

OBESITY IN THE INUIT - ADIPOSE TISSUE AND ISCHAEMIC HEART DISEASE

Obesity is a major, and growing, health problem in many regions of the world. It is not, however, obesity per se that matters from a health perspective, but rather the diseases which are associated with it. These include type 2 diabetes, heart disease and certain cancers. Obesity is a concern in the Inuit, as in many other groups, and data from the International Obesity Task Force have indicated that Inuit men are in the top half of nearly 80 countries and territories in the extent of overweight and obesity (1). The position is worse for Inuit women in that they rank on these measures in the top quintile of over 100 countries/territories (1).

The measurement of overweight and obesity is generally based on Body Mass Index (weight in Kg/height in m²), with overweight being 25.0-29.9 and obesity ≥ 30.0 . These definitions are derived from Europeans and North Americans of Caucasian origin, and it is recognised that they are not appropriate for other ethnic groups, such as the Inuit and those from parts of Asia (1). In several Asian regions a lower BMI is now used as a threshold for obesity, reflecting higher levels of body fat than Caucasians for a given BMI as a consequence of different frame sizes.

It is not, however, simply the total amount of body fat that matters, but the distribution with a high waist circumference reflecting an abdominal deposition of fat being particularly linked to the adverse health consequences of obesity. Data from the MONICA survey from the mid-1990's, indicate that Inuit women have a high waist circumference; indeed, it was the highest from all the study areas in North America, Europe, and Australasia (1). Despite this fat distribution,

the Inuit appear at lower, or similar, risk than matched Caucasian populations in relation to other components of the metabolic syndrome, such as lipid profile and hypertension. A survey in 1992 found that Inuit from the Nunavik region of Northern Quebec had a lower risk of ischaemic heart disease (IHD) than James Bay Cree and Caucasians from Southern Quebec (2), although they had the highest rates of obesity and smoking.

Expansion of white adipose tissue mass is, of course, the defining feature of obesity. The tissue is now recognised as much more than a site of fat storage – it is a dynamic endocrine and signalling organ with a pervasive role in metabolic regulation (3). This is because the tissue synthesises and secretes a wide range of protein factors (>100), termed adipokines. The hormones leptin and adiponectin are the best known adipokines, but others include the cytokines TNF α and IL-6 (3). One of the key concepts to emerge in obesity research in recent years is that metabolic dysregulation within adipose tissue is central to the initiation of the associated pathologies - due to changes in the secretion of key adipokines, particularly those linked to inflammation with an inflammatory response developing as adipose mass increases in obesity (3).

Several adipokines play roles in lipid metabolism, and prominent among them is acylation stimulating protein (ASP). This product of the alternative complement system is involved in the clearance of dietary lipids, stimulating triglyceride synthesis within white adipose tissue (4). As such, it may provide a link between hyperlipidaemia and the risk of IHD. A study reported in

this issue of IJCH demonstrates that plasma ASP is elevated in the Inuit as compared with Quebec Caucasians, the circulating levels being >2-fold higher in both males and females (5). The level in the Inuit groups was similar to Caucasians with IHD. Surprisingly, there was no correlation between plasma ASP and any index of obesity; nor was there any correlation with lipid-related risk factors for IHD (5). This may relate partly to the issue of the appropriate cut-off for obesity in the Inuit and whether differences in fat distribution are important. In the case of adipokines such as leptin, differences in the extent to which subcutaneous and internal adipose tissue depots produce these hormones are recognised.

The lower risk of IHD in the Inuit may, of course, be a reflection of genetic variation, particularly in view of the selective pressures to which they will have been exposed in the Arctic environment over thousands of years, or to lifestyle factors. Foremost among the lifestyle factors is diet, with the Inuit exhibiting a high consumption of marine mammals and of fish rich in omega-3 fatty acids (2). These fatty acids are viewed as anti-inflammatory and cell culture studies on adipocytes have shown that the production and secretion of several adipokines, including adiponectin, leptin and TNF α , are modulated by them (6). However, in the study of Smith et al (5) no relationship was observed

between plasma ASP and the omega-3 levels in erythrocyte cell membranes, and neither did a 6-week supplementation with omega-3 fatty acids lead to changes in ASP.

From a broad biomedical perspective, the Inuit may provide important new insights on the relationship between body fat, both amount and distribution, and the diseases associated with obesity. Mechanistic information on the link between the production of key adipokines in obesity and their modulation by diet may also be provided.

REFERENCES

1. Young TK. Are the circumpolar Inuit becoming obese? *Am J Human Biol* 2007;19:181-189.
2. Dewailly E, Blanchet C, Lemieux S, Sauve L, Gingras S, Ayotte P, Holub BJ. n-3 Fatty acids and cardiovascular disease risk factors among the Inuit of Nunavik. *Am J Clin Nutr* 2001;74: 464-473.
3. Trayhurn P. Endocrine and signalling role of adipose tissue: new perspectives on fat. *Acta Physiol Scand* 2005; 184:285-293.
4. Cianflone K, Xia Z, Chen LY. Critical review of acylation-stimulating protein physiology in humans and rodents. *Biochim Biophys Acta* 2003;1609:127-143.
5. Smith JD, Cianflone K, Dewailly E, Château-Dégat M-L, Vohl M-C, Julien P. Acylation stimulating protein is higher in Inuit from Nunavik compared to a southern Quebec population. *Int J Circumpolar Health* 2009;68: in press - this issue.
6. Pérez-Matute P, Marti A, Martínez JA, Fernández-Otero MP, Stanhope KL, Havel PJ. Eicosapentaenoic fatty acid increases leptin secretion from primary cultured rat adipocytes: role of glucose metabolism. *Am J Physiol Reg Integr Comp Physiol* 2005;288:R1682-R1688.

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