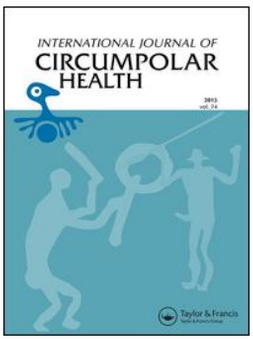

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ORIGINAL ARTICLE

ACYLATION STIMULATING PROTEIN IS HIGHER IN INUIT FROM NUNAVIK COMPARED TO A SOUTHERN QUEBEC POPULATION

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ABSTRACT

Objectives. The Inuit of Nunavik in northern Quebec have a lower risk for ischemic heart disease (IHD) compared to Caucasian populations. Acylation stimulating protein (ASP), which is involved in the storage of dietary fat, may play a role. The objective of the study was to determine plasma concentration of ASP in an Inuit and a southern Quebec Caucasian population.
Study design. This is a cross-sectional study evaluating the relationship between ASP and dietary factors, such as retinol, whose intake is higher in the Inuit. As well, concentrations of ASP were evaluated in relationship to components of the metabolic syndrome.
Methods. Medical history was collected via a questionnaire and anthropometric measurements and blood samples were collected.
Results. ASP was significantly higher in both the Inuit men and women compared to Caucasian men (66.1±4.1 nM vs 27.5±2.5 nM, $p<0.0001$) and women (71.8±3.8 nM vs 29.4±1.3 nM, $p<0.0001$). In addition, ASP significantly correlated with total retinol ($r=0.17$, $p=0.02$) and free retinol ($r=0.15$, $p=0.04$) in Inuit men but not with other distinctive dietary markers such as omega-3 fatty acids.
Conclusions. Inuit men and women have higher ASP which was unrelated to the number of risk factors for IHD that were present.
(Int J Circumpolar Health 2009; 68(5): 421–432)

Keywords: acylation stimulating protein (ASP), Inuit, retinol, metabolic syndrome

INTRODUCTION

The Inuit population of northern Quebec, specifically in the Nunavik region, has health characteristics distinct from southern populations of Quebec. Up until the 1950s, the population was relatively isolated and was reliant on its own food supply and cultural traditions (1). The past 50 years have been a time of immense change for the Inuit, affecting many aspects of their way of life, especially diet (1–3). The recent and dramatic changes taking place within this community provide an opportunity to evaluate the effects of changing diet on the health of a homogenous population.

In an extensive survey conducted in 1992 examining the risk of the Inuit to two other populations, the James Bay Cree and Caucasians in southern Quebec, the Inuit population had the lowest IHD risk (4). This lower IHD risk was present in spite of having the higher rate of obesity and smoking (5). This disparity asks the "nature versus nurture" question.

Investigations into both genetic differences and lifestyle differences have taken place. The genetic evidence is still nascent and ambivalent (6) but there is strong evidence to support the hypothesis that the dietary habits of the Inuit may contribute to their low IHD risk (4). The 1992 Health Survey found that the Inuit had the highest consumption of marine mammals and fish compared to other Quebecers. In addition, dietary consumption of omega-3 correlated strongly with high density lipoprotein cholesterol in the Inuit (4).

Several mechanistic studies have shown that omega-3 fatty acids have anti-inflammatory and insulin sensitizing properties (4,7–11). Omega-3 fatty acids have also been shown to directly affect adipocyte production and the secretion of hormones such as adiponectin, leptin and TNF-alpha (7–9). These adipokines are associated with IHD risk (9). Acylation stimulating protein (ASP) is one such adipokine which positively correlates with IHD risk factors (12).

ASP is a product of the alternative complement immune pathway. It is a cleavage product of complement C3 (C3), also identified as C3adesArg and stimulates the synthesis of triglycerides within adipose tissue, thereby increasing the clearance of dietary fat from circulation (12). This has been demonstrated both ex vivo and in vivo (12). This role in dietary fat clearance provides a potential mechanistic link between ASP, hyperlipidemia and IHD risk (13). Therefore, we sought to evaluate three interrelated factors together in the Inuit population, which has unique dietary, genetic and lifestyle characteristics, compared to a southern Quebec population: the adipokine ASP, dietary factors believed to be higher in a traditional Inuit diet, such as retinol and IHD risk factors.

MATERIAL AND METHODS

Inuit study group

The target population consisted of permanent residents of Nunavik over the age of 18 years. The Inuit population in the current study is a subset of a larger study organized by the Nunavik regional Board of Health and Social Services (NRBHSS) and the Ministère de la Santé et des Services Sociaux (MSSS) du Québec. The survey used a stratified random

sampling of private Inuit households. For more information on the entire survey population, refer to *Nunavik Inuit Health Survey 2004/ Qanuippitaa? How are we? Methodology Report* available at http://www.inspq.qc.ca. A subset of Inuit participants (215 men and 265 women) above the age of 33 were randomly selected to participate in the current study.

Caucasian study group

The Caucasian population consisted of 175 men and 238 women, derived from a database of control subjects from various studies conducted within our laboratory during the years 1991 to 2001. All participants were healthy and had no known diseases, and were recruited from the general population via advertisements. None of the participants were taking medication that affected blood lipids, blood glucose or metabolism. Subjects were selected to be between the ages of 26 and 80, and no further restrictions were applied.

Caucasian participants identified with diabetes or ischemic heart disease (IHD) were recruited through cardiovascular, lipid and/or diabetes clinics or in response to advertisements at the McGill University Health Centre (MUHC) in Montreal, Quebec. All of these subjects were examined in the absence of lipid-lowering medication. The presence of the diseases was confirmed by a physician. The studies were approved by the Comité d'ethique à la recherche de l'Université Laval, the Comité d'ethique de santé publique du Québec in Nunavik and the McGill University Health Centre ethics committee.

Inuit questionnaire and anthropometric measurements

Medical history and lifestyle information were collected via a nurse-administered questionnaire as part of the Nunavik Inuit Health Survey conducted from 27 August to 1 October 2004. Anthropometric measurements were collected using standard techniques. Bioelectrical impedance was taken using the Tanita™ technique, consisting of a leg-to-leg system based on pressure contact footpad electrodes. Blood pressure was taken using the Canadian Coalition for High Blood Pressure technique.

Plasma parameters

A fasting blood sample of 60 ml was collected from Inuit participants into EDTA containing tubes for measurement of lipids, insulin, glucose, inflammation and adipose tissue related hormones and vitamin A plus fatty acid composition of red blood cells. Caucasian participants had 7 to 15 ml of blood collected into EDTA-containing tubes. For both populations, the blood was immediately centrifuged and plasma and red blood cells were stored at -80°C. For both populations, analyses for total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglyceride (TG), apolipoprotein B (apoB) and insulin were measured according to standardized clinical biochemistry laboratory techniques. LDL cholesterol was calculated with the Friedewald formula for plasma triglyceride levels <4.5 mmol/L. Plasma OxLDL was measured by ELISA (Mercodia AB, Uppsala, Sweden) (14). Erythrocyte fatty acid profiles were obtained by gas-liquid chromatography (HP 5890; Hewlett Packard,

Toronto, Ontario, Canada) using an Innowax capillary column (30 m × 0.25 mm × 0.25 μm; Agilent, Mississauga, Ontario, Canada). Fatty acid data were expressed as the percentage of total erythrocyte membrane fatty acids (15). Plasma insulin levels were measured using the Elecsys2010 system from Roche.

Omega-3 fatty acid dietary treatment

A group of 28 men were recruited to participate in a 6-week dietary intervention in which 3 g of omega-3 fatty acid was supplemented to their regular diet. For more detailed information regarding the study protocol, please see the following reference (16). All subjects gave their written informed consent and the project was approved by the ethics committees of Laval University Hospital Research Centre and Laval University.

Acylation stimulating protein (ASP) and complement C3 determination

ASP was measured using an in-house sandwich ELISA, following previously published methodology (17). Complement C3 (C3) was measured in the Inuit population using an immunoturbidimetric assay (Kamiya Biomedical Company, Seattle, WA) modified for use in a 96 well plate.

Statistical analysis

Statistical analysis was performed using GraphPad Prism or SigmaStat 3.5. Values reported as mean±standard error (SEM). Differences between two groups were evaluated using a t-test and for 3 or more groups one-way ANOVA with Dunnett's multiple comparison post-hoc test to assess significance compared to control group. $P<0.05$ was considered significant.

RESULTS

Anthropometric, blood lipid, hormonal and nutritional status of two Quebec-based populations, the Inuit population of Nunavik and a healthy control Caucasian population from the southern regions of Quebec (primarily from the Montreal area), were evaluated. The Inuit study group is a subset of a larger study undertaken by Santé Québec. The subset of subjects for this study was a random selection of men and women between the ages of 33 and 70. The Caucasian population was derived from a database of healthy control subjects who were used as reference populations in previous studies.

Of the Inuit men, 9 (4.2%) identified themselves as having had a myocardial infarction, 14 (6.5%) reported having had a previous stroke, 19 (8.8%) reported having other ischemic heart disease and 12 (5.6%) had diabetes. Of the Inuit women, 5 (1.9%) identified themselves as having had a myocardial infarction, 15 (5.7%) reported having a previous stroke, 22 (8.3%) reported having other ischemic heart disease and 30 (11.3%) had diabetes. These groups were not exclusive to one another.

Table I summarizes the anthropometric and blood lipid profile of both the Inuit and Caucasian men and women. There was no significant difference in age between the Inuit and Caucasian populations (Table I). Both the Inuit men and women were significantly shorter than Caucasian men and women, respectively; however, there were no differences in average body weight and only the Inuit men had a significantly higher BMI than the Caucasian men (Table I). Despite the same (women) or higher (men) BMI, Inuit

individuals had significantly higher HDL-C than Caucasian men and women, with no other significant difference in any lipid parameter except for higher total cholesterol and higher LDL-C in the Inuit women (Table I). Exclusion of all Inuit men (31 of 215, 14.4%) and women (44 of 265, 16.6%) on lipid-lowering and insulin-sensitizing medication or insulin did not affect any of the above-mentioned parameters or any of the following analysis. For that reason, we chose to keep these subjects in the analysis.

Despite the lack of a clear difference in risk factors for IHD, Inuit men and women had higher ASP (Men: 66.1±4.1 nM vs 27.5±2.5 nM, p<0.0001; Women: 71.8±3.8 nM vs 29.4±1.3 nM, p<0.0001). Because ASP displayed a skewed distribution, ASP values were log transformed (Fig 1. A and B). The mean value for complement C3, the precursor protein to ASP, was within normal reported ranges (0.83 g/L to 1.45 g/L) (12) for both Inuit men (1.16±0.02 g/L) and Inuit women (1.13±0.02 g/L). Therefore, the elevated ASP values seen in this population were not due to increased availability of the precursor protein. Because ASP is typically elevated in concert with increased risk factors for IHD and diabetes (12) we further investigated which factors may be influencing the elevated ASP in the Inuit population.

ASP does not change with increasing number of components of the metabolic syndrome in the Inuit population

The Inuit population was divided into four groups based on the number of diagnostic criteria of the metabolic syndrome (MetS) according to the ATPIII criteria (Table II and III) (18). Of Inuit men, 6.4% (13 of 204) and 10.5% (26 of 248) of Inuit women met the criteria for having components of MetS, whereas no women had all 5 of the criteria. The most prevalent component of the MetS in both the men and women was increased waist circumference (25.5% of Inuit men and 61.7% of Inuit women) while the least prevalent component was elevated fasting glucose.

Table I. Anthropometric characteristics and lipoprotein profile of Inuit and Caucasian populations.

	Inuit men n=215	Caucasian men n=175	p-value	Inuit women n=265	Caucasian women n=238	p-value
Age (years)	47.0±0.8	49.8±1.3	ns	47.1±0.7	45.3±0.9	ns
BMI kg/m^2	27.7±0.4	25.3±0.3	<0.0001	28.6±0.4	28.2±0.7	ns
Height (cm)	165.2±0.4	174.6±0.8	<0.0001	152.7±0.3	163.1±0.5	<0.0001
Weight (kg)	75.8±1.1	76.1±1.2	ns	66.8±1.0	65.3±1.1	ns
TG mmol/L	1.30±0.05	1.43±0.09	ns	1.25±0.05	1.20±0.05	ns
TC mmol/L	5.23±0.07	5.14±0.08	ns	5.39±0.06	4.89±0.08	<0.0001
HDL-C mmol/L	1.55±0.03	1.22±0.03	<0.0001	1.92±0.03	1.37±0.03	<0.0001
LDL-C mmol/L	3.08±0.07	3.14±0.09	ns	2.90±0.05	2.74±0.06	0.05
apoB mg/dL	101.7±1.7	103.2±2.4	ns	99.3±1.4	96.3±2.3	ns

Values are given as mean ± standard error (SEM). BMI, body mass index; TG, triglycerides; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; apoB, apolipoprotein B. P values based t-test with analyses done separately for men and women. P<0.05 was taken as significant.

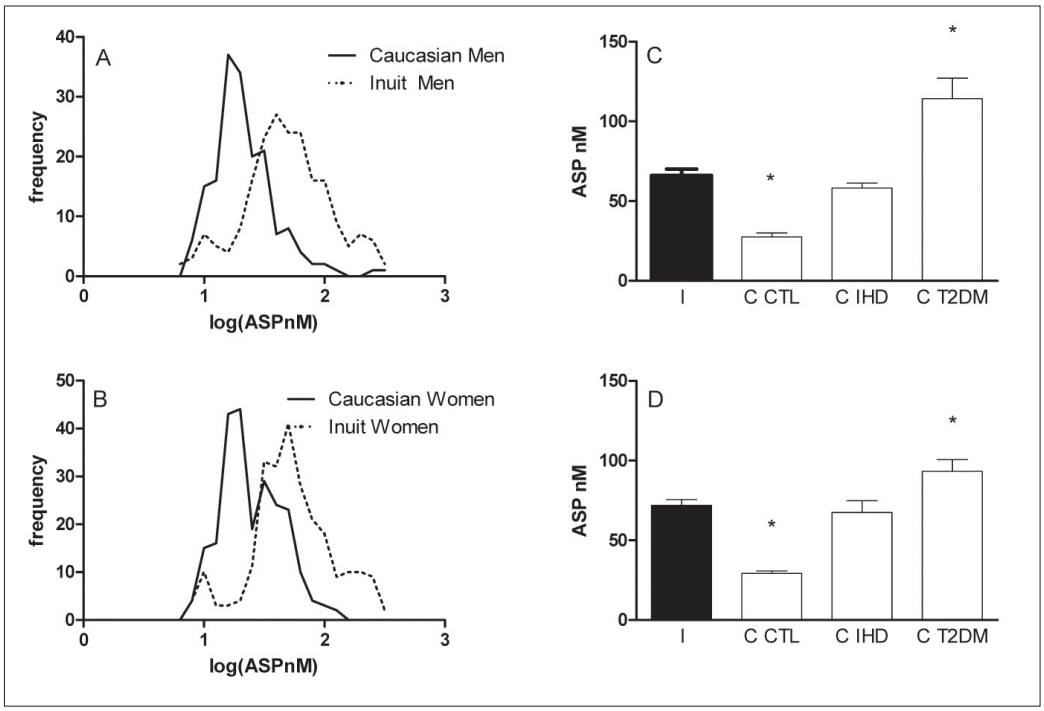

Figure 1. Acylation stimulating protein (ASP) values in Inuit and Caucasian men and women. In panels A and B, ASP values were log transformed due to a skewed distribution. Panel A shows the frequency distribution of ASP for Inuit men (n=204) and Caucasian men (n=175). Panel B is the frequency distribution for Inuit women (n=248) and Caucasian women (n=236), where average values are Inuit men 66.1±4.1 nM versus Caucasian men 27.5±2.5 nM, $p<0.0001$; Inuit women 71.8±3.8 nM versus Caucasian women 29.4±1.3 nM, $p<0.0001$. Panel C: ASP was higher in the Inuit men compared to Caucasian control men and was not different from Caucasian IHD men. T2DM men had the highest ASP (one way ANOVA $p<0.0001$). Panel D: ASP was higher in the Inuit women compared to Caucasian control women and was not different from Caucasian IHD women. T2DM women had the highest ASP (one way ANOVA $p<0.0001$). Differences amongst groups were assessed using one way ANOVA with Tukey post hoc test. * denotes $p<0.05$ for post hoc test compared to Inuit group.

Table II. Anthropometric and blood parameters according to the number of metabolic syndrome criteria in Inuit men.

Inuit men	MetS0 n=104	MetS1 n=59	MetS2 n=28	MetS≥3 n=13	One-way ANOVA p-value
Age years	45.4±1.1	47.3±1.5	49.8±2.3	49.5±2.9	0.21
BMI kg/m^2	25.0±0.3	28.7±0.6*	33.8±0.9*	33.9±1.0*	<0.0001
BF%	19.4±0.6	25.3±1.0*	32.8±1.3*	32.7±2.1*	<0.0001
WC cm	87.0±0.8	97.0±1.5*	109.7±2.1*	111.8±2.7*	<0.0001
SBP mmHg	117.9±1.2	130.2±2.1*	128.7±2.8*	130.6±4.3*	<0.0001
DBP mmHg	73.3±0.8	81.3±1.3*	79.7±2.2*	84.1±2.4*	<0.0001
TG mmol/L	0.93±0.03	1.43±0.09*	1.92±0.20*	2.40±0.25*	<0.0001
TC mmol/L	5.00±0.09	5.54±0.13*	5.44±0.21	5.55±0.29	0.004
HDL-C mmol/L	1.66±0.04	1.55±0.05	1.32±0.06*	1.00±0.05*	<0.0001
LDL-C mmol/L	2.92±0.09	3.34±0.13*	3.24±0.18	3.45±0.31	0.02
oxLDL %	50.7±1.6	59.0±2.1*	63.7±3.6*	66.1±5.7*	<0.0001
apoB g/L	0.96±0.02	1.08±0.03*	1.11±0.04*	1.20±0.08*	0.0001
apoA1 g/L	1.69±0.02	1.67±0.03	1.55±0.05*	1.38±0.03*	<0.0001
apoCIII mg/dL	151.3±3.2	177.3±4.8*	201.4±11.1*	210.2±16.4*	<0.0001
ASP nM	57.9±5.5	80.2±10.8	83.3±13.5	79.3±18.8	0.07
IL-6 pg/mL	2.42±0.21	2.62±0.25	3.61±0.59*	3.10±0.78	0.10
CRP mg/L	2.35±0.37	3.33±0.58	6.03±1.84*	3.16±0.65	0.01
TNF-alpha pg/mL	2.57±0.36	2.41±0.27	2.13±0.21	2.68±0.82	0.90

Values are given as mean ± standard error of the mean (SEM). BMI, body mass index; BF%, percentage body fat; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; TG, triglycerides; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; oxLDL, oxidized low density lipoprotein; apoB, apolipoprotein B, apoA1, apolipoprotein A1; apoCIII, apolipoprotein CIII; ASP, acylation stimulating protein; IL-6, interluken 6; CRP, C-reactive protein; TNF-alpha, tumour necrosis factor alpha. p-values based ANOVA with p<0.05 was taken as significant and * indicates a p-value <0.05 for the Dunnett's multiple comparison post hoc test.

Table III. Anthropometric and blood parameters according to the number of metabolic syndrome criteria in Inuit women.

Inuit women	MetS0 n=81	MetS1 n=102	MetS2 n=39	MetS≥3 n= 26	One-way ANOVA p-value
Age years	43.4±0.9	47.7±1.1*	51.1±2.2*	48.7±2.0*	0.001
BMI kg/m^2	23.1±0.3	30.0±0.5*	33.7±1.0*	33.0±1.2*	<0.0001
BF%	25.1±0.7	36.7±0.7*	40.4±1.1*	39.9±1.2*	<0.0001
WC cm	80.0±0.5	98.5±1.1*	105.7±2.1*	105.4±2.4*	<0.0001
SBP mmHg	110.8±1.4	119.0±1.6*	127.4±3.0*	124.8±3.9*	<0.0001
DBP mmHg	70.7±0.9	74.3±0.9*	77.5±1.4*	76.8±2.0*	0.0003
TC mmol/L	5.26±0.10	5.39±0.10	5.45±0.14	5.51±0.20	0.57
TG mmol/L	0.84±0.03	1.03±0.04	1.63±0.10*	2.45±0.20*	<0.0001
HDL-C	2.17±0.05	1.97±0.05	1.68±0.07*	1.32±0.06*	<0.0001
LDL-C	2.71±0.09	2.95±0.08*	3.03±0.14*	3.08±0.17	<0.0001
oxLDL U/l	49.1±1.7	51.3±1.3	58.4±1.9*	60.5±2.9	0.0002
apoB g/L	0.91±0.02	0.99±0.02*	1.06±0.04*	1.14±0.04*	<0.0001
apoA1 g/L	1.93±0.03	1.90±0.03	1.77±0.04*	1.57±0.05*	<0.0001
apoCIII mg/L	152.0±4.3	169.8±3.7*	190.3±6.6*	213.8±11.6*	<0.0001
ASP nM	65.2±6.3	80.5±6.8	66.0±9.9	73.2±10.8	0.38
IL-6 pg/mL	2.37±0.22	3.06±0.24	2.86±0.31	3.02±0.40	0.18
CRP mg/L	2.11±0.38	4.31±0.56*	3.04±0.36	5.07±1.27	0.005
TNF-alpha pg/mL	2.63±0.25	2.91±0.28	2.29±0.19	2.41±0.34	0.51

Values are given as mean ± standard error of the mean (SEM). BMI, body mass index; BF%, percentage body fat; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; TG, triglycerides; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; oxLDL, oxidized low density lipoprotein; apoB, apolipoprotein B, apoA1, apolipoprotein A1; apoCIII, apolipoprotein CIII; ASP, acylation stimulating protein; IL-6, interluken 6; CRP, C-reactive protein; TNF-alpha, tumour necrosis factor alpha. p-values based ANOVA with p<0.05 was taken as significant and * indicates a p-value <0.05 for the Dunnett's multiple comparison post hoc test.

We also found that BMI, percentage of body fat, insulin, LDL-C, oxLDL, apoB and apoCIII (Table II and III) and total and free retinol (Fig. 2) increased in both the Inuit men and women with increasing MetS components. Total cholesterol also increased among Inuit men, but not among the Inuit women. ApoA1 decreased in both the men and women with increasing MetS components. However, CRP was the only inflammatory marker to change with increasing MetS criteria and there was no significant change in IL-6, TNF-alpha or ASP. However, there appeared to be a trend for increasing ASP with increasing MetS criteria among the Inuit men.

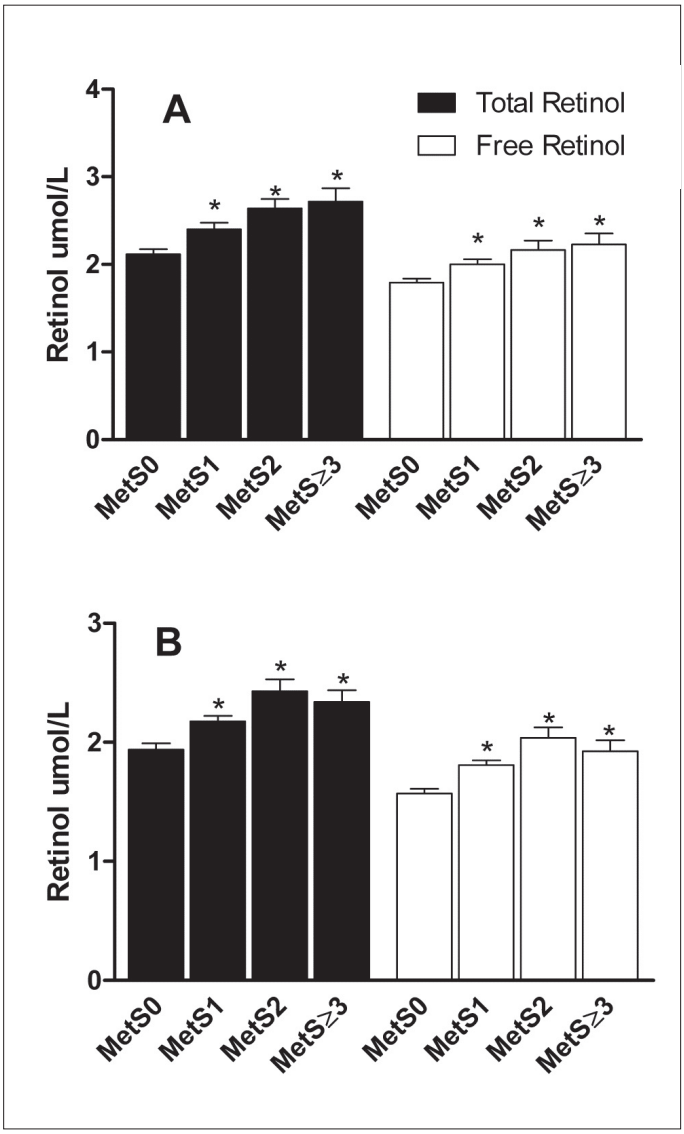

Figure 2. Total and free retinol stratified based on the number of metabolic syndrome criteria present in Inuit men (panel A) and women (panel B). Inuit men and women were categorized based on the number of metabolic syndrome criteria present according to the ATPIII definition. Panel A: Total retinol ($p<0.0001$) and free retinol ($p=0.0001$) were significantly higher in Inuit men with one or more metabolic syndrome criteria (MetS1, MetS2 and MetS≥3) compared to men with none of the criteria (MetS0). Panel B: Total retinol ($p<0.0001$) and free retinol ($p<0.0001$) was also significantly higher in Inuit women with one or more metabolic syndrome criteria (MetS1, MetS2 and MetS≥3) compared to women with none of the criteria (MetS0). * denotes $p<0.05$ for Dunnett's multiple comparison post-hoc test versus MetS0 group for total and free retinol, respectively.

It has previously been reported in the literature that chronic inflammatory conditions, such as type 2 diabetes mellitus and IHD are associated with increased ASP levels. However, even in the Inuit group with no components of MetS (MetS0), ASP was still elevated compared to the Caucasian men and women, suggesting that the increased ASP in this population is not due to increased IHD or metabolic syndrome risk. Despite the low IHD risk profile in the Inuit population and their reported low incidence of cardiovascular mortality, the ASP of Inuit men and women was comparable to a Caucasian IHD group, yet was lower than the Caucasian type 2 diabetes group (Fig 1. C and D).

Omega-3 intake does not affect ASP values

Based on data indicating that the high levels of dietary omega-3 fatty acids (DHA and EPA) increased insulin sensitivity and have anti-inflammatory properties, we evaluated ASP in the context of omega-3 fatty content of red blood cell membranes. There was no correlation between ASP level and the percent content of omega-3 in the red blood cell membranes. In addition to omega-3 fatty acids, omega-6 fatty acid, oleate (monounsaturated, abundant dietary fat) and trans fatty acid (linked to heart disease) content of the erythrocyte plasma membranes did not correlate with ASP (data not shown).

Also, we divided the Inuit men and women into quartiles according to their percentage of omega-3, and there was no difference in ASP between the low omega-3 and the high omega-3 groups. In addition, CRP and TNF-alpha (markers of inflammation associated with insulin resistance) were not different between the low omega-3 and high omega-3 groups (data not shown).

To further examine the potential impact of omega-3 fatty acids on ASP production, we studied a group of 28 men who underwent a 6 week dietary treatment with 3 g/day omega-3 fatty acids supplementation of their regular diet. There was no change in ASP after the 6 week intervention (pre-treatment ASP 15.4±2.6 nM vs post-treatment ASP 13.3±1.3 nM, pNS).

However, both total and free retinol did correlate with ASP in Inuit men (total retinol r=0.17, p=0.02; free retinol r=0.15, p=0.04). In addition, total and free retinol also increased with increasing MetS components (Fig. 2). Similarly, we found that ASP correlated positively with apoA1 in Inuit men (r=0.16, p=0.02) and Inuit women (r=0.14, p=0.02) and decreased with increasing MetS components (Table II and Table III). There were no other significant correlations with lipids or lipoproteins. We performed forward stepwise multiple linear regression analysis to determine if other variables, including plasma lipids and lipoproteins, contributed to the relationship between retinol and ASP in the Inuit men. Only total retinol (p=0.02) significantly contributed to predicting ASP values (r=0.17) while body fat percentage (BF%) (p=0.90), plasma TG (p=0.31) and age (p=0.10) did not further contribute. We obtained similar results for free retinol.

DISCUSSION

IHD has a complex etiology determined by dietary factors, body composition, blood lipids and adipose tissue-derived hormones (19). In this study, we investigated the ASP concentrations in the Inuit of northern Quebec both with respect to their IHD risk and biological markers of nutrition.

Unique to our study was the evaluation of the adipose tissue-derived hormone, ASP. ASP concentration was higher in the Inuit than the Caucasian Quebec population, yet did not correlate with any markers of adiposity, including BMI, BF%, waist circumference or hip circumference. This contrasts with previous studies which have shown that ASP, which is produced by adipose tissue, often increases with increasing levels of obesity (12). As well, ASP often correlates with increasing risk factors for IHD including apoB and TG (12). Once again, we found no such correlations in the present study. Interestingly, ASP concentrations were elevated even in the group of Inuit who had no components of the metabolic syndrome, and the ASP levels were comparable to Caucasian groups with IHD.

As suggested by Young, obesity may have a different "dose-response" relationship with metabolic correlates in the Inuit (20). Hypotheses have been presented that the colder climate of the circumpolar region in which the Inuit have lived for thousands of years have led to greater stores of subcutaneous body fat (20). Although this has not yet been studied, the function of this fat may be different, and potentially less metabolically deleterious, than the Caucasian adipose tissue. Our results showed that Inuit men had a higher BMI than Caucasian men, and for both Inuit men and women the average BMI was 27.7 ± 0.4 kg/m^2 and 28.6 ± 0.4 kg/m^2, respectively, which is considered overweight. However, the usefulness of BMI as a marker of IHD risk has been questioned for the Inuit (20). BMI cut points have been derived from Caucasian populations, and therefore may not have the same relationship with morbidity and mortality in the Inuit (20,21). A similar problem has been noted for other populations including Asian Indians and Chinese (22,23).

It is also possible that their dietary composition is providing some metabolic protection from the development of cardiovascular risk factors and/or stimulating ASP production. Due to the uniquely high intake of omega-3 fatty acids in the Inuit (4), and the abundance of research supporting the anti-atherogenic, insulin-sensitizing properties of omega-3 (7,9–11,24–27), we studied the relationship between the level of omega-3 fatty acids in the cell membranes of the Inuit and ASP concentrations and found no correlation. Further, dietary treatment with omega-3 fatty acids in men did not change systemic ASP concentrations after a 6-week period. However, previous studies have determined that adipose tissue specific changes in ASP production, such as those evident in a trans-adipose tissue gradient after a fat load, can occur without acute changes in systemic concentrations (17). Potentially, chronic, long-term consumption of omega-3 may increase systemic ASP. Additionally, acute changes in ASP may occur in response to omega-3 but only within the adipose tissue bed. Retinol, or vitamin A, found abundantly in marine mammals and fish, has been shown ex vivo to increase the production of ASP by adipocytes (28). In the present study, we did find a positive relationship between both total and free retinol and ASP in the Inuit men.

Many data on ASP have displayed elevated ASP with increasing risk factors for IHD suggesting an "ASP resistance" similar to insulin resistance (12,18,29,30). On the other hand, there are also data to support an "ASP

compensation" in which higher ASP may stimulate higher adipose TG synthetic activity and therefore, promote postprandial TG clearance by adipose tissue (13,31,32). Perhaps the traditionally high-fat diet of the Inuit has played a role in the higher average ASP values in this population. Therefore, high ASP values of the Inuit may not be associated with IHD risk as has previously been shown in Caucasian populations.

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