Plasma Lipids Concentrations in Obese Children
Living in a Cold Area*

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Plasma free fatty acids (FFA), triglycerides (TG) and uric acid (UA), and skinfold thickness at three sites (triceps, inferior tip of scapula and abdomen) were determined in the postabsorptive state in obese and non-obese boys of ages from 12 to 14, who were born in Hokkaido, and living in the intense cold area, Asahikawa, Hokkaido.

The subjects were selected according to Mizuno's tables for standard and obese height-weight (1968).

In obese groups skinfold thicknesses at the three sites were appreciably greater than that in non-obese group. Plasma TG level doubled in obese children as compared with that in non-obese children, while plasma FFA and UA levels were not significantly different between the groups.

There was a significant correlation between skinfold thickness at the inferior tip of the scapula or at (the triceps+the inferior tip of the scapula) /2 and plasma FFA level in obese subjects, while no such association was found in a non-obese group.

During recent years much attention has been paid to obese children, since an appreciable group of these subjects is reported to pass into an adult form of obesity1, 2) with unfavorable complications.3) A great number of metabolic differences between obese and non-obese adults have been demonstrated,4) while there are very few observations of metabolic disturbances, especially on lipid metabolism, in obese children and adolescents.

Several investigators reported that obese children were characterized by elevated blood levels of total lipids,5) total cholesterol, 5,6) triglycerides (TG), 5, 6) glycerol7) and free fatty acids (FFA) 5,6,7,8) after overnight fasting, in comparison with those in non-obese children. However, when fasting is prolonged up to 19 to 24 hours, blood FFA level in obese children becomes similar to6) or conversely surpassed that in non-obese subjects,8) even though blood glycerol level remains higher in the former.8) Thus, it was suggested that an increased re-esterification of mobilized FFA to TG due to prolonged fasting might occur in obese children. Elevated FFA level under basal conditions might be explained by an increased sympathetic activity in obese children.9)

Recently Itoh et al10) reported that plasma FFA levels showed stepwise changes according to experiences in cold exposure. The lowest level of FFA was observed in subjects who were considered to be well adapted to cold, while the highest in subjects who were not so during the winter time. These results imply that lipid metabolism could be modified in the process of cold adaptation.

* Presented in part at The 15th Japanese School Health Society Meeting, Kyoto, November 1968.
Therefore from the viewpoint of lipid metabolism it would appear to be worthwhile to investigate obese children living in a cold area and being considered to be well adapted to cold.

Materials and Methods

The study was made from the end of June to the beginning of July on 22 obese and 26 non-obese junior high school boys of ages from 12 to 14 who were born in Hokkaido and living in the intense cold area, Asahikawa, Hokkaido. The mean temperatures in Asahikawa were shown in Table 1 with corresponding values in a rather mild area, Sapporo, and in a comparatively warm area, Tokyo.

Table 1 Mean monthly temperature (1931-1960) in Asahikawa, Sapporo and Tokyo, JAPAN

<table>
<thead>
<tr>
<th>Place</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>Jun</th>
<th>Jul</th>
<th>Aug</th>
<th>Sept</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asahikawa</td>
<td>-8.9</td>
<td>-7.9</td>
<td>-3.3</td>
<td>4.1</td>
<td>10.9</td>
<td>16.0</td>
<td>20.3</td>
<td>21.1</td>
<td>15.4</td>
<td>8.6</td>
<td>1.3</td>
<td>-5.1</td>
<td>6.0</td>
</tr>
<tr>
<td>Sapporo</td>
<td>-5.9</td>
<td>-4.7</td>
<td>-1.0</td>
<td>5.7</td>
<td>11.3</td>
<td>15.5</td>
<td>20.0</td>
<td>21.7</td>
<td>16.8</td>
<td>10.4</td>
<td>3.6</td>
<td>-2.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Tokyo</td>
<td>3.7</td>
<td>4.3</td>
<td>7.6</td>
<td>13.1</td>
<td>17.6</td>
<td>21.1</td>
<td>25.1</td>
<td>26.4</td>
<td>22.8</td>
<td>16.7</td>
<td>11.3</td>
<td>6.1</td>
<td>14.7</td>
</tr>
</tbody>
</table>

The subjects studied were selected by the use of Mizuno's tables\textsuperscript{11} for standard height-weight and under-limits of obese height-weight.

Blood specimens were obtained from the antecubital veins into heparinized syringes, in the A.M., and in a fasting state, about 12 hours following a last meal. Plasma was immediately separated and kept frozen until analysed for lipids. Free fatty acids were determined by the colorimetric method of Itaya and Ui.\textsuperscript{12} Triglycerides were analyzed by the method of Laurell.\textsuperscript{13} Uric acid was determined by the sodium carbonate method using Iatron reagents kit,\textsuperscript{14} essentially described by Caraway.\textsuperscript{15}

Skinfold thickness was measured at the time of blood collection with Harpenden skinfold calipers at three sites on the right side; (1) at the triceps, midway between the acromial and olecranon processes, (2) at the inferior tip of the scapula and (3) at the abdomen to the right of the umbilicus.

Body fat was estimated from skinfold thickness at the triceps and at the inferior tip of the scapula by the nomogram of Parizkova.\textsuperscript{16}

Results

The average heights and weights, skinfold thickness and estimated body fat in the term of per cent of body weight were presented in Table 2. The average body weight in the obese group was about 50% more than that in non-obese group. The average height showed no significant difference between groups. The skinfold thickness in obese subjects were appreciably greater in all sites measured than in non-obese subjects. Estimated body fat doubled in obese children as compared with that in non-obese children. National Institute of Nutrition\textsuperscript{17} recently proposed a classification of obesity in children on the basis of body fat into three
Table 2 Skinfold thickness and estimated body fat

<table>
<thead>
<tr>
<th>Subjects</th>
<th>No.</th>
<th>Height cm</th>
<th>Body Weight kg</th>
<th>Skinfold thickness mm</th>
<th>abdomen</th>
<th>Body fat %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-obese</td>
<td>26</td>
<td>155.5±1.9</td>
<td>44.0±1.5</td>
<td>5.3±0.35</td>
<td>5.3±0.23</td>
<td>3.9±0.22</td>
</tr>
<tr>
<td>Obese</td>
<td>22</td>
<td>157.6±1.8</td>
<td>66.2±2.2</td>
<td>13.8±0.93</td>
<td>12.3±0.64</td>
<td>14.1±1.20</td>
</tr>
<tr>
<td>P vs non-obese</td>
<td>N.S.</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mean±Standard error
N.S.: not significant

categories; slight (+), moderate (++) and intense (+++) obesity. According to this, obese subjects in the present study are placed to the slight obesity. The Rohrer-Index in the obese group was 167 on an average, also indicating a slight degree of obese condition in the subjects studied here.

Figure 1 summarized the results of plasma FFA, TG and uric acid levels. In obese subjects plasma FFA levels was 507±46.6 μEq/liter, which was not significantly different from that in non-obese subjects, 549±56.4 μEq/liter. This result was not in accordance with previous reports, which referred to unanimously higher blood levels of FFA in obese children. Plasma TG level in obese group was approximately twice that in non-obese group, 104±14.1mg/dl and 51±3.5mg/dl respectively, conforming to the results by other investigators.

Adequate evidence is now available to indicate a relationship between uric acid and lipid metabolism, although no definite mechanism remains to be explained. An elevated uric acid level in blood was reported in obese adults, while no observation in obese children has appeared so far. The present result indicated that there was no significant difference in the plasma uric acid level between the obese (6.3±0.27mg/dl) and non-obese (7.0±0.36mg/dl) group.

Although we failed to find a significant difference in the plasma FFA level between the obese and the non-obese group, it was of great interest to note a correlation between skinfold thickness and plasma FFA level as shown in Figure 2-1, II, III and IV.
Interrelationships between skinfold thickness and plasma FFA levels in non-obese and obese children.

I: Correlation between skinfold at the inferior tip of scapula and plasma FFA level.

II: Correlation between skinfold at the triceps and plasma FFA level.

III: Correlation between skinfold at the abdomen and plasma FFA level.

IV: Correlation between (skinfold at the inferior tip of scapula + skinfold at the triceps)/2 and plasma FFA level.

Discussion

Elevated levels of FFA and TG have been unanimously observed after overnight fasting in obese children in previous reports. Therefore it was indeed somewhat surprising that we found no significant difference in plasma FFA levels between obese and non-obese subjects in the present study. In this context, it is interesting to note a report by Persson and Sterky. They found that prolonged fasting decreased the rate of the rising of plasma FFA level and after 23 hours of fasting the plasma FFA level became significantly less in obese than in non-obese children, whereas plasma glycerol remained significantly higher throughout the fasting period up to 23 hours in obese group. Since glycerol is poorly utilized by adipose tissue, owing to lack of glycerokini-
nase, the released glycerol could indicate the degree of lipolysis. Therefore an apparent decrement in plasma FFA in the obese might indicate an increased reesterification of released FFA. It was reported that such factors as epinephrine,7 8) exercise8) and posture change7) which are known to stimulate the release of FFA from adipose tissue were found to bring about less elevation of blood FFA level in obese children than in non-obese subjects. These results could explain either a decreased ability of FFA release or an increased reesterification of FFA. It is also interesting to refer to the results by Zimmer19) suggesting that the adipose organism is adapted to a quantitatively increased fat oxidation. He observed that lean subjects exhibited a higher level of acetoacetate in serum although no difference in the serum FFA and glycerol level between the obese and lean group was observed after 42 hours fasting. The fact that the present result demonstrates no difference in the plasma FFA level between obese and non-obese groups living in cold area might be due to a different timing in lipolysis-reesterification cycle and a different oxidation rate of fat from those of other studies. This possibility is very likely, since obese children in cold area might be affected in a certain site of lipid metabolism owing to their acclimatization to cold as mentioned earlier.10) It is necessary to follow up blood glycerol and acetoacetate as well as FFA in order to get further information on this point.

Finally, failure to find a difference in plasma FFA levels between the groups might be attributed to the intensity of obesity. As described above, obese subjects in the present study appear to include a slight obese group. An elevated FFA level might occur only in the intense obese subjects. However it is unlikely, because an appreciably higher level of TG was observed in obese than in non-obese subjects studied here, although there was no significant correlation between FFA and TG levels in obese group.

From the present findings, it would appear to be pertinent to state that lipid metabolism in obese children living in cold areas might be influenced in its certain site by the process of cold adaptation.

In adult obesity a good correlation between the degree of obesity and plasma FFA level was reported,20,21) while there was no association in obese children.7) The present study clearly indicated a significant correlation between skinfold thickness and plasma FFA level in the obese group. The result should be considered to indicate a reflection of the size of the body fat mass on plasma FFA in obese subjects, while failure to find association between these indices in non-obese subjects suggests that plasma FFA levels are affected by other factors such as the nervous or endocrine mechanisms rather than that of the body fat mass. No significant relationship between skinfold thickness and TG or uric acid was demonstrated.

Recently Albrink and Meigs found22) blood TG to correlate best with several indices of body fatness in adults, while Berkowitz23) reported no elevation of blood TG in obese adult. As to this discrepancy, it was suggested that variation in lipid levels of obese subjects might be due to the existence of two types of obesity, congenital and acquired.22) Another possibility is that blood TG elevation may well be associated with an increasing phase of body fat.5) If such is the case, in some cases of stable obesity, normal level of blood TG might be expected. In the present study, the average value of blood TG was significantly greater in obese group. However some exhibited
Fig. 3  Distribution of TG levels in non-obese and obese children. Horizontal bars indicate average values.

Fig. 4  Correlation between plasma TG and uric acid (UA) in non-obese (○) and obese (●) children. Correlation was calculated only on obese subjects.

low levels which were comparable to those in non-obese group (Figure 3). For this reason, it seems to be essential to know the duration of obese conditions and a longitudinal picture of heights and weights in order to analyze obese conditions dynamically.

In male subjects, blood uric acid level increases steeply up to the age of 24 and thereafter remains constant. Some investigators pointed to a significant association in adult subjects between blood uric acid level and body fatness, while others found no or little relationship. However no report as to uric acid in obese children was found. It was interesting to see the blood uric acid level in obese subjects with hypertriglyceridemia, since TG is shown to be a primary factor in the concomitant uric acid values. However there was no significant difference in the uric acid level between obese and non-obese group. In addition no association between TG and uric acid levels in the former was found (Figure 4).

Recently a close relationship between blood TG level and diabetes mellitus or atherosclerosis have been stressed. Therefore it is quite possible that obese children with hypertriglyceridemia might develop the disorders mentioned above. An elevated TG level in obese children as well as obese adults should be considered to be a potentially pathological state which should require attention.
References

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23) Berkowitz, D.: Metabolic changes associated with obesity, JAMA, 187, 399-403 (1964)
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寒冷地肥満児に関する研究
特に脂質代謝について

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最近肥満児に関する生理化学的および疫学的研究が数多く報告されているが，寒冷地における肥満児に関する系統的研究はほとんど行なわれていない。われわれは寒冷地肥満児の実態を明らかにする目的で旭川市の肥満児を対象に脂質代謝を中心に検討を行なった。

12才から14才の中学生男子で北海道に住，旭川に居住している者から「青少年体力標準表」（水野，1968）により肥満児（22名）を抽出し，対照児（26名）とともに6月下旬から7月中旬にかけて早朝空腹時皮厚を測定，また採血を行なない血漿中の遊離脂肪酸（FFA），中性脂肪（TG），尿酸の測定を行なった。

肩甲骨下，上腕部，腹部皮厚は肥満児においては対照児に比べて著しく大であった。

血中のFFAレベルは507±46.6 μEq/Lit. で，対照児の549±56.4 μEq/Lit.との間に有意の差がみられなかった。また尿酸も肥満児（7.0±0.36mg/dl）と对照児（6.3±0.27mg/dl）の間で差がみられなかった。

しかしながら肥満児においては皮厚と血中のFFAレベルの間に相関の傾向がみられ，特にFFAレベルと肩甲骨下皮厚および（肩甲骨下皮厚+上腕部皮厚）/2の間に有意に正の相関がみられた。

血中TGのレベルは肥満児では104±14.1mg/dl と对照児の51±3.5mg/dlに比べて有意に高かった。

従来の報告は一本児肥満においては血中のFFA，TGレベルが高いと述べているが，われわれの結果ではFFAレベルは両群の間で全く差異が認められず，寒冷地における脂質代謝の特異性という点から興味ある知見と考えられ，今後さらに検討されるべきである。

血中の尿酸レベルは脂質代謝と密接な関係のあることが知られており，成人肥満では血中レベルの上昇が報告されているが，小児肥満では従来報告がなく，われわれの結果では両群の間に差を認めなかった。

（本論文の一部は第15回日本学校保健学会，京都1968において発表した）

（受付 1968年11月11日）