Fatty Acid Composition of Human Serum Lipids at Birth

Lars Ivar Hardell and Göran Walldius

Department of Paediatrics, University Hospital, Uppsala, King Gustaf V Research Institute and Department of Internal Medicine, Karolinska Hospital, Stockholm, Sweden

ABSTRACT

Umbilical cord blood was collected immediately after birth from 55 unselected newborn infants. Fatty acid spectra of serum cholesterol esters, triglycerides, phospholipids and free fatty acids were determined by a combination of thin layer and gas liquid chromatography. Triglyceride and cholesterol concentrations were determined in total serum and in the three major lipoprotein classes. The three major fatty acids in cholesterol esters, triglycerides and free fatty acids were palmitic, oleic and linoleic acid, comprising 75 per cent of all acids. In phospholipids palmitic, stearic and arachidonic acid comprised about 75 per cent of all acids. The greatest amounts of linoleic acid were obtained in cholesterol esters (about 20 per cent) and free fatty acids (about 15 per cent), whereas arachidonic acid was most common in cholesterol esters (about 12 per cent) and phospholipids (about 18 per cent). In addition phospholipids contained 16 per cent highly unsaturated fatty acids besides linoleic and arachidonic acid. There were no sex differences within any lipid fraction. There was a striking difference in the fatty acid pattern between cord blood and adult blood. The relative content of linoleic acid was 60-70 per cent lower in cholesterol esters and phospholipids. Further, much higher relative contents of arachidonic acid were found in all serum lipids at birth. The ratio between polyunsaturated and saturated fatty acids in triglycerides and free fatty acids was the same in newborns and adults, but the ratio was lower in cholesterol esters and phospholipids at birth. There was also a positive correlation between linoleic and arachidonic acids in cholesterol esters and in triglycerides. For most of the fatty acids there were positive correlations between cholesterol esters and triglycerides. The various correlations suggest similar steps in the foetal liver metabolism and/or in the placental transfer and metabolism of different acids. There were weak positive correlations between the serum triglyceride concentration and the relative content of linoleic acid in triglycerides and of linoleic and arachidonic acid in cholesterol esters. Only very weak or no correlations were present between
total serum cholesterol and the different fatty acids. The correlations between fatty acids and the very low, the low and the high density lipoproteins were similar or weaker than those between fatty acids and total serum lipids.

INTRODUCTION

Fatty acids are transported in serum either as albumin-bound free fatty acids or as fatty acids in cholesterol esters, triglycerides and phospholipids. These lipids are carried in different lipoproteins. The concentration and composition of lipoproteins influence their properties. Thus increased concentrations of triglycerides (6) and/or cholesterol (21) as well as a low content of polyunsaturated fatty acids (20), are associated with an increased risk of atherosclerotic vascular disease. A high dietary intake of linoleic acid, the most common polyunsaturated fatty acid, is thought to be beneficial, since it lowers the serum cholesterol concentration (27). At birth the concentration of serum lipids is low and seems to be independent of the mother's nutritional status or ethnic group (2, 14, 16, 26), and in most investigations no correlation with maternal serum lipids has been found (28, 29, 39). Cholesterol esters, triglycerides and phospholipids do not pass the human placenta (reviewed in 3, 15, 31). Free fatty acids, on the other hand, are to some extent transferred through the placenta (36); short-chained fatty acids easily (7), but longer-chained probably with limitations (8, 9).

Linoleic acid with 18 carbon atoms and two double bonds (18:2) and arachidonic acid (20:4) are considered to be essential fatty acids, that is they are not synthesized in the human body, but must be supplied in the diet (reviewed in 1, 37). Furthermore the chain length of these fatty acids suggests a limited transport from mother to foetus. Previous studies of cord blood have also shown lower contents of linoleic acid, but mostly higher contents of arachidonic acid in cholesterol esters (12, 29, 39, 41), triglycerides (12, 29, 39), total or fractions of phospholipids (28, 29, 35, 40, 41) and free fatty acids (29, 30). Differences have been found between the investigated populations and the materials have mostly been small. Only one description (29) concerned fatty acids in the four different lipids.

The aim of this study was therefore to describe the normal fatty acid spectrum of cholesterol esters, triglycerides, phospholipids and free fatty acids in a reasonably large population of normal newborns to obtain a control material for further studies on abnormal pregnancies and deliveries and for prospective analyses of normal and abnormal development after birth. We also analysed the distributions and relationships of fatty acids within and between the different lipids and their relations to serum lipid concentrations, with special reference to the essential fatty acids. The values were compared with those of healthy adult men to distinguish principal differences and similari-
ties.

This study was a part of a one-year population study of newborn infants undertaken to investigate the possibilities of early detection of atherogenic hyperlipidaemias. A preliminary note on our major findings has been presented earlier (18).

MATERIALS

Cord blood samples from 55 full-term, healthy newborns with a birth weight of 3675 ± 445 g (mean ± standard deviation; range 2640-5010 g) were studied. They were collected consecutively during 48-hour periods once a week in the course of 6 weeks in May-June 1975. All infants were born at the Department of Obstetrics and Gynaecology, University Hospital, Uppsala, and only births after normal pregnancies and uncomplicated deliveries were accepted in the study. The adult reference material comprised a random sample from the city of Stockholm of 26 forty-year old healthy men (24), from whom venous blood was drawn after an overnight fast and abstinence from smoking. The two materials were analysed by the same methods at the King Gustaf V Research Institute.

METHODS

Sampling procedure

Free-flowing cord blood from the placental end of the umbilical cord was collected immediately after the umbilical artery pulsations had ceased. No deviations were made from the routine practice of deliveries at the department. After allowing 2-3 hours for clotting, serum was separated by centrifugation and 5 per cent EDTA was added to a final concentration of 0.05 per cent. The specimens were stored at +4°C prior to analyses of lipids and lipoproteins, which were performed within 72 hours after sampling. Serum for gas-liquid chromatographic determination of fatty acid spectrum was frozen and stored at -20°C for less than 2 months before analysis.

Fatty acid analysis

Fatty acid spectra of serum cholesterol esters, triglycerides, phospholipids and free fatty acids were determined by a combination of thin-layer and gas-liquid chromatography as described in detail elsewhere (38). After lipid extraction free fatty acids were selectively methylated by diazomethane and all lipids were separated as described (38). Cholesterol esters, triglycerides and phospholipids were methylated by 5 per cent H_2SO_4 dissolved in methanol at +60°C for 12-16 hours under nitrogen. Methyl esters were extracted into petroleum ether. Aliquots of each lipid fraction were separated isothermally at +180 or +190°C on a 1.8 metre glass column with an internal diameter of 2 mm with a 10 per cent DEGS-PS phase in an automatic (7671A) Hewlett Packard
chromatograph. The peaks were identified by relative retention times and the area was integrated with an Autolab system SP-4000 integrator. On each day of analyses standards of NIH series and PUFA 1-2 purchased from Supelco were run. The eight most common fatty acids were identified according to relative retention times compared to standards and the sum was taken as 100 per cent. In addition, longer polyunsaturated fatty acids were also tentatively identified in the phospholipid fraction and the relative composition was recalculated with including of these acids, as described under Results. An example of an assay of phospholipids in cord serum is shown in Fig. 1.

Figure 1. Fatty acid spectrum of total serum phospholipids. Each fatty acid is indicated by its number of carbon atoms and the number of double bonds. Identified fatty acids are indicated as further described in the section on methods.

Lipids and lipoprotein measurements

Fractionation of lipoproteins into the main classes, very low, low and high density lipoproteins, was performed by preparative ultracentrifugation at densities of 1.006 and 1.063 (5). Total serum and the three fractions were then extracted by isopropanol for determination of cholesterol (4) and triglycerides (22). The results of the lipoprotein determinations were acceptable in 44 newborns in whom the recovery of cholesterol and triglycerides in the lipoprotein classes was within the range of 87-113 per cent of the total serum lipid concentration. The values from these 44 infants were representative for the larger material of newborns for whom concentrations of triglycerides and cholesterol in total serum and lipoproteins have been described (17).

Statistical methods

Statistical analyses were performed as described by Snedecor and Cochran (34).
RESULTS

Serum triglycerides and cholesterol

In total serum the concentration of triglycerides was 0.40±0.02 mmol/l (mean ± SEM; range 0.19-1.01) and of cholesterol 1.76±0.05 (range 1.27-2.77). The cholesterol and triglyceride concentrations in very low, low and high density lipoproteins were the same as in the larger material described earlier (17).

Sex differences

No sex difference was found in the relative fatty acid content in cholesterol esters, triglycerides, phospholipids and free fatty acids. Neither was there any sex-related correlation between birth weights and either lipid concentrations or fatty acid composition of lipids. Since no differences were found between the sexes in the composition of lipids, boys and girls were pooled in the further analyses.

Fatty acid composition of serum lipids

Details with mean values, SEM and ranges are given in Table 1.

Cholesterol esters, triglycerides and free fatty acids. The three major fatty acid constituents were palmitic (16:0), oleic (18:1) and linoleic acid, totally about 75 per cent of the fatty acids. Linoleic acid occurred in about 20 per cent in cholesterol esters and in about 15 per cent in the other fractions. The percentage of arachidonic acid in cholesterol esters was about 10.

Phospholipids. The dominating fatty acid was palmitic acid (about 40 per cent of the fatty acids). The percentages of stearic (18:0) and arachidonic acid were about 20 and of linoleic acid about 10. In all cases longer and highly unsaturated fatty acids, i.e., 20:3, 20:5, 22:4 and 22:5, were also determined. These acids comprised 8, 1, 1 and 6 per cent of all fatty acids.

![Cumulative frequency distribution of linoleic acid in serum lipids at birth](image1)

![Cumulative frequency distribution of arachidonic acid in serum lipids at birth](image2)
Table 1.
Relative content (mean, SEM and range) of fatty acids in per cent of the total fatty acids, the sum of the saturated (14:0, 16:0, 18:0) (S), monounsaturated (16:1, 18:1), and polyunsaturated (18:2, 18:3, 20:4) (P) fatty acids and P/S ratio in each lipid fraction of serum lipids from 55 newborn infants.

<table>
<thead>
<tr>
<th></th>
<th>Myristic</th>
<th>Palmitic</th>
<th>Palmitoleic</th>
<th>Stearic</th>
<th>Oleic</th>
<th>Linoleic</th>
<th>Linolenic</th>
<th>Arachidonic</th>
<th>Saturated</th>
<th>Monounsaturated</th>
<th>Polyunsaturated</th>
<th>Ratio P/S</th>
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<td>10.54</td>
<td>3.02</td>
<td>32.93</td>
<td>19.38</td>
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<td>43.48</td>
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<tr>
<td></td>
<td>SEM</td>
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<td>0.23</td>
<td>0.36</td>
<td>0.10</td>
<td>0.38</td>
<td>0.34</td>
<td>0.03</td>
<td>0.32</td>
<td>0.24</td>
<td>0.53</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Range</td>
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<td>17.70-</td>
<td>3.21-</td>
<td>1.16-</td>
<td>26.13-</td>
<td>12.60-</td>
<td>trace-</td>
<td>7.14-</td>
<td>21.00-</td>
<td>35.09-</td>
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<td>9.62</td>
<td>4.26</td>
<td>36.16</td>
<td>13.52</td>
<td>0.69</td>
<td>3.98</td>
<td>36.02</td>
<td>45.77</td>
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<td>0.20</td>
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<td>0.40</td>
<td>0.32</td>
<td>0.03</td>
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<td></td>
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<td>1.70</td>
<td>19.18</td>
<td>12.90</td>
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<td>0.20</td>
<td>0.20</td>
<td>0.17</td>
<td>0.06</td>
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<td>15.81-</td>
<td>9.46-</td>
<td>5.72-</td>
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<td>trace-</td>
<td>53.46-</td>
<td>11.21-</td>
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<td>5.51</td>
<td>10.52</td>
<td>27.01</td>
<td>11.74</td>
<td>0.67</td>
<td>3.24</td>
<td>48.82</td>
<td>32.53</td>
<td>18.65</td>
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<tr>
<td></td>
<td>SEM</td>
<td>0.19</td>
<td>0.23</td>
<td>0.18</td>
<td>0.26</td>
<td>0.36</td>
<td>0.31</td>
<td>0.10</td>
<td>0.18</td>
<td>0.37</td>
<td>0.47</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>trace-</td>
<td>30.91-</td>
<td>2.04-</td>
<td>6.88-</td>
<td>21.77-</td>
<td>9.17-</td>
<td>trace-</td>
<td>trace-</td>
<td>43.77-</td>
<td>25.95-</td>
<td>11.90-</td>
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<td></td>
<td></td>
<td>-10.24</td>
<td>-38.39-</td>
<td>-8.05-</td>
<td>-15.68</td>
<td>-34.22-</td>
<td>-22.77-</td>
<td>-2.63</td>
<td>-6.88</td>
<td>-53.88</td>
<td>-39.84</td>
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</table>
The cumulative frequency distributions of the essential fatty acids in the different lipids are shown in Fig. 2 and 3. The S-shaped curves suggest fairly normal distributions.

**Distribution of fatty acids in newborn infants compared to adult men**

In Fig. 4 the spectra of the eight most common fatty acids in cholesterol

![Graphs showing distribution of fatty acids in different lipids](image)

**Figure 4.** Spectra of the eight most common fatty acids in serum lipids in newborn infants and adults. x) p<0.05, xx) p<0.01, and xxx) p<0.001 indicates the degree of significance in the difference of fatty acid content between newborns and adults. Abbreviations of fatty acids as in Table I.
esters, triglycerides, phospholipids and free fatty acids in both newborns and adults are illustrated. The fatty acid composition of the different lipids showed both similarities and differences between newborns and adults. In newborn infants the fatty acid spectrum was displaced towards shorter-chained acids in cholesterol esters, triglycerides and free fatty acids. The most striking difference was the much lower relative content of linoleic acid in cholesterol esters and phospholipids at birth. At birth the relative content of arachidonic acid was more than double that in adults in all serum lipids. The highest contents were present in cholesterol esters and phospholipids.

The ratio between total polyunsaturated and saturated fatty acids (P/S, Table 1) in triglycerides and free fatty acids was the same as in adults, but the newborns had lower ratios in their cholesterol esters and phospholipids (30 and 75 per cent of the corresponding values in adults).

**Relationship between fatty acids within each lipid fraction**

Only significant correlation coefficients are summarized in Table 2. In cholesterol esters and triglycerides the essential fatty acids correlated negatively with the monounsaturated fatty acids. There was a positive correlation between linoleic and arachidonic acid in both fractions.

In phospholipids there were negative correlations between linoleic acid and palmitic and stearic acid, respectively, as well as between arachidonic acid and palmitic and oleic acid, respectively. In free fatty acids the essential fatty acids correlated negatively with monounsaturated fatty acids. There was a negative correlation between linoleic acid and palmitic acid and a positive correlation between arachidonic and stearic acid.

**Relationship between fatty acids in different lipid fractions**

Significant correlation coefficients are summarized in Table 3. Positive correlations were found between many of the same fatty acids in cholesterol esters and in triglycerides.

A positive correlation was present both between linoleic acid ($r = 0.39$, $p<0.01$) and between arachidonic acid in cholesterol esters and in phospholipids.

No relationship was found between the essential fatty acids in free fatty acids and in the other lipids.

**Relationship between concentration of serum triglycerides and cholesterol and the relative contents of different fatty acids**

Correlations were determined between triglycerides and cholesterol in total serum and in very low, low and high density lipoproteins, on the one hand, and the relative fatty acid content in each lipid fraction, on the other. The relationships between fatty acids and the lipid concentrations in lipoproteins...
Table 2.
Correlation coefficients between fatty acids within each lipid fraction in 55 newborn infants. Abbreviations of fatty acids as in Table 1.

<table>
<thead>
<tr>
<th>Cholesterol esters</th>
<th>18:1</th>
<th>18:2</th>
<th>20:4</th>
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<td>14:0</td>
<td>0.63</td>
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<td></td>
</tr>
<tr>
<td>16:1</td>
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<td>-0.50</td>
<td>-0.51</td>
</tr>
<tr>
<td>18:0</td>
<td>0.58</td>
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<td></td>
</tr>
<tr>
<td>18:1</td>
<td></td>
<td>-0.42</td>
<td>-0.50</td>
</tr>
<tr>
<td>18:2</td>
<td></td>
<td>-0.56</td>
<td>-0.71</td>
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<table>
<thead>
<tr>
<th>Triglycerides</th>
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<th>18:0</th>
<th>18:2</th>
<th>20:4</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:0</td>
<td>0.53</td>
<td></td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>16:1</td>
<td></td>
<td>-0.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:1</td>
<td></td>
<td>-0.59</td>
<td>-0.75</td>
<td></td>
</tr>
<tr>
<td>18:2</td>
<td></td>
<td></td>
<td>-0.66</td>
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<th>20:4</th>
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<td>0.46</td>
<td></td>
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<td>18:1</td>
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<td>-0.44</td>
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<table>
<thead>
<tr>
<th>Free fatty acids</th>
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<th>18:0</th>
<th>18:2</th>
<th>20:4</th>
</tr>
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<tbody>
<tr>
<td>14:0</td>
<td>0.51</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:1</td>
<td></td>
<td>-0.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:0</td>
<td></td>
<td>-0.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:1</td>
<td></td>
<td></td>
<td>-0.52</td>
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</table>

xxx) p<0.001

were never higher than those between fatty acids and lipids in total serum.

There was a positive correlation between total triglycerides, on the one hand, and linoleic acid in triglycerides (r = 0.46, p<0.001) and the essential fatty acids in cholesterol esters (18:2, r = 0.39, p<0.01 and 20:4, r = 0.45, p<0.001), on the other.

Only weak correlations existed between total cholesterol and linoleic acid in triglycerides (r = 0.36, p<0.01) and arachidonic acid in phospholipids (r = 0.36, p<0.01), respectively.

DISCUSSION

Linoleic and arachidonic acid are of particular interest in cord blood as these fatty acids are so called essential, which in adults means that an exogenous supply is necessary. They were present in all circulating lipids at
Table 3.
Correlation coefficients between fatty acids in different serum lipids in 55 newborn infants. Abbreviations of fatty acids as in Table 1.

<table>
<thead>
<tr>
<th>Cholesterol esters</th>
<th>Triglycerides</th>
<th>Phospholipids</th>
<th>Free fatty acids</th>
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<td>0.47 (xxx)</td>
<td>-0.43 (xxx)</td>
</tr>
<tr>
<td>18:0</td>
<td>0.46 (xxx)</td>
<td>0.57 (xxx)</td>
<td>0.46 (xxx)</td>
</tr>
<tr>
<td>18:1</td>
<td>0.67 (xxx)</td>
<td>0.56 (xxx)</td>
<td>-0.49 (xxx)</td>
</tr>
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<td>18:2</td>
<td>-0.51 (xxx)</td>
<td>-0.55 (xxx)</td>
<td>0.45 (xxx)</td>
</tr>
<tr>
<td>18:3</td>
<td>-0.70 (xxx)</td>
<td>-0.70 (xxx)</td>
<td></td>
</tr>
<tr>
<td>20:4</td>
<td></td>
<td>0.43 (xxx)</td>
<td></td>
</tr>
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</table>

Birth, even in substantial amounts in the free fatty acid and triglyceride fractions. Similar relative amounts of these acids have been reported previously (12, 28, 29, 32, 36, 39, 40, 41). However, there were comparatively few subjects in each of those studies, and only few investigations concerned all lipid fractions (29).

Our results were obtained from a well defined material of normal newborn infants with a fully analysed and normal lipoprotein spectrum representative of our previously larger sample (17). As the values for the different fatty acids in the circulating lipids were similar for the two sexes, they were pooled and plotted in cumulative frequency curves. The values for the essential fatty acids are probably the most interesting and yield basic information for future studies on preterm, small for gestational age or otherwise abnormal infants and children in whom nutritional disorders may be present.

The essential fatty acids recovered in the foetal circulation may either be transferred directly from the maternal circulation or result from exchange mechanisms for fatty acids across the placenta. A direct transport is probable for free fatty acids (7, 8, 36) and has been shown for fatty acids with up to 16 carbon atoms and for linoleic acid (9). Placental transfer of arachidonic acid — with a low transfer rate compared to shorter chained fatty acids — has
so far only been reported in other species (10). Free arachidonic acid is, however, present in high amounts in human placenta (32), suggesting that it might be transferred as such to the foetus. Several results indicate that cholesterol esters, triglycerides and phospholipids do not pass the human placenta (3, 15, 31). Thus the foetal essential fatty acids in these lipid fractions may be derived from hydrolysis of maternal lipids with reesterification of these acids in the placental tissue (30, 31, 32) or in the foetal organism, as further discussed below for the different lipid fractions.

In adult men free fatty acids are precursors in the liver synthesis of triglycerides, and correlations exist between the relative amounts of essential fatty acids in these two lipid fractions (24). At birth, however, no such relation was found for any of these acids, indicating other metabolic conditions in newborns. In the foetus the contribution of free fatty acids to the synthesis of very low density lipoprotein triglycerides may be much less than in adult man, where in the fasting state at least free fatty acids play a major role. The foetal essential fatty acids in free fatty acids and triglycerides may be derived not only from maternal free fatty acids but also from maternal triglycerides. Lipoprotein lipase in human placenta (25) may split maternal triglycerides into fatty acids. These may then enter the placental cells to be utilized for resynthesis and storage of triglycerides. From these triglycerides fatty acids may again be liberated by foetal lipoprotein lipase to penetrate to the foetal organism for further metabolism. Alternatively the triglycerides may be secreted as very low density lipoprotein molecules directly from the placenta to the foetal circulation. The rather high P/S ratio in free fatty acids and triglycerides at birth, which was almost equal to that later in life, suggests that the essential fatty acids are rapidly distributed into these lipids.

There were great differences in the fatty acid spectra of triglycerides and cholesterol esters in newborns, but many direct correlations were found between individual fatty acids, including the essential ones, in these two lipids. The relationships indicate close metabolic connections between cholesterol esters and triglycerides, including their incorporation into lipoproteins either in the foetal liver or intestine or in the placenta.

Cholesterol esters and phospholipids form a major part of the high density lipoproteins (11), which have been suggested to mediate exchange of lipids over membranes (13). Some of the relations between the unsaturated fatty acids, which were positively correlated between linoleic and arachidonic acid in phospholipids and cholesterol esters but not in phospholipids and triglycerides or phospholipids and free fatty acids, may reflect such mechanisms. This is possibly mediated by the LCAT enzyme which converts mainly unsaturated fatty acids from phospholipids to cholesterol esters (13) and is present in the
foetal circulation (23). Placental phospholipase (30) probably also plays a role in the metabolism and exchange of fatty acids between phospholipids and cholesterol esters.

Newborns had a low linoleic acid content in cholesterol esters and phospholipids, about one third of the value in adults, but they had a higher content of arachidonic acid. Unless the high arachidonic acid content is the result of pure exchange over the membranes in the placenta, the findings suggest that the newborn infant has enzymes involved in desaturation and chain elongation of fatty acids. In this process linoleic acid is utilized for synthesis of longer chained and more polyunsaturated fatty acids (reviewed in 1). This was most obvious in the phospholipids, which were relatively rich in acids with 20 carbon atoms or more. The site and mode of action of these enzymes is unknown. No attempt was made to determine the relative amount of 20:3ω9 in phospholipids. This acid is used to indicate an essential fatty acid deficiency (19), and for this purpose isolation of lecithin would have been necessary.

The correlation between different fatty acids within each lipid fraction may indicate the means by which these fatty acids are interconverted by desaturases and chain elongation enzymes. In all lipid fractions there was a negative correlation between poly- and monounsaturated fatty acids, findings similar to those obtained in adults (38).

There were only weak or no correlations between individual fatty acids and cholesterol concentration in total serum or in the lipoprotein fractions. This suggests that the essential fatty acids do not determine the serum cholesterol levels, at least not in healthy newborns with normal lipids. A direct or indirect relationship may exist between linoleic acid and the triglyceride concentrations, as there were significant positive correlations between linoleic acid in some lipid fractions and the triglyceride concentration in total serum, as well as in very low and high density lipoproteins.

Our qualitative analyses of the lipid fractions thus showed a low content of polyunsaturated fatty acids, at least in cholesterol esters, as compared with adults. The variation in the individual compositions were small, and in no case was there an extremely low content of the total polyunsaturated fatty acids.

Nothing can so far be said about the influence of the comparatively low, but physiological content of the essential fatty acids at birth on the metabolism of arteries and the development of atherosclerotic vascular disease. There are several reasons, however, to give an early, adequate dietary supplement of essential fatty acids after birth, as these substances are important in many intermediate metabolic events and for growth (1, 37).

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REFERENCES


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Address for reprints:
Lars Ivar Hardell, M.D.
Department of Paediatrics
University Hospital
S-750 14 Uppsala
Sweden