Alaskan Arctic Eskimo: responses to a customary high fat diet¹²

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After a multidisciplinary study of some unique biological characteristics of the Masai of East Africa (1–3), we turned our interests to the lipid and cholesterol metabolism of the Arctic Alaskan Eskimos and the relationship of this metabolism to the customary high protein, high fat, low carbohydrate diet of the Eskimo. A detailed description of the study is at the present time in press elsewhere (4). This guest editorial will summarize the interesting and essential parts of the study.

The Eskimos are descended from the Thule people who migrated from Asia through Siberia and the Bering Strait to North America approximately 3,000 years ago (5). Today they number approximately 45,000, with 60% of them living in Alaska and the remainder in Arctic Canada and Greenland (6). Their physiognomy is, in general, remarkably uniform, having the appearance of a mixture of Mongol and Indian (5). Their skulls are usually large and massive, with a distinct occipital protuberance. As a rule, Eskimos are powerfully built with relatively nonobese, short, and large musculoskeletal physiques. Although the trunk of an Eskimo is comparatively long, his arms and legs are short in proportion to his total height.

Our study was conducted at Point Hope, Alaska. The village is located at the end of a gravel spit on the western edge of the North Slope of Alaska on the western shore of the Chukchi Sea. This site was selected for the study because of its isolation from inland Alaska by the imposing Brooks Mountain range (the most northerly portion of the Rocky Mountains) and its stable and genetically homogeneous population of approximately 250, a number that has remained constant since the first population estimate in 1880.

Dietary habits and cholesterol intake

The Eskimos' economy has depended heavily upon hunting of sea and land mammals and fishing. The Point Hope inhabitants represent one of the few remnants of the Eskimo whale, sea, and walrus hunting cultures in the world. Each summer the village of Point Hope captures from three to seven (40-ton) whales. The meat and fat are distributed among the villagers and preserved in continuously frozen subterranean caches (undoubtedly, the world's oldest and most dependable "deep-freezer"). Additional food items obtained from the ocean include seal, walrus, and small amounts of fish caught during brief migratory periods in the spring and early summer. Additional food is ob-

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tained from caribou, available in summer, and an occasional polar bear trapped during the winter months. Grain products and simple carbohydrates are virtually absent from the diet, as they must be imported from a great distance at considerable cost.

The marine mammals and the herds of caribou, upon which the Eskimos depend, tend to be migratory, and famines occur occasionally, especially during the long dark winters (5, 6). In the summertime, their diet is usually plethoric. In general, they have no fixed time for meals and eat as they please, but they usually do have one good meal toward the end of each day. Much of their food is eaten uncooked, partly from preference and especially from necessity, because fuel is scarce.

In order to evaluate the daily intake of cholesterol in this ecologically isolated group of Eskimos, the cholesterol content of their major indigenous dietary items, such as fat and meat of seal, whale, caribou, and fish was determined. Generally speaking, on the basis of unit wet weight of tissue, the cholesterol content is lower in whole fish and meats of sea mammals but higher in isolated adipose tissue. For example, seal fat contains three times as much cholesterol as seal meat (0.27 versus 0.09 g/100 g wet tissue).

By careful and meticulous recording of varieties and quantities of foods eaten by the eight healthy adult Eskimos selected for our special cholesterol metabolic studies, we learned that their average daily cholesterol intakes ranged from 420 mg/day to 1,650 mg/day. Even in an individual subject, the daily consumption of cholesterol varied from time to time. The variation ranged from 6 to 45% with an average of 20%. In general, the cholesterol intakes of this group of Eskimos during the period of the experiment, which was in the summer, were comparable to those of the usual overnourished United States population (7). In the winter or during periods of famine when the supply of food is low, they undoubtedly have a lower cholesterol intake (5).

The daily caloric intake during the experiment was calculated for these eight subjects, the results of which were quite similar to the report on an Alaskan dietary survey by the United States Public Health Service. Average total daily caloric intake was approximately 3,000 kcal per person, ranging from 2,300 to 4,500 kcal. Approximately 50% of the calories were derived from fat and 30 to 35% from protein. Carbohydrate accounted for only 15 to 20% of their calories, largely in the form of glycogen from the meat they consumed. Grain products were scarce and although sucrose was not unknown, the average adult ingested less than 3 g/day, primarily for sweetening tea or coffee.

**Serum lipids**

One hundred sixty-eight subjects over the age of 6 years (representing approximately 70% of the entire population of Point Hope) were included in the survey of serum lipids. Sixty-two of them were 12 years old or younger and sixteen were over the age of 60. The average age of the population in Point Hope is 26 years.

**Cholesterol.** The mean serum total cholesterol concentration in the population as a whole was 221 mg/100 ml with a standard deviation of 66. Approximately 25% of the total cholesterol was nonesterified. This value was in general agreement with that obtained from other mass samplings of Arctic Eskimos (8–11) but was slightly higher than those values obtained from the Eskimos living on the Pacific Coast of Alaska, as reported by Scott et al. (9). A generalization was made by Scott and co-workers from their study on 842 Eskimos that northern Alaskan Eskimos have higher serum cholesterol levels than southern Eskimos. The reason for this difference might well be related to the differences in their diets, as the main staple of northern Eskimos is marine mammals, whereas that of the southern Eskimos includes some vegetables and fish (12).

The serum cholesterol levels of the Point Hope population showed no sexual difference and were not related to prandiality but tended to rise linearly with increasing age. The regression equation for the serum cholesterol levels (Y in mg/100 ml) based upon their ages (X in years) was $Y = 201.7 + 0.7X$ with a standard error of estimate (SEE) of 4.3 ($r = 0.22, P < 0.05$). By comparing a similar regression equation, $Y = 158.8 + 1.97X$,
obtained by Scott et al. (9) derived from the 842 Eskimo men between the ages of 17 and 53 who were members of the Alaska National Guard, the young Eskimos at Point Hope tended to have a higher cholesterol level than the general Eskimo population. The cholesterol levels increased with advancing age, but the increment of Point Hope Eskimos was not as great as that of the general Alaskan male population (0.7 versus 1.97 mg/year). Therefore the cholesterol levels of Point Hope Eskimos over age 36 were not different from those of the general population. Moreover, the distribution of serum cholesterol levels in the Point Hope and general male Eskimo population was not significantly different from the general United States population except for the sexual differences observed in the latter.

**Triglycerides.** A fascinating and significant finding was that of a markedly lower serum triglyceride concentration in Point Hope Eskimos than in the general Caucasian population in the United States (14). The average of serum triglyceride concentrations of the Point Hope Eskimos was 85.2 mg/100 ml, whereas that of the Caucasians was usually over 100 mg/100 ml. Recently Bang et al. (15) reported an even lower concentration of plasma triglyceride (less than 60 mg/100 ml) in Greenlandic west coast Arctic Eskimos. A diet rich in carbohydrates, particularly simple sugars, elevates serum triglyceride levels due to the increased availability of triglyceride precursors, such as acetyl-CoA and glycerol-6-phosphate, which favors a net increased synthesis of triglycerides (16). The reverse conditions were true for Point Hope Eskimos. Their lipogenesis must be inhibited by the relative paucity of these precursors (a low carbohydrate intake). Moreover, it would be expected that Point Hope Eskimos would have low insulin values that stimulate tissue lipolytic enzymes, thus reducing serum triglycerides and raising free fatty acid levels (17).

**Free fatty acids.** The serum free fatty acid (FFA) concentrations of the Point Hope Eskimos were also quite different from those of the United States white population. The average Eskimo fasting FFA was 34 mg/100 ml or 1.5 mEq/liter, with a range of 0.4 mEq/liter, with a range from 0.3 to 0.8 mEq/liter for United States whites (14). In the prolonged postprandial period, the serum FFA of the Eskimos reached levels of 2.4 mEq/liter, a finding seen only in prolonged starvation or diabetic ketoacidosis in the United States whites. Each Eskimo's serum was tested for the presence of ketone bodies by the strip paper technique (18), which is sensitive to concentrations of 1 mg/100 ml or greater and all serums were negative. This does not preclude an increase in ketone body production during this time; usually these substances do not attain noxious concentrations until after fasting periods longer than 50 hr. The fact that the Eskimos had high serum FFA and low glucose levels (approximately 65 mg/100 ml) indicated that free fatty acids played a major role in body energy production.

**Lipoproteins.** There was a significantly lower concentration of pre-beta lipoproteins in the Eskimos than in United States whites; alpha- and beta-lipoprotein concentrations were, however, similar in both ethnic groups. Pooled lipoprotein ultracentrifugation confirmed this observation. The average absolute concentration of the very low density lipoproteins was less than 35 mg/100 ml in the Eskimos, as compared with a normal range of 60 to 200 mg/100 ml in the Caucasians. A similar low level of pre-beta or very low density lipoproteins was also observed by Bang et al. (15) in Greenlandic west coast Eskimos, which was consonant with their low dietary carbohydrate ingestion. The concentration of low density lipoproteins, high density lipoproteins and, indeed, total lipoprotein concentrations were identical in both populations.

**Cholesterol metabolic studies**

**Kinetic analysis.** Eight healthy adult volunteers, age 39 to 66, three males and five females, were selected for a special cholesterol metabolic study. Each of them received a single dose of 40 μCi cholesterol-4-14C intravenously. Compartmental analyses of the disappearance curves of serum cholesterol specific activity were carried out by a computerized program based on the combination of the kinetic analysis reported by Gurpide.
et al. (19) and the input–output analysis shown by Perl and Samuel (20). The curves of all cases uniformly fit a two-compartment model. The following kinetic parameters could be obtained by this program: total input (IT), output, or turnover rate of cholesterol in the system, mean transit time of cholesterol (1/α), total traced mass (MT), and individual pool sizes (MA and MB), exchange rates between compartments A and B (KABMA, KBA, MBA), and turnover times of pools A and B (1/α and 1/β). With additional analysis of the radioactivity of fecal sterols and by some mathematical manipulations, it was possible to determine the rates of absorption and synthesis of cholesterol in these eight subjects.

Figure 1 summarizes the above kinetic parameters (means of the eight subjects) together with those obtained recently by our group in a study of 15 average United States white males for comparison (21). There were striking similarities of the kinetic parameters of these two ethnic groups except for the average rates of absorption and synthesis of cholesterol. The mean sizes of rapidly and slowly exchangeable pools of the Eskimos were 25.0 and 43.1, respectively, which were slightly smaller than those of United States whites on the basis of absolute amounts. However, on the basis of per unit of body weight, the sizes of these two pools were exactly the same. The turnover times of the cholesterol in the rapidly and slowly exchangeable pools were 5.37 and 65.11 days, respectively, for the Eskimos and 6.45 and 72.69 days for the United States whites. The mean turnover rate of body exchangeable cholesterol was 1,315 mg/day for the former and 1,412 mg/day for the latter.

**Cholesterol absorption.** Individual Eskimos absorbed from 157 to 912 mg/day of cholesterol in this study on diets containing from 420 to 1,650 mg cholesterol/day. A statistically significant correlation of the rate of cholesterol absorption (Y in milligrams/day) with the daily cholesterol intake (X in milligrams/day) was found (r = 0.919, P < 0.001) with the following regression equation: Y = -65.63 + 0.57X (see = 92.63). The slope of the equation, 0.57, indicated that the efficiency of absorption was 57% of dietary cholesterol. The mean percent absorption could also be calculated from diet and absorbed, for each individual. The results showed 48.62 ± 11.00% (mean ± SD), which was quite comparable to the value obtained by regression analysis.

It has been generally accepted that Caucasians in the United States have a limited ability to absorb dietary cholesterol (22–24). Their maximal capacity is approximately 300 mg/day as calculated from the experiment by Kaplan et al. (22) and confirmed by the studies by Wilson and Lindsey (25) and of Grundy and Ahrens (26). Our recent study of a group of 15 Caucasians in the United

![Diagram of kinetic parameters](image-url)
States revealed that the rate of cholesterol absorption ($Y$) was also proportional to their daily cholesterol intake ($X$) (the regression equation: $Y = 7.05 + 0.38X$ ($\gamma = 0.945$, $P < 0.001$, $\text{SEE} = 31.37$ (21)). Similar findings were reported by Kudchodkar et al. (27) in 10 Canadian whites. Both studies showed similar, fixed absorption efficiencies, approximately 37 ± 5% of dietary cholesterol within the range of 300 to 1,250 mg/day. Although there was no leveling off of the amount absorbed even at the highest amount of cholesterol intake, the maximal absorption rates of these subjects were approximately 500 mg/day or less; the mean absorption rate was between 200 and 300 mg/day. The authors feel that an important and, as yet, incompletely studied parameter is the presence or absence of a high residue diet.

In our previous studies on the Masai (1–3) who live primarily on a diet composed almost exclusively of milk, blood, and meat, we found that they were capable of absorbing 653 ± 124 mg (mean ± sd, n = 11), or 33% of the 2,000 mg crystalline cholesterol added to their individual rations. This might not be the maximal capacity of their intestinal absorption because higher doses of cholesterol have not been tested, and the cholesterol given was in the crystalline form, which is absorbed less efficiently than that in the micellar form as in egg yolks (28). Nevertheless, the Masai did absorb more cholesterol than did the United States whites. In the present study, the Eskimos exhibited an even greater capacity for cholesterol absorption. The rate of absorption was linearly proportional to the amount of cholesterol present in the diet, ranging from 420 to 1,650 mg/day. The absorption efficiency was approximately 50% throughout the above dietary cholesterol range. The maximal absorption noted for the Eskimos in this study was 912 mg/day, which may not be their true maximal capacity, however, as higher amounts of dietary cholesterol were not ingested. Such an enormous capacity for intestinal absorption of cholesterol in the Eskimos reflected an extraordinarily long-term adaptation to their customary high fat diet that is essential for their survival.

**Homeostatic response to cholesterol absorption.** There are four hypothetical homeostatic mechanisms for control of cholesterol metabolism, namely $a)$ limitation of absorption, $b)$ suppression of synthesis, $c)$ increase of excretion, and $d)$ reversible tissue cholesterol storage. Because Eskimos seem to have an enormous capacity for intestinal absorption of cholesterol, they cannot prevent hypercholesteremia by limiting absorption of cholesterol by the intestine.

A statistically significant linear correlation between the turnover rate ($Y$) and absorption rate ($X$) was found in this study. The regression equation was $Y = 841 + 1.04X$ ($X = 0.64, P = 0.01, \text{SEE} = 293$). It is quite interesting that not only was the turnover rate directly proportional to the absorption rate, but also the slope of the regression equation approached unity. These data strongly suggest that there was a constant fixed rate of cholesterol synthesis in these free-living Eskimos with an average of 841 mg/day, and in addition to this fixed rate of synthesis, the amount of cholesterol absorbed contributed directly and additively to the same amount synthesized, in each subject, and to the daily turnover of body exchangeable cholesterol. This conclusion was further verified by studying the relationship between absorption rate and synthetic rate. There was no significant linear correlation between these two parameters ($\gamma = 0.03, P > 0.8$), supporting the observation that in the experimental Eskimos, the rate of synthesis was rather constant and was not affected by the rate of absorption.

As the average Eskimo may probably synthesize 1,315 mg of cholesterol when consuming a cholesterol-free diet, he probably suppressed 36% of his endogenous cholesterol synthesis on a diet containing 420 mg or more of cholesterol. As soon as this maximal degree of suppression was reached, no further suppression could be observed, even if there were a further increase of dietary cholesterol. Such a degree of maximal suppression (36%) is higher than that of the average Caucasian in the United States (25%) (21, 22), but lower than that of the African Masai (50%) (1–3) (Table 1) and is apparently not sufficient to compensate
perfectly for the intestinal influx of dietary cholesterol.

The fact that the turnover rate of cholesterol was proportional to the absorption rate indicated that there was an increase of sterol excretion as an important homeostatic mechanism to compensate for excessive absorption of dietary cholesterol in Eskimos. No such phenomenon was observed in both United States whites and Masai (Table 1). It should be added that Masai have only been challenged with daily intakes of 2 g cholesterol; perhaps if they ingested larger amounts of cholesterol, they might maintain serum cholesterol homeostasis by further endogenous suppression and an increased excretion of fecal neutral and acid sterols. However, the Eskimo's ability to increase sterol excretion was not great enough to compensate for his intestinal absorption. Furthermore, the mean transit time of body exchangeable cholesterol was not shortened by the increased rates of absorption and excretion.

As a result of excessive intestinal absorption of dietary cholesterol and insufficient suppression of endogenous synthesis, as well as an insufficient increase of excretion, the serum cholesterol levels of the Eskimos were elevated and reflected by a statistically significant correlation between their rate of cholesterol absorption (X) and serum cholesterol level (Y). \( Y = 211.31 + 0.048X, \text{ SEE } = 16.58, \gamma = 0.562, P = 0.02 \) The regression analyses also revealed that as a result of the elevation of serum cholesterol levels, there was an expansion of the rapidly exchangeable pool and consequently an expansion of the total exchangeable pool; the slowly exchangeable pool was not affected. Figure 2 summarizes the homeostatic responses of Eskimos to an increased dietary intake of cholesterol in a simplified diagram.

**Relation to atherosclerotic cardiovascular disease**

Because Eskimos ingest a carnivorous diet, which undoubtedly elevates their serum cholesterol levels, a hypothesis may be proposed that Eskimos should experience a high incidence of atherosclerosis. It has been, how-

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**TABLE 1**

Comparison of various homeostatic control mechanisms of cholesterol metabolism among Alaskan Arctic Eskimos, United States whites, and African Masai

<table>
<thead>
<tr>
<th></th>
<th>Alaskan Arctic Eskimos (n = 8)</th>
<th>U.S. whites* (n = 15)</th>
<th>African Masaib (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absorption:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal, mg/day</td>
<td>Up to 912</td>
<td>Up to 500</td>
<td>Up to 653</td>
</tr>
<tr>
<td>Average, mg/day</td>
<td>400-500</td>
<td>200-300</td>
<td></td>
</tr>
<tr>
<td>Efficiency, %</td>
<td>50</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td><strong>Synthesis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal suppression, %</td>
<td>36</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Average suppression, %</td>
<td>36</td>
<td>16.6</td>
<td></td>
</tr>
<tr>
<td><strong>Excretion</strong></td>
<td>Proportional increase with absorption rate</td>
<td>No change</td>
<td>No significant change under our experimental conditions</td>
</tr>
<tr>
<td><strong>Tissue storage</strong></td>
<td>Proportional expansion of rapidly exchangeable pool with absorption rate</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td><strong>Serum cholesterol</strong></td>
<td>Proportional elevation with absorption rate</td>
<td>Elevated but not proportional to the absorption rate</td>
<td>Low and not affected by absorption rate</td>
</tr>
</tbody>
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* See (21).  b See (1-3).
Figure 2. Simplified diagram of the homeostatic responses of Alaskan Arctic Eskimos to the intestinally influx of cholesterol.

However, a generally held, albeit not firmly established, contention that the Eskimo tends to develop atherosclerotic heart disease at a much slower rate than the general United States population (8, 15, 29, 30). Rennie and his colleagues (personal communication) have recently attempted to determine the prevalence of heart disease among North Slope Eskimos via the combined diagnostic techniques of the physical examination, chest X-ray, and electrocardiography. Their as yet unpublished data indicate that the rate of ischemic heart disease among 779 North Slope Eskimos is approximately 5/1,000. This is to be compared with an incidence of 50/1,000 among the American population as reported by the National Health Survey (31). The discrepancy between the observed fact (low incidence of atherosclerotic cardiovascular disease) and the well-established hypothesis (positive correlation of serum cholesterol levels and incidence of atherosclerotic cardiovascular disease) (32) could be explained by the following observations:

1) This Eskimo population is young with a mean age of 26 years, whereas atherosclerotic cardiovascular disease is usually not manifested until after middle age (fifth decade and later).

2) A serum cholesterol level of over 250 mg/100 ml was rarely observed in these Eskimos, less than 3% in the population of individuals 40 years of age and over but is more common among the whites.

3) Two series of postmortem studies disclosed that approximately 10% of the Eskimo patients did have a certain degree of atherosclerosis (33, 34), but the severity was usually not enough to produce clinically recognizable symptoms and signs.

4) As shown in previous studies on animals (35, 36) during periods of dietary induced hypercholesteremia, the cholesterol was deposited in most of the tissues in rabbits (35) and monkeys (36); during subsequent periods on cholesterol-free diets, the excessive amounts of cholesterol in most tissues was removed rapidly but the removal from aortas was slow and incomplete. During the lifetime of an individual Eskimo, there must be annual alternate periods of hyper- and hypocholesteremia, depending upon the abundance of food and types of foods available. During the hypercholesteremic period, a net influx of cholesterol into the vascular wall would be expected, but it would be removed slowly during the subsequent hypocholesteremic period. The slowness and incompleteness of removal would result in a net retention of cholesterol in the aorta and other arteries and atherosclerosis. Thus atherosclerosis indeed exists in Eskimos.
mos but is less severe and only rarely produced clinical manifestations and fatal complications. In contrast, Caucasians in the United States seem to have a continuous influx of lipid into their vascular wall because of their persistent hypercholesterolemia and consequently, they are suffering from a high incidence of atherosclerotic cardiovascular disease.

References


31. Coronary Heart Disease in Adults, United


