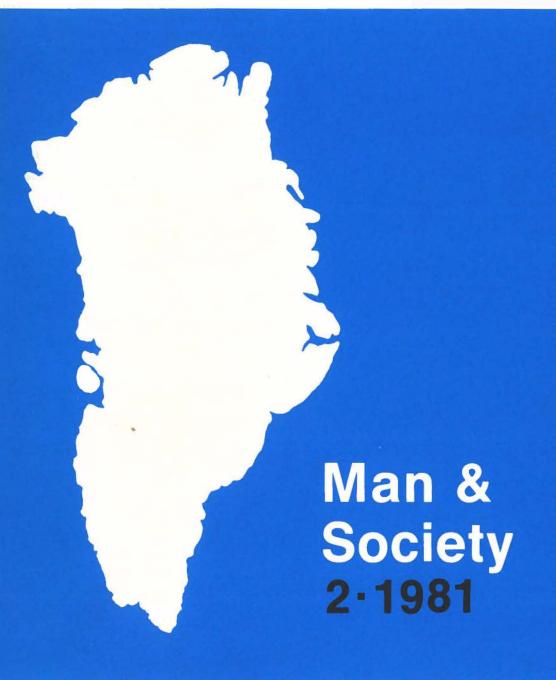
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The Lipid Metabolism in Greenlanders

H. O. Bang and Jørn Dyerberg



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# The Lipid Metabolism in Greenlanders

H. O. Bang and Jørn Dyerberg

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# The Lipid Metabolism in Greenlanders

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In the years 1970, 1972 and 1976 the blood lipids in Greenlanders living in the Umanak district and the composition of their food, especially that of their dietary fat were examined in an attempt to explain the rarity of ischaemic heart disease in Greenlanders.

Decreased concentrations of serum cholesterol, triglycerides, low density and very low density lipoproteins and increased concentration of high density lipoprotein in male Eskimos were found. The fatty acid pattern of the serum lipids was different from that of Danes. Especially remarkable was the high concentration of eicosapentaenoic and low concentration of arachidonic acids compared with Danes. The serum lipids of Greenlanders living in Denmark were found similar to that of Danes.

The Eskimo food was found rich in protein and poor in carbohydrate. The fatty acid pattern of the dietary fat was similar to that found in their blood.

We could show – by in-vitro experiments – that eicosapentaenoic acid can act as precursor for thrombocyte active prostaglandins in stead of arachidonic acid in Europeans, giving rise to an anti-aggregatory prostaglandin, probably PGI<sub>3</sub>, but to no pro-aggregatory thromboxane. This causes a shift in the balance towards the anti-aggregatory – and consequently anti-thrombotic – side.

During a fourth expedition in 1978 to the Umanak district our theory from the in-vitro experiments was confirmed by in-vivo observations in the Eskimos. We found decreased platelet aggregability and increased bleeding time.

The rare incidence of ischaemic heart disease and other thrombotic diseases in Greenlanders can be explained by their low serum lipids, their high content of  $\alpha$ -lipoprotein and – probably most important – by their special serum fatty acid pattern giving rise to a decreased platelet aggregability and consequently a decreased tendency to thrombosis.

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#### Introduction

One of the most important causes of death in western populations is ischaemic heart disease. The incidence of this disease has increased during several decades and it has become one of the major challenges in medicine to find prophylactic measures against it. There is still some uncertainties concerning the causes of ischaemic heart disease and other atherosclerotic conditions, but it is a general opinion that the lipid level in blood, primarily that of cholesterol, is of importance for the development of atherosclerosis. Furthermore, that the level of the blood lipids is influenced by the composition of the food. Epidemiological studies in most parts of the world (Keys 1965) have shown correlation between fat consumption and death of ischaemic heart disease. It has been shown that the composition of the dietary fat especially the relation of saturated to polyunsaturated fats - is of importance for the incidence of this disease.

Nothing has hitherto been published concerning the lipid metabolism of Greenlanders and only little about the composition of their food, especially about that of their dietary fat.

Ischaemic heart disease is very rare in Greenlanders (Harvald 1974). In his extensive nosography of Greenland, Berthelsen (1940) does not even mention ischaemic heart disease, although he gives some information about atherosclerosis in the Greenlanders. Other thrombotic diseases, both in the arterial and the venous systems, are mentioned very scarcely by him or not described at all. In the annual report on the state of health in Greenland (Bøggild et al. 1978) covering the years 1973-1976 death from ischaemic heart disease constitutes on an average 3.5 per cent of all causes of death. In this and other official medical statistics no distinction is made between true Greenlanders and Danes living in Greenland and almost invariably carrying their western style of life with them. However, the Danish fraction of the total population of about 50.000 inhabitants of Greenland is small. Life expectancy is rapidly increasing after tuberculosis has been successfully defeated, now being over 60 years. The most common cause of death is accidents, amounting to about one third of all deaths. In the medical statistical report of Greenland is mentioned that an annual average of 9.5 cases of myocardial infarction is admitted to the hospitals in Greenland. The main part of these patients as well as of the reported deaths from ischaemic heart disease comes from the southern and most »westernized« part of Greenland, whereas not a single death from ischaemic heart disease nor case of myocardial infarction is reported from the Umanak district (population of about 2600) in the decade 1968–78 where the present investigation has been carried out.

In 1969 we decided to start examinations in Greenland with the purpose of attempting to find the cause of the nearly non-existence of thrombotic diseases in Greenlanders. If an explanation could be given, it might be of importance for maintaining the absence of these diseases in Greenlanders and for establishing prophylactic measures against them in other parts of the world.

During the years 1970–78 we have carried out four expeditions to the Umanax district with the aim to study the lipid metabolism in the Greenlanders and – by means of food examinations – to try to find the cause of eventual peculiarities of the Greenlanders' blood lipids, and possibly to deduct from our analytical results an explanation of the infrequency of ischaemic heart disease in Greenlanders.

## First Umanak Expedition 12 August – 17 September 1970

The purpose of this expedition was to collect blood samples from Greenlanders, preferably persons living as hunters and/or fishermen and their wives in order to carry out extensive analyses of the composition of their blood lipids.

The expedition comprised three members, namely the authors and Aase Brøndum Nielsen who served as laboratory technician.

We chose the Umanak district for the examinations because the conditions of life here at that time was still rather typical Greenlandic, with hunting and fishing as the main occupations.

The Umanak district is located on the west coast of Greenland at latitude 70°40′ north, about 500 km north of the Arctic circle. There is one main city: Umanak with about 1100 inhabitants, and seven settlements with from 70 to 280 inhabitants. The population of the whole district is about 2600 inhabitants of whom very few are born outside Greenland.

In the settlements a great deal of the adult males are occupied by seal hunting, occasionally whale hunting, and fishing. In the city of Umanak part of the population is working in offices, service institutions and trade, and the hunting and fishing is of less importance.

As an example of the extent of the seal and whale hunting, the reported figures for the seals and whales caught in the district in the year of 1970 is given in table 1. The figures are minimum figures because not all seals caught are reported, even if the hunters are asked to do so. Almost all the meat from seals and whales is eaten by the local population. The sledge dogs are mainly fed on fish. No calculations exist of the amount of fish landed in the district. The shooting of reindeer, ptarmigan and marine birds is of little nutritional importance in the district.

In the city of Umanak as well as in the settlements there are shops where food and other necessities can be bought. In the settlements the population will mainly buy flour, bisquits, sugar, rice, margarine, tea, coffee, beer and spirits for consumption. All meat is eaten boiled if not raw. Frying is not used.

#### Material and methods

Blood samples were taken in the fasting state in the morning in 130 Greenlanders, 61 males and 69 females,

Table 1. Captured seals and whales in the Umanak district in 1970 and calculations of the meat consumed from these sources (Bang and Dyerberg 1972).

		Whales				Seals		
	Lesser Rorqual <sup>a</sup>	Narwhale <sup>b</sup>	Belugac	Ringed seal <sup>d</sup>	Bearded seale	Harp seal	Hooded seal <sup>8</sup>	Total
Animals captured (n)	22	23	8	11.904	28	476	75	12.536
Estimated average weight of meat and edible entrails (kg)	2.000	250	225	22	110	35	100	
Estimated total weight of meat and edible entrails (kg)	44.000	5.750	1.800	261.888	7.080	16.660	7.500	340.678
Meat sold outside the Umanak district (kg)	1.900							1.900
Meat and entrails consumed in the Umanak district (kg)	42.100	5.750	1.800	261.888	3.080	16.660	7.500	338.778
seal meat per person (2.400 inhabitants) and day (kg)								0.387

<sup>&</sup>lt;sup>a</sup> Balaenoptera acutorostrata L, <sup>b</sup> Monodon moneceros L, <sup>c</sup> Delphinapterus leucas P, <sup>d</sup> Pusa hispida S, <sup>e</sup> Eriguathus barbatus E, <sup>f</sup> Pagophilus groenlandicus E, <sup>g</sup> Cystophora cristata E.

aged 30-83 years. The results of the analyses were compared with those of two groups of persons, namely 32 Greenlanders living in Denmark, and 193 Danes of the same age and sex distribution (Dyerberg 1972).

The following measurements were carried out:

Total lipid content in serum Cholesterol content in serum Triglycerides content in serum Phospholipids content in serum Chylomicron content in serum

 $\beta$ -lipoprotein (Low density lipoprotein, LDL) content in serum

Pre- $\beta$ -lipoprotein (Very low density lipoprotein, VLDL) content in serum

 $\alpha\text{-lipoprotein}$  (High density lipoprotein, HDL) content in serum

Fatty acids in ester bound with cholesterol in serum Fatty acids in ester bound as triglycerides in serum Fatty acids in ester bound as phospholipids in serum

Serum or plasma was separated from the blood samples shortly after the venipuncture and was kept in ice-water during transportation in up to ten hours to the hospital in Umanak. Here the samples were frozen to about -20°C and kept deep frozen until they were analysed in the Department of Clinical Chemistry in the Aalborg Hospital, section North. The analyses were carried out by traditional clinical chemical techniques. The determinations of the fatty acid pattern were done gasliquid-chromatographically after separation of cholesterol esters, triglycerides and phospholipids by silica gel column chromatography. A Beckman GCM gas chromatograph equipped with a 2 m glass column of 3 mm internal diameter was used. Supporting medium was chromosorb WAW, mesh 80-100, and the stationary phase was 10 per cent w/w diethylene glycol succinate. The injection temperature was 250°C, and the column was kept at 180°C with a column flow of 30 ml/min of nitrogen. A hydrogen flame ionization detector was used at a temperature of 250°C. The signal was analysed by a disc integrator and compared with those of assays on mixtures of pure fatty acids from Nu-Check Prep, Elysian, Minnesota, U.S.A.

As lipoproteins are rather unstable, the measurements of these compounds were carried out in the laboratory of the Umanak Hospital within 12 hours from the venipuncture using the method of Dyerberg & Hjørne (1970).

#### Results

The concentration of plasma total lipids, cholesterol, triglycerides and phospholipids in the two sexes together with those of a control group of healthy Danes are given in table 2 and 3. The significances of possible differences between the Greenlanders and the controls (p-values) are stated.

Table 4 and 5 show the results of quantitative lipoprotein assays with the corresponding values from healthy Danish controls.

In order to examine if the described differences in the blood lipid patterns between Greenlanders and Danes were due to racial peculiarities of the lipid metabolism of Greenlanders, we examined the blood lipids in 32 Greenlanders living in Denmark under ordinary Danish dietary conditions. There was found no differences between the concentrations of the blood lipids in these Greenlanders and Danes.

In table 6-8 are given the results of the fatty acid determinations in serum cholesterol esters, in triglycerides and phospholipids in Greenlanders and Danish controls.

It has been stressed by several authors that the ratio saturated/polyunsaturated fatty acids in the food is determinant for the cholesterol level of the blood. As the fatty acid pattern of the blood to some degree reflects that of the food, we have calculated the sum of the

Table 2. Average concentrations of plasma total lipids and cholesterol in Greenlanders and Danish controls (Bang and Dyerberg 1972; Dyerberg 1972; Dyerberg et al. 1977).

		Total li	pids g/liter				Chole	sterol mme	ole/liter	
(	Greenlander			Danes		Greenl	anders		Danes	
Males aged	mean	SD	mean	SD	Sign. of diff.	mean	SD	mean	SD	Sign. of diff.
31-40	6.01	0.99	6.29	0.74	no	4.75	0.723	5.46	0.801	p < 0.01
41-50	6.42	1.17	7.42	1.63	p < 0.05	4.98	0.786	6.28	1.027	p < 0.005
51-60	6.46	1.02	7.17	1.16	p = 0.05	5.33	0.782	6.24	1.004	p < 0.005
≧61	5.95	0.56	7.04	1.28	p < 0.005	5.07	0.766	5.83	1.053	p < 0.05
Females								343		
aged 31–40	5.71	0.93	6.32	0.97	p < 0.05	4.59	0.951	5.52	1.044	p < 0.005
							0.931	6.04	1.036	p < 0.005
41-50	6.18	0.91	6.77	1.05	no	5.02				1
51-60	6.50	0.89	8.02	1.29	p < 0.001	5.32	0.822	7.00	1.182	p < 0.005
≧61	6.21	0.86	8.19	1.26	p < 0.001	5.19	0.639	7.08	1.524	p < 0.005

SD = standard deviation. The statistical comparisons are performed after logarithmic transformation. Student's t-test.

saturated, monounsaturated and polyunsaturated fatty acids in the serum lipids. The results are given in table 9.

#### Discussion

The only examinations of plasma lipids in Greenlanders hitherto, namely the cholesterol concentration, have been carried out by U. Sagild in cooperation with Ancel Keys. The results have not been published, but Sagild has informed us that the cholesterol level in the Greenlanders' blood was found lower than that of Danes. Our study of the blood cholesterol level in Greenlanders confirmed this finding.

Table 3. Average concentrations of plasma triglycerides and phospholipids in Greenlanders and Danish controls (Bang and Dyerberg 1972; Dyerberg 1972).

	Triglycerides mmole/liter						Phospl	holipids mm	ole/liter	
G	reenlander			Danes		Greenla		•	Danes	
Males aged	mean	SD	mean	SD	Sign. of diff.	mean	SD	mean	SD	Sign. of diff.
31-40	0.66	0.44	1.15	0.53	p < 0.001	2.94	0.50	2.75	0.44	no
41-50	0.62	0.26	1.65	0.79	p < 0.001	2.99	0.51	2.91	0.85	no
51-60	0.61	0.21	1.32	0.62	p < 0.001	3.42	0.55	2.84	0.60	p < 0.003
≧61	0.68	0.32	1.35	0.81	p < 0.001	3.14	0.49	2.79	0.57	p < 0.05
Females aged		-			,		-			
31-40	0.41	0.16	0.95	0.40	p < 0.001	2.82	0.64	2.83	0.62	no
41-50	0.47	0.14	1.02	0.43	p < 0.001	3.05	0.85	2.98	0.40	no
51-60	0.54	0.19	1.10	0.41	p < 0.001	3.27	0.46	3.28	0.47	no
≧61	0.59	0.15	1.30	0.47	p < 0.001	2.94	0.33	3.30	0.54	p < 0.02

Table 4. Average concentrations of plasma chylomicrons and LDL in Greenlanders and Danish controls (Bang and Dyerberg 1972; Dyerberg 1972).

		LDL g/liter					rons g/liter	Chylomic		
	Danes		nders	Greenla		Danes			Greenlanders	
Sign. of diff.	SD	mean	SD	mean	Sign. of diff.	SD	mean	SD	mean	Males aged
no	0.85	4.55	0.88	4.32	p < 0.05	0.10	0.18	0.18	0.31	31-40
no	1.52	5.19	1.56	4.58	no	0.11	0.23	0.27	0.30	41 - 50
p < 0.003	1.08	5.32	0.70	4.52	p < 0.001	0.08	0.16	0.12	0.30	51-60
p < 0.003	1.20	5.22	0.71	4.23	no	0.13	0.21	0.12	0.28	≧61
										emales ged
no	1.23	4.29	1.00	4.03	p < 0.005	0.10	0.16	0.18	0.36	31-40
no	1.22	4.86	0.74	4.56	no	0.09	0.15	0.10	0.18	41 - 50
p < 0.00	1.45	6.02	0.81	4.48	no	0.10	0.19	0.14	0.23	51-60
p < 0.003	1.52	6.26	1.16	4.88	no	0.08	0.23	0.10	0.21	≧61

Table 5. Average concentrations of plasma VLDL and HDL in Greenlanders and Danish controls (Bang and Dyerberg 1972; Dyerberg 1972).

		VLD	L g/liter					HDL g/lite	r	
	Greenlanders			Danes		Greenla	anders		Danes	
Males aged	mean	SD	mean	SD	Sign. of diff.	mean	SD	mean	SD	Sign. of diff.
31-40	0.62	0.36	1.17	0.59	p < 0.005	3.47	1.02	2.90	0.69	no
41 - 50	0.44	0.42	1.81	0.87	p < 0.001	4.20	1.54	2.84	1.08	p < 0.01
51-60	0.42	0.28	1.58	0.77	p < 0.001	4.41	1.61	2.78	0.89	p < 0.001
≧61	0.30	0.27	1.45	1.02	p < 0.001	4.09	1.51	2.75	0.80	p < 0.01
Females										
aged	0.15	0.20	0.00	0.51	- 0.005	2 2 4	1.20	2 7 .	0.00	
31-40	0.45	0.30	0.99	0.54	p < 0.005	3.31	1.20	3.71	0.92	no
41 - 50	0.43	0.35	1.11	0.49	p < 0.001	4.03	1.51	3.57	1.10	no
51 - 60	0.39	0.39	0.98	0.55	p < 0.005	4.74	1.90	4.35	1.04	no
≧61	0.42	0.31	1.23	0.68	p < 0.001	3.74	1.19	3.78	0.97	no

Table 6. The average fatty acid composition of plasma cholesterol esters in % of total.

	Greenlanders	Danes
8:0–12:0	0.0	4.6
14:0	1.2	0.7
14:1	0.0	0.7
16:0	19.2	11.4
16:1	9.2	3.4
17:0	0.0	0.2
18:0	1.0	1.1
18:1	25.3	18.3
18:2	20.3	51.0
18:3	0.1	0.5
19:0	0.1	0.0
20:0	0.1	0.0
20:1	0.1	0.0
20:2	0.0	0.0
20:3	3.4	0.0
20:4	1.0	5.8
20:5	15.8	0.9
22:0	0.0	0.0
22:1	0.1	0.0
22:3	0.1	0.0
2:5	0.1	0.0
22:6	1.0	0.4
24:0	0.4	0.0
24:1	0.9	0.0
24:2	0.9	0.0

The data for the Greenlanders are those given by Dyerberg et al., 1975, whereas the Danish figures are new and not earlier published results. Fatty acids are indicated by the number of carbon atoms in the molecule, followed by a ":" and a figure indicating the number of double bonds. Due to 1–2% of unidentified components the sums of the percentages are not exactly 100.

Table 7. The average fatty acid composition of plasma triglycerides including free fatty acids in % of total (Dyerberg et al. 1975).

al. 1975).		
	Greenlanders	Danes
12:0	0.2	0.2
14:0	2.1	2.1
14:1	0.1	0.2
16:0	25.1	26.3
16:1	9.4	4.6
16:2	0.1	0.0
17:0	0.1	0.3
18:0	5.8	5.5
18:1	35.0	37.2
18:2	6.2	17.9
18:3		1.1
20:0	0.5	0.1
20:1	3.3	0.4
20:2	0.1	0.1
20:3		0.0
20:4		1.5
20:5	4.2	0.7
22:0	1.1	0.2
22:1	0.1	0.4
22:3	0.2	0.0
22:4	0.2	0.0
22:5	0.3	0.0
22:6	2.4	0.6
24:0	0.6	0.0
24:1	0.2	0.0
24:2	0.6	0.0

See footnote to table 6.

Table 8. The average fatty acid composition of plasma phospholipids in % of total (Dyerberg et al. 1975).

	Greenlanders	Danes
14:0	0.1	0.3
16:0	34.8	30.0
16:1	2.6	0.8
17:0	0.0	0.7
18:0		14.6
18:1	15.9	12.4
18:2	6.6	22.3
18:3	0.0	0.2
20:0	0.3	0.4
20:1		0.1
20:2	0.0	0.2
20:3		0.0
20:4		7.4
20:5		1.8
22:0		1.4
22:1	0.0	0.8
22:5	0.2	0.2
22:6	3.9	2.2
24:0	2.1	0.5
24:1	0.1	1.1
24:2	0.1	0.0

See footnote to table 6.

Our observations concerning the other blood lipids and lipoproteins are new. They may be summarized as follows: The concentration of plasma triglycerides in Greenlanders was found much lower than in Danes. The level of phospholipids did not differ from that of Danes. The concentration of plasma  $\beta$ -lipoprotein (LDL) was found lower in Greenlanders, while that of pre- $\beta$ -lipoprotein (VLDL) was much lower than in Danes.

The sex difference in some plasma lipids (cholesterol, triglycerides, VLDL) described in western countries by several authors was not found in Greenlanders.

The level of plasma α-lipoprotein (HDL) was found higher in male Greenlanders than in male Danes. It has been shown by several authors (Miller & Miller 1975, Miller et al. 1977) that a high concentration of α-lipoprotein in plasma is strongly negatively correlated to ischaemic heart disease. Our finding of a high level of HDL in male Greenlanders supports this concept and is in fact the first epidemiological observation of an association between a high HDL and a low incidence of ischaemic heart disease.

The concentrations of several of the fatty acids in esterbound differed dramatically from the Danish pattern. The concentration of linoleic (C  $18:2\omega-6$ )\* and linolenic (C  $18:3\omega-3$ ) acids were found lower in the

<sup>\*</sup> The nomenclature of the fatty acids is as follows: C means carbon atom. The following figure gives the number of carbon atoms. The figure after the colon is the number of double bonds in the molecule. The figure after the  $\omega$  indicates the number of the carbon atom where the first double bond is situated as counted from the opposite end of the molecule than the carboxyl group.

Table 9. The distribution of esterified fatty acids in plasma lipids divided in saturated, mono- and polyunsaturated acids (Dyerberg et al. 1975).

	Cholester	ol esters	Trigly	cerides	Phosph	olipids	To	tal
Fatty acids	G	D	G	D	G '	D	G	D
Saturated	22	18	36	35	58	49	39	34
Monounsaturated	36	23	45	43	21	16	34	27
Polyunsaturated	42	59	19	22	21	35	27	39

Values in % of total. G = Greenlanders, D = Danes.

Greenlanders. This might be expected as these fatty acids essentially arise from vegetable oils which are scarce in the Eskimo diet.

Remarkable is the high level of the long-chained polyunsaturated fatty acid 5, 8, 11, 14, 17-eicosapentaenoic acid (C  $20:5\omega-3$ ) which is known to be abundant in the body fats of arctic marine animals. Eicosapentaenoic acid of which only very small amounts are normally found in the blood of western populations was one of the major components of the esterified fatty acids in plasma of Greenlanders, constituting up to 16 per cent of the total fatty acids in ester-bound with cholesterol.

The concentration of arachidonic acid (C  $20:4\omega-6$ ) which is rather high especially in the phospholipids of Danes was found much lower in the Greenlanders' cholesterol esters and phospholipids.

Even if linolenic acid (C  $18:3\omega-3$ ) is very low in Greenlanders, the differences in the polyunsaturated fatty acids between Greenlanders and Danes are essentially that the  $\omega-6$  class is replaced in the Eskimos by the  $\omega-3$  class. This is most clearly seen in the content of linoleic (C  $18:2\omega-6$ ) and arachidonic (C  $20:4\omega-6$ ) acids which are both lower in the Greenlanders. The corresponding dominating  $\omega-3$  polyunsaturated fatty acid in the Eskimos is eicosapentaenoic acid (C  $20:5\omega-3$ ). This shift in polyunsaturated fatty acid composition, especially the dominance of eicosapentaenoic acid should – as it turned out later – be of main importance when considering the prostaglandin synthesis and the regulation of haemostasis.

The finding of almost identical plasma lipid values in Greenlanders living under Danish conditions in Denmark as compared with Danes lead to the conclusion that the differences in plasma lipid levels between Greenlanders and Danes are not due to racial peculiarities in the Eskimos' lipid metabolism, but must be of exogenous, presumably nutritional origin.

It has been established by several authors that there exists a strong correlation between the cholesterol level in blood – or rather the level of the mainly cholesterol containing LDL – and the incidence and death of ischaemic heart disease. Consequently, the lower level of blood cholesterol in Greenlanders, found by Sagild and ourselves, can be expected to lead to a decreased incidence of ischaemic heart disease, probably due to a delayed development of atherosclerosis. Our finding of a

low level of cholesterol and of  $\beta$ -lipoprotein (LDL) in plasma of Greenlanders confirm this concept.

It is difficult to combine the generally accepted concept of the advantage of a relatively high intake of polyunsaturated fatty acids and consequently a high plasma level of polyunsaturated fatty acids, as it involves a low blood cholesterol level, with our present results. The discrepancy is that a generally higher proportion of polyunsaturated fatty acids was *not* found in the plasma of Greenlanders (table 9). In fact the sum of the saturated fatty acids was found to be higher, and that of the polyunsaturated fatty acids lower in the Greenlanders.

#### Conclusion

The low level of blood lipids, especially that of cholesterol and  $\beta$ -lipoprotein (LDL), and the high level (in males) of  $\alpha$ -lipoproteins (HDL) in Greenlanders should be expected to lead to a lower incidence of ischaemic heart disease as compared with that of western populations.

However, there is still need for a supplementary explanation of the almost non-existence of this disease. It was felt that further examinations in Greenland were necessary in order to get closer to a satisfactory understanding.

# Second Umanak Expedition 7 August – 4 September 1972

As mentioned our theory concerning the cause of the almost non-existence of ischaemic heart disease in Greenlanders was that it was mainly due to the special Greenlandic nutrition. The peculiarities of the blood lipids in Greenlanders must be expected to be of nutritional origin. Consequently, it was felt that a thorough examination of the Greenlanders' food was indicated, and this was the aim of the second expedition.

The members of the expedition were the same as those of the first expedition.

The settlement of Igdlorssuit about 100 km north of Umanak was chosen as particularly suitable for a food examination as the population of this settlement are

Table 10. Average amounts of protein, fat and carbohydrate (caloric %) in the diet of arctic populations and of the Danish population in 1972 (Bang, Dyerberg and Hjørne 1976).

Authors	Year of publication	Place of study	Protein	Fat	Carbo- hydrate
Krogh and Krogh	1914 1935–43	Northwest Greenland Greenland	44	47	8
		Hunters	19	27	53
		Fishermen	40	10	50
Rodahl	1954	Alaska		37	
Uhl et al	1955 1972	Northwest Greenland Alaska inland	36	25	39
		In 1955-57	33	41	26
		In 1965	15	40	45
Feldman et al	1972	Northwest Greenland	30-35	50	15-20
Present investigation	1974	Northwest Greenland	26	37	37
Helms	1972	Denmark	11	42	47

active hunters and/or fishermen. The inhabitants of the settlement, about 140 persons, all live to a greater or lesser degree on catch from hunting and fishing, predominantly seal, whale and fish.

#### Material and methods

The study comprised seven persons, five males and two females, aged 32–76 years. During a period of seven days all meals of these seven persons were collected and weighed in accordance with similar nutritional studies by Keys & Kimura (1970) (the "double-portion-technique"). The subjects were asked not to change their dietary habits and to collect and deliver quantitative dublicates of all their meals. They were visited once a day and interviewed concerning the composition of the meals of the previous day. After collection the food specimens comprising – hopefully – complete day rations were weighed, homogenized, and aliquots were taken out and kept frozen until they could be analysed in Denmark.

The following analyses were carried out: Water content after freeze-drying and weighing of the residue, protein content by the Kjeldahl method, fat content after extraction and weighing by the method of Folch et al. (1951), and content of minerals after burning and weighing the ashes. The carbohydrate content was calculated as the difference between dry weight and the sum of protein, fat and minerals. The caloric values were calculated by means of Atwater's factors, protein and carbohydrate 4 Kcal/g, fat 9 Kcal/g.

In the fat extracts cholesterol was determined gasliquid-chromatographally on a 3 per cent OV column at 260°C. The fatty acids were determined – after hydrolysis and methylation – by gas-liquid-chromatography with the same equipment and reagents as mentioned for the fatty acid determinations in serum.

Comparisons with average Danish food were made with figures given by Helms (1975) based on food analyses carried out by the Danish State Institute of Food.

#### Results

In table 10 are listed the average amounts of food components in caloric per cent from seven Greenlanders. The corresponding figures from other studies of arctic and Danish diets are given for comparison.

In table 11 are given the average daily energy and fat intake in the Eskimos.

In table 12 are listed the relative amount (percentage of total) of the fatty acids in the food portions collected

Table 11. Total energy and fat intake per day of Eskimos.

	Energy (Kcal/day)	Fat (g/day)
Mean	1541	69.9
Midrange	4762	303.6
Range	117-9407	3.9-603.3

Table 12. Average content of fatty acids (percentage of the total fatty acids) in the food consumed by seven Eskimos during seven days and corresponding mean values for common Danish food (Bang, Dyerberg and Hjørne 1976).

	Eski	Eskimos					
Fatty acid	mean	SD	mean				
C12:0	1.1	1.0	5.9				
C14:0	5.7	1.1	7.5				
C16:0	19.2	4.7	25.5				
C16:1	13.5	4.5	3.8				
C18:0	4.9	2.5	9.5				
C18:1	29.7	5.3	29.2				
C18:2	4.7	2.7	10.0				
C18:3	0.4	0.3	2.0				
C20:0	0.6	0.8	4.3				
C20:1	6.9	3.5	0.4				
C20:4	0.1	0.4	0.0				
C20:5	2.3	1.4	0.4				
C22:0	1.8	2.3	0.0				
C22:1	4.6	2.9	1.2				
C22:6	2.2	2.2	0.3				
C24:0	0.4	0.8	0.0				
C24:1	1.9	2.1	0.0				

in seven days, calculated as average of all portions and subjects. Average values for Danish food are given for comparison.

In table 13 are given the sums of the contents of saturated, monounsaturated and polyunsaturated fatty acids in the diet of Greenlanders and Danes.

#### Discussion

Several investigations concerning the nutrition of arctic populations have been published (table 10). However, most of the studies deal with the net composition of the diets in terms of protein, fat and carbohydrates, and do not include the chemical composition of the nutritional fat in detail. No study has to our knowledge hitherto been carried out with the specific aim of elucidating the fatty acid composition of the dietary fat.

Generally it has been found that arctic populations consume more protein and less carbohydrates than western populations. The arctic diets are generally considered to contain more fat than in the western world. Our examination of the 49 food portions from seven persons could confirm the general opinion with the exception that we found the Greenlanders' diets containing less fat than average Danish food.

The high proportion of protein in the food is in accordance with the fact that meat – from seal, whale and fish – is the predominant nutrition of this population.

From hunting statistics from 1970 we calculated that each subject in the Umanak district consumed an average of about 400 g seal and/or whale meat a day (table 1).

In table 14 are listed the average number of meals

Table 13. Sums of the saturated, monounsaturated, and polyunsaturated fatty acids (percentage of total fatty acids) in Eskimo and Danish food (Bang, Dyerberg and Hjørne 1976).

Fatty acids	Eskimos	Danes		
Saturated	33.7	52.7		
Monounsaturated	56.6	34.6		
Polyunsaturated	9.7	12.7		

Table 14. Average number of meals during one week, which contain one or several of the food components listed (Bang, Dyerberg and Hjørne 1976).

Whale (meat and blubber)	. 5.7
Seal (meat and blubber)	. 6.4
Seal (intestines)	. 0.6
Wildfowl	. 0.6
Fish	. 1.4
Soup with seal meat	. 2.3
Tinned food	. 0.7
Potatoes	. 1.9
Milk (powder)	. 0.7
Bread	. 13.6
Biscuits	. 1.0
Sugar	. 35.4
C	

during one week which contained one or several of the food components mentioned. It can be seen that whale and/or seal meat was eaten every day. Sugar was used abundantly about five times a day, mostly in tea or coffee.

The Eskimo pattern of eating habits gives rise to enormous variations in the daily energy intake (table 11). The fat intake may occasionally exceed 600 g a day giving an energy intake of 9000 Kcal!

It is interesting that the fat intake of Greenlanders was found to be even a little less than that of Danes, considering the large meat/fish consumption and the relatively high fat content of seals and whales, especially in blubber and intestines, part of which is eaten. However, the large amount of fat in Danish diets originates mostly from diary products which are very scarce in the Greenlanders' diet.

As expected the composition of the Eskimo nutritional lipids was found very different from that of Danes (table 12). The pattern grossly reflects that of the serum fatty acid pattern (table 6–8). The Eskimo food was found to contain much more of the monoenes C 16:1, C 20:1 and C 22:1 than Danish food.

Also remarkable was the much higher intake of eicosapentaenoic acid (C  $20.5~\omega$ -3) in Eskimos giving rise to a high plasma concentration of this fatty acid which later on should appear to be of paramount importance.

However, later examinations of the freeze-drying technique used for the food samples showed that this technique – even if it is carried out in a temperature below –20°C and under strongly reduced air pressure, and the samples afterwards were kept under nitrogen in tightly closed vials – do not completely prevent some oxidation of the highly reactive polyunsaturated fatty acids. The figures for these fatty acids in table 12 must therefore be considered to be somewhat too low. This influences to a similar degree the other figures of the table as the amounts are listed as per cent of total. In the food analyses of the portions collected during the third Umanak expedition in 1976 (see later), the technique has been changed as to warrant correct results.

As demonstrated by Keys et al. (1965) and Hegsted et al. (1965) the level of serum cholesterol is, among other things, a function of the dietary intake of polyunsaturated fatty acids relative to that of saturated ones. The influence of fatty acid intake on the serum cholesterol level is determined by the amount af saturated fatty acids minus half the amount of polyunsaturated fatty acids, expressed as caloric per cent, according to the formula of Keys et al. (1965):

s. chol. = 2.7 (S-1/2P) + 1.5 (
$$\sqrt{C_2}$$
- $\sqrt{C_1}$ )

where S and P are the caloric percentages of saturated and polyunsaturated acids respectively, omitting stearic acid (C 18), and  $C_1$  and  $C_2$  are mg cholesterol/1000 calories in the two diets to be compared.

Applying this formula to our data a change from

Danish food (Helms 1975) to the Greenlandic food observed in this study, assuming an unchanged intake of energy, would cause the serum cholesterol level to decrease 7.6 mg/100 ml or 0.20 mmol/l. This is not in accordance with the definitely lower serum cholesterol found by us in Greenlanders (table 2) as compared with that of Danes of the same age, this difference being averagely 1.15 mmol/l. It must be concluded that Key's formula which was worked out from data from young Americans is not valid for Greenlanders whose dietary and other life habits are so different.

#### Conclusion

The results of the examination of Greenlanders' food confirm earlier observations concerning the high protein and low carbohydrate content. The slightly lower fat content as compared with Danish food is remarkable. The fatty acid pattern of the food reflected that of the blood, observed during the first Umanax expedition, especially concerning the high content of the monoenes C 16:1, C 20:1, and C 22:1, and of the long-chained polyunsaturated acid C 20:5 $\omega$ -3, the content of which is probably even higher than our results show.

After the conclusion of the analytical work on the food samples we felt that our material was too small as to warrent definite inferences, especially concerning the diverging fatty acid pattern. Consequently, we determined to repeat the food examination in Greenland and preferably with a bigger amount of food samples.

# Third Umanak Expedition 19 April – 12 May 1976

The purpose of this expedition was to collect food samples for supplementary analyses of the Greenlanders' diet.

The members of the expedition were – besides the authors who acted as scientific leaders –

Professor Hugh M. Sinclair, Oxford.

Anna Rosenquist, dietician, Aarhus Universitet.

Ivars Silis, author and arctic traveller, responsible for the practical problems of the expedition, Julianehåb.

Ruth Edgar, clinical chemical technician, Aalborg Hospital.

Grete Jespersen, clinical chemical technician, Aalborg Hospital.

Kaj Fogh, electrical engineer, Aalborg Hospital. In Greenland two interpreters were engaged.

The place of the examinations was again the settlement of Igdlorssuit in the Umanak district. Winter climate was still prevailing. For all transportations dog sledging on the frozen ice was used. The temperature went down to about 20–25°C below zero during night and often rose to about zero at noon.

The collection of food samples was carried out in the same way as earlier, using the double-portion-technique. More emphasis was laid on the interviews about the composition of the meals.

50 Greenlanders, 25 male and 25 females, aged 20-76 years, all hunters and/or fishermen and their wives, participated in the examination. The collection of food samples was carried out during five to seven consecutive days. A total of 178 samples of day rations were collected, homogenized and frozen as earlier.

The chemical procedures were the same as earlier, carried out in the clinical chemical department of the Aalborg Hospital, section North.

However, one important change of analytical technique was introduced. As we found that freeze-drying of the food samples from the second expedition involved some risk of oxigenation of the polyunsaturated fatty acid in the food, even if the freeze-drying procedure took place under low pressure and the samples after drying were kept under nitrogen in closed vials, we kept the food samples from this expedition deep-frozen in closed vials, but without freezedrying. The extraction of the lipids was carried out without preceding freeze-drying.

Comparison with average Danish food was made with data from 1972 given by Helms (1975).

#### Results

The average gross composition of the food samples is given in table 15 and the average fatty acid pattern of the food lipids in table 16 together with the results from 1972 and for common Danish food.

The sums of the saturated, mono- and polyunsaturated fatty acids in the Greenlanders' food are listed in table 17 together with the results from 1972 and corresponding Danish figures. In table 18 are given the amounts of fatty acids of the linoleic ( $\omega$ -6) and linolenic ( $\omega$ -3) classes of essential fatty acids eaten daily by Eskimos and Danes respectively, calculated on the basis of an estimated daily energy intake of 3000 Kcal. In table 19 are given the amounts of monoene fatty acids other than palmitoleic (C 16:1) and oleic (C 18:1) acids in Eskimo and Danish food, assuming a daily energy in-

Table 15. Average percentage amounts of energy from protein, fat and carbohydrate in the diet of Greenland Eskimos and in Danes (Helms 1975). Values in brackets are corresponding figures from 1972.

	Eskimos	Danes	
Protein	23 (26)	11	
Fat	39 (37)	42	
Carbohydrate	38 (37)	47	

take of 3000 Kcal. In table 20 the total energy intake and the actual fat consumption of the Eskimos are given.

#### Discussion

The composition of the food samples was found in all essentials similar to those collected in 1972. At that time the collecting of the food samples took place during summer time, the present investigation during winter time. The seal hunting was during our stay in Igdlorssuit very profitable, several seals being delivered almost every day. Consequently, the food was genuine Greenlandic during the examination.

However, there were a few, but important differences between the results from 1972 and 1976. The average concentration of eicosapentaenoic (C  $20:5\omega-3$ ) and docosahexaenoic (C  $22:6\omega-3$ ) acids was in 1972 found to be 2.3 and 2.2 per cent respectively. In the 1976 study the results were 4.6 and 5.9 per cent respectively. The discrepancy may be explained at least partly by technical reasons as mentioned earlier.

Since about 1950 most Eskimos, particularly in Alaska and Canada, have been on diets rich in "western" food. The settlement of Igdlorssuit was established in 1859. The first shop was opened in 1918 and in 1966 a new and bigger shop was built. At the time of our expedition it was stocked with quantities of "western" food of which sugar and white flour were in great demand. In 1975 the shop sold 3147 kg of soft sugar and 1920 kg of lump sugar. This gives a daily consumption of nearly 100 g sugar/person. Between January 1st and

Table 16. Average content of fatty acids as percentage of total fatty acids in Eskimo food as compared with Danish food (Helms 1975). Values in brackets are corresponding figures from 1972.

	Es	Danes	
	Mean	S.E.M.	Mean
C12:0	1.1	0.08 (1.1)	5.9
C14:0	3.7	0.06 (5.7)	7.5
C16:0	13.6	0.26 (19.2)	25.5
C16:1	9.8	0.25(13.5)	3.8
C16:2 (C17:0)	0.4	0.04	
C18:0	4.0	0.15 (4.9)	9.5
C18:1	24.6	0.22(29.7)	
C18:2	5.0	0.28 (4.7)	
C18:3	0.6	0.04 (0.4)	
C20:0	0.1	0.02 (0.6)	
C20:1	14.7	0.37 (6.9)	0.4
C20:2	0	0.01	
C20:4	0.4	0.04 (0.1)	0
C20:5	4.6	0.15 (2.3)	
C22:0	0.1	0.02 (1.8)	
C22:1	8.0	0.23 (4.6)	
C22:5	2.6	0.10 (0)	0
C22:6	5.9	0.16 (2.2)	_
C24:0	0	0.01 (0.4)	
C24:1	0.1	0.02 (1.9)	0

Table 17. Sums of the saturated, monounsaturated and polyunsaturated fatty acids (percentage of total fatty acids) in Eskimo food and in Danish food (Helms 1975). Values in brackets are corresponding figures from 1972.

	Eskimos	Danes
Saturated (S)	22.8 (33.7)	52.7
Monounsaturated		34.6
Polyunsaturated (P)	19.2 (9.7)	12.7
P/S ratio	0.84	0.24

Table 18. Sums of fatty acids in g of the linoleic ( $\omega$ -6) and linolenic ( $\omega$ -3) classes respectively eaten daily by Eskimos and Danes (Helms 1975), assuming a daily intake of 3000 Kcal.

	Eskimos	Danes
Linoleic class (ω–6)	5.4	10.0
Linolenic class (ω–3)	13.7	2.8

Table 19. Sums of monoenes in g other than palmitoleic and oleic acids eaten daily by Eskimos and Danes (Helms 1975) assuming a daily intake of 3000 Kcal.

	Eskimos	Danes
Monoenes	29.6	2.1

Table 20. Total energy intake and fat consumption per day of Eskimo volunteers.

	Energy (kcal/day)	Fat (g/day)
Mean	1541	69.9
Median	1328	53.2
Midrange	4762	303.6
Range	117-9407	3.9-603.3

May 8th 1976 the sale of sugar even was about 175 g per day and person. During the second Umanak expedition 1972 the sugar consumption was calculated to about 165 g per day and person. The energy coming from sugar can be estimated to about 700 Kcal (1976) while white bread, bisquits and rye flour provided about 335, rice 112 and potatoes 35 Kcal per day. The daily carbohydrate consumption from these food items amounted to about 280 g. Whereas whale and seal meat was eaten almost every day, on an average of 400 g per day and person, sugar was taken about five times and bread and bisquits twice a day.

The traditional Eskimo diet, however, contained no sugar or cereals. 25 years ago, Sinclair (1953) observed in Canadian Eskimos the absence of non-infective discases (cardiovascular diseases, diabetes mellitus, appendicitis, cancer, dental caries), but a high prevalence of epistaxis. He calculated that the Eskimo diet in 1855 contained 377 g protein, 162 g fat and only 59 g car-

bohydrate. Obviously, without any "western" contact, the Eskimos would have been totally carnivorous and almost free of carbohydrates, except for a few berries, roots and leaves in the summer.

Therefore the Igdlorssuit Eskimos we have examined are not eating the traditional high fat and protein diet, but their dietary fat is rich in long-chained fatty acids of the linolenic ( $\omega$ -3) class with very little of the linoleic ( $\omega$ -6) class (table 18), and this is reflected in their serum fatty acid pattern (table 6-8).

The results of the examination of the dietary fatty acids may be summarized as follows: The Eskimo food was found to contain much more of the monoenes C 16:1, C 20:1 and C 22:1 than Danish food (table 16). The high consumption of cetoleic acid (C 22:1 $\omega$ -11) by the Eskimos is interesting in view of the known toxicity of docosaenoic acids to all lower mammals reviewed by Beare-Rogers (1977) and FAO/WHO (1977). Cetoleic acid is an isomer of erucic acid (C 22:1 $\omega$ -9) which is a predominant fatty acid of most rape seed oils. Cetoleic acid is a predominant fatty acid of marine oils, constituting about 12 per cent of the fatty acid of herring oil, 15 per cent of capelin oil and 4 per cent of Greenland halibut and seal oils. It causes in certain species cardiac fibrosis because myocardial mitochondria have difficulty in metabolizing it, leading to accumulation of lipid droplets. Adaptation occurs to low doses, which may explain that Eskimos - and seals - do not get cardiac damage. They receive cetoleic acid as foetuses and from the breast feeding.

Another essential difference between Eskimo and Danish food is that the Eskimo intake of linoleic (C  $18:2\omega-6$ ) and linolenic (C  $18:3\omega-3$ ) acids is much less than in Danes. The intake by Eskimos of linoleic acid is less than half of that of Danes, whereas the consumption of linolenic acid is only one fifth.

As linoleic acid in "western" food is the precursor of arachidonic acid (C 20:4 $\omega$ -6), the amount in the Eskimo food of only half of that in Danish food is notable. Also notable is the finding of the high intake by Eskimos of the long-chained polyunsaturated fatty acids eicosapentaenoic (C 20:5 $\omega$ -3), docosapentaenoic (C 22:5 $\omega$ -3) and docosahexaenoic (C 22:6 $\omega$ -3) acids as compared with that of Danes. The sum of these fatty acids – all belonging to the  $\omega$ -3 class – is in Eskimo 13.1 against 0.8 per cent in Danish food. This means that the polyunsaturated fatty acids of the  $\omega$ -3 class (the linolenic acid family) are dominant in the Eskimo food, whereas the  $\omega$ -6 class (the linoleic acid family) dominates in Danish food. This is also reflected in the plasma fatty acid pattern of the Eskimos (table 6-8).

Based on our finding in the 1972 study and using the formula of Keys for calculating changes in the serum cholesterol level when changing one diet with another (p. 10), we found that a change from Danish food to the Eskimo food, assuming an unchanged energy intake, would cause the serum cholesterol to decrease substantially less than the actual difference found be-

tween Eskimos and Danes (table 2). Based on our present findings the calculation by Keys' formula gives a difference between average serum cholesterol level in Eskimos and Danes of 0.67 mmol/l whereas the actual difference is 1.15 mmol/l as found in 1972. This discrepancy between the calculated and actually found differences in serum cholesterol level when going from the Danish to the Eskimo diet stresses that calculations of the influence of dietary alterations on serum cholesterol level are only valid when these are not substantially influenced by major alterations in the composition of the food. They are valid only for quantitative, not for qualitative changes.

In-vitro experiments (Dyerberg & Bang 1978) have shown that the low concentration of serum arachidonic acid (C 20:4ω-6) and high concentration of serum eicosapentaenoic acid (C 20:5ω-3) may be of great importance for the aggregability of thrombocytes in-vivo. The basis for this is that eicosapentaenoic acid can be converted to a potent antiaggregatory agent by the vessel wall, probably  $\triangle$ -17-prostacyclin (PGI<sub>3</sub>), whereas a proaggregatory agent cannot be formed in the platelets from this fatty acid. This is in contrast to the biologically active metabolites of arachidonic acid (C 20:4ω-6) from which as well a potent proaggregatory prostaglandin (TXA<sub>2</sub>) as a potent antiaggregatory substance (PGI<sub>2</sub>) can be formed (Moncada & Vane 1978)\*. In this way the tendency to thrombus formation is diminished in Eskimos, as the aggregation of thrombocytes has been shown to be the initial stage of any thrombotic process.

The results from the two food examinations in Greenland carried out by us represent the first thorough analysis of the composition of the nutritional fat in an arctic population.

#### Conclusion

The findings of the food examination in the summer 1972 were in all essentials confirmed in the winter 1976, now based on a much bigger amount of food samples. The content of the long-chained polyunsaturated fatty acid eicosapentaenoic acid which we found in rather high concentration in the blood of Greenlanders in 1970 was found higher in the food examination in 1976 than in 1972, probably due to better technique. The result from 1976 as regards this important fatty acid must be regarded as the correct one.

Our findings could up to this point – concerning the explanation of the almost non-existing ischaemic heart disease and other thrombotic diseases in Greenlanders – only confirm the earlier established concept of the

<sup>\*</sup> Prostaglandins derived from dihomogamma-linolenic acid (C 20:3ω-6) belong to the 1-family, those derived from arachidonic acid (C 20:4ω-6)to the 2-family and those derived from eicosapentaenoic acid (C 20:5ω-3) to the 3-family.

favourable effect of low blood cholesterol and – perhaps – triglyceride levels. This fact must be considered a delaying factor in the development of atherosclerosis in Greenlanders, but scarcely explains the almost non-existence of coronary thrombosis.

The experiments concerning the formation of thrombocyte active prostaglandins from eicosapentaenoic acid – as mentioned above – open a new possibility of explaining the rarity of ischaemic heart disease in Eskimos. In-vivo evidence concerning this matter was the aim of the fourth Umanak expedition.

# Fourth Umanak Expedition 28 July – 18 August 1978

#### Introduction

After the biological very active group of compounds named *prostaglandins* had been discovered, a very rapid development of the knowledge about these substances has taken place.

The elucidation of how the prostaglandin thromboxane  $A_2$  (TXA<sub>2</sub>) is formed in platelets and of its pro-aggregatory ability (Hamberg et al. 1975), and the discovery of prostacyclin (PGI<sub>2</sub>), a powerful anti-aggregatory agent formed by the vessel wall (Moncada et al. 1976) has led to the suggestion that a balance between the formation of these two compounds controls platelet aggregability in vivo (Moncada and Vane 1978). Both substances have arachidonic acid (C 20:4,  $\omega$ -6) as precursor.

We were able to show that eicosapentaenoic acid (C 20:5,  $\omega-3$ ), in the respect of being substrate for prostaglandins regulating haemostasis, acted in quite a different way than arachidonic acid. Eicosapentaenoic acid cannot be converted by the platelets to a potent pro-aggregatory substance, but actually inhibits platelet aggregation (Dyerberg and Bang 1978). Vascular tissue, however, can convert it to a potent antiaggregatory substance, probably  $\Delta-17$ -prostacyclin (PGI<sub>3</sub>) (Dyerberg et al. 1978), an observation which has been confirmed later (Needleman et al. 1979).

The difference can be illustrated in this way:

Platelets Fatty acid Vessel wall 
$$TXA_2 \leftarrow Arachidonic acid \rightarrow PGI_2$$
 (proaggregatory) (antiaggregatory)

No pro-  $\leftarrow$  Eicosapentaenoic acid  $\rightarrow PGI_3$  (antiaggregatory compound aggregatory)

This means that the balance between pro- and anti-aggregatory prostaglandins in Eskimos seems to be displaced towards the anti-aggregatory side. The consequence of this is that the tendency to bleeding will be increased and the inclination to thrombotic diseases decreased in Greenlanders, as the very first stage of a thrombus formation is an aggregation of the thrombocytes on a lesion in the intimal layer of the vessel. This initiates a sort of chain reaction as the aggregated platelets release thromboxane which will cause further platelets to aggregate on the spot. Furthermore, the aggregated platelets will release blood clotting factors resulting in local coagulation of the blood and giving rise to formation of a thrombus.

This process takes place both as a part of the natural haemostasis in accidental lesions of vessels and in pathological lesions of the inner layer of the vessel wall. From thrombocytes aggregated on the arterial inner wall compounds are released which promote the growth of some pathological cells (myointimal cells), which are essential in the atherosclerotic process, worsening the already existing atherosclerotic condition.

On this background we returned to the peculiarities of the blood fatty acid pattern in Greenlanders, especially the low concentration of arachidonic acid and high concentration of eicosapentaenoic acid. The aim of the next expedition to Greenland was to measure platelet aggregability and other factors in the haemostasis mechanism in Greenlanders.

The members of the expedition were – besides the authors.

Ruth Edgar, clinical chemical technician, Aalborg. Erik Stoffersen, clinical chemical technician, Aalborg.

Kaj Fogh, electrical engineer, Aalborg.

In Greenland an interpreter was engaged.

#### Material and methods

21 Greenlanders, 14 males and 7 females, aged between 21 and 77 years, took part in the study as volunteers. All were free of any medication and none had consumed alcohol for three days prior to the examination.

The following examinations were carried out:

- Determination of the ADP (adenosine diphosphate) threshold for secondary phase thrombocyte aggregation.
- If this threshold was increased to more than 7.8
   µmol/l, platelet aggregation stimulated by two fixed
   doses of collagen was examined in order to find out if
   any secondary phase aggregation could be induced at
   all.
- 3. The bleeding time after Ivy's method with the Simplate device.
- 4. Fatty acid pattern in the thrombocytes (not fractionated in lipid classes).
- Routine haemostatic examinations including thrombocyte count, platelet adhaesivity, one-stage prothrombin time, activated partial thromboplastin time (APTT) and plasma fibrinogen determination.

For comparison a group of 21 healthy Danes were examined. They were chosen as to match each Greenlander according to age and sex and they were submitted to the same restrictions concerning medication and alcohol as the Greenlanders.

Blood for coagulation studies was collected in sodium citrate 3.8 per cent (w/v), one part to nine parts of blood. All analyses took place within 2 hours after sampling, during which period platelet suspensions were kept at room temperature, the rest of the samples were kept on ice. Platelet rich plasma (PRP) was obtained by centrifugation at 200 g for five minutes, and platelet poor plasma (PPP) by centrifugation at 1500 g for ten minutes.

Platelet aggregation studies were performed with a Fibromate ®, Bie and Berntsen, Copenhagen. Adenosine diphosphate (ADP) and arachidonic acid was obtained from Sigma Chemicals, St. Louis, USA, and collagen from General Diagnostics, Warner-Lambert Co., New Jersey, USA. The platelet aggregation studies were carried out to determine the concentration of ADP in PRP that would induce a secondary phase aggregation response using the following concentrations: 0.4, 0.5, 0.64, 0.8, 1.0, 1.25, 1.6, 2.0, 2.5, 3.2, 4.0, 4.9, 5.5, 6.7 and 7.8 µmol/l. If no secondary phase aggregation response was recorded at an ADP concentration of 7.8 µmol/l, or if the result was doubtful, PRP was stimulated with collagen at 2 and 4 µg/ml. The absence of any platelet aggregation after this collagen stimulation indicated no secondary phase aggregation response. Platelets were counted in a counting chamber using phase contrast light microscopy.

The following coagulation studies were performed on the Fibromate: Fibrinogen concentration, activated partial thromboplastin time (APTT) and two-stage prothrombin time (PT) using Cephotest ® and Normotest ® reagents from Nycomed, Oslo, Norway.

For other analyses, K-EDTA-stabilized blood 1 mg/ml was used from which platelets were isolated after washing repeatedly in saline. Fatty acid pattern in thrombocytes was determined after lipid extraction. The fatty acids were methylated and analysed by gasliquid-chromatography as described earlier.

Bleeding time (Ivy) was measured with a disposable device Simplate II ® from General Diagnostics. Platelet adhesiveness was recorded using citrated whole blood.

#### Results

In table 21 are given the results of determinations of bleeding time, ADP threshold of secondary phase thrombocyte aggregation and platelet count. In the ten cases in whom the maximal ADP concentration of 7.8  $\mu$ mol/l was unable to induce any aggregation at all, or the result was doubtful, the aggregability was examined after stimulation with collagen 2 and 4  $\mu$ g/ml. This compound is a potent stimulator of platelet aggregation. In none of the cases it induced any aggregation.

Table 21. Bleeding time (BT), ADP threshold for secondary phase aggregation (ADP-AG) and platelet count (PC) in 21 Greenlanders (G) and 21 Danish controls (D). In brackets are Danish reference values.

	BT		ADP	-AG	PC				
(	3-8 min	)	(1-4)	umol/	(140-340×10 <sup>9</sup> / liter)				
			lite	er)					
	G D		G	D	G	D			
	14	6.5	7.8	1.6	140	221			
	8	5.5	00	1.25	220	333			
	6	5	00	1.6	135	179			
	15	6	$\infty$	4.9	121	193			
	8	8	4.9	2.5	199	330			
	15 6 8 8 10 5		4.9	1.25	134	242			
	8	4.5	3.2	1.25	220	274			
	8	4.5	5.5	2.5	166	276			
	9	3.5	4.0	1.6	205	211			
	10	6	$\infty$	1.25	92	203			
	9	4	00	2.0	200	299			
	5	4	00	2.0	153	298			
	9 5 7 7 7 6	3.5	00	1.0	125	162			
	7	4	$\infty$	3.2	175	145			
	7	3.5	3.2	1.25	159	229			
	6	3	2.5	1.25	151	241			
	6	3.5	3.2	2.5	318	194			
	7	4	00	2.0	191	246			
	5	3 7	3.2	1.25	95	227			
	6 7 5 7 7		$\infty$	2.0	102	174			
	7	6	6.7	4.0	288	185			
mean	8.05	4.74			171	232			
SD	2.56	1.39			58.8	53.8			

 $\infty$  in ADP-AG means that an ADP concentration of 7.8  $\mu$ mol/liter was unable to induce any aggregation.

SD = Standard deviation.

In the Eskimos in whom no platelet aggregation could be induced, even after stimulation with collagen, incubation of the platelets with arachidonic acid in a final concentration of 0.6 mmol/l induced a normal aggregation response, indicating a normal ability of synthetizing prostaglandins.

The bleeding time was found significantly longer in the Greenlanders, averagely 8.1 as compared with 4.8 min in the Danish controls (P < 0.01 Wilcoxon matched pair test).

The thrombocyte count was found significantly lower in the Eskimos. No difference in platelet adhaesivity was observed between Greenlanders and Danes. Prothrombin time and APTT were found similar in the two groups. The concentration of plasma fibrinogen was found significantly higher in the Greenlanders.

In the four Greenlanders with the longest bleeding time this measurement was repeated 24 h after the intake of 1.5 g acetylsalicylic acid which is known to block the cyclo-oxigenase which catalyses the transformation of fatty acids to endoperoxides that are the precursors of prostaglandins. In all four individuals the bleeding time was shortened.

The fatty acid pattern of platelet lipids is shown in table 22. Even if the platelets obviously have a certain preference for taking up arachidonic acid, the same

Table 22. The distribution of fatty acids in platelet lipids in Eskimos and Danes.

	14:0	16:0	16:1	18:0	18:1	18:2	18:3	20:0	20:1	20:4	20:5	22:0	22:1	22:5	22:6	24:0		Jniden- tified
E	0.2 (0.06)	20.6 (0.30)	2.3 (0.14)	11.5 (0.26)	17.5 (0.27)	3.9 (0.34)	-	0.6 (0.07)	4.8 (0.22)	8.5 (0.21)	8.0 (0.36)	1.0 (0.08)	2.7 (0.18)	3.3 (0.16)	5.8 (0.36)	0.3 (0.07)	4.4 (0.17)	4.6
D	0.1 (0.04)	19.0 (0.45)	1.4 (0.22)	17.2 (0.78)	17.2 (0.20)	8.2 (0.33)	_	1.3 (0.07)	1.0 (0.15)	22.1 (0.47)	0.5 (0.20)	3.1 (0.14)	1.1 (0.16)	1.0 (0.14)	1.5 (0.09)	0.7 (0.16)	1.1 (0.12)	3.6 (0.37)

Fatty acids are indicated as in table 6. Values are % of total. Figures in brackets are standard error of the mean.

pattern as that of the Eskimo food and plasma fatty acids could be found in the platelets. What should be noted especially is the ratio between eicosapentaenoic and arachidonic acids, being 0.94 in Eskimos against 0.02 in Danes.

#### Discussion

The basis for our examination of the haemostatic function in Greenlanders was the experimental in-vitro evidence that eicosapentaenoic acid as a substitute for arachidonic acid may influence haemostasis and consequently the thrombosis tendency in an anti-thrombotic direction (Dyerberg and Bang 1978, Dyerberg et al. 1978). These findings have been confirmed recently by other authors (Needleman et al. 1979).

In earlier descriptions of the morbidity in Greenland Eskimos (Berthelsen 1940) an enhanced bleeding tendency has been stressed. This was seen especially in the frequent nose bleeding in the Eskimos as well as the numerable haemoptyses observed when pulmonary tuberculosis was still prevailing. Our results confirm this bleeding diathesis and indicate that the mechanism of the rarity of thrombotic diseases in Greenlanders is substantially a decreased platelet aggregability. The complete absence of ADP- and collagen-induced secondary phase platelet aggregation in half of the Greenlanders examined by us, in spite of a normal ability of synthetizing prostaglandins, demonstrates the extent to which a physiological mechanism can be displaced by exogenous influences.

If prostaglandins belonging to the 3-family substantially influence haemostasis, one would expect that inhibition of the prostaglandin synthesis, such as brought about by acetylating cyclo-oxigenase with acetylsalicylic acid, would have an effect mainly by blocking the synthesis of the anti-aggregatory prostacyclin, whereas a blocking of the ineffective thromboxane  $A_3$  is of no influence. The administration of acetylsalicylic acid to four Greenlanders resulted in all in a consistent shortening of their bleeding time.

Platelet adhaesivity was found similar in Greenlanders and Danes. This is not surprising as it seems to be regulated by other factors quite independent of prostaglandin formation. The factor VII (von Willebrand

factor) plays an important role for platelet adhaesivity, but the mechanism is still not clear.

The lower platelet count found in the Eskimos as compared with Danes are in our opinion not related to any effect on haemostasis as demonstrated by the lack of correlation between platelet count and bleeding time (table 21). Measurable influence on the bleeding time by low platelet counts is first seen at substantially lower levels than those observed. The reason for the differences found in platelet count and concentration of plasma fibrinogen between Greenlanders and Danes is not clear.

The data presented here represent the first major investigation of the haemostatic function in Greenland Eskimos.

#### Conclusion

Our theory of eicosapentaenoic acid as a possible substitute for arachidonic acid in the formation of pro- and anti-aggregatory prostaglandins based upon in-vitro experiments was consistently confirmed by our finding during the fourth Umanak expedition of a changed haemostatic function in Greenlanders. The decreased or invalidated secondary phase platelet aggregability and the increased bleeding time found in all Greenlanders examined as compared with Danish controls is essential. The ability of the platelets to produce prostaglandins after incubation with arachidonic acid and the shortening of the bleeding time after acetylsalicylic acid further shows that our theory comes true.

Our findings give for the first time a well supported explanation of the bleeding tendency in Greenlanders known for centuries (Bang and Dyerberg 1980).

# Conclusions based upon all four Umanak expeditions

The question we asked 10 years ago why thrombotic diseases and especially ischaemic heart disease are so rare in Greenland Eskimos can be answered – based on our examinations in Greenland – as follows:

1. The low level of serum lipids that we found in the Greenlanders, especially of cholesterol and  $\beta$ -lipopro-

tein, probably also of triglycerides and pre-β-lipoprotein, are known to be associated with a low risk of ischaemic heart disease, probably due to a slower development of atherosclerosis.

- 2. The high level of  $\alpha$ -lipoprotein which we saw in the male Eskimos is strongly negatively correlated with ischaemic heart disease.
- 3. The high plasma level of eicosapentaenoic and low level of arachidonic acids – originating from the speciel Eskimo diet, rich in marine arctic animals – gives rise to a displaced balance between pro- and anti-aggregatory platelet active prostaglandins towards the anti-aggregatory and consequently anti-thrombotic side.

Ischaemic heart disease is a multifactorial disease. Of the three causes of the rarity of this disease we consider the third to be by far the most important. The new knowledge originating from our Greenland studies may become the basis for prophylactic measures against thrombotic diseases.

The knowledge about the causes of the rarity of thrombotic diseases in Greenlanders can probably be utilized in an effort of maintaining the favorable situation concerning thrombotic diseases which prevail in Greenland Eskimos. However, our findings may become of more global importance as they point at measures - dietary or medicamentary - acting as a prophylaxis against ischaemic heart disease, one of the most frequent ailments in the modern western world.

Our study of the serum lipids in Greenlanders is the most detailed ever done and may become of importance also in other connections. This is also valid for the analysis of the composition of Eskimo food, especially that of the dietary fat.

The study of the haemostatic function in Greenlanders gives a series of new observations and explains the hitherto unexplained bleeding tendency in Eskimos.

# Acknowledgements

All the Greenlanders, especially those of Igdlorssuit who with never failing readiness took part as volunteers in our studies are heartily thanked. We thank the medical and municipal authorities in the Umanak district for their assistance in our project. The different clinical chemical technicians who have worked with the extensive analytical task are thanked heartily.

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#### Meddelelser om Grønland, Geoscience

1979.

1. C. K. Brooks:

»Geomorphological observations at Kangerdlugssuaq, East Greenland«. 21 pp.

The Kangerdlugssuaq area is mainly comprised of two contrasting rock groups: on the one hand the easily-eroded lavas and sediments of late Mesozoic to early Tertiary age and on the other the highly resistant Precambrian gneisses. Intermediate between these two types in terms of behaviour with respect to erosion are the Tertiary plutonic complexes and the basaltic areas along the coast which have been intruded by intense dyke swarms.

In the late Mesozoic the area was a peneplain, and low relief apparently persisted throughout the volcanic episode as there is good evidence that the lava plateau subsided during its formation. During this period ocean-floor spreading gave rise to the embryonic Danmark Stræde. Shortly after the volcanic episode the Kangerdlugssuaq area became the centre of a massive domal upwarping which has been a dominant feature of the land-forms up to the present day. The original surface of the dome has been reconstructed on the basis of topographic and geological evidence to show that it was elliptical in form with a major axis of at least 300 km in length and a height above present sea-level of about 6.5 km. However, subsequent isostatic effects are not considered in deriving these figures. The updoming is estimated to have occurred about 50 m.y. ago.

Several kilometres thickness of sediments and lavas were eroded off this dome at an early stage exposing the gneissic core, which still stands in alpine peaks up to about 2.7 km altitude in the central part, and dumping ca. 50000 km³ of sediment on the continental shelf. The erosion was effected by a radial, consequent drainage system, relicts of which can still be found. Kangerdlugssuaq itself may owe its origin to a tectonic line of weakness formed in response to doming, but there are also good arguments for its being purely erosional. The erosion of the dome was probably fluviatile but all trace of this stage has been obliterated the subsequent glaciation.

In the period between the Eocene and the early Miocene, possibly around 35 m.y. ago, the entire area underwent epeirogenic uplift raising the undeformed parts of the original lava plateau to around 2.5 km above sea-level. At present this plateau is undergoing dissection from the seaward side, but considerable areas are still preserved under thin, horizontal ice-caps.

A brief description of the various types of glaciers, an impermanent, ice-dammed lake and the areas of ice-free land is given. In the Pleistocene, the Kangerdlugssuaq glacier was considerably thicker than at the present time and extended far out over the shelf, excavating a deep channel here. Finally some observations on the coastlines are presented.

1979.

2. Sven Karup-Møller and Hans Pauly:

»Galena and associated ore minerals from the cryolite at Ivigtut, South Greenland«. 25 pp.

Silver- and bismuth-rich galena concentrates have been produced for more than 70 years as a byproduct in the dressing of the crude cryolite from Ivigtut, South Greenland.

Concentrates from the years 1937 to 1962 contained from 0.44 % Ag and 0.74 % Bi to 0.94 % Ag and 1.93 % Bi. Conspicuous increases in the content of these elements appeared twice within this time interval, namely in 1955 and in 1960. Thus it seems that crude cryolite from specific areas within the mine carried galena high in silver and bismuth. This promoted a detailed study of the common Ivigtut galena and associated sulphides.

An outline of the geological setting of the deposit is given. The deposit is divided into two main bodies – the cryolite body and the quartz body. Both are subdivided into units characterized by their content of siderite and fluorite. Galena samples from these units and from rock types surrounding the deposit have been studied.

Galena from units characterized by siderite follows the compositional pattern found in the galena concentrates, whereas the sparse galena mineralizations from units characterized by fluorite contain much smaller amounts of silver and bismuth, less than 0.2%. However, within the fluorite-bearing units, two peculiar parageneses reveal high contents of silver and bismuth expressed by the presence of particular minerals such as marildite-aikinite and gustavite cosalite respectively.

Further trace element studies on selected galena samples emphasize Sn and Te as chemically characteristic of the galena and of the sulphide-carbonate phase of the deposit.

The temperature of formation of the main part of the deposit is placed at 550-400°C, and between 300 and 200°C certain parts of the fluorite cryolite and the fluorite zone.

 John C. Rucklidge, Charles Kent Brooks and Troels F. D. Nielsen: »Petrology of the coastal dykes at Tugtilik, southern East Greenland«. 17 pp.

Dolerite and lamprophyre dikes from Tugtilik in the southern part of the onshore exposure of the East Greenland coastal dike swarm are described. The dolerites, which are earlier, are similar to other tholeiites from the dike swarm and the plateau basalts and also to many Icelandic tholeiites. Transitional varieties have been identified from the Angmagssalik district. The lamprophyres have a nephelinitic composition and are rich in phenocrysts and xenocrysts. In one case, abundant low pressure inclusions occur. Rocks identical to these lamprophyres have not previously been described from Greenland but are well known, for instance, in the African Rift.

## Meddelelser om Grønland, Bioscience

1979.

 Erik L. B. Smidt: »Annual cycles of primary production and of zooplankton at Southwest Grenland«. 53 pp.

Annual hydrographic observations, measurements of primary production, and samplings of zooplankton were undertaken in Southwest Greenland waters in the 1950s and –60s. In the coastal area and at the entrance to Godthåbsfjord winter cooling normally extends to the bottom, resulting in a vertical mixing of the water and an effective replenishment of nutrients at the surface. The subsequent production rate is, therefore, high with an average annual gross production calculated to about 160 g C m<sup>-2</sup>. In the inner fjord regions the stratification is normally much more stable with persisting warm bottom water, and the production is, therefore, lower here than in the coastal area. The seasonal variation in the relations between daylight, primary production, phosphate, and quantity of zooplankton is, presumably, representative of the coastal waters at SW Greenland. A maximum in primary production in spring is normally followed by another maximum in late summer. The number of animals in the microplankton samples from the upper 30 m (the productive layer) is at its maximum simultaneously with the second maximum of the primary production, while the maximum of the macroplankton biomass (taken by stramin net) extends until late autumn in the coastal and outer fjord regions.

A maximum of the macroplankton biomass during winter in the deep water layers in the inner Godthåbsfjord, caused by inflow of warm bottom water, stable stratification and cooled outflowing surface water acting as a barrier to the ascent of the animals, is assumed to be normal to the open, non-threshold, W Greenland fjords.

Seasonal vertical migration of the zooplankton is indicated by Hensen net hauls from different depths. There is a concentration of zooplankton in the upper water layers in April–September and a deeper concentration from autumn to spring.

Annual cycles of various animal groups are described for holoplankton and meroplankton, separately. Holoplankters are normally dominant, copepods being the most numerous group. Meroplankters, especially bottom invertebrate larvae, are relatively numerous in the microplankton in spring and summer with *Balanus* naupli dominant in spring and lamellibranch larvae in the following months. In a special section on fish eggs and larvae it is shown *I.a.* that cod eggs and larvae are normally concentrated in the upper 50 m, where they are much exposed to temperature variations, while eggs and larvae of American plaice occur also in deeper water. This may partly explain why the cod stock is more vulnerable to low temperatures.

It is shown that the epipelagic plankton fauna in the survey area in terms of growth and mode of development is more similar to the arctic than to the boreal fauna. It could therefore be termed subarctic, which also corresponds to the environmental conditions in the area.

2. Jean Just:

»Amphipoda (Crustacea) of the Thule area, Northwest Greenland: Faunistics and Taxonomy«. 61 pp.

The material reported on was collected in the Thule area, NW Greenland, in 1968 and includes 105 species. Four of these, Aceroides goesi, Bathymedon antennarius, Monoculodes vibei and Parametopa crassicornis, are new to science. An additional 6 species are new to Greenland, while 9 species have previously been found in E Greenland but not in W Greenland. Four genera, Lembos, Arrhinopsis, Arctopleustes and Parametopa, are recorded from Greenland for the first time.

Specimens belonging to 15 additional taxa are for various reasons not referred to species. Major taxonomic problems, warranting broadly based revisions, are outlined in the genera *Byblis, Gitanopsis, Ischyrocerus, Tmetonyx, Monoculodes* and *Stenula*. Three different forms of *Paroediceros lynceus* are discussed.

All known amphipod species from the Thule area are included in an annotated list. Forty-nine taxa are discussed and figured.

## Meddelelser om Grønland, Man & Society

1980

1. Isi Foighel: »Home Rule in Greenland«. 18 pp.

By Danish Act of 29 November, 1978, Home Rule was established in Greenland within the Unity of the Danish Realm. The Act was prepared by a Danish-Greenlandic Commission.

The Act on Home Rule is discussed with special reference to the historical and political background.

By the establishing of Home Rule, powers which hitherto had been vested in the Danish Government and Parliament were transferred to the Greenlandic authorities. The scope of these powers and their legal characteristics are outlined.

Home Rule makes no changes in the international competence or in the relationship between Greenland and the international or interregional organizations. Greenland's membership of the EEC creates some special problems.

The question of ownership of the natural resources was of great importance in the debate in the Home Rule Commission. The Act contains a solution which seeks to give the Danish Government as well as the Greenlanders equal rights in the decision-making procedure, in the administration, and in the sharing of the revenue.

Furthermore, the financing of the Home Rule system, the language problem, the organizing of fishing and trade are being dealt with.

#### Instructions to authors

Manuscripts will be forwarded to referees for evaluation. Authors will be notified as quickly as possible about acceptance, rejection, or desired alterations. The final decision rests with the editor. Authors receive two page proofs. Prompt return to the editor is requested.

Alterations against the ms. will be charged to the author(s). Twenty five offprints are supplied free. Order form, quoting price, for additional copies accompanies 2nd proof. Manuscripts (including illustrations) are not returned to the author(s) after printing unless especially requested.

## Manuscript

General. – Manuscripts corresponding to less than 16 printed pages (of 6100 type units), incl. illustrations, are not accepted. Two copies of the ms. (original and one good quality copy), each complete with illustrations should be sent to the Secretary.

All Greenland place names in text and illustrations must be those authorized. Therefore sketch-maps with all the required names should be forwarded to the Secretary for checking before the ms. is submitted.

Language. – Manuscripts should be in English (preferred language), French, or German. When appropriate, the language of the ms. must be revised before submission.

Title. – Titles should be kept as short as possible and with emphasis on words useful for indexing and information retrieval.

Abstract. – An English abstract should accompany the ms. It should be short, outline main features, and stress novel information and conclusions.

Typescript. – Page 1 should contain: (1) title, (2) name(s) of author(s), (3) abstract, and (4) author's full postal address(es). Large mss. should be accompanied by a Table of Contents, typed on separate sheet(s). The text should start on p. 2. Consult a recent issue of the series for general lay-out.

Double space throughout and leave a 4 cm left margin. Footnotes should be avoided. Desired position of illustrations and tables should be indicated with pencil in left margin.

Underlining should only be used in generic and species names. The use of italics in other connections is indicated by wavy line in pencil under appropriate words. The editor undertakes all other type selection.

Use three or fewer grades of headings, but do not underline. Avoid long headings.

References. – Reference to figures and tables in the text should have this form: Fig. 1; Figs 2–4; Table 3. Bibliographic references in the text are given as: Shergold (1975: 16) and (Jago & Daily 1974b).

In the list of references the following usage is adopted:

Journal: Macpherson, A. H. 1965. The origin of diversity in mammals of the Canadian arctic tundra. – System. Zool. 14: 153–173.

Book: Marsden, W. 1964. The lemming year. – Chatto & Windus, London: xxx pp.

Chapter (part): Wolfe, J. A. & Hopkins, D. M. 1967. Climatic changes recorded by Tertiary landfloras in northwestern North America. – In: Hatai, K. (ed.), Tertiary correlations and climatic changes in the Pacific. – 11th Pacific Sci. Congr. Tokyo 1966, Symp.: 67–76.

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