was labelled to any significant extent (Fig. 1b). The specific activity of secreted PC was more than four times that of the cell PC. Serine is therefore selectively incorporated into secreted PC rather than cell PC.

These observations indicate that PS formed by base exchange in the c.e. is selectively channelled into a pool of PC at the cisternal side of the membrane, which is used for assembly of very low density lipoprotein in the cisternae of the c.e. or the Golgi membranes (Higgins & Hutson, 1984; Higgins & Fieldsend, 1987). Thus, membrane phospholipids are not mixed, but appear to be sequestered in functional compartments which may have different metabolic fates.

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Circulating insulin concentrations and lipogenesis in inbred lines of mice differing in fatness

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Investigations seeking to identify the biochemical mechanisms underlying differences in body fat content have frequently employed grossly obese rats and mice as models. The hyperinsulinaemia commonly associated with such obesities is accompanied in many cases by hyperglycaemia and increased fatty acid biosynthesis (Bray & York, 1971; Herberg & Coleman, 1977). This study was undertaken to determine whether similar metabolic differences accompanied less extreme variations in fat accumulation. Plasma
Evidence for the presence of hormone-sensitive lipase in heart muscle

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Hormone-sensitive lipase (HSL) is a single polypeptide of Mr 84,000 which catalyses the initial, rate-limiting reaction in adipose tissue lipolysis. The enzyme is under acute hormonal control via the reversible phosphorylation of a single serine residue. Phosphorylation of this residue by cyclic AMP-dependent protein kinase results in activation of the enzyme, which is reversed by protein phosphatase-catalysed dephosphorylation (Yeaman et al., 1987).

Lipolytic activity has also been observed in the heart, where endogenous triacylglycerol is the major energy store. Lipolysis is controlled in response to the energy demands of the heart, achieved, at least in part, by hormonal regulation of the lipase responsible (Severson, 1979). The nature of the heart lipase is controversial, with conflicting views that either an intracellular form of lipoprotein lipase (Oscat, 1979; Palmer et al., 1981), or a distinct neutral lipase (Goldberg, 1988), exists. 

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Table 1. Age variation of lipogenic activity of liver and gonadal fat, and plasma insulin concentrations, in VL and SWR mice

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Activity/g of liver VL</th>
<th>Activity/g of liver SWR</th>
<th>Total gonadal fat activity VL</th>
<th>Total gonadal fat activity SWR</th>
<th>Plasma insulin concn. (ng/ml) VL</th>
<th>Plasma insulin concn. (ng/ml) SWR</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>38.98 ± 18.35</td>
<td>15.59 ± 2.60</td>
<td>0.66 ± 0.14</td>
<td>0.25</td>
<td>2.52 ± 0.16</td>
<td>3.90 ± 0.14</td>
</tr>
<tr>
<td>27</td>
<td>34.20 ± 9.71</td>
<td>28.90 ± 8.63</td>
<td>1.48 ± 0.29</td>
<td>0.25</td>
<td>3.59 ± 0.55</td>
<td>2.93 ± 0.38</td>
</tr>
<tr>
<td>34</td>
<td>19.91 ± 5.01</td>
<td>9.85 ± 1.93</td>
<td>0.83 ± 0.32</td>
<td>0.54 ± 0.28</td>
<td>4.12 ± 0.88</td>
<td>2.89 ± 0.14</td>
</tr>
<tr>
<td>39</td>
<td>23.33 ± 3.50</td>
<td>10.14 ± 1.50</td>
<td>1.79 ± 0.31</td>
<td>0.56 ± 0.09</td>
<td>9.68 ± 3.21</td>
<td>3.53 ± 0.16</td>
</tr>
<tr>
<td>45</td>
<td>22.65 ± 2.97</td>
<td>12.86 ± 1.28</td>
<td>1.24 ± 0.18</td>
<td>0.84 ± 0.30</td>
<td>5.41 ± 0.63</td>
<td>4.00 ± 0.36</td>
</tr>
<tr>
<td>51</td>
<td>17.73 ± 2.64</td>
<td>11.36 ± 1.37</td>
<td>1.11 ± 0.25</td>
<td>0.61 ± 0.18</td>
<td>5.33 ± 0.34</td>
<td>3.87 ± 0.33</td>
</tr>
<tr>
<td>124</td>
<td>24.80 ± 4.62</td>
<td>11.27 ± 2.54</td>
<td>0.69 ± 0.43</td>
<td>0.28 ± 0.12</td>
<td>8.27 ± 3.36</td>
<td>3.37 ± 0.40</td>
</tr>
</tbody>
</table>

Values are mean ± s.e.m. for three to six animals (except for insulin (n = 2) and gonadal fat lipogenesis (n = 1) in SWR mice at 21 days; µg at., microgram atoms.

The higher rates of lipogenesis and plasma concentrations of insulin in the line of fatter mice are similar to observations made when comparing grossly obese mice with their lean littermates or controls (Herberg & Coleman, 1977). However, the fall in the lipogenic activity of most tissues with age appears to occur in spite of the increase in the plasma concentration of insulin, which normally stimulates lipogenesis. The lack of difference between mouse lines in the lipogenic rate/g of gonadal fat may be due to a greater increase in the cellular fat content of VL mice and consequent reduction in the cell number/g of fat. However, as fat cell number is likely to increase with age, as in the rat (Hirsch & Han, 1969), the expression of lipogenic rate in gonadal fat on a whole-tissue basis may not be entirely appropriate. It is possible that the lower lipogenic rate in the heads of VL mice may in part be due to their containing a relatively larger proportion of brain tissue, this having little lipogenic activity (Hollands & Cawthorne, 1981). The precise relationship between circulating insulin concentrations and fat deposition requires clarification, as does the role of insulin in other genetic differences in fat content.

Vernon, R. G. (1975) Lipids 10, 284-289

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