

PLASMA LIPID PROFILES IN THE WINTER OF HOKKAIDO INHABITANTS

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Although considerable number of reports have appeared as to plasma lipid concentrations in relation to cold acclimation, data are not consistent. Moreover, most studies have been made in mammals, particularly in the rat, but little work done on this problem in man. HICKS¹⁾ reported that serum cholesterol level showed some increase only during early months of one year stay at an Antarctic station. MAGER and IAMPIETRO²⁾ found in their experiments on the effect of two week period starvation plus cold on plasma lipids in normal men that plasma cholesterol, phospholipids and total lipids increased during early phases of cold and starvation, but were restored to control levels by the end of two week period, and that plasma FFA rose to over 200 per cent of control levels within 2 days and remained constant thereafter. Our previous study on seasonal variations of plasma lipid profiles indicated that plasma levels of FFA were considerably high in the winter and low in the summer. Average value in the winter was 21 per cent over the level in the summer³⁾. Moreover, we noticed in the same experiment particularly high levels of plasma FFA, amounting to 626 and 741 μ Eq/l respectively, in the winter in two subjects who were born on the main island of Japan. The elevated plasma level of FFA in the winter might be related to hypermetabolism in this season. Accordingly, it seemed of interest to compare plasma FFA levels as well as other lipid components in different subject populations in the winter in cold districts.

METHODS

Eight groups, totalling 128 male subjects, including two groups of the Ainu, were used for the present study. They were (i) students who were born on the main island and living in Sapporo for 2 to 3 years, (ii) students and professionals born on Hokkaido and living in Sapporo, (iii) policemen in Asahikawa, (iv) farmers in Huren and (v) in

Received for publication May 30, 1968

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Niikappu, (vi) fishermen and fish factory workers in Monbetsu, and (vii) Ainu in Asahikawa and (viii) in Niikappu. These Ainu are mostly hybrids, but not pure. Among the places listed above Huren is the coldest, followed by Asahikawa and Monbetsu. Niikappu and Sapporo are rather warm in winter. Monthly mean temperatures at these places were indicated elsewhere⁴⁾.

The study was made during a period from January to the beginning of March. In the morning before breakfast under resting conditions, blood specimens were obtained from the antecubital vein. The blood samples were promptly centrifuged and plasma kept frozen until use. Concentrations of total lipids⁵⁾, triglycerides⁶⁾, phospholipids⁷⁾, total and free cholesterol⁸⁾, esterified⁹⁾ and free fatty acids¹⁰⁾ were determined respectively.

RESULTS

Plasma lipid levels observed in eight groups of subjects are summarized in TABLE 1, in which Group I are Japanese subjects born on the main island, Group II-VI those born on Hokkaido, and Group VII and VIII the Ainu.

Among Group II-VI there observed some differences in the concentrations of plasma lipid components. Plasma levels of phospholipids were high in Niikappu farmers and low in Huren farmers, total cholesterol and esterified fatty acids high in Asahikawa policemen, and FFA high in students and professionals in Sapporo. Furthermore, two groups of the Ainu showed some differences in the concentrations of total lipids and phospholipids. However, as a whole significant differences were not found in the levels of total lipids, triglycerides, phospholipids, total and free cholesterol, and esterified fatty acids between Group I and Group II-VI. On the other hand, esterified fatty acid levels were lower in the Ainu than in the Hokkaido-born Japanese subjects (Group II-VI),

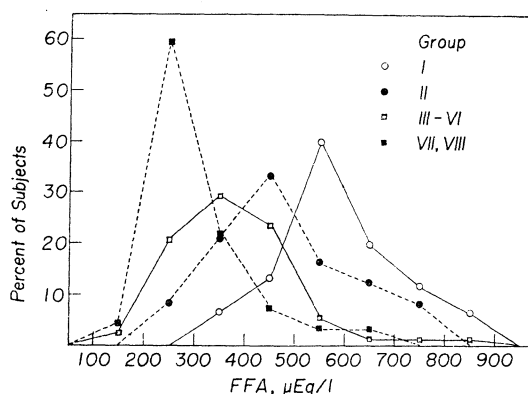


FIG. 1. Frequency distributions of plasma FFA levels in Japanese subjects born on the main island (Group I: open circle), those born on Hokkaido and living in Sapporo (Group II: closed circle), those in rural districts in Hokkaido (Group III-VI: open square) and Ainu (Group VII and VIII: closed square).

TABLE I.
Plasma lipid profiles in winter.

Group	Living place	No. of subjects	age (average)	Total lipids (mg/dl)	Trigly- cerides (mg/dl)	Phospho- lipids (mg/dl)	Cholesterol Total (mg/dl)	Cholesterol Free (mg/dl)	Fatty acids Ester. (mg/dl)	Fatty acids Free (μ Eq/l)
I	Students (born on main island)	15	21-26(22)	491 \pm 18.4	84 \pm 10.6 (8)	139 \pm 5.0	171 \pm 8.7	46 \pm 3.0	340 \pm 16.5	598 \pm 23.0
II	Students and professionals	24	20-34(23)	439 \pm 12.8	69 \pm 6.3 (14)	148 \pm 3.6 (23)	160 \pm 4.2	53 \pm 2.4	305 \pm 9.8	481 \pm 29.5
III	Policemen	15	21-40(27)	451 \pm 22.4	79 \pm 5.0 (14)	154 \pm 4.9	193 \pm 9.2	45 \pm 4.0	401 \pm 22.2	376 \pm 32.5
IV	Farmers	15	28-39(35)	505 \pm 21.8		133 \pm 8.4	164 \pm 6.9	53 \pm 4.4	334 \pm 15.4	393 \pm 29.5
V	Farmers	11	20-50(33)	481 \pm 32.2	87 \pm 13.9 (10)	166 \pm 11.6	153 \pm 11.1	42 \pm 3.5	340 \pm 35.1	357 \pm 25.5
VI	Fishermen and fish factory workers	21	20-50(38)	434 \pm 23.1	71 \pm 7.3	147 \pm 8.9	177 \pm 7.7	39 \pm 3.0	370 \pm 14.4	382 \pm 37.3
II-VI TOTAL		86	20-50(31)	457 \pm 9.3	75 \pm 4.0 (39)	149 \pm 3.5 (85)	168 \pm 3.6	47 \pm 1.6	350 \pm 8.5	407 \pm 14.8
vs I				NS	NS	NS	NS	NS	NS	P<0.001
VII	Ainu	17	17-45(28)	403 \pm 24.5	75 \pm 7.8	135 \pm 8.9	161 \pm 6.0	49 \pm 5.0	294 \pm 15.7	314 \pm 26.5
VIII	Ainu	10	22-58(42)	505 \pm 34.1	86 \pm 8.4	167 \pm 9.0	168 \pm 9.9	55 \pm 6.6	317 \pm 44.7	294 \pm 41.0
VII-VIII TOTAL		27	17-58(33)	441 \pm 21.2	79 \pm 5.8	147 \pm 7.1	164 \pm 4.7	51 \pm 3.1	303 \pm 10.9	306 \pm 22.2
vs I				NS	NS	NS	NS	NS	NS	P<0.001
vs II-VI				NS	NS	NS	NS	NS	P<0.01	P<0.001

Values are means and standard errors of the means. NS: not significant. Numbers in parentheses under the values indicate number of determinations which were less than number of subjects.

though the difference between the Ainu and main island-born students (Group I) was not significant. The most striking differences were observed in plasma FFA levels which were the highest in subjects born on the main island, followed by those born on Hokkaido and the lowest in the Ainu. The differences among these groups were highly significant each other. Frequency distributions of plasma FFA levels of the groups are shown in FIG. 1. Apparently peaks were located at different levels of FFA. The peak of the Ainu (Group VII and VIII) was at the lowest level and it moved to higher levels in the following order: Japanese in rural districts in Hokkaido (Group III-VI), those born Hokkaido and living in Sapporo (Group II), and the subjects born on the main island (Group I).

DISCUSSION

Total lipids Average value of plasma total lipids in the Ainu was somewhat low, as compared with those of the Japanese, but the difference was not significant. Values reported by BOYD¹¹⁾ and MAGER and IAMPIETRO²⁾ are similar to that presented in this paper. However, others found considerably higher values. For instance, LUND et al.¹²⁾ reported 567 ± 11 mg/100 ml (mean \pm S.E.) for males and 569 ± 15 mg/100 ml for females, and SVANBORG and SVENNERHOLM¹³⁾ 610 ± 15.3 and 648 ± 21.1 respectively. The great difference between our results and those of the latter investigators might be interpreted to be mostly due to differences in total cholesterol and phospholipids, as will be indicated below, although methodological differences will not be excluded.

Triglycerides Plasma levels of triglycerides of the Ainu were not different from the levels of the Japanese. Values obtained in the present experiments were similar to those on Japanese subjects by OYAMA et al.¹⁴⁾ and on the white by several investigators^{18,15-20)}, though higher average values amounting to 138 and 152 mg/100 ml were also reported by SCHWARTS et al.²¹⁾ and DUNN and MOSES²²⁾ respectively. Such differences may occur according to different racial groups and different methods employed for the determination.

Cholesterol Appreciable differences in the plasma total cholesterol were not observed among Japanese born on the main island, those born on Hokkaido, and Ainu. The values obtained in these groups were on the same level reported by OKINAKA²³⁾ who summarized 6977 determinations of total cholesterol in the plasma of Japanese in the main and southern islands (TABLE 2). According to NAMIKI et al.²⁴⁾, the plasma levels of cholesterol were 152 ± 8.1 mg/100 ml (mean \pm S.D.) for 24 Ainu, the figure being significantly less than the level of 189 ± 10.7 mg/100 ml for 26 Japanese in the same place. When our values of the both ethnic groups were compared each other in subjects younger than 40 years, the levels were 155 ± 5.3 mg/100 ml (mean \pm S.E.) for 17 Ainu and

TABLE 2.
Plasma levels of cholesterol (mg/100 ml).

Age group, yr.	Ainu		Japanese		Main island*
	No.	Mean	No.	Mean	
17-19	4	154			
20-29	8	154	57	167	164
30-39	5	158	32	172	173
40-49	6	182	9	160	183
50-59	4	173	3	183	195

* OKINAKA²²⁾

169±3.3 mg/100 ml for 90 Japanese ($P<0.05$). It might be therefore true that the plasma levels of total cholesterol are less in the Ainu than in the Japanese.

It should be noted that the plasma cholesterol was particularly high in policemen, averaging 193±9.2 mg/100 ml. The subjects are engaged in patrol of 24 hour duty every other day. Such occupational stress might be a cause of the increase in plasma cholesterol concentration²⁵⁾.

Plasma cholesterol level of the Japanese is markedly low in comparison with the values of Americans and Europeans. Although SVANBORN and SVENNERHOLM¹³⁾ and STAMP et al.²⁶⁾ found the average values of 192 and 195 mg/100 ml respectively, others reported the values more than 200 mg/100ml^{8,12,20,22,27)}. LEWIS et al.²⁸⁾ who measured total serum cholesterol on 10,690 men and 3,404 women also reported the average values of over 200 mg/100 ml. One of the principal causes of the difference in plasma cholesterol between Japanese and Americans or Europeans might be differences in the dietary habits.

Plasma levels of free cholesterol in three groups of the present study were on the same level and the values were not very much different from those observed by others^{2,11,29)}.

Phospholipids Plasma phospholipid levels of subjects born on the main island were slightly low, though the difference was not significant, as compared with other two groups of Japanese and Ainu subjects born on Hokkaido. However, in general the average value were found to be considerably lower than those reported in literatures. This might be due, at least in part, to the method employed in this study. OYAMA et al.¹⁴⁾ found the average value of 182 mg/100 ml in Japanese in the main island, GJONE and ORNING³⁰⁾ reported 170 mg/100 ml for males and 182 for females, SVANBORG and SVENNERHOLM¹³⁾ 208±4.4 mg/100 ml for males and 232±8.2 for females, and DUNN and MOSES²²⁾ as high as 297 mg/100 ml. ADLERSBERG et al.²⁷⁾ also described high average values as much as 249 mg/100 ml for males in the year of 23 to 27, and the values increased gradually with age. When our results were divided according to age groups, values of old subjects were shown to be higher than those of younger

ones (TABLE 3). Moreover, four Ainu subjects in ages between 17 and 19 showed extremely low values, averaging 106 mg/100 ml.

A close relationship between phospholipids and cholesterol was demonstrated in the Ainu (FIG. 2), as already reported by others, while the relation was not significant in the Japanese. This is probably due to variety of the groups studied which include various subjects with different occupations from different districts.

Esterified fatty acids Average value of esterified fatty acids was somewhat lower in the Ainu than in the Japanese. The difference between Ainu and Japanese born on Hokkaido was significant. This is mostly ascribed to high levels of esterified cholesterol in Asahikawa policemen (148 mg/100 ml) and fishermen and fish factory workers in Monbetsu (138 mg/100 ml), in comparison with low average value of 113 mg/100 ml in the Ainu. As a whole, values obtained in the present study were on the same level to the observations of BOYD¹¹⁾ and VERHEYDEN and NYS⁹⁾.

Free fatty acids In the present study the most striking differences were found in FFA levels which were the highest in the Japanese subjects born on the main island, followed by those born on Hokkaido. The lowest value was observed in the Ainu. The differences among these three groups were highly significant (FIG. 3). As summarized in TABLE 4, fasting levels of plasma FFA

TABLE 3.
Plasma levels of phospholipids (mg/100 ml).

Age group, yr.	No.	Ainu Mean	No.	Japanese Mean
17-19	4	106		
20-29	8	143	57	147
30-39	5	137	32	145
40-49	6	163	9	144
50-59	4	174	3	201

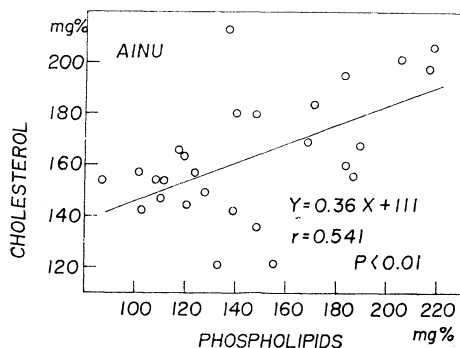


FIG. 2. Relationship between plasma cholesterol and phospholipid levels in the Ainu.

in normal subjects are within the range between 470 and 750 μ Eq/l. In a previous study³³ we also found similar levels of FFA, that is, $448 \pm 28.9 \mu$ Eq/l in summer and $544 \pm 29.4 \mu$ Eq/l in winter (FIG. 3). Among the results obtained in this study, values of Sapporo subjects were in the same range as above, while Japanese in rural districts showed considerably low levels and the Ainu very low average value of $306 \pm 22.2 \mu$ Eq/l.

It is of great interest that the plasma levels of FFA showed such step-wise changes according to the experiences in cold exposure. The lowest was observed in subjects who were considered to be well adapted to cold, while

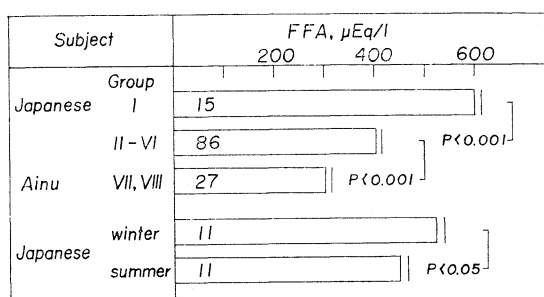


FIG. 3. Comparison of plasma FFA levels in Japanese subjects born on the main island (Group I), those born on Hokkaido (Group II-VI) and Ainu (Group VII and VIII), and seasonal changes of plasma FFA levels in Japanese subjects in Sapporo³³.

TABLE 4.
Plasma levels of FFA (μ Eq/l).

Source	Sex	No. of subjects	FFA
TROUT et al. ³¹⁾		12	584 ± 11.2 (S.E.)
SVANBORG and SVENNERHOLM ¹⁸⁾	male	62	750 ± 34 (S.E.)
	female	29	781 ± 45
ANSTALL and TRUJILLO ³²⁾	male	24	540
	female	6	514
	total	30	534
BJÖRNTORP et al. ³³⁾		8	631 ± 150 (S.D.)
STAMP et al. ²⁶⁾	male	50	575 ± 160 (S.D.)
DE CARO et al. ³⁴⁾		12	460 ± 26 (S.E.)
REITSMA ³⁵⁾		17	570
GLENNON et al. ³⁶⁾	male	21	474 ± 39 (S.E.)
	female	21	487 ± 43
	total	42	482 ± 29

the highest in subjects who were not so. The finding may suggest that FFA mobilization from fat stores is stimulated markedly in non-acclimatized men, owing to the accelerated demand of metabolic fuel necessary for thermoregulation in the cold. However, further investigations are required to know the reason why plasma FFA level is so low in the Ainu. Turnover rate of FFA which might be affected by cold adaptation should be examined to elucidate the mechanism involved in lipid metabolism in this ethnic group.

It is known that during fasting the release of FFA is increased as glucose entry into adipose tissue is decreased. Therefore, the plasma level of FFA might be affected by the time of blood sampling after food intake. As to this problem, we have observed diurnal variations of plasma FFA level and influence of starvation on its level on 10 subjects³⁷⁾. It was demonstrated that the plasma FFA level began to increase 10 hours after meal and thereafter was elevated progressively with the elapse of time. In the present study blood samples were obtained in the morning without breakfast, but the elapse of time after dinner was somewhat different from individual to individual. Therefore, some doubt might be raised to the evaluation of the data. However, it was shown that the plasma FFA level was significantly higher in subjects born on the main island than in those born on Hokkaido, when the sampling of blood were made exactly 15.5 hours after dinner³⁷⁾. The observation would appear to exclude the possibility that the variations of FFA levels might be related to different time of blood sampling.

At all events, in regard to the present observations nutritional surveys of the groups studied should be evaluated, since it is possible that dietary habits influence the plasma lipid levels.

SUMMARY

Plasma lipid profiles in the winter were studied in 128 male subjects. They were Japanese subjects born on the main island, those born on Hokkaido, and Ainu.

Appreciable differences were not detected among these three groups in the concentrations of total lipids, triglycerides, phospholipids, total and free cholesterol, and esterified fatty acids in the plasma, although average values of total cholesterol and phospholipids were considerably low, as compared with values reported by American or European investigators.

Highly significant differences were observed in the plasma levels of FFA; the lowest values were obtained in the Ainu who were considered to be well adapted to cold, while the highest in subjects born on the main island and not adapted to cold.

The results suggest that FFA mobilization is related in some way to the thermoregulation in the cold and the development of cold acclimatization.

The authors are greatly indebted to Dr. K. KUMAGAI, Director of the Monbetsu General Hospital, Dr. K. MATSUMOTO, Director of the Huren Hospital, Mr. K. OTSUKA, Asahikawa Police Station, and Dr. N. YAZAWA in Niikappu for their cordial help. This work was supported by a grant from the Japan Society for the Promotion of Science (M-8) and in part by a grant from the Ministry of Education.

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